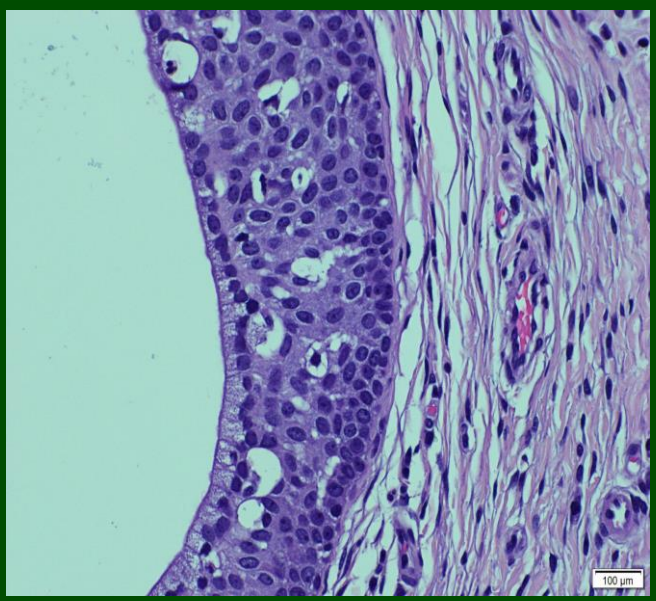
DOAJ DIRECTORY OF OPEN ACCESS JOURNALS

pISSN 0854-0381
eISSN 2598-1013

Majalah Obstetri & Ginekologi

JOURNAL OF OBSTETRICS & GYNECOLOGY SCIENCE
Vol. 33 No. 2 August 2025



Histopathology of low grade squamous intraepithelial lesion (LSIL)

Published by
Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga
In Collaboration with Indonesian Society of Obstetrics and Gynecology

Accredited by Ministry of Education, Culture, Research, and Technology, Republic of Indonesia
No. 105/E/KPT/2022

Vol. 33 No. 2 August 2025

pISSN 0854-0381
eISSN 2598-1013

Majalah Obstetri & Ginekologi

JOURNAL OF OBSTETRICS & GYNECOLOGY SCIENCE

ACCREDITED
Ministry of Education, Culture, Research, and Technology, Republic of Indonesia
No. 105/E/KPT/2022

EDITORIAL TEAM

Address

Department of Obstetrics and Gynecology
Faculty of Medicine, Universitas Airlangga - Dr. Soetomo General Academic Hospital
Jl. Mayjen Prof dr Moestopo no. 6 – 8, Surabaya 60286, Indonesia. Phone: 62-31-5501185, Facs: 62-31-5037733
https://e-journal.unair.ac.id/MOG/
Email: mog@journal.unair.ac.id, mog.obgsby@gmail.com

Vol. 33 No. 2 August 2025

pISSN 0854-0381
eISSN 2598-1013

Majalah Obstetri & Ginekologi

JOURNAL OF OBSTETRICS & GYNECOLOGY SCIENCE

CONTENT

Cover :
Histopathology of low grade squamous intraepithelial lesion (LSIL)

This edition page 174

AUTHOR GUIDELINES

Majalah Obstetri & Ginekologi publishes original articles on all aspects of obstetrics and gynecology. Articles can be classified as **original research, case series, review article, systematic review,** and **meta-analysis** that keep the readers informed of current issues, innovative thinking in obstetrics and gynecology. We welcome submissions that contribute to the advancement of knowledge in obstetrics and gynecology. Articles are considered for publication with the condition that they have not been published, submitted, or being under consideration for publication elsewhere. Manuscript must be written in American English with proper grammar. Authors should follow the **Author Guidelines** and the manuscript is arranged according to the **Manuscript Template**. Manuscript must be submitted through online submission by registered users. Authors can register themselves in the journal system. For further question contact us at: mog@journal.unair.ac.id.

General Principles

The manuscript must be free of typing errors and have a proportional length. The length of each manuscript is 5-10 pages of A4 size paper (1.5 spaces, Times New Roman font size 12, with normal margins page layout of 2.54 cm on each side). The recommended references are the updated ones in the last ten (10) years from the date of current submission (minimal of 20 references), unless in a special case accepted by the editors due to scientific reasons.

Total number of tables and figures should be limited, advisably no more than five. Tables should be numbered with Arabic numbers, and the title of each table should be written center-aligned at the top of the table, in normal Times New Roman, font size 12. Text within tables should be written in 1 space, normal Times New Roman font size 10 or less. Figures (including graphs, diagrams, charts, drawings, and photographs) should be produced at least 300 dpi in jpg, jpeg, or png format, have clear legends, numbered with Arabic numerals, and the title of each figure should be written center-aligned at the bottom of the figure, in normal Times New Roman, font size 12. All words in Latin must be written in italics. The use of abbreviations is generally agreed upon, and an extension must be given in the first mention of the abbreviation. Decimal numbers are marked with points (.).

All types of manuscripts must consist of:

- **Title**, which must be concise, specific, and informative. The title must consist of no more than 30 words, written on the top line with bold Gill Sans MT font size 12, left-aligned, and in sentence case. Latin name is italicized (italic).
- **The author's name(s)** is complete (without title) and the home institutions of the authors are written with an initial capital letter for each word in Gill Sans MT font, size 10, left-aligned, without ending points. If there is more than 1 author, all is written, separated by commas. Numeric code in superscript is added behind the author's name. The author's home institution is written under the author's name beginning with a numeric code (superscript). The name of the institution is followed by the name of the city and the country where the institution is located. At least one of the authors is required to add their **ORCID IDs** listed on https://orcid.org/. The link should be embedded on the ORCID logo after the authors' names. At least 1 of the authors must include external (more than 1, if necessary) affiliation(s) outside the Majalah Obstetri & Ginekologi publisher.
- **Abstract** must be arranged with a brief description (containing no more than 250 words). The abstract is written in English.
  a. Abstract of original research report, systematic review/scoping review or meta-analysis must consist of objective, materials and methods, results, and conclusion each written as one paragraph.
  b. Abstract of narrative review article must consist narration summarizing the content of the manuscript, written in one paragraph.
  c. Abstract of case series must consist of background, objective, case(s), and conclusion, each written in one paragraph.
- **Keywords** consist of 3-5 words and/or phrases, written under abstract as seen in the template, in English, started with a capital letter (sentence case), separated with semi-colon, and without an ending point. Keywords should apply terms present in **Medical Subject Headings (MeSH)**. The keywords must contain at least one keyword of **Sustainable Development Goals (SDGs)**.
- **Running title** (short version of full title or abbreviated title) must be written as a header of the manuscript on the right side.
- **Correspondence** is written under the keywords including the name, full address, and email address of one of the authors responsible as corresponding author.

- **Highlights** of the manuscript, which consist of minimally two keypoints representing the novel contributions of the study and must not be the copy-paste and/or repetition of sentences of any other parts of the manuscript. These two highlights should be written before the introduction using number bullets (see template).

Article Types

The journal accepts the following types of articles:

a. Original research

Original research reports a substantial body of laboratory or clinical work, presenting the outcome of a large trial, case control, observational or retrospective study. The authors must confirm in the manuscript that they have ethical clearance for the conduct of the reported research. The procedure in the research should be in accordance with the **Declaration of Helsinki 2013**. The ethical clearance should be submitted along with the manuscript. The manuscript should be approximately 3500 words. Total number of tables and figures are limited, advisably not more than five, and references are minimally 20 from the last 10 years before the date of submission. The text consists of **Abstract, Introduction, Materials and Methods, Results and Discussion, Conclusion,** and **Disclosures**. The Disclosures consist of **Acknowledgment, Conflict of Interest, Funding, and Authors Contribution**.

b. Case series

Case series highlights important innovations with wide applicability or previously unpublished complications of new techniques or medications. The authors must confirm in the manuscript that they have obtained **written permission** of those whose case is being presented. The manuscript should be approximately 3500 words. Total number of tables and figures are limited, advisably not more than five, and references are minimally 20 from the last 10 years before the date of submission. The text consists of **Abstract, Introduction, Case Series, Discussion, Conclusion,** and **Disclosures**. The Disclosures consist of **Acknowledgment, Conflict of Interest, Patient Consent for Publication, Funding,** and **Authors Contribution**.

c. Review article

Review article is a survey of previously published research on a topic. It should give an overview of current thinking on the topic. The manuscript should be approximately 3500 words. Total number of tables and figures are limited, advisably not more than five, and references are minimally 20 from the last 10 years before the date of submission. The text consists of **Abstract, Introduction, any subheadings as needed by the author(s), Conclusion,** and **Disclosures**. The Disclosures consist of **Acknowledgment, Conflict of Interest, Funding,** and **Authors Contribution**.

d. Systematic review/Scoping review

Systematic review is a synthesis of the evidence on a clearly presented topic using critical methods to identify, define and assess research on the topic, extracting and interpreting data from published studies on the topic, then analyzing, describing, and summarizing interpretations into a refined conclusion. Appropriate methodology should be followed, such as PROSPERO, the online international register for systematic reviews. Total number of tables and figures are limited, advisably not more than five, and references are minimally 20 from the last 10 years before the date of submission. A scoping review is a type of literature review that aims to map the existing research literature on a broad topic area, identifying key concepts, evidence sources, and gaps in knowledge. Unlike systematic reviews, scoping reviews typically have less stringent inclusion criteria and may include a wide range of study designs to provide a comprehensive overview of the literature. They are often used to explore emerging research areas, clarify key concepts, and inform future research directions. Scoping reviews use a systematic approach to searching, selecting, and summarizing relevant studies but do not typically assess the quality of included studies. The authors should refer to existing guidelines and frameworks to ensure rigor and transparency in conducting scoping reviews, such as the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). Both systematic and scoping review consists of **Abstract, Introduction, Materials and Methods, Results and Discussion, Conclusion,** and **Disclosures**. The Disclosures consist of **Acknowledgment, Conflict of Interest, Funding,** and **Authors Contribution**.

e. Meta-analysis

Meta-analysis is a statistical analysis combining the results of multiple scientific studies, analyzing multiple scientific studies addressing the same question, with each individual study reporting measurements that are expected to have some degree of error. Total number of tables and figures are limited, advisably not more than five, and references are minimally 20 from the last 10 years before the date of submission. The text consists of **Abstract, Introduction, Materials and Methods,**

Results and Discussion, Conclusion, and **Disclosures**. The Disclosures consist of **Acknowledgment, Conflict of Interest, Funding,** and **Authors Contribution**.

Authors must also supply the **Author Statement and Copyright Transfer Agreement** issued by Majalah Obstetri & Ginekologi. The form can be downloaded from the website of the journal. The statement should be submitted along with the submission of the manuscript.

References

Number of references depends on each types of article (see "Article types") and should in general be limited to ten years before the date of submission. References must be numbered in the order in which they are mentioned in the text. Use the style of the examples below, which are based on the **International Committee of Medical Journal Editors (ICMJE)** Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals: Sample References. Avoid using abstracts as references. Information from manuscripts submitted but not yet accepted should be cited in the text as "unpublished observations" with written permission from the source. Papers accepted but not yet published may be included as references; designate the journal and add "Forthcoming". Avoid citing "personal communication" unless it provides essential information not available publically, name the person and date of communication, obtain written permission and confirmation of accuracy from the source of a personal communication. Authors is recommended to use reference management software, in writing the citations and references such as: Mendeley®, Zotero®, EndNote®, and Reference Manager®.

Here are some examples of the references:

1. Journal

Up to three authors, list all the authors.

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002;347(4):284-7.

More than three authors, list the first three authors, followed by et al.

Rose ME, Huerbin MB, Melick J, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.

2. Books

Butler SW. Secrets from the black bag. London: The Royal College of General Practitioners; 2005.

Chapter of an edited book

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

Translated book

Luria AR. The mind of a mnemonist. Solotaroff L, translator. New York: Avon Books; 1969.

Electronic book/E-book

Chapter from an electronic book

Darwin C. On the origin of species by means of natural selection or the preservation of favoured races in the struggle for life [Internet]. London: John Murray; 1859. Chapter 5, Laws of variation. [cited 2010 Apr 22]. Available from: http://www.talkorigins. org/faqs/origin/ chapter5.html

Full text electronic book

Macdonald S. editor. Maye's midwifery 14th ed. [eBook]. Edinburgh: Bailliere Tindall; 2011 [cited 2012 Aug 26]. Available from: Ebrary.

Proceeding book

Offline proceeding

Kimura J, Shibasaki H, editors. Recent advances in clinical neurophysiology. Proceedings of the 10th International Congress of EMG and Clinical Neurophysiology; 1995 Oct 15-19; Kyoto, Japan. Amsterdam: Elsevier; 1996.

Online proceeding

Muller S, editor. Proceedings of the 10th international conference on head-driven phrase structure grammar [Internet]; 2003 Jul 18-20; East Lansing (MI). Stanford (CA): CSLI Publications; 2003 [cited 2017 Nov 16]. Available from: http://web.stanford.edu/group/ csli publicationsSta/cslipublications/HPSG/2003/toc.shtml

Thesis/dissertation

Offline thesis/dissertation

Kay JG. Intracellular cytokine trafficking and phagocytosis in macrophages [dissertation]. St Lucia, Qld: University of Queensland; 2007

Online thesis/dissertation

Pahl KM. Preventing anxiety and promoting social and emotional strength in early childhood: an investigation of risk factors [dissertation on the Internet]. St Lucia, Qld: University of Queensland; 2009 [cited 2017 Nov 22]. Available from: https://espace.library.uq.edu.au/view/UQ:178027

3. Website

With author

Diabetes Australia. Gestational diabetes [Internet]. Canberra (ACT): Diabetes Australia; 2015 [updated 2015; cited 2017 Nov 23]. Available from: https://www.diabetesaustralia.com.au/gestational-diabetes

No author

The family impact of Attention Deficit Hyperactivity Disorder (ADHD) [Internet]. 2009 Nov 1 [updated 2010 Jan 1; cited 2010 Apr 8]. Available from:http://www.virtualmedical centre.com.au/healthandlifestyle.asp?sid=192&title=The-Family-Impact-of-Attention-Deficit-Hyperactivity-Disorder-%28ADHD%29page=2.

CITATION WRITING

As the general rule, the reference numbers:

- should be placed outside full stops and commas
- the citation number can be place next to the author name where emphasis is place on the author eg. Smith[2]
- When multiple references are cited at a given place in the text, use a hyphen to join the first and last numbers that are inclusive. Use commas (without spaces) to separate non-inclusive numbers in a multiple citation e.g. ([2,3,4,5,7,10]) is abbreviated to ([2-5,7,10]).
- Do not use a hyphen if there are no citation numbers in between that support your statement e.g. ([1-2]). Use instead ([1,2])

For example:

Moir and Jessel maintain "that the sexes are interchangeable".[1]
Numerous studies[20-22] have.....
Smith's research .....[21]
Smith and Jones'[22] research .....

Up to 3 authors eg. Smith, Jones and McDonald reported that .....[23]

More than 3 authors eg. Smith et al.[24] reports.

ORIGINAL RESEARCH

Long COVID in vaccinated women with Polycystic Ovary Syndrome: A retrospective cohort pilot study

R Muharam[1,2,3]*, Aswan Bagastoro[1], Anindita Abigail Faradina[1], Edward Christopher Yo[1], Alisha Nurdya Irzanti[1], Kanadi Sumapraja[1,2,3], Achmad Kemal Harzif[1,2,3], Gita Pratama[1,2,3], Mila Maidarti[1,2,3], Vita Silvana[1,2,3], Budi Wiweko[1,2,3], Andon Hestiantoro[1,2,3]

[1]Department of Obstetrics and Gynecology, Faculty of Medicine Universitas Indonesia, dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia
[2]Yasmin IVF Clinic, dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia
[3]Human Reproduction, Infertility, and Family Planning Cluster, Indonesia Reproductive Medicine Research and Training Center, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Article Info

Received Oct 6, 2024
Revised Dec 17, 2024
Accepted Dec 20, 2024
Published Aug 1, 2025

***Corresponding author:**
R. Muharam
rmuharam@yahoo.com

Keywords:
COVID-19
COVID-19 Vaccines
Maternal health
Post-Acute COVID-19 Syndrome
Polycystic Ovary Syndrome

ABSTRACT

Objective: Long COVID, or the persistence of symptoms after acute COVID-19 illness, can affect individuals with pre-existing health conditions such as polycystic ovary syndrome (PCOS). Long COVID and PCOS may share overlapping pathogenesis which potentially exacerbate one another. The aim of this study was to evaluate the symptoms of long COVID in women with PCOS who have been vaccinated and investigate whether COVID-19 vaccination or infection worsened PCOS symptoms.

Materials and Methods: We carried out a retrospective cohort study on 44 women with PCOS who have been vaccinated and previously diagnosed with COVID-19. Questionnaires were distributed to find out the effect of COVID infection and vaccines in these women, as well as the symptoms of long COVID-19.

Results: Of all participants, 28 women (70%) continued to report persistent long COVID symptoms, with the highest number of complaints being fatigue and hair loss. The results, using Mann-Whitney test, showed that there was no difference in PCOS symptoms before and after COVID-19 vaccination ($p = 0.520$) or after COVID-19 infections ($p = 0.241$). Although this study revealed a substantial prevalence of long COVID symptoms among women with PCOS, an encouraging finding emerged: neither the administration of COVID-19 vaccination nor prior infection with COVID-19 had a significant impact on PCOS-associated symptoms.

Conclusion: This study further underscores the importance of vaccination for all individuals, including women with a history of PCOS. Furthermore, the purpose of COVID-19 vaccination is to mitigate symptom severity, thus potentially diminishing the occurrence of long-term COVID-19 symptoms in future cases.

How to cite: Muharam R, Bagastoro A, Faradina AA, et al. Long COVID in vaccinated women with Polycystic Ovary Syndrome: A retrospective cohort pilot study. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):89-96. doi: 10.20473/mog.V33I22025.89-96.

Highlights:

1. Among women with PCOS, many still reported persistent long COVID symptoms such as hair loss and fatigue.
2. COVID-19 vaccination does not exacerbate symptoms of PCOS, which further emphasizes the importance of completing COVID-19 doses for women with PCOS to avoid long COVID sequelae.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex reproductive system disorder affecting women of reproductive age. It involves a combination of endocrine imbalances, leading to various health issues such as infertility, insulin resistance, obesity, and cardiovascular problems, among others. PCOS is characterized by a multifaceted nature, involving multiple genes and factors, and it manifests as a systemic, inflammatory, dysregulated steroid state with autoimmune components, often influenced by lifestyle factors.[1] The main contributors to PCOS are disruptions in the liver and ovary functions, leading to elevated levels of androgen, insulin, estrone, LH, and lipids.[2]

COVID-19, caused by the SARS-CoV-2 virus, emerged as a global pandemic in early 2020, challenging healthcare systems and disrupting lives worldwide. While most individuals with COVID-19 experience mild to moderate symptoms and recover within a few weeks, a significant number face prolonged health issues even after the acute phase.[3] This condition is known as Long COVID, or post-acute sequelae of SARS-CoV-2 infection (PASC). Long COVID is characterized by persistent symptoms that persist for weeks or months after the initial infection, affecting individuals of all ages, regardless of the severity of their initial illness. The symptoms of Long COVID can vary widely and may include fatigue, shortness of breath, brain fog, muscle and joint pain, chest pain, and even psychological distress.[4]

The severity and persistence of Long COVID symptoms can vary widely among individuals, regardless of their pre-existing health conditions. Factors that have been associated with an increased risk of Long COVID include the severity of the initial COVID-19 infection, age, and certain pre-existing health conditions, such as diabetes, obesity, and asthma. Recent studies have indicated a potential link between PCOS and an increased risk of developing Long COVID symptoms in women who contract COVID-19. When women with PCOS contract COVID-19, their pre-existing immune dysregulation may contribute to a more pronounced and prolonged inflammatory response to the viral infection. This chronic inflammation can lead to a wide range of Long COVID symptoms persisting well beyond the acute phase of the illness. Furthermore, the hormonal imbalances and insulin resistance commonly observed in PCOS may also exacerbate the impact of COVID-19 on the body's systems.[5,6]

On the other hand, recent literature suggested that long COVID or even COVID-19 vaccination may also exacerbate PCOS symptoms such as metabolic syndrome, weight gain, and menstrual irregularities. Infection with SARS-CoV-2 may worsen insulin resistance which is already experienced by PCOS patients. The virus can bind to its receptors on pancreatic islet cells, causing temporary damage and insulin deficiency. The infection also raises inflammatory markers, which may destroy pancreatic fat cells and trigger insulin resistance through ketogenesis and adipocyte dysregulation.[7,8] Chronic inflammation due to long COVID has also been found to disrupt the hypothalamic-pituitary-ovarian (HPO) axis, which is essential for normal function of the ovaries and their responsiveness towards estrogen and progesterone. The inflammatory cytokines released may interfere with follicle development, ovarian angio-genesis, hormone production, timing of ovulation, and corpus luteum formation that all occur within the ovaries.[9] The aim of this study was to evaluate the symptoms of long COVID in women with PCOS who have been vaccinated and investigate whether COVID-19 vaccination or infection also affected PCOS symptoms.

MATERIALS AND METHODS

Study design and participants

This retrospective study was conducted on PCOS patients in Cipto Mangunkusumo Hospital medical record admitted from 2021 to 2023, involving 40 women with PCOS who have been vaccinated and previously diagnosed with COVID-19. Criteria for inclusion comprised women aged 18 years or older and diagnosed with PCOS according to Rotterdam criteria (oligo/anovulation, hyperandrogenism features, polycystic ovaries on ultrasonography). PCOS patients who were also diagnosed with other reproductive endocrinology disorders were excluded. The ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo Hospital, Jakarta, Indonesia, with protocol number 24-02-0201 (KET-467/UN2.F1/ETIK/ PPM.00 .02/2024; approved 25 March 2024). We designed a special questionnaire to inquire about the current health status of patients and their persistent symptoms in the post-COVID period, as well as their PCOS symptoms before and after 3 months following COVID-19 infection, and contacted all eligible patients. All research subjects included in this study had given their informed consent.

Content of survey

The information included in the questionnaire were age, weight, height, comorbid diseases, obstetric history, characteristics of acute COVID-19, history of hospita-

lization (disease severity, length of hospital stay, need for respiratory supports, and need for intensive care unit [ICU]), long COVID symptoms, COVID-19 vaccination, and their PCOS symptoms before and after 3 months following COVID infection.

Statistical analysis

All analysis were performed using IBM SPSS software version 27.0. The analysis was conducted using SPSS software version. Descriptive statistics were reported as mean ± standard deviation (SD) or medians with quartiles. Student t-test was utilized to compare continuous variables with normal distribution, while the Mann–Whitney U test was employed for non-normal distribution. The $\chi 2$ test was used to compare categorical variables under parametric conditions. A p-value below 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

From the study, a total of 40 women were followed up. We investigated the long COVID symptoms in women with PCOS who had been vaccinated, as well as their PCOS symptoms during the acute COVID-19 infection compared to the chronic infection >3 months after being confirmed positive. We found that there was no difference in PCOS symptoms before and after COVID-19 vaccination (p = 0.520) or after COVID-19 infections (p = 0.241).

Out of the 40 respondents, 28 of them (70%) still complained of long COVID symptoms to time of survey. The most frequently experienced symptom was fatigue, with a total of 17 individuals reporting it (42.50%). The second most common complaint was hair loss, with 10 out of 28 respondents experiencing it (25%). This was followed by other complaints such as tingling sensations, shortness of breath, concentration difficulties, as well as disturbances in the sense of smell and taste, of which each of the symptoms was experienced by 5 respondents (12.5%). Other complaints included joint pain (10%), chest pain (2.5%), palpitations (2.5%), and cough, allergies, and skin rashes, each reported by 7.5% (Figure 1).

All respondents were asked about their PCOS symptoms shortly after being infected with COVID or during the acute onset (<3 months) as well as during the chronic onset (>3 months). During the acute onset, a total of 11 out of 40 respondents had already received the COVID vaccine. Among them, 26 reported weight gain (65%), 34 experienced infertility (85%), 15 had acne breakouts (37.5%), 25 experienced hair loss or balding symptoms (62.5%), 15 had hirsutism (37.5%), 7 had amenorrhea for more than 6 months (17.5%), and irregular menstruation was reported by 33 respondents (82.5%) (Figure 2).

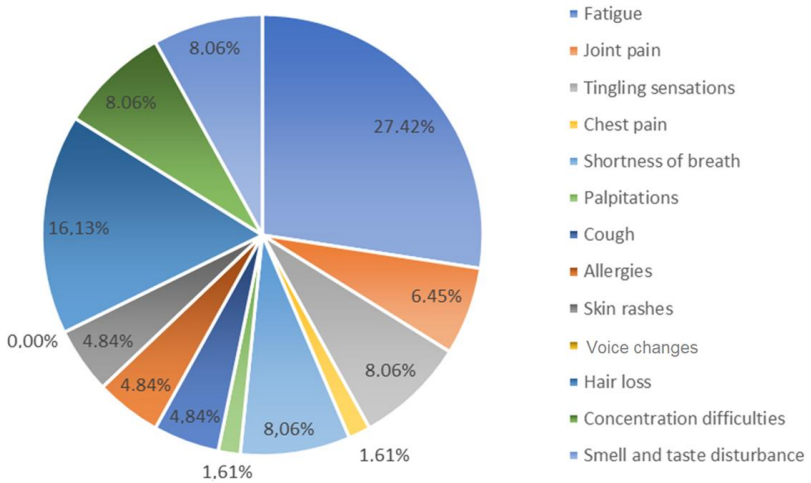


Figure 1. Long COVID symptoms reported among PCOS patients.

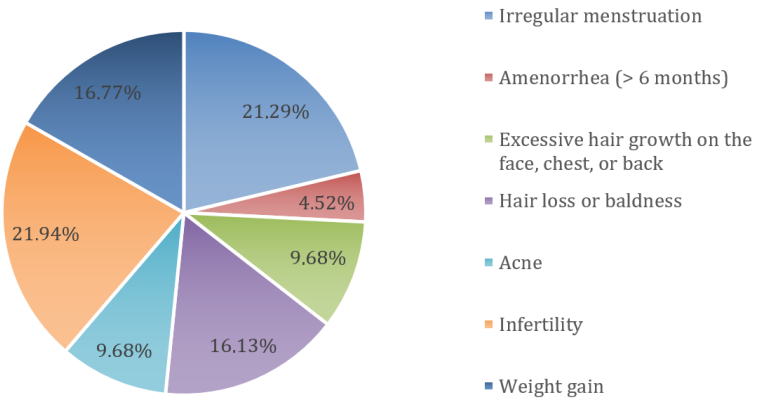


Figure 2. PCOS symptoms shortly after COVID-19 infection.

During the chronic onset of COVID infection (>3 months), they were re-evaluated regarding the PCOS symptoms they experienced. All respondents had already received the COVID vaccine. Only 17 out of 40 individuals reported weight gain (42.5%), 20 experienced infertility (50%), 6 had acne breakouts (15%), 22 had hair loss or balding symptoms (55%), 9 had hirsutism (22.5%), 8 had amenorrhea (20%), and irregular menstruation was reported by 23 respondents (57.5%) (Figure 3, Table 1).

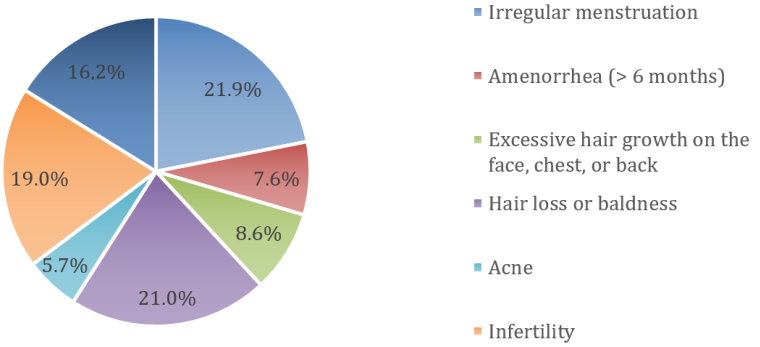


Figure 3. PCOS symptoms 3 months or more after COVID-19 infection.

Table 1. Association between PCOS symptoms reported and onset of COVID-19 infection.

Symptoms	Category	< 3 months (Acute onset)	> 3 months (Chronic onset)	*p*-values
Weight gain	Yes	26 (65.0)	17 (42.5)	0.035
	No	14 (35.0)	23 (57.5)	
Infertility	Yes	34 (85.0)	20 (50.0)	0.000
	No	6 (15.0)	20 (50.0)	
Acne	Yes	15 (37.5)	6 (15.0)	0.022
	No	25 (62.5)	34 (85.0)	
Hair loss / Baldness	Yes	25 (62.5)	22 (55.0)	0.508
	No	15 (37.5)	18 (45.0)	
Hirsutism	Yes	15 (37.5)	9 (22.5)	0.070
	No	25 (62.5)	31 (77.5)	
Amenorrhea	Yes	7 (17.5)	8 (20.0)	1.000
	No	33 (82.5)	32 (80.0)	
Irregular menstruation	Yes	33 (82.5)	23 (57.5)	0.002
	No	7 (17.5)	17 (42.5)	

Long COVID, which is defined by the persistence of symptoms after the acute phase of COVID-19, has become a subject of significant interest in recent research. Previous research indicated that women with PCOS may have a heightened risk of contracting COVID-19 and experiencing more severe clinical manifestations of the disease.[5] A comprehensive review by de Medeiros et al. predicted that PCOS patients had 28-50% higher risk of contracting COVID-19 infection.[5] A large-scale cohort study among the British population by Subramanian et al. also found that the incidence rate of COVID-19 infection was higher in women with PCOS (18.1 per 1000 person-years) compared to that in healthy women (11.9 per 1000 person-years).[10] Hence, many have suggested that PCOS should be considered an independent risk factor for COVID-19. On the other hand, past epidemiological studies found that lockdowns and anxiety related to risk of COVID-19 infection were negatively associated with the wellbeing of PCOS patients.[11,12] Up to present, however, there is a lack of evidence from clinical studies regarding how COVID-19 infection might affect the severity of PCOS-related symptoms. The potential mechanisms underlying the association between PCOS and long COVID symptoms are not yet fully understood, but there are several hypotheses based on recent research.[5]

PCOS is associated with chronic low-grade inflammation, which may contribute to the development of long COVID symptoms. Long COVID is also characterized by chronic inflammation, which may be exacerbated in PCOS patients.[13] Previously, it has been found that as many as 30% of all PCOS patients have chronic low-grade inflammation. The key components that constitute low-grade inflammation in PCOS include over-production of pro-inflammatory cytokines, endothelial cell dysfunction, and leukocytosis, and all of this likely stem from hyperandrogenism.[14] Excessive androgen level stimulates monocytic infiltration inside the ovaries and increased production of inflammatory factors such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α).[14,15] Other pro-inflammatory factors that have been found to be higher in PCOS patients than in healthy women include interleukin-17 (IL-17), interleukin-18 (IL-18), interleukin-1B (IL-1B), C-reactive protein (CRP), monocyte chemoattractant protein-1 (MCP1), soluble intercellular adhesion molecule (sICAM), and soluble endothelial leukocyte adhesion molecule (SE selectin).[16,17] Low-grade chronic inflammation in PCOS may then act as a prerequisite to the incidence of various metabolic diseases such as dyslipidemia and diabetes. It also impairs how the innate and adaptive immune system respond to pathogenic triggers, allowing infection to take over.[18,19] Therefore, a low-grade prolonged inflammatory state is integral to the pathophysiology of poor COVID-19 symptoms.[5] The inflammatory state is more pronounced in PCOS patients who are also obese, since adipose tissue can act as a reservoir for SARS-CoV-2 spread, shedding, activation of immune system, and cytokine cascade amplification, further contributing to a state of cytokine storm.[20]

Moreover, women with PCOS have been shown to have immune dysfunction, which may make them more susceptible to COVID-19 infection and more likely to develop long COVID symptoms. 19 PCOS is characterized by hyperandrogenism, which may play a role in the pathophysiology of COVID-19 infection and long COVID symptoms. Previous research has shown a correlation between gender and COVID-19 mortality or morbidity, in which men tend to be more susceptible compared to women. The immune dysregulation in men is likely due to higher androgen levels, as testosterone can regulate the transcription of TMPRSS2 gene which helps facilitate entry of virus into the cells.[5,21,22] The levels of androgens inside the body are also correlated with the number of ACE2 receptors, which are the main receptor for SARS-CoV-2 in target cells.[23] In women with PCOS, the resulting immune susceptibility towards COVID-19 may also be explained by the higher levels of testosterone. Nevertheless, the role of testosterone in COVID-19 is still widely debated as other studies found that it can also be a protective factor in certain conditions. Low testosterone level has been linked with poorer outcomes following COVID-19 infections.[24] Recent evidence has pointed out the beneficial role of testosterone against COVID-19, which lies upon its ability to inhibit inflammatory signalling cascade, endothelial dysfunction, and oxidative stress. These conflicting findings on testosterone's role can be made clearer through future studies that measure the concentration of testosterone before, during, and after a COVID-19 infection.[24,25]

In conjunction with higher androgen levels, there is also overactivation of the renin-angiotensin-aldosterone (RAAS) system in PCOS. Overactivation of the RAAS system results in excess angiotensin II, which causes disassociation of ACE2 from angiotensin II receptor type 1 (AT1R) that allows angiotensin II to bind to AT1R instead. Excessive angiotensin II stimulation leads to increased vascular permeability, severe inflammation, pulmonary fibrosis, pulmonary edema, and eventually acute respiratory distress syndrome (ARDS). In addition, the detachment of ACE2 from AT1R allows more virus entry into lung pneumocytes.[5,26]

Vitamin D deficiency is common in PCOS patients and has been associated with an increased risk of severe

COVID-19 infection. The role of vitamin D in innate and adaptive immunity has been thoroughly studied. Low vitamin D levels in the body contribute to higher serum levels of proinflammatory cytokines that are released from macrophages. Furthermore, PCOS is often associated with comorbidities such as obesity, diabetes, and hypertension, which are also risk factors for severe COVID-19 infection and long COVID symptoms.[5,13,19] While the provided references do not specifically discuss long COVID symptoms in PCOS patients, they provide valuable insights into the overall understanding of long COVID and the association between PCOS and COVID-19. Further research is needed to explore the specific symptoms and impacts of long COVID in PCOS patients.

Finally, we also need to consider the impact of COVID-19 pandemic on lifestyle changes of women with PCOS. PCOS symptoms may be influenced not only by the COVID-19 infection itself but also by the stress and lifestyle changes that accompany it. A survey by McGowan et al. found that women with PCOS tended to exercise less, increase sugar intake, and gain more weight during the COVID-19 2020 pandemic era.[27] In addition to the infection itself, these unhealthy habits can lead to worsening of PCOS symptoms. However, there are limited long-term studies that track lifestyle adjustments in years after the post-COVID era and their association with PCOS symptoms.

Overall, this study presented several strengths that can be highlighted. Firstly, this study underscored women with PCOS as a vulnerable group at risk of developing persistent long COVID symptoms due to overlapping pathogenesis pathways. Several key pathogenesis pathways such as chronic low-grade inflammation, immune dysregulation, excessive androgen level, overactivation of RAAS system, and vitamin D deficiency, have been elaborated above in the context of PCOS and COVID-19. Moreover, this study proved that COVID-19 vaccination does not exacerbate PCOS-associated symptoms, which further emphasizes the importance of completing COVID-19 doses for women with PCOS to avoid persistent long COVID symptoms. Findings from this study can be used as a foundation for future research, for example to investigate whether lean PCOS patients also exhibit similar long COVID-19 risk with their obese counterparts. Nevertheless, despite the novel insight presented in this study, there remain some limitations. Our sample size is limited since many of our PCOS patients were not advised to come to the hospital for medical consultation unless for emergency at the time of pandemic, especially during lockdown periods. Additionally, since we used a survey to ask about long COVID symptoms and PCOS symptoms experienced by the patients, recall bias to some extent might have occurred.

CONCLUSION

Women with PCOS are considered a high-risk group for experiencing long COVID symptoms. Chronic low-grade inflammation and immune system dysregulation associated with PCOS are likely to contribute to the persistence of long COVID symptoms. Even among PCOS patients who had been vaccinated, some women still reported lingering long COVID symptoms. Therefore, vaccination is essential to potentially reduce the severity of these symptoms. It is reassuring to note that COVID-19 vaccination does not worsen PCOS symptoms. However, further studies are needed to explore the potential relationship between PCOS, long COVID, and vaccination to gain a better understanding of their interactions. Understanding the relationship between PCOS and COVID-19 also opens new research avenues on the link between PCOS and respiratory infections or even other infections.

DISCLOSURES

Acknowledgment

The researchers extend their sincere appreciation to the Indonesian Reproductive Medicine Research and Training Center (INAREPROMED), as well as the dedicated teams at Yasmin Clinic and Cipto Mangunkusumo National General Hospital, for their indispensable collaboration and assistance during the entire course of this research project.

Conflict of interest

The authors declare that they have no competing interests.

Funding

No financial support or funding was provided for the publication of this journal article.

Author Contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript. R. M., G. P., A. K. H.; Conceptualization, Methodology, Validation. R. M., K. S. M. M.; Project Supervision. V. S., B. W., A. H.; Administration. A. B., A. A. F.; Formal Analysis, Writing - Original Draft,

Data Curation. E. C. Y., A.N.I; Writing - Review & Editing, Visualization.

REFERENCES

1. Patel S. Polycystic ovary syndrome (PCOS), an inflammatory, systemic, lifestyle endocrinopathy. J Steroid Biochem Mol Biol. 2018;182:27-36. doi: 10.1016/j.jsbmb.2018.04.008. Epub 2018 Apr 17. PMID: 29678491.
2. Li Y, Chen C, Ma Y, et l. Multi-system reproductive metabolic disorder: significance for the pathogenesis and therapy of polycystic ovary syndrome (PCOS). Life Sci. 2019;228:167-75. doi: 10.1016/j.lfs.2019.04.046. Epub 2019 Apr 25. PMID: 31029778.
3. Burhan E. Long COVID: Diagnosis and treatment of respiratory syndrome in post COVID-19 conditions. Jurnal Respirologi Indonesia. 2022;42 (3):250 -6. doi: 10.36497/jri.v40i3.279.
4. Kenny G, Townsend L, Savinelli S, et al. Long COVID: Clinical characteristics, proposed pathogenesis and potential therapeutic targets. Front Mol Biosci. 2023;10:1157651. doi: 10.3389/fmolb.2023.1157651. PMID: 37179568; PMCID: PMC10171433.
5. de Medeiros SF, Yamamoto MMW, de Medeiros MAS, et al. Polycystic ovary syndrome and risks for COVID-19 infection: A comprehensive review : PCOS and COVID-19 relationship. Rev Endocr Metab Disord. 2022;23(2):251-64. doi: 10.1007/s11154-022-09715-y. Epub 2022 Feb 26. PMID: 35218458; PMCID: PMC8881900.
6. Stewart S, Newson L, Briggs TA, et al. Long COVID risk - a signal to address sex hormones and women's health. Lancet Reg Health Eur. 2021;11:100242. doi: 10.1016/j.lanepe.2021.100242. Epub 2021 Nov 2. PMID: 34746909; PMCID: PMC8561426.
7. Man DE, Andor M, Buda V, et al. Insulin resistance in long COVID-19 Syndrome. J Pers Med. 2024; 14(9):911. doi: 10.3390/jpm14090911. PMID: 39338165; PMCID: PMC11433386.
8. Conte C, Cipponeri E, Roden M. Diabetes mellitus, energy metabolism, and COVID-19. Endocr Rev. 2024;45(2):281-308. doi: 10.1210/endrev/bnad032. PMID: 37934800; PMCID: PMC10911957.
9. Maham S, Yoon MS. Clinical spectrum of long COVID: Effects on female reproductive health. Viruses. 2024;16(7):1142. doi: 10.3390/v16071142. PMID: 39066303; PMCID: PMC11281454.
10. Subramanian A, Anand A, Adderley NJ, et al. Increased COVID-19 infections in women with polycystic ovary syndrome: a population-based study. Eur J Endocrinol. 2021;184(5):637-45. doi: 10.1530/EJE-20-1163. PMID: 33635829; PMCID: PMC8052516.
11. Atkinson L, Kite C, McGregor G, et al. Uncertainty, anxiety and isolation: Experiencing the COVID-19 pandemic and lockdown as a woman with Polycystic Ovary Syndrome (PCOS). J Pers Med. 2021;11(10):952. doi: 10.3390/jpm11100952. PMID: 34683093; PMCID: PMC8539750.
12. Kite C, Atkinson L, McGregor G, et al. Sleep disruption and depression, stress and anxiety levels in women with Polycystic Ovary Syndrome (PCOS) during the lockdown measures for COVID-19 in the UK. Front Glob Womens Health. 2021;2: 649104. doi: 10.3389/fgwh.2021.649104. PMID: 34816205; PMCID: PMC8593975.
13. Kyrou I, Karteris E, Robbins T, et alS. Polycystic ovary syndrome (PCOS) and COVID-19: an overlooked female patient population at potentially higher risk during the COVID-19 pandemic. BMC Med. 2020;18(1):220. doi: 10.1186/s12916-020-01697-5. PMID: 32664957; PMCID: PMC7360476.
14. Luan YY, Zhang L, Peng YQ, et al. Immune regulation in polycystic ovary syndrome. Clin Chim Acta. 2022;531:265-72. doi: 10.1016/j.cca.2022.04.234. Epub 2022 Apr 18. PMID: 35447143.
15. Wang D, Weng Y, Zhang Y, et al. Exposure to hyperandrogen drives ovarian dysfunction and fibrosis by activating the NLRP3 inflammasome in mice. Sci Total Environ. 2020;745:141049. doi: 10.1016/j.scitotenv.2020.141049. Epub 2020 Jul 22. PMID: 32758727.
16. Dey R, Bhattacharya K, Basak AK, et al. Inflammatory perspectives of polycystic ovary syndrome: role of specific mediators and markers. Middle East Fertility Society Journal. 2023;28(33). doi: 10.1186/s43043-023-00158-2.
17. Rudnicka E, Suchta K, Grymowicz M, et al. Chronic low grade inflammation in pathogenesis of PCOS. Int J Mol Sci. 2021;22(7):3789. doi: 10.3390/ijms22073789. PMID: 33917519; PMCID: PMC8038770.
18. Dhurandhar NV, Bailey D, Thomas D. Interaction of obesity and infections. Obes Rev. 2015;16(12): 1017-29. doi: 10.1111/obr.12320. Epub 2015 Sep 10. PMID: 26354800.
19. Morgante G, Troìa L, De Leo V. Coronavirus Disease 2019 (SARS-CoV-2) and polycystic ovarian disease: Is there a higher risk for these women? J Steroid Biochem Mol Biol. 2021;205: 105770. doi: 10.1016/j.jsbmb.2020.1057 70. Epub 2020 Oct 13. PMID: 33065278; PMCID: PMC7550902.
20. Ryan PM, Caplice NM. Is adipose tissue a reservoir for viral spread, immune activation, and cytokine amplification in Coronavirus Disease 2019?

Obesity (Silver Spring). 2020;28(7):1191-4. doi: 10.1002/oby.22843. Epub 2020 May 31. PMID: 32314868; PMCID: PMC7264526.
21. Stopsack KH, Mucci LA, Antonarakis ES, et al. TMPRSS2 and COVID-19: Serendipity or opportunity for intervention? Cancer Discov. 2020; 10(6):779-82. doi: 10.1158/2159-8290.CD-20-0451. Epub 2020 Apr 10. PMID: 32276929; PMCID: PMC7437472.
22. Sah P, Fitzpatrick MC, Zimmer CF, et al. Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis. Proc Natl Acad Sci U S A. 2021;118(34):e2109229118. doi: 10.1073/pnas.2109229118. PMID: 34376550; PMCID: PMC8403749.
23. Kalidhindi RSR, Borkar NA, Ambhore NS, et al. Sex steroids skew ACE2 expression in human airway: a contributing factor to sex differences in COVID-19? Am J Physiol Lung Cell Mol Physiol. 2020;319(5):L843-L847. doi: 10.1152/ajplung.00391.2020. Epub 2020 Sep 30. PMID: 32996784; PMCID: PMC7789973.
24. Yassin A, Shabsigh R, Al-Zoubi RM, et al. Testosterone and Covid-19: An update. Rev Med Virol. 2023;33(1):e2395. doi: 10.1002/rmv.2395. Epub 2022 Sep 3. PMID: 36056748; PMCID: PMC9537909.
25. Al-Kuraishy HM, Al-Gareeb AI, Faidah H, et al. Testosterone in COVID-19: An adversary bane or comrade boon. Front Cell Infect Microbiol. 2021;11:666987. doi: 10.3389/fcimb.2021.666987. PMID: 34568081; PMCID: PMC8455954.
26. Moin ASM, Sathyapalan T, Atkin SL, et al. Renin-Angiotensin System overactivation in polycystic ovary syndrome, a risk for SARS-CoV-2 infection? Metabol Open. 2020;7:100052. doi: 10.1016/j.metop.2020.100052. Epub 2020 Aug 18. PMID: 32838280; PMCID: PMC7434315.
27. McGowan M, Lim S, O'Reilly SL, et al. Impact of COVID-19 restriction on weight, physical activity, diet and psychological distress on people with PCOS. Nutrients. 2023;15(11):2579. doi: 10.3390/nu15112579. PMID: 37299542; PMCID: PMC10255147.

ORIGINAL RESEARCH

Maternal, socioeconomic and healthcare factors associated with postpartum maternal mortality in Papua Province, Indonesia, based on secondary data analysis of IDHS 2020

Dian Laily Safitri[1]*, Samsriyaningsih Handayani[2], Budi Prasetyo[1], Ratna Dwi Jayanti[1]
[1]Midwifery Study Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2]Department of Public Health and Preventive Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

Article Info
Received Nov 10, 2024
Revised Jan 30, 2025
Accepted Feb 14, 2025
Published Aug 1, 2025

***Corresponding author:**
Dian Laily Safitri
lailysvirgo@gmail.com

Keywords:
Indonesia Demographic Health Survey (IDHS)
Maternal health
Postpartum maternal mortality
Socioeconomic factors

ABSTRACT

Objective: This study utilized data from the Indonesia Demographic Health Survey (IDHS) 2020 to examine the relationship between postpartum maternal mortality and several determinants, including maternal, socioeconomic, and healthcare-related factors in Papua Province.

Materials and Methods: A cross-sectional design with a quantitative analytical framework was applied, drawing on secondary data from IDHS 2020. The sample comprised 14,802 women aged 15–49 years. Data were analyzed through a simple logistic regression test for bivariate analysis with a 95% confidence level (α = 0.05). Subsequently, multivariate multiple logistic regression analysis was conducted on variables with a p-value of less than 0.25.

Results: Findings demonstrated that all variables (parity p<0.001 AOR=0.533 95% CI 0.375–0.758; place of residence p=0.001 AOR=2.526 95% CI 1.438–4.436; proficiency in Indonesian language p<0.001 AOR=0.039 95% CI 0.031–0.050; delivery attendant and place of birth p<0.001 AOR=0.118 95% CI 0.142–0.249, whereas wealth index status p=0.972 AOR=1.010 95% CI 0.565–1.806) showed a significant negative association with postpartum maternal mortality (p<0.05), except for the wealth index. The strongest association, with an odds ratio (OR) of 0.039, was identified in Indonesian language proficiency, indicating a 25.64-fold increase.

Conclusion: The findings provide a crucial evidence base for the development of policies and interventions aimed at lowering postpartum maternal mortality in Papua Province. Proficiency in the Indonesian language emerged as the most influential factor, underscoring the potential for targeted interventions and improved healthcare outcomes.

How to cite: Safitri DL, Handayani S, Prasetyo B, et al. Maternal, socioeconomic and healthcare factors associated with postpartum maternal mortality in Papua Province, Indonesia, based on secondary data analysis of IDHS 2020. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):97-104. https://doi.org/10.20473/mog.V33I22025.97-104.

Highlights:

1. Postpartum maternal mortality demonstrates associations with determinants including parity, place of residence, proficiency in the Indonesian language, socioeconomic status or wealth index, type of delivery attendant, and place of childbirth.
2. Proficiency in the Indonesian language constitutes the most dominant factor, plausibly indicating inequalities in healthcare access, levels of health literacy, and conditions of geographic or social marginalization.

INTRODUCTION

Strategic initiatives to strengthen health systems constitute an essential component of the 2030 development agenda within the Sustainable Development Goals (SDGs).[1] To reduce the global maternal mortality ratio (MMR), the World Health Organization (WHO) recommends intensifying strategies to improve health outcomes. Maternal mortality is defined as death during pregnancy or within 42 days of pregnancy termination, excluding accidental or incidental causes, but attributable to pregnancy or its management. According to the Indonesia Demographic Health Survey (IDHS), the maternal mortality rate in 2020 was 189 per 100,000 live births. By 2030, the SDGs target 70 per 100,000 live births. In Papua Province, the MMR was 289 per 100,000 live births in 2017 and increased to 565 per 100,000 live births in 2020, reflecting a substantial rise within three years.[2] This increase underscores persistent disparities in healthcare provision, regional infrastructure, and access to skilled health professionals, which remain major challenges in achieving national and global maternal health targets.

Maternal mortality is classified into direct and indirect causes. Direct maternal deaths primarily result from complications of pregnancy, delivery, and the postpartum period. Approximately 75% of maternal deaths are attributed to hemorrhage, infection, hyper-tensive disorders of pregnancy, obstructed labor, and unsafe abortion. Indirect maternal mortality arises from pre-existing conditions or comorbid illnesses aggravated during pregnancy.[3] In Indonesia, the prevalence of Four High and Three Delays represents the leading indirect contributors to maternal mortality. The Four High cases encompass conditions that, when not adequately identified and managed, may result in fatal outcomes, with risk factors including maternal age and parity.[3] The Three Delays involve slow decision-making regarding referral to appropriate health facilities, delayed recognition of pregnancy danger signs, and delayed access to suitable care once at medical centers. Family-level decision-making often contributes to referral delays, highlighting the necessity to strengthen determinants influencing health-seeking behavior and recognition of puerperal complications. Expanding transportation infrastructure is critical to reduce referral delays and facilitate prompt access to healthcare. Furthermore, prolonged administrative processes, inadequate referral centers, insufficient medical personnel, lack of pre-facility readiness, and limited blood supply contribute to treatment delays, necessitating Regional Government reforms to support maternal mortality reduction in Papua Province.[4]

Parity, defined as the number of children a woman has delivered alive or deceased, is closely related to maternal mortality during the postpartum period. Parity serves as an indirect marker of maternal well-being during pregnancy and neonatal outcomes at birth.[3] Social determinants associated with residential settings, particularly rural versus urban environments, reflect health disparities in specific populations. Variations in population density, demographic structure, lifestyle patterns, employment, health perceptions, living standards, and sanitation contribute to differences in morbidity and mortality across rural and urban areas.[5] Another social determinant is proficiency in the Indonesian language. Limited fluency often reflects social isolation, especially among populations in remote areas lacking access to education and technology, such as rural communities in Papua. In this context, linguistic capacity functions not only as a communication skill but also as a critical determinant of health literacy, shaping how women understand medical instructions, navigate health systems, and utilize preventive services.

In Indonesia, many individuals are bilingual, speaking local languages as their mother tongue while using Indonesian as a second language.[6] Economic determinants, including the status/wealth index, affect household financial resources and consequently influence healthcare utilization. Households with lower socioeconomic status must expend greater effort to access healthcare services compared to wealthier households.[5] Healthcare-related factors also include delivery attendants, professionals committed to maternal health, whose skills and expertise are acquired through formal training and regulated licensure, which is essential to ensure safe healthcare practices.[7] Additionally, the place of delivery remains a critical factor, distinguishing between healthcare-based and non-healthcare-based settings. Non-healthcare delivery sites include the mother's home, residences of untrained personnel, or other locations without access to adequate health infrastructure.[8]

MATERIALS AND METHODS

This research was quantitative analytical, using secondary data from SDKI 2020. This research was conducted in Surabaya with data from October 2023 to March 2024. The study consisted of 20,482 women aged 15 to 49. There were originally 439,562 data for this study, but only 14,802 data remained after cleaning. This study was a total sample with inclusion criteria using data on postpartum maternal deaths that occurred within two years. Exclusion criteria in this study included incomplete data and different RUTA IDs. SPSS software version 26 for Windows was used to

classify and organize the study findings. This study received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine Universitas Airlangga Surabaya, numbered 41/EC/KEPK/FKUA/2024. This ethics declaration applies from February 6, 2024 until February 6, 2025. Variables independent in this study are parity, living place, Indonesian language ability, status/wealth index, delivery attendant, and place of delivery. Variable Independent in this study is postpartum maternal mortality.

RESULTS AND DISCUSSION

The 2020 SDKI data classify the dependent variable into four distinct categories of maternal mortality: pregnancy, abortion, delivery process, and postpartum period. Results from the Central Bureau of Statistics indicate that maternal mortality in Papua Province is substantially higher than in other provinces. Table 1 presents the distribution of maternal mortality in Papua Province in 2020.

The study evaluated several independent variables, namely parity, place of residence, Indonesian language proficiency, socioeconomic status or wealth index, delivery attendant, and place of delivery. Table 2 illustrates the distribution of parity, living place, Indonesian language ability, status/wealth index, delivery attendant, and place of delivery.

A logistic regression analysis was performed to determine the association between parity and maternal mortality in Papua Province in 2020. The regression results demonstrated a p-value of less than 0.05, indicating a statistically significant relationship between parity and maternal mortality at the 0.05 level. The association between parity and postpartum maternal mortality revealed a negative Odds Ratio. Mothers with more than three children were at greater risk of maternal death compared with mothers having fewer than three children.[9] Logistic regression was further applied to evaluate the association between place of residence and maternal mortality in Papua Province in 2020. The test yielded a p-value of less than 0.05, establishing a significant association between place of residence and maternal mortality at the 0.05 significance level.

The odds ratio demonstrated a negative correlation between place of residence and postpartum maternal mortality. Mothers residing in urban areas were found to be at greater risk of maternal death compared with those in rural areas.[9] Logistic regression was also employed to examine the relationship between Indonesian language proficiency and maternal mortality in Papua Province in 2020. The analysis revealed a p-value of less than 0.05, indicating a significant association between Indonesian language ability and maternal mortality at the 0.05 level. The Odds Ratio further indicated a negative association, whereby mothers proficient in Indonesian were at higher risk of maternal death compared with mothers without proficiency.[9]

Table 1. Distribution of maternal mortality in Papua Province 2020

Maternal mortality	Death n (%)	Life n (%)
Pregnancy	121 (26.30)	
Abortion	66 (14.35)	
Delivery process	204 (44.35)	
Postpartum period	69 (15)	
Total	460 (3.10)	14.342 (96.90)

Table 2. Distribution of parity, living place, Indonesian language ability, status/wealth index, delivery attendant, place of delivery

Factors	Categories	n (%)
Parity	> 3 children	2421 (16.36)
	≤ 3 children	12.381 (83.64)
Living place	Urban	4.136 (27.94)
	Rural	10.666 (72.06)
Indonesian language ability	Able	14.316 (96.72)
	Not capable	486 (3.28)
Status/wealth index	Middle to upper	3.693 (24.95)
	Middle to lower	11.109 (75.05)
Delivery attendant	Healthcare professional	10.562 (71.36)
	Non-healthcare professional	4.240 (28.64)
Place of delivery	Healthcare facility	10.562 (71.36)
	Non-healthcare facility	4.240 (28.64)

Table 3. Results from simple logistic regression parity, living place, Indonesian language ability, status/wealth index, delivery attendant, place of delivery with postpartum maternal mortality

Postpartum maternal mortality factors	Categories	p-values	Odds Ratio (95%CI)
Parity	> 3 children ≤ 3 children	0.000	0.478 (0.345-0.664)
Living place	Urban Rural	0.000	0.542 (0.425-0.691)
Indonesian language ability	Able Not capable	0.000	0.026 (0.021-0.033)
Status/wealth index	Middle to upper Middle to lower	0.000	0.513 (0.395-0.665)
Delivery attendant	Healthcare professional Non-healthcare professional	0.000	0.159 (0.130-0.195)
Place of delivery	Healthcare facility Non-healthcare facility	0.000	0.159 (0.130-0.195)

A logistic regression analysis assessed the relationship between the status/wealth index and maternal mortality in Papua Province in 2020. The regression produced a p-value of less than 0.05, confirming a significant association between the status/wealth index and maternal mortality. This association was statistically significant at the 0.05 level. The Odds Ratio indicated a negative relationship between the status/wealth index and postpartum maternal mortality. Mothers from middle-to-upper socioeconomic groups were found to be at greater risk of maternal death compared with mothers from middle-to-lower groups.[9]

A logistic regression test was conducted to analyze the correlation between delivery attendants and maternal mortality in Papua Province in 2020. The regression yielded a p-value of less than 0.05, indicating a statistically significant association between delivery attendants and maternal mortality at the 0.05 level. The Odds Ratio demonstrated a negative correlation between delivery attendants and postpartum maternal mortality. Mothers attended by healthcare professionals during delivery were more likely to experience maternal death compared with those attended by non-healthcare providers.[9] Logistic regression was further applied to assess the association between place of delivery and maternal mortality in Papua Province in 2020. The regression test produced a p-value of less than 0.05, confirming a significant association between place of delivery and maternal mortality at the 0.05 level. The Odds Ratio demonstrated a negative association between place of delivery and postpartum maternal mortality. Mothers who delivered in healthcare facilities were at higher risk of maternal death compared with mothers delivering in non-healthcare settings.[9] Referral delays were identified as a contributing factor to deaths occurring in healthcare facilities. These referral delays in Papua are attributed to difficult geographic accessibility, which results in prolonged processing times. Table 3 presents the regression outcomes.

Hazairin et al. (2021) reported that the weakening and decline in reproductive organ function increase the likelihood of complications, low birth weight, and other health problems that threaten maternal safety. Furthermore, high parity is generally associated with advanced maternal age and shortened birth intervals, both of which heighten maternal risk. Based on the findings of this study, it is recommended that the government strengthen family planning programs within communities to enhance awareness of the risks during pregnancy, childbirth, and the postpartum period that may arise when parity is high or non-ideal, defined as more than three children.[3] Rosales et al. (2019) emphasized that postpartum hemorrhage represents a critical danger sign, requiring the decision to seek medical help to be made as quickly as possible. Within Papuan communities, however, decision-making is predominantly influenced by the husband.

Pregnancy and postpartum care are often still conducted at home by non-healthcare providers when immediate intervention is required. In most cases, care is sought outside the household but not at established health facilities, as mothers and families frequently fail to recognize danger signs of pregnancy through the postpartum period. Decisions to seek emergency care in formal health facilities are generally made only after non-healthcare personnel are unable to manage the condition. Maternal mortality is strongly associated with delays in seeking professional assistance, which result from both limitations in recognizing obstetric danger signs and delays in receiving definitive treatment at the health facility level.[10]

To date, no studies have explicitly reported that mothers fluent in Indonesian face an elevated risk of maternal death; however, Fiharsono (2021) emphasized that the socio-cultural heterogeneity of Papua can be characterized through distinctions between urban, rural, and remote communities. This investigation further identified that populations proficient in Indonesian are more commonly concentrated in rural areas.[11] Khayati et al. (2018) additionally observed that families within the middle-to-upper socioeconomic strata were often associated with maternal employment. Their study demonstrated a significant correlation between maternal occupational status, heightened stress levels during pregnancy, and the occurrence of preeclampsia. Persistent stress sustains a physiologically activated state marked by excessive secretion of adrenaline and cortisol, stress hormones that compromise the maternal immune system. As a result, pregnant women become more vulnerable to multiple disorders, with preeclampsia representing a major concern. Complications arising from preeclampsia commonly persist throughout labor and frequently extend into the postpartum period.[12]

Afrida et al. (2022) reported that the crisis in healthcare professional availability across Indonesia has markedly influenced the effectiveness of national health development efforts. Papua Province remains among the regions experiencing uneven distribution of healthcare personnel, undermining the quality of maternal health services and directly contributing to maternal mortality. Fatalities frequently occur due to referral delays and treatment initiation, even after mothers have reached the presence of healthcare providers.[13] Munro et al. (2022) observed that Papuans place strong cultural emphasis on vaginal delivery while generally avoiding cesarean section. In practice, women and their families often confront or negotiate with physicians, decline recommended cesarean procedures, or insist upon clear justification before granting consent. Some avoid hospitals altogether to avert surgical intervention. These practices constitute an important contributor to maternal mortality, as they lead to substantial delays in decision-making and the initiation of treatment within health facilities.[14]

The initial study hypothesis proposed that parity was the most dominant determinant of maternal mortality in Papua Province in 2020. Nevertheless, results from multiple logistic regression analysis revealed that proficiency in Indonesian demonstrated the strongest association with postpartum maternal mortality, with negative test outcomes. The Indonesian language variable yielded a correlation coefficient of 0.039, corresponding to a 25.64-fold greater risk of postpartum maternal death. Mothers fluent in Indonesian were determined to be at higher risk of mortality compared to mothers lacking such proficiency.[15] The analysis results are displayed in Table 4. This outcome is likely attributable to the predominance of Indonesian-speaking populations in rural villages (OR=0.063), where referral delays are substantially more common. Therefore, in addition to implementing health promotion strategies, it is essential to encourage pregnant and postpartum women to reside closer to healthcare facilities. Furthermore, government efforts should prioritize expanding the establishment of healthcare centers in rural settings, particularly in areas where difficult terrain and limited accessibility hinder timely referral to the nearest facility.[16]

The development of rural healthcare facilities is fundamental in reducing maternal mortality by guaranteeing the provision of critical services, such as antenatal care, skilled attendance at delivery, and emergency obstetric management. These centers are equally vital in enhancing community awareness of safe maternal health behaviors and potential risks associated with pregnancy.[17] The presence of trained healthcare personnel, including midwives and physicians, during childbirth ensures the early detection and treatment of life-threatening complications such as obstructed labor and postpartum hemorrhage.[18] Regular antenatal visits at these centers enable timely detection of pregnancy-related complications and strengthen postnatal care, thereby reducing the risk of maternal and neonatal morbidity and mortality.[19] In emergency situations, village-based healthcare facilities serve as critical stabilization points, providing immediate care and organizing referral to higher-level institutions—an indispensable role in areas with limited transport networks. Furthermore, these centers function as focal points for health education, equipping mothers and families with essential knowledge on birth preparedness, danger sign recognition, and utilization of available maternal health services.[20]

Table 4. Results from multiple logistic regression factor with postpartum maternal mortality

Maternal mortality	Factors	p-values	Odds Ratio (95% CI)
Postpartum maternal mortality	Parity	0.000	0.533
	Living place	0.001	2.526
	Indonesian language ability	0.000	0.039
	Status/wealth index	0.972	1.010
	Delivery attendant	0.000	0.188
	Place of delivery	0.000	0.188

Table 5. Relationship between Indonesian language ability and living place

Factors	p-values	Odds Ratio (95% CI)
Indonesian language ability	0.000	0.063
Living place	0.000	0.063

The strong association between the ability to speak Indonesian and postpartum maternal mortality, as revealed in this study, may initially appear unexpected—especially given that language proficiency is generally assumed to facilitate access to healthcare (Table 5). However, in the sociocultural and geographic context of Papua, this finding can be meaningfully interpreted through a broader understanding of structural health determinants. In this case, Indonesian language ability appears not as a protective factor but rather as a proxy for other underlying risks. The study found that women who speak Indonesian are more likely to reside in rural areas of Papua with limited access to health facilities, skilled birth attendants, and emergency obstetric care.

Thus, contrary to typical assumptions, proficiency in the national language does not necessarily translate to better health outcomes in this setting. Instead, it may reflect exposure to circumstances that increase vulnerability—such as poor infrastructure, social exclusion, or the absence of culturally appropriate services. The limited availability of quality maternal healthcare in these rural communities likely contributes more significantly to maternal mortality than language proficiency alone. Furthermore, the extraordinarily high adjusted odds ratio (AOR = 0.039) suggests a complex interplay of risk factors. Indonesian language ability, in this context, may signal a subset of the population that, despite linguistic fluency, remains marginalized in terms of access to timely and adequate maternal care.

In summary, Indonesian language ability in Papua should not be interpreted as a straightforward advantage in maternal health. Instead, it reflects deeper systemic vulnerabilities—geographic isolation, healthcare inequity, and limited service reach—which must be addressed through inclusive, community-based, and regionally tailored health interventions.

Strength and limitation

The advantage of secondary data lies in the rapid and straightforward data collection method. The Secondary Data Analysis of IDHS offers a range of intriguing data that yield comprehensive insights into Indonesian society's demographic and health aspects. The constraints of secondary data research arise from the outcomes of interviews. Completing questionnaires necessitates that respondents depend solely on recollection, potentially leading to recall bias and insufficient clarity of the essential information. The data employed is solely from the datasheet, limiting the factors analyzed. Secondary data necessitates a process of elimination to obtain the requisite information for researchers, along with a coding procedure due to inconsistencies in specific codes relative to the research.

CONCLUSION

The results indicated that all factors—parity, living place, Indonesian language ability, delivery attendant, and place of delivery—were significantly associated with postpartum maternal mortality, except for the status/wealth index. The strongest association was observed in Indonesian language ability. This finding likely reflects broader disparities in healthcare access, health literacy, and geographic or social marginalization. The research provides a strong foundation for future policies and interventions to reduce postpartum maternal mortality in Papua Province, with Indonesian language ability emerging as the most dominant factor,

highlighting the need for targeted, inclusive, and linguistically accessible healthcare strategies.

DISCLOSURES

Acknowledgment

The author thanks the Midwifery Study Program, Faculty of Medicine, Universitas Airlangga Surabaya, for academic guidance and support in completing this research. Appreciation is also extended to all individuals who contributed to the development of this article.

Conflict of interest

This study presents no potential physical or psychological risks, as it utilizes secondary data derived from IDHS 2020. The author declares no conflict of interest associated with this research.

Funding

This study was supported through the author's personal funding.

Author contribution

All authors contributed equally to every stage of the research process, including study design, data acquisition and analysis, manuscript drafting, and final approval of the version submitted for publication.

REFERENCES

1. Maternal mortality [Internet]. [cited 2023 Nov 21]. Available from: https://www.who.int/news-room/fact-sheets/detail/maternal-mortality
2. Preventing Pregnancy-Related Deaths | CDC [Internet]. 2023 [cited 2023 Nov 21]. Available from: https://www.cdc.gov/reproductivehealth/maternal-mortality/preventing-pregnancy-related-deaths.html
3. Kurniawan R, Melaniani S. Hubungan paritas, penolong persalinan dan jarak kehamilan dengan angka kematian bayi di Jawa Timur [Relationship between parity, birth attendant and pregnancy spacing with infant mortality rate in East Java]. Jurnal Biometrika dan Kependudukan. 2018;7(2): 113–121. doi: 10.20473/jbk.v7i2.2018.113-121.
4. Ulfah M. Analisis kematian ibu ditinjau dari Tiga Terlambat pada rujukan maternal desa siaga dengan P4K di Kabupaten Bojonegoro tahun 2016-2018 [Analysis of maternal mortality given Three Delays in maternal referral of alert village with P4K in Bojonegoro Regency in 2016-2018] [Repository]. Surabaya: Universitas Airlangga; 2019.
5. Lengkong GT, Langi FL, Posangi J. Factors associated with infant mortality in Indonesia. Journal of KESMAS. 2020;9(4).
6. Language Center of Papua Province. Indonesian language development in Papua province in 2020. [Internet]. Available from https://www.pusatbahasa provinsipapua
7. Ulfa DN. Analisis determinan antara pada kasus kematian ibu di kota Tasikmalaya tahun 2018 [Analysis of intermediate determinants in maternal mortality cases in Tasikmalaya City in 2018]. [Repository]. Tasikmalaya: Universitas Silliwangi; 2019.
8. Ray JG, Fu L, Austin PC, et al. Teen pregnancy and risk of premature mortality. JAMA Netw Open. 2024;7(3):e241833. doi: 10.1001/jamanetworkopen.2024.1833. PMID: 38483391; PMCID: PMC10940968.
9. Hosmer DW, Lemeshow S, Sturdivant RX. Applied Logistic Regression. New York: John Wiley & Sons; 2013.
10. Rosales A, Sulistyo S, Miko O, et al. Recognition of and care-seeking for maternal and newborn complications in Jayawijaya district, Papua province, Indonesia: a qualitative study. J Health Popul Nutr. 2017;36(Suppl 1):44. doi: 10.1186/s41043-017-0122-0. PMID: 29297380; PMCID: PMC5764054.
11. Fiharsono A, Carey M, Hyde M. et al. Culturally based learning needs of Korowai students in a lowland-remote area of Indonesian Papua:school physical environment and building design. Aust Educ Res. 2024:51;611–29. doi: 10.1007/s13384-023-00615-x.
12. Khayati YN, Veftisia V. Hubungan stress dan pekerjaan dengan preeklamsia di wilayah Kabupaten Semarang [Relationship between stress and work with preeclampsia in Semarang Regency Area]. Indonesian Journal of Midwifery. 2018;1:35-40. doi: 10.35473/ijm.v1i1.38.
13. Afrida ND, Wulandari SP. Pemetaan fasilitas tenaga kesehatan berdasarkan kabupaten/kota di Provinsi Papua [Health care facility mapping based on districts/towns in Papua Province]. Jurnal Sains dan Seni ITS. 2022;11(1):D57–63. doi: 10.12962/j23373520.v11i1.62871.
14. Munro J, Katmo ETR, Wetipo M. Hospital births and frontier obstetrics in urban West Papua. The Asia Pacific Journal of Anthropology. 2022;23(4–5):388–406. doi: 10.1080/14442213.2022.2115121.
15. Bursac Z, Gauss CH, Williams DK, et al. Purposeful selection of variables in logistic regression. Source Code Biol Med. 2008;3:17. doi:

10.1186/1751-0473-3-17. PMID: 19087314; PMCID: PMC2633005.
16. Laksono AD, Wulandari RD. Urban–rural disparities of facility-based childbirth in Indonesia. In: Proceedings of the 4th International Symposium on Health Research (ISHR 2019). Advances in Health Sciences Research. 2020;22. Atlantis Press, pp. 33-9. ISBN 10.2991/ahsr.k.200215.007
17. Mathar I, Klevina MD, Sebtalesy CY. A literature review of maternal mortality in the countryside. What are the policies and prevention? Asian Journal of Healthy and Science. 2024;3(8):197-209. doi: 10.58631/ajhs.v3i8.110.
18. Regif SY, Nasution FA, Pattipeilohy A, et al. Revitalizing rural healthcare: a case study of village maternity cottages in Indonesia. International Journal of Sustainable Development and Planning. 2023;18(10):3309-16. doi: 10.18280/ijsdp.181030.
19. Chhabra S, Kanade M. Need of going beyond creating rural health facilities and community based care for prevention of maternal deaths. J Clin Exp Reprod Med. 2024;1(1):12-25. doi: 10.46439/reproductivemed.1.003.
20. Damayanti NA, Wulandari RD, Ridlo IA. Maternal health care utilization behavior, local wisdom, and associated factors among women in urban and rural areas, Indonesia. Int J Womens Health. 2023;15: 665-77. doi: 10.2147/IJWH.S379749. PMID: 37163191; PMCID: PMC10164391.

ORIGINAL RESEARCH

Maternal and fetal characteristics associated with successful Vaginal Birth After Cesarean (VBAC) in Dr. Soetomo and Universitas Airlangga Hospitals, Surabaya, Indonesia

Syihab Armawa[1]*, Agus Sulistyono[2], Muhammad Ilham Aldika Akbar[3], Risa Etika[4]
[1]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2]Department of Obstetrics and Gynecology, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
[3]Universitas Airlangga General Academic Hospital, Surabaya, Indonesia.
[4]Department of Pediatrics, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

Article Info
Received Dec 7, 2024
Revised Mar 11, 2025
Accepted Apr 25, 2025
Published Aug 1, 2025

***Corresponding author:**
Syihab Armawa
syihab.armawa.putera-2021@fk.unair.ac.id

Keywords:
Cervical dilation
Cesarean section
Maternal health
Vaginal birth
VBAC

ABSTRACT

Objective: This study aimed to assess maternal and fetal characteristics associated with successful vaginal birth after cesarean (VBAC) at Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital in Surabaya, Indonesia.

Materials and Methods: A retrospective analytic design was applied using a total sampling method to examine medical records from January 2021 to December 2022. Inclusion criteria were singleton pregnancies with one prior low-segment cesarean section, vertex presentation, and absence of contraindications to vaginal delivery. A total of 46 eligible cases were evaluated after applying exclusion criteria.

Results: Among the analyzed parameters, cervical dilation at admission and the 5-minute Apgar score were significantly associated with successful VBAC ($p < 0.05$). All women admitted with cervical dilation >4 cm achieved vaginal delivery, underscoring its strong predictive value. Conversely, those with dilation <4 cm demonstrated a markedly increased likelihood of repeat cesarean section. A higher Apgar score was also positively correlated with VBAC success, reflecting favorable neonatal outcomes in such cases. Maternal BMI showed no statistically significant association with VBAC success ($p > 0.05$), probably due to the predominance of obesity within the cohort. Other variables, including maternal age, parity, birth interval, gestational age, and neonatal birth weight, exhibited no significant relationship with the outcome.

Conclusion: Although most maternal and fetal parameters were not significantly related to VBAC success, cervical dilation on admission proved to be a crucial clinical predictor. These findings highlight the value of intrapartum evaluation, particularly cervical assessment, in informing delivery planning for women with previous cesarean sections.

How to cite: Armawa S, Sulistyono A, Akbar MIA, et al. Maternal and fetal characteristics associated with successful Vaginal Birth After Cesarean (VBAC) in Dr. Soetomo and Universitas Airlangga Hospitals, Surabaya, Indonesia. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):105-112. doi: 10.20473/mog.V33I22025.105-112.

Highlights:

1. High VBAC success rate demonstrated with effective patient selection and intrapartum management.
2. Cervical dilation >4 cm at admission identified as a critical predictor of VBAC success.

INTRODUCTION

Cesarean-section (CS) deliveries have experienced a marked global rise, shaping maternal preferences for delivery methods, largely due to anxiety regarding vaginal birth, fear of labor pain, and other determinants influencing the decision to undergo CS. The increasing prevalence is especially pronounced in high- and middle-income nations, where rates of non-medically indicated CS have escalated, often motivated by maternal preference to avoid vaginal delivery and sociocultural influences surrounding childbirth.[1]

Worldwide, the CS rate increased from 6.7% in 1990 to 19.1% in 2014, with Asia recording the second-highest rise at 15.1% during this interval.[2] This growth is linked to advances in surgical safety, including the availability of modern antibiotics, improved transfusion methods, enhanced anesthesia, and supportive medical technologies. Nevertheless, despite these advances, CS is associated with higher risks and complications compared with vaginal birth, such as elevated infection rates, hemorrhage, thromboembolic events, and prolonged recovery.[3] Vaginal birth after cesarean (VBAC) represents an important strategy to decrease repeat CS rates, with global success ranging between 60–80%.[4] In light of the increasing CS prevalence and its associated risks, identifying determinants of successful VBAC is essential to optimize maternal and neonatal outcomes. This study therefore aimed to evaluate maternal and fetal characteristics associated with successful VBAC at Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital in Surabaya, Indonesia, between 2021 and 2022, to guide clinical decision-making and strengthen patient selection for VBAC attempts.

MATERIALS AND METHODS

A retrospective analytic study design was adopted, employing a total sampling technique to review medical records at Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital from January 2021 to December 2022. Inclusion criteria consisted of live fetuses, a single prior low-segment transverse cesarean section, singleton gestation, vertex presentation, and the absence of contraindications to vaginal delivery (e.g., placenta previa, active genital herpes, or severe fetal distress). Exclusion criteria comprised incomplete documentation, multiple pregnancies, or non-vertex presentations. Data extracted from both electronic and paper-based records included maternal age, BMI, gravidity, interpregnancy interval, gestational age, history of vaginal birth, neonatal birth weight, Apgar scores, and cervical dilation on admission. Accuracy of extracted data was confirmed by cross-verification with labor and delivery logs. From 70 records initially identified, 46 fulfilled the inclusion criteria after excluding 24 for incomplete data or ineligibility. Data were summarized in frequency distribution tables and analyzed with the Chi-square test to examine associations between maternal and fetal characteristics and VBAC success. Statistical analysis was conducted using SPSS version 25, with significance set at $p<0.05$. Ethical approval was secured from the institutional review boards of both hospitals, with confidentiality maintained in compliance with standards for retrospective research, thereby ensuring adherence to accepted principles of medical ethics and patient data protection.

RESULTS AND DISCUSSION

Retrospective Chi-square analysis of medical records from Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital between January 2021 and December 2022 included 70 women undergoing attempted VBAC, of which 24 records were excluded according to study criteria, leaving 46 cases for analysis through tabulation and graphical representation. The results demonstrated that cervical dilation on admission and 5-minute Apgar scores were significantly associated with successful VBAC ($p<0.05$), whereas maternal BMI, age, gravidity, and interpregnancy interval were not statistically significant. This analysis underscores the influence of cervical dilation and neonatal condition on VBAC outcomes and provides clinically relevant insights for practice, particularly in facilities with similar resource settings and patient populations.

Table 1 summarizes the data distribution and outcomes of patients undergoing VBAC (N=46), demonstrating significant associations for Apgar score and cervical dilation with p-values <0.05. The final analysis indicated that selected maternal and fetal characteristics can serve as predictors for evaluating VBAC risk at Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital. Accordingly, accurate prediction plays a crucial role in clinical decision-making for women with a high likelihood of VBAC success.5 In support of these findings, a study from China reported VBAC success rates as high as 84% among post-cesarean women, although elective repeat CS remains the most common delivery mode in this population, reflecting persistent clinical caution and maternal concerns.[6]

Table 1. Data distribution of patients with VBAC procedure

Variables	Margin	Method of delivery		Total percent	p-values
		VBAC	CS		
Maternal age	20-35	31 (86.1%)	5 (13.9%)	36 (78.2%)	0.244
	>35	7 (70%)	3 (30%)	10 (22.8%)	
Maternal BMI	<25 kg/m^2	8 (100%)	-	8 (17.4%)	0.067
	25-30 kg/m^2	14 (87.5%)	2 (12.5%)	16 (34.8%)	
	>30 kg/m^2	16 (72.7%)	6 (27.3%)	22 (47.8%)	
Gravidity	G2	16 (80%)	4 (20%)	20 (43.5%)	0.614
	G3	13 (81.3%)	3 (18.8%)	16 (34.8%)	
	G4	5 (100%)	-	5 (10.8%)	
	>G4	4 (80%)	1 (20%)	5 (10.8%)	
Birth interval	<2 years	8 (88.9%)	1 (11.1%)	9 (19.6%)	0.589
	>2 years	30 (81.1%)	7 (18.9%)	37 (80.4%)	
Gestational weeks	<34 weeks	2 (100%)	-	2 (4.3%)	0.299
	34-37 weeks	5 (62.5%)	3 (37.5%)	8 (17.5%)	
	>37 weeks	31 (86.1%)	5 (13.9%)	36 (78.2%)	
Vaginal birth history	Yes	20 (83.3%)	4 (16.7%)	24 (52.2%)	0.895
	No history	18 (81.8%)	4 (18.2%)	22 (48.8%)	
Baby birth weight	<2 kg	2 (100%)	-	2 (4.3%)	0.842
	2-2.5 kg	5 (71.4%)	2 (28.6%)	7 (15.2%)	
	2.6-2.9 kg	12 (85.7%)	2 (14.3%)	14 (30.4%)	
	3-3.5 kg	19 (86.4%)	3 (13.6%)	22 (47.8)	
	>3 kg	-	1 (100%)	1 (2.3%)	
APGAR score	0-3	1 (100%)	-	1 (2.2%)	0.023
	4-6	7 (58.3%)	5 (41.7%)	12 (26.1%)	
	7-10	30 (90.0%)	3 (9.1%)	33 (72.7%)	
Cervical dilation	<4 cm	7 (46.7%)	8 (53.3%)	15 (32.6%)	0.000
	>4 cm	31 (100%)	-	31 (68.4%)	

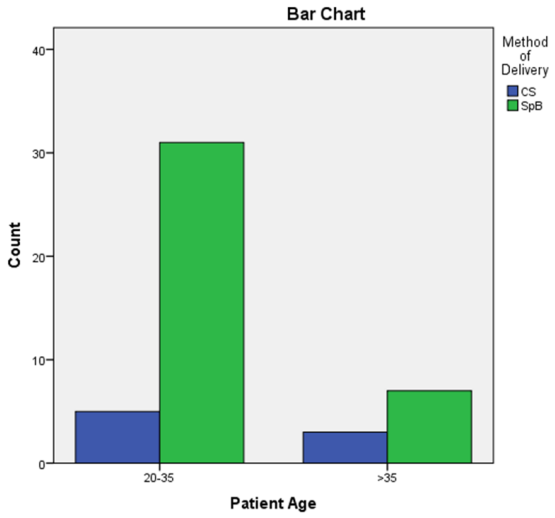


Figure 1. Distribution and frequency of patients based on age.

Figure 1 illustrates that the predominant cohort comprised 36 women (78.2%) aged 20–35 years, with a VBAC success rate of 86.1%, compared with a 70% success rate in patients older than 35 years (N=10, 22.8% of the sample), yielding a p-value of 0.244. Younger patients may benefit from enhanced pelvic adaptability and fewer comorbidities, thereby facilitating vaginal delivery. Nevertheless, the relatively small number of older participants limited the ability to demonstrate significant differences. Most patients in the 20–35 age group who experienced failed VBAC exhibited obesity, short interpregnancy intervals, or additional maternal conditions that elevated risk, consistent with reports indicating that maternal age below 35 and primiparity are associated with increased likelihood of successful vaginal birth.[7] Many older women likewise presented with higher BMI or reduced interpregnancy intervals, contributing to greater repeat cesarean rates within this subgroup. This multifactorial interaction highlights the importance of comprehensive risk stratification, suggesting that younger women with normal BMI and a history of vaginal delivery represent ideal VBAC candidates, whereas older women with concomitant risk factors require closer surveillance or consideration of alternative delivery strategies.

Figure 2 presents the distribution and frequency of patients according to BMI, where a p-value of 0.067 indicated a suggestive but non-significant trend toward higher repeat cesarean rates with increasing BMI. The obese group (BMI >30 kg/m²) represented 47.8% of the sample (N=22) and demonstrated a 27.3% cesarean rate, compared with 12.5% in the overweight group (BMI 25–30 kg/m², N=16) and 0% in the normal BMI group

(<25 kg/m², N=8). Cesarean section rates increased progressively from 28% among overweight women to 41.2% among obese women.[8] VBAC success was most frequently observed in the obese subgroup, which accounted for 47.82% of all cases, whereas the lowest frequency occurred in the normal BMI group at 17.39%. This trend suggests that obesity may adversely influence labor progression, potentially through prolonged labor or heightened uterine rupture risk. The high prevalence of obesity in this population may have reduced statistical power to achieve significance, given that nearly half of participants were obese. These findings underscore the importance of individualized counseling for women with elevated BMI, including preconception weight optimization and nutritional guidance to reduce risks of labor complications and repeat cesarean. Clinicians should incorporate enhanced intrapartum monitoring for obese patients to facilitate timely interventions in the presence of labor challenges.

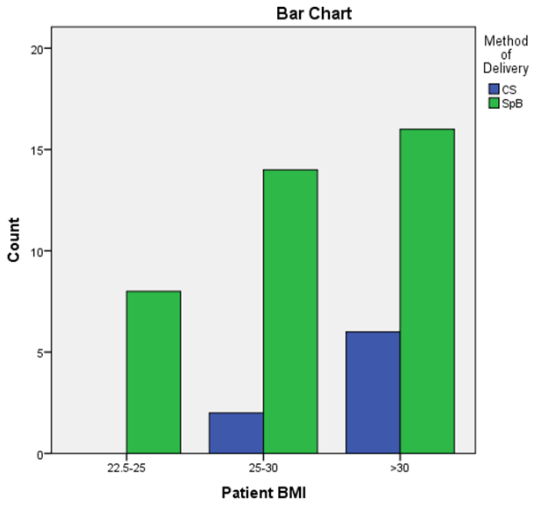


Figure 2. Distribution and frequency of patients based on BMI.

Figure 3 illustrates the subgroup of patients presenting with cervical dilation greater than 4 cm, in which all 31 women (100%) achieved spontaneous vaginal delivery, highlighting the pivotal influence of advanced labor progression upon admission. Conversely, among patients with dilation less than 4 cm, 58.3% required repeat cesarean delivery, with only 7 of 15 achieving vaginal birth. The strong association (correlation coefficient 0.660, p-value <0.02) underscores the necessity for clinicians to evaluate cervical status early during labor as a guide to clinical decision-making. For patients presenting with minimal dilation, early intrapartum interventions, such as augmentation of labor or intensified monitoring, may enhance VBAC outcomes, while concurrent preparation for potential cesarean delivery could optimize maternal and neonatal safety. The findings also suggest that a history of labor arrest in prior pregnancies affects VBAC success. Women with a history of arrest during the second stage of labor tend to exhibit higher rates of successful VBAC, whereas those with first-stage arrest demonstrate lower success, likely reflecting underlying limitations in labor progression. Supporting evidence from other studies indicates that 90.5% of VBAC attempts with cervical dilation greater than 4 cm culminate in successful vaginal birth, and women admitted with dilation exceeding 1 cm show an increased likelihood of VBAC achievement.7,9 Prior maximal cervical dilation likewise represents a prognostic determinant, with second-stage arrest linked to higher VBAC success, while first-stage arrest corresponds to approximately 65% success in subsequent VBAC attempts.10,11

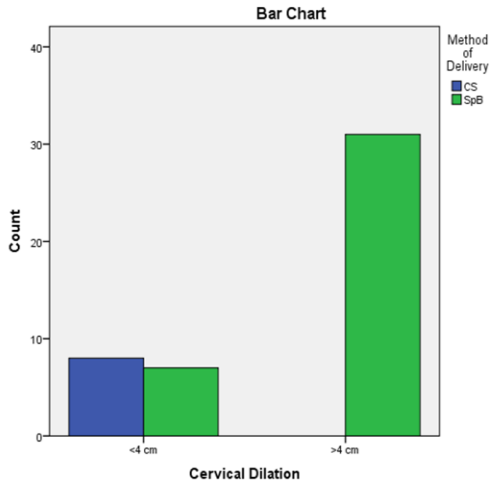


Figure 3. Distribution and frequency of patients based on cervical dilation.

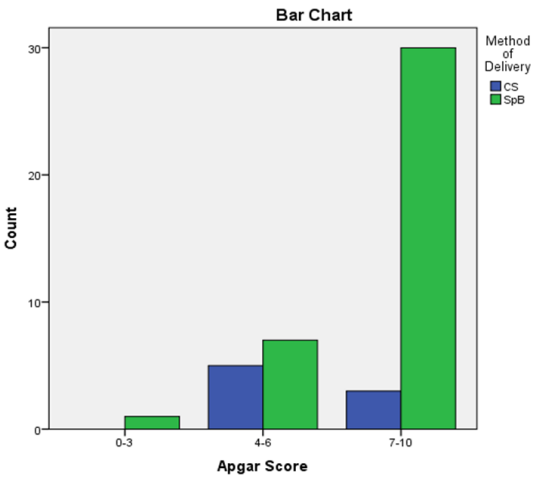


Figure 4. Distribution and frequency of patients based on 5-minute APGAR Score.

Figure 4 illustrates comparable outcomes in neonatal performance, with Apgar scores at 5 minutes post-delivery demonstrating significant prognostic relevance. Specifically, 71.7% of VBAC patients (N=33) achieved Apgar scores of 7–10 within one to five minutes after birth, with 90.9% of this subgroup delivered vaginally, reflecting favorable neonatal outcomes associated with successful VBAC. The mean Apgar score for successful VBAC was higher at 1 minute (7.21) compared with failed trial of labor after cesarean (TOLAC) cases (6.91), and this pattern persisted at 5 minutes.[12] Conversely, those with Apgar scores of 4–6 exhibited a reduced VBAC success rate of 58.3%, implying that fetal distress or intrapartum complications may necessitate cesarean delivery. Within the VBAC cohort, 13 neonates (28.3%) had scores below the 7–10 range, underscoring a notable distinction in Apgar outcomes between successful and unsuccessful VBAC attempts. These findings emphasize the critical importance of vigilant intrapartum surveillance, including continuous electronic fetal monitoring, to promptly identify early compromise that may lower Apgar scores, enabling timely adjustments in delivery mode.[13] However, the differences in Apgar scores between successful and unsuccessful VBAC attempts were not sufficiently marked to suggest that neonatal outcomes alone dictate delivery success, as maternal characteristics and labor dynamics also substantially influence results.[14]

Gravidity and parity (p=0.614) revealed no significant association with VBAC outcome, with consistently high success rates across gravidity groups. Patients in the G4 group achieved a 100% success rate (N=5), though the limited sample constrains interpretation. The elevated success rates may reflect stringent selection criteria, particularly inclusion of women with a single prior low-segment cesarean section. Moreover, the presence of women with prior vaginal births (52.2%, N=24) likely enhanced overall success, since previous vaginal delivery is a recognized predictor of VBAC success. Women with such a history, regardless of gravidity, represent promising candidates; however, clinicians should exercise caution with higher-gravidity cases, given cumulative risks from repeated uterine scarring.[15]

Birth interval (p=0.589) similarly showed no significant effect, with success rates of 88.9% for intervals shorter than 2 years (N=9) and 81.1% for intervals exceeding 2 years (N=37). Although short interpregnancy intervals are typically associated with incomplete uterine healing or increased risk of rupture, the high success rates observed in both groups suggest that judicious patient selection and vigilant monitoring can mitigate such risks. The limited number of women with short intervals, however, reduced the ability to discern subtle differences. Counseling regarding optimal inter-pregnancy spacing remains advisable to further optimize VBAC safety and outcomes.[16]

Gestational age and birth weight, with p-values of 0.299 and 0.842, respectively, also demonstrated no significant correlation with VBAC success. The majority of participants (78.2%, N=36) delivered at term (>37 weeks), achieving an 86.1% success rate, indicating that term gestation favors VBAC through enhanced fetal maturity and readiness for labor. Two preterm deliveries (<34 weeks) achieved 100% success, suggesting that VBAC may be feasible in carefully selected preterm cases. Birth weight similarly showed no consistent trend, with high success rates across most categories, although the single neonate exceeding 3 kg delivered by cesarean highlights potential concerns with macrosomia, underscoring the need for heightened monitoring in such scenarios.

The overall VBAC success rate of 82.6% underscores the effectiveness of stringent patient selection, incorporating factors such as singleton gestation, cephalic presentation, and absence of contraindications to vaginal delivery. Evidence from a Chinese study demonstrated a comparable success rate of 84% among post-cesarean women, although repeat cesarean remains the predominant choice for many with a prior cesarean section.[6] These observations highlight the necessity of individualized risk stratification and collaborative decision-making in VBAC planning.[15] Cervical dilation and Apgar scores should be emphasized as primary predictors, whereas maternal BMI and age should be integrated into a comprehensive evaluation. This final analysis indicates that specific maternal and fetal characteristics may serve as predictors of VBAC outcomes, making accurate prediction essential for identifying women with a high probability of successful VBAC.[5]

The increased VBAC success rate illustrates the potential of this strategy to reduce repeat cesarean sections, which are associated with increased risks of complications, including infection, hemorrhage, and prolonged recovery relative to vaginal delivery. The pivotal role of cervical dilation, as presented in Figure 3, suggests that intrapartum management protocols should prioritize optimizing cervical progress through timely interventions, such as oxytocin augmentation or artificial rupture of membranes, when clinically appropriate.[17] Clinicians should also apply partograms to systematically monitor labor progression and identify delays at an early stage, particularly among patients admitted with cervical dilation less than 4 cm.[18] The correlation between higher Apgar scores and successful VBAC, as depicted in Figure 4, further reinforces the importance of vigilant fetal monitoring to safeguard

neonatal outcomes, guiding decisions regarding continuation of VBAC attempts or conversion to cesarean delivery.

The non-significant results concerning maternal BMI, as shown in Figure 2, underscore the multifactorial nature of VBAC outcomes, which are determined by the interaction of multiple influences rather than a single variable in isolation. The observed tendency toward increased cesarean rates with rising BMI suggests that obesity-related factors, such as diminished uterine contractility or augmented soft tissue obstruction, may contribute to failed VBAC.[19] This emphasizes the need for a multidisciplinary approach to VBAC counseling, involving obstetricians, nutritionists, and maternal–fetal medicine specialists to address modifiable risks, such as obesity, prior to conception.[20] Likewise, the lack of significance for maternal age, as illustrated in Figure 1, may be attributable to confounding variables, including comorbidities or additional maternal conditions, which should be carefully evaluated in prenatal care to optimize candidacy for VBAC.

The high success rate among women with prior vaginal deliveries highlights the importance of incorporating obstetric history into VBAC counseling and management. A history of vaginal birth likely reflects enhanced myometrial adaptability to labor, thereby increasing the likelihood of success. This finding supports the development of predictive models integrating obstetric history alongside clinical factors, such as cervical dilation and fetal well-being.[21] Such predictive tools could enable stratification of patients into low-, intermediate-, and high-risk categories for VBAC success, facilitating personalized counseling and tailored intrapartum management strategies.

The lack of significant impact from birth interval is particularly relevant for women planning subsequent pregnancies after a cesarean section. While shorter intervals are often considered a risk factor, the high success rate in this study suggests that with appropriate patient selection—such as ensuring a low-segment cesarean scar and no other contraindications—VBAC can be safely attempted even with intervals less than 2 years.[22] However, clinicians should remain vigilant for signs of uterine rupture, a rare but serious complication, particularly in women with shorter intervals. Regular ultrasound assessments of the uterine scar during pregnancy could provide additional reassurance in these cases.[23]

The findings on gestational age and birth weight further reinforce the importance of fetal maturity and size in VBAC planning. Term deliveries are generally associated with better labor outcomes due to the fetus's readiness for delivery and the mother's physiological preparedness for labor. The small number of preterm deliveries in this study limits definitive conclusions, but the 100% success rate in this group suggests that preterm VBAC may be a viable option in carefully selected cases, such as those with spontaneous preterm labor and favorable cervical conditions. Conversely, the single case of macrosomia resulting in a cesarean delivery underscores the need for careful monitoring of fetal size, as larger fetuses may increase the risk of labor dystocia or shoulder dystocia, which could complicate VBAC attempts.[24]

Future research could build on these findings by exploring additional variables that may influence VBAC outcomes, such as the impact of labor induction, the role of maternal comorbidities like diabetes or hypertension, or the effect of different labor management protocols. Larger cohort studies would enhance statistical power to detect differences in non-significant variables like maternal age and birth interval, providing a more comprehensive understanding of VBAC predictors. Additionally, qualitative studies exploring patient preferences and experiences with VBAC could inform strategies to increase its acceptance among women with a prior cesarean section, addressing barriers such as fear of labor or lack of awareness about VBAC benefits.

Strengths and limitations

The study's strengths include its retrospective design, utilizing comprehensive medical records from two major hospitals, ensuring robust data collection, and focusing on key predictors like cervical dilation and Apgar scores, which showed significant associations with VBAC success. The careful patient selection criteria enhanced the reliability of the findings. Limitations include the small sample size (N=46), which reduced statistical power for non-significant variables like maternal BMI and age. The retrospective nature may introduce selection bias, and the lack of data on labor induction or maternal comorbidities limits generalizability. Larger, prospective studies could address these gaps.

CONCLUSION

This study highlights the potential of vaginal birth after cesarean (VBAC) as a viable strategy to reduce repeat cesarean deliveries in multiparous women, provided that rigorous patient selection and thorough risk assessment are prioritized. VBAC represents a safer alternative to repeat cesarean section in the absence of contra-indications, such as placenta previa or fetal distress, thereby safeguarding maternal and neonatal outcomes.

These findings enrich the existing scientific evidence and seek to promote greater awareness of the benefits of VBAC. This study demonstrates that VBAC procedures conducted at Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital, Surabaya, Indonesia, achieved a high probability of success. Greater cervical dilation at the time of admission is a pivotal determinant strongly correlated with successful VBAC. Favorable neonatal outcomes, as reflected by higher Apgar scores, are consistently associated with successful VBAC, underscoring positive indicators of fetal well-being.

DISCLOSURES

Acknowledgment

The authors express their sincere gratitude to Dr. Agus Sulistyono, Dr. Risa Etika, and Dr. Muhammad Ilham Aldika Akbar for their valuable guidance, constructive input, and support throughout the stages of study design, data collection, analysis, and manuscript preparation. Their contributions were essential to the successful completion of this work.

Conflict of interest

No conflict of interest occurred in this study

Funding

This research did not receive any funding

Author contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

REFERENCES

1. Boerma T, Ronsmans C, Melesse DY, et al. Global epidemiology of use of and disparities in caesarean sections. Lancet. 2018;392(10155):1341-8. doi: 10.1016/S0140-6736(18)31928-7. PMID: 30322 584.
2. Betrán AP, Ye J, Moller AB, et al. The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. PLoS One. 2016;11(2):e0148343. doi: 10.1371/journal.pone. 0148343. PMID: 26849801; PMCID: PMC4743 929.
3. Gee ME, Dempsey A, Myers JE. Caesarean section: techniques and complications. Obstet Gynaecol Reprod Med. 2020;30(4):97–103. doi:10.1016/j. ogrm.2020. 02.004.
4. Vishesha Y, Vidyadhar B, Sai B. Predictors of successful vaginal birth after caesarean section. Indian J Basic Appl Med Res. 2017;6(4):380–8. Available from: https://www.ijbamr.com/assets/ images/issues/pdf/September%202017%20%20380 -388.pdf.pdf
5. Mesay F, Melese E, Wudie G, et al. A prognostic study for the development of risk prediction model for the success of vaginal birth following a cesarean surgery at Felege Hiwot Comprehensive Specialized Hospital, Northwest Ethiopia. Risk Manag Healthc Policy. 2023;16:55-68. doi: 10.2147/ RMHP.S395388. PMID: 36714193; PMCID: PMC9880561.
6. Li H, Sheng W, Cai M, et al. A predictive nomogram for a failed trial of labor after cesarean: A retrospective cohort study. J Obstet Gynaecol Res. 2022;48(11):2798-806. doi: 10.1111/jog.15398. Epub 2022 Sep 2. PMID: 36055678; PMCID: PMC9825937.
7. Dunn MC, Ananth CV, Zhang Y, et al. Association of BMI and success of trial of labor after cesarean: systematic review and meta-analysis. Am J Obstet Gynecol. 2023;228(1):S372. doi: 10.1016/j.ajog. 2022.11.650.
8. Birara M, Gebrehiwot Y. Factors associated with success of vaginal birth after one caesarean section (VBAC) at three teaching hospitals in Addis Ababa, Ethiopia: A case control study. BMC Pregnancy Childbirth. 2013;13(1):1. doi: 10.1186/1471-2393-13-31.
9. Singh P, Bamaniya J, Shah A. Factors predicting success of trial of labour after caesarean in current scenario. Int J Reprod Contraception, Obstet Gynecol. 2016;5(11):3893–7. doi: 10.18203/2320-1770.ijrcog20163860.
10. Levin G, Tsur A, Tenenbaum L, et al. Prediction of successful vaginal birth after cesarean in women with diabetic disorders and no prior vaginal delivery. Int J Gynaecol Obstet. 2022;157(1):165-72. doi: 10.1002/ijgo.13736. Epub 2021 Jun 2. PMID: 33969481.
11. Trojano G, Damiani GR, Olivieri C, et al. VBAC: antenatal predictors of success. Acta Biomed. 2019;90(3):300-9. doi: 10.23750/abm.v90i3.7623. PMID: 31580319; PMCID: PMC7233729.
12. Siddiqui SA. Obstetric factors for unsuccessful trial of labor in second-order birth following previous cesarean. Ann Saudi Med. 2013;33(4):356-62. doi: 10.5144/0256-4947.2013.356. PMID: 24060714; PMCID: PMC6078504.

13. Grivell RM, Alfirevic Z, Gyte GM, et al. Antenatal cardiotocography for fetal assessment. Cochrane Database Syst Rev. 2015;2015(9):CD007863. doi: 10.1002/14651858.CD007863.pub4. PMID: 26363287; PMCID: PMC6510058.
14. Herwanto ES, Hudiyanto PS, Muhammad I (2024) Factors of maternal influence on Low Birth Weight. Asian J Heal Res. 3 (1): 5-10. doi: 10.55561/ajhr.v3i1.144.
15. Habak PJ, Khaparde G, Vadakekut ES. Vaginal Birth After Cesarean Delivery. 2025 Feb 15. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29939621.
16. American College of Obstetricians and Gynecologists; Society for Maternal-Fetal Medicine. Obstetric Care Consensus No. 8: Interpregnancy Care. Obstet Gynecol. 2019;133(1): e51-e72. doi: 10.1097/AOG.0000000000003025. PMID: 30575677.
17. Myers ER, Sanders GD, Coeytaux RR, et al. Labor dystocia [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020. Report No.: 20-EHC007. PMID: 32479038.
18. Lavender T, Cuthbert A, Smyth RM. Effect of partograph use on outcomes for women in spontaneous labour at term and their babies. Cochrane Database Syst Rev. 2018;8(8):CD00 5461. doi: 10.1002/14651858.CD005461.pub5. PMID: 30080256; PMCID: PMC6513424.
19. Šišljagic D, Blažetic S, Heffer M, et al. The interplay of uterine health and obesity: A comprehensive review. Biomedicines. 2024;12(12): 2801. doi: 10.3390/biomedicines12122801. PMID: 39767708; PMCID: PMC11673887.
20. Wingert A, Hartling L, Sebastianski M, et al. Clinical interventions that influence vaginal birth after cesarean delivery rates: Systematic Review & Meta-Analysis. BMC Pregnancy Childbirth. 2019;19(1):529. doi: 10.1186/s12884-019-2689-5. PMID: 31888540; PMCID: PMC6937863.
21. Jenkins SM, Mikes BA. Preterm Labor. 2025 Feb 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 30725624.
22. Carauleanu A, Tanasa IA, Nemescu D, et al. Risk management of vaginal birth after cesarean section (Review). Exp Ther Med. 2021;22(4):1111. doi: 10.3892/etm.2021.10545. Epub 2021 Aug 3. PMID: 34504565; PMCID: PMC8383756.
23. Cheng XL, Cao XY, Wang XQ, et al. Diagnosing early scar pregnancy in the lower uterine segment after cesarean section by intracavitary ultrasound. World J Clin Cases. 2022;10(2):547-53. doi: 10.12998/wjcc.v10.i2.547. PMID: 35097080; PMCID: PMC8771384.

ORIGINAL RESEARCH

The development of "TAMENG" flipchart for eradication of anemia in pregnancy in Sumber, Kabupaten Probolinggo, Indonesia

Manggala Pasca Wardhana[1]*, Agus Sulistyono[1], Riska Wahyuningtyas[1], Rizqy Rahmatyah[1], Amrina Rosyada[1], Salsabila Nabilah Rifdah[1], Mirani Ulfa Yusrika[2]
[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2]Department of Pediatrics, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

Article Info
Received Dec 28, 2024
Revised May 2, 2025
Accepted May 16, 2025
Published Aug 1, 2025

***Corresponding author:**
Manggala Pasca Wardhana
manggala.pasca
@fk.unair.ac.id

Keywords:
Anemia in pregnancy
Educational intervention
Maternal health
Nutritional status
TAMENG flipchart

ABSTRACT

Objective: This study aimed to evaluate the effectiveness of the "TAMENG" flipchart as an educational tool to improve knowledge about anemia prevention among pregnant women in Sumber, Kabupaten Probolinggo, Indonesia, and to explore associated risk factors for anemia, including nutritional status and supplementation practices.

Materials and Methods: A community-based cross-sectional study was conducted in August 2024 as part of Universitas Airlangga's Community Service Program. Pregnant women attending antenatal care in Sumber, Kabupaten Probolinggo were recruited based on ANC attendance and availability of hemoglobin test results. The "TAMENG" flipchart, designed with culturally relevant visuals and content on anemia prevention, was implemented during interactive education sessions. Demographic data, obstetric histories, and pre- and post-test knowledge assessments were collected. Statistical analysis was performed using chi-square tests to identify significant associations between variables.

Results: Among 65 participants, 35.38% were anemic. Significant factors associated with anemia included nutritional status (60.9% of anemic women had mid-upper arm circumference <23.5 cm; p = 0.019) and history of anemia (30.4% vs. 9.5%; p = 0.032). Knowledge scores significantly improved post-intervention for 90.5% of non-anemic women and 100% of anemic women. Employment status and supplementation practices showed notable trends but were not statistically significant.

Conclusion: The "TAMENG" flipchart effectively increased knowledge and awareness about anemia prevention. Tailored interventions addressing nutritional deficiencies, supplementation adherence, and family involvement can enhance maternal health outcomes in rural communities.

How to cite: Wardhana MP, Sulistyono A, Wahyuningtyas R, et al. The development of "TAMENG" flipchart for eradication of anemia in pregnancy in Sumber, Kabupaten Probolinggo, Indonesia. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):113-120. doi: 10.20473/mog.V33I22025.113-120.

Highlights:

1. The "TAMENG" flipchart significantly improved knowledge about anemia prevention among pregnant women.
2. Nutritional status (mid-upper arm circumference) and history of anemia were strongly associated with anemia prevalence.
3. Community-based, culturally relevant tools like the flipchart can effectively promote sustainable maternal health behaviors.

INTRODUCTION

Anemia occurs when red blood cells are unable to provide enough oxygen to meet tissue requirements. This condition can be detected by low hemoglobin (Hb) levels, erythrocyte counts, and hematocrit (Hct) concentrations.[1] The World Health Organization (WHO) defines anemia in pregnancy as Hb <11 g/dL. Meanwhile, the Centers for Disease Control and Prevention (CDC) defines anemia in pregnancy as Hb <11 g/dL in the first and third trimesters and Hb <10.5 g/dL in the second trimester.[2,3] Iron deficiency accounts for around 50% of pregnant women's anemia. Other causes include deficits in folic acid (B9) and other micronutrients (vitamins A, riboflavin (B2), B6, and B12), acute or chronic infections (such as malaria, hookworm, schistosomiasis, TB, and HIV), and congenital hemoglobin synthesis abnormalities.[1,3] Anemia in pregnancy has a negative impact on the growth and development of the fetus. It can cause difficulties from pregnancy until delivery, including maternal and fetal mortality.[1]

The global prevalence of anemia in pregnancy is 38.2, with Southeast Asia having the highest prevalence (48.75).[2] According to Riset Kesehatan Dasar (Riskesdas) or Indonesian Basic Health Research in 2018, the incidence of anemia among pregnant women in Indonesia was 48.9%, an increase of 11.8% compared to 2013. It can be interpreted that anemia affects up to two out of every five pregnant women in Indonesia.[4] According to data from Dinas Kesehatan Provinsi Jawa Timur or East Java Provincial Health Office, anemia affects 15.6% of all women of reproductive age in East Java. A study in Probolinggo in 2020 found that 501 out of 4075 pregnant women had anemia.[5] Another study reported that the frequency of anemia among pregnant women in Probolinggo was 48.5%.[6] The prevalence of anemia in pregnancy varies with socioeconomic status, lifestyle, diet, attitudes, and health practices.[2]

The provision of iron and folic acid supplements (*tablet tambah darah* or TTD) during pregnancy is one of the initiatives to prevent and treat iron and folic acid deficiency anemia. Through antenatal care (ANC) service standards, the Indonesian Government requires pregnant women to take the supplement daily during pregnancy, or at least 90 tablets. In East Java, only 49.8% of pregnant women received supplementation of more than 90 tablets. In comparison, only 35.6% consumed more than 90.[4] Based on the 2023 Nutrition Plan at the Sumber Community Health Center, the coverage of supplementation only reached 72.2% of the target set at 81%.[7] In Sumber, Kabupaten Probolinggo, the prevalence of anemia among pregnant women highlights the need for effective educational interventions. This study explores the development and impact of the "TAMENG" flipchart as an educational tool designed to address knowledge gaps, promote behavior change for eradicating anemia, and explore the risk factors among pregnant women in Sumber, Kabupaten Probolinggo, East Java, Indonesia.

MATERIALS AND METHODS

Study population and design

This community-based cross-sectional study was part of the 2024 Universitas Airlangga Community Service, implemented in August 2024 in Sumber, Kabupaten Probolinggo. Participants were recruited through community health posts and classes for pregnant women in Sumber, Kabupaten Probolinggo. Inclusion criteria included all pregnant women who had attended at least one antenatal care session and had available hemoglobin laboratory test results. Recruitment involved collaboration with local midwives and community health volunteers, ensuring broad participation across various villages. Data were collected through demographic surveys, obstetric histories, and knowledge assessments (pre- and post-tests). The data recorded and stored both manual and digital entry using initial for the confidentiality is being kept for the researchers only. Informed consent was provided for each individual before participation.

Hypothesis of the study

We hypothesized that TAMENG is effective in evaluating knowledge improvement and is associated with anemia prevalence.

Development of the flipchart

The "TAMENG" flipchart was designed based on input from obstetrics and gynecology specialists. The content covered anemia prevention, dietary practices, and the importance of iron supplementation, the acronym "TAMENG" in Indonesian, a protective shield. Visual aids and culturally relevant illustrations were incorporated to enhance comprehension among participants with low literacy levels. The material underwent a pilot test with a small group of pregnant women and was revised based on their feedback. To ensure the effectiveness of the educational content, the flipchart was reviewed, and later, pre- and post-intervention assessments were conducted to measure the validity and reliability.

Implementation and outcome

The educational activity involved delivering a comprehensive socialization program to pregnant women. In collaboration with health center officers, the research team provided education on anemia's definition, epidemiology, risk factors, clinical symptoms, impacts, and prevention strategies using the "TAMENG" flipchart. This program was integrated with pregnant women's classes and antenatal care examinations. Pre-tests and post-tests were administered to assess changes in community knowledge before and after the sessions. The activity concluded with a discussion session, allowing participants to clarify questions and engage further with the presented material.

Statistical analysis

Numerical data were reported with mean with standard deviation, and categorical data were reported as n(%). Cross-tabulation with a chi-square test was used to examine relationships between variables, with significance set at $p < 0.05$. Pretest and posttest using Mann-Whitney due to not normally distributed data. Data was analyzed using The Statistical Package for the Social Sciences (SPSS) version 29 for Mac (IBM Corp., Armonk, NY, USA).

Ethical clearance

This research is registered in the 2024 Universitas Airlangga Community Service and has received ethical clearance from the Faculty of Medicine, Universitas Airlangga, with number 107/EC/KEPK/FKUA/2024.

RESULTS AND DISCUSSION

A total of 65 pregnant women from 81 registered pregnant women participated in the study (participation rate 80.25%), who came from 9 villages in Sumber. The demographic data (Table 1) revealed that the mean age of participants in the anemia group was 23.45 years, while the mean age in the non-anemia group was 21.86 years. Employment status showed a significant difference between the two groups, with 65.2% of anemic women being housewives compared to 92.9% of non-anemic women ($p = 0.004$). Educational levels were predominantly low in both groups, with 52.2% of women in the anemia group and 45.2% in the non-anemia group having lower education levels.

Maternal history and nutritional status are provided in Table 2. Regarding obstetric and health history, the prevalence of primigravida was similar in both groups, at 60.9% for the anemia group and 61.9% for the non-anemia group ($p = 0.037$). However, a significant history of anemia was more common in the anemic group (30.4%) compared to the non-anemic group (9.5%; $p = 0.032$). Nutritional status also differed notably between the groups, with 60.9% of anemic women having an upper-arm circumference of less than 23.5 cm, compared to 31.0% of non-anemic women ($p = 0.019$).

Regarding supplementation practices (Table 3), routine iron tablet supplementation was more common among non-anemic women (76.2%) than anemic women (56.5%), though the difference was not statistically significant ($p = 0.100$). Finally, the impact of education on knowledge improvement post-intervention was significant. A greater proportion of non-anemic women (90.5%) showed an increase in their knowledge scores compared to 37.7% of anemic women. Knowledge of anemia is provided in Table 4.

The findings underscore the importance of targeted educational interventions in addressing anemia during pregnancy. The "TAMENG" flipchart's success aligns with global studies highlighting the effectiveness of community-based tools in improving maternal health outcomes. Until now, patient education has been conducted using self-made posters that lack standardization. Therefore, the use of standardized educational media such as TAMENG can help unify the knowledge provided, ensuring that the information received by patients is more consistent and of higher quality. For instance, educational programs in rural India and sub-Saharan Africa have demonstrated that visual and interactive learning materials significantly enhance knowledge retention and behavior modification among pregnant women.[8] In line with SDGs goal number 3 of ensuring healthy lives and promoting well-being for all ages, community service programs focusing on maternal and child health are essential. This goal includes targets to reduce maternal mortality, end preventable child deaths, and end the spread of communicable diseases by 2030.[9] Up to one thousand days after delivery, addressing anemia in pregnancy can automatically improve the nutritional status of pregnant women, affecting the growth and development of the fetus and infant.[1,3] Some significant findings in this study are employment status, nutritional status, history of anemia, supplementation practices, and knowledge levels.

Table 1. Demographic data

Variables			Anemia (n=23)	Non-Anemia (n=42)	p-Values
			n (%)	n (%)	
Demographic data					
Age	Mean		23.45	21.86	0.384
	≥19 years		14 (60.9)	30 (71.4)	
	<19 years		9 (39.1)	12 (28.6)	
Village	Cepoko		4 (17.4)	7 (16.7)	0.735
	Gemito		3 (13.0)	6 (14.3)	
	Ledok Ombo		2 (8.7)	1 (2.4)	
	Pandansari		4 (17.4)	5 (11.9)	
	Rambaan		1 (4.3)	3 (7.1)	
	Sumber		3 (13.0)	13 (31.0)	
	Sumberanom		2 (8.7)	1 (2.4)	
	Tukul		3 (13.0)	4 (9.5)	
	Wonokerso		1 (4.3)	2 (4.8)	
Employment status*	Housewife		15 (65.2)	39 (92.9)	0.004*
	Working		8 (34.8)	3 (7.1)	
Education level	Low	No school	3 (13.0)	2 (4.8)	0.288
		Primary school	12 (52.2)	19 (45.2)	
	Intermediate	Middle school	7 (30.4)	14 (33.3)	
	High	High school/above	1 (4.3)	7 (16.7)	
Marriage	First		18 (78.3)	36 (85.7)	0.443
	Second or More		5 (21.7)	6 (14.3)	

*significant

Table 2. Maternal history and nutritional status

Variables			Anemia (n=23)	Non-Anemia (n=42)	p-Value
			n (%)	n (%)	
Maternal history and nutritional status					
Pregnancy*	Primigravida	1	14 (60.9)	26 (61.9)	0.037*
	Multigravida	2	2 (8.7)	12 (28.6)	
		3	5 (21.7)	2 (4.8)	
		4	1 (4.3)	2 (4.8)	
		5	1 (4.3)	0 (0)	
Number of children	0		16 (69.6)	26 (61.9)	0.507
	1		6 (26.1)	14 (33.3)	
	2		0 (0)	1 (2.4)	
	4		1 (4.3)	0 (0)	
	6		0 (0)	1 (2.4)	
History of miscarriage	Yes		6 (26.1)	5 (11.9)	0.145
	No		17 (73.9)	37 (88.1)	
History of anemia*	Yes		7 (30.4)	4 (9.5)	0.032
	No		16 (69.6)	38 (90.5)	
History of hypertension	Yes		2 (8.7)	3 (7.1)	0.822
	No		21 (91.3)	39 (92.9)	
History of bleeding	Yes		1 (4.3)	22 (95.7)	0.939
	No		2 (4.8)	40 (95.2)	
Smoking	Yes		1 (4.3)	1 (2.4)	0.661
	No		22 (95.7)	41 (97.6)	
Menstrual cycle	Regular		22 (95.7)	40 (95.2)	0.939
	Irregular		1 (4.3)	2 (4.8)	
Menstrual period*	2-4 days		7 (30.4)	9 (21.4)	0.026
	5-7 days		14 (61.0)	32 (76.2)	
	>7 days		2 (8.6)	1 (2.4)	
Amount of menstruation	1-2 pads/day		5 (21.7)	15 (35.8)	0.265
	3-4 pads/day		18 (78.2)	24 (57.1)	
	>5 pads/day		0 (0.0)	3 (7.1)	
Antenatal care	Routine		19 (82.6)	37 (88.1)	0.540
	Non-routine		4 (17.4)	5 (11.9)	
Body Mass Index	Normal		22 (95.7)	38 (90.5)	0.454
	Obesity		1 (4.3)	4 (9.5)	
Blood Pressure	Normal		21 (91.3)	37 (88.1)	0.690
	Hypertension		2 (8.7)	5 (11.9)	
Mid-Upper Arm Circumference*	<23.5 cm		14 (60.9)	13 (31.0)	0.019
	>23.5 cm		9 (39.1)	29 (69.0)	

*significant

Table 3. Iron and folic acid supplementation practice

Variables		Anemia (n=23) n (%)	Non-Anemia (n=42) n (%)	p-Value
Iron and Folic Acid Supplementation Practice				
Supplementation Compliance	Routine	13 (56.5)	32 (76.2)	0.100
	Non-routine	10 (43.5)	10 (23.8)	
Supplementation Schedule	Morning	6 (26.1)	9 (21.4)	0.118
	Afternoon	7 (30.4)	5 (11.9)	
	Evening	10 (43.5)	28 (66.7)	
Moment	After eating	19 (82.6)	34 (81.0)	0.869
	Before eating	4 (17.4)	8 (19.0)	
Consumption with	Water	16 (69.6)	36 (85.7)	0.120
	Other drinks (tea, coffee, milk)	7 (30.4)	6 (14.3)	
Side effect	Non	11 (47.8)	21 (50.0)	0.265
	Headache	1 (4.3)	7 (16.7)	
	Nausea-vomiting	11 (47.8)	14 (33.3)	
Control Card*	Routine	7 (30.4)	25 (59.5)	0.025*
	Non-routine	16 (69.6)	17 (40.5)	
Controller	Non	9 (39.1)	16 (38.1)	0.899
	Husband	13 (56.5)	25 (59.5)	
	Family/others	1 (4.3)	1 (2.4)	

Table 4. Knowledge of anemia

Variables		Anemia (n=23) n (%)	Non-Anemia (n=42) n (%)	p-Value
Knowledge of anemia				
Knowledge*	Low	6 (26.1)	1 (2.4)	0.011*
	Intermediate	11 (47.8)	23 (54.8)	
	High	6 (26.1)	18 (42.9)	
Pre-test Score	Median (Min,Max)	60 (10, 80)	70 (10, 90)	0.088
Post-test Score	Median (Min,Max)	80 (50, 90)	90 (50, 100)	0.203
Improvement	Increases	23 (37.7)	38 (90.5)	0.311
	Persists	0 (0)	2 (4.8)	
	Decreases	0 (0)	2 (4.8)	

*significant

Employment and nutritional status showed a significant association with anemia. Housewives were found to be less anemic compared to working women (p = 0.004). This finding may relate to the higher likelihood of housewives adhering to antenatal care recommendations and dietary guidelines due to more flexible schedules. However, it also underscores the need for tailored interventions for working women, who may face time constraints and workplace challenges that hinder healthy behaviors.[10]

Nutritional status can be measured from low mid-upper arm circumference. The prevalence of low mid-upper arm circumference (MUAC <23.5 cm) or chronic energy deficiency (CED) among anemic women (60.9%) compared to non-anemic women (31.0%) (p = 0.019) indicates a strong link between malnutrition and anemia. This highlights the critical role of addressing nutritional deficiencies, particularly in rural areas with limited dietary diversity. Providing fortified foods or nutrition supplementation programs alongside educational tools could enhance the overall impact.[11]

A significant history of anemia (30.4% vs. 9.5%, p = 0.032) among anemic participants reflects the chronic nature of the issue. This finding emphasizes the importance of early screening, consistent monitoring, and integrating anemia prevention strategies into preconception care.[12] While the difference in routine iron supplementation between anemic (56.5%) and non-anemic women (76.2%) was not statistically significant, the results indicate room for improvement. Non-compliance with supplementation may be linked to misconceptions about side effects, as noted in reports of headache, nausea, and vomiting. Interventions should address these barriers by educating women about proper supplementation techniques and managing potential side effects.[13]

The significant improvement in knowledge scores post-intervention highlights the flipchart's effectiveness in bridging information gaps. The stark contrast between pre-intervention knowledge levels (26.1% low in anemic women) and post-intervention scores suggests that educational tools are pivotal in promoting behavior change.[14,15] Future studies should explore how sustained knowledge impacts long-term health outcomes.

Cultural factors, such as traditional dietary practices and perceptions about anemia, play a critical role in intervention success. In Sumber, Kabupaten Probolinggo, dietary staples like rice and vegetables may lack sufficient iron content, necessitating targeted messaging on incorporating iron-rich foods, such as meat, legumes, and fortified products.[16] Moreover, local beliefs about pregnancy-related dietary restrictions may hinder adherence to nutritional advice. Engaging community leaders and incorporating culturally relevant examples can improve acceptance of educational programs.[17]

Additionally, the involvement of primary healthcare cadres and family members, particularly husbands, enhanced the intervention's reach. Previous studies have shown that spousal support significantly influences maternal health behaviors, underscoring the need to include family-centered approaches in anemia prevention strategies.[18]

These findings suggest several actionable recommend-dations. First, integrating flipchart-based education into routine antenatal care services could improve knowledge sustainability about anemia in pregnancy. Second, addressing systemic barriers, such as access to affordable iron supplements and fortified foods, is crucial.[19] Lastly, further research is needed to evaluate the long-term effectiveness of the "TAMENG" flipchart and its adaptability to other rural settings. Exploring its integration with digital platforms could also open up new outreach and education possibilities.[20] The findings underscore the importance of targeted educational interventions. Compared to previous studies, the "TAMENG" flipchart's success aligns with global findings emphasizing the role of community-based education in improving maternal health outcomes. For instance, studies from similar rural Southeast Asian settings have shown that culturally tailored educational tools significantly enhance knowledge and compliance with anemia prevention strategies.[5,6,16] Addressing factors such as nutritional deficits and low educational levels is crucial for the success of anemia eradication programs.[14]

Specific regional factors, such as dietary habits and socioeconomic conditions in Kabupaten Probolinggo, may have influenced the outcomes. The predominance of low educational attainment and nutritional deficits in this population mirrors broader national trends, as reported in Indonesian health surveys. Moreover, the involvement of community health workers and local leaders in delivering the intervention likely enhanced its acceptability and effectiveness. These cultural and social dynamics underscore the importance of locally adapted approaches in addressing anemia.[5–7]

Strength and limitation

This study demonstrates notable strengths, including the application of the culturally adapted "TAMENG" flipchart, which effectively enhanced participants' knowledge regarding anemia prevention. The robust methodological approach, incorporating pre- and post-intervention assessments alongside the involvement of local community leaders and healthcare providers, further increased the study's contextual relevance and acceptability. Moreover, the findings offer practical insights into key factors associated with anemia, such as nutritional deficiencies and employment status, facilitating the development of targeted interventions. Nonetheless, the study is subject to certain limitations, including a relatively small sample size and a focus on a single geographic region, which may constrain the generalizability of the findings. The absence of a control group poses challenges in isolating the intervention's impact, while the short duration of follow-up limits the ability to assess sustained behavioral and health outcomes.

CONCLUSION

The "TAMENG" flipchart is a promising tool for improving anemia awareness and prevention practices among pregnant women in Sumber, Kabupaten Probolinggo. Although that iron supplementation compliance was not significantly associated with anemia prevalence in this study and suggest further investigation. Key findings, such as the significant association between employment status, nutritional deficiencies, and anemia, underline the need for comprehensive strategies, including nutritional supple-mentation, early screening, and tailored interventions for working women. This study also could be use as discussion maternal for designing future health policies in maternal and ANC education program. Future efforts should expand the use of tools like the "TAMENG" flipchart, enhance access to affordable iron-rich supplements, and consider digital adaptations to broaden outreach. By addressing these critical factors and involving family members and community leaders,

sustainable improvements in maternal and fetal health outcomes can be achieved.

DISCLOSURES

Acknowledgment

This study was supported by the 2024 Universitas Airlangga Community Service grant funding. We thank the healthcare professionals and participants who participated.

Conflict of interest

All authors have no conflict of interest.

Funding

Funding sources of the research by the 2024 Universitas Airlangga Community Service.

Author contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting, and approval for publication of this manuscript.

REFERENCES

1. Wibowo N, Irwinda R, Hiksas R. Anemia defisiensi besi pada kehamilan [Iron deficiency anemia in pregnancy]. Jakarta: UI Publishing; 2021.
2. World Health Organization (WHO). The Global Prevalence of Anaemia in 2011 [Internet]. Geneva: WHO; 2015. Available from: https://www.who.int/publications/i/item/9789241564960
3. Breymann C. Iron deficiency anemia in pregnancy. Semin Hematol. 2015;52(4):339-47. doi: 10.1053/j.seminhematol.2015.07.003. Epub 2015 Jul 10. PMID: 26404445.
4. Ministry of Health, Republic of Indonesia. Riset Kesehatan Dasar (RISKESDAS) 2018 [Health Basic Resarch 2018]. 2018.
5. Putri SI, Sumarmi S. Perbandingan konsumsi zat gizi, status gizi, dan kadar hemoglobin pengantin wanita di wilayah pantai dan pertanian kabupaten Probolinggo [Comparison of nutrient, nutritional status, and hemoglobin level of female bride in coastal and agricutural area of Probolinggo]. Media Gizi Indonesia. 2013;9(1):72-7.
6. Azizah AN, Achyar K. Status gizi pada wanita pranikah di wilayah kerja Puskesmas Purwojati [Pre-marriage nutritional status in women at Community Health Center, Purwojati] 2022;12(2):55-8. doi: https://doi.org/10.61902/involusi. v12i2.429.
7. Puskesmas Sumber. Laporan Rencana Umum Kegiatan (RUK) Gizi Puskesmas Sumber Tahun 2023 [Report on Nutrition Activity General Plan of Sumber Health Center, 2023]. Probolinggo; 2023.
8. Mathias EG, Dhyani V, Krishnan JB, et al. Community based health literacy interventions in India: A scoping review. 2023;22. doi: 10.1016/j.cegh.2023.101310.
9. UN Women. Women and Sustainable Development Goals [Internet]. 2015 [cited 2024 Dec 1]. Available from: https://www.unwomen.org/en/news/in-focus/women-and-the-sdgs/sdg-3-good-health-well-being
10. Abdisa DK, Jaleta DD, Tsegaye D, et al. Effect of community based nutritional education on knowledge, attitude and compliance to IFA supplementation among pregnant women in rural areas of southwest Ethiopia: a quasi experimental study. BMC Public Health. 2023;23(1):1923. doi: 10.1186/s12889-023-16798-y. PMID: 37794346; PMCID: PMC10552188.
11. Munyogwa MJ, Gibore NS, Ngowi AF, et al. Effect of nutritional education intervention to reduce anaemia during pregnancy in Dodoma City, Tanzania: protocol for a cluster randomized controlled trial. Biol Methods Protoc. 2021;6(1):bpab012. doi: 10.1093/biomethods/bpab012. PMID: 34222670; PMCID: PMC8242494.
12. Alem AZ, Efendi F, McKenna L, et al. Prevalence and factors associated with anemia in women of reproductive age across low- and middle-income countries based on national data. Sci Rep. 2023;13(1):20335. doi: 10.1038/s41598-023-46739-z. PMID: 37990069; PMCID: PMC10663544.
13. Rahman WKSAE, Ahmed AA, Atwa AMES. Effect of Educational Instructions on Pregnant Women's Knowledge and Practice regarding Iron Deficiency Anemia. 2022;13(2):2007-20. doi: 10.21608/ejhc.2022.282806.
14. Hairiyah S, Toaha A, Abri N, et al. The Effect of SEKAR (Sumber Edukasi Anemia yang Relevan) Card-Based Nutrition Education on Knowledge and Iron Intake in Pregnant Women. 2023;2(3):146-57. doi: 10.56303/jhnresearch.v2i3.176.
15. Salam SS, Ramadurg U, Charantimath U, et al. Impact of a school-based nutrition educational intervention on knowledge related to iron deficiency anaemia in rural Karnataka, India: A mixed methods pre-post interventional study. BJOG. 2023;130 Suppl 3:113-123. doi: 10.1111/1471-0528.17619. Epub 2023 Aug 2. PMID: 37530624.

16. Abd Rahman R, Idris IB, Isa ZM, et al. The Prevalence and Risk Factors of Iron Deficiency Anemia Among Pregnant Women in Malaysia: A Systematic Review. Front Nutr. 2022;9:847693. doi: 10.3389/fnut.2022.847693. PMID: 35495961; PMCID: PMC9051477.
17. Amani Z, Sebayang SK. The Effect of Iron Supplementation and Other School-Based Support on Anemia Status in Adolescents: A Systematic Literature Review. 2024;8(3):312-25. doi: 10.20473/imhsj.v8i3.2024.312-325.
18. Kucukkaya B, Basgol S. The effect of perceived spousal support on childbirth self-efficacy on pregnant women in turkey. BMC Pregnancy Childbirth. 2023;23(1):173. doi: 10.1186/s12884-023-05508-6. PMID: 36915041; PMCID: PMC10012433.
19. Balcha WF, Eteffa T, Tesfu AA, et al. Factors associated with anemia among pregnant women attended antenatal care: a health facility-based cross-sectional study. Ann Med Surg (Lond). 2023;85(5):1712-1721. doi: 10.1097/MS9.0000000000000608. PMID: 37228917; PMCID: PMC10205215.
20. Ali AM, Salah H, Mataria A, et al. Enhancing nutrition specific interventions through public health policies and public-private partnerships in the Eastern Mediterranean Region: a desk review. 2021:1-10. doi: 10.12688/f1000research.27710.1.

SYSTEMATIC REVIEW

Cranberry extract for urinary tract infection treatment in pregnancy: A systematic review

Rahmawati Abdul Hakim*, Dhian Eka Putri, Rahajeng
Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Brawijaya,
Saiful Anwar General Hospital, Malang, Indonesia.

Article Info
Received Nov 24, 2024
Revised Feb 6, 2025
Accepted Feb 14, 2025
Published Aug 1, 2025

***Corresponding author:**
Rahmawati Abdul Hakim
rahma.hakimtya@gmail.com

Keywords:
Cranberry extract
Maternal health
Phenolic chemicals
Pregnancy
Proanthocyanidins
Urinary Tract Infection

ABSTRACT

Objective: Urinary tract infections (UTIs) represent the second most common infectious disease worldwide, affecting nearly 150 million people annually. Owing to anatomical and physiological alterations, UTIs are especially frequent during pregnancy, manifesting with symptoms including dysuria, cloudy urine, increased urinary frequency, and occasionally hematuria. Recurrent UTIs are defined as two or more episodes within six months or three episodes within a year. Cranberries are widely recognized for their potential in preventing UTIs during pregnancy. Their protective action involves blocking the adhesion of uropathogenic bacteria to the urinary tract epithelium, a process mediated by phenolic compounds and A-type proanthocyanidins (PACs).

Materials and Methods: In this systematic review, the authors searched PubMed, ScienceDirect, ResearchGate, and Google Scholar for eligible articles published from 2013 to 2024. The search strategy employed Medical Subject Headings (MeSH) and keywords pertaining to Cranberry Extract/Juice and UTI Assessment Methods in Pregnancy. Search expressions were adapted to the specific requirements of each database to optimize retrieval precision. All identified studies were assessed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results: Of the 30 studies included, a daily administration of 500 mg cranberry extract over six months exhibited notable effectiveness as an alternative therapeutic approach for UTIs in pregnancy.

Conclusion: Cranberry (*Vaccinium macrocarpon*) extract prevents UTIs by impeding bacterial adherence and exerting antibacterial properties. This review supports cranberry as a promising and safe alternative for UTI prevention and management in pregnancy, appropriate for routine daily use.

How to cite: Hakim RA, Putri DE, Rahajeng. Cranberry extract for urinary tract infection treatment in pregnancy: A systematic review. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):121-131. doi: 10.20473/mog.V33I22025.121-131.

Highlights:

1. Cranberry represents a promising and effective alternative for both the treatment and prevention of urinary tract infections during pregnancy.
2. Cranberry acts by inhibiting bacterial adhesion to the urinary tract epithelium and exerting direct antibacterial activity.

INTRODUCTION

Due to their pelvic anatomy, women are more susceptible to urinary tract infections (UTIs) than men, as bacteria readily ascend from the urethra into the bladder and may extend to the kidneys. The warm, moist vulvar environment near the rectum further increases contamination risk.[1] UTIs are the second most common infection worldwide, often presenting as a significant complication in pregnancy, frequently progressing to recurrent urinary tract infections (RUTIs).[2-4] Their increased incidence in pregnancy results from anatomical and physiological changes, including ureteral dilation and reduced bladder tone.[5] Symptoms include dysuria, cloudy urine, urinary frequency, and occasionally hematuria. Recurrent UTI is defined as two or more episodes within six months or three episodes in one year.[6] Uncomplicated UTIs, especially prevalent in women, have a 20–30% recurrence rate, creating a persistent health burden.[7]

Uncomplicated UTI symptoms, typically managed in primary care, are usually treated with antibiotics. Their high occurrence during pregnancy has increased antibiotic use, raising concerns about antimicrobial resistance (AMR).[8] AMR is a major global health threat, responsible for 2.8 million infections and more than 35,000 deaths annually in the United States in 2019.[9] Consequently, alternative approaches, including herbal therapies, are being explored for UTI prevention and as novel treatments for RUTIs to reduce antibiotic reliance.

Cranberry (Vaccinium macrocarpon) is a widely applied medicinal plant, recognized for its role in preventing UTIs during pregnancy.[10,11] The mechanism underlying cranberry's preventive action has not been fully defined. Evidence shows that phenolic compounds and A-type proanthocyanidins (PACs) inhibit adhesion of uropathogenic bacteria to the urinary tract epithelium.[10,12,13] These agents limit bacterial binding to bladder cells but do not dislodge attached bacteria.[14] Cranberry also exhibits antibiofilm, antiproliferative, immunomodulatory, and anti-inflammatory effects, strengthening its principal antiadhesive action.[15-17] By lowering antibiotic exposure, cranberry extract reduces the risk of resistant pathogens, offering important clinical benefits.[18]

Recent metabolomics analyses reveal that cranberry juice alters the urinary metabolome, increasing excretion of exogenous and endogenous metabolites. As cranberries are not metabolized, they are eliminated in urine, likely contributing to their antiadhesive effect.[18] This study investigated cranberry extract's efficacy in preventing and treating UTIs in pregnancy, determines its optimal dosage, and examines its potential to mitigate AMR-related complications in practice.

MATERIALS AND METHODS

Literature searching

This review involved a comprehensive and systematic search of the literature performed in PubMed, ScienceDirect, ResearchGate, and Google Scholar to identify publications directly relevant to the research question. The search strategy integrated both MeSH terms and carefully selected keywords, focusing on Cranberry Extract/Juice and Methods of Measurement and Analysis for UTIs during pregnancy. Search expressions were specifically customized to the requirements of each database to optimize precision and completeness of retrieval. Articles published between 2013 and 2024 were collected, screened, and assessed in detail. This systematic review was conducted in full compliance with PRISMA guidelines and prospectively registered in PROSPERO (CRD42024620931).

Eligibility criteria

The data used in this review were classified according to explicit inclusion and exclusion criteria. Eligible studies encompassed experimental research, cohort investigations, longitudinal studies, case reports, social or pilot studies, and observational designs that were published within the last decade and written in English. The study population consisted of healthy pregnant women, irrespective of race, with or without Urinary Tract Infections (UTIs), with particular emphasis on those presenting recurrent UTI symptoms. These groups were selected as the central focus of this review. Inclusion further required that studies employ uniform measurement units, or where variations occurred, that they were appropriately standardized through validated calculations to ensure accuracy and comparability. Exclusion criteria incorporated all review articles, editorials, letters to editors, and conference abstracts. Studies were also excluded if titles or abstracts were judged irrelevant, if complete full texts could not be accessed, if reporting of measurement units was insufficient, or if datasets were incomplete.

Study selection and screening

Screening was carried out independently by a team of reviewers. Titles, abstracts, and keywords were systematically evaluated in several steps. PRISMA guidelines and the Mixed Methods Appraisal Tool (MMAT) were utilized to assess both methodological quality and reporting clarity of studies included in this systematic review. The MMAT applies five criteria to each methodological category, with responses rated as Y (YES = 1), N (NO = 0), or C (Cannot tell = 0). Final

quality scores were derived from the total number of affirmative responses obtained (see Table 1).

Data extraction

Urinary Tract Infections (UTIs) are identified based on characteristic clinical manifestations of genitourinary tract infection and microbiological confirmation by the presence of one or more microorganisms in urine exceeding a recognized diagnostic threshold (102 to 103 colony-forming units/mL).19,20 Recurrent Urinary Tract Infections (RUTIs) are defined as three positive urine cultures in a 12-month interval or two infections within a six-month period.21 Cranberry Extract, derived from the fruits and leaves of Vaccinium macrocarpon, is a traditional herbal preparation widely used in UTI prophylaxis. Numerous clinical and preclinical studies, including those supported by the National Center for Complementary and Alternative Medicine, have examined its potential protective role in urinary tract health.22 Eligible studies comprised experimental, cohort, review, and observational designs directly addressing this systematic review. The target population included women of reproductive age (20–50 years) and older. In addition to the six domains outlined, detailed information was extracted regarding study duration, geographic setting, characteristics of intervention and control groups, outcome measurement tools (e.g., standardized questionnaires), and principal findings—such as the effectiveness of interventions on clinical and psychological outcomes, adherence to therapy, and any reported adverse events.

RESULTS AND DISCUSSION

Overview of literature searching

The PRISMA flow diagram illustrating the study selection process is presented in Figure 1. A total of 743 studies were initially retrieved from PubMed, ResearchGate, ScienceDirect, and Google Scholar. After removal of 805 duplicate entries, 358 records remained for title and abstract screening. In accordance with the predefined eligibility criteria, 253 articles were excluded. Subsequently, 105 full-text articles were reviewed, of which 59 were excluded due to irrelevant outcomes, the use of active control groups, or publication in languages other than English or Indonesian. Ultimately, 30 studies fulfilled all inclusion criteria and were incorporated into the qualitative synthesis.

Table 1. RCT (Randomized Controlled Trial; Y=YES, N=NO, C=Cannot Tell)

Design	Methodological quality criteria / study ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Quantitative RCT	Is randomization appropriately performed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are the group comparable at baseline?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are there complete outcome data?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are outcome assessors blinded to the intervention provided?	C	C	C	C	Y	Y	C	C	C	C	C	Y	Y	Y	Y
	Did the participants adhere to the assigned intervention?	C	Y	C	C	C	C	C	Y	Y	Y	Y	Y	Y	Y	Y
	Is randomization appropriately performed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are the group comparable at baseline?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are there complete outcome data?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are outcome assessors blinded to the intervention provided?	C	C	C	C	Y	C	C	C	Y	C	C	Y	Y	Y	Y
	Did the participants adhere to the assigned intervention?	C	Y	Y	Y	C	C	Y	Y	Y	Y	Y	Y	Y	Y	Y

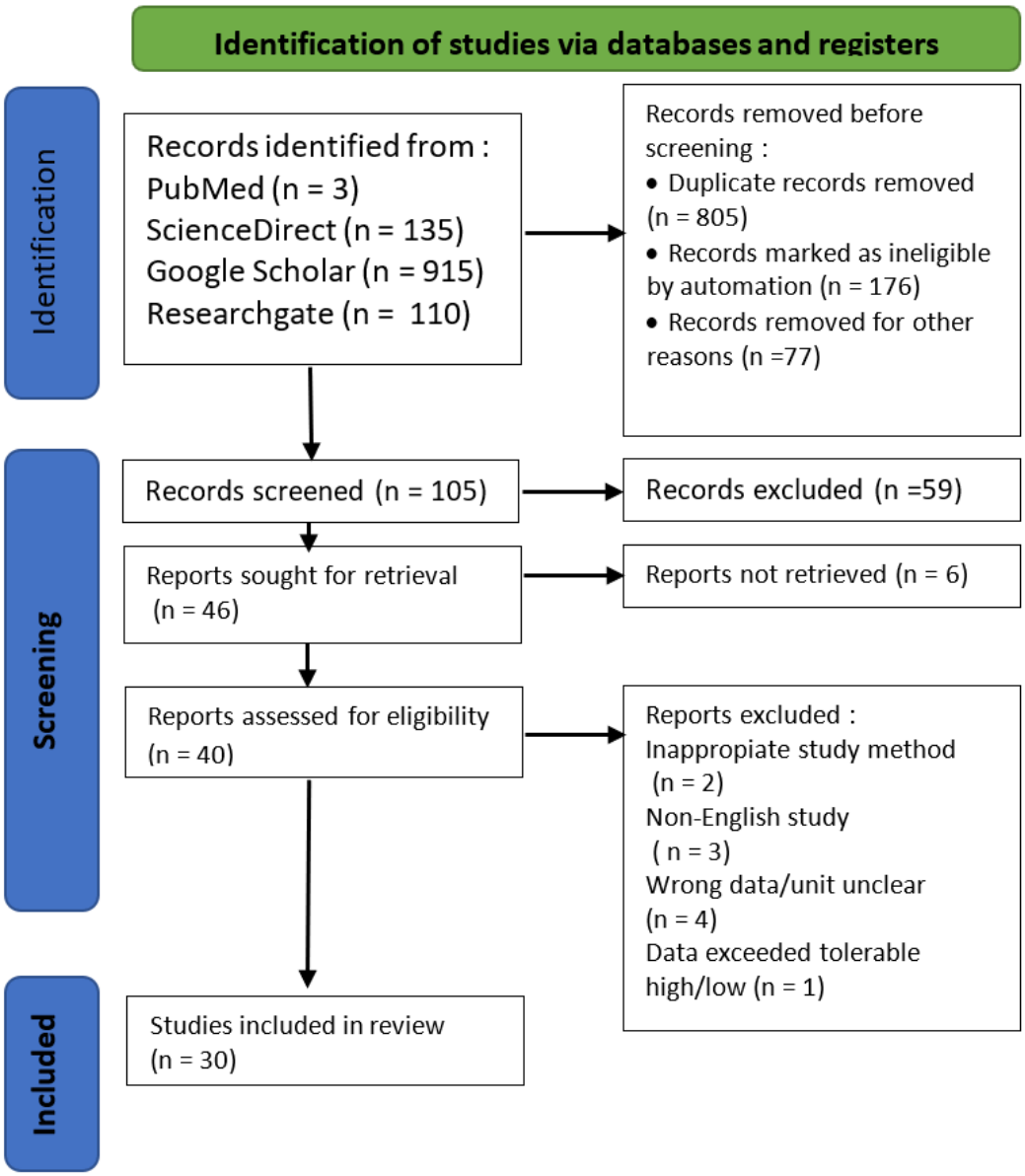


Figure 1. PRISMA Flowchart of The Literature Selection

Study characteristics

The characteristics of the 30 studies included in this qualitative analysis are summarized in Table 2. Altogether, 30 studies involving participants assessed for the use of Cranberry Extract in the treatment of Urinary Tract Infections (UTIs) during pregnancy were reviewed. The majority of investigations were conducted in the United States (10), followed by the United Kingdom (3), Spain (2), China (2), the Netherlands (2), Germany (2), and one study each from Canada, Switzerland, Norway, Italy, Mexico, Australia, Iraq, Poland, and Finland. Collectively, these 30 studies provided analytical evaluation of the preventive application of Cranberry (*Vaccinium macrocarpon*) extract in the management of UTIs during pregnancy.

Table 2. Characteristics of included study

Countries	Authors	Years	Study designs
Spain	Llano, Dolores Gonzales et al	2020	Observational Study
Canada	Babar, Asma et al	2018	Double Blind Randomized Controlled Study
USA	Zhuxuan, Fu et al	2017	Cohort Study
UK	Gbinigie, Oghenekome et al	2019	Randomized Clinical Study
USA	Hudson, Rachel E et al	2021	Cohort Study
USA	Bolgarina, Zoryana et al	2023	Clinical Trial and Observational Study
Switzerland	Gbinigie, Oghenekome et al	2020	Cohort Study
USA	Wing, Deborah A et al	2014	Clinical Trial and Observational Study
China	Wang, Chih-Hung et al	2013	Randomized Control Study
Norway	Heitmann, Kristine et al	2013	Cohort Study
Germany	Jeitler, Michael et al	2022	Prospective, Uncontrolled Exploratory Study
Italy	Ledda, A et al	2017	Clinical Study
Germany	Vostalova, Jitka et al	2015	Randomized Double Blind and Placebo Controlled Study
USA	Wing, Deborah A et al	2013	Pilot Study
USA	Stapleton, Ann E. et al	2013	Randomized Controlled Study
Netherland	Beerepoot, Marielle A.J et al	2013	Randomized Double-Blind Non-Inferiority Study
Spain	Perez-Lopez, Faustino R et al	2013	Observational Study
USA	Koradia, Parshottam et al	2019	Controlled Pilot Study
Mexico	Monroy-Torres, Rebeca et al	2018	Observational Actual Evidence Study
Australia	Konesan, Jenane et al	2022	Cohort Study
UK	Maki, Kevin C et al	2016	Double-blind Randomized Placebo-controlled Study
USA	Liska, DeAnn J et al	2016	Cohort Study
Iraq	Al Gaoale, Zubaidah Ibrahim Younus et al	2022	Observational Study
Poland	Wawrysiuk, Sara et al	2019	Cohort Study
UK	Griffiths, Peter	2013	Observational Social Study
USA	Efros, Mitchell et al	2013	Clinical Study
Netherland	van Wietmarschen, Herman et al	2022	Observational Study
USA	Gupta, K et al	2013	Clinical Study
Finland	Kontiokari, Tero et al	2013	Randomized Study
China	Xia, Jia-yue et al	2021	Sequential Analysis Study

Table 3 contains detailed descriptions of the 30 primary articles selected for the systematic review on Cranberry Extract in Urinary Tract Infections (UTIs) during pregnancy, comprising a total sample size of 3,657 women in healthy reproductive age, pregnant, or breastfeeding.

UTIs represent the second most common infectious condition globally, affecting approximately 150 million individuals. This infection is highly prevalent during pregnancy, with frequent recurrence attributed to anatomical and physiological changes associated with gestation.[2,23] The prevalence of UTIs is higher in women due to shorter urethral anatomy, which facilitates bacterial colonization and ascending infection to the bladder and kidneys.[1] During pregnancy, UTIs are often associated with complications affecting both the mother and fetus. Studies have reported a higher incidence of preterm birth among women experiencing recurrent UTIs.[3] Recurrent UTIs (r-UTIs) are defined as two episodes within six months or three within twelve months.[24] This condition often necessitates extended or higher-dose antibiotic therapy. Some women may present with asymptomatic UTIs, posing challenges for timely diagnosis and effective treatment. Standard treatment for UTIs primarily involves antimicrobial or antibiotic therapy. However, growing concerns have emerged due to increasing antibiotic resistance associated with recurrent infections.[8,9] This situation has led to a growing interest in alternative therapies, such as herbal medicine, for their protective effects. Beyond resistance, additional concerns regarding antibiotic use in pregnancy include risks of miscarriage and increased incidence of sick leave, as also reported in the literature.[13]

Table 3. PICO table summary of primary articles sources with sample size (n = 3657 women)

Author (Year)	Country	Sample	P	I	C	O
Llano, Dolores Gonzales et al (2020)	Spain	170 women	100 pregnancy women (50 primiparous and 50 nulliparous) and 70 healthy women in reproductive ages with or without recurrent or uncomplicated UTIs for 3 – 6 months	Cranberry extract from small dosage to high dosage	Placebo	Protective effect of cranberry extract for UTIs
Babar, Asma et al (2018)	Canada	148 women; ages ≥ 18 years old, with ≥ 2 symptoms of UTIs in 6 months or ≥ 3 symptoms of UTIs in 12 months	Divided into 2 groups (74 women for each group)	2x18,5 mg PACs per day for 6 months	2x1 mg PACs per day for 6 months	New standardized of High Doses of cranberry extract for Prevention of r-UTI
Zhuxuan, Fu et al (2017)	USA	154 women; ages ≥ 18 years old with history of UTI in pregnancy	Divided into 2 groups (77 women for each group)	Cranberry juice and extract	Placebo	Effect of cranberry for UTIs in women
Gbinigie, Oghenekome et al (2019)	UK	45 women; ages ≥ 18 years old consulting in primary care for pregnancy and problems of acute UTIs; get antibiotic for prescription	20 women with problem of UTIs who got the early prescription of first line antibiotics; 25 women with UTIs who got delayed or never get antibiotics	Cranberry extract combines with primary line antibiotics	Antibiotics	Effect of cranberry for acute UTIs and how much it can reduce antibiotics use for treatment of UTIs
Hudson, Rachel E et al (2021)	USA	100 women with symptoms of UTIs in pregnancy	25 women as control group get conventional treatment for UTIs; 75 women in intervention group divided into 2 groups; 35 women with standard dosage of cranberry and 40 women with high dosage of cranberry extract	Standard dosage of cranberry extract and high dosage of cranberry extract	Conventional Treatment for UTIs	Examine the complementary and dosage of cranberry for better treatment
Bolgarina, Zoryana et al (2023)	USA	200 women; with symptoms of UTIs or RUTIs in pregnancy	Divided into 2 groups	Cranberry supplement	Placebo	Evaluate the effectiveness of cranberry supplement for UTIs in pregnancy women
Gbinigie, Oghenekome et al (2020)	Switzerland	140 women; ages ≥18 years old, outpatient in primary care with symptoms of UTIs	Divided into 2 groups	Cranberry extracts	Placebo	Efficacy of cranberry extract for acute UTIs in pregnancy
Wing, Deborah A et al (2014)	USA	49 pregnant women with gestational ages between 12 to16 weeks	Divided into 2 groups	Cranberry capsules	Placebo	Preventive effect of cranberry for UTIs in pregnancy
Wang, Chih-Hung et al (2013)	China	414 women; ages ≥18 years old with UTIs symptoms in pregnancy	Divided into 2 groups (consist of 207 each group), then divided into 2 smaller groups each; 1 group for r-UTIs during pregnancy and 1 group without r-UTIs symptoms	Cranberry juice and extract for 3 until 6 months prior to the symptoms	Placebo	Analyze the effect of cranberry extract for treatment in UTIs of pregnant women
Heitmann, Kristine et al (2013)	Norway	300 women; gestational age between 12 to 16 weeks	Divided into 2 groups base on primiparous and nulliparous	Cranberry extract	Placebo	Pregnancy UTIs symptoms and condition after consume cranberry extract
Jeitler, Michael et al (2022)	Germany	23 women; ages ≥18 years old reported with chronic recurrent UTIs problem in pregnancy	Divided into 2 groups	Cranberry supplement within 6 months consumption	Cranberry supplement for 1 – 3 months consumption	UTIs outcome with different duration of cranberry supplement consumption
Ledda, A et al (2017)	Italy	36 women; ages ≥18 years old suffering with r-UTI in pregnancy	Divided into 2 groups consisting of 17 women as control (get the standard management for UTIs) and 19 women as intervention who obtained oral cranberry supplementation	Oral cranberry supplementation contain of 120 mg cranberry extract, standardized to 36 mg proanthocyanidins for 60 days	Standard management and medication	Effectiveness of prevention of UTIs in pregnancy

Vostalova, Jitka et al (2015)	Germany	182 women; history of pregnancywith 2 or more UTIs episodes in the last year	Divided into 2 groups; 89 received the cranberry extract and 93 as control received the placebo	Daily 500 mg cranberry extract for 6 months	Placebo	Efficacy of high dosage of proanthocyanidins as the key of successful treatment and prevention of UTIs in pregnancy
Wing, Deborah A et al (2013)	USA	28 pregnant women and 15 non-pregnant women in reproductive age	Both category divided into 2 and randomly made into 2 large groups, consisted of 24 intervention groups (14 pregnant women and 10 non-pregnant) and the rest as the control group	Low calorie cranberry juice (consist of 100% cranberry) 240 ml two times daily	Placebo	Antimicrobial effect of cranberry juice cocktail daily
Stapleton, Ann E. et al (2013)	USA	176 women; ages between 18 to 45 years old which history of clinical diagnosed UTIs in pregnancy	Divided into 2 groups of 120 women in intervention group and 56 women in control group. The intervention group divided into 2 groups obtaining different intervention	Group 1A : received 4 oz of cranberry juice Group 2A : received 8 oz of cranberry juice	Placebo	The preventive effect of cranberry juice for recurrent UTIs and Urinary *Eschericia colli* Infection in women
Beerepoot, Marielle A.J et al (2013)	Netherland	221 women; ages between 18 to 45 with history of UTIs symptoms in pregnancy or breastfeeding (at least 3 symptomatic UTIs) that have been receiving antibiotics treatment	Divided into 3 groups; consisted of 2 intervention groups and 1 placebo	Group (1) : obtained *Trimetrophim-sulfamethoxazole* (TMP) with placebo Group (2) : TMP and 500 mg capsule of cranberry, 1 capsule, twice, daily	Placebo	Analyze the preventive effect between antibiotics and cranberry for UTIs problem in women
Perez-Lopez, Faustino R et al (2013)	Spain	20 women; ages ≥18 years old with history of UTIs in pregnancy	Divided into 2 groups	Cranberry extract	Placebo	The effect of cranberry for prevent the case of recurrent UTIs
Koradia, Parshottam et al (2019)	USA	115 women; which 90 enrolled and 81 subjects completed the study; ages 18 to 55 years old which have history of UTIs in pregnancy	Divided into 2 groups for 26 weeks treatment	180 days (full treatment) of cranberry capsule	90 days cranberry capsule	Evaluate the duration of probiotic and cranberry capsule for recurrent UTIs in women
Monroy-Torres, Rebeca et al (2018)	Mexico	150 pregnant women (early pregnancy or first semester) with the history of UTIs, but not in active UTIs problem	Divided into 2 groups, each consisted of 75 women	Cranberry juice daily for 6 months	Placebo	The efficacy of cranberry juice for prevention of r-UTIs in pregnant women
Konesan, Jenane et al (2022)	Australia	172 women; ages between middle 20 to 50s years old with history of UTIs in pregnancy	Divided into 2 groupss	Cranberry extract	Placebo	The effect of cranberry for UTIs in women
Maki, Kevin C et al (2016)	UK	373 women; ages 20 – 70 years old with history of UTIs in pregnancy and BMI < 40, that have been treated in health care professional	Divided into 2 groups; 185 women in intervention group and 188 women in control group	240 mL of cranberry beverages/day	240 ml placebo beverages/day	Evaluate the effect of cranberry beverages for UTIs problem
Liska, DeAnn J et al (2016)	USA	90 women; ages 18 – 45 years old with history of recurrent UTIs in pregnancy and breastfeeding	Divided into 2 groups; 50 women in intervention group and 40 women in control group	Cranberry extract	Placebo	The effect in cranberry extract consumption for UTIs problem
Al Gaoale, Zubaidah Ibrahim Younus et al (2022)	Iraq	24 pregnant women with uncomplicated UTIs problem	Divided into 2 groups	Cranberry (combination) supplement	Placebo	Therapeutic effect of cranberry for anti-relapse uncomplicated UTIs in women
Wawrysiuk, Sara et al (2019)	Poland	30 women; ages ≥18 years old with history of UTIs in pregnancy or r-UTI	Divided into 2 groups	Cranberry extract	Placebo	Evaluate the preventive and treatment effect of cranberry in UTIs

Griffiths, Peter (2013)	UK	20 women; ages ≥18 years old outpatient in primary health care with history of UTIs in pregnancy	Divided into 2 groups	Cranberry juice for 7 days	Cranberry juice for ≥14 days (standardized)	Role of cranberry for treatment and prevention of UTIs
Efros, Mitchell et al (2013)	USA	28 women; ages ≥18 years old with history of UTIs in pregnancy and breastfeeding in minimum 6 months	Divided into 5 groups	Oral cranberry extract at : Group (1) 15 mL, (2) 30 mL, (3) 45 mL, (4) 60 mL and (5) 75 mL for 12 weeks	-	The recommend dose of cranberry extract to get the preventive effect of recurrent UTIs problem
van Wietmarschen, Herman et al (2022)	Netherland	40 women; ages ≥18 years old with history of UTIs in pregnancy	Divided into 2 groups	Cranberry extract	Placebo	The preventive effect of cranberry extract for recurrent UTIs
Gupta, K et al (2013)	USA	20 women; ages ≥18 years old with history of specific UTIs in pregnancy (*E. coli)* infection	Divided into 2 groups	Cranberry supplement (consist of 9 mg proanthocyanidin per gm)	Placebo	The effect of cranberry extract in inhibit adherence of P-Fimbriated *Eschericia coli* in UTIs problem
Kontiokari, Tero et al (2013)	Finland	150 women; have the history of pregnancy UTIs caused by *Eschericia coli* bacteria in Oulu University Hospital	Divided into 3 groups, consisted 2 intervention groups and 1 control group	Group 1A : 50 women received 50 mL of cranberry juice concentrate a day for 6 months Group 2A : 50 women received 100 mL *Lactobacillus* GG drink 5 days a week for one year	Placebo	Evaluate better option for prevention of recurrent UTIs caused by *E.coli*
Xia, Jia-yue et al (2021)	China	24 women; reproductive age, with history of UTIs in pregnancy that have been treated by antibiotics	Divided into 2 groups	Cranberry extract	Primary Line of Antibiotics	Evaluate the effect of cranberry as the adjuvant therapy of UTIs problem in women

Herbal therapies for UTI prevention include cranberry (*Vaccinium macrocarpon*). Cranberry contains polyphenols, flavonoids, and phenolic acids, which have been demonstrated to contribute to UTI prevention.[5,6] Early investigations proposed that cranberry acted by increasing urinary acidity, whereas more recent studies suggest its mechanism primarily involves inhibiting bacterial adhesion to the urinary tract epithelium.[25,26] Consumption of cranberry has been associated with a reduced incidence of UTIs among women.[5] While multiple studies support its efficacy in both symptom alleviation and UTI prevention, some have produced inconsistent findings. Results from in vivo and in vitro experiments strongly endorse cranberry as a preventive intervention for UTIs.[5] In this review, such claims are corroborated by more than 20 included studies. Evidence indicates that cranberry extract, administered either as juice or in capsule formulation, may be utilized as an adjunct to antibiotic therapy or as a standalone treatment.[27-29] Both approaches demonstrate beneficial outcomes in reducing recurrent UTIs.[9] Nevertheless, challenges persist, including insufficient knowledge regarding product formulation, lack of standardization, uncertainty about optimal dosing regimens, and ongoing concerns about toxicity and adverse effects.[6,10]

One study evaluated in this review demonstrated that daily supplementation of 500 mg cranberry containing 2.8 mg of proanthocyanidins (PACs) over six months reduced UTI recurrence.[18] Another investigation revealed that cranberry exhibited antibacterial activity against Escherichia coli, with decreased colony counts observed following single or double doses of cranberry intake.[19] Although issues of tolerability remain, several trials have reported statistically significant reductions in recurrent UTIs in women consuming cranberry.[30-32] Furthermore, evidence suggests that daily cranberry use for 6 to 12 months is safe in pregnant women and children.[33,34] Additional investigations confirm the high efficacy of cranberry for UTI prevention during pregnancy, particularly given its practicality for daily consumption.[35,36]

Despite these positive findings, two studies included in the review reported no significant differences in the protective effects of cranberry. Additionally, extended study durations led to high rates of loss to follow-up, thereby limiting the robustness of available evidence.[4-7] The incidence of symptomatic UTIs across cranberry, antibiotic, and placebo groups demonstrated minimal variation.[7,8] The limitations of this review include the lack of well-designed trials published beyond 2018, insufficient data to establish definitive clinical guidelines, and continued absence of standardized formulations as of 2022. Nonetheless, the evidence presented highlights the potential of cranberry as a viable alternative treatment and preventive approach for UTIs in pregnancy, thereby underscoring the therapeutic role of herbal medicine in infectious disease management.

Strength and limitation

An important strength of this review is the consistent finding that cranberry represents a promising and effective alternative for both the prevention and treatment of UTIs during pregnancy. The primary limitation, however, is the restricted number of high-quality trials and the limited availability of comprehensive sources suitable for inclusion.

CONCLUSION

This systematic review highlights that UTIs remain a common and clinically significant health concern among women, particularly in pregnancy. At present, this infection may be managed and prevented using alternative interventions in addition to conventional approaches. Cranberry (*Vaccinium macrocarpon*) extract has been frequently employed for its prophylactic potential against UTIs. Based on the studies included in this review, daily intake of 500 mg cranberry extract for six months provides an effective option for UTI prevention in pregnancy, with no adverse effects reported. The mechanism of action is thought to involve inhibition of bacterial adherence to the uroepithelial surface, in addition to demonstrating antibacterial properties. Collectively, these findings reinforce the conclusion that cranberry is a promising and effective alternative therapeutic strategy for both treatment and prevention of UTIs in pregnancy, appropriate for routine use.

DISCLOSURES

Acknowledgment

None

Conflict of interest

None

Funding

None

Author contribution

All of the authors prepared, collected, analyzed, wrote, and approved this work.

REFERENCES

1. Hoffman BL, Schorge JO, Bradshaw KD, et al. William Gynecology. 3rd Edition. McGraw Hill Education, 2016.

2. Getaneh T, Negesse A, Dessie G, et al. Prevalence of urinary tract infection and its associated factors among pregnant women in Ethiopia: A systematic review and meta-analysis. Biomed Res Int. 2021 ;2021:6551526. doi: 10.1155/2021/6551526. PMID: 34901276; PMCID: PMC8654570.
3. Balachandran L, Jacob L, Al Awadhi R, et al. Urinary tract infection in pregnancy and its effects on maternal and perinatal outcome: A retrospective study. Cureus. 2022;14(1):e21500. doi: 10.7759/cureus.21500. PMID: 35223276; PMCID: PMC8860729.
4. Schneeberger C, Geerlings SE, Middleton P, et al. Interventions for preventing recurrent urinary tract infection during pregnancy. Cochrane Database Syst Rev. 2012;11:CD009279. doi: 10.1002/14651858.CD009279.pub2. Update in: Cochrane Database Syst Rev. 2015;(7):CD009279. doi: 10.1002/14651858.CD009279.pub3. PMID: 23152271.
5. González de Llano D, Moreno-Arribas MV, Bartolomé B. Cranberry polyphenols and prevention against urinary tract infections: Relevant considerations. Molecules. 2020;25(15):3523. doi: 10.3390/molecules25153523. PMID: 32752183; PMCID: PMC7436188.
6. Babar A, Moore L, Leblanc V, et al. High dose versus low dose standardized cranberry proanthocyanidin extract for the prevention of recurrent urinary tract infection in healthy women: a double-blind randomized controlled trial. BMC Urol. 2021;21(1):44. doi: 10.1186/s12894-021-00811-w. PMID: 33757474; PMCID: PMC7986024.
7. Fu Z, Liska D, Talan D, et al. Cranberry reduces the risk of urinary tract infection recurrence in otherwise healthy women: A systematic review and meta-analysis. J Nutr. 2017;147(12):2282-88. doi: 10.3945/jn.117.254961. Epub 2017 Oct 18. PMID: 29046404.
8. Gbinigie O, Allen J, Boylan et al. Does cranberry extract reduce antibiotic use for symptoms of acute uncomplicated urinary tract infections (CUTI)? Protocol for a feasibility study. Trials. 2019;20(1): 767. doi: 10.1186/s13063-019-3860-z. PMID: 31870413; PMCID: PMC6929469.
9. Hudson RE, Job KM, Sayre CL, et al. Examination of complementary medicine for treating urinary tract infections among pregnant women and children. Front Pharmacol. 2022;13:883216. doi: 10.3389/fphar.2022.883216. PMID: 35571128; PMCID: PMC9094615.
10. Bolgarina Z, Gonzalez-Gonzalez LF, Rodroiguez GV, et al. Cranberry supplements for urinary tract infection prophylaxis in pregnant women: A systematic review of clinical trials and observational studies on efficacy, acceptability, outcomes measurement methods, and studies' feasibility. Cureus. 2023;15(10):e46738. doi: 10.7759/cureus.46738. Erratum in: Cureus. 2023;15(10):c140. doi: 10.7759/cureus.c140. PMID: 38022216; PMCID: PMC10631496.
11. Gbinigie OA, Spencer EA, Heneghan CJ, et al. Cranberry extract for symptoms of acute, uncomplicated urinary tract infection: a systematic review. Antibiotics (Basel). 2020;10(1):12. doi: 10.3390/antibiotics10010012. PMID: 33375566; PMCID: PMC7824375.
12. Wing DA, Rumney PJ, Hindra S, et al. Pilot study to evaluate compliance and tolerability of cranberry capsules in pregnancy for the prevention of asymptomatic bacteriuria. J Altern Complement Med. 2015;21(11):700-6. doi: 10.1089/acm.2014.0272. Epub 2015 Aug 21. PMID: 26535612; PMCID: PMC4642828.
13. Wang CH, Fang CC, Chen NC, et al. Cranberry-containing products for prevention of urinary tract infections in susceptible populations: a systematic review and meta-analysis of randomized controlled trials. Arch Intern Med. 2012;172(13):988-96. doi: 10.1001/archinternmed.2012.3004. PMID: 22777630.
14. Heitmann K, Nordeng H, Holst L. Pregnancy outcome after use of cranberry in pregnancy - the Norwegian Mother and Child Cohort Study. BMC Complement Altern Med. 2013;13:345. doi: 10.1186/1472-6882-13-345. PMID: 24314317; PMCID: PMC3924191.
15. Stapleton AE, Dziura J, Hooton TM, et al. Recurrent urinary tract infection and urinary *Escherichia coli* in women ingesting cranberry juice daily: A randomized controlled trial. Mayo Clin Proc. 2012;87(2):143-50. doi: 10.1016/j.mayocp.2011.10.006. PMID: 22305026; PMCID: PMC3497550.
16. Liska DJ, Kern HJ, Maki KC. Cranberries and urinary tract infections: How can the same evidence lead to conflicting advice? Adv Nutr. 2016;7(3): 498-506. doi: 10.3945/an.115.011197. PMID: 27184277; PMCID: PMC4863270.
17. Konesan J, Liu L, Mansfield KJ. The clinical trial outcomes of cranberry, D-mannose and NSAIDs in the prevention or management of uncomplicated urinary tract infections in women: A systematic review. Pathogens. 2022;11(12):1471. doi: 10.3390/pathogens11121471. PMID: 36558804; PMCID: PMC9788503.
18. Jeitler M, Michalsen A, Schwiertz A, et al. Effects of a supplement containing a cranberry extract on recurrent urinary tract infections and intestinal microbiota: A prospective, uncontrolled exploratory study. J Integr Complement Med. 2022;28(5):399-406. doi: 10.1089/jicm.2021.0300. Epub 2022 Mar 14. PMID: 35285701; PMCID: PMC9127832.

19. Guay DR. Cranberry and urinary tract infections. Drugs. 2009;69(7):775-807. doi: 10.2165/00003495-200969070-00002. PMID: 19441868.
20. Ledda A, Belcaro G, Dugall M, et al. Highly standardized cranberry extract supplementation (Anthocran®) as prophylaxis in young healthy subjects with recurrent urinary tract infections. Eur Rev Med Pharmacol Sci. 2017;21(2):389-93. PMID: 28165546.
21. Vostalova J, Vidlar A, Simanek V, et al. Are high proanthocyanidins key to cranberry efficacy in the prevention of recurrent urinary tract infection? Phytother Res. 2015;29(10):1559-67. doi: 10.1002/ptr.5427. Epub 2015 Aug 13. PMID: 26268913.
22. Wing DA, Shell A, Lee YL, et al. Antimicrobial activity of urine after ingestion of differing daily doses of cranberry juice cocktail in pregnancy: A pilot study. Open Complement. Med. J. 2001;2: 15–9. doi: 10.2174/1876391X01002010015.
23. Salari N, Khoshbakht Y, Hemmati M, et al. Global prevalence of urinary tract infection in pregnant mothers: a systematic review and meta-analysis. Public Health. 2023;224:58-65. doi: 10.1016/j.puhe.2023.08.016. Epub 2023 Sep 19. PMID: 37734277.
24. Koradia P, Kapadia S, Trivedi Y, et al. Probiotic and cranberry supplementation for preventing recurrent uncomplicated urinary tract infections in premenopausal women: a controlled pilot study. Expert Rev Anti Infect Ther. 2019;17(9):733-40. doi: 10.1080/14787210.2019.1664287. Epub 2019 Sep 13. Erratum in: Expert Rev Anti Infect Ther. 2019;17(11):939. doi: 10.1080/14787210.2019.1673041. PMID: 31516055.
25. van Wietmarschen H, van Steenbergen N, van der Werf E, et al. Effectiveness of herbal medicines to prevent and control symptoms of urinary tract infections and to reduce antibiotic use: A literature review. Integr Med Res. 2022;11(4):100892. doi: 10.1016/j.imr.2022.100892. Epub 2022 Oct 9. PMID: 36345487; PMCID: PMC9636546.
26. Gupta K, Chou MY, Howell A, et al. Cranberry products inhibit adherence of p-fimbriated *Escherichia coli* to primary cultured bladder and vaginal epithelial cells. J Urol. 2007;177(6):2357-60. doi: 10.1016/j.juro.2007.01.114. PMID: 17509358; PMCID: PMC3684265.
27. Xia JY, Yang C, Xu DF, et al. Consumption of cranberry as adjuvant therapy for urinary tract infections in susceptible populations: A systematic review and meta-analysis with trial sequential analysis. PLoS One. 2021;16(9):e0256992. doi: 10.1371/journal.pone.0256992. PMID: 34473789; PMCID: PMC8412316.
28. Kontiokari T, Sundqvist K, Nuutinen M, et al. Randomised trial of cranberry-lingonberry juice and *Lactobacillus GG* drink for the prevention of urinary tract infections in women. BMJ. 2001;322(7302):1571. doi: 10.1136/bmj.322.7302.1571. PMID: 11431298; PMCID: PMC33514.
29. Maki KC, Kaspar KL, Khoo C, et al. Consumption of a cranberry juice beverage lowered the number of clinical urinary tract infection episodes in women with a recent history of urinary tract infection. Am J Clin Nutr. 2016;103(6):1434-42. doi: 10.3945/ajcn.116.130542. Erratum in: Am J Clin Nutr. 2017;106(2):708. doi: 10.3945/ajcn.117.161851. PMID: 27251185.
30. Gurley BJ. Cranberries as antibiotics?: Comment on "Cranberries vs antibiotics to prevent urinary tract infections: a randomized double-blind non-inferiority trial in premenopausal women". Arch Intern Med. 2011;171(14):1279-80. doi: 10.1001/archinternmed.2011.332. PMID: 21788543.
31. Pérez-López FR, Haya J, Chedraui P. *Vaccinium macrocarpon*: an interesting option for women with recurrent urinary tract infections and other health benefits. J Obstet Gynaecol Res. 2009;35(4):630-9. doi: 10.1111/j.1447-0756.2009.01026.x. PMID: 19751320.
32. Monroy-Torres R, Medina-Jiménez AK. Cranberry juice and other functional foods in urinary tract infections in women: a review of actual evidence and main challenges. Bentham Science. 2019;29:183–211. doi: 10.2174/9781681086378119050007.
33. Younus Al Gaoale ZI, Sheekhoo Al Azzawi KG, Dhannooon Al-Sabaawi MB. Urinary tract infections in pregnant women. New opportunities anti-relapse therapy. Medico-Legal Updat. 2022;22(3). doi: 10.37506/mlu.v22i3.3307.
34. Wawrysiuk S, Naber K, Rechberger T, et al. Prevention and treatment of uncomplicated lower urinary tract infections in the era of increasing antimicrobial resistance-non-antibiotic approaches: a systemic review. Arch Gynecol Obstet. 2019;300(4):821-8. doi: 10.1007/s00404-019-05256-z. Epub 2019 Jul 26. PMID: 31350663; PMCID: PMC6759629.
35. Griffiths P. The role of cranberry juice in the treatment of urinary tract infections. Br J Community Nurs. 2003;8(12):557-61. doi: 10.12968/bjcn.2003.8.12.11853. PMID: 14688663.
36. Efros M, Bromberg W, Cossu L, et al. Novel concentrated cranberry liquid blend, UTI-STAT with Proantinox, might help prevent recurrent urinary tract infections in women. Urology. 2010;76(4):841-5. doi: 10.1016/j.urology.2010.01.068. PMID: 20399486.

SYSTEMATIC REVIEW

Efficacy and role of vitamin D (25-OH-D serum) in the treatment of endometriosis: A systematic review

Yuli Ayu Diani*, I Wayan Arsana Wiyasa
Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

Article Info
Received Mar 15, 2025
Revised Apr 30, 2025
Accepted May 16, 2025
Published Aug 1, 2025

***Corresponding author:**
Yuli Ayu Diani
yuliayu.obgynfkub
@gmail.com

Keywords:
25-OH-D serum
Chronic inflammation
Endometriosis
Immunologic response
Maternal health
Plasma level
Vitamin D

ABSTRACT

Objective: Vitamin D, an essential element in women's reproductive health, has shown potential benefits in endometriosis management by improving plasma concentrations and modulating immune responses in chronic inflammatory conditions, including endometriosis. This study aimed to elucidate the pivotal role of vitamin D in alleviating chronic pain and infertility associated with endometriosis and to provide new insights into its therapeutic application in reproductive medicine.

Materials and Methods: This systematic review examined literature retrieved from PubMed, ScienceDirect, ResearchGate, and Google Scholar, screening 1,156 records and including 20 studies for qualitative assessment. The review focused on the therapeutic contribution of vitamin D in endometriosis management. Eligible studies were those published in the last decade, in English, involving non-pregnant, healthy women, particularly patients with chronic pelvic pain or infertility. Accepted study designs comprised experimental, cohort, longitudinal, case reports, pilot, and observational studies. Excluded were non-English articles, animal or pregnant populations, reviews, inaccessible full texts, and studies lacking relevance to vitamin D or endometriosis.

Results: Twenty selected studies were analyzed, encompassing 5,346 women and 60 girls aged 12–50 years, with or without endometriosis, from Iran, the USA, South Korea, Russia, Turkey, Brazil, Poland, Italy, Germany, and Japan. These studies indicated that multiple therapeutic approaches were attempted, suggesting that endometriosis may be partially ameliorated by vitamin D administration.

Conclusion: This systematic review highlights that women with endometriosis presented with lower vitamin D levels; however, the evidence regarding supplementation efficacy remains uncertain. Further large-scale, rigorously designed trials are necessary to establish vitamin D's therapeutic role in the management of endometriosis.

How to cite: Diani YA, Wiyasa IWA. Efficacy and role of vitamin D (25-OH-D serum) in the treatment of endometriosis: A systematic review. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(1):132-140. doi: 10.20473/mog.V33I22025.132-140.

Highlights:

1. Endometriosis frequently causes pelvic damage and infertility, and vitamin D has been proposed as a therapeutic option owing to its involvement in immune regulation and reproductive health.
2. Vitamin D may contribute to the modulation of inflammatory pathways and decrease the risk of hyperplasia and malignancy, with several studies indicating that it might also impact infertility related to endometriosis.

INTRODUCTION

Endometriosis is a gynecological disorder defined by the ectopic presence of endometrial glands and stroma outside the uterine cavity, and it is widely recognized as an estrogen-dependent pathology.[1,2] Globally, this condition represents the most prevalent gynecological disease, affecting 10 to 15% of reproductive-aged women and occurring at higher rates among infertile women (30 to 50%).[2] Despite multiple hypotheses proposed to explain the pathophysiology of endometriosis, its underlying cause and associated risk factors remain uncertain. Endometriosis is regarded as a multifactorial illness, with genetic, hormonal, immunological, and environmental factors all implicated in its development.[3]

Although the etiology of endometriosis has not been fully established, inflammatory mechanisms are considered to play a pivotal role in disease onset and progression.[3] Moreover, the high prevalence of autoimmune disorders in women with endometriosis has been suggested as an additional contributing factor.[4] The ectopic growth of endometrial tissue beyond the uterus may result in pelvic damage and impair fertility by disrupting uterine blood vessels, thereby compromising uterine oxygenation and nutrient supply. Clinical manifestations of endometriosis commonly include chronic pelvic pain and infertility.[5] These complications significantly affect quality of life. Several investigations have reported that this pro-inflammatory state is associated with elevated cytokine and growth factor levels, diminished apoptosis, and increased angiogenesis, collectively contributing to symptom severity and pain.[1,5]

Multiple therapeutic strategies have been proposed for endometriosis. Vitamin D acts through specific receptors and enzymes expressed in cervical and uterine tissues, vagina, endometrium, cervical epithelium, fallopian tubes, ovaries, and pituitary gland.[6] It is recognized to exert immunomodulatory effects in chronic inflammatory states. This observation suggests that it may serve as a potential treatment for endometriosis, which shares features with autoimmune and neoplastic disorders.[7] Several studies have indicated that polymorphisms of Vitamin D receptors (VDR) binding to Retinoid X Receptors (RXR) may constitute genetic risk factors associated with endometriosis-related infertility.[8] Conversely, other research demonstrated that its capacity to increase plasma levels underscores a distinctive therapeutic role in endometriosis.[8] Additional studies have also reported that vitamin D may reduce hyperplasia and malignancy risk by attenuating cellular proliferation and inducing apoptosis in tumor cells.[9]

This review explored the potential therapeutic role and efficacy of vitamin D (25-OH-D serum) in the management of endometriosis, with emphasis on alleviating chronic pain and infertility. We hypothesized that vitamin D supplementation may enhance clinical outcomes through modulation of inflammatory pathways and reduction of disease-related symptoms. Nonetheless, while numerous studies support beneficial effects of vitamin D in regulating immune responses and improving endometriosis manifestations, other findings have shown no significant improvement, highlighting inconsistency in available data and the necessity for further rigorous investigations.

MATERIALS AND METHODS

Literature searching

The present study comprised a comprehensive review of published literature. For this analysis, relevant articles were retrieved from electronic databases including PubMed, ScienceDirect, ResearchGate, and Google Scholar. The search strategy combined Medical Subject Headings (MeSH) with keyword phrases for Vitamin D, alongside MeSH and keyword terms for Endometriosis, Measurement Methods and Analysis, or Endometriosis in Gynecology. To optimize retrieval, search phrases were adapted according to the requirements of each database. For this review, all publications from 2014 to 2024 were identified and carefully evaluated for relevance and scientific rigor. The process was meticulously conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and reproducibility.

Eligibility criteria

The dataset for this review was classified into two categories: inclusion and exclusion criteria. Eligible designs included experimental studies, cohort studies, longitudinal investigations, case reports, social or pilot studies, and observational research, published within the last decade and written in English. Subjects were restricted to non-pregnant, healthy women, with or without endometriosis, regardless of ethnicity, with a particular focus on individuals experiencing chronic pain and infertility. An additional inclusion criterion required studies to report outcomes using a comparable unit of measurement, and when discrepancies occurred, standardized calculations were applied to ensure consistency and comparability across findings.

Study selection and screening

The reviewers independently conducted the screening of retrieved records. All titles, abstracts, and keywords were systematically assessed. Study quality was evaluated using both the PRISMA framework and the Mixed Methods Appraisal Tool (MMAT). The MMAT comprises five criteria for each study category, with assessments scored as Y (YES = 1), N (NO = 0), or C (Cannot tell = 0). Accordingly, the cumulative favorable responses determined the final methodological score and provided a structured framework for assessing overall study validity.

Data extraction

The methodology for this review adhered to defined core elements. The systematic review concentrated on endometriosis, a chronic, estrogen-dependent disorder associated with pain and infertility due to ectopic proliferation of endometrial tissue,7,10 and on vitamin D, particularly 25-hydroxyvitamin D (25-OH-D), which is central in maintaining calcium homeostasis and influencing immune regulation.11 Included studies comprised experimental, cohort, review, and observational designs involving women of reproductive age (12–50 years). Various biochemical approaches were utilized across the studies, while extracted data encompassed study period, geographical setting, characteristics of intervention and control groups, outcome measures, and principal findings—including treatment effects on psychological symptoms as well as any documented adverse events or reported safety considerations.

RESULTS AND DISCUSSION

A total of 1,156 studies were initially identified, and following the removal of 710 duplicates, 446 articles remained eligible for title and abstract screening. Based on the predefined selection criteria, 313 studies were excluded. Subsequently, 133 full-text articles were assessed for eligibility, with 123 records excluded due to irrelevant outcomes, active control group designs, or non-English publication. Ultimately, 20 studies were included in the qualitative synthesis. Figure 1 illustrates the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart outlining the research selection process.

In this systematic review, the overall population encompassed 5,346 women and 60 female rats with and without endometriosis, aged 12–50 years. The majority of studies were conducted in Iran,[7] USA,[3] South Korea,[2] Russia,[2] Turkey,[1] Brazil,[1] Poland,[1] Italy,[1] Germany,[1] and Japan.[1] Table 1 provides descriptions of the 20 primary articles that were analyzed in this review.

Endometriosis is a chronic, painful, and persistent gynecological disorder characterized by the ectopic growth of endometrial glands, stroma, and endometrial-like tissue beyond the uterine cavity.[14,15] It affects approximately 6–10% of women of reproductive age, increasing to 25–38% among those with chronic pelvic pain and 30–50% among infertile women.[1,2,15] The clinical presentation commonly includes dysmenorrhea, dyspareunia, chronic pelvic pain, abnormal uterine bleeding, and infertility.[15] Several theories, including retrograde menstruation and metaplasia, have been proposed, although these alone cannot explain the disease. Genetic, hormonal, and immunological factors are also considered significant contributors.[4] Evidence from Iranian research indicates that endometriosis mimics autoimmune and malignant disorders by promoting angiogenesis and invasion of endometrial tissue into surrounding organs.[5,7] Multiple treatment modalities have been recommended to improve patients' quality of life, including hormonal and metabolic therapy, surgical interventions, and lifestyle modifications such as exercise and dietary adjustments.[5]

Vitamin D, often referred to as the "secosteroid" vitamin because of its steroid-like structure with a cleaved carbon ring, is critical for numerous metabolic processes, particularly within female reproductive physiology.[6] Several investigations suggest that vitamin D plays a role in regulating appropriate cellular proliferation and differentiation.[7] It also modulates immune responses by enhancing anti-inflammatory cytokines while reducing pro-inflammatory cytokines.[6,7] Vitamin D supplementation is considered essential in endometriosis, given the presence of receptors and enzymes required for its activation.[6] All studies included in this review reported that women with endometriosis exhibited reduced serum concentrations of vitamin D compared with the general population. One study specifically identified hypovitaminosis D3 as a risk factor for endometriosis.[5] Nevertheless, vitamin D levels were not significantly associated with disease severity, although one study demonstrated that serum 25-OH-D levels correlated with gravidity.[3,4]

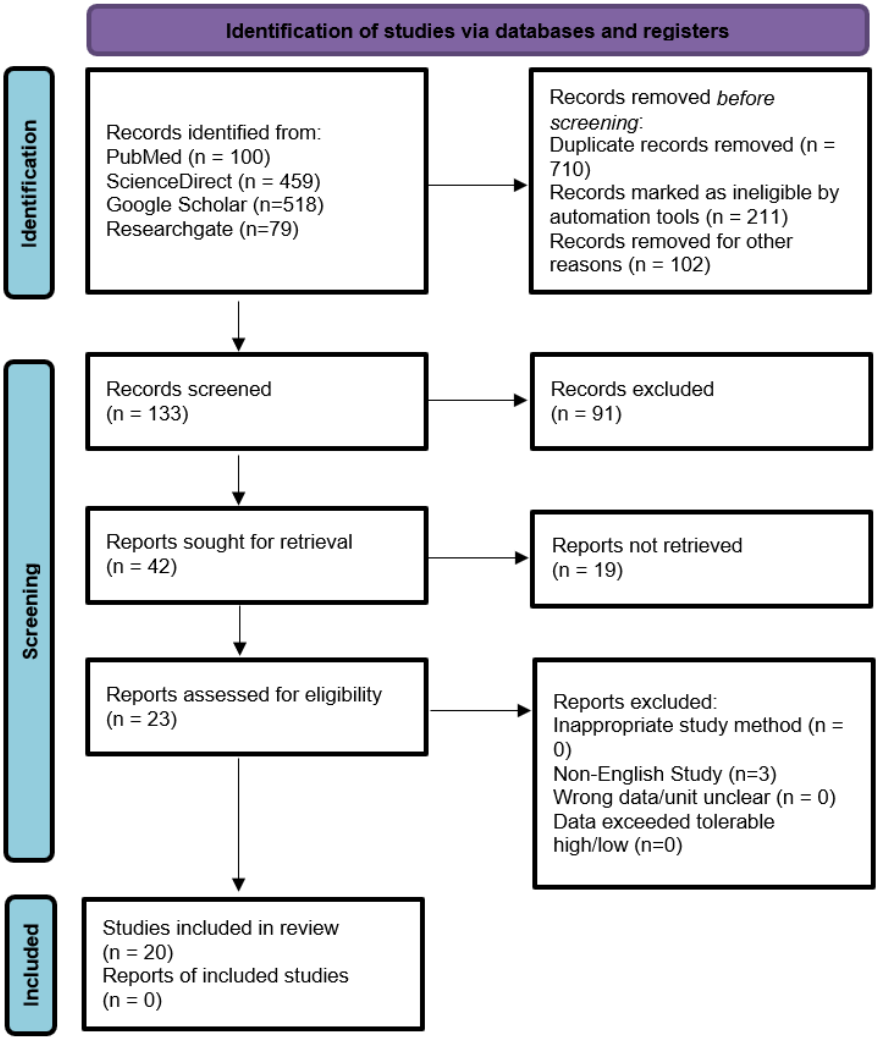


Figure 1. PRISMA flowchart of the literature selection

Table 1. Selected review studies

	Author(s) and article titles	Methods	Determinant variables	Conclusions
1	Nodler, James L et al (2020) With the title "Supplementation with vitamin D or ω-3 fatty acids in adolescent girls and young women with endometriosis (SAGE)"	1. Study Design: A double-blind, randomized, placebo-controlled experiment. 2. Research location: Pediatric Gynecology Clinic at Boston Children's Hospital (BCH). 3. Population: aged 12-25 females having a surgical diagnosis of endometriosis. 4. Sample: 69 participants	1. Age 2. Race 3. BMI 4. VAS pain score 5. Severity or staging of diagnosis (endometriosis)	Supplementing teenage women with Vitamin D after surgically diagnosed endometriosis resulted in a statistically significant improve in pelvic pain status.
2	Akyol, Alpaslan et al (2015) With the title "Efficacies of vitamin D and omega-3 polyunsaturated fatty acids on experimental endometriosis"	1. Study Design: Prospective, single-blind, randomized, controlled experimental investigation. 2. Research location: Firat University Experimental Research Center. 3. Population: mature female Wistar albino rats weighing 200-220 g. 4. Sample: 30 female rats	1. Weight 2. Endometriosis induction 3. Laparoscopic surgery	The study found that Vitamin D supplementation reduced the size and histopathologic changes in endometriosis. However, the regression of omega-3 fatty acids is more substantial than Vitamin D.

3	Baek, Jong Chul et al (2019) With the title "Differences in 25-hydroxy vitamin D and vitamin D-binding protein concentrations according to the severity of endometriosis"	1. Study Design: Observational Study 2. Research Location: Gyeongsang National University Hospital, Jinju, Korea 3. Population: All patients underwent laparoscopy to stage the severity of their endometriosis Sample: 32 participants	1. Age 2. Race 3. BMI 4. Gravidity 5. Parity 6. Diagnosis 7. Laparoscopy diagnostic 8. Vitamin D serum level	According to research, the blood level of 25(OH)D is not substantially connected with the severity of endometriosis, however it is correlated with pregnancy. It is determined that the 25(OH)D serum level correlates with the frequency of births.
4	Cho, Min-Chul et al (2019) With the title "Analysis of vitamin D-binding protein (VDBP) gene polymorphisms in Korean women with and without endometriosis"	1. Study Design: Prospective, observational study 2. Research Location: Gyeongsang National University Hospital, Jinju, Korea 3. Population: All patients with endometriosis had a definitive diagnosis on a pathological review of their surgical specimens 4. Sample: 32 participants	1. Age 2. Race 3. BMI 4. Diagnosis 5. Laparoscopy diagnostic 6. Vitamin D serum level	This study showed that Korean women with endometriosis disease have lower level of Vitamin D serum
5	Nameni, Farah and Mahssadat Ebrahimmosavi (2023) With the title "The Effects of Vitamin D3 Supplementation and Simultaneous Exercise on Aldehyde Dehydrogenase Gene Expression in Endometriosis Female Rats"	1. Study Design: The experimental method with a post-test design 2. Research Location: Islamic Azad University, Varamin, Iran 3. Population: three-month-old female Wistar rats (mean weight = 200 - 250 g) 4. Sample: 30 female rats divided into 6 categories: (1) healthy group, (2) endometriosis group, (3) endometriosis and placebo group, (4) endometriosis and Vitamin D group, (5) endometriosis and simultaneous exercise, (6) endometriosis and simultaneous exercise and Vitamin D	1. Age 2. Weight 3. Endometriosis Induction 4. Exercise 5. Vitamin D supplementation	Hypovitaminosis D3 is a risk factor for endometriosis, and vitamin D supplementation increases the ALDH genes for detoxification of endometriosis-produced aldehydes. Exercise is shown to reduce endometriosis symptoms.
6	Lopes, Vinicius Medina et al (2017) With the title "Highly prevalence of vitamin D deficiency among Brazilian women of reproductive age"	1. Study Design: retrospective cross-sectional design 2. Research Location: record of patients who visited a Brazilian assisted reproduction center between January 1, 2012 and May 15, 2012 3. Population: all infertile patients who were treated between January 1 and May 15, 2012. The control group included 30–45-year-old women who were treated at the clinic 4. Sample: 369 eligible women	1. Age 2. Race 3. Infertility condition 4. Chronical pain 5. Endometriosis	The study found that 32.9% of Brazilian women met the criterion for vitamin D supplementation; however, there was no significant variation in 25(OH)D blood levels based on reproductive status.
7	Almassinokiani, Fariba et al (2016) With the title "Effects of Vitamin D on Endometriosis-Related Pain"	1. Study Design: randomized, double-blind clinical trial 2. Research Location: single tertiary university hospital in Iran 3. Population: Women with age of 15–40 years, proven endometriosis by laparoscopy and a VAS test score of 3 or more for dysmenorrhea and/or pelvic pain 4. Sample: 39 participants	1. Age 2. Race 3. BMI 4. Laparoscopic diagnostic 5. VAS test 3 for dysmenorrhea and/or pelvic pain	Although there may be a link between vitamin D with endometriosis pathogenesis, our study found that vitamin D was ineffective in treating endometriosis-related pain. Larger clinical trials had to establish the potential benefits of vitamin D supplementation in endometriosis therapy.
8	Szczepanska, Malgorzata et al (2015) With the title "Polymorphic variants in vitamin D signaling pathway genes and the risk of endometriosis-associated infertility"	1. Study Design: Prospective, Observational Study 2. Research Location: The Gynecologic and Obstetrical University Hospital, Division of Reproduction at Poland 3. Population: A total of 154 subjects were infertile women with endometriosis, and 347 women	1. Age 2. Race 3. BMI 4. Laparoscopic Diagnostic for endometriosis or infertility 5. Duration of infertility	The study demonstrated that the genetic factor can be one of the risk factors of endometriosis. VDR haplotype had a risk factor for endometriosis-associated infertility and supplementation of Vitamin D can help improvement of the endometriosis symptoms.

		were used as fertile controls 4. Sample: 501 participants	6. Parity	
9	Tabassi, Zohreh et al (2017) With the title "Clinical and Metabolic Response to Vitamin D Supplementation in Endometrial Hyperplasia"	1. Study Design: randomized double-blind placebo-controlled clinical trial 2. Research Location: Naghavi Clinic in Kashan, Iran 3. Population: premenopausal women diagnose with endometrial disorder (such as endometrial hyperplasia, endometriosis etc), aged 35–55 years old 4. Sample: 60 participants	1. Weight 2. Height 3. Race 4. Age	Vitamin D supplementation for 12 weeks effect in glucose metabolism, serum hs-CRP, and plasma TAC concentration. Vitamin D may play indirect role to decrease the complication of endometrial disorder.
10	Yarmolinskaya, Maria et al (2021) With the title "Vitamin D significance in pathogenesis of endometriosis"	1. Study Design: Observational Study 2. Research Location: The Research Institute of Obstetrics, Gynecology and Reproductology, Russia 3. Population: women of reproductive age with GE diagnosis and confirmed morphologically 4. Sample: 211 participants	1. Age 2. Race 3. BMI 4. Gynecological Endometriosis confirmed after laparoscopic diagnostic	This study found that the cholecalciferol level and pain syndrome in endometriosis are conflicting. There is no significant difference in dysmenorrhea and persistent pelvic pain reduction following colecalciferol treatment compared to placebo.
11	Delbandi, Ali-Akbar et al (2015) 1,25-Dihydroxy Vitamin D3 Modulates Endometriosis-Related Features of Human Endometriotic Stromal Cells	1. Study Design: Pilot Study 2. Research Location: Iran University of Medical Sciences, Tehran, Iran 3. Population: women with ovarian endometriosis aged 29 and nonendometriosis with mean age 32 4. Sample: 45 participants	1. Age 2. Laparoscopy diagnostic 3. Three months not taken any hormonal medication	Overall, the study demonstrated for the very first time that 1,25(OH)2D3 has several favorable impacts on endometriosis-related aspects of ESCs from endometriotic patients, indicating the potential utility of this hormone in endometriosis treatment.
12	Mehdizadehkashi, Abolfazl et al (2021) The effect of vitamin D supplementation on clinical symptoms and metabolic profiles in patients with endometriosis	1. Study Design: randomized double-blind placebo-controlled clinical trial 2. Research Location: Rasoul Akram Hospital, Tehran, Iran 3. Population: women with endometriosis aged 18–40 year without diabetes mellitus, thyroid disease, hypertension, hyperprolactemia, and Cushing syndrome 4. Sample: 40 participants	1. Age 2. BMI 3. Malondialdehyde (MDA) status 4. Other metabolic status correlate to endometriosis	The current study found that Vitamin D administration in endometriosis patients resulted in a substantial reduction in chronic pain, total cholesterol/HDL ratio, hs-CRP, and TAC levels. Another clinical and metabolic symptom has no effect.
13	Xie, Baoli et al (2023) With the title "Association between vitamin D and endometriosis among American women: National Health and Nutrition Examination Survey[12]"	1. Study Design: population-based cross-sectional survey 2. Research Location: The National Center for Health Statistics 3. Population: American women around aged 20–54 years from 2001 to 2006 4. Sample: 3,232 women, of whom 257 had endometriosis and 2,975 did not	1. Age 2. Pregnancy 3. Race 4. Marital Status 5. Education Level 6. Vigorous/Moderate activity 7. Smoking status	In representative sample of American women, higher serum of 25(OH)-D concentration will decrease the risk of endometriosis.
14	Yaghoubi, Hadi Mohagheghian et al (2020) Immunomodulatory effects of vitamin D3 on gene expression of MDGF, EGF and PDGFB in endometriosis	1. Study Design: In–vitro Experimental study 2. Research Location: Iran University of Medical Sciences, Iran 3. Population: Thirty-eight patients with a clinical diagnosis of endometriosis and 26 non-endometriotic women with benign gynaecological problems 4. Sample: PFMC from 10 women with endometriosis and 10 control participants	1. Age 2. BMI 3. Cycle phase 4. Marital status 5. Infertility	This study discovered that in-vitro results suggested that Vitamin D3 might significantly reduce PDGFB and EGF gene expression, which was reported to be enhanced in the peritoneal fluids of endometriosis patients.
15	Chamgordani, Samira Najafi et al (2024) Evaluation of the natural killer cell subsets and their relationship with	1. Study Design: Case-control study 2. Research Location: The Immunology Department of Isfahan University of Medical Sciences, Iran	1. Age 2. Race 3. BMI 4. Marital status	In conclusion of this study, the level of serum in vitamin D and IFN-γ has increased in women with endometriosis compared to control group

	serum interferon gamma and vitamin D levels in women with stages III and IV endometriosis[13]	3. Population: women of reproductive age (18–45 yr) 4. Sample: 59 participants		
16	Ciavattini, Andrea et al (2016) With the title "Ovarian endometriosis and vitamin D serum levels"	1. Study Design: Cohort, Observational study 2. Research Location: Polytechnic University of Marche, Ancona, Italy 3. Population: childbearing-age women diagnosed with singleton ovarian endometrioma 4. Sample: 49 participants	1. Age 2. BMI 3. Tobacco use 4. Menarche 5. Infertility 6. Number of pregnancies	This study examined that the hypotaminosis D could have role in development of endometriosis disease and correlate with the severity of this disease. This study also suggested that supplementation of Vitamin D is novel, safe, and low-cost treatment of endometriosis.
17	Agic, Admir (2014) Relative Expression of 1,25-Dihydroxyvitamin D3 Receptor, Vitamin D 1α-Hydroxylase, Vitamin D 24-Hydroxylase, and Vitamin D 25-Hydroxylase in Endometriosis and Gynecologic Cancers	1. Study Design: Experimental Study 2. Research Location: University of Schleswig-Holstein, Department of Gynecology and Obstetrics, Ratzeburgerallee, Germany 3. Population: women undergoing laparoscopy and women with endometrial and ovarian cancer 4. Sample: 79 participants	1. Age 2. BMI 3. Marital status 4. Menarche 5. Infertility	Given the emerging evidence of vitamin D's anti-proliferative and anti-inflammatory actions,40 we hypothesize that the vitamin may influence the activity of local immune cells and also their cytokine production, which have previously been identified as important factors in the development and also maintenance of endometriosis.
18	Miyashita, Mariko et al (2016) With the title "Effects of 1,25-Dihydroxy Vitamin D3 on Endometriosis"	1. Study Design: Experimental, in-vitro Study 2. Research Location: University of Tokyo 3. Population: Endometriosis tissues in patients with ovarian endometriosis 4. Sample: 35 participants	1. Age 2. BMI 3. Endometriosis status	This study indicated that Vitamin D supplementation may reduce disease development, and lower Vitamin D levels were connected with endometriosis.
19	Denisova, Alexander S. et al (2021) With the title "Assessment of 25(OH)D status in patients with genital endometriosis and clinical efficacy of cholecalciferol in the treatment of the disease"	1. Study Design: Observational Study 2. Research Location: D.O. Ott Scientific Research Institute of Obstetrics, Gynecology, and Reproduction 3. Population: patients with genital endometriosis with age aroung 33.7 ± 5.8 years and had various degrees of disease prevalence 4. Sample: 440 participants	1. Age 2. BMI 3. Endometriosis-associated pain 4. EGE grades I-IV	This study found that a dosage of 2 mg combined with cholecalciferol was the most beneficial for endometriosis.
20	Pazhohan, Azar et al (2020) With the title "The modulating effects of vitamin D on the activity of b-catenin in the endometrium of women with endometriosis"	Study Design: randomized exploratory trial Research Location: Alzahra hospital, Iran Population: women with endometriosis stage III and VI diagnosed using laparoscopic with age 22–37 year Sample: 34 participants	1. Age 2. BMI 3. Endometriosis diagnosed after laparoscopic 4. Menstrual cycle	This study demonstrated that vitamin D can change the defective pathway of wnt/b-catenin and signaling in the endometrium of endometriosis patients by inactivating b-catenin.

Several in vitro experiments and population-based investigations among American women have demonstrated that adequate serum levels of vitamin D may inhibit the progression of endometriosis, indicating that lower vitamin D concentrations are associated with increased prevalence of this disease.[16-19] Multiple reports have emphasized the significant role of vitamin D as both an anti-proliferative and anti-neoplastic factor, exerting effects through genomic and non-genomic pathways. The genomic pathway, mediated through the vitamin D receptor (VDR), appears particularly critical since VDR expression is markedly elevated in endometriotic tissue. When vitamin D supplementation binds to VDR, it may reduce disease progression.[19] A Russian study highlighted the genetic contribution of vitamin D in endometriosis-associated infertility, demonstrating that reduced serum 25-OH-D levels correlate with specific gene variations, thereby playing an important role in limiting the progression of endometriosis.[10] Supporting this hypothesis, another study identified a particular VDR haplotype within endometrial tissue of affected women as a risk factor for endometriosis.[8] In contrast, research from Brazil found no significant relationship between vitamin D serum levels and infertility status in women with endometriosis, thereby underscoring persistent controversy regarding the association of vitamin D with the disease.[6]

Oral vitamin D3 supplementation has been suggested as a potentially safe, accessible, and low-cost therapeutic approach for managing endometriosis.[19-20] Mechanistic evidence indicates that vitamin D may inactivate ß-catenin signaling in endometriosis patients, thereby limiting disease progression.[21] Moreover, supplementation has been shown to decrease peritoneal fluid concentrations of sCD44 in affected individuals.[22] Several studies reported improved outcomes in chronic pain management following vitamin D supplementation when combined with surgical intervention. Additional findings support that vitamin D intake enhances not only chronic pelvic pain relief but also improves metabolic parameters such as total/HDL cholesterol ratio, hs-CRP levels, and TAC activity.[23] Nevertheless, a study from Iran revealed no significant efficacy of vitamin D supplementation in alleviating endometriosis-associated pain.[7] Further evidence suggests that vitamin D may contribute primarily to delaying or regressing disease progression rather than exerting substantial effects on pain or infertility management.[9]

This review provides a comprehensive synthesis of the association between vitamin D levels and endometriosis, offering an important preliminary foundation for evaluating vitamin D as both a potential risk factor and therapeutic adjunct in disease management. However, inconsistent findings across studies regarding supplementation outcomes complicate the ability to establish definitive conclusions. Furthermore, the lack of adequately powered, large-scale randomized clinical trials remains a major limitation in confirming the clinical significance and therapeutic benefit of vitamin D supplementation for endometriosis.

CONCLUSION

This review indicates that women with endometriosis exhibit lower vitamin D levels, and deficiency of vitamin D has been described as one of the potential risk factors for endometriosis. However, the association between vitamin D supplementation and endometriosis treatment remains controversial. While certain studies demonstrate clinical improvement, others report no significant correlation or therapeutic benefit of vitamin D supplementation in the management of endometriosis. Therefore, larger well-designed trials are required to further investigate and clarify the possible therapeutic effects of vitamin D supplementation in endometriosis treatment.

DISCLOSURES

Acknowledgment

No recognition and/or acknowledgement is present.

Conflict of interest

No conflicting interests are present in this review.

Funding

This review has not received any funding or sponsorship.

Author contribution

All authors have contributed to all process in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

REFERENCES

1. Nodler JL, DiVasta AD, Vitonis AF, et al. Supplementation with vitamin D or ω-3 fatty acids in adolescent girls and young women with endometriosis (SAGE): a double-blind, randomized, placebo-controlled trial. Am J Clin Nutr. 2020;112(1):229-36. doi: 10.1093/ajcn/nqaa096. PMID: 32453393; PMCID: PMC7326593.
2. Akyol A, Şimşek M, İlhan R, et al. Efficacies of vitamin D and omega-3 polyunsaturated fatty acids on experimental endometriosis. Taiwan J Obstet Gynecol. 2016;55(6):835-9. doi: 10.1016/j.tjog.2015.06.018. PMID: 28040129.
3. Baek JC, Jo JY, Lee SM, et al. Differences in 25-hydroxy vitamin D and vitamin D-binding protein concentrations according to the severity of endometriosis. Clin Exp Reprod Med. 2019;46(3):125-31. doi: 10.5653/cerm.2018.00416. Epub 2019 Aug 1. PMID: 31370113; PMCID: PMC6736508.
4. Cho MC, Kim JH, Jung MH, et al. Analysis of vitamin D-binding protein (VDBP) gene polymorphisms in Korean women with and without endometriosis. Clin Exp Reprod Med. 2019;46(3):132-9. doi: 10.5653/cerm.2019.00122. Epub 2019 Aug 13. PMID: 31405270; PMCID: PMC6736509.
5. Nameni F, Ebrahimmosavi M. The effects of vitamin d3 supplementation and simultaneous exercise on aldehyde dehydrogenase gene expression in endometriosis female rats. Gene, Cell and Tissue. 2023;11(1):1-7. doi: 10.5812/gct-138359.

6. Lopes VM, Lopes JR, Brasileiro JP, et al. Highly prevalence of vitamin D deficiency among Brazilian women of reproductive age. Arch Endocrinol Metab. 2017;61(1):21-7. doi: 10.1590/2359-3997000000216. Epub 2016 Oct 10. PMID: 27737331; PMCID: PMC10522115.
7. Almassinokiani F, Khodaverdi S, Solaymani-Dodaran et al. Effects of vitamin D on endometriosis-related pain: A double-blind Clinical Trial. Med Sci Monit. 2016;22:4960-6. doi: 10.12659/msm.901838. PMID: 27986972; PMCID: PMC5189720.
8. Szczepańska M, Mostowska A, Wirstlein P, et al. Polymorphic variants in vitamin D signaling pathway genes and the risk of endometriosis-associated infertility. Mol Med Rep. 2015;12(5):7109-15. doi: 10.3892/mmr.2015.4309. Epub 2015 Sep 10. PMID: 26398313.
9. Tabassi Z, Bagheri S, Samimi M, et al. Clinical and Metabolic Response to Vitamin D Supplementation in Endometrial Hyperplasia: a Randomized, Double-Blind, Placebo-Controlled Trial. Horm Cancer. 2017;8(3):185-95. doi: 10.1007/s12672-017-0290-9. Epub 2017 Mar 10. PMID: 28283863; PMCID: PMC10355957.
10. Yarmolinskaya M, Denisova A, Tkachenko N, et al. Vitamin D significance in pathogenesis of endometriosis. Gynecol Endocrinol. 2021;37(sup1):40-3. doi: 10.1080/09513590.2021.2006516. PMID: 34937505.
11. Aridan DA. Hubungan antara defisiensi vitamin D dengan kadar interleukin 6 pada anak obes [Correlation between vitamin D deficiency and IL-6 level in obese children]. [Dissertation]. Makassar. Universitas Hasanuddin.
12. Xie B, Liao M, Huang Y, et al. Association between vitamin D and endometriosis among American women: National Health and Nutrition Examination Survey. PLoS One. 2024;19(1):e0296190. doi: 10.1371/journal.pone.0296190. PMID: 38215179; PMCID: PMC10786361.
13. Najafi Chamgordani S, Esmaeil N, Hashemi M, et al Evaluation of the natural killer cell subsets and their relationship with serum interferon gamma and vitamin D levels in women with stages III and IV endometriosis: A case-control study. Int J Reprod Biomed. 2024;22(7):593-604. doi: 10.18502/ijrm.v22i7.16933. PMID: 39355310; PMCID: PMC11441287.
14. Delbandi AA, Mahmoudi M, Shervin A, et al. 1,25-dihydroxy vitamin D3 modulates endometriosis-related features of human endometriotic stromal cells. Am J Reprod Immunol. 2016;75(4):461-73. doi: 10.1111/aji.12463. Epub 2015 Dec 22. PMID: 26691009.
15. Sayegh L, Fuleihan Gel-H, Nassar AH. Vitamin D in endometriosis: a causative or confounding factor? Metabolism. 2014;63(1):32-41. doi: 10.1016/j.metabol.2013.09.012. Epub 2013 Oct 14. PMID: 24135500.
16. Ciavattini A, Serri M, Delli Carpini G, et al. Ovarian endometriosis and vitamin D serum levels. Gynecol Endocrinol. 2017;33(2):164-7. doi: 10.1080/09513590.2016.1239254. Epub 2016 Nov 4. PMID: 27809683.
17. Miyashita M, Koga K, Izumi G, et al. Effects of 1,25-Dihydroxy Vitamin D3 on Endometriosis. J Clin Endocrinol Metab. 2016;101(6):2371-9. doi: 10.1210/jc.2016-1515. Epub 2016 Apr 1. PMID: 27035829.
18. Denisova AS, Yarmolinskaya MI, Tkachenko NN. Assessment of 25 (OH) D status in patients with genital endometriosis and clinical efficacy of cholecalciferol in the treatment of the disease. Journal of Obstetrics and Women's Diseases. 2021;70(4):125-33. doi: 10.17816/JOWD70796.
19. Agic A, Xu H, Altgassen C, et al. Relative expression of 1,25-dihydroxyvitamin D3 receptor, vitamin D 1 alpha-hydroxylase, vitamin D 24-hydroxylase, and vitamin D 25-hydroxylase in endometriosis and gynecologic cancers. Reprod Sci. 2007;14(5):486-97. doi: 10.1177/1933719107304565. PMID: 17913968.
20. Mohagheghian Yaghoubi H, Samadi M, Tajik N, et al. Immunomodulatory effects of vitamin D3 on gene expression of MDGF, EGF and PDGFB in endometriosis. Reprod Biomed Online. 2020;41(5):782-9. doi: 10.1016/j.rbmo.2020.05.013. Epub 2020 May 26. PMID: 32883565.
21. Pazhohan A, Danaei-Mehrabad S, Mohamad-Rezaeii Z, et al. The modulating effects of vitamin D on the activity of β-catenin in the endometrium of women with endometriosis: a randomized exploratory trial. Gynecol Endocrinol. 2021;37(3):278-82. doi: 10.1080/09513590.2020.1858780. Epub 2020 Dec 11. PMID: 33305626.
22. Pazhohan A, Amidi F, Akbari-Asbagh F, et al. Expression and shedding of CD44 in the endometrium of women with endometriosis and modulating effects of vitamin D: A randomized exploratory trial. J Steroid Biochem Mol Biol. 2018;178:150-8. doi: 10.1016/j.jsbmb.2017.12.001. Epub 2017 Dec 9. PMID: 29229305.
23. Mehdizadehkashi A, Rokhgireh S, Tahermanesh K, et al. The effect of vitamin D supplementation on clinical symptoms and metabolic profiles in patients with endometriosis. Gynecol Endocrinol. 2021;37(7):640-5. doi: 10.1080/09513590.2021.1878138. Epub 2021 Jan 29. PMID: 33508990.

SYSTEMATIC REVIEW

Differences in factors associated with postpartum hemorrhage in developed and developing countries: A systematic review

Sri Astuti Handayani*, Farida Kartini
Midwifery Master Program, Faculty of Health Science, Universitas 'Aisyiyah, Yogyakarta, Indonesia.

Article Info
Received Dec 6, 2024
Revised Mar 20, 2025
Accepted Apr 25, 2025
Published Aug 1, 2025

***Corresponding author:**
Sri Astuti Handayani
sriastuti6115@gmail.com

Keywords:
Developed countries
Developing countries
Maternal health
Postpartum hemorrhage
Puerperium
Risk factors

ABSTRACT

Objective: This study aimed to assess maternal and fetal risk factors for post-partum hemorrhage in both developed and developing countries.

Materials and Methods: A systematic review methodology was employed, incorporating a descriptive design. The study followed Joanna Briggs Institute (JBI) techniques, the PCC framework, and the PRISMA-ScR checklist. Article searches were conducted across four databases: Research Rabbit, Science Direct, Wiley, and PubMed. Articles published in English between 2019 and 2024 that met the inclusion criteria were selected. The search terms included combinations of "Postpartum women" OR "Puerperium" AND "Risk factors" OR "Risky conditions" AND "Postpartum hemorrhag*" "Postpartum bleeding" and "Developed countr*" AND "Developing countr*".

Results: Out of 906 articles, 20 met the inclusion criteria, representing both developed and developing countries. The findings were categorized into two themes: risk factors in developed versus developing countries. In developed countries, PPH risk factors are often linked to medical interventions and prolonged labor management, while in developing countries, the focus shifts to conditions like anemia, uterine overdistension, and trauma from delivery practices. Sociocultural disparities further exacerbate risks in both settings.

Conclusion: The study reveals significant differences in PPH risk factors between developed and developing countries. By reviewing existing research, it identifies factors that can influence PPH occurrence. The findings emphasize the need for developing policies to screen pregnant, maternity, and postpartum women to mitigate PPH risk.

How to cite: Handayani SA, Kartini F. Differences in factors associated with postpartum hemorrhage in developed and developing countries : A systematic review. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):141-151. doi: 10.20473/mog.V33I22025.141-151.

Highlights:

1. Analysis of maternal and fetal risk factors associated with postpartum hemorrhage, comparing data from both developed and developing countries.
2. There are differences in the risk factors for postpartum hemorrhage between developed and developing countries.

INTRODUCTION

Maternal health has been a global concern. In some countries, especially developed and developing countries, mothers face various risks during childbirth. This situation has prompted the international community to make greater efforts in addressing this issue.[1] According to estimates from the World Health Organization (WHO), 287.000 women will pass away in 2020 as a result of pregnancy and delivery. By 2020, problems from pregnancy and childbirth will kill over 800 women daily. In 2020, rich countries accounted for about 95% of all maternal deaths; the majority of these deaths might have been avoided.[2]

The Maternal Mortality Ratio (MMR) in low-income countries in 2020 was 430 per 100.000 live births versus 13 per 100 000 live births in high income countries.[2] Indonesia has a comparatively high MMR of 305 per 100,000 live births, whereas the IMR is 16.9 per 1,000 live births, according to data from the Central Bureau of Statistics.[3] It falls short of the 2020–2024 National Medium-Term Development Plan (RPJMN) MMR and Infant Mortality Rate (IMR) objectives, which are 183 per 100,000 live births and 16 per 1,000 live births, respectively.[4] Among Southeast Asian countries, Indonesia's MMR remains in the third-highest ranking.[5]

Complications that arise during or after pregnancy and childbirth can have devastating consequences for women. Pregnancy is the time when many of these problems first appear, but they are frequently avoidable or treatable with the right care. If left untreated, several pre-existing diseases can also get worse during pregnancy. Roughly 75% of maternal deaths are caused by high blood pressure conditions like pre-eclampsia and eclampsia, infections that usually occur after childbirth, severe bleeding, especially postpartum hemorrhage (PPH), delivery complications, and unsafe abortion practices.[2]

The standard definition of PPH is blood loss of more than 500 milliliters after vaginal delivery or more than 1000 milliliters after cesarean delivery.[6] However, in 2017, PPH was redefined by the American College of Obstetrics and Gynecologists (ACOG) as a blood loss associated with hypovolemia symptoms or indicators, as well as a cumulative blood loss of 1000 milliliters or more, regardless of the delivery method, within the first 24 hours of the birth.[7] Clinical signs and symptoms typical of hypovolemia resulting from postpartum hemorrhage, symptoms like tachycardia and hypotension could not show up until blood loss exceeds 25% of the total volume of blood (>1500 ml in late pregnancy).[8] Maternal mortality rates remain a significant challenge, with PPH being a leading cause. The complexity of contributing factors complicates the issue. Currently, there are no review articles comparing the risk factors for postpartum hemorrhage in developed and developing countries. The purpose of this systematic review is to distinguish between postpartum hemorrhage risk factors in developed and developing countries.

MATERIALS AND METHODS

A systematic review maps and identifies research gaps by following Arkshey & O'Malley and Daniel Levac's methodology, which includes formulating research questions, selecting articles based on inclusion and exclusion criteria, charting data, and extracting relevant information.

Identifying research questions

Usage of the PCC framework is recommended (Population, Concept, Context) to establish specific objectives and prerequisites for a systematic study (Table 1). This will enable the organized identification of pertinent data items.[9] This review addresses the research question: "What are the differences in factors contributing to PPH in developed versus developing countries?"

Table 1. PCC framework

P (Population)	C (Concept)	C (Context)
Postpartum women	The factor which influence PPH	Developed countries, developing countries

Identifying relevant articles

In article searches for this systematic review, specific inclusion and exclusion criteria are established to streamline the selection process (Table 2).

Table 2. Eligibility criteria

"Inclusion Criteria"	"Exclusion Criteria"
1. Original research article 2. Articles published in the last 5 years (2019-2024) 3. Research articles published in English 4. Full text 5. Factors contributing to PPH	1. Review/ comment articles 2. Book chapters

Literature searching

The researcher employed various search strategies, including truncation and Boolean operators,[10] to identify relevant articles. Databases used were PubMed, Science

Direct, Wiley Online Library, and manual searches through Research Rabbit. Keywords were chosen to align with inclusion criteria and bibliography: "Postpartum women" OR "Puerperium" AND "Risk factors" OR "Risky condition" AND "Postpartum hemorrhag*" OR "Postpartum bleeding" AND "Developed countr*" AND "Developing countr*".

Article selection

Researchers followed the Arksey & O'Malley framework for article selection, which included database identification, duplication screening, title and abstract review, full-text screening, and categorization for inclusion or exclusion. Documentation was provided using PRISMA flow charts (Figure 1).[11]

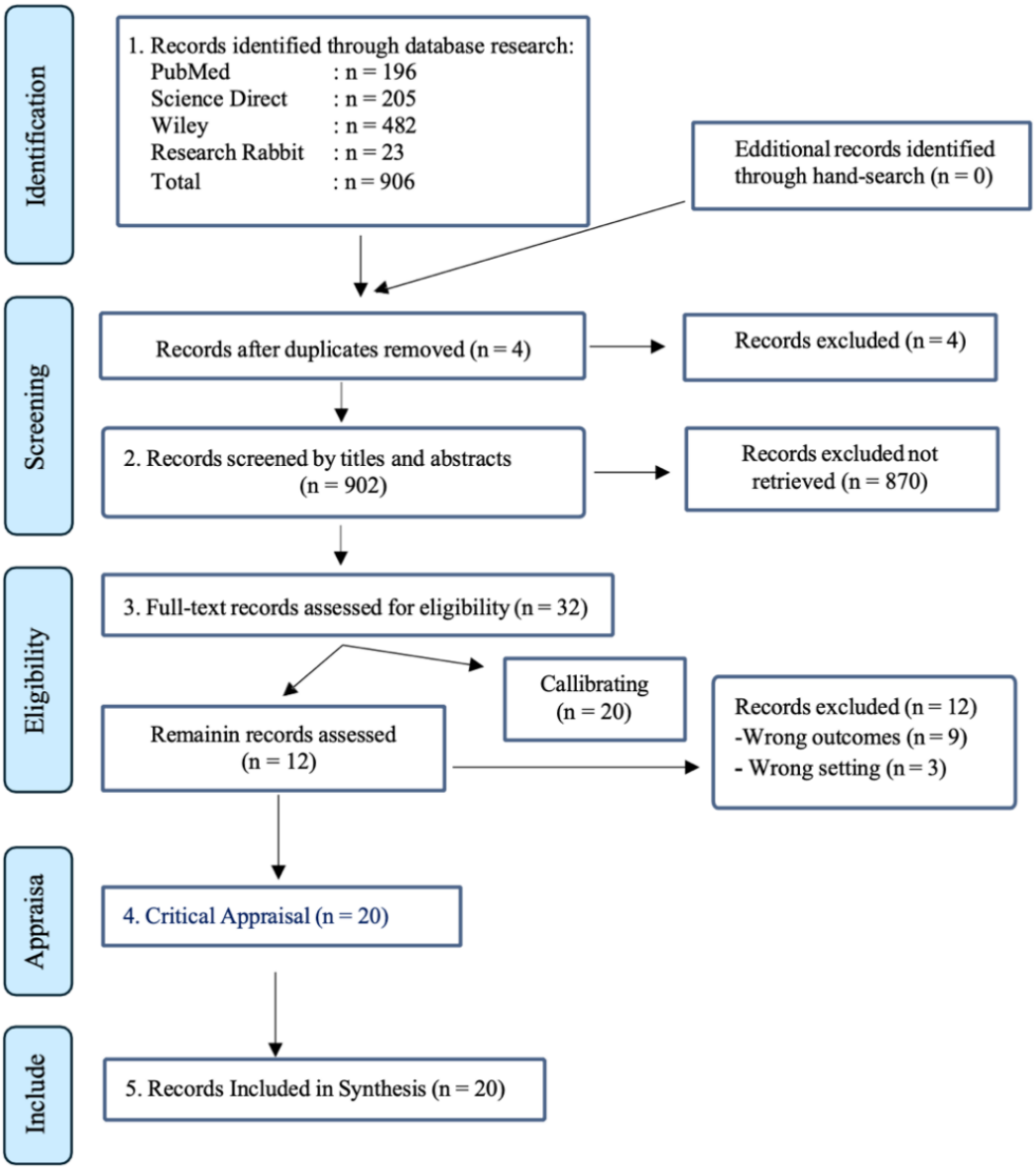


Figure 1. PRISMA flowchart

Based on the search for articles using keywords and inclusion and exclusion criteria in 3 databases and 1 manual research. It was found as many as 906 articles and then duplication checks were carried out. After that, 870 items were eliminated based on a screening of the abstract and title of 902 articles. Twelve papers were eliminated after 32 were vetted for publication in full. Twenty articles were reviewed in this systematic review. The articles are subsequently chosen for critical appraisal to evaluate their quality. In order to assess articles quality, the Joanna Brigs checklist from the Joana Brigs Institute (JBI) is needed.

Data charting

At this point, all of the chosen articles data were entered into a table and included the following: the article title, the name of the author, the year, the nation, the goal of the study, the study design, the data collection method, the number of participants and sample size, and the results, as shown in Table 3.

Table 3. Data charting

No	Title/author/year	Country	Aim	Study design	Data collection/ participant/Sample size	Results
A1	Risk factors for postpartum hemorrhage in The Northern Province of Rwanda[12]	Republic of South Africa	To research and simulate primary PPH risk factors	Case Control	Between January 1 and June 30, 2020, information was gathered from medical records for 430 women, 108 of whom had PPH.	The most common risk factors for primary PPH were hemoglobin levels less than 11 g/dL before admission, cultural differences, and multiple pregnancies.
A2	Association of oxytocin augmentation and duration of labour with postpartum hemorrhage[13]	Norway	To look into the relationship between the length of labor and the increase of oxytocin for PPH	Cohort	From December 2014 to January 2017, a secondary analysis was carried out on 14 birth-care units located in all four health regions of Norway. In the LaPS study, 4,943 of the 7,277 women satisfied the inclusion requirements.	The interpretation of oxytocin and labor time as predictors of PPH is complicated by the intricacy of clinical practice.
A3	Twin growth discordance and risk of postpartum hemorrhage[14]	China	To determine whether prenatal growth abnormalities and PPH are related	Cohort	All twin pregnant women who had cesarean sections between August 2013 and July 2020 had their obstetric records examined. 3,180 of them were examined.	Rather than FGR, twin growth discordance was linked to a higher incidence of PPH.
A4	Relation of meconium-stained amniotic fluid and postpartum hemorrhage[15]	China	To determine whether MSAF poses a risk for PPH following vaginal birth	Cohort	Medical records of all patients with vaginal deliveries from January 1, 2013, to December 31, 2018, were analyzed. Of 55,197 deliveries, 13,686 were classified in the MSAF group, and 41,511 in the clear AF group.	To ascertain whether MSAF increases the risk of PPH after vaginal delivery
A5	Postpartum hemorrhage and risk for postpartum readmission[16]	The United States of America	To evaluate and to determine risk factors for postpartum readmission	Cohort	The analysis utilized the 2010–2014 Nationwide Readmissions Database (NRD) and included women aged 15–54 years.	The general risk of all-cause readmission shortly after delivery suggests that these women may benefit from closer postpartum surveillance.
A6	Analysis of perinatal outcome of forceps delivery and risk factors of postpartum hemorrhage[17]	China	To exploring the perinatal outcomes of forceps delivery and the risk factors of PPH	Cohort	The study included mothers aged 15 to 54 years with PPH extending up to 60 days. Of 1,520 pregnant women, 1,454 were in the normal vaginal delivery group.	The incidence of PPH is higher in the forceps-assisted delivery group, particularly with occipital posterior position, abnormal coagulation function, soft birth canal tears, and lateral perineal incisions.

A7	Incidence and risk factors for postpartum hemorrhage among transvaginal deliveries at a tertiary perinatal medical facility in Japan[18]	Japan	To assess the incidence of, and risk factors for PPH among transvaginal deliveries	Cohort	Health care providers were trained to collect data and measure PPH. Among 1,920 deliveries from June 2013 to July 2016, 93 cases of PPH were identified.	Risk factors for PPH included the use of ART, pregnancy-induced hypertension (PIH), severe vaginal/perineal lacerations, and macrosomia neonates.
A8	Postpartum hemorrhage in Sub-Saharan Africa—a prospective study in metropolitan Mozambique[19]	Mozambique	To analyze MM, PPH, and associated risk factors	Cohort	Data were extracted from the paper charts of all pregnant women delivering at MCH, between February 2019 and January 2021. Of 8,879 women, 5,011 were local and 3,495 were non-local; these groups were analyzed and compared separately.	For women from nonmetropolitan areas, PPH was strongly associated with correctable risk factors such as prepartum anemia and uterine atony.
A9	Risk factors for postpartum hemorrhage following cesarean delivery[20]	Israel	To identify risk factors for PPH following cesarean delivery (CD)	Cohort	Data were collected from departmental electronics between January 2014 and December 2015. Out of 15,564 deliveries, 3,208 women met the inclusion criteria.	In women undergoing cesarean section, the duration of surgery and the number of previous cesarean deliveries are associated with the risk of PPH.
A10	Risk factors and recurrence of cause-specific postpartum hemorrhage[21]	Norway	To explore and recurrence risks in a subsequent delivery	Cohort	Data from The Medical Birth Registry of Norway and Statistics Norway (1967–2017) identified 277,746 cases of PPH out of 3,003,025 births, representing 9.3% of the total.	Retained placenta was most commonly associated with severe PPH, while a history of cesarean delivery increased the risk of PPH due to dystocia.
A11	Incidence and risk factors of postpartum hemorrhage in China[22]	China	To investigate the incidence and the risk factors of PPH in Chinese women	Cohort	This study, conducted across 14 medical centers in 10 provinces from October 1, 2016, to September 30, 2017, enrolled 99,253 women, including 95,967 with singleton pregnancies and 3,286 with twin pregnancies.	Risk factors for PPH varied slightly with the number of fetuses and the mode of delivery, with placenta previa and placenta accreta being the two major contributors.
A12	Prevalence and risk factors of severe postpartum hemorrhage[23]	China	To determine the prevalence and risk factors of SPPH	Cohort	This study utilized a database from medical records, including all women who gave birth after 28 weeks of gestation from January 2015 to August 2019, totaling 34,178 women.	Risk factors for SPPH included previous cesarean section, history of PPH, pre-delivery anemia, prolonged labor, placenta previa, placental abruption, and macrosomia.
A13	Risk factors for postpartum hemorrhage and its severe forms with blood loss evaluated objectively[24]	Brazil	To identify risk factors related to PPH and severe PPH with blood loss quantified objectively	Cohort	Data were collected through interviews and medical records from February 1, 2015, to March 31, 2016. Of 319 eligible women, 8 declined participation and 41 underwent cesarean sections, resulting in the inclusion of 270 women.	A prolonged second stage of labor, use of forceps, and episiotomy are associated with PPH and should prompt delivery assistants to recognize and treat PPH early.
A14	Postpartum hemorrhage in maternal mothers at Anutapura Public Hospital in Palu[25]	Indonesia	To know the risk factors of the incidence of PPH in birth mothers	Case control	This study used secondary data from complete patient medical records in 2017. Out of 50 PPH cases, 27 involved mothers aged below 20 or over 35 years, indicating high risk.	Anemia, parity, and maternal age are risk factors for PPH in childbirth.
A15	Risk factors for postpartum hemorrhage in a tertiary hospital in South-Central	The United States of America	To determine prevalence, risk factors, and causes for PPH	Cohort	Data were extracted from electronic medical records for 30,674 women between October 1, 2015, and September 30, 2020. Among them, 1,869 experienced	Black race, increased BMI, cesarean delivery, and anemia are associated with PPH, with anemia at

	Louisiana[26]				PPH.	delivery increasing the risk of severe maternal morbidity in PPH cases.
A16	Prevalence, related factors and maternal outcomes of primary postpartum haemorrhage in governmental hospitals in Kabul-Afghanistan[27]	Afghanistan	To determine the prevalence, related factors and maternal outcomes of primary PPH in governmental hospitals	Cohort	This study focused on women who gave birth between August and October 2018. Data were collected using a structured checklist for those with primary PPH. Out of 8,652 women observed, 215 had primary PPH, and 2 died during cesarean section.	Among demographic characteristics of women with primary PPH, education level, being a housewife, and the self-employment status of their husbands were the most common related factors.
A17	Incidence and risk factors for postpartum hemorrhage[28]	Greece	To estimate the rate of primary PPH, as well as to investigate the potential risk factors	Case control	Singleton pregnancies complicated by PPH were recorded from January 2015 to December 2021. Out of 8,545 deliveries, 219 cases (2.5%) of PPH were identified.	Most cases of PPH were managed with uterotonic medications. Advanced maternal age, prematurity, and multiparity significantly impacted PPH occurrence.
A18	Risk factors for postpartum hemorrhage in a Thai–Myanmar border community hospital[29]	Thailand	To assess the incidence and relevant risk factors for PPH	Cohort	Medical and obstetric records were reviewed to identify a cohort of 4,845 women who delivered at the hospital between 2014 and 2018.	Risk factors for PPH included nulliparity, a history of PPH, BMI ≥ 35 kg/m², manual placenta removal, fetal weight > 4000 g, ethnicity, and cultural beliefs.
A19	Risk factors for postpartum hemorrhage after elective cesarean deliveries for twin pregnancies[30]	China	To identify the high-risk factors associated with PPH after an elective cesarean delivery of twins	Cohort	The study, conducted at the Women's Hospital, School of Medicine, Zhejiang University from September 2014 to April 2019, enrolled 532 pregnant women. PPH occurred in 70 of these women (13.2%).	Twin pregnancies and elective cesarean deliveries are high-risk factors for PPH, leading to increased PPH rates in women undergoing elective cesarean sections for twin pregnancies.
A20	Factors associated with primary postpartum hemorrhage in elderly women undergoing repeated cesarean deliveries[31]	China	To analyze the risk factors for primary PPH in elderly parturients undergoing repeat cesarean deliveries.	Cohort	Medical records were analyzed for all patients from May 2011 to March 2020, dividing them into a PPH group (116 women) and a non-PPH group (1,559 women).	The number of cesarean sections, placenta previa, placenta implantation, placenta attachment position, and fetal position are independent risk factors for PPH.

RESULT AND DISCUSSION

The data charting process produced 20 articles from the database search. These articles were categorized based on several characteristics. First, the study characteristics by country revealed that 13 articles came from developing nations, including South Africa, China, Mozambique, Brazil, Indonesia, Afghanistan, and Thailand, while seven articles were from developed countries, such as Norway, the United States, Japan, Israel, and Greece. In terms of article type, 16 of the selected papers were cohort studies, four were case-control studies, and none were qualitative. Finally, using theme mapping, the researchers identified two main topics: Both the risk factors for postpartum hemorrhage in industrialized and underdeveloped nations should be considered.

Risk factors for postpartum hemorrhage in developed countries

One dose-dependent risk factor for PPH has been found as the use of oxytocin for labor augmentation, with studies demonstrating that prolonged administration increases PPH risk.[13] Specifically, a significant retrospective study in the United States found that oxytocin administered for longer than four hours when in spontaneous labor and longer than seven hours when

in labor induction significantly raises the likelihood of PPH.[32] Additionally, prolonged labor duration, particularly beyond 16 hours, is strongly associated with a higher incidence of PPH.[33] Severe PPH is also more frequent in cases where active labor exceeds 12 hours,[34] and the duration of the third stage of labor (TSL) plays a critical role in postpartum bleeding risk. Bleeding correlates positively with TSL duration, increasing sharply up to 10 minutes and more gradually thereafter, with a notable rise in PPH risk when TSL exceeds 18 minutes.[35]

Women with a prior diagnosis of PPH are more likely to experience a recurrence in subsequent pregnancies.[16,21] This recurrent risk is often linked to persistent underlying conditions such as uterine atony, coagulation disorders, or trauma from previous deliveries. It may also indicate that initial risk factors were not adequately managed or have worsened in later pregnancies.[36] Compounding these issues, challenges in recognizing bleeding signs, particularly in patients with darker skin tones, can delay timely intervention, potentially increasing PPH morbidity.[37] Black patients, in particular, face higher rates of severe PPH-related complications, including transfusions, disseminated intravascular coagulation, and hysterectomy, partly due to receiving less extensive treatment for PPH, which exacerbates maternal morbidity and mortality.[38]

Preterm birth is another factor that raises the likelihood of PPH. Women who deliver prematurely are more susceptible to postpartum bleeding due to the immaturity of the vascular and uterine muscle systems, which can exacerbate uterine atony, a leading cause of PPH. Furthermore, preterm births often involve complex medical interventions, such as cesarean sections, which further elevate the risk of bleeding.[39] Larger infant birth weight is similarly associated with an increased risk of PPH. Mothers who deliver infants weighing over 4,000 grams are twice as likely to develop PPH as those delivering infants of average weight, primarily due to excessive uterine distension, which impairs normal uterine contractions.[40] Uterine atony, a primary cause of PPH, often results from the uterus's inability to contract efficiently after the delivery of a large baby.

Another important risk factor for postpartum hemorrhage is cesarean sections; studies show that women who have cesarean deliveries are more likely to have PPH than those who deliver vaginally.[41] The heightened risk is attributed to several factors, including greater trauma to the uterine tissue during surgery, which impairs the uterus's ability to contract effectively after delivery. Complications such as uterine atony, where the uterine muscles fail to contract properly, are more frequently observed in women following cesarean sections.[42]

Risk factors for postpartum hemorrhage in developing countries

Uterine atony is what causes PPH, as evidenced by multiple studies emphasizing its high prevalence across various populations.[12,27,43] This condition is marked by inadequate contraction of myometrial cells when endogenous oxytocin is released during childbirth.[36] Inadequate compression of the blood vessels within myometrial fibers leads to improper closure at the placental implantation site, resulting in the inability to stop postpartum bleeding.[44] This is more frequently seen in more pregnancies than in ones that were singletons, primarily due to excessive uterine distension, which impairs contractions and increases the risk of uterine atony.[14] Mechanical factors such as uterine overdistension, which compromise myometrial contractility, contribute to approximately 80% of PPH cases.[45]

Additionally, meconium-stained amniotic fluid (MSAF) has been consistently shown as a significant risk factor for PPH after vaginal delivery. Studies reveal that MSAF, compared to clear amniotic fluid, is linked to a higher risk of moderate and severe PPH.[46] Epidemiological and retrospective studies further confirm meconium contamination as a notable contributor to PPH.[47] Another identified risk factor is the use of forceps during labor, which, although it expedites delivery and reduces labor duration, is associated with an increased risk of PPH due to trauma to vaginal and perineal tissues, potential uterine atony, and the need for episiotomy or larger tears.[48]

Hemoglobin levels below 10 g/dL also show a strong negative correlation with the likelihood of PPH.[19,25,49] Severe prenatal anemia, by impairing uterine contractions during labor, increases PPH risk, as weaker contractions are more common in anemic women and lead to inadequate uterine contraction and subsequent bleeding after delivery.[50] Similarly, women with placenta previa are at a significantly higher risk, facing a 6- to 20-fold increased chance of PPH compared to those without the condition.[22,30,31,49] Placenta previa hinders the uterus's ability to contract efficiently, which is critical for controlling postpartum bleeding, and it is often associated with placenta accreta, further increasing the risk of PPH through disruption of uterine smooth muscle contractions.[22]

Furthermore, obesity, specifically a BMI over 35 kg/m², serves as an independent risk factor for both PPH and severe PPH.[29] Research shows that women who are overweight or classified as class I obese are more likely

to experience PPH and uterine atony compared to those with a normal BMI.[51] Obesity impacts uterine contractility, as high-fat and high-cholesterol diets reduce the expression of contractility-related proteins, thus decreasing contractile activity during labor and elevating PPH risk.[52] Another contributing factor is preeclampsia, which is linked to a higher likelihood of transfusion following twin deliveries and is an independent risk factor for severe PPH.[30] Preeclampsia may exacerbate PPH risk through decreased anti-thrombin III activity or platelet counts, with severe preeclampsia (SPE) also correlating with increased prenatal plasma D-dimer levels, further linking it to PPH.[53]

Multiparity, particularly in women with higher parity, is another significant risk factor for primary PPH.[27,29] Women with more than four births may experience reduced uterine muscle elasticity, resulting in less effective contractions, thus raising the risk of PPH.[54] Additionally, higher parity increases the likelihood of placenta previa, further elevating PPH risk.[44] Racial and ethnic differences also play a crucial role in PPH incidence, with the Southeast Asian ethnic group identified as a higher-risk population.[12,29] Ethnic disparities in PPH outcomes[55] are influenced by biological, cultural, and socioeconomic factors, impacting treatment options and the overall management of peripartum complications, including peripartum hysterectomy.[56]

The strength of this article lies in its selection of studies from various countries, both developed and developing, encompassing a wide range of postpartum hemorrhage risk factors, thus providing a more comprehensive perspective. However, the limitation of this article is the restricted database used, which narrows the scope of the findings obtained.

CONCLUSION

Based on the 20 articles reviewed, 7 came from developed countries and 13 reports came from developing countries. The research findings reveal differences in the risk factors contributing to PPH between developed and developing countries. PPH in developed countries is primarily linked to medical interventions and prolonged labor, while in developing countries, anemia, uterine overdistension, and delivery trauma are key factors, with sociocultural disparities exacerbating risks globally. It is hoped that this systematic review will serve as evidence of previous research, thereby providing a reference for identifying factors that can influence the occurrence of PPH. Given the various risk factors identified, it is hoped that a policy will be established for screening pregnant, maternity, and postpartum women to reduce the risk of PPH.

DISCLOSURES

Acknowledgment

The Master of Midwifery study program at ‘Aisyiyah University in Yogyakarta provided funding for this study. Furthermore, the writer expresses gratitude to all those who contributed to the preparation of this systematic review.

Conflict of interest

Every author has no competing interests.

Funding

There has been no external funding for this research.

Author Contribution

All authors participated in all phases of this research, including planning, collecting and analyzing data, drafting, and approving the manuscript for publication.

REFERENCES

1. Gustiani R, Kartini F. Factors affecting postpartum haemorrhage on postpartum mother. Placentum. Jurnal Ilmiah Kesehatan dan Aplikasinya. 2023;11(1):13-22. doi: 10.20961/ placentum.v11i1.55528.
2. WHO. Maternal Mortality [Internet]. 2024 [Cited 2024 Jul 13]. Available From: https://www.who.int/news-room/fact-sheets/detail/maternal-mortality
3. Ministry of Health, Republic of Indonesia. Turunkan angka kematian ibu melalui deteksi dini dengan pemenuhan USG di Puskesmas [Reduction of maternal mortality rate by early detection with USG at health centers] [Internet]. 2023 [Cited 2024 Jul 13]. Available from: https://kemkes.go.id/id/turunkan-angka-kematian-ibu-melalui-deteksi-dini-dengan-pemenuhan-usg-di-puskesmas
4. Ministry of Health, Republic of Indonesia. Dana Alokasi Khusus (DAK) fisik bidang kesehatan dalam mendukung target penurunan angka kematian ibu dan anak [Physical Special Allocation Fund (DAK) for the health sector to support the target of reducing maternal and child mortality rates]. In: Analisis RKP dan Pembicaraan Pendahuluan APBN [RKP Analysis and Preliminary Discussion of the State Budget]. 2021.

Available from: https://share.google/sUplaWL0YbiCbKLfr.
5. World Bank. Angka Kematian Ibu Indonesia Ketiga Tertinggi Di Asia Tenggara [Indonesia's Maternal Mortality Rate is the Third Highest in Southeast Asia] [Internet]. 2021. [Cited 2024 Jul 13]. Available from: https://databoks.katadata.co.id/demografi/statistik/3df25d0a2d01f36/angka-kematian-ibu-indonesia-ketiga-tertinggi-di-asia-tenggara
6. Abecassis A, Wainstock T, Sheiner E, et al. Risk factors for early postpartum hemorrhage: A retrospective, population-based, cohort analysis. Int J Gynaecol Obstet. 2024;166(2):812-8. doi: 10.1002/ijgo.15414. Epub 2024 Feb 6. PMID: 38321817.
7. Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 183: Postpartum hemorrhage. Obstet Gynecol. 2017;130(4):e168-e186. doi: 10.1097/AOG.0000000000002351. PMID: 28937571.
8. Bienstock JL, Eke AC, Hueppchen NA. Postpartum hemorrhage. N Engl J Med. 2021;384(17):1635-45. doi: 10.1056/NEJMra1513247.
9. Pollock D, Peters MDJ, Khalil H, et al. Recommendations for the extraction, analysis, and presentation of results in scoping reviews. JBI Evid Synth. 2023;21(3):520-32. doi: 10.11124/JBIES-22-00123. PMID: 36081365.
10. Bramer WM, de Jonge GB, Rethlefsen ML, et al. A systematic approach to searching: an efficient and complete method to develop literature searches. J Med Libr Assoc. 2018;106(4):531-41. doi: 10.5195/jmla.2018.283. Epub 2018 Oct 1. PMID: 30271302; PMCID: PMC6148622.
11. Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. Ann Intern Med. 201;169(7):467-73. doi: 10.7326/M18-0850. Epub 2018 Sep 4. PMID: 30178033.
12. Bazirete O, Nzayirambaho M, Umubyeyi A, et al. Risk factors for postpartum haemorrhage in the Northern Province of Rwanda: A case control study. PLoS One. 2022;17(2):e0263731. doi: 10.1371/journal.pone.0263731. PMID: 35167600; PMCID: PMC8846539.
13. Bernitz S, Betran AP, Gunnes N, et al. Association of oxytocin augmentation and duration of labour with postpartum haemorrhage: A cohort study of nulliparous women. Midwifery. 2023;123:103705. doi: 10.1016/j.midw.2023.103705. Epub 2023 May 9. PMID: 37244235.
14. Cao X, Luo Y, Zhou S, et al. Twin growth discordance and risk of postpartum hemorrhage: A Retrospective Cohort Study. Front Med (Lausanne). 2022;9:876411. doi: 10.3389/fmed. 2022.876411. PMID: 35692549; PMCID: PMC91 74790.
15. Fang ZJ, Liu HF, Zhang YL, et al. Relation of meconium-stained amniotic fluid and postpartum hemorrhage: a retrospective cohort study. Eur Rev Med Pharmacol Sci. 2020;24(20):10352-10358. doi: 10.26355/eurrev_202010_23384. PMID: 33155191.
16. Fein A, Wen T, Wright JD, et al. Postpartum hemorrhage and risk for postpartum readmission. J Matern Fetal Neonatal Med. 2021;34(2):187-94. doi: 10.1080/14767058.2019.1601697. Epub 2019 Apr 9. PMID: 30919702; PMCID: PMC7135873.
17. Feng J, Zhang X. Analysis of perinatal outcome of forceps delivery and risk factors of postpartum hemorrhage. Altern Ther Health Med. 2024;30(4):102-7. PMID: 38064601.
18. Fukami T, Koga H, Goto M, et al. Incidence and risk factors for postpartum hemorrhage among transvaginal deliveries at a tertiary perinatal medical facility in Japan. PLoS One. 2019;14(1):e0208873. doi: 10.1371/journal.pone.0208873. PMID: 30625154; PMCID: PMC6326562.
19. Glenzer MM, Correia M, Nhantumbo V, et al. Postpartum hemorrhage in Sub-Saharan Africa-a prospective study in metropolitan Mozambique. J Thromb Haemost. 2023;21(12):3463-76. doi: 10.1016/j.jtha.2023.09.002. Epub 2023 Sep 13. PMID: 37709148.
20. Ashwal E, Bergel Bson R, Aviram A, et al. Risk factors for postpartum hemorrhage following cesarean delivery. J Matern Fetal Neonatal Med. 2022;35(18):3626-30. doi: 10.1080/14767058.2020.1834533. Epub 2021 Jan 28. PMID: 33508987.
21. Linde LE, Rasmussen S, Moster D, et al. Risk factors and recurrence of cause-specific postpartum hemorrhage: A population-based study. PLoS One. 2022;17(10):e0275879. doi: 10.1371/journal.pone.0275879. PMID: 36240210; PMCID: PMC9565392.
22. Li S, Gao J, Liu J, et al. Incidence and Risk Factors of Postpartum Hemorrhage in China: A Multicenter Retrospective Study. Front Med (Lausanne). 2021;8:673500. doi: 10.3389/fmed.2021.673500. PMID: 34497812; PMCID: PMC8419315.
23. Liu CN, Yu FB, Xu YZ, et al. Prevalence and risk factors of severe postpartum hemorrhage: a retrospective cohort study. BMC Pregnancy Childbirth. 2021;21(1):332. doi: 10.1186/s12884-021-03818-1. PMID: 33902475; PMCID: PMC8077797.
24. Borovac-Pinheiro A, Ribeiro FM, Pacagnella RC. Risk Factors for Postpartum Hemorrhage and its Severe Forms with Blood Loss Evaluated Objectively - A Prospective Cohort Study. Rev Bras Ginecol Obstet. 2021;43(2):113-8. doi: 10.1055/s-0040-1718439. Epub 2021 Jan 28. PMID: 33511619; PMCID: PMC10183850.

25. Nur R, Sarina HS, Patui NS, et al. Postpartum hemorrhage in maternal mothers at Anutapura Public Hospital in Palu, 2017. Gac Sanit. 2021;35 Suppl 2:S148-S151. doi: 10.1016/j.gaceta.2021.10.014. PMID: 34929799.
26. Taylor K, Noel E, Chapple AG, et al. Risk factors for postpartum hemorrhage in a tertiary hospital in South-Central Louisiana. J Matern Fetal Neonatal Med. 2022;35(25):7353-9. doi: 10.1080/14767058.2021.1948528. Epub 2021 Jul 25. PMID: 34304671.
27. Shahbazi Sighaldeh S, Nazari A, Maasoumi R, et al. Prevalence, related factors and maternal outcomes of primary postpartum haemorrhage in governmental hospitals in Kabul-Afghanistan. BMC Pregnancy Childbirth. 2020;20(1):428. doi: 10.1186/s12884-020-03123-3. PMID: 32723320; PMCID: PMC7390104.
28. Mitta K, Tsakiridis I, Dagklis T, et al. Incidence and Risk Factors for Postpartum Hemorrhage: A Case-Control Study in a Tertiary Hospital in Greece. Medicina (Kaunas). 2023;59(6):1151. doi: 10.3390/medicina59061151. PMID: 37374355; PMCID: PMC10303199.
29. Thepampan W, Eungapithum N, Tanasombatkul K, et al. Risk Factors for Postpartum Hemorrhage in a Thai-Myanmar Border Community Hospital: A Nested Case-Control Study. Int J Environ Res Public Health. 2021;18(9):4633. doi: 10.3390/ijerph18094633. PMID: 33925427; PMCID: PMC8123817.
30. Wan X, Zhao W, Zhao L, et al. Risk factors for postpartum hemorrhage after elective cesarean deliveries for twin pregnancies. Ginekol Pol. 2024;95(7):531-5. doi: 10.5603/GP.a2023.0071. Epub 2023 Aug 7. PMID: 37548501.
31. Yang Y, He J, Deng N. Factors associated with primary postpartum hemorrhage in elderly women undergoing repeated cesarean deliveries. Int J Womens Health. 2021;13:1261-1267. doi: 10.2147/IJWH.S332020. PMID: 35002333; PMCID: PMC8721015.
32. Klemettilä E, Rahkonen L, Nuutila M, et al. Role of oxytocin in prevention of postpartum hemorrhage in unplanned out-of-hospital deliveries treated by emergency medical services. Acta Obstet Gynecol Scand. 2020;99(7):901-908. doi: 10.1111/aogs.13804. Epub 2020 Jan 28. PMID: 31943125.
33. Bernitz S, Betran AP, Gunnes N, et al. Association of oxytocin augmentation and duration of labour with postpartum haemorrhage: A cohort study of nulliparous women. Midwifery. 2023;123:103705. doi: 10.1016/j.midw.2023.103705. Epub 2023 May 9. PMID: 37244235.
34. Chikkamath SB, Katageri GM, Mallapur AA, et al. Duration of third stage labour and postpartum blood loss: a secondary analysis of the WHO Champion trial data. Reprod Health. 2021;18 (1):230. doi: 10.1186/s12978-021-01284-8. PMID: 34775959; PMCID: PMC8591926.
35. Nyfløt LT, Stray-Pedersen B, Forsén L, et al. Duration of labor and the risk of severe postpartum hemorrhage: A case-control study. PLoS One. 2017;12(4):e0175306. doi: 10.1371/journal.pone.0175306. PMID: 28384337; PMCID: PMC5383278.
36. Gill P, Patel A, Van Hook JW. Uterine Atony. 2023 Jul 4. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29630290.
37. Sekar H, Joash K. Why is ethnicity a risk factor for postpartum haemorrhage? J Obstet Gynaecol. 2024;44(1):2380084. doi: 10.1080/01443615.2024.2380084. Epub 2024 Jul 17. PMID: 39016305.
38. Guan CS, Boyer TM, Darwin KC, et al. Racial disparities in care escalation for postpartum hemorrhage requiring transfusion. Am J Obstet Gynecol MFM. 2023;5(6):100938. doi: 10.1016/j.ajogmf.2023.100938. Epub 2023 Mar 21. PMID: 36948294; PMCID: PMC10481353.
39. Wang W, Liao C, Zhang H, et al. Postpartum haemorrhage risk prediction model developed by machine learning algorithms: A single-centre retrospective analysis of clinical data. Clinical and Experimental Obstetrics & Gynecology. 2024;51 (3):60. doi: 10.31083/j.ceog5103060.
40. Quezada-Robles A, Quispe-Sarmiento F, Bendezu-Quispe G, et al. Fetal macrosomia and postpartum hemorrhage in Latin American and Caribbean Region: Systematic review and meta-analysis. Rev Bras Ginecol Obstet. 2023;45(11):e706-e723. doi: 10.1055/s-0043-1772597. Epub 2023 Nov 29. PMID: 38029773; PMCID: PMC10686756.
41. Gong J, Chen Z, Zhang Y, et al. Risk-factor model for postpartum hemorrhage after cesarean delivery: a retrospective study based on 3498 patients. Sci Rep. 2022;12(1):22100. doi: 10.1038/s41598-022-23636-5. PMID: 36543795; PMCID: PMC9772352.
42. Banu D, Jikria N, Naim J, et al. Comparison of risk factors of postpartum hemorrhage among normal versus cesarean delivery cases at a secondary care center in Naogaon. Int J Reprod Contracept Obstet Gynecol. 2024;13(3):535-9. doi: 10.18203/2320-1770.ijrcog20240451.
43. Sultana R, Manzoor S, Humayan S. Primary post-partum hemorrhage: Risk factors, causes and maternal outcome. J Soc Obstet Gynaecol Pak. 2020;10(1):40–6. Avalable from: https://jsogp.net/index.php/ jsogp/article/view/320.
44. Basir F, Gnd HA, Handayani D, et al. Risk factors for uterine atony in postpartum hemorrhage patients

at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. Bioscientia Medicina: Journal of Biomedicine & Translational Research. 2023;6(17):2891–4. doi: 10.37275/bsm. v6i17.719.
45. di Marco G, Bevilacqua E, Passananti E, et al. Multiple pregnancy and the risk of postpartum hemorrhage: retrospective analysis in a tertiary level center of care. Diagnostics (Basel). 2023; 13(3):446. doi: 10.3390/diagnostics13030446. PMID: 36766551; PMCID: PMC9914228.
46. Bouchè C, Wiesenfeld U, Ronfani L, et al. Meconium-stained amniotic fluid: a risk factor for postpartum hemorrhage. Ther Clin Risk Manag. 2018;14:1671-5. doi: 10.2147/TCRM.S150049. PMID: 30254448; PMCID: PMC6140737.
47. Gallo DM, Romero R, Bosco M, et al. Meconium-stained amniotic fluid. Am J Obstet Gynecol. 2023;228(5S):S1158-S1178. doi: 10.1016/j.ajog. 2022.11.1283. Epub 2023 Apr 1. PMID: 37012128; PMCID: PMC10291742. xxx
48. Sivasambu G, Kempaiah SB, Thukral U. Risk factors for post-partum hemorrhage in patients who underwent operative vaginal delivery in a tertiary care center. International Journal of Reproduction Contraception Obstetrics and Gynecology. 2021;10(11):4085-9. doi: 10.18203/2320-1770. ijrcog20214066.
49. Liu CN, Yu FB, Xu YZ, et al. Prevalence and risk factors of severe postpartum hemorrhage: A retrospective cohort study. BMC Pregnancy Childbirth. 2021;21(1):332. doi: 10.1186/s12884-021-03818-1. PMID: 33902475; PMCID: PMC8077797.
50. Omotayo MO, Abioye AI, Kuyebi M, et al. Prenatal anemia and postpartum hemorrhage risk: A systematic review and meta-analysis. J Obstet Gynaecol Res. 2021;47(8):2565-76. doi: 10.1111/ jog.14834. Epub 2021 May 17. PMID: 34002432; PMCID: PMC9258034.
51. Butwick AJ, Abreo A, Bateman BT, et al. Effect of maternal body mass index on postpartum hemorrhage. Anesthesiology. 2018;128(4):774-83. doi: 10.1097/ALN.0000000000002082. PMID: 29346134; PMCID: PMC5849500.
52. Polic A, Curry TL, Louis JM. The impact of obesity on the management and outcomes of postpartum hemorrhage. Am J Perinatol. 2022;39(6):652-7. doi: 10.1055/s-0040-1718574. Epub 2020 Oct 14. PMID: 33053594.
53. Shao H, Gao S, Dai D, et al. The association of antenatal D-dimer and fibrinogen with postpartum hemorrhage and intrauterine growth restriction in preeclampsia. BMC Pregnancy Childbirth. 2021; 21(1):605. doi: 10.1186/s12884-021-04082-z. PMID: 34482843; PMCID: PMC8420001.
54. Hidayati SN, Budihastuti UR, Widyaningsih V. Path analysis on determinants of postpartum bleeding at Dr. Moewardi Hospital, Central Java. Journal of Maternal and Child Health. 2019;4(6): 35-47. doi: 10.26911/thejmch.2019.04. 06.04.
55. Dai J, Shi Y, Wu Y, et al. The interaction between age and parity on adverse pregnancy and neonatal outcomes. Front Med (Lausanne). 2023;10:1056 064. doi: 10.3389/fmed.2023.1056064. PMID: 36910494; PMCID: PMC9995429.
56. Wang L, Pan JY. Predictive model for postpartum hemorrhage requiring hysterectomy in a minority ethnic region. World J Clin Cases. 2024;12(22): 4865-72. doi: 10.12998/wjcc.v12.i22. 4865. PMID: 39109042; PMCID: PMC11238818.

BIBLIOMETRIC ANALYSIS

Global research trends in partograph: A bibliometric analysis

Alfun Dhiya An[1]*, Asri Nur Maulidya[2], Maria Ulfa[3]
[1]Department of Obstetrics and Gynecology, Faculty of Medicine and Health Science, Universitas Muhammadiyah Yogyakarta, Yogyakarta, Indonesia.
[2]Department of Health Administration and Policy, Faculty of Public Health, Universitas Indonesia, West Java, Indonesia.
[3]School of Medicine, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, Yogyakarta, Indonesia.

Article Info
Received Apr 14, 2025
Revised May 23, 2025
Accepted June 12, 2025
Published Aug 1, 2025

***Corresponding author:**
Alfun Dhiya An
alfundhiyaan
@fkik.umy.ac.id

Keywords:
Healthcare quality
Intrapartum care
Maternal health
Network analysis
Partograph
Performance analysis
Research trends

ABSTRACT

Objective: The present study aimed to clarify the emerging patterns in partograph utilization, its development, and its impact on clinical practice.

Materials and Methods: A bibliometric analysis was conducted using Scopus as the primary database. Articles were retrieved using the keywords "Partograph" or "Partogram" and analyzed using two strategies: performance analysis (Scopus "analyze" function) and network analysis (VOSviewer and NVivo).

Results: Five hundred and thirteen articles published between 1965 and 2025 were analyzed. Performance analysis revealed that the most cited studies focused on labor management, labor progression, and maternal and neonatal health outcomes. The leading publishing countries included Ethiopia, the United States, the United Kingdom, India, and South Africa. Network analysis identified strong connections between partograph research and healthcare quality, personnel delivery, and facilities. Research trends evolved from early studies on spontaneous delivery, dystocia, and maternal mortality to more recent investigations into partograph utilization as a healthcare service quality improvement tool. Pearson correlation analysis showed strong associations between partograph use and birth outcomes (0.81), mortality (0.78), and healthcare workers' perspectives (0.76).

Conclusion: Research on partograph utilization continues to expand, focusing on labor monitoring and its impact on maternal and neonatal outcomes. Recently, studies have shifted toward labor-management quality, healthcare service improvement, and patient safety. However, certain areas remain underexplored, presenting opportunities for further research.

How to cite: Dhiya An A, Maulidya AN, Ulfa M. Global research trends in partograph: A bibliometric analysis. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):152-163. doi: 10.20473/mog.V33I22025.152-163.

Highlights:

1. This study highlights growing global attention on the partograph as a part of labor monitoring.
2. Partograph use remains inconsistent and affects clinical decision-making and management of labor.
3. Future studies should focus on digital monitoring and policy effectiveness in intrapartum care as a part of enhancing maternal and neonatal outcomes.

INTRODUCTION

Facility-based birth has been the main focus of global efforts to lower maternal mortality over 20 years, with the coverage rising from 50% in 2000 to 77% in 2020.[1] Maternal mortality is still high despite these advancements, especially in low- to lower-middle-income countries, where 94% of maternal deaths occur.[2] Although prompt measures are necessary for labor complications and postpartum hemorrhage, poor mother and newborn outcomes are nevertheless a result of care delays. A low-cost labor monitoring tool, partograph, has been widely promoted for the early detection of labor complications.[3]

Existing studies highlight low completion rates and poor interpretation of partographs, often due to a lack of training and the perception that it is merely a documentation formality rather than a clinical decision-making tool.[4,5] In settings with high workloads and workforce shortages, partograph documentation is frequently neglected, leading to inadequate emergency obstetric care.[6] Asphyxia continues to be an avoidable contributor to neonatal mortality, and poor partograph adherence limits its potential to aid early fetal distress detection and timely interventions.[7] These challenges highlight a persistent gap between policy recommendations and real-world implementation.

Research has predominantly focused on the partograph's clinical benefits, yet studies remain fragmented and lack a comprehensive overview of its adoption, implementation barriers, and evolving role in labor management.[8,9] Moreover, no study has systematically mapped global research trends on partograph utilization to identify knowledge gaps and future research directions.

This study addresses a gap in the literature by conducting a bibliometric analysis of partograph-related research. No comprehensive bibliometric study has mapped the evolution of partograph research or identified thematic trends and underexplored areas in obstetric care. The findings aim to provide a foundation for future research and policy recommendations to optimize partograph utilization as an effective labor monitoring tool in reducing maternal and neonatal morbidity and mortality.

MATERIALS AND METHODS

Source information

This study used an electronic online database, Scopus (https://www.scopus.com/). Scopus is the most comprehensive abstract and references database, which has been carefully chosen and has more information about peer-reviewed literature. The online search was performed on 25 March 2025. The data gathered during the same period to prevent bias caused an increase in the number of published journals in the database. The search results were then analyzed using bibliometric analysis that combines two procedures: (1) performance analysis as the main technique and (2) network analysis as an enrichment technique.

Search strategy

The keywords were selected to filter the information, so a search within the Scopus database can be conducted. The keywords used were "Partograph" or "Partogram". Side functions in the Scopus menu bar allow the researcher to refine the obtained data by publication year, subject area, document type, geographical distribution, or even language used. This study did not set time limitations to capture research trends from the beginning of the first article related to keywords, which was published in 1965.[10]

The search strategy is shown in Figure 1. The search query employed to obtain the necessary data was: (title-abs-key(partograph) or title-abs-key(partogram)) and (limit-to(subjarea, "medi") or limit-to(subjarea, "nurs") or limit-to(subjarea, "mult") or limit-to(subjarea, "bioc") or limit-to(subjarea, "comp") or limit-to(subjarea, "engi") or limit-to(subjarea, "soci") or limit-to(subjarea, "heal") or limit-to(subjarea, "agri") or limit-to(subjarea, "busi")) and (limit-to(doctype, "ar")) and (limit-to(pubstage, "final")) and (limit-to(srctype, "j")) and (limit-to(language, "English")).

Bibliometric indicators, analytics, and mapping

Performance analysis was done by applying the "analyze" feature in the Scopus menu section to present the various research constituents. Performance analysis using Scopus search results was analyzed descriptively. This article presents a performance analysis consisting of publication and citation numbers per year, number of contributing authors, most cited articles, and most active countries. Publication of the article represents productivity. Citation is a metric that quantifies the influence or impact of an area of study.[11]

All data from the Scopus Search query were exported in *.ris format to be processed for the network analysis. Network analysis was done using two strategies: (1) network visualization generated using VOSviewer and (2) qualitative interpretation using the NVivo software. Vosviewer analysis visualizes the most dominant keywords and the correlation between one topic and

another. The advantage of using VOSviewer analysis was that the researcher could adjust the study's desired or less relevant keywords. The NVivo software facilitated the qualitative interpretation of the prior study's indicators, variables, and keywords. The minimum occurrence of keywords was kept under 10 to maintain relevance. Finally, bibliometric research does not involve humans or animals as subjects. Consequently, this study did not require ethical approval as it was based on publicly available data from Scopus-indexed publications and did not involve human subjects or identifiable personal data.

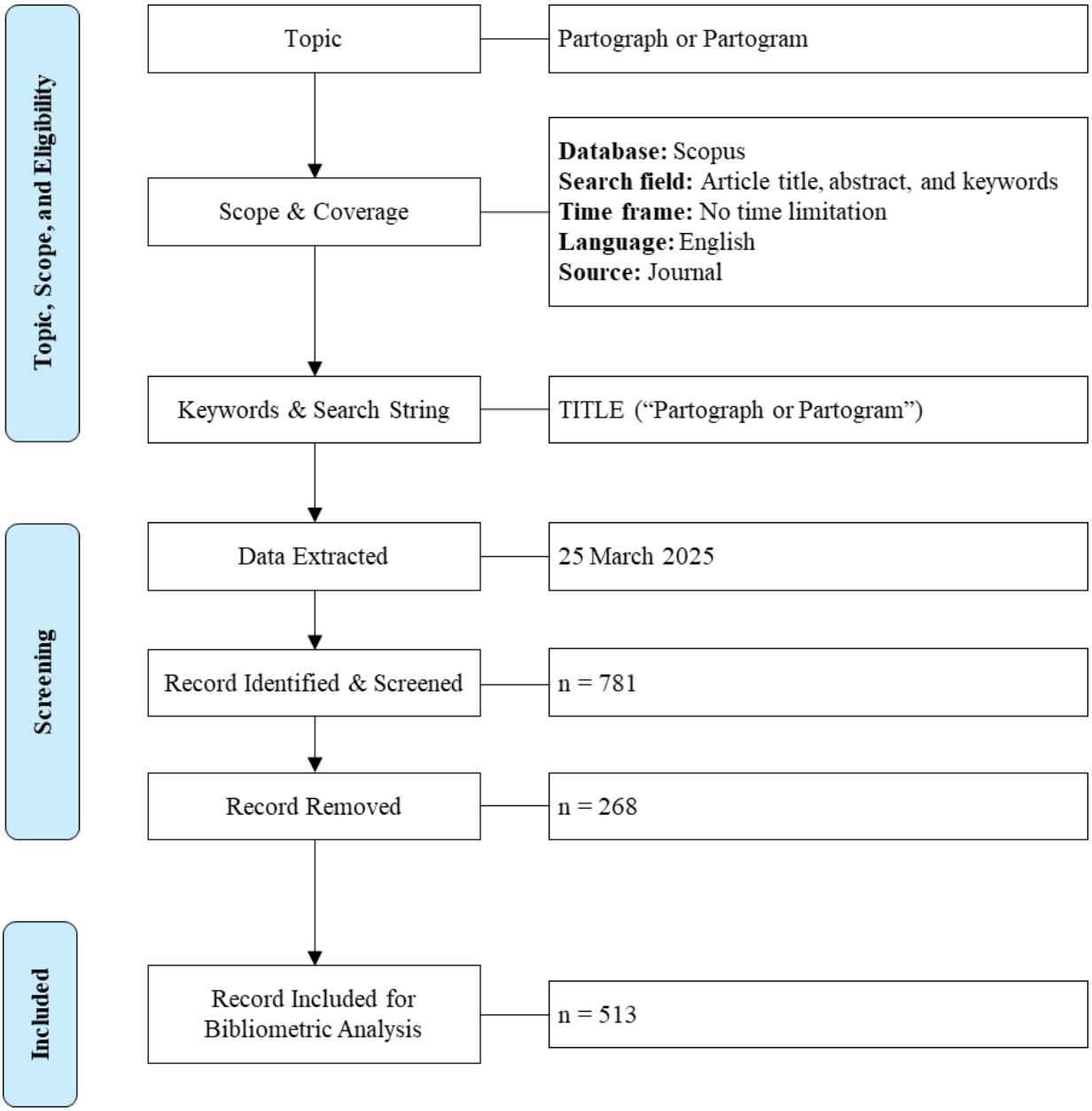


Figure 1. Flow diagram of search strategy

RESULTS AND DISCUSSION

Performance analysis is conducted based on journals, articles, authors, institutions, and countries. Performance analysis represents the usage of "Partograph" or "Partogram" in the title, abstract, and keywords. First, performance analysis was carried out to show the research trend related to "Partograph" or "Partogram" since the first article published in 1965, as shown in Figure 2. From 1965 until the online search was performed, 513 articles were retrieved. The first article was titled "Introduction, use, and results of a new Partogram".[10] The trend shows a gradual increase in publications, with a significant surge in recent decades and substantial growth between 2010 and 2021. This suggests increasing global recognition of the importance of the partograph in obstetric care.

The number of citations of the articles was then analyzed to reflect the impact and influence of the "Partograph" or "Partogram" written in the scientific community's title, abstract, and keywords.[11,12] Table 1 displays the top 10 most frequently cited articles in the partograph study.[13–22] The highest-cited article was "Contemporary Patterns of Spontaneous Labour with Normal Neonatal Outcomes," published in Obstetrics and Gynaecology and received 605 citations.[13] The three most cited articles primarily focus on spontaneous labor patterns, partograph in labor management, and birth attendant skills, which are critical aspects of intrapartum care.[13–15]

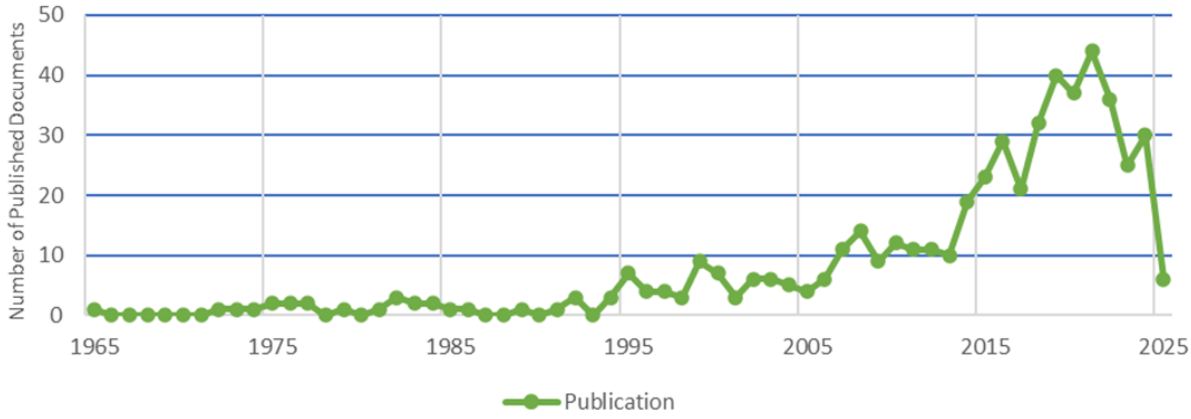


Figure 2. Annual growth of publication activity

Table 1. Top 10 cited articles

No.	Article title	Author	Year	Journal	Number of citations
1.	Contemporary patterns of spontaneous labor with normal neonatal outcomes	Zhang J, et al.	2010	Obstetrics and Gynecology	605
2.	World Health Organization partograph in management of labour	WHO	1994	The Lancet	249
3.	Are skilled birth attendants really skilled? A measurement method, some disturbing results and a potential way forward	Harvey S A, et al	2007	Bulletin of the world health organization	170
4.	Association between anaemia during pregnancy and blood loss at and after delivery among with vaginal births in Pemba Islam, Zanzibar, Tanzania	Kavle J A, et al	2008	Journal of Health, Population and Nutrition	126
5.	Partograms and Nomograms of cervical dilataion in management of primigravid labour	Studd J, et al	1973	British Medical Journal	108
6.	Progress in childbirth care in brazil: preliminary results of two evaluation studies	Leal M D C, et al	2019	Cadernos de saude publica	83
7.	Use and abuse of oxytocin for augmentation of labor	Selin L, et al	2009	Acta Obstetricia et Gynecologica Scandinavica	75
8.	Predictive value of cervimetric labour patterns in primigravida	Cardozo, L D, et al	1982	BJOG: An International Journal of Obstetrics & Gynecology	70
9.	Duration of second stage of labor and instrumental delivery as risk factors for severe perineal lacerations: population-based study	Simic M, et al	2017	BMC Pregnancy and Childbirth	69
10.	The sonopartogram: a novel method for recording progress of labor by ultrasound	Hassan W A, et al	2014	Ultrasound in Obstetrics and Gynecology	67

To highlight the research productivity of the article publications globally, the data were visualized using Microsoft Excel 365. As shown in Figure 3, the darker shades represent higher publication output, indicating a strong academic focus on this topic. National contributions to scientific research are the key indicators of research engagement, maternal health research initiatives, and healthcare prioritization.[23] The most published were from Ethiopia, the United States, the United Kingdom, India, and South Africa.

Network analysis was conducted using VOSviewer and NVivo to visually analyze dominance and interconnections between keywords. VOSviewer provides three visualization modes: network, overlay, and density, where the node and label size reflect keyword significance. From 513 Scopus-indexed articles from 1965 to 2025, 2.337 keywords were extracted. Then, the extracted keywords were filtered, and 72 met the criteria after filtering for a minimum occurrence of 10 keywords.

The VOSviewer network analysis (Figure 4) identified five distinct research clusters, each represented by colors, highlighting key themes in partograph-related studies. The most dominant keyword, "Partograph," was strongly associated with "healthcare quality, healthcare personnel, delivery, and healthcare facility." The peripheral positioning suggests underexplored research areas in this study. This analysis provides insight into major themes, research gaps, and future directions.[24,25]

Table 2 and Figure 4 show that Cluster 1 (Red, 31.9%) focused on the relationship between partograph utilization, healthcare protocols, and medical decision-making, particularly in diagnosing dystocia and guiding hospital referrals. A lack of understanding of the normal labor curve among healthcare personnel has resulted in sub-optimal decision-making, limiting the effectiveness of maternal health protocols during labor. This gap contributes to missed opportunities for life-saving interventions, unnecessary cesarean sections, and adverse maternal and neonatal outcomes, including neonatal asphyxia and post-partum hemorrhage.[3,26,27]

Cluster 2 (Green, 23.6%) emphasized structural challenges in partograph utilization, linking underuse to deficiencies in clinical practice monitoring, utilization review, and the need for in-service training. The findings suggest that inadequate institutional support and insufficient training programs hinder effective implementation of the partograph in maternal healthcare management.[6,8,9]

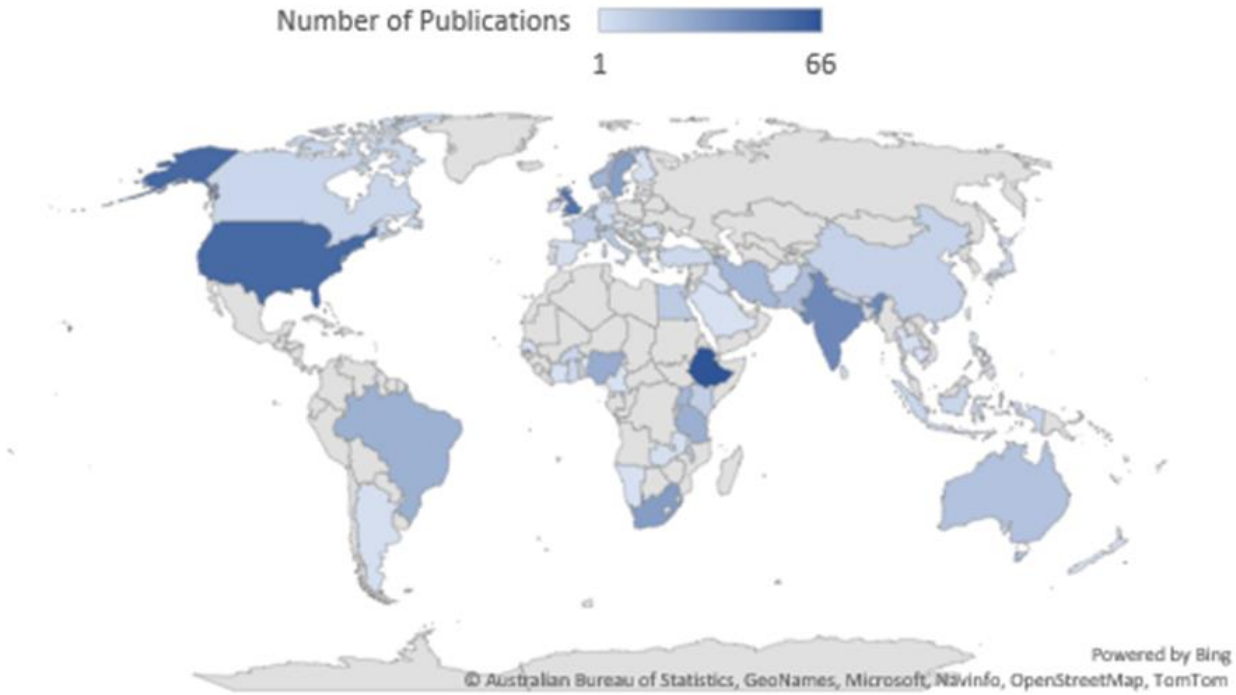


Figure 3. Geographical distribution of publications

Table 2. Cluster analysis

Cluster	Keyword items	Total	Percentage	Theme	Article titles	Authors, and (years)	Study findings
Cluster 1	Asphyxia neonatorum, cesarean section, clinical protocol, dystocia, emergency surgery, fetus weight, forceps delivery, information processing, instrumental delivery, labor curve, labor onset, malpresentation, maternal morbidity, medical decision making, medical record, newborn hypoxia, partogram, postpartum hemorrhage, prolonged labor, time factors, treatment indication, trial of labor, vacuum extraction.	23 items	31.9%	Clinical decision-making and maternal health outcomes	Disclosing suboptimal indications for emergency cesarean sections due to fetal distress and prolonged labor: a multicenter cross-sectional study at 12 public hospitals in Nepal	Helena L, et al. (2020)	This study identified that an 18% CS rate was linked to suboptimal CS indications due to inadequate fetal heart rate during labor monitoring and poor partograph use.[27]
Cluster 2	Attitude to health, clinical competence, decision support technique, diagnostic techniques, obstetrical and gynecological, fetal monitoring, health care personnel, health care utilization, health knowledge, attitude, practice, in-service training, in-service training, obstetric procedure, organizational and management, partograph, physiologic monitoring, uterine activity monitoring utilization, utilization review.	17 items	23.61%	Clinical competence and structural issues	Level of partograph utilization and its associated factors among obstetric caregivers at public health facilities in East Gojam Zone, Northwest Ethiopia.	Zelellw and Tegegne (2018)	This study evaluated the utilization of the Partograph and the factors associated with obstetrics caregivers. The study indicated that healthcare personnel possessed substantial knowledge, yet their application was limited. On-the-job training has the potential to enhance health outcomes substantially.[6]
Cluster 3	Cause of death, cervical dilatation, delivery, documentation, health care facility, health services accessibility, maternal mortality, medical audit, obstetrical surgery, patient referral, perinatal mortality, referral, and consultation.	12 items	16.67%	Medical documentation and referral system	Quality of comprehensive emergency obstetric care through the lens of clinical documentation on admission to labour ward.	Kosgei RJ, et al. (2016)	This study determined the comprehensive emergency obstetric quality care level through clinical documentation indicators. This study found that completion of partograph parameters varied: cervical dilatation (73%), contractions (72%), fetal heart rate (71%), maternal blood pressure (67%), fetal head descent (65%), maternal pulse rate (59%), liquor (48%), degree of moulding (36%), maternal temperature (42%), maternal respiratory rate (31%). The variation of partograph completion limits partograph effectiveness and affects labor management decisions. Poor record-keeping could compromise the continuity of care and timely interventions during labor.[28]
Cluster 4	Clinical assessment tool, health care planning, healthcare quality, intrapartum care, labor pain, newborn care, patient safety, protocol compliance, quality improvement, scoring system, skilled birth attendant, total quality management.	12 items	16.67%	Healthcare planning and quality management	Effect of partograph use on outcomes for women in spontaneous labour at term and their babies.	Lavender T, Cuthbert A, and Smyth R (2018)	This study determined the efficacy and safety of partograph utilization on pregnancy outcomes. The study found that routine partograph use as a standard labor management tool remains uncertain. A comparison of action line placement shows that the three-hour action line group is linked to a higher cesarean rate compared to the four-hour action line (RR 1.7, 95% CI 1.07-2.70). This early identification increases the intervention rate without clear benefits on maternal and neonatal outcomes. A partograph with an alert line only resulted in a lower cesarean section than one with an alert and action line (RR 0.68, 95% CI 0.50-0.93). This resulted from reduced mandatory interventions and an emphasis on clinical judgment regarding labor progression.[29]

Cluster 5	Clinical evaluation, clinical practice, health personnel attitude, labor management, medical documentation, outcome assessment, patient monitoring, perception.	8 items	11.11%	Healthcare personnel attitudes and practices	A cross-sectional study of partograph utilization as a decision-making tool for referral of abnormal labour in primary health care facilities of Bangladesh	Khan, et al. (2018)	The study assessed how health workers practice on a partograph. The study found that Interview data showed that health workers interpret referral indications poorly from partographs. Supporting health workers in primary health centers in interpreting and decision-making related to partograph is needed to improve maternal care quality and prevent poor neonatal outcomes.[5]

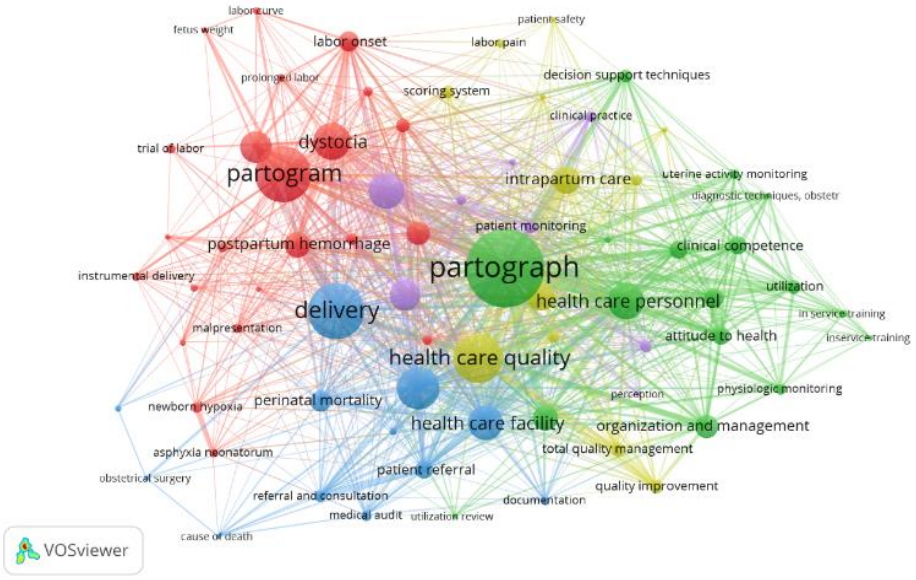


Figure 4. Network visualization

Cluster 3 (Blue, 16.7%) explored the role of the partograph in medical documentation, particularly in determining causes of death during audits and improving communication in referral coordination. Its underutilization exposed inefficiencies in healthcare communication and bureaucratic delays, which could negatively impact maternal and neonatal outcomes. Strengthening referral systems and ensuring partograph use as a standardized documentation tool may improve coordination between healthcare facilities.[28,30]

Cluster 4 (Yellow, 16.7%) examined partograph use in intrapartum healthcare planning, highlighting its role in improving care quality. The effectiveness of intrapartum care is a key indicator of total quality management in healthcare facilities. Recent maternal health paradigms emphasize positive birth experiences, making high-quality intrapartum care essential in shaping women's perceptions of childbirth. Integrating clinical excellence with patient-centered approaches enhances maternal health outcomes and aligns with efforts to improve overall service quality.[29]

Cluster 5 (Purple, 11.1%) analyzed healthcare personnel's perceptions of patient monitoring, medical documentation, and clinical practice related to partograph use. The findings suggest that many providers view the partograph as a routine formality rather than a critical decision-support tool, leading to gaps in clinical practice and ineffective labor monitoring. Many studies focus on how partograph is viewed from a clinical perspective rather than as a basis for policy enforcement or the digitalization of labor monitoring. Addressing this issue requires a shift in clinical training and policy enforcement to ensure the partograph is fully utilized to improve maternal and neonatal health outcomes.[5]

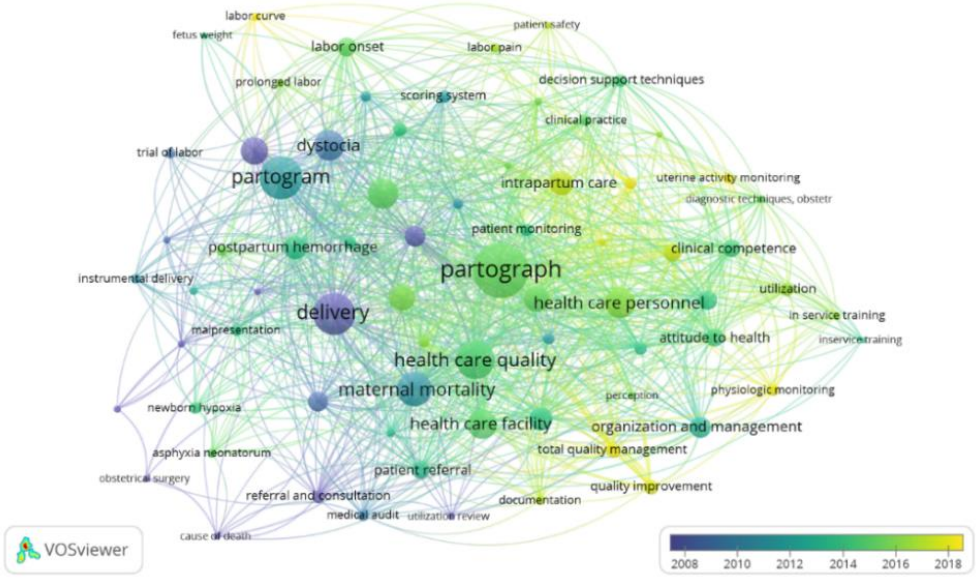


Figure 5. Overlay visualization

The cluster analysis offers important clinical insights into the practical use of the partograph. By identifying key thematic groupings, such as clinical decision-making, structural issues, referral system, healthcare planning and quality management, and healthcare personnel practices. This analysis highlights which aspects of partograph utilization are well-studied and which remain underexplored. Additionally, cluster focusing on clinical competence and training reinforces the need for capacity building among healthcare personnel in using the partograph effectively. The peripheral clusters reveal opportunities for future research in areas such as digital monitoring, quality assurance, and patient-centered care, which can strengthen the integration of the partograph into routine obstetric services. The cluster analysis provides actionable evidence for clinicians, health managers, and policy makers to improve maternal care systems and ensure timely, lifesaving interventions during labor.

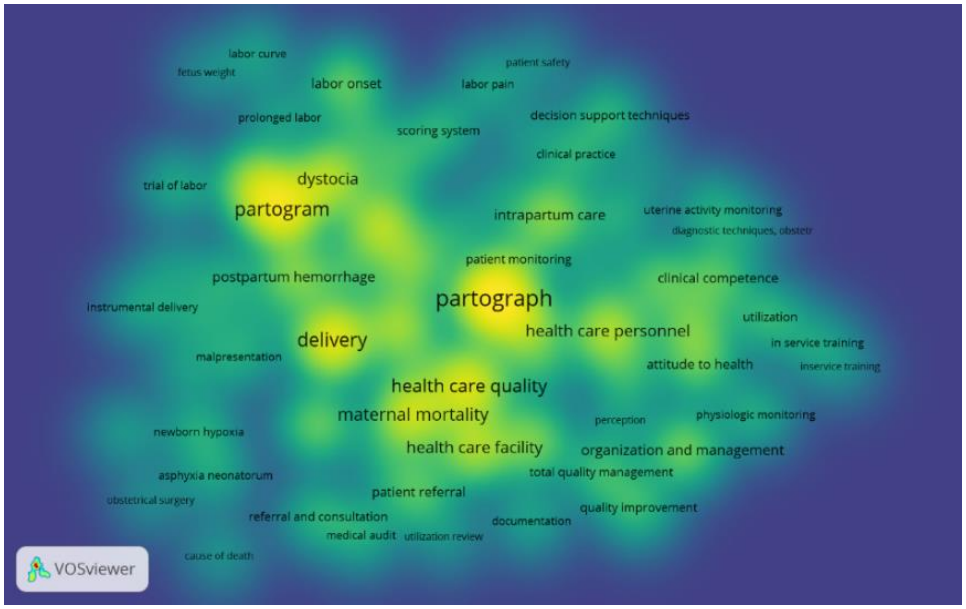


Figure 6. Density visualization

The overlay visualization (Figure 5) classifies the research shift from labor management to maternal mortality and healthcare access, then evolving to service quality. Meanwhile, the density visualization (Figure 6) provides an overview of the research landscape, highlighting key focus areas. The red and yellow regions represent higher keyword density and significance, while blue areas indicate less-explored topics. Figure 6 shows that no subject has been extensively developed and remains underexplored, suggesting ongoing gaps in maternal healthcare studies. Keywords such as "partograph, partogram, healthcare quality, delivery, and maternal mortality" have the highest density as research themes.

The trending topic of the keyword presented in Table 3 resulted from NVivo analysis. It shows the authors' size of frequency words. Since the first article was published in 1965, health (n=16.488), care (n=12.099), labor (n=10.127), pregnancy (n=7.472), and delivery (n=5.654) are the most trending terms used in the articles. Furthermore, the researchers found that partograph research trends were highly used as part of healthcare during labor,[30,31] as a basis to maintain clinical quality,[8,28] prevent mortality for both mother and fetus,[7,32] and as a part of childbirth management.[5]

The relation trend in Table 4 resulted from NVivo, which showed the Pearson Correlation Coefficient to reflect the correlation value between words. A strong correlation was found between Partograph with mortality, neonatal, perinatal mortality, and monitoring. Besides that, "Partogram" keywords strongly correlate with healthcare workers' perspectives. "Partogram" keywords found are quite strong with monitoring, rural health facilities, health facilities, and primary healthcare facilities.[6,33]

The bibliometric analysis holds practical relevance for clinicians, health managers, and policymakers by identifying critical gaps in the implementation, documentation, and training related to the routine clinical practice of the partograph. Addressing these gaps is essential to strengthen intrapartum care and reduce preventable maternal and neonatal complications. The bibliometrics analysis demonstrates how partograph research has been evolving from a basic labor monitoring tool to broader themes like maternal safety, health worker competency, and health system quality improvement.[8,27]

The partograph is a real-time monitoring tool that facilitates timely and evidence-based clinical decisions during labor. The deficiencies in implementation, training, and documentation contribute to inaccuracies in clinical decision making and delays in referrals.[9,31] The proper use of partograph is vital in low-resource settings, where the third phase delay is often caused by insufficient labor assessment and late referral, as it remains a major barrier to quality care.[34] The partograph supports early identification of complications such as prolonged labor, enabling prompt referral and management to reduce further morbidity risk, such as a low 5th APGAR Score, especially in primary care and rural health facilities.[35] The strong correlation between partograph and neonatal mortality further underscores its potential role in reducing preventable deaths when properly utilized.[36]

Table 3. Trending topic of the keyword

Words	Length	Count	Words	Length	Count
Health	6	16.488	Clinical	8	3.372
Care	4	12.099	Quality	7	3.273
Labor	5	10.127	Birth	5	3.241
Pregnancy	9	7.472	Mortality	9	3.122
Delivery	8	5.654	Hospital	8	3.027
Obstetric	9	5.630	Section	7	2.977
Maternal	8	5.596	Cesarean	8	2.898
Labor	6	4.132	Childbirth	10	2.478
Newborn	7	3.799	Management	10	2.345
Partograph	10	3.602	Outcome	7	2.232

Table 4. Relation of partograph or partogram keywords

Code A	Code B	Pearson Correlation Coefficient
Partograph	Birth	0.807609
	Mortality	0.78269
	Neonatal	0.777066
	Perinatal mortality	0.769482
	Monitoring	0.751678
Partogram	Health care workers perspectives	0.761183
	Monitoring	0.478388
	Rural health facilities	0.451084
	Health facilities	0.445508
	Primary health care facilities	0.441794

While this study provides a comprehensive, longitudinal overview of the global partograph literature, it is limited by its reliance on the Scopus database. It does not include a critical appraisal of individual articles. Furthermore, although network mapping identifies associations among keywords, it does not reflect the context-specific barriers or the real-world complexity of implementing the partograph in everyday practice. Future studies should bridge this gap by exploring qualitative insights from healthcare providers and evaluating digital tools that integrate partograph function into maternal care pathways.

CONCLUSION

The emerging trends in Partograph or Partogram remain developing. Despite its recognized potential, the partograph continues to be underutilized, posing a critical barrier to improving maternal and child health outcomes. This study found an underutilized partograph deeply rooted in structural challenges within maternal healthcare systems, including inadequate clinical monitoring, lack of utilization review, and insufficient in-service training. Underutilized partograph reflects poor communication and bureaucratic inefficiencies in the referral process. A persistent gap between clinical protocols and real clinical practice persisted in health-care personnel's perception that the partograph was just a procedural formality rather than a vital decision-support tool. Despite the underexplored and under-developed ongoing partograph research, the paradigm of maternal healthcare has shifted, emphasizing positive birth experiences and integrating clinical excellence with patient-centered care. Future research should prioritize integrating partograph utilization with digital monitoring technologies and embedding it into health systems as a strategic component of quality intrapartum care.

DISCLOSURES

Acknowledgment

The authors thank Universitas Muhammadiyah Yogyakarta for their assistance and guidance throughout the paper writing process.

Conflict of interest

The authors declared no conflict of interest with respect to the material presented in this study.

Funding

The authors received no external funding.

Author contribution

Study conceptualization by Alfun Dhiya An and Maria Ulfa, format analysis by Asri Nur Maulidya and Maria Ulfa, methodology by Maria Ulfa, writing original draft by Asri Nur Maulidya, and review and editing by Alfun Dhiya An.

REFERENCES

1. UNICEF. Despite recent progress, millions of births still occur without any assistance from a skilled attendant each year [Internet]. 2024 [cited 2025 Mar 27]. Available from: https://data.unicef.org/topic/maternal-health/delivery-care/
2. UNICEF. Cross-Sector Indicators: Maternal Mortality Ratio (Number of Maternal Deaths per 100.000) [Internet]. UNICEF Data Warehouse. 2019 [cited 2022 May 4]. Available from: https://data.unicef.org/resources/data_explorer/unicef/
3. Dol J, Hughes B, Bonet M, et al. Timing of maternal mortality and severe morbidity during the postpartum period: a systematic review. JBI Evid Synth. 2022;20(9):2119-94. doi: 10.11124/JBIES-

20-00578. PMID: 35916004; PMCID: PMC9594153.
4. Dhiya An AD, Emilia O. Knowledge, attitude, and skills of partograph utilization among health workers: a systematic review. Bali Medical Journal. 2023;12(1):626-30. doi: 10.15562/bmj.v12i1.3975.
5. Khan ANS, Billah SM, Mannan I, et al. A cross-sectional study of partograph utilization as a decision making tool for referral of abnormal labour in primary health care facilities of Bangladesh. PLoS One. 2018;13(9):e0203617. doi: 10.1371/journal.pone.0203617. PMID: 30188940; PMCID: PMC6126840.
6. Zelellw DA, Tegegne TK. Level of partograph utilization and its associated factors among obstetric caregivers at public health facilities in East Gojam Zone, Northwest Ethiopia. PLoS One. 2018;13(7):e0200479. doi: 10.1371/journal.pone.0200479. PMID: 30001358; PMCID: PMC6042737.
7. Löwensteyn YN, Housseine N, Masina T, et al. Birth asphyxia following delayed recognition and response to abnormal labour progress and fetal distress in a 31-year-old multiparous Malawian woman. BMJ Case Rep. 2019;12(9):e227973. doi: 10.1136/bcr-2018-227973. PMID: 31511259; PMCID: PMC6738677.
8. Taneja G, Sarin E, Bajpayee D, et al. Care around birth approach: a training, mentoring, and quality improvement model to optimize intrapartum and immediate postpartum quality of care in India. Glob Health Sci Pract. 2021;9(3):590-610. doi: 10.9745/GHSP-D-20-00368. PMID: 34593584; PMCID: PMC8514027.
9. Hagos AA, Teka EC, Degu G. Utilization of Partograph and its associated factors among midwives working in public health institutions, Addis Ababa City Administration, Ethiopia, 2017. BMC Pregnancy Childbirth. 2020;20(1):49. doi: 10.1186/s12884-020-2734-4. PMID: 31964349; PMCID: PMC6975085.
10. Rodesch F, Ehman-Ellinger C, Wilkin P, et al. Introduction, use, and results of a new Partogram. BJOG Int J Obstet Gynaecol. 1965;72(6):930–5. doi: 10.1111/j.1471-0528.1965.tb01515.x.
11. Donthu N, Kumar S, Mukherjee D, et al. How to conduct a bibliometric analysis: An overview and guidelines. Journal of Business Research. 2021; 133:285–96. doi: 10.1016/j.jbusres.2021.04.070.
12. Hirsch JE. An index to quantify an individual's scientific research output that takes into account the effect of multiple coauthorship. Scientometrics. 2010;85(3):741–54. doi: 10.1007/s11192-010-0193-9.
13. Zhang J, Landy HJ, Ware Branch D, et al. Contemporary patterns of spontaneous labor with normal neonatal outcomes. Obstet Gynecol. 2010;116(6):1281-7. doi: 10.1097/AOG.0b013e3181fdef6e. PMID: 21099592; PMCID: PMC3660040.
14. World Health Organization partograph in management of labour. World Health Organization Maternal Health and Safe Motherhood Programme. Lancet. 1994;343(8910):1399-404. PMID: 7910888.
15. Harvey SA, Blandón YC, McCaw-Binns A, et al. Are skilled birth attendants really skilled? A measurement method, some disturbing results and a potential way forward. Bull World Health Organ. 2007;85(10):783-90. doi: 10.2471/blt.06.038455. PMID: 18038060; PMCID: PMC2636500.
16. Kavle JA, Stoltzfus RJ, Witter F, et al. Association between anaemia during pregnancy and blood loss at and after delivery among women with vaginal births in Pemba Island, Zanzibar, Tanzania. J Health Popul Nutr. 2008;26(2):232-40. PMID: 18686556; PMCID: PMC2740668.
17. Studd J. Partograms and nomograms of cervical dilatation in management of primigravid labour. Br Med J. 1973;4(5890):451-5. doi: 10.1136/bmj.4.5890.451. PMID: 4758447; PMCID: PMC1587584.
18. Leal MDC, Bittencourt SA, Esteves-Pereira AP, et al. Progress in childbirth care in Brazil: preliminary results of two evaluation studies. Cad Saude Publica. 2019;35(7):e00223018. doi: 10.1590/0102-311X00223018. PMID: 31340337.
19. Selin L, Almström E, Wallin G, et al. Use and abuse of oxytocin for augmentation of labor. Acta Obstet Gynecol Scand. 2009;88(12):1352-7. doi: 10.3109/00016340903358812. PMID: 19878049.
20. Cardozo LD, Gibb DM, Studd JW, et al. Predictive value of cervimetric labour patterns in primigravidae. Br J Obstet Gynaecol. 1982;89(1):33-8. doi: 10.1111/j.1471-0528.1982.tb04631.x. PMID: 7059543.
21. Simic M, Cnattingius S, Petersson G, et al. Duration of second stage of labor and instrumental delivery as risk factors for severe perineal lacerations: population-based study. BMC Pregnancy Childbirth. 2017;17(1):72. doi: 10.1186/s12884-017-1251-6. PMID: 28222704; PMCID: PMC5320686.
22. Hassan WA, Eggebø T, Ferguson M, et al. The sonopartogram: a novel method for recording progress of labor by ultrasound. Ultrasound Obstet Gynecol. 2014;43(2):189-94. doi: 10.1002/uog.13212. PMID: 24105734.
23. King DA. The scientific impact of nations. Nature. 2004;430(6997):311-6. doi: 10.1038/430311a. Erratum in: Nature. 2004 Nov 4;432(7013):8. PMID: 15254529.
24. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric

mapping. Scientometrics. 2010;84(2):523-38. doi: 10.1007/s11192-009-0146-3. Epub 2009 Dec 31. PMID: 20585380; PMCID: PMC2883932.
25. Eck NJV, Waltman L. VOSviewer Manual. 2022 [cited 2025 Mar 27]; Available from: https://www.vosviewer.com/documentation/Manual_VOSviewer_1.6.18.pdf
26. Kune G, Oljira H, Wakgari N, et al. Determinants of birth asphyxia among newborns delivered in public hospitals of West Shoa Zone, Central Ethiopia: A case-control study. PLoS One. 2021; 16(3):e0248504. doi: 10.1371/journal.pone.0248504. PMID: 33725001; PMCID: PMC7963050.
27. Litorp H, Gurung R, Målqvist M, Kc A. Disclosing suboptimal indications for emergency caesarean sections due to fetal distress and prolonged labor: a multicenter cross-sectional study at 12 public hospitals in Nepal. Reprod Health. 2020;17(1):197. doi: 10.1186/s12978-020-01039-x. PMID: 33334355; PMCID: PMC7745386.
28. Kosgei RJ, Gathara D, Kamau RK, et al. Quality of comprehensive emergency obstetric care through the lens of clinical documentation on admission to labour ward. East African Medical Journal. 2016; 93(2):82–90. Available from: https://erepository.uonbi.ac.ke/handle/11295/96279
29. Lavender T, Cuthbert A, Smyth RM. Effect of partograph use on outcomes for women in spontaneous labour at term and their babies. Cochrane Database Syst Rev. 2018;8(8):CD005461. doi: 10.1002/14651858.CD005461.pub5. PMID: 30080256; PMCID: PMC6513424.
30. Lavender T, Bernitz S. Use of the partograph - Current thinking. Best Pract Res Clin Obstet Gynaecol. 2020;67:33-43. doi: 10.1016/j.bpobgyn.2020.03.010. Epub 2020 Mar 26. PMID: 32321672.
31. Negash BT, Alelgn Y. Proper partograph utilization among skilled birth attendants in Hawassa city public health facilities, Sidama region, Ethiopia, in 2021. BMC Womens Health. 2022;22(1):539. doi: 10.1186/s12905-022-02117-x. PMID: 36550470; PMCID: PMC9773518.
32. Said A, Malqvist M, Pembe AB, et al. Causes of maternal deaths and delays in care: comparison between routine maternal death surveillance and response system and an obstetrician expert panel in Tanzania. BMC Health Serv Res. 2020;20(1):614. doi: 10.1186/s12913-020-05460-7. PMID: 32623999; PMCID: PMC7336440.
33. Bedwell C, Levin K, Pett C, et al. A realist review of the partograph: when and how does it work for labour monitoring? BMC Pregnancy Childbirth. 2017;17(1):31. doi: 10.1186/s12884-016-1213-4. PMID: 28086823; PMCID: PMC5237234.
34. Beyene MG, Zemedu TG, Gebregiorgis AH, et al. Cesarean delivery rates, hospital readiness and quality of clinical management in Ethiopia: national results from two cross-sectional emergency obstetric and newborn care assessments. BMC Pregnancy Childbirth. 2021;21(1):571. doi: 10.1186/s12884-021-04008-9. PMID: 34412599; PMCID: PMC8377989.
35. Tantu T, Tantu T, Hailu Y, et al. Prevalence and factors associated with low 5th minute APGAR score among mothers who birth through emergency cesarean section: prospective cross-sectional study in Ethiopia. BMC Pregnancy Childbirth. 2025; 25(1):342. doi: 10.1186/s12884-025-07456-9. PMID: 40133944; PMCID: PMC11934554.
36. Blankenship SA, Raghuraman N, Delhi A, et al. Association of abnormal first stage of labor duration and maternal and neonatal morbidity. Am J Obstet Gynecol. 2020;223(3):445.e1-445.e15. doi: 10.1016/j.ajog.2020.06.053. PMID: 32883453.

REVIEW ARTICLE

Pregnancy: A window of opportunity for refining and mitigating the fetal origins of adult health and disease, and maternal cardiovascular futures

Hermanto Tri Joewono*
Master Program in Medical Education, Universitas Airlangga Teaching Hospital, RSIA(MCH) IBI Surabaya, Indonesia.

Article Info
Received Dec 20, 2024
Revised Mar 18, 2025
Accepted Apr 25, 2025
Published Aug 1, 2025

***Corresponding author:**
Hermanto Tri Joewono
hermanto.tri@fk.unair.ac.id

Keywords:
Health & disease
Longterm consequences
Maternal health
Mother & child
Pregnancy

SUMMARY

This review explores the profound impact of pregnancy on fetal development and long-term maternal cardiovascular health, emphasizing how early-life conditions shape lifelong health. The concept of Fetal Origins of Adult Disease (FOAD) or Developmental Origins of Health and Disease (DOHaD) is discussed, highlighting how maternal nutrition and environmental factors during pregnancy predispose offspring to chronic diseases later in life. Maternal mental health is also explored, with depression and anxiety during pregnancy linked to lasting effects on offspring, including increased risks of mental health disorders and chronic conditions in adulthood. The study "Like Mother, Like Daughter" is examined to illustrate intergenerational risks such as preeclampsia and intrauterine growth restriction (IUGR), emphasizing the role of maternal health. Additionally, the long-term cardiovascular consequences of adverse pregnancy outcomes—such as preeclampsia, gestational diabetes, and preterm birth—are discussed, noting that they elevate the mother's risk of cardiovascular disease (CVD) in later life. The rising prevalence of obesity during pregnancy further exacerbates these risks. The paper calls for a shift in obstetrics from a narrow focus on pregnancy management to a broader approach that addresses both maternal and fetal health for long-term benefits. By recognizing pregnancy as a critical window to influence future health, comprehensive strategies could help mitigate chronic diseases in both mothers and children.

How to cite: Hermanto TJ. Pregnancy: A window of opportunity for refining and mitigating the fetal origins of adult health and disease, and maternal cardiovascular futures. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2):164-172. doi: 10.20473/mog.V33I22025.164-172.

Highlights:

1. Maternal nutrition, mental health, and environmental factors during pregnancy significantly influence the long-term physical and mental health of offspring, supporting the concept of Fetal Origins of Adult Disease (FOAD) and Developmental Origins of Health and Disease (DOHaD).
2. Adverse pregnancy outcomes like preeclampsia and gestational diabetes increase the mother's future risk of cardiovascular disease, highlighting the need for broader maternal health strategies beyond childbirth.

INTRODUCTION

Pregnancy is a critical period that offers a unique window of opportunity to shape the future health of both the child and the mother. This review begins with the understanding that human brain growth and development commence in the womb, making the prenatal environment crucial for optimal neurological outcomes.[1-4] It then proceeds to explore the concept that early-life conditions can set the stage for lifelong health outcomes,[5-9] as evidenced by unintended historical events such as the Dutch Hunger Winter.[10-11]

The influence of maternal mental health on fetal development is also a key area of concern.[12] The study by Sherf et al., "Like Mother, Like Daughter," exemplifies how maternal conditions such as preeclampsia and intrauterine growth restriction (IUGR) can transmit health risks across generations, further highlighting the intergenerational impact of maternal health.[13]

Adverse pregnancy outcomes, such as preeclampsia, gestational diabetes, preterm birth, and IUGR, are now recognized as significant risk factors for the development of cardiovascular disease (CVD) in mothers. The rising prevalence of obesity during pregnancy exacerbates the future risk of CVD for mothers, underscoring the need for comprehensive strategies to address maternal health.[14-30]

This review explores the profound impact of pregnancy on both fetal development and maternal cardiovascular health, advocating for a broader understanding of pregnancy as a crucial period for long-term health intervention. By expanding the focus beyond the traditional approach that narrowly addresses pregnancy, birth, and the puerperium, this paper aims to highlight the importance of addressing the broader and long-term implications of maternal and fetal health. Such an approach holds significant potential to mitigate the risk of chronic diseases in both the child and the mother, leading to healthier futures for both

OVERVIEW

Human brain growth and development – the forgotten amazing growth and development

Research, particularly by Stiles and Jernigan, has highlighted the critical importance of brain growth and development that begins in the womb, encompassing key processes such as neurulation, proliferation, migration, differentiation, myelination, apoptosis, and synaptogenesis. These foundational events in brain development occur prenatally and may be more crucial than those occurring after birth. Notably, by around 26 weeks of pregnancy, neuronal proliferation ceases, meaning that humans are born with fewer neurons than they had in utero. This challenges earlier models, such as Shonkoff's brain growth chart, which emphasized postnatal growth and development. Prenatal brain development is also significantly influenced by environmental enrichment and genetic factors, setting the stage for lifelong cognitive and neurological function.

Interestingly, hearing is the first sense to develop fully while the fetus is still in the womb, underscoring the complexity and early onset of sensory development (Figure 1). This prenatal period is therefore not only crucial for establishing the basic architecture of the brain but also for determining how it will interact with and adapt to the environment after birth.[1-4] Studies on environment enrichment by Mozart compositions during pregnancy by Hermanto TJ et al in Surabaya on human and animal models, should be noted even though on small number of population.[30]

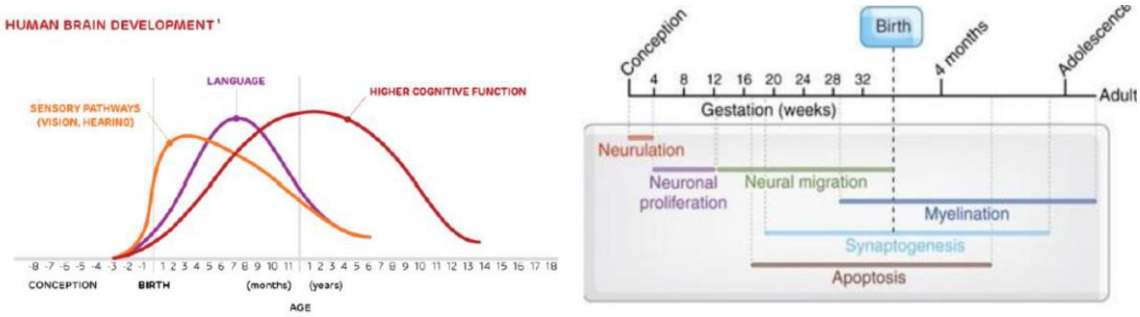


Figure 1. We have to change our perspective on human brain growth: the milestones are in the womb.[3,4]

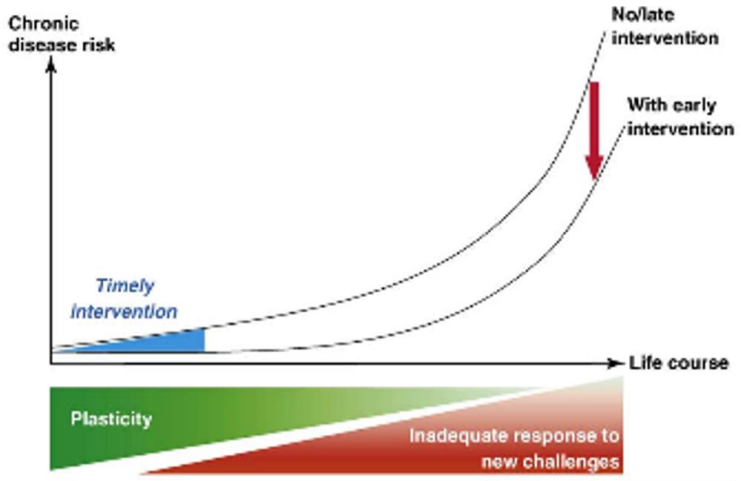


Figure 2. Relationship between early intervention vs impact,[7] but it does not explain the importance of the pregnancy period compared to the postnatal period

FOAD (fetal origins of adult disease) – important of life in the womb

The fetal origins of adult disease hypothesis, pioneered by David Barker, posits that the conditions experienced by a developing fetus can significantly influence long-term health outcomes. This groundbreaking theory emerged from Barker's observations in the 1980s, where he noted a correlation between low birth weight and higher rates of chronic diseases such as cardiovascular conditions and diabetes in adulthood. Barker suggested that environmental factors, particularly maternal nutrition during pregnancy, play a crucial role in shaping the fetal environment. Stress, inadequate nutrition, and other prenatal exposures can lead to adaptive changes in the developing fetus, which may predispose individuals to various health issues later in life. This paradigm shift not only emphasizes the importance of maternal health and prenatal care but also highlights the intricate connections between early life experiences and long-term physiological outcomes, underscoring a critical window during pregnancy that can have profound implications for public health and disease prevention strategies.[5]

DOHaD (developmental origins of health and disease) – not only in the womb or birthweight

The developmental origins of health and disease (DOHaD) hypothesis, articulated by Mark Hanson and Peter Gluckman, expands upon the ideas of fetal programming by emphasizing the intricate relationship between early life exposures and subsequent health outcomes throughout an individual's lifespan. This hypothesis posits that the environment experienced by a fetus—shaped by maternal nutrition, stress, and overall health—can lead to biological adaptations that, while beneficial for survival in the short term, may predispose individuals to chronic diseases such as obesity, diabetes, and cardiovascular issues later in life. Hanson and Gluckman argue that these adaptations are a response to the anticipated conditions of the external environment, meaning that a mismatch between early life conditions and later life realities can lead to adverse health effects. Their work underscores the importance of ensuring optimal maternal health and nutrition during pregnancy, as well as addressing social determinants of health, to improve outcomes not just for mothers and infants, but for future generations. By framing health as a continuum that begins in utero, the DOHaD hypothesis has significant implications for public health strategies, highlighting the need for early interventions that can mitigate risk factors and promote healthier lives (Figure 2).[6-9]

Dutch Hunger Winter – an unintended clinical trials study

The Dutch Hunger Winter of 1944-1945 serves as a poignant case study in the effects of maternal mal-nutrition during pregnancy, illuminating the profound impact that extreme environmental stressors can have on fetal development. During this harrowing period, a severe food blockade led to widespread famine in the Netherlands, with pregnant women facing acute shortages of essential nutrients. Research has shown that infants born during this time exhibited not only reduced birth weights but also increased susceptibility to a range of health issues later in life, including cardiovascular diseases, metabolic disorders, and mental health challenges.[10]

The experiences of those affected by the Hunger Winter underscore the principles of the developmental origins of health and disease hypothesis, revealing how prenatal exposures to starvation can trigger lasting biological changes. For instance, studies tracking this cohort have demonstrated that individuals who were exposed to starvation in utero exhibited altered epigenetic patterns, which may influence gene expression related to growth and metabolism. This phenomenon illustrates the critical role that early life conditions play in shaping lifelong health trajectories, reinforcing the importance of maternal nutrition as a foundational aspect of public health.[11]

Furthermore, the legacy of the Dutch Hunger Winter extends beyond individual health outcomes, highlighting the broader societal implications of maternal well-being. The psychological and social impacts of famine on families and communities during this time serve as a reminder that maternal and child health cannot be isolated from the socio-political context. This historical event has spurred ongoing research into the long-term effects of prenatal adversity, advocating for policies that prioritize maternal nutrition and health as vital components of disease prevention strategies, ultimately fostering healthier future generations.[10-11]

Maternal mental health: Standing ovation for Alain Gregoire at Paris FIGO Congress 2023

Maternal mental health is a crucial aspect of prenatal care, as conditions such as depression during pregnancy can have profound implications not only for the mother but also for the developing child. Research indicates that maternal depression can disrupt the intricate bonding process between mother and child, potentially leading to attachment issues and emotional disturbances in the offspring. This disruption may manifest in various ways, including behavioral problems and cognitive delays, which can persist into adulthood. Of note, Alain Gregoire, a prominent expert in perinatal psychiatry, has consistently emphasized the critical importance of addressing women's mental health during pregnancy. He argues that the psychological well-being of expectant mothers is not only vital for their own health but also for the development and future well-being of their children. Gregoire highlights that pregnancy is a period of immense physical and emotional change, making women particularly vulnerable to mental health issues such as depression and anxiety. He advocates for comprehensive mental health support systems that are integrated into prenatal care, ensuring that women receive the necessary resources and interventions to manage stress, trauma, and other psychological challenges during this crucial time. By prioritizing mental health care during pregnancy, Gregoire believes that we can significantly improve outcomes for both mothers and their children, leading to healthier families and communities.[12,13]

The intergenerational transmission of mental health issues is a significant concern. Children of mothers who experience depression during pregnancy are at a higher risk of developing their own mental health disorders, such as anxiety and depression later in life. The underlying mechanisms may involve both genetic predispositions and environmental factors including the quality of the mother-child relationship and the home environment. For instance, a mother's depressive symptoms can affect her parenting style, leading to less responsive and nurturing interactions, which are essential for healthy emotional development. Furthermore, the stress experienced by mothers during pregnancy can alter fetal development. Elevated levels of stress hormones, such as cortisol, may affect brain development, potentially leading to long-term cognitive and emotional challenges for the child. Studies have shown that children exposed to high maternal stress during pregnancy are more likely to exhibit behavioral issues, mood disorders, and difficulties in social relationships as they grow older. Addressing maternal mental health is therefore critical not only for the well-being of the mother but also for breaking the cycle of mental health issues across generations. Early intervention and support for expectant mothers can significantly reduce the risk of developing long-term mental health problems in their children. Creating a strong support system, including mental health resources, social support, and prenatal education, can foster resilience and promote healthier outcomes for both mothers and their children. Understanding the link between maternal depression during pregnancy and long-term mental health outcomes in offspring highlights the need for comprehensive mental health care in prenatal settings. By prioritizing maternal mental health, we can create a positive ripple effect that enhances the well-being of families and mitigates the risk of mental health disorders across generations.[12-14]

Study of Sherf et al., "Like Mother, Like Daughter"

In the triad study "Like Mother, Like Daughter" by Sherf et al., the researchers explore the transgenerational implications of preeclampsia and intrauterine growth restriction (IUGR). The narrative begins with the recognition that maternal health conditions during pregnancy can have lasting effects, not only on the immediate offspring but also on subsequent generations. The study highlights how daughters of mothers who experienced preeclampsia are at a heightened risk of developing similar complications in their own

pregnancies, suggesting a hereditary component to these conditions. Sherf et al. delve into the biological mechanisms that may underpin this transgenerational transmission, examining genetic, epigenetic, and environmental factors that contribute to the susceptibility of future generations. The researchers emphasize the importance of understanding these dynamics, as they can inform preventative strategies and clinical interventions aimed at mitigating risks for women with a family history of preeclampsia and IUGR. The findings underscore the critical need for healthcare providers to consider family history when assessing risks during prenatal care. By recognizing patterns that span generations, practitioners can better tailor monitoring and treatment plans. This study not only sheds light on the complex interplay of maternal health and offspring outcomes but also calls for further research to unravel the intricate pathways linking maternal experiences to the health of future generations. Ultimately, Sherf et al. advocate for a more holistic approach to maternal-fetal medicine that takes into account the legacy of maternal health conditions.[15] The "Collab team" appears to have explained the mechanism in their 2022 paper.[16]

Adverse Pregnancy Outcomes (APO) vs Maternal Future CardioVascular Disease (MFCVD)

Pregnancy is a critical period that can significantly influence a woman's long-term health, particularly concerning cardiovascular disease (CVD). Emerging research has highlighted a concerning link between adverse pregnancy outcomes—such as preeclampsia, gestational diabetes, preterm birth, and obesity—and an increased risk of future cardiovascular complications.[17,18] Preeclampsia, characterized by high blood pressure and damage to other organ systems, is one of the most significant pregnancy complications. Studies indicate that women who experience pre-eclampsia face a heightened risk of developing hyper-tension and cardiovascular disease later in life. The underlying mechanisms may include persistent vascular damage and altered metabolic profiles that persist long after delivery.[19-25]

Gestational diabetes mellitus (GDM) is another pregnancy-related condition that has been associated with long-term health implications. Women with a history of GDM are at increased risk for type 2 diabetes, which is a well-known risk factor for cardiovascular disease. The metabolic disturbances caused by GDM can contribute to endothelial dysfunction, a precursor to cardiovascular issues, highlighting the importance of monitoring these women post-pregnancy.[26-30]

Preterm birth also raises alarms regarding maternal health. Research suggests that women who deliver preterm may experience an increased risk of cardiovascular events later in life. The stress of preterm delivery and potential complications may lead to lasting changes in the cardiovascular system, necessitating ongoing surveillance for heart health in this population.[31,32]

Lastly, obesity during pregnancy compounds these risks. Maternal obesity is linked to a higher incidence of the aforementioned adverse outcomes, creating a cyclical pattern that exacerbates long-term cardiovascular risk. Women who enter pregnancy with obesity are more likely to develop complications like preeclampsia and gestational diabetes, further increasing their future cardiovascular burden.[33,34]

Table 1. Most probable mechanisms

Items	Mechanisms
FOAD DOHaD	Fetal programming via epigenetic modifications at least involving • altered DNA Methylation and • changes in histone acetylation/methylation
Dutch Hunger Winter	• Epigenetic Reprogramming of Metabolism • Stress-Induced HPA Axis Dysregulation • Endothelial Dysfunction & Cardiovascular Risk • Mismatch Hypothesis & Metabolic Adaptation
APO vs MFCVD	Complex and multifactorial, involving endothelial dysfunction, chronic inflammation, metabolic disturbances, oxidative stress, epigenetic changes, and shared genetic and lifestyle factors.
Environment Enrichment	Prenatal exposure to Mozart's 14-sequence music may enhance neuroplasticity by increasing BDNF and synapsin, while reducing neuronal apoptosis, supporting optimal brain development and cognitive function in the offspring

Environmental enrichment and fetal brain capacity

Environmental enrichment during pregnancy, such as exposure to stimulating environments and adequate nutrition, has been shown to enhance fetal brain development. Research suggests that maternal engagement in cognitive activities, physical exercise, and a balanced diet can foster neurodevelopment, potentially increasing cognitive capacities in offspring. This emphasizes the significant role of the prenatal environment in shaping brain health and cognitive outcomes, pointing to the importance of maternal lifestyle and environment during pregnancy. The interplay between pregnancy outcomes, maternal health, and fetal development represents a complex and critical area of research. Understanding these relationships is essential for developing interventions that can promote better health outcomes for both mothers and their children. Continued exploration of how prenatal experiences influence long-term health can inform public health strategies aimed at reducing the burden of chronic diseases that are linked to early life conditions. This discussion highlights the need for a holistic approach to prenatal care that not only addresses immediate pregnancy outcomes but also considers the broader, long-term implications for maternal and child health.[35-41]

Most probable mechanism

The most probable mechanism remains a subject of ongoing investigation, marked by its inherent ambiguity due to its recent discovery and the intricate interplay of multiple contributing factors (Table 1). Rather than a singular, linear pathway, emerging evidence suggests a network of interconnected mechanisms operating in parallel or sequentially, influenced by dynamic physiological, molecular, or environmental variables. This complexity challenges traditional reductionist models, requiring an integrative approach that synthesizes diverse perspectives and methodologies. As research progresses, refining our understanding of this mechanism will necessitate advanced analytical techniques and interdisciplinary collaboration to disentangle its layered intricacies.

Relationship with SDG 3's goal

This paper aligns closely with the 3rd Sustainable Development Goal (SDG) on Good Health and Well-being by advocating for a holistic approach to maternal and fetal health that extends beyond pregnancy. By emphasizing the long-term benefits of addressing maternal mental health, managing conditions like preeclampsia, gestational diabetes, and intrauterine growth restriction (IUGR), the paper highlights how proactive maternal care can lead to healthier outcomes for both mothers and their children (Figure 3). This approach not only improves immediate pregnancy outcomes but also reduces the future burden of chronic diseases such as cardiovascular disease (CVD) in mothers, supporting healthier lifespans. Additionally, by focusing on intergenerational health—how maternal health impacts the child's lifelong well-being—the paper underscores the importance of addressing both maternal and fetal health comprehensively. This contributes directly to SDG 3's goal of ensuring healthy lives and promoting well-being for all ages by fostering a healthcare system that is empathetic, informed, and preventive, thus breaking cycles of poor health across generations.[42]

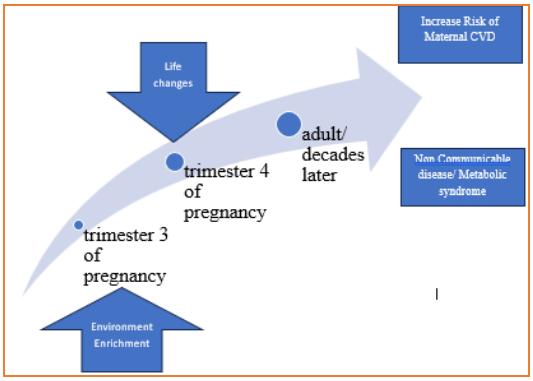


Figure 3. Proposed model for mitigating adult disease in the unborn child through environmental enrichment during third trimester of pregnancy, and reducing the increased maternal risk of future cerebrovascular disease through lifestyle changes during the fourth trimester — laying the groundwork for a healthier generation and ultimately transforming the landscape of public health for years to come.

CONCLUSION

In conclusion, the intricate interplay between maternal health during pregnancy and the long-term outcomes for both mother and child underscores the critical importance of this unique developmental window. As we have explored throughout this paper, pregnancy is not merely a period of gestation but a pivotal phase that holds the potential to shape lifelong health trajectories.

By refining our understanding of the fetal and developmental origins of adult health and disease, we can identify key interventions that may mitigate adverse outcomes. This knowledge empowers healthcare

providers to implement evidence-based strategies that promote maternal cardiovascular health and foster optimal fetal development.

Moreover, addressing maternal health proactively during pregnancy can lead to significant public health benefits, reducing the burden of chronic diseases that often emerge later in life. By recognizing and acting upon the vulnerabilities and opportunities present during this time, we can pave the way for healthier futures for both mothers and their children.

Ultimately, the narrative of pregnancy as a window of opportunity calls for a paradigm shift in how we approach maternal and child health. It emphasizes the need for a holistic view that integrates medical, social, and environmental factors, encouraging collaborative efforts among healthcare professionals, policymakers, and communities. As we move forward, let us commit to harnessing this critical period not only to improve maternal cardiovascular outcomes but also to lay the groundwork for a healthier generation, ultimately transforming the landscape of public health for years to come.

DISCLOSURES

Acknowledgment
N/A

Conflict of interest
N/A

Funding
N/A

Author contribution
N/A

REFERENCES

1. Stiles J, Jernigan TL. The basics of brain development. Neuropsychol Rev. 2010;20(4):327-48. doi: 10.1007/s11065-010-9148-4. Epub 2010 Nov 3. PMID: 21042938; PMCID: PMC2989000.
2. Ackerman S. Discovering the Brain. Washington (DC): National Academies Press (US); 1992. 6, The Development and Shaping of the Brain. Available from: https://www.ncbi.nlm.nih.gov/books/NBK234146/
3. Tau GZ, Peterson BS. Normal development of brain circuits. Neuropsychopharmacology. 2010;35(1):147-68. doi: 10.1038/npp.2009.115. PMID: 19794405; PMCID: PMC3055433.
4. National Research Council (US) and Institute of Medicine (US) Committee on Integrating the Science of Early Childhood Development. From Neurons to Neighborhoods: The Science of Early Childhood Development. Shonkoff JP, Phillips DA, editors. Washington (DC): National Academies Press (US); 2000. PMID: 25077268.
5. Calkins K, Devaskar SU. Fetal origins of adult disease. Curr Probl Pediatr Adolesc Health Care. 2011;41(6):158-76. doi: 10.1016/j.cppeds.2011.01.001. PMID: 21684471; PMCID: PMC4608552.
6. Godfrey KM, Gluckman PD, Hanson MA. Developmental origins of metabolic disease: life course and intergenerational perspectives. Trends Endocrinol Metab. 2010;21(4):199-205. doi: 10.1016/j.tem.2009.12.008. Epub 2010 Jan 14. PMID: 20080045.
7. Lacagnina S. The Developmental Origins of Health and Disease (DOHaD). Am J Lifestyle Med. 2019;14(1):47-50. doi: 10.1177/1559827619879694. PMID: 31903081; PMCID: PMC6933571.
8. Monk C, Fernández CR. Neuroscience advances and the developmental origins of health and disease research. JAMA Netw Open. 2022;5(4):e229251. doi: 10.1001/jamanetwork_open.2022.9251. PMID: 35486407.
9. Holme AM, Sitras V. Developmental origin of health and disease-Evidence and time for action. Acta Obstet Gynecol Scand. 2020;99(8):961-2. doi: 10.1111/aogs.13915. PMID: 32683681.
10. Ramirez D, Haas SA. Windows of vulnerability: consequences of exposure timing during the Dutch hunger winter. Popul Dev Rev. 2022;48(4):959-89. doi: 10.1111/padr.12513. Epub 2022 Sep 14. PMID: 37063488; PMCID: PMC10087479.
11. Lumey LH, Van Poppel FW. The Dutch famine of 1944-45: mortality and morbidity in past and present generations. Soc Hist Med. 1994;7(2):229-46. doi: 10.1093/shm/7.2.229. PMID: 11639327.
12. Bush NR, Noroña-Zhou A, Coccia M, et al. Intergenerational transmission of stress: Multi-domain stressors from maternal childhood and pregnancy predict children's mental health in a racially and socioeconomically diverse, multi-site cohort. Soc Psychiatry Psychiatr Epidemiol. 2023;58(11):1625-36. doi: 10.1007/s00127-022-02401-z. Epub 2023 Feb 3. PMID: 36735003; PMCID: PMC10397362.
13. Ganho-Avila A, Gregoire A. Breaking the Silence of Maternal Mental Health. Video by Make Mothers Matters
14. WHO. Guide for integration of perinatal mental health in maternal and child health services. 2022. Geneva: World Health Organization; Licence: CC BY-NC-SA 3.0 IGO. Available from: https://www.who.int/publications/i/item/9789240057142

15. Sherf Y, Sheiner E, Shoham Vardi I, et al. Like mother like daughter: low birth weight and pre-eclampsia tend to reoccur at the next generation. J Matern Fetal Neonatal Med. 2019;32(9):1478-84. doi: 10.1080/14767058.2017.1410124. Epub 2017 Dec 7. PMID: 29172830.
16. Korzeniewski SJ, Sutton E, Escudero C, et al. The Global Pregnancy Collaboration (CoLab) symposium on short- and long-term outcomes in offspring whose mothers had preeclampsia: A scoping review of clinical evidence. Front Med (Lausanne). 2022;9:984291. doi: 10.3389/fmed. 2022.984291. PMID: 36111112; PMCID: PMC9470009.
17. Panah LG, Park K., Honigberg, M.C. The Fourth Trimester: Adverse Pregnancy Outcomes and Long-Term Cardiovascular Risk. In: Sharma G, Scott NS, Davis MB, et al. (eds) Contemporary Topics in Cardio-Obstetrics. Contemporary Cardiology. 2023. Humana, Cham. https://doi.org/10.1007/978-3-031-34103-8_8
18. Kurkani A, Liu J, Virani SS. Adverse Pregnancy Outcomes: A Window into Cardiovascular Disease Prevention. 2020 Sept. ACC: Latest in Cardiology
19. Antipolis S. Pre-eclampsia linked with four-fold higher risk of heart attack in decade after delivery. European Journal of Preventive Cardiology. 2023 26 Jan 23. doi: 10.1093/eurjpc/zwad003
20. Aditiawarman, Zulhijayanti NA, Ernawati E, et al. A retrospective cohort study of hypertension, cardiovascular disease, and metabolic syndrome risk in women with history of preterm and term preeclampsia five years after delivery. Pregnancy Hypertens. 2023;32:57-63. doi: 10.1016/j.preghy.2023.04.003. Epub 2023 Apr 26. PMID: 37104925.
21. Carey C, Mulcahy E, McCarthy FP, et al. Hypertensive disorders of pregnancy and the risk of maternal dementia: a systematic review and meta-analysis. Am J Obstet Gynecol. 2024;231(2):196-210. doi: 10.1016/j.ajog.2024.01.013. Epub 2024 Jan 24. PMID: 38278201.
22. Khosla K, Heimberger S, Nieman KM, et al. Long-term cardiovascular disease risk in women after hypertensive disorders of pregnancy: Recent advances in hypertension. Hypertension. 2021;78 (4):927-35. doi: 10.1161/HYPERTENSIONAHA.121.16506. Epub 2021 Aug 15. PMID: 34397272; PMCID: PMC8678921.
23. Turbeville HR, Sasser JM. Preeclampsia beyond pregnancy: long-term consequences for mother and child. Am J Physiol Renal Physiol. 2020;318(6) :F1315-F1326. doi: 10.1152/ajprenal.00071.2020. Epub 2020 Apr 6. PMID: 32249616; PMCID: PMC7311709.
24. Shaw LJ, Patel K, Lala-Trindade A, et al. Pathophysiology of preeclampsia-induced vascular dysfunction and implications for subclinical myocardial damage and heart failure. JACC Adv. 2024;3(6):100980. doi: 10.1016/j.jacadv.2024.100980. PMID: 38938863; PMCID: PMC11198310.
25. Veiga ECA, Rocha PRH, Caviola LL, et al. Previous preeclampsia and its association with the future development of cardiovascular diseases: a systematic review and meta-analysis. Clinics (Sao Paulo). 2021;76:e1999. doi: 10.6061/clinics/2021/e1999. PMID: 33503177; PMCID: PMC7798130.
26. Kim C. Gestational diabetes mellitus and risk of future maternal cardiovascular disease. Expert Rev Cardiovasc Ther. 2010;8(12):1639-41. doi: 10.1586/erc.10.167. PMID: 21108545.
27. Lee SM, Shivakumar M, Park JW, et al. Long-term cardiovascular outcomes of gestational diabetes mellitus: a prospective UK Biobank study. Cardiovasc Diabetol. 2022;21(1):221. doi: 10.1186/s12933-022-01663-w. PMID: 36309714; PMCID: PMC9618212.
28. Ormazabal V, Nair S, Carrión F, et al. The link between gestational diabetes and cardiovascular diseases: potential role of extracellular vesicles. Cardiovasc Diabetol. 2022;21(1):174. doi: 10.1186/s12933-022-01597-3. PMID: 36057662; PMCID: PMC9441052.
29. Yu Y, Arah OA, Liew Z, et al. Maternal diabetes during pregnancy and early onset of cardiovascular disease in offspring: population based cohort study with 40 years of follow-up. BMJ. 2019;367:l6398. doi: 10.1136/bmj.l6398. PMID: 31801789; PMCID: PMC6891797.
30. Hildén K, Magnuson A, Montgomery S, et al. Previous pre-eclampsia, gestational diabetes mellitus and the risk of cardiovascular disease: A nested case-control study in Sweden. BJOG. 2023;130(10):1209-16. doi: 10.1111/1471-0528.17454. Epub 2023 Mar 27. PMID: 36974033.
31. Tanz LJ, Stuart JJ, Williams PL, et al. Preterm delivery and maternal cardiovascular disease in young and middle-aged adult women. circulation. 2017;135(6):578-89. doi: 10.1161/ CIRCULATIONAHA.116.025954. PMID: 281539 93; PMCID: PMC5308562.
32. Wu P, Gulati M, Kwok CS, et al. Preterm delivery and future risk of maternal cardiovascular disease: a systematic review and meta-analysis. J Am Heart Assoc. 2018;7(2):e007809. doi: 10.1161/JAHA.117.007809. PMID: 29335319; PMCID: PMC5850169.
33. Krewson C. Obesity increases cardiovascular risk from pregnancy complications. Contemp Ob/gyn 2023 October 16. Available from: https://www.contemporaryobgyn.net/view/obesity-increases-cardiovascular-risk-from-pregnancy-complications
34. O'Kelly AC, Michos ED, Shufelt CL, et al. Pregnancy and reproductive risk factors for cardio-

vascular disease in women. Circ Res. 2022;130(4): 652-72. doi: 10.1161/CIRCRESAHA. 121.319895. Epub 2022 Feb 17. PMID: 35175837; PMCID: PMC8870397.
35. Joewono HT. The evidence for the influence of musical compositions during pregnancy to the structure and functions of the offsprings' brain. Majalah Obstetri & Ginekologi. 2020;28(1):44-51. doi: 10.20473/mog.V28I12020.44-51.
36. Hermanto TJ. Bersujud dalam rahim II. Mencerdaskan janin sejak dalam rahim dengan kombinasi 11-14 lagu karya Mozart dan Nutrisi [Prostrating in the womb II: Enriching the fetus from within the womb with a combination of 11-14 Mozart Songs and Nutrition]. 2012. Surabaya: Global Persada Press.
37. Hermanto TJ. New Role for Obstetricians: Preparing Headstart in the Womb. 2002. Malang: Indonesia Society for Obstetrics-Gynecology Annual Meeting
38. Hermanto TJ. Prenatal University. Indonesiatrek: Toward a New Brighter Generations. 2002. Surabaya: Symposium on Innovation in Medical Education
39. Hermanto TJ. New Antenatal Care. 2007. Mataram: Indonesia Society for Obstetrics-Gynecology Annual Meeting
40. Hermanto TJ. Antenatal Care: Monsternity or Maternity Care? 2008. Jakarta: Maternal Fetal-Medicine Annual Meeting IX
41. Hermanto TJ. Obstetrics Revisited. 2024 – under the publication process
42. United Nations. Sustainable Development Goals. Geneve: UN.

CASE SERIES

Cervical cancer screening before hysterectomy in pelvic organ prolapse patients: Is it essential? A case series

Ekarini Aryasatiani[1,2], Raymond Surya[1]*, Dyonesia Ary Harjanti[3], Florinda Ilona[4], Chandra Dewi Kartika[4], Catalya Christina Cantika[1], Lisda Tenka[4]
[1]Department of Obstetrics and Gynecology, Tarakan Regional General Hospital, Jakarta, Indonesia.
[2]Faculty of Medicine and Health Science, Krida Wacana Christian University, Jakarta, Indonesia.
[3]Department of Anatomic Pathology, St. Carolus Hospital, Jakarta, Indonesia.
[4]Department of Anatomic Pathology, Tarakan Regional General Hospital, Jakarta, Indonesia.

Article Info
Received Oct 20, 2024
Revised Dec 6, 2024
Accepted Dec 20, 2024
Published Aug 1, 2025

***Corresponding author:**
Raymond Surya
raymond_s130291
@yahoo.co.id

Keywords:
Cervical cancer
Cervical cancer screening
Maternal health
Pap test
Pelvic organ prolapse
Vaginal hysterectomy

ABSTRACT

Objective: Pelvic organ prolapse (POP) results from weakening of the pelvic floor musculature. The reported prevalence of unexpected premalignant and malignant pathologies following hysterectomy ranges from 0.2 to 0.8%. This study aims to present a case series of patients with POP who underwent vaginal hysterectomy (VH) after preoperative evaluation for abnormal cervical cytology, which subsequently demonstrated more advanced histopathological findings.

Case Series: Case 1: A 55-year-old woman, P3A0, was diagnosed with third-degree uterine prolapse and cystocele. Pap smear revealed atypical glandular cells of undetermined significance (AGUS). Histopathological examination after VH demonstrated vaginitis and metaplastic chronic cervicitis with atypia progressing to mild dysplasia of endocervical epithelial cells/low-grade squamous intraepithelial lesion (LSIL). Case 2: A 62-year-old woman, P5A0, was diagnosed with third-degree uterine prolapse. Pap smear revealed atypical squamous cells of undetermined significance (ASCH). Histopathological evaluation after VH demonstrated high-grade squamous intraepithelial lesion (HSIL) up to carcinoma in situ with microinvasive glandular involvement and focal extension.

Conclusion: Given that cervical cancer remains the second leading cause of mortality among women in Indonesia, preoperative screening for precancerous gynecological lesions and malignancy is strongly recommended.

How to cite: Aryasatiani E, Surya R, Harjanti DA, et al. Cervical cancer screening before hysterectomy in pelvic organ prolapse patients: Is it essential? A case series. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2025;33(2): 173-179. doi: 10.20473/mog.V33I22025. 173-179.

Highlights:

1. More advanced cervical precancerous histopathological findings compared with cervical cytology are observed in POP patients undergoing vaginal hysterectomy.
2. Routine use of preoperative biopsy or ultrasound in POP patients undergoing vaginal hysterectomy cannot be recommended.

INTRODUCTION

Pelvic organ prolapse (POP) results from weakening of the pelvic floor musculature and constitutes a global health issue affecting quality of life. The prevalence of POP ranges between 2% and 20%.[1] The incidence of POP reaches its peak among women aged 60 to 69 years. Consequently, hysterectomy in postmenopausal women is frequently performed due to POP.[2] Protrusion of the uterus beyond the vulva may result in infection, bleeding, and, rarely, malignancy. Cervical carcinoma and uterine prolapse are common in developing countries; however, their coexistence is uncommon.[3]

The World Health Organization (WHO) has reported that cervical cancer remains the fourth most prevalent malignancy among women, with up to 604,000 new cases and 342,000 deaths in 2020. The highest mortality rates occur in low- and middle-income countries owing to limited access to HPV vaccination, cervical screening, early therapeutic intervention, and social as well as economic determinants.[4] Cervical cancer generally develops gradually from precancerous lesions described as dysplasia or cervical intraepithelial neoplasia (CIN). These changes arise in the trans-formation zone in association with squamous meta-plasia. The cervical smear (Pap smear) is a simple test enabling detection of precancerous lesions for early diagnosis and timely treatment as part of secondary prevention.[5] In POP, direct mechanical irritation of the cervix is associated with chronic inflammation in at least third-degree prolapse, predisposing to cervical malignancy.[1] Conversely, another study suggested that uterine prolapse rarely coexists with cervical carcinoma, as cornified cervical epithelium confers resistance, while reduced vaginal secretions, absence of infection, and adequate drainage provide protective mechanisms against carcinoma.[6] Nevertheless, this issue remains controversial.

The prevalence of unexpected premalignant and malignant pathologies following hysterectomy varies between 0.2% and 0.8%.[7–9] However, this remains an important concern for surgeons performing pelvic reconstructive procedures, as it may influence both surgical technique and patient outcomes.[9] Accordingly, this report aims to present a case series of POP patients undergoing vaginal hysterectomy (VH) with pre-operative identification of abnormal cervical cytology ultimately associated with more advanced histopathological results.

CASE SERIES

Case 1

A 55-year-old woman, P3A0, presented with a protruding vaginal mass that had developed two years prior to admission. She had a history of three previous cesarean deliveries with birth weights ranging from 3,000 grams to 3,800 grams. She had been in menopause for four years and remained sexually active. On Pelvic Organ Prolapse Quantification (POP-Q) assessment, she was diagnosed with third-degree uterine prolapse accompanied by cystocele. She elected to undergo VH. During preoperative evaluation, her Pap smear revealed atypical glandular cells of undetermined significance (AGUS) (Figure 1). Histopathological examination following VH demonstrated vaginitis and metaplastic chronic cervicitis with atypia progressing to mild dysplasia of endocervical epithelial cells/low-grade squamous intraepithelial lesion (LSIL) (Figure 2).

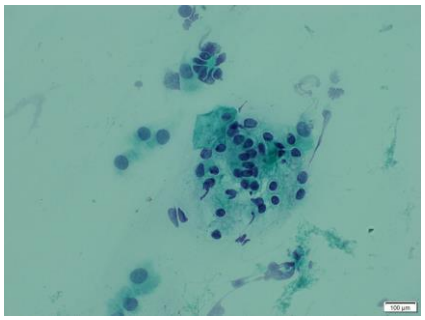


Figure 1. Pap smear of atypical glandular cells of undetermined significance (AGUS).

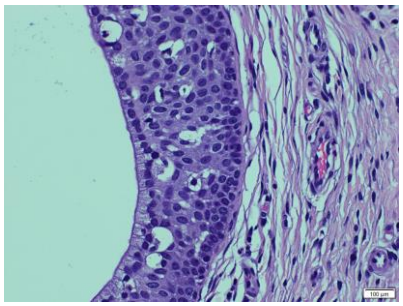


Figure 2. Histopathology of low grade squamous intraepithelial lesion (LSIL).

Case 2

A 62-year-old woman, P5A0, presented with a protruding vaginal mass that had developed five years earlier. She had experienced five vaginal deliveries, with the largest birth weight recorded at 4,000 grams. She had been menopausal for 10 years and was not

sexually active. On POP-Q assessment, she was diagnosed with third-degree uterine prolapse and elected to undergo VH followed by colpocleisis.

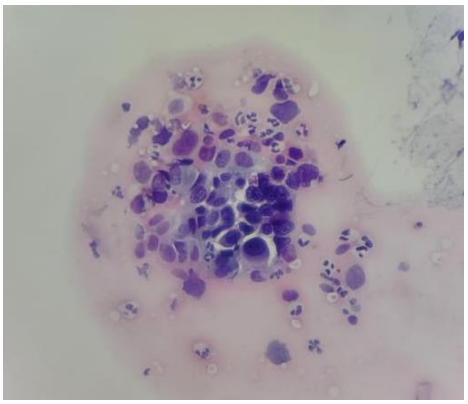


Figure 3. Pap smear of atypical squamous cells of cannot excluded HSIL (ASCH).

Preoperative Pap smear demonstrated atypical squamous cells, cannot exclude HSIL (ASCH) (Figure 3). Histopathological examination after VH revealed high-grade squamous intraepithelial lesion (HSIL) progressing to carcinoma in situ with microinvasive glandular involvement and focal extension (Figure 4). These cases underscore the need to evaluate the role of cytological cervical screening in POP patients prior to hysterectomy.

SCOPING REVIEW

This scoping review was carried out in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA-ScR). The search strategy was implemented through PubMed, Ebscohost, Cochrane, and Google Scholar for studies published up to August 1, 2024, without restriction on earlier publications. The following keywords were applied: "pelvic organ prolapse," "cervical cancer screening," and "Papanicolaou test." In Cochrane and PubMed, Medical Subject Headings (MeSH) terms were employed as provided by the databases. All study types were included, encompassing original articles, case reports, systematic reviews, and meta-analyses. Exclusion criteria comprised studies consisting only of abstracts, editorials, conference or meeting proceedings, letters, lack of available full text, and animal studies.

Results of the scoping review

Figure 5 illustrates the PRISMA flow diagram of the study selection process. Initially, 256 articles were identified across PubMed, Ebscohost, Cochrane, and Google Scholar. Two duplicate entries were removed, yielding 254 records. After abstract screening for relevance to the topic, 6 studies were selected for eligibility assessment. Ultimately, 4 articles were included in the review. Table 1 summarizes the findings of the scoping review (n = 4).

DISCUSSION

In the aging population, POP is commonly encountered with diverse manifestations ranging from vaginal and lower urinary tract symptoms to defecatory and sexual dysfunction. As a less invasive procedure, vaginal hysterectomy has become a preferred treatment option for patients with POP.[10]

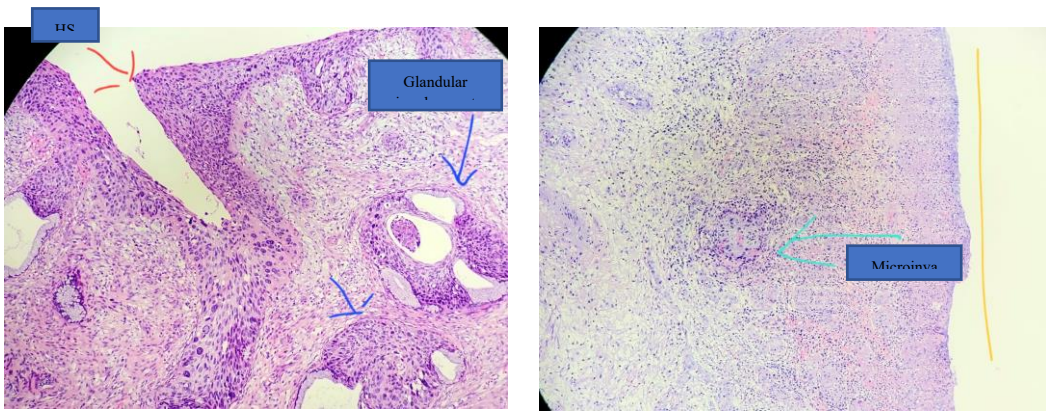


Figure 4. Histopathological result of HSIL up to in situ carcinoma

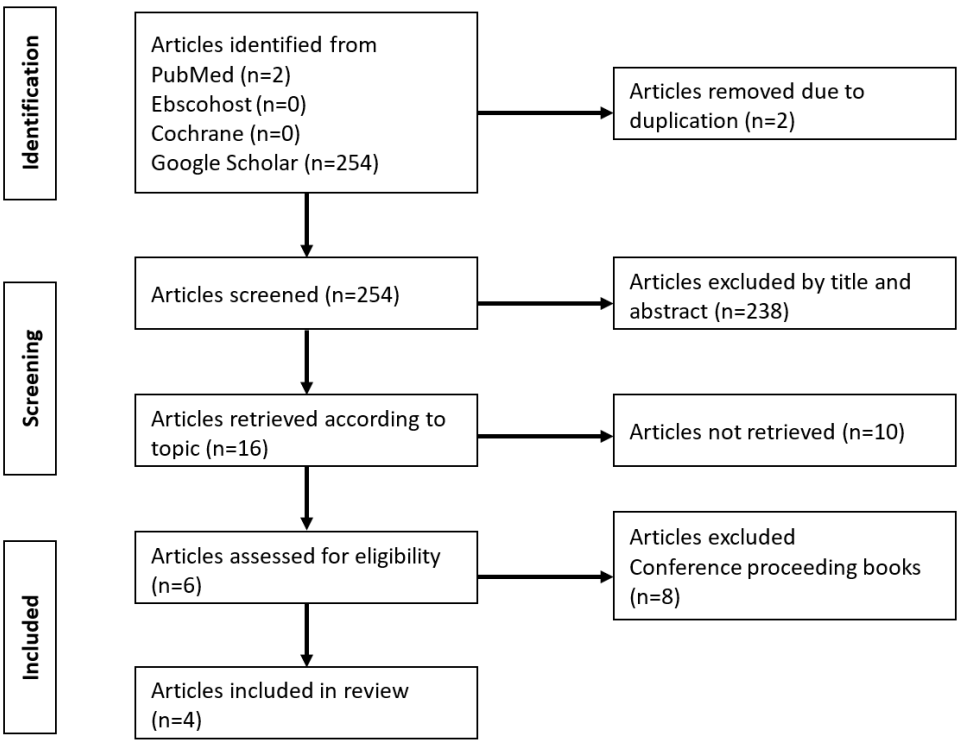


Figure 5. PRISMA flowchart of article selection process

Table 1. The results of scoping review (n=4)

References	Type of Study	Focus	Results
Tailor HJ, 2015	Retrospective cohort study	To evaluate the Pap smear finding in patients with uterine prolapse and compare it with nonprolapse cases	Of 1,427 cases, we have received only 5 cases of ASCUS in 233 uterine prolapse cases.
Grigoriadis T, 2015	Retrospective study	The incidence of malignant and premalignant gynecological histopathological findings among POP women who underwent a VH	Five out of 333 women who underwent VH consisted of 1 case of cervical cancer (0.3 %), 1 case of cervical intraepithelial neoplasia (CIN) III (0.3 %), and 3 cases of CINI (0.9 %).
Barakzai S, 2023	Retrospective study	The rates of unanticipated premalignancy and malignancy at the time of hysterectomy performed for pelvic organ prolapse in an underscreened population	For patients undergoing hysterectomy for pelvic organ prolapse in an underscreened population, the rates of cervical dysplasia or cancer were 0.42% (3/729).
Suphattanaporn O, 2023	Retrospective cohort study	Prevalence of precancerous or malignant lesions of the cervix among POP patients underwent vaginal hysterectomy	Nine of the 530 patients (1.7%) had precancerous or malignant lesions of the cervix and/ or endometrium. Precancerous cervical lesions were found in five patients (0.95%): ciN ii 0.38% and ciN iii 0.57%.

Unexpected premalignant and malignant pathologies identified during hysterectomy may arise in both endometrial and cervical tissues. According to the International Federation of Gynecology and Obstetrics Working Group guidelines, preoperative biopsy or ultrasonography in POP patients is not recommended as a routine procedure prior to hysterectomy.[11] The 2019 guidelines of the American Society for Colposcopy and Cervical Pathology (ASCCP) did not address the management of cytological abnormalities in POP patients scheduled for hysterectomy.[12] Conversely, several studies have reported that women with POP who are candidates for VH should undergo preoperative diagnostic evaluations including blood testing, cervical cancer screening, ultrasonography, and endometrial sampling, particularly in those presenting with abnormal uterine bleeding.[13,14]

Bayan M, et al.[15] in a study from Jordan reported that among 5,000 routine Pap smears, the prevalence of abnormal results in the general population was only 3.8%. Meanwhile, Syem B, et al.[9] concluded that the incidence of unexpected cervical premalignancy (CIN2 or higher) was 0.42% (3/729 cases) in POP patients undergoing hysterectomy. Another study by Ornthicha, et al.[14] demonstrated a prevalence of CIN II and CIN III of 0.38% and 0.57%, respectively. All patients were postmenopausal and Pap test–negative, with no transformation zone (TZ) detected. The reliability of cervical cancer screening is limited due to the high false-negative rate of Pap testing, estimated at approximately 5% to 35%.[16,17] In fact, co-testing with HPV increases detection of CIN3 or greater lesions two- to threefold. Furthermore, co-testing has demonstrated a higher negative predictive value compared with cytology alone.[18] Data published in 2023 confirmed that high-risk (HR) HPV screening exhibited high sensitivity (98.66%) and specificity (87.15%) for detecting preneoplastic lesions in clinical practice.[19] Although HR-HPV testing is highly sensitive, false-negative outcomes may still occur since no screening tool achieves 100% sensitivity. Co-testing is therefore considered an alternative strategy to improve sensitivity in detecting HPV-negative subtypes of adenocarcinoma (ADC).[20,21] Unfortunately, in Indonesia, HR-HPV screening is not performed routinely due to its high cost.

In Indonesia, data from 2020 indicated 36,633 new cases of cervical cancer and 21,003 deaths related to the disease. Cervical cancer remains the second most common cause of mortality among Indonesian women, as nearly 70% of cases are diagnosed at an advanced stage.[22] Thus, early detection of cervical cancer is crucial to decrease preventable deaths. Our cases demonstrated worse histopathological findings compared with cytological results. In the first case, AGUS identified on cytology corresponded to mild dysplasia or LSIL on histopathology. In the second case, ASCH detected during screening was confirmed as HSIL progressing to carcinoma in situ on histopathology following VH. According to the ASCCP guideline, patients who have undergone hysterectomy for benign disease but present with high-grade cytology (HSIL, atypical squamous cells—cannot exclude high-grade squamous intraepithelial lesion/ASC-H, or atypical glandular cells/AGC) should immediately undergo vaginal colposcopy.[12]

Although cytology is the standard primary method for cervical precancer screening, in low-resource settings such as rural Indonesia, significant barriers exist including limited availability of specialists, high costs, and the requirement for multiple visits.[1] Visual inspection with acetic acid (VIA) and Lugol's iodine offers a simpler approach for early detection of cervical precancerous lesions. VIA involves identifying acetowhite plaques near the squamocolumnar junction of the cervix following application of acetic acid.[1] Reported sensitivity and specificity of VIA range between 50–88.6% and 66.7–89.7%. A study by Wang S, et al.[1] in China found that among HPV-positive women, adherence with VIA was 93.9%, reducing colposcopy referral rates to 18.3%. Another study from India concluded that VIA performed by trained female health workers was safe, acceptable, and effective for detecting precancerous lesions in resource-limited rural regions.[1]

Given the slow progression of cervical cancer and its high prevalence in Indonesia, preoperative screening for precancerous gynecological lesions and malignancy is strongly recommended. This should include endometrial assessment by transvaginal ultrasound and cervical evaluation through cytology or co-testing in asymptomatic postmenopausal women. Although the incidence of unanticipated cervical pathology at hysterectomy for POP is relatively low, cytology screening performed preoperatively can guide clinicians in optimizing management and counseling of patients undergoing VH.

The strength of this case series is to emphasize to gynecologists that cytological screening in postmenopausal POP women prior to VH may yield less severe results than histopathological findings. Even though the incidence of unexpected cervical premalignancy is reported at less than 1%, gynecologists should counsel patients to undergo cytology and HPV testing before VH in POP, particularly in consideration of life expectancy in Indonesia. In addition, careful history-taking regarding prior cervical and endometrial cancer screening is essential to assess individual risk

factors. The limitation of this case series was the absence of further follow-up after VH.

CONCLUSION

There is no routine recommended guideline of pre-operative biopsy or ultrasound in POP patient. Since cervical cancer still become the second most common cause of mortality in Indonesia, it is recommended to screen preoperatively for precancerous gynecological lesion and cancer before POP surgery.

DISCLOSURES

Acknowledgment

The authors express gratitude to Tarakan General Hospital and St. Carolus Hospital Jakarta for facilitating access to these unique cases. In addition, appreciation is extended to the Departments of Obstetrics and Gynecology and Anatomical Pathology for their assistance in data acquisition and completion of the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest related to this study.

Patient consent for publication

The patients included in this study provided signed consent for publication to contribute to the advancement of knowledge in gynecological cases.

Funding

No funding was declared.

Author contribution

All authors contributed to this study, including preparation, data collection, case description, drafting, revising, and submission of the manuscript for publication.

REFERENCES

1. Tailor HJ, Bhagat VM, Patel PR, et al. Pap smear findings in uterine prolapse: a coincidence or indicator for impending malignancy. International Journal of Medical Science and Public Health. 2015;5(4):819–22. doi: 10.5455/ijmsph.2016.20022015375
2. Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. Lancet. 2007;369(9566):1027-38. doi: 10.1016/S0140-6736(07)60462-0. PMID: 17382829.
3. Merrill RM, Layman AB, Oderda G, et al. Risk estimates of hysterectomy and selected conditions commonly treated with hysterectomy. Ann Epidemiol. 2008;18(3):253-60. doi: 10.1016/j.annepidem.2007.10.011. PMID: 18280923.
4. World Health Organization. Cervical cancer [Internet]. 2023 [cited 2023 Nov 29]. Available from: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
5. Safaeian M, Solomon D, Castle PE. Cervical cancer prevention--cervical screening: science in evolution. Obstet Gynecol Clin North Am. 2007;34(4):739-60, ix. doi: 10.1016/j.ogc.2007.09.004. PMID: 18061867; PMCID: PMC2762353.
6. Guthrie D, Bache W. The infrequency of carcinoma of the cervix with complete procidentia. Ann Surg. 1932;96(4):796-800. doi: 10.1097/00000658-193210000-00027. PMID: 17866871; PMCID: PMC1391809.
7. Aydin S, Bakar RZ, Mammadzade A, et al. The incidence of concomitant precancerous lesions in cases who underwent hysterectomy for prolapse. Journal of Clinical and Analytical Medicine. 2016;7:676-80. doi: 10.4328/jcam.4385.
8. Grigoriadis T, Valla A, Zacharakis D, et al. Vaginal hysterectomy for uterovaginal prolapse: what is the incidence of concurrent gynecological malignancy? Int Urogynecol J. 2015;26(3):421-5. doi: 10.1007/s00192-014-2516-5. Epub 2014 Oct 8. PMID: 25293812.
9. Barakzai S, Koltun-Baker E, Melville SJF, et al. Rates of unanticipated premalignant and malignant lesions at the time of hysterectomy performed for pelvic organ prolapse in an underscreened population. AJOG Glob Rep. 2023;3(2):100217. doi: 10.1016/j.xagr.2023.100217. PMID: 37275440; PMCID: PMC10232886.
10. Aimjirakul K, Ng JJ, Saraluck A, et al. A Retrospective cohort study on the prevalence, risk factors, and improvement of overactive bladder symptoms in women with pelvic organ prolapse. Int J Womens Health. 2023;15:1039-46. doi: 10.2147/IJWH.S413670. PMID: 37469654; PMCID: PMC10352122.
11. Ramm O, Gleason JL, Segal S, et al. Utility of preoperative endometrial assessment in asymptomatic women undergoing hysterectomy for pelvic floor dysfunction. Int Urogynecol J. 2012;23(7):913-7. doi: 10.1007/s00192-012-1694-2. Epub 2012 Mar 8. PMID: 22398824.

12. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis. 2020;24(2):102-31. doi: 10.1097/LGT.0000000000000525. Erratum in: J Low Genit Tract Dis. 2020 Oct;24(4):427. doi: 10.1097/LGT.0000000000000563. PMID: 32243 307; PMCID: PMC7147428.
13. Elbiaa AA, Abdelazim IA, Farghali MM, et al. Unexpected premalignant gynecological lesions in women undergoing vaginal hysterectomy for utero-vaginal prolapse. Prz Menopauzalny. 2015;14(3): 188-91. doi: 10.5114/pm.2015.54344. Epub 2015 Sep 30. PMID: 26528108; PMCID: PMC4612556.
14. Suphattanaporn O, Saraluck A, Mononai J, et al. Prevalence of precancerous gynecological lesions and gynecological cancer in patients undergoing vaginal hysterectomy for pelvic organ prolapse. Ann Med. 2023;55(2):2273428. doi: 10.1080/0785 3890.2023.2273428. Epub 2023 Oct 26. PMID: 37883921; PMCID: PMC10836294.
15. Maraqa B, Lataifeh I, Otay L, et al. Prevalence of Abnormal Pap Smears: A Descriptive Study from a Cancer Center in a Low-Prevalence Community. Asian Pac J Cancer Prev. 2017;18(11):3117-21. doi: 10.22034/APJCP.2017.18.11.3117. PMID: 29172288; PMCID: PMC5773800.
16. Koonmee S, Bychkov A, Shuangshoti S, et al. False-negative rate of papanicolaou testing: A national survey from the Thai Society of Cytology. Acta Cytol. 2017;61(6):434-40. doi: 10.1159/00047 8770. Epub 2017 Jul 25. PMID: 28738387.
17. Grimes DR, Corry EMA, Malagón T, et al. Challenges of false positive and negative results in cervical cancer screening [Internet]. medRxiv; 2020 [cited 2023 Dec 10]. p. 2020.03.17.20037440. Available from: https://www.medrxiv.org/content/ 10.1101/2020.03.17.20037440v1
18. Melnikow J, Henderson JT, Burda BU, et al. Screening for cervical cancer with high-risk human papillomavirus testing: Updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2018;320(7):687-705. doi: 10.1001/jama.2018.10400. PMID: 30140883.
19. Fleider LA, de Los Ángeles Tinnirello M, Gómez Cherey F, et al. High sensitivity and specificity rates of cobas® HPV test as a primary screening test for cervical intraepithelial lesions in a real-world setting. PLoS One. 2023;18(2):e0279728. doi: 10.1371/journal.pone.0279728. PMID: 36745 662; PMCID: PMC9901754.
20. Macios A, Nowakowski A. False negative results in cervical cancer screening-risks, reasons and implications for clinical practice and public health. Diagnostics (Basel). 2022;12(6):1508. doi: 10.3390/diagnostics12061508. PMID: 35741319; PMCID: PMC9222017.
21. Schiffman M, Kinney WK, Cheung LC, et al. Relative Performance of HPV and Cytology Components of Cotesting in Cervical Screening. J Natl Cancer Inst. 2018;110(5):501-8. doi: 10.1093/ jnci/djx225. PMID: 29145648; PMCID: PMC627 9277.
22. Nuranna L. See and treat: Cervical cancer prevention strategy in Indonesia with VIA-DoVIA screening and prompt treatment. The Indonesian Journal of Cancer Control. 2022;2(1):32–8. doi: 10.52830/inajcc.v2i1.70.

MAJALAH OBSTETRI & GINEKOLOGI
Journal of Obstetrics & Gynecology Science

SUBSCRIPTION FORM

To subscribe to the journal and/or to purchase individual issue of the journal, please complete this form and send the completed form to e-mail address: mog@journal.unair.ac.id.

Name : .....
Institution : .....
: .....
Address : .....
: .....
Phone : ..... E-mail : .....

I intend to :

☐ subscribe to the journal for ..... publication year(s) starting from publication year of ..... to ..... with payment* in the following currency :
- ☐ IDR 300,000 per publication year
- ☐ USD 30 per publication year

☐ Purchase individual issue of the journal. Please specify the edition/year of the journal and the quantity of the issue(s) :

No.	Edition no.	Year	Quantity

No.	Edition no.	Year	Quantity

with payment* in the following currency :
- ☐ IDR 100,000 per issue
- ☐ USD 10 per issue

*the mentioned prices have not included the delivery fee

The ordered journal(s) will be delivered to :

Name : .....
Institution : .....
: .....
Address : .....
: .....
Phone : ..... E-mail : .....

On the payment method and other related costs, kindly contact Ms. Priska Dwi Wahyurini, Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Jalan Prof dr. Moestopo 6-8, Surabaya 60286, Indonesia. Phone: +6281227593208. E-mail: mog@journal.unair.ac.id

Date of order (DD/Month/YYYY) : .....

Signature : .....


0854 0386
9 772598 101001