

## Tummy Time and Development of 6- to 12-Month-Old Infants

Marvella Graceria Titah,<sup>1</sup> Edward Surjono,<sup>2</sup> Johanes A. C. Prabowo,<sup>2</sup> Andy Setiawan,<sup>2</sup> Rita Dewi<sup>3</sup>

<sup>1</sup>Faculty of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia  
<sup>2</sup>Department of Pediatrics, Faculty of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

<sup>3</sup>Department of Biochemistry, Faculty of Medicine and Health Sciences Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

### Abstract

Early childhood development, particularly within the first 1,000 days of life, is a critical period. Globally, 5–16% of children experience developmental delays. This figure is higher in Indonesia with approximately 13–18% of children under five are facing growth and developmental issues. Adequate stimulation, including activities like tummy time, plays a vital role in a child's growth and development. This study aimed to investigate the correlation between tummy time and the developmental outcomes of infants aged 6–12 months. An analytical descriptive design with a cross-sectional approach was employed in this study that was conducted at Public Health Centers in North Sulawesi Province, Indonesia. Data collection involved questionnaires assessing the onset, frequency, and duration of tummy time, alongside the use of the Child Development Pre-Screening Questionnaire. With a minimum sample size of 96 respondents, data were analyzed using Spearman's correlation. Findings indicated that performing tummy time more than 1–2 times per week, with each session lasting 6–20 minutes, was significantly associated with better developmental outcomes. However, no significant relationship was observed between early initiation of tummy time or the number of daily sessions with infant development. The study concluded that engaging in tummy time more than 1–2 times per week for 6–20 minutes per session can promote optimal infant development.

**Keywords:** Infant development, sensory stimulation, tummy time

### Introduction

Early childhood development during the first 1,000 days of life is a critical period, beginning from fetal development in the womb through the child's second year of life.<sup>1</sup> During this stage, rapid brain development takes place, encompassing the growth of the sensory system, hippocampus, myelination, and the neurotransmitter system.<sup>2</sup>

Global estimates suggest that the prevalence of developmental delays in infants and preschoolers ranges from 5–16%.<sup>3</sup> According to the Indonesian Pediatrician Association (IDAI), 5 to 10% of children are believed to encounter developmental delays. In 2014,<sup>4</sup> national data from the Indonesian Ministry of Health indicated that approximately 13–18% of Indonesian

infants suffered from growth and developmental problems.<sup>5</sup>

Interruptions in an infant's growth and development can jeopardize their future stages of life. Maximizing Development during this critical period is essential. Stimulation is a significant factor influencing infant growth and Development. Offering appropriate and positive stimuli from the environment can contribute to achieving optimal growth and developmental outcomes. One effective form of stimulation for growth and Development is engaging infants in tummy time activities.<sup>6</sup>

Tummy time is an important activity that supports the growth and development of infants, when a baby is placed on their stomach, they are encouraged to lift their head and push with their arms, which helps strengthen the neck, back, and shoulder muscles. It also enhances gross motor skills such as rolling over, crawling, and eventually walking.

Acknowledging the significance of infant development during the First 1,000 days of life

### Corresponding Author:

Edward Surjono  
 Department of Pediatrics, Faculty of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia  
 Email: [edward.surjono@atmajaya.ac.id](mailto:edward.surjono@atmajaya.ac.id)

and its implications for future developmental stages, along with the existing research gap regarding tummy time and infant development, this study seeks to explore the correlation between tummy time and the growth and development of infants aged 6–12 months.

## Methods

This cross-sectional analytical study was conducted at Paniki Bawah, Tuminting, and Tagulandang Health Centers in North Sulawesi Province from July 2023 to September 2024. The study utilized a questionnaire to gather information on variables such as the initiation age of tummy time, weekly frequency, daily sessions, and duration per session, which were treated as independent variables. The Child Development Pre-Screening Questionnaire (KPSP) was used to evaluate infant development as the dependent variable. KPSP is a tool to detect the development of children aged 0–72 months, consisting of 9–10 age-appropriate questions, using aids such as pencils, paper, a tennis ball, rattle, blocks, raisins, peanuts, or small biscuits. The interpretation of results is as follows: 9–10 “Yes” answers indicate appropriate development, 7–8 “Yes” answers indicate doubtful development, and fewer than 6 “Yes” answers suggest potential developmental delays.

Inclusion criteria were infants aged 6–12 months who had received tummy time stimulation from birth until 6 months, with parental or caregiver consent. Exclusion criteria included prematurity or post-term, congenital abnormalities, neuromuscular diseases, central nervous system disorders, hearing impairments, speech disorders, vision impairments, incomplete vaccination records, mothers with infectious diseases during childbirth, improper tummy time positioning, and infants engaging in tummy time for more than six months.

The minimum required sample size was 96. Data were analyzed using univariate and bivariate methods. Spearman’s correlation was used due to non-normally distributed data. Ethical approval was obtained from the Atma Jaya Catholic University Ethics Committee (No: 18/07/KEP-FKIKUAJ/2023).

## Results

Of 109 respondents, nine were excluded (two post-term births, six who began tummy time

**Table 1 Demographic Characteristics of the Study Population**

Variable	n=100	%
Age		
6 Month	14	14
7 Month	7	7
8 Month	7	7
9 Month	20	20
10 Month	12	12
11 Month	13	13
12 Month	27	27
Gender		
Male	56	56
Female	44	44

after six months, and one with Down syndrome), leaving 100 eligible participants. Table 1 presents the demographic characteristics of the study population. Table 2 summarizes tummy time practices, including age of initiation, weekly frequency, daily sessions, and session duration. Developmental outcomes were classified as normal, borderline, or abnormal. The data revealed that most infants (82%) showed normal Development, with the largest group (22 infants) starting tummy time at four months of age.

Interestingly, no abnormal cases were observed among infants who began tummy time at 1, 2, or 5 months. The study included 100 infants, ranging in tummy time initiation from less than one month to 6 months. The study reports a p-value of 0.106 and a correlation coefficient of -0.163, indicating the statistical analysis of the relationship between the age of tummy time initiation and developmental outcomes. However, further context is needed to interpret these findings accurately.

Table 3 shows the association between the number of tummy time sessions per day and developmental outcomes in infants aged 6–12 months. Among those who engaged in 1–2 sessions per day, 7% demonstrated appropriate development, 5% were questionable, and 2% were deviant. In the 2–3 sessions group, 25% achieved appropriate development, 4% were questionable, and no deviant cases were recorded. For infants performing 3–4 sessions per day, 22% were appropriate and 1% deviant, with no questionable outcomes. The largest group, those practicing tummy time more than four times daily, included 28% appropriate, 4%

**Table 2 Tummy Time Assessment**

Variable	n	%
Age to Start Tummy Time		
<1 Month	5	5
1 Month	3	3
2 Month	8	8
3 Month	24	24
4 Month	28	28
5 Month	18	18
6 Month	14	14
Intensity (1 weeks)		
1-2x	9	9
3-4x	15	15
5-6x	3	3
Every day	73	73
Session (per day)		
1-2x	14	14
2-3x	29	29
3-4x	23	23
>4x	34	34
Duration (per session)		
<1-5 min	40	40
6-20 min	47	47
>20 min	13	13
Developmental		
Appropriate	82	82
Questionable	13	13
Deviant	5	5

questionable, and 2% deviant cases.

Statistical analysis revealed a p-value of 0.098 and a correlation coefficient of 0.167, indicating a weak, nonsignificant positive correlation between the number of daily tummy time sessions and developmental outcomes.

Table 4 presents the relationship between the number of daily tummy time sessions and developmental outcomes in infants aged 6-12

months. The study categorizes daily tummy time sessions into four groups: 1-2 times, 2-3 times, 3-4 times, and more than four times. For each group, the table presents the count and percentage of infants categorized as showing normal, borderline, or abnormal Development. Among the 100 infants studied, 82 (82%) demonstrated normal Development, 13 (13%) were classified as borderline, and 5 (5%) as abnormal. Significantly, infants who underwent more than four tummy time sessions per day exhibited the highest incidence of normal Development, with 28 cases (28%). The group with 2-3 tummy time sessions showed no abnormal cases, while the 3-4 group had no borderline cases. Additionally, Table 4 includes a p-value of 0.098 and a coefficient of 0.167, indicating a potential weak positive correlation between tummy time frequency and developmental outcomes. However, interpreting these findings accurately would necessitate additional statistical context.

Table 5 presents the association between tummy time session duration and developmental outcomes in infants aged 6-12 months. Of the 100 infants, 82% demonstrated appropriate development, 13% were borderline, and 5% were deviant. The highest proportion of appropriate outcomes was observed among infants who engaged in sessions lasting 6-20 minutes (42%). No abnormal cases occurred in the group with sessions longer than 20 minutes. Statistical analysis showed a p-value of 0.014 and a correlation coefficient of 0.244, indicating a statistically significant positive correlation between session duration and developmental outcomes. These findings suggest that sessions of 6-20 minutes are particularly beneficial, and longer durations may also support favorable developmental progress.

Table 6 illustrates the association between weekly tummy time frequency and developmental outcomes in infants aged 6-12 months. Tummy

**Table 3 Correlation Between the Session Frequency of Tummy Time per Day and Developmental Outcomes in Toddlers Aged 6-12 Months**

Tummy Time Sessions/Day	Appropriate n (%)	Questionable n (%)	Deviant n (%)	p-value	Correlation (r)
1-2x	7 (7.0)	5 (5.0)	2 (2.0)	0.098	0.167
2-3x	25 (25.0)	4 (4.0)	0 (0.0)		
3-4x	22 (12.0)	0 (0.0)	1 (1.0)		
>4x	28 (28.0)	4 (4.0)	2 (2.0)		

**Table 4 Correlation Between the Age to Start Tummy Time and Developmental Outcomes in Infants Aged 6-12 Months**

Age to Start Tummy Time	Toodlers Age 6 to 12 Months Development			p-value	Correlation
	Appropriate n (%)	Questionable n (%)	Deviant n (%)		
<1 Month	3 (3.0)	1 (1.0)	1 (1.0)		
1 Month	2 (2.0)	1 (1.0)	0 (0.0)		
2 Month	8 (8.0)	0 (0.0)	0 (0.0)		
3 Month	21 (21.0)	2 (2.0)	1 (1.0)	0.106	-0.163
4 Month	22 (22.0)	4 (4.0)	2 (2.0)		
5 Month	15 (15.0)	3 (3.0)	0 (0.0)		
6 Month	11 (11.0)	2 (2.0)	1 (1.0)		
TOTAL	82 (61)	13 (13.0)	5 (5.0)		

**Table 5 Correlation Between the Duration of Tummy Time Sessions and Developmental Outcomes in Infants Aged 6-12 Months**

Duration of Tummy Time/Session	Appropriate n (%)	Questionable n (%)	Deviant n (%)	p-value	Correlation
<1-5 min	28 (28.0)	9 (9.0)	3 (3.0)		
6-20 min	42 (42.0)	3 (3.0)	2 (2.0)	0.014	0.244
>20 min	12 (12.0)	1 (1.0)	0 (0.0)		
TOTAL	82 (61.0)	13 (13.0)	5 (5.0)		

time intensity was categorized into four groups: 1-2 times, 3-4 times, 5-6 times, and daily. Among the 100 infants, 82 (82%) demonstrated normal development, 13 (13%) were classified as borderline, and 5 (5%) as abnormal. Infants who engaged in daily tummy time had the highest proportion of normal development, totaling 64 (64%). Notably, no abnormal cases were observed among infants practicing tummy time 3-4 times or 5-6 times per week.

Furthermore, Table 6 reports a p-value of 0.002 and a correlation coefficient of 0.300, indicating a statistically significant positive correlation between the frequency of tummy

time per week and developmental outcomes. This suggests that increasing the frequency of tummy time sessions throughout the week may correlate with better developmental outcomes in infants of this age group. The robust statistical significance ( $p<0.01$ ) and moderate positive correlation further underscore the beneficial impact of consistent tummy time on infant development.

The Kruskal-Wallis test results indicate a significant difference in tummy time intensity per week concerning developmental outcomes (Asymp. Sig.<0.05). Pairwise comparisons demonstrate that tummy time performed

**Table 6 Correlation Between the Frequency of Intensity Tummy Time Per Week and Developmental Outcomes in Infants Aged 6 To 12 Months**

Intensity of Tummy Time / Week	Appropriate n (%)	Questionable n (%)	Deviant n (%)	p-value	Correlation (r)
1-2x	2 (2.0)	5 (5.0)	2 (2.0)		
3-4x	13 (13.0)	2 (2.0)	0 (0.0)	0.002	0.300
5-6x	3 (3.0)	0 (0.0)	0 (0.0)		
Everyday	64 (64.0)	6 (6.0)	3 (3.0)		

1–2 times per week significantly differs from intensities exceeding 1–2 times per week (3–4 times per week, 5–6 times per week, and daily). This indicates that performing tummy time more than 1–2 times per week is more beneficial for development.

The results of the Kruskal-Wallis test indicate a significant difference in tummy time duration concerning developmental outcomes (Asymp. Sig.<0.05). Pairwise comparisons show that durations of less than 1–5 minutes significantly differ from durations of 6–20 minutes. Therefore, it can be concluded that the duration of tummy time per session that impacts Development is 6–20 minutes.

## Discussion

There is a notable correlation between tummy time and infant development, particularly regarding the frequency of tummy time sessions per week and the duration of each session. These findings are consistent with Hewitt et al., who reported that regular tummy time is associated with improved locomotor skills such as rolling, crawling, and sitting, as well as earlier achievement of milestones. Moreover, among six observational studies, it was observed that infants who engage in longer durations of tummy time tend to reach developmental milestones earlier. Additionally, significant correlations were identified between tummy time and cognitive development, as well as social communication skills.<sup>6</sup>

Koren et al.,<sup>6</sup> investigated the association of tummy time with growth and development in infants aged 2 and 4 months. The authors reported that infants who engaged in longer durations of tummy time achieved developmental milestones earlier, including lifting the head, turning the head, making eye contact, bringing hands to the mouth, and kicking. Similarly, a study by Sabang and Yuliati demonstrated significant improvements in psychomotor development among infants aged 6–9 months before and after tummy time, with a Z value of -4.231 and p<0.0001.<sup>7</sup>

These findings are consistent with previous studies, supporting the association between tummy time and developmental progress.<sup>6,7</sup> This study shows age-appropriate developmental outcomes in infants aged 6–12 months who engage in tummy time, as assessed using the pre-screening developmental questionnaire, in line with previous studies. No studies to date

have reported an absence of association between tummy time and development. This study further evaluated the timing of initiation, weekly frequency, daily sessions, and session duration to identify criteria for optimal tummy time. The results obtained that an ideal frequency of tummy time for optimal development is more than 1–2 times per week, as there was a significant difference observed between frequencies of 1–2 times per week and those exceeding 1–2 times per week in terms of developmental outcomes (Asymp. Sig.<0.05). Similarly, the study identified the optimal duration of tummy time to be 6–20 minutes, with a notable difference noted between durations of less than 1–5 minutes and 6–20 minutes in relation to development (Asymp. Sig.<0.05).

No significant correlation was found between the initiation age of tummy time or the number of daily sessions and developmental outcomes in infants aged 6–12 months. This may be explained by the study's sample selection, which included only infants who began tummy time early (before 6 months of age, consistent with WHO guidelines) and excluded those who started later. The lack of variation in initiation age likely contributed to the nonsignificant findings. In summary, infants who performed tummy time more than 1–2 times per week, with sessions lasting 6–20 minutes, were more likely to achieve age-appropriate developmental milestones.

## References

1. Widyahening IS, Aufa MA, Alhas MF, Widodo AB, Friska D. Knowledge, attitude, and practice of mothers on the first 1000 Days of Life. *eJournal Kedokteran Indonesia*. 2021;9(2):129. doi:10.23886/ejki.9.65.129
2. Schwarzenberg SJ, Georgieff MK, Daniels S, Corkins M, Golden NH, Kim JH, et al. Advocacy for improving nutrition in the first 1000 days to support childhood development and Adult Health. *Pediatrics*. 2018;141(2):2–6. doi:10.1542/peds.2017-3716
3. Institute for Public Health, National Institutes of Health, Ministry of Health Malaysia. National Health and Morbidity Survey 2016 (NHMS 2016): Maternal and Child Health. Vol. II: Maternal and child health findings. Selangor, Malaysia: Institute for Public Health, National Institutes of Health, Ministry of Health; 2016.
4. Gunardi H, Nugraheni RP, Yulman AR, Soedjatmiko, Sekartini R, Medise BE, et al.

- Growth and developmental delay risk factors among under-five children in an inner-City Slum Area. *Paediatrica Indonesiana*. 2019;59(5):276-83.
- 5. Hewitt L, Kerr E, Stanley RM, Okely AD. Tummy time and infant health outcomes: a systematic review. *Pediatrics*. 2020;145(6):13-25. doi:10.1542/peds.2019-2168
  - 6. Koren A, Kahn-D'angelo L, Reece SM, Gore R. Examining childhood obesity from infancy: The relationship between tummy time, infant BMI-Z, weight gain, and motor development—an exploratory study. *J Pediatr Health Care*. 2019;33(1):80-91. doi:10.1016/j.pedhc.2018.06.006
  - 7. Sabang R, Yuliati L. Tummy time to improve psychomotor development Babies 6-9 months. 2023;11(2):317-20. doi:10.35335/midwifery.v11i2.1274
  - 8. Silva BF, Sampaio SS, Moura JR, de Medeiros CE, de Lima-Alvarez CD, Simão CR, et al. "I am afraid of positioning my baby in prone": Beliefs and knowledge about Tummy time practice. *Int J Pediatr*. 2023;2023:1-7. doi:10.1155/2023/4153523
  - 9. Wentz EE. Importance of initiating a "Tummy time" intervention early in infants with down syndrome. *Pediatric Physical Therapy*. 2017;29(1):68-75. doi:10.1097/pep.0000000000000335
  - 10. Direktorat Kesehatan Keluarga, Departemen Kesehatan Republik Indonesia. Pedoman pelaksanaan stimulasi, deteksi dan intervensi dini tumbuh kembang anak. Jakarta: Bakti Husada; 2016.

## Clinical Approach to Differentiating Epileptic Seizures from Bipolar Disorder

Wardah Rahmatul Islamiyah, Rudolph Mulianwan Putera

Department of Neurology, Faculty of Medicine Airlangga University, Surabaya, Indonesia

### Abstract

Distinguishing between epileptic seizures and bipolar disorder in clinical setting presents a significant challenge due to overlapping symptoms and the complex mechanism underlying both conditions. This study offers a novel perspective by integrating the latest research and clinical practices to explore this intricate diagnostic landscape. Unlike previous studies that primarily focused on isolated aspects, this study synthesizes recent advancements in neuroimaging, wearable technology, and machine learning to enhance diagnostic accuracy. Data sources searched were Google Scholar, PubMed, and ScienceDirect using the keywords of 'epileptic seizures', 'bipolar disorder', 'diagnosis', 'neuroimaging', 'wearable technology', and 'machine learning'. Following the Preferred Reporting Item for Systematic Review and Meta-Analysis (PRISMA) methodology, the findings highlight how the variability of mood episodes and their resemblance to seizure activity often complicate differential diagnosis. Moreover, they underscore the potentials of emerging technologies, such as real-time monitoring via wearable devices and AI-driven diagnostic tools, in refining current clinical approaches. This study emphasizes the necessity of clinic awareness regarding subtle but crucial distinctions between bipolar disorder and epileptic seizures. By leveraging continuous monitoring and data-driven insights, an innovative framework that combines clinical expertise with advanced technology is proposed, paving the way for more precise and effective diagnostic methods.

**Keywords:** Bipolar disorder, differential diagnosis, diagnosis, epileptic seizures

### Introduction

Epileptic seizures are temporary neurological events caused by excessive or unusually synchronous neuronal activity in the brain. Their clinical manifestations vary based on factors such as the site of onset, brain maturity, and confounding conditions.<sup>1</sup> Seizures are unpredictable, potentially life-threatening, and classified into focal onset, generalized onset, or unknown onset.<sup>2</sup> Despite advances in epilepsy research, determining its etiology remains challenging due to heterogeneity, requiring sophisticated diagnostic tools.

Bipolar disorder is a chronic psychiatric condition comprising bipolar I disorder (BD I) and bipolar II disorder (BD II). BD I presents with manic episodes, while BD II includes hypomanic

and major depressive episodes.<sup>3</sup> Diagnosing bipolar disorder is complex due to symptom overlap with other psychiatric conditions, frequent comorbidities, and the absence of objective biomarkers. This overlap creates a significant challenge in distinguishing between epileptic seizures and bipolar disorder, as both conditions share clinical similarities, including transient mood and behavioral changes.<sup>4</sup>

The difficulty in differentiating epileptic seizures from bipolar disorder has significant clinical consequences. Epileptic seizures can be diagnosed using clinical manifestations, EEG, ECG, neuroimaging, and laboratory findings. However, due to variations in symptoms, distinguishing epileptic from non-epileptic seizures remains difficult. Similarly, bipolar disorder diagnosis is hindered by symptom overlap, lack of patient awareness, and societal stigma.<sup>4</sup> Misdiagnosis can lead to inappropriate treatment strategies, exposing patients to ineffective or even harmful interventions, thereby worsening their prognosis.<sup>5</sup> Given the potential for severe morbidity and mortality

---

#### Corresponding Author:

Wardah Rahmatul Islamiyah  
Department of Neurology, Faculty of Medicine, Airlangga  
University, Surabaya  
Email: wardah-ri@fk.unair.id

associated with both conditions, improving diagnostic accuracy is crucial.

Advancements in neuroimaging techniques have enhanced the diagnosis of both epileptic seizures and bipolar disorder by identifying structural abnormalities.<sup>5</sup> Recent research has also explored the role of wearable devices and machine learning in refining diagnostic precision.<sup>4</sup> These technologies offer promising solutions by providing objective and quantifiable diagnostic markers. However, previous studies have mainly focused on comparing epilepsy with non-epileptic seizures or bipolar disorder with other psychiatric illnesses, often without an integrated interdisciplinary approach.<sup>3,6,7</sup>

This study provides a novel interdisciplinary approach by integrating genetic biomarkers, neuroimaging techniques, and immune factor analysis to improve diagnostic accuracy between epileptic seizures and bipolar disorder. Unlike previous studies that focused on isolated diagnostic tools, this research examines the combined potential of genetic markers (SCN1A for epilepsy and CACNA1C for bipolar disorder),<sup>8,9</sup> immune response biomarkers (IL-6 and TNF- $\alpha$ ),<sup>1,10</sup> and neurophysiological assessments (VEEG, MRI, and machine learning-based tools)<sup>5,6,11</sup> to establish a comprehensive and evidence-based diagnostic framework. The findings of this study will bridge the gap between neurology and psychiatry, offering a more integrated diagnostic pathway for clinicians.

To address these diagnostic challenges, this study proposes an interdisciplinary approach combining expert opinions from neurology and psychiatry alongside an extensive survey of current diagnostic methodologies and technological advancements. The integration of neuroimaging innovations, molecular genetics, and expert consensus provides a robust diagnostic framework that enhances accuracy. Additionally, the study evaluates the utility of emerging technologies such as machine learning-based assessment tools to improve real-time diagnostic precision.<sup>9</sup>

This study aims to establish an evidence-based diagnostic framework that improves the differentiation of epileptic seizures from bipolar disorder. By investigating advanced neuroimaging methods, molecular biomarkers, and interdisciplinary diagnostic techniques, this research seeks to refine clinical decision-making and optimize patient care. The findings will contribute to developing a standardized diagnostic approach that minimizes misdiagnosis and enhances patient outcomes, particularly

in clinical settings where diagnostic ambiguity remains a challenge.

## Methods

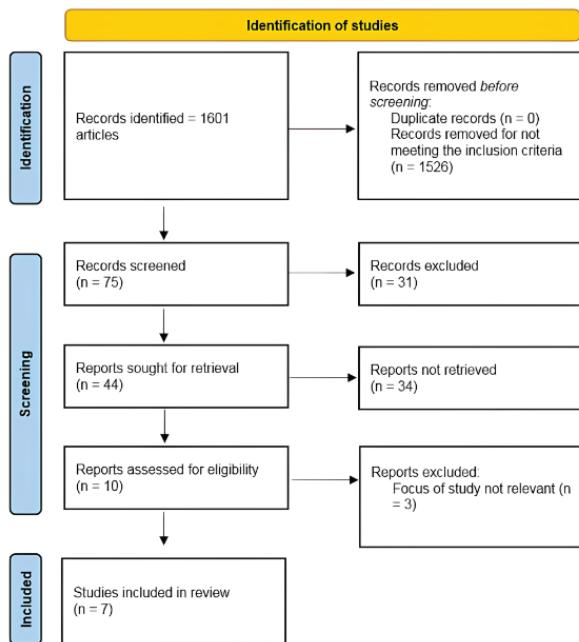
This study uses a narrative review approach based on research articles available on Google Scholar, PubMed, and Science Direct with the keywords "epileptic seizures" and "bipolar disorder" combined with "detection", "diagnostics", "wearable devices", and the "machine" is learning". The method for conducting this review is to follow the Preferred Reporting Item for Systematic Review and Meta-Analysis (PRISMA) method.<sup>26</sup> The literature review is carried out in four stages, namely; selection criteria, information sources, filtering, and Data analysis. The selection criteria in this review are published in English, published during 2014–2024, full text articles are available, topics discussed are epilepsy or bipolar disorder. Exclusion criteria are only abstract articles, and Science Direct.

## Results

Article filtering was carried out using a combination of keywords as stated in the method section. Initial identification found 1601 articles. After screening, including the inclusion criteria, 75 articles were obtained. 31 of 75 articles were excluded due to ineligible methodology and 44 articles were further screened. There were 10 articles eligible for review and based on their relevance, 7 articles were included for review. The detailed screening process can be seen in Figure 1.

This summary covers seven studies on epilepsy, seizure detection, and psychiatric disorders. Research highlights challenges in epilepsy diagnosis, with machine learning and deep learning improving seizure detection and prediction. Genetic markers aid epilepsy classification, while ML enhances psychiatric disorders diagnosis. Neuroimaging studies identify cerebellar and frontoparietal biomarkers for bipolar disorder, supporting early diagnosis and treatment. Table 1 provides detailed findings.

Article 1 states that in determining the diagnosis and prognosis of epilepsy, immune factors in the blood can be considered as biomarkers of epileptic seizures. According to article 2, the symptoms of epileptic attacks originate from abnormal brain function.



**Figure 1 Article Screening Process**

Furthermore, article 3 states that genetic biomarkers are considered as one of the etiological factors of epileptic seizures. In identifying new genes associated with epilepsy, genetic testing can be used because differences in genetic results cause different types of epilepsy.<sup>8</sup> In article 4 it is stated that seizure activity depends on the localization of the epileptogenic zone in the brain.

Articles 5 and 6 state that genetic expression in the brain, particularly the cerebellum, is found to be a biomarker for bipolar disorder and other neuropsychiatric diseases. Identification of biomarkers can be used for classification and provide insight into the biology underlying behavioral symptoms in psychiatric disorders.<sup>9,15</sup> Article 7 states that changes in function and morphology in several local parts of the brain are found in patients with bipolar disorder.<sup>10</sup> Biomarker detection can be useful for early treatment of patients.

In article 1 it is stated that a video-electroencephalogram or vEEG is needed to verify the interictal, ictal and postictal periods in the evaluation of seizures. Neuroimaging via vEEG can verify immune factors in temporal lobe seizures in adults. Article 2 finds that an electroencephalogram or EEG is used to determine electrical recordings of brain activity which are then used to categorize epilepsy

patients.<sup>8</sup> Neuroimaging such as EEG is necessary in delineating the epileptogenic zone of epilepsy. EEG combined with other neuroimaging tools can increase accuracy in localizing the epileptogenic zone. Article 4 found that Electrical Impedance Tomography (EIT) has the potential to improve localization of the epileptogenic zone. In bipolar disorder, article 7 states that neuroimaging techniques such as MRI are used to identify functional brain abnormalities and classify the type of bipolar disorder. With neuroimaging, pathological mechanisms that trigger manic episodes can be identified.<sup>7</sup>

Advances in medical equipment and neuroimaging are being made to improve the diagnostics and detection of diseases and disorders, including epileptic seizures and bipolar disorder. The detection model was proven to be 99% more accurate in evaluating epileptic seizures, reducing the False Alarm Rate (FAR) in a shorter time. Article 2 finds that by using machine learning algorithms, classification and prediction accuracy can be improved. Meanwhile, article 3 found that advances in genetic testing also helped reclassify epilepsy with clinical correlation and segregation studies. For bipolar disorder, article 5 finds that machine learning is also used in optimizing genetic analysis for diagnostics and classification. Machine Learning tools can minimize human error and increase

**Table 1 Summary of 7 Articles**

Article	Author	Subject	Method	Result	Key Finding
1	Elger CE, Hoppe C. (2018) <sup>1</sup>	Epilepsy-diagnostic challenges	Clinical evaluation, EEG, patient self-reporting	Challenges in accurate seizure reporting and diagnosis	Under-reporting and misdiagnosis are common in epilepsy
2	Thangarajoo RG et al. (2021) <sup>13</sup>	Machine learning for epileptic seizure detection	Wavelet and EMD-Based Decomposition Techniques	Improved epileptic seizure detection using ML techniques	ML-based methods improve seizure detection significantly
3	Akbar F et al. (2022) <sup>8</sup>	Genetic testing in pediatric epilepsy	Genetic testing for epilepsy classification	Genetic markers identified for epilepsy classification	Genetic markers can refine epilepsy classification
4	Jaishankar B et al. (2023) <sup>14</sup>	Deep learning for seizure prediction	Deep learning model for seizure prediction	Deep learning model enhanced seizure prediction accuracy	AI models increase accuracy of seizure onset prediction
5	Yang Q et al. (2022) <sup>9</sup>	Machine learning for psychiatric disorder classification	Machine learning-based classification	Machine learning improved psychiatric disorder classification	Machine learning enhances psychiatric diagnosis accuracy
6	Thomaidis GV et al. (2023) <sup>15</sup>	Cerebellar biosignature in bipolar disorder	Automatic machine learning analysis	Identified unique cerebellar patterns in bipolar disorder	Cerebellar abnormalities serve as bipolar biomarkers
7	Gao Y et al. (2023) <sup>10</sup>	Neuroimaging biomarker for bipolar disorder	MRI-based frontoparietal network analysis	Frontoparietal network homogeneity as a bipolar biomarker	Neuroimaging biomarkers aid in bipolar disorder treatment

classification accuracy. According to article 6, this is very useful in the diagnosis of psychiatric disorders.<sup>16</sup>

## Discussion

Epileptic seizures are temporary occurrences of signs and/or indications due to strange or synchronous nerve movements in the brain. The hallmarks of seizures are chaos, muscle twitching, and twitching, all caused by a multitude of electrical actions within the brain's neurons. These seizures disrupt normal brain function, varying in strength and duration, ranging from momentary loss of consciousness to prolonged attacks.

The mental illness known as manic depression, or bipolar disorder, causes severe and unpredictable mood swings. Bipolar disorder is an episodic up-and-down flow of

mood swings. Affected individuals experience increased mood, energy, and impulsivity during manic or hypomanic episodes. After a manic episode, the person usually experiences a major depressive episode, which makes them feel sad, hopeless, and disinterested in activities. The severity and duration of mood episodes are used to categorize the condition into different types. Severe manic episodes define bipolar I disorder and are often followed by depressive episodes, whereas hypomanic episodes and major depressive episodes are characteristic of bipolar II conditions. Cyclothymic disorder is a milder form, featuring several periods of hypomanic symptoms and depressive symptoms that do not meet the criteria for a severe episode.

Previous research suggests that epilepsy and bipolar disorder can coexist in individuals. Within ten years or more post-hospital admission, the ratio of epilepsy following bipolar disorder is higher compared with shorter time spans. The

cause was likely due to epileptic seizures which were initially diagnosed as bipolar disorder which were later reclassified. Conditions coded as bipolar disorder can include interictal dysphoric and other cases of bipolar disorder. Treatment of bipolar disorder may benefit from epilepsy medications such as brain stimulation and epilepsy treatment using anticonvulsants.

The episodic nature of these two diseases is one notable similarity. Experiences of mania, hypomania, and depression occur regularly in people with bipolar disorder, while seizures or seizure episodes sporadically affect people with epilepsy. Disorders such as bipolar and epilepsy are difficult to diagnose because the patterns of seizures and mood attacks are almost indistinguishable. Adding to this puzzle is the fact that the glutamate, GABA, and dopamine systems that influence brain neurotransmitter activity are common to both conditions. When this pathway is damaged, the disorder can worsen and increase. Additionally, the data suggests a possible genetic vulnerability shared by bipolar disorder and epilepsy. Susceptibility to both disorders has been associated with certain hereditary variables and differences in genes relevant to neuronal excitability and synaptic function. This genetic overlap highlights the complex interplay between genetic factors and environmental influences in the manifestation of these disorders.

Apart from being episodic, epilepsy and bipolar disorder also have the same probability in the kindling model and the use of antiepileptic drugs (AED) for the management of both. In the kindling model, repetitive electrical stimulation causes profound changes and may prolong episodes of epilepsy and bipolar disorder.<sup>17</sup> A future-oriented learner-centered 'Empowerment Paradigm' that empowers and endorses all learners with future success. It is an influential and tempting way of restructuring and reorganizing engineering education. Washington Accord, an International accreditation convention, an independent agreement between signatory organizations to provide an external accreditation to undergraduate engineering programs. The accredited engineering programs that qualify an engineer to enter into the practice of professional engineers are equally recognized and acknowledged by other signatory countries and responsible organizations Pakistan Engineering Council (PEC). The ignition mechanism may explain the common underlying pathophysiology between epilepsy and bipolar disorder. Several neurotransmitters such as

GABA, excitatory amino acids (EAA), dopamine, and serotonin imbalance are known to impact epilepsy and bipolar disorder. It is important to know whether mood stabilizers, especially AEDs, can provide neuroprotective effects. This is because excessive neurotoxicity may be associated with epilepsy and bipolar disorder.

In the treatment of epilepsy, vagus nerve stimulation (VNS) is an option for pharmacoresistant epilepsy patients aged four years and over who cannot undergo or fail to undergo resective surgery. Approximately 8% of patients achieved seizure freedom after >2 years of VNS treatment and approximately 50% experienced a reduction in seizure frequency of at least 50%. Despite the low rate of seizure freedom, epilepsy patients are still advised to undergo neuromodulation treatments such as VNS. Interest is increasing in brain stimulation as an adjunct or alternative to medication and psychotherapy for bipolar disorder, and the evidence base is growing rapidly. Treatment options such as deep brain stimulation or vagus nerve stimulation may address some of the challenges associated with the complex clinical picture of bipolar disorder in difficult-to-treat patients. Additionally, Vagus nerve stimulation (VNS) has been proposed to improve attention and working memory. Vagus nerve stimulation (VNS) is intended to treat major depression or resistant bipolar disorder when the patient is refractory to conventional treatment or is indifferent to medications or convulsive seizure therapy. However, it was found that VNS took longer to improve the condition.

Over the past two decades, the use of anticonvulsants for the treatment of bipolar disorder has increased rapidly in accordance with recent findings of the efficacy of valproate, carbamazepine, and lamotrigine. Previous research found that carbamazepine and valproate proved effective as mood stabilizers in bipolar disorder patients. Lamotrigine is also known to have a much better effect in treating depressive episodes in bipolar disorder compared to placebo. Valproate has been found to be a safe option with favorable side effects in association with short-term mania or mixed states. Meanwhile, carbamazepine has the best efficacy in treating mania and lamotrigine has the mildest side effects and is mainly used to prevent depression recurrence. These similarities may stem from similar pathophysiology. Therefore, epileptic seizures and bipolar disorder may benefit from the use of neuroimaging and machine learning.<sup>7</sup>

Pathobiological differences between epileptic seizures and bipolar disorder can be seen through neurotransmitter imbalances, ion channel dysfunction, neural networks, irregularities, genetic factors, and neuroinflammation and neuroprotection. Considering the imbalance of neurotransmitters, in epileptic seizures, abnormalities in excitability and neural synchronization arise from an imbalance of neurotransmitters, namely glutamate and gamma-aminobutyric acid (GABA), which triggers epileptic attacks. Meanwhile, in bipolar disorder, changes in mood and changes in energy levels are symptoms of bipolar disorder which are caused by an imbalance in the neurotransmitter system of serotonin, dopamine and norepinephrine. From ion channel dysfunction, epileptic seizures can be triggered by abnormal discharges and brain hyperexcitability that may be caused by mutations in ion channel genes, particularly those related to voltage-gated sodium channels. Meanwhile, in bipolar disorder, involvement of ion channels, particularly calcium channels, has been linked to the pathophysiology of bipolar disorder, potentially affecting mood regulation and neural communication. However, ion channel damage is not the main cause.<sup>9</sup>

For neural network disorders, epileptic seizures caused by abnormal synchronized neural activation patterns in certain brain regions or tissues can disrupt the balance between excitatory and inhibitory neurons and cause epilepsy. Meanwhile, a common characteristic of bipolar disorder is disruption of the prefrontal cortex and limbic system, the two main brain networks that regulate emotions. Genetic factors also play an important role in epileptic seizures and bipolar disorder. Several genetic disorders that impact ion channels, neurotransmitter receptors, or synaptic proteins can make a person more susceptible to epilepsy. Bipolar disorder is known to have a complex genetic basis consisting of many susceptible genes, each with minimal impact, and has been implicated in genes related to synaptic plasticity, neurotransmitter pathways, and circadian rhythms.

The final pathobiological difference between bipolar disorder and epileptic seizures can be seen from their neuroinflammation and neuroprotection. Neuroinflammation and disruption of the neuroprotective system may be involved in the development of epileptogenesis, which can lead to recurrent seizures and nerve damage. Investigations into the exact relationship are still ongoing, but low-grade

chronic neuroinflammation has been observed in bipolar disorder, which may be related to oxidative stress and altered neuroprotective mechanisms.

According to Goodwin and Jamison, the differences between epileptic seizures and bipolar disorder can be determined from the nature of the episodes, duration and frequency, consciousness and awareness, motor symptoms, triggering and precipitating factors, as well as post-episode conditions.

Judging from its episodic nature, epileptic attacks are usually caused by abnormalities in the electrical activity of the brain, which are characterized by seizures, muscle twitches, or changes in consciousness and sensory disturbances. Meanwhile, bipolar disorder is a sporadic mental illness with symptoms of euphoria and high energy for a week or month followed by extreme sadness and despair. Considering their duration and frequency, epileptic seizures can last anywhere from a few seconds to a few minutes, and are not very common, whereas periods of bipolar disorder with abnormal mood can last for days to months, with intermittent periods. separated. normal mood. The duration and frequency of these mood episodes can vary greatly between individuals.

Regarding consciousness and consciousness, seizures can alter consciousness, causing loss of awareness and responsiveness during the episode, while individuals with bipolar disorder maintain full awareness and awareness during mood episodes. For motor symptoms, muscle stiffness, repetitive movements, or twitching are often experienced during epileptic attacks, whereas psychomotor symptoms in bipolar disorder are known to be the main characteristics of increased or decreased activity during manic or depressive episodes. These include agitation or retardation of movement. It is important to pay attention to the motor symptoms associated with this condition.

Triggers and precipitating factors for epileptic attacks are lack of sleep and stress, while bipolar disorder can be triggered by various factors including life events, sleep disorders, and changes in daily routine. Further differences in trigger factors between epileptic seizures and bipolar disorder can be seen in Table 1. In the post-episode state, after a seizure, sufferers may experience a post-tictal state characterized by confusion, fatigue, and memory impairment, whereas after a mood episode they experience a post-seizure state. In bipolar disorder, individuals often return to baseline levels of functioning,

**Table 2 Differences in Precipitating Factors Between Epileptic Seizures and Bipolar Disorder**

Trigger Factors	Bipolar disorder	Epilepsy
Emphasize*	✓ Strong evidence based on retrospective and prospective reports linking stress to mania may be due to endocrinological responses	✓ Strong evidence from retrospective and prospective reports linking stress to seizures. The most affected is the PS of the temporal lobe
Achievement of objectives Program*	✓ Susceptibility to mania-higher life ambitions. Higher levels of manic symptoms following goal attainment events	There is no proof
Emotion**	✓ Tentatively more evidence is required because it can confuse state and trait markers. Fun and entertainment = greater manic symptoms. Lability in those whose relatives express high levels of emotion	✓ In epileptic excitement, fear, anger and anxiety-the number of seizures is greater. Strongly related to PS in TLE
Sleep deprivation*	✓ Sleep deprivation serves as a marker for mania and depression. Animals and humans are associated with manic and manic-like behavior in bipolar disorder. Prospective evidence to support sleep deprivation and transition to mania	✓ Associated with focal seizures in TLE self-report. A seizure diary—to say the least A sleep reduction of 1.5 hours can cause more seizures
Moon phases	Associated with a high incidence of hospital admission. There is no direct evidence for bipolar disorder.	No effect on epileptic seizures, possible effect on non-epileptic seizures
Seasonal variations	✓ Spring and summer are associated with mania in bipolar disorder which may be caused by the effects of light and/or sleep deprivation	✓ Epileptiform discharge occurs more frequently in winter. Seizures are more common in winter focal seizures are less common on sunny days
Puberty/ menarche	Related to the beginning. There is no specific evidence that this is a triggering factor	Possible predisposing factors are inconsistent findings related to menarche
Period	Symptom fluctuations but not mania specifically, are strong candidates for future research	✓ Focal seizures in TLE—catamenial epilepsy
Postpartum	✓ Associated with mania and psychosis	Possible predisposing factors
Fairy/ menopause	Worsening/fluctuating symptoms require more research into hormonal levels verification. Possible predisposing factors	More research is needed on possible predisposing factors
Antidepressant Treatment*	✓ The mechanism is unknown, suggesting a role for neurotransmitters in initiation mania	✓ Lowers the seizure threshold

\* indicates the same precipitating factor in both disorders; \*\*tentative precipitating factors ✓ indicates precipitating factor<sup>18</sup>

with periods of euthymia (normal mood).

A combination of clinical assessment, medical history, electroencephalogram (EEG) data, and, in certain situations, neuroimaging examination is usually used to make a diagnosis. However, the level of support for this technique can vary. An example of the application of this technique can be seen below; however, for any modification of

diagnostic criteria or instruments, it is important to refer to the most recent research.

In differentiating epileptic seizures from bipolar disorder, several tools can be used to investigate them. These tools include clinical evaluation, ictal video encephalogram (EEG), neuroimaging studies (MRI, CTScan), and neuropsychological assessment. Clinical

evaluation by experienced neurologists and psychiatrists is considered essential for accurate diagnosis, although the level of evidence may be relatively lower due to its subjective nature. EEG, especially long-term video EEG monitoring (including ictal EEG), is an important tool in capturing and analyzing brain wave patterns during seizure events. This provides valuable information for diagnosing epileptic seizures.<sup>6</sup> Neuroimaging studies, such as magnetic resonance imaging (MRI) or computerized tomography (CT) scans, can help identify structural abnormalities in the brain and rule out certain causes of seizures.<sup>11</sup> Identifying specific patterns associated with mood disorders or epileptic seizures can be facilitated with the help of a neuropsychological assessment. This assessment is useful in evaluating cognitive function.<sup>20</sup> Given the importance of a thorough evaluation, diagnosing such conditions often requires examination of the medical and family background, as well as the manifestation of certain indications.

Several studies have explored the application of different tools in diagnosing epileptic seizures and bipolar disorder. The seven articles included in this study provide insights into their advantages and disadvantages. For instance, neuroimaging techniques such as MRI and CT scans have been effective in identifying structural abnormalities, but their accessibility and high costs in certain regions limit their use.<sup>6</sup> Video-EEG monitoring is considered optimal for diagnosing psychogenic non-epileptic seizures (PNES), yet its availability remains a challenge in resource-limited settings.<sup>11</sup> Meanwhile, machine learning-based diagnostic tools have shown promise in improving accuracy and early detection, though concerns about data bias and interpretability need to be addressed.<sup>9</sup>

Recent genetic studies have identified potential biomarkers for both epilepsy and bipolar disorder. Article no. 3 highlights specific gene variants that may serve as new biomarkers. Among these, CACNA1C and SCN1A have been implicated in both conditions due to their roles in neuronal excitability and synaptic function.<sup>8</sup> The identification of such genes could pave the way for more precise diagnostic and therapeutic strategies, emphasizing the need for further genetic screening and validation studies.<sup>9</sup> Genetic testing should be considered in cases where a hereditary component is strongly suspected, particularly when there is a family history of epilepsy or psychiatric disorders. Specific gene variants have been identified as

potential biomarkers for these conditions. The SCN1A gene has been primarily associated with epilepsy, particularly generalized epilepsies and Dravet syndrome, due to its role in neuronal excitability and sodium channel regulation.<sup>8</sup> Mutations in SCN1A can lead to hyperexcitability of neurons, increasing seizure susceptibility. On the other hand, the CACNA1C gene has been strongly linked to bipolar disorder, as it encodes a subunit of voltage-gated calcium channels that influence neuronal signaling and synaptic plasticity.<sup>9</sup> Studies have shown that variations in CACNA1C contribute to altered calcium channel function, which is implicated in mood regulation and psychiatric disorders, making it a key biomarker for bipolar disorder.

Additionally, immune system factors have been increasingly recognized as potential biomarkers for epilepsy. Article no. 1 discusses the role of pro-inflammatory cytokines, such as IL-6 and TNF- $\alpha$ , in epileptic conditions.<sup>1</sup> Elevated levels of these cytokines have been observed in epilepsy patients, suggesting an inflammatory component in seizure pathophysiology. These findings align with other studies emphasizing neuroinflammation as a critical mechanism in epilepsy, further supporting the potential role of immune biomarkers in diagnosis and treatment strategies.<sup>10</sup> Future studies should explore how these immune markers interact with genetic predispositions to refine diagnostic accuracy and therapeutic approaches.

Given the evolving landscape of epilepsy and bipolar disorder diagnostics, integrating multimodal approaches—including neuroimaging, genetic screening, immune profiling, and machine learning—may significantly enhance clinical decision-making. However, challenges such as accessibility, cost, and validation of new biomarkers need to be addressed through collaborative interdisciplinary research efforts.

Differentiating epileptic seizures from bipolar disorder presents persistent challenges for clinicians and researchers. Accurate distinction is essential for effective management and improved patient outcomes, yet both conditions share overlapping symptoms, genetic predispositions, and environmental triggers. Recognition of these similarities underscores the need for comprehensive and multidisciplinary assessment. Collaboration among specialists in neurology, psychiatry, and neuropsychology is fundamental to refining diagnostic strategies.

Recognition of the similarity of symptoms, genetic predisposition, and environmental

triggers between epileptic seizures and bipolar disorder underscores the need for differentiated and comprehensive assessment. Genetic testing should be considered in cases where a hereditary component is strongly suspected, particularly when there is a family history of epilepsy or psychiatric disorders. Specific gene variants, such as CACNA1C and SCN1A, have been associated with both conditions and may serve as potential biomarkers to refine diagnosis and tailor treatment strategies.<sup>8,9</sup> Similarly, video-electroencephalogram (vEEG) should be used in cases where non-epileptic seizures are suspected, such as psychogenic non-epileptic seizures (PNES), or when routine EEG findings are inconclusive.<sup>11</sup> vEEG remains a critical tool in capturing ictal events and distinguishing between epileptic and non-epileptic seizures, particularly in patients with atypical presentations or treatment-resistant cases.<sup>6,7</sup>

This review is limited by heterogeneity in diagnostic techniques, lack of quantitative synthesis, and potential publication bias, which restrict generalizability. Furthermore, while emerging biomarkers and neuroimaging hold promise, their clinical validation remains incomplete and requires large-scale studies.

Future research should integrate genetic, neuroimaging, and immunological biomarkers to enhance diagnostic accuracy and support individualized treatment planning. Continued interdisciplinary collaboration and technological advances are essential for developing standardized frameworks that improve patient care and quality of life.

## References

1. Elger CE, Hoppe C. Diagnostic challenges in epilepsy: seizure under-reporting and seizure detection. *Lancet Neurol*. 2018;17(3):279–88. doi:10.1016/S1474-4422(18)30038-3
2. Yu S, Atrache RE, Tang J, Jackson M, Makarucha A, Cantley S, et al. Artificial intelligence-enhanced epileptic seizure detection by wearables. *Epilepsia*. 2023;64(12):3212–26. doi:10.1111/epi.17774
3. McIntyre RS, Berk M, Brietzke E, Goldstein BI, López-Jaramillo C, Kessing LV, et al. Bipolar disorders. *Lancet*. 2020;Dec 5;396(10265):1841–56. doi:10.1016/S0140-6736(20)31544-0
4. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. *Epilepsia*. 2017;58(4):512–21. doi:10.1111/epi.13709
5. Pambudi P, Sidabutar O. Headache Patients hubungan antara derajat stres psikologis dengan intensitas nyeri pada pasien nyeri kepala tipe tegang. 2024;33(1):6–10.
6. Lapalme-Remis S, Nguyen DK. Neuroimaging of Epilepsy. *Continuum (Minneapolis Minn)*. 2022;28(2):306–38. doi:10.1212/CON.0000000000001080
7. Leibetseder A, Eisermann M, LaFrance Jr WC, Nobili L, Oertzen TJ von. How to distinguish seizures from non-epileptic manifestations. *Epileptic Disord Int epilepsy J with videotape*. 2020;22(6):716–38. doi:10.1684/epd.2020.1234
8. Akbar F, Saleh R, Kirmani S, Chand P, Mukhtiar K, Jan F, et al. Utility of genetic testing in pediatric epilepsy: Experience from a low to middle-income country. *Epilepsy Behav Reports*. 2022;20(100575). doi:10.1016/j.ebr.2022.100575
9. Yang Q, Xing Q, Yang Q, Gong Y. Classification for psychiatric disorders including schizophrenia, bipolar disorder, and major depressive disorder using machine learning. *Comput Struct Biotechnol J*. 2022;20:5054–5064. doi:10.1016/j.csbj.2022.09.014
10. Gao Y, Guo X, Wang S, Huang Z, Zhang B, Hong J, et al. Frontoparietal network homogeneity as a biomarker for mania and remitted bipolar disorder and a predictor of early treatment response in bipolar mania patient. *J Affect Disord*. 2023;339:486–94. doi:10.1016/j.jad.2023.07.033
11. Ali A. Global health: epilepsy. *Semin Neurol*. 2018;38(2):191–9. doi:10.1055/s-0038-1646947
12. Nurfianto S, Suhanda R, Yuarta FA, Refani P, Nina T, Sembiring A, et al. Review determinan sectio caesarea nonmedis di Indonesia: sebuah kajian sistematis. 2024;33(1):54–61.
13. Thangarajoo RG, Reaz MBI, Srivastava G, Haque F, Ali SHM, Bakar ASA, et al. Machine learning-based epileptic seizure detection methods using wavelet and emd-based decomposition techniques: a review. *Sensors (Basel)*. 2021;21(24):8485. doi:10.3390/s21248485
14. Jaishankar B, M AA, D V, Raja L. A novel epilepsy seizure prediction model using deep learning and classification. A novel epilepsy seizure prediction model using deep learning and classification. *Healthc*

- Anal. 2023;4:100222. doi:10.1016/j.health.2023.100222.
15. Thomaidis G V, Papadimitriou K, Michos S, Chartampilas E, Tsamardinos I. A characteristic cerebellar biosignature for bipolar disorder, identified with fully automatic machine learning. *IBRO Neurosci Reports.* 2023;15:77–89. doi:10.1016/j.ibneur.2023.06.008
16. Almustafa KM. Classification of epileptic seizure dataset using different machine learning algorithms. *Informatics Med Unlocked.* 2020;21:100444. doi:10.1016/j imu.2020.100444
17. Shaheen S. Theoretical perspectives and current challenges of outcome-based education framework. *Int J Eng Educ.* 2019;1(2):122–9. doi: 10.14710/ijee.1.2.122-129
18. Bostock ECS, Kirkby KC, Garry MI, Taylor BVM. Comparison of precipitating factors for mania and partial seizures: Indicative of shared pathophysiology?. *J Affect Disord.* 2015;183:57–67. doi:10.1016/j.jad.2015.04.057

## Correlation Between Anemia, Sexually Transmitted Infections, and Low Birth Weight Among Pregnant Women

Elviara Martha Tinova Suprapto,<sup>1</sup> Mega Memory Rahasa Putra,<sup>1</sup> Thomas Yan Bangun,<sup>2</sup> Nur Azizah,<sup>2</sup>

<sup>1</sup>General Practitioner in the Scholoo Keyen Hospital South Sorong, South West Papua, Indonesia

<sup>2</sup>Obstetrics and Gynecology Specialists in the Scholoo Keyen Hospital South Sorong, Southwest Papua, Indonesia

### Abstract

Anemia in pregnancy and sexually transmitted infections (STIs) are global health issues linked to low birth weight. This study explored the correlation between these factors and low birth weight at the General Hospital of Scholoo Keyen, South Sorong, Southwest Papua, Indonesia. A cross-sectional observational analytic study was conducted from September 2022 to March 2023, involving pregnant women who gave birth at the General Hospital of Scholoo Keyen. The correlation between risk factors and low birth weight was analyzed using the chi-square test with a significance threshold of  $p<0.05$ . Results showed that among 162 pregnant women (average age:  $27.72\pm6.62$  years), anemia severity was distributed as follows: severe (3.7%), moderate (16.0%), and mild (40.1%). However, no significant relationship was found between anemia and birth weight ( $p=0.850$ ,  $p>0.05$ ). The incidences of HIV, syphilis, and hepatitis B were 3.1%, 13.6%, and 7.4%, respectively. A significant association was identified between HIV infection and low birth weight ( $p=0.000$ ), while no such association was found for syphilis ( $p=0.160$ ) or hepatitis B infection ( $p=0.852$ ). In conclusion, HIV infection is associated with low-birth-weight newborns, but there are no apparent relationships between anemia, syphilis, or hepatitis B infection and low-birth-weight newborns. This study implies the importance of nutritional support among pregnant mothers with HIV and delaying pregnancy in HIV-positive women until their immune system improve.

**Keywords:** Anemia, low birth weight, sexually transmitted infections

### Introduction

Low birth weight (LBW) affects 15% to 20% of all births globally, which corresponds to over 20 million births annually. The prevalence of low birth weight varies significantly across different regions.<sup>1</sup> In the Southeast Asian region, the prevalence of low birth weight ranges from 7% to 21%.<sup>2</sup> Based on data analysis from 2017 Indonesia Demographic and Health Survey, the prevalence of low birth weight in Indonesia is recorded at 6.1%.<sup>3</sup> Meanwhile, the prevalence of LBW in West Papua in 2019, based on West Papua Public Health Office, is 10.4%.<sup>4</sup> Several factors contribute to low birth weight during pregnancy, including maternal age, occupation, body weight, number of pregnancies, smoking

history, gestational length, previous childbearing, reproductive health, poor nutritional status, socioeconomic disparities, inadequate attention to proper diet and supplement intake during pregnancy, season of birth, frequency of prenatal care, anemia, birth defects, pre-pregnancy health conditions, and the family's socioeconomic status.<sup>5</sup>

Anemia is a common nutritional deficiency that significantly impacts pregnant women. Lower levels of hemoglobin in the blood lead to alterations in placental angiogenesis, which restricts the oxygen supply to the developing fetus.<sup>6</sup> Research on the relationship between anemia during pregnancy and low birth weight remains controversial. Tabrizi, in a study conducted in Iran in 2015, stated that low hemoglobin levels during pregnancy are associated with low birth weight.<sup>7</sup> However, a study by Sibuea et al. in 2022 revealed no significant relationship between anemia in pregnant mothers and the occurrence of low birth weight.<sup>8</sup>

### Corresponding Author:

Elviara Martha Tinova Suprapto  
 General Practitioner in the Scholoo Keyen Hospital South Sorong, South West Papua, Indonesia  
 Email: nova.elviara@gmail.com

Maternal infection is a significant cause of low birth weight.<sup>5</sup> Sexually transmitted infections (STIs) during pregnancy are associated with various adverse birth outcomes, including preterm birth, low birth weight, perinatal death, and congenital infections, which may lead to increased mother-to-child transmission.<sup>9</sup> In addition, Human Immunodeficiency Virus (HIV), Syphilis, and Hepatitis B are included in the "Triple elimination", a government program to prevent the transmission of infections from mother to her child. Moreover, Papua is one province contributing most to sexually transmitted diseases in Indonesia.<sup>2</sup> Furthermore, various studies show that HIV, syphilis, and hepatitis B infections during pregnancy are associated with LBW.<sup>10,11,12</sup> Therefore, this study also assessed the association of these three sexually transmitted diseases with LBW.

The study focused on investigating the risk factors associated with low-birth-weight infants, with specific emphasis on risk factors including anemia and three sexually transmitted diseases including HIV, Hepatitis B, and Syphilis infections at the General Hospital of Scholoo Keyen, located in South Sorong, Southwest Papua.

## Methods

This observational analytic study with a cross-sectional design was conducted at Scholoo Keyen General Hospital, South Sorong, from September 2022 to March 2023. Ethical approval was obtained from the Faculty of Medicine, Brawijaya University (No. 112/EC/KEPK/05/2024).

Using total sampling, 162 pregnant women delivering at the hospital during the study period were included. Inclusion criteria consisted of newborns born at the General Hospital of Scholoo Keyen, South Sorong, Southwest Papua, during the specified study period, ensuring that they were alive, and that the delivery mothers had completed medication and data collection. Exclusion criteria encompassed newborns born outside the hospital, intrauterine fetal demise (IUFD), premature labor (<36 weeks gestation), cases where delivery mothers left against medical advice, and instances of incomplete data.

The study investigated various variables, including socio-demographic factors, obstetric factors, anemia, and sexually transmitted diseases (STDs) infection. Socio-demographic factors encompassed age, body mass index, and nutritional status. Obstetric factors included labor history and newborn weight. Anemia

characteristics were categorized as normal, mild anemia (Hb 9–10.9 mg/dL), moderate anemia (Hb 7–8.9 mg/dL), and severe anemia (Hb <7 mg/dL). Nutritional status was classified into underweight (BMI 17–18.4 kg/m<sup>2</sup>), normal (BMI 18.5–25 kg/m<sup>2</sup>), overweight (BMI 25.1–27 kg/m<sup>2</sup>), and obese (BMI >27 kg/m<sup>2</sup>). Sexually transmitted disease infections comprised hepatitis B, syphilis, and HIV infection. Low birth weight infants were defined as those weighing less than 2500 grams.

Data were presented using mean and standard deviation. Categorical data were presented using totals and percentages. The association between risk factors and the incidence of low birth weight was analyzed using chi-square test. Data analysis was conducted using IBM SPSS Statistic version 26 with the significance level set at p<0.05.

**Table 1 Sample Characteristics**

Variable	Frequency (n=126)	%
Anemia		
Severe	6	3.7
Moderate	26	16
Mild	65	40.1
Normal	65	40.1
Age (years)		
≤20	27	16.7
21–34	108	66.7
≥ 35	27	16.7
Nutritional status		
Obesity	77	47.5
Overweight	32	19.8
Normal	52	32.1
Underweight	1	0.6
Syphilis		
Yes	22	13.6
No	140	86.4
Hepatitis B (HbsAg)		
Yes	12	7.4
No	150	92.6
HIV		
Yes	5	3.1
No	157	96.9

## Results

The study participants were selected based on baby weight information gathered from 162 respondents. It was observed that sixteen respondents (9.9%) had babies with low birth weight (LBW), while 146 respondents (90.1%) had babies with normal birth weight. The study results revealed the hemoglobin (Hb) status in pregnant women among the 162 respondents. In the normal category, there were sixty-five respondents (40.1%). In the mild anemia category, there were sixty-five respondents (40.1%). The moderate category included twenty-six respondents (16%), while the severe anemia category consisted of six respondents (3.7%) (Table 1).

Mothers with anemia in the third trimester

had eleven babies born with LBW and 102 babies born without LBW. The statistical analysis revealed that there was no association. Most pregnant mothers had an obese nutritional status, specifically seventy-seven participants (47.5%), and most pregnant mothers were in their productive age, specifically between twenty-one and thirty-four years old, totaling 108 mothers (66.7%). Four mothers with syphilis had four babies with LBW, and eighteen mothers with syphilis had no LBW babies. The statistical analysis indicated that there was no association. A mother with positive HbsAg had one baby with LBW, and eleven mothers with positive HbsAg had no LBW babies. The statistical analysis indicated that there was no significant difference. Three mothers with positive HIV had three babies with LBW, and two others with

**Table 2 Association Between Risk Factors and Low Birth Weight**

Risk Factor	Low Birth Weight		p-value
	Yes	No	
Anemia			
Severe	1 (0.6%)	5 (3.1%)	
Moderate	3 (1.9%)	23 (14.2%)	
Mild	7 (4.3%)	58 (35.8%)	0.85
Normal	5 (3.1%)	60 (37%)	
Nutritional Status			
Obesity	7 (4.3%)	70 (43.2%)	
Overweight	3 (1.9%)	29 (17.9%)	
Normal	6 (3.7%)	46 (28.4%)	0.95
Underweight	0 (0.0%)	1 (0.6%)	
Age			
≥35 Years Old	2 (1.2%)	25 (15.4%)	
21–34 Years Old	9 (5.6%)	99 (61.1%)	0.25
≤20 Years Old	5 (3.1%)	22 (13.6%)	
Syphilis			
Yes	4 (2.5%)	18 (11.1%)	
No	12 (7.4%)	128 (79.0%)	0.16
Hepatitis B (HbsAg)			
Yes	1 (0.6%)	11 (6.8%)	
No	15 (9.3%)	135 (83.3%)	0.85
HIV			
Yes	3 (1.9%)	2 (1.2%)	
No	13 (8%)	144 (88.9%)	*0.001

\*Chi-square test, statistically significant ( $p < 0.05$ )

positive HIV had no LBW babies (Table 2).

## Discussions

This study investigated 162 mothers who delivered at Scholoo Keyen General Hospital, Southwest Papua, to examine associations between LBW and maternal anemia, HIV, hepatitis B, and syphilis. The findings showed no significant association between LBW and maternal anemia, syphilis, or hepatitis B, whereas HIV infection was significantly associated with LBW.

Pregnancy-related anemia can result from insufficient nutrient intake, failure to adhere to the prescribed iron and folic acid supplementation, inadequate preconception and conception care, pregnancy-related health issues such as helminthiasis, and suboptimal dietary habits. These elements, either directly or indirectly, contribute to the occurrence of low birth weight.<sup>13</sup>

Maternal anemia reduces hemoglobin levels and alters placental angiogenesis, restricting oxygen supply to the fetus and potentially impairing intrauterine growth.<sup>14</sup> Inadequate hemoglobin levels impede the mother's capacity to provide oxygen and nutrients to the fetus, impacting both oxygen delivery in the body and placental growth. These negative effects result in prolonged fetal hypoxia and insufficient nutrient supply, leading to suboptimal fetal weight gain and unfavorable birth outcomes, including low birth weight. However, other research showed that birth weight is not exclusively determined by the hemoglobin levels of pregnant mothers. It is influenced by two maternal factors that impact intrauterine fetal growth, the internal and external factors related to pregnant mothers. Hemoglobin levels are categorized as one of the internal factors associated with pregnant mothers.<sup>15</sup>

HIV infection was significantly associated with LBW, consistent with findings from prior studies. For example, a retrospective cohort study in Southern Ethiopia reported that infants born to HIV-negative women had significantly higher mean birth weight ( $3.1 \pm 0.7$  kg) compared to those born to HIV-positive mothers ( $3.0 \pm 0.6$  kg), with a higher prevalence of LBW in the HIV-exposed group (22.2%) compared to the non-exposed group (13.7%). The multivariable analysis revealed that HIV-positive women had a fourfold increased odds of giving birth to LBW infants.<sup>16</sup> Another research in China also showed that HIV infection was strongly associated with

increased risks of LBW and preterm.<sup>17</sup>

Exposure to HIV before or during pregnancy is associated with an increased risk of adverse pregnancy outcomes (APOs) through various mechanisms. Firstly, HIV infection can compromise the immune system, leading to lower immune activation and an elevated risk of preterm birth (PTB). Additionally, immunosuppression and decreased CD4+T cells in HIV-infected pregnancies are linked to low birth weight (LBW). Secondly, HIV-infected mothers exhibit abnormal placenta characteristics and altered placental angiogenesis, contributing to lower placental weight and area, which are significantly associated with reduced infant birth weight. Lastly, the ascending genital tract infection is proposed as a potential mechanism for HIV-associated PTB, with correlations observed between genital-tract matrix-metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinases-1 (TIMP-1) levels, inflammation, and vaginal bacteria in HIV-positive pregnant women. These findings highlight the complex interplay of factors contributing to APOs in the context of HIV exposure during pregnancy.<sup>17</sup> However, another study in the General Hospital of dr. Soebandi, Jember, East Java reported no correlation between LBW and HIV infections in pregnancy, which contrasts with this study.<sup>18</sup>

A study suggested that in HIV-HBV co-infected women, high HBV viral loads increase the risk of low birth weight and potentially HIV perinatal transmission.<sup>11</sup> Maternal HBV status was not associated with low birth weight in this study, which is in line with several other studies.<sup>19,20,21</sup> In this study, maternal HBV status was not associated with LBW, consistent with several reports. However, Sirilert et al. found that maternal positivity for HBsAg and HBeAg increased the likelihood of LBW.<sup>22</sup>

Additionally, syphilis has also been identified as a risk factor for low birth weight.<sup>11</sup> Several studies showed that maternal syphilis is associated with low birth weight.<sup>23,24</sup> During pregnancy, syphilis can lead to these outcomes through the mechanism by which *T. pallidum* sp. *pallidum* spreads to different organs of the fetus, causing damage to the placenta and umbilical cord, usually from the 16th gestational week. Thus, gestational syphilis involves an inflammatory response that can negatively impact the unborn child, resulting in stillbirth, premature birth, and low birth weight.<sup>25</sup> However, this study showed no association between LBW and syphilis infection. This could be due to the

small sample size applied in this study.

This study has several limitations. First, the sample size was relatively small. Second, the analysis focused on selected risk factors and may have overlooked other determinants of LBW. Third, socioeconomic factors were not fully addressed, though they can strongly influence birth outcomes. Therefore, further research with a larger sample size is necessary. In summary, this study concludes that there is a correlation between HIV infection and low birth weight incidence at the General Hospital of Scholoo Keyen, Southwest Papua.

## References

1. Thapa P, Poudyal A, Poudel R. Prevalence of low birth weight and its associated factors: hospital-based cross-sectional study in Nepal. *PLOS Global Public Health*. 2022;2(11):e0001220. doi:10.1371/journal.pgph.0001220
2. Wulandari F, Mahmudiono T, Rifqi MA. Maternal Characteristics and socio-economic factors as determinants of low birth weight in Indonesia: analysis of 2017 Indonesian Demographic and Health Survey (IDHS). *Int J Environ Res Public Health*. 2022;19(21):13892. doi:10.3390/ijerph192113892.
3. Sadarang RAI. The study on low birth weight in Indonesia: Analysis on the 2017 Indonesia Demographic and Health Survey. *Jurnal Kesehatan Jambi*. 2021;5(2):28-35.
4. West Papua Provincial Health Office (WP-PHO). Health profile of West Papua. Manokwari: WP-PHO; 2019.
5. Khazaei S, Mansori K, Khazaei Z, Sani M, Ayubi E. Infant and young child feeding status in Iran compared the different United Nation Regions. *Int J Pediatr* 2016;4:3639-41.
6. Figueiredo ACMG, Gomes-Filho IS, Silva RB. Maternal anemia and low birth weight: a systematic review and meta-analysis. *Nutrients*. 2018;10(5):601. doi:10.3390/nu10050601.
7. Tabrizi Moghaddam F, Barjasteh S. Maternal hemoglobin levels during pregnancy and their association with birth weight of neonates. *Iran J Ped Hematol Oncol*. 2015;5(4):211-7.
8. Sibuea R, Raja SNL. Correlation of anemia in pregnancy and low birth weight in public health centers. *Sci Midwifery*. 2022;10(4):2985-91.
9. Medina-Marino A, Cleary S, Muzny CA. Sexually transmitted infection screening to prevent adverse birth and newborn outcomes: study protocol for a randomized-controlled hybrid-effectiveness trial. *Trials*. 2022;23(1):441. doi:10.1186/s13063-022-06400-y.
10. Fentie EA, Yeshita HY, Bokie MM. Low birth weight and associated factors among HIV positive and negative mothers delivered in northwest Amhara region referral hospitals, Ethiopia, 2020: a comparative cross-sectional study. *PLoS One*. 2022;17(2):e0263812. doi:10.1371/journal.pone.0263812.
11. Bhattacharya D, Guo R, Tseng CH. Maternal HBV viremia and association with adverse infant outcomes in women living with HIV and HBV. *Pediatr Infect Dis J*. 2021;40(2):e56-e61. doi:10.1097/INF.0000000000002980.
12. Wan Z, Zhang H, Xu H. Maternal syphilis treatment and pregnancy outcomes: a retrospective study in Jiangxi Province, China. *BMC Pregnancy Childbirth*. 2020;20(1):648. doi:10.1186/s12884-020-03314-y.
13. Engidaw MT, Eyayu T, Tiruneh T. The effect of maternal anaemia on low birth weight among newborns in Northwest Ethiopia. *Sci Rep*. 2022;12:15280.
14. Stangret A, Wnuk A, Szewczyk G, Pyzak M, Szukiewicz D. Maternal hemoglobin concentration and hematocrit values may affect fetus development by influencing placental angiogenesis. *J Matern Fetal Neonatal Med*. 2017;30(2):199-204. doi:10.3109/14767058.2016.1168395.
15. Sah SK, Sunuwar DR, Baral JR, Singh DR, Chaudhary NK, Gurung G. Maternal hemoglobin and risk of low birth weight: A hospital-based cross-sectional study in Nepal. *Heliyon*. 2022;8(12):e12174. doi:10.1016/j.heliyon.2022.e12174.
16. Zenebe A, Eshetu B, Gebremedhin S. Association between maternal HIV infection and birthweight in a tertiary hospital in southern Ethiopia: retrospective cohort study. *Ital J Pediatr*. 2020;46(1):70. doi:10.1186/s13052-020-00834-3.
17. Yingjuan L, Peng J, Liu Y. Association between maternal HIV infection and the risks of preterm birth and low birth weight in Chengdu, China: a propensity score matching approach. *BMJ Open*. 2023;13(9):e071205. doi:10.1136/bmjopen-2022-071205.
18. Shodikin MA, Kusumastuti I, Indasyah WA. The Correlation Between Human Immunodeficiency Virus (HIV) Infection in

- Pregnancy and Low Birth Weight Infants. *JHS*. 2021;14(3):209–13. doi: 10.33086/jhs.v14i3.2186
19. Cui AM, Cheng XY, Shao JG, Li HB, Wang XL, Shen Y, et al. Maternal hepatitis B virus carrier status and pregnancy outcomes: A prospective cohort study. *BMC Pregnancy Childbirth*. 2016;16:87. doi: 10.1186/s12884-016-0884-1.
20. Bajema KL, Stankiewicz Karita HC, Tenforde MW, Hawes SE, Heffron R. Maternal hepatitis B infection and pregnancy outcomes in the United States: a population-based cohort study. *Open Forum Infect Dis*. 2018;5(6):ofy134. doi: 10.1093/ofid/ofy134.
21. Tan J, Huang S, He G, Tang L, Ren Y, Zheng J, et al. Maternal hepatitis B surface antigen carrier status and its impact on neonatal outcomes: A cohort study of 21 947 singleton newborns in China. *J Matern Fetal Neonatal Med*. 2017;30(18):2219–24. doi: 10.1080/14767058.2016.1243098.
22. Sirilert S, Traisrisilp K, Sirivatanapa P, Tongsong T. Pregnancy outcomes among chronic carriers of hepatitis B virus. *Int J Gynaecol Obstet*. 2014;126(2):106–10. doi: 10.1016/j.ijgo.2014.02.019
23. Sun M, Luo M, Wang T, Zhong T, Chen Q, Liu H. Associations between maternal syphilis infection during pregnancy and low birth weight and preterm birth: a prospective cohort study. *Arch Gynecol Obstet*. 2024;310(1):203–211. doi:10.1007/s00404-023-07321-0
24. da Silva HBM, de Cássia Ribeiro-Silva R, Junior EPP, Barreto ML, Paixão ES, Ichihara MY. Syphilis in pregnancy and adverse birth outcomes: A nationwide longitudinal study in Brazil. *Int J Gynaecol Obstet*. 2024;166(1):80–89. doi:10.1002/ijgo.15561
25. Tsai S, Sun MY, Kuller JA, Rhee EHJ, Dotters-Katz S. *Obstet Gynecol Surv*. 2019;74(9):557–64. doi:10.1097/OGX.0000000000000713

## Antibacterial Activity of Mangrove Leaves Extract (*Rhizophora Apiculata*) Against *Salmonella typhi* Growth

Nurfadly,<sup>1</sup> Sevani Ayu Harahap,<sup>2</sup> Ance Roslina,<sup>3</sup> Munauwarus Sarirah<sup>1</sup>

<sup>1</sup>Parasitology Department, Faculty of Medicine, Universitas Muhammadiyah Sumatera Utara, Indonesia

<sup>2</sup>Faculty of Medicine Universitas Muhammadiyah Sumatera Utara, Indonesia

<sup>3</sup>Microbiology Department, Faculty of Medicine, Universitas Muhammadiyah Sumatera Utara, Indonesia

### Abstract

Mangrove leaves (*Rhizophora apiculata*) contain antibacterial chemical compounds with antibacterial properties against various pathogens. *Salmonella typhi*, the causative agent of typhoid fever, triggers a systemic infectious disease that can lead to complications and deaths if not treated properly. This study aimed to screen the phytochemical content of *R. apiculata* leaf extract, evaluate its antibacterial activity against *S. typhi*, and determine the optimal inhibitory concentration. Leaves were collected from the Sicanang mangrove forest in Belawan, North Sumatra, Indonesia, and extracted using the maceration method with 96% ethanol. Antibacterial effectiveness was assessed using disc diffusion method by measuring the zone of inhibition after exposure to mangrove leaf extract at concentrations of 40%, 60%, 80%, and 100%, with chloramphenicol as a positive control, to determine the most effective concentration for inhibiting the growth of *Salmonella typhi*. The results of the study showed that there were differences in inhibition zones in each group. Mangrove leaves extract at a concentration of 100% is the most effective in inhibiting the growth of *Salmonella typhi* compared to 80%, 60%, and 40% concentrations.

**Keywords:** Mangrove leaves, *rhizophora apiculata*, *salmonella typhi*

### Introduction

Mangroves (*Rhizophora apiculata*) of the Rhizophoraceae family are widely distributed along the Indonesian coastline and have long been used in traditional medicine. Previous studies have highlighted their pharmacological potential, including anticancer, antitumor, anti-inflammatory, antifungal, antibacterial, antiviral, and antidiabetic properties.<sup>1</sup> Phytochemical analysis revealed that the mangrove leaves contain flavonoids, alkaloids, sterols, tannins, saponins, and phenols.<sup>2,3</sup> The environment and a plant's physiological adaptability affect an organism's capacity to create secondary metabolites.<sup>4</sup>

Several investigations have demonstrated the antibacterial activity of mangrove-derived extracts against diverse pathogens.<sup>5,6</sup> Given their

promising antimicrobial potential in Indonesia and other regions, this study explores the antibacterial activity of *R. apiculata* leaf extract collected from the Sicanang mangrove forest, Belawan, North Sumatra, Indonesia.

*Salmonella typhi* is a bacterium that causes typhoid fever. Typhoid fever is a systemic infectious disease that, if not treated properly, can cause complications and death. It is usually spread through contaminated food or water. Despite considerable progress in water and sanitation facilities in most areas, typhoid fever is often found worldwide.<sup>7,8</sup> An estimated nine million people get typhoid fever, and 110,000 people die from it worldwide every year. The prevalence of typhoid in Indonesia is 1.60 %, and the age group 5–14 is the highest.<sup>9</sup> Moreover, according to the place of residence, typhoid fever cases are higher in rural areas than urban areas, with low levels of education and low economic conditions. The prevalence of typhoid varies from one region to another. The difference in the incidence of this disease between rural and urban areas is caused by the provision of

### Corresponding Author:

Nurfadly

Parasitology Department, Faculty of Medicine, Universitas Muhammadiyah Sumatera Utara, Indonesia  
 Email: nurfadly@umsu.ac.id

drinking water, sanitation, and waste disposal.<sup>10</sup>

Typhoid fever treatment usually uses antimicrobial monotherapy, but the choice of drug and duration of therapy is optimal depending on the pattern of antimicrobial resistance.<sup>11</sup> The World Health Organization (WHO) recommends treating typhoid and paratyphoid (enteric fever) with azithromycin, ciprofloxacin, or ceftriaxone because of widespread resistance to first-line antimicrobials, such as chloramphenicol.<sup>12</sup> The prevalence of bacterial antibiotic resistance is increasing and becoming a significant problem in treating infectious diseases.<sup>13</sup> Therefore, the discovery of new antibacterial compounds is an important priority.<sup>14</sup> The discovery of bioactive compounds as an antibacterial in mangrove leaves is expected to lower incident drug resistance and increase efficacy for treating typhoid fever.

This study aimed to screen the phytochemical constituents of *R. apiculata* leaf extract, evaluate its antibacterial activity against *S. typhi*, and determine the optimal inhibitory concentration.

## Methods

This experimental study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Muhammadiyah Sumatera Utara (No. 1063/KEPK/FKUMSU/2023). This study involves six groups of experimental objects. Four groups receive mangrove leaf extracts with concentrations of 40%, 60%, 80%, and 100%, while two control groups receive chloramphenicol as a positive control and aquadest as a negative control. The measurement values taken in the treatment groups are compared with the control group. The sample in this research is *Salmonella typhi* ATCC 14028 bacteria. The number of research samples is calculated using the Federer formula:  $(n-1)(t-1) \geq 15$ ; where is n: sample size, t: number of groups. There are four samples for each group, and the experiments are repeated four times, so the total sample used in this study is twenty-four. Data are collected by measuring the clear zone of *Salmonella typhi* growth using a vernier caliper. Mangrove leaf extract uses the maceration method with 96% ethanol solvent. One kilogram of the mangrove leaves from Sicanang wisata hutan mangrove Belawan, Sumatera Utara, Indonesia is washed clean and dried without direct sunlight exposure. Then, the mangrove leaves are blended and sifted into powder. The mangrove leaf powder is soaked in 3 liters

of 96% ethanol solvent for the first 6 hours, stirred occasionally, then left for 18 hours. The mass is separated by filtration, then evaporated using a rotary evaporator until a thick extract is obtained, and a phytochemical test is carried out. The extract obtained is diluted using DMSO (Dimethyl Sulfoxide) solvent to make extracts with concentrations of 40%, 60%, 80%, and 100%.<sup>12</sup>

Moreover, this study uses phytochemical test of mangrove leaf extract. The phenol test is carried out by adding 1% FeCl<sub>3</sub> to 2 ml of mangrove leaf extract, then observing whether there was a color change. It is positive when the color turns blackish blue. The Alkaloid test is carried out by mixing 2 ml of mangrove leaf extract with 2 ml of HCl and Mayer's reagent, then observing whether there is a color change. It is positive when a white precipitate forms. The flavonoid test is carried out by mixing several ml of mangrove leaf extract with 5 ml of ethanol, then adding several drops of concentrated HCl and 1.5 grams of magnesium. It is positive when it turns red. The tannin test is carried out by mixing 2 ml of mangrove leaf extract with FeCl<sub>3</sub> and 2-3 drops of H<sub>2</sub>SO<sub>4</sub> solution, then observing whether there is a color change. Positive if it turns brownish yellow. The Saponin test was carried out by mixing 2 ml of mangrove leaf extract with 5 ml of distilled water, shaking until stable foam formed, then adding another 1 drop of HCl 2N. It is positive when foam forms remain stable. The Steroid test is carried out by adding one drop of anhydrous acetic acid and one drop of concentrated sulfuric acid (Liebermann Burchard reagent) to the mangrove leaf extract. It is positive if it turns blue or green.<sup>10</sup>

The diffusion method inhibition test is conducted by making a suspension of *Salmonella typhi* colonies in 0.9% NaCl with a McFarland turbidity standard of 0.5 (comparable to the density of a bacterial suspension with a 1.5 x 10<sup>8</sup> CFU/mL). Blank discs are first sterilized by autoclaving. Mangrove leaf extract testing is carried out by immersing a sterilized blank disk in each extract concentration with a volume of 1 ml for 15 minutes so the solution could be properly absorbed into the blank disk. Next, the suspension of *Salmonella typhi* bacterial colonies is planted using a sterile tube evenly over the entire surface of the Muller Hinton Agar. Then, the blank disk containing the test material is placed in the middle of the agar surface using sterile tweezers and pressed slightly to adhere well. After that, it is incubated at 37°C for 18-24 hours. Then, the resistance of the clear zone

around the additional blank disk is measured using a vernier caliper.<sup>13</sup>

Statistical tests are used to determine the differences in the clear zone between the four treatment groups and the control groups. The normality and homogeneity tests found that the data in this study were not normally distributed and homogeneous. As a result, the Kruskal-Wallis test is carried out and followed by the Mann-Whitney test. All tests are considered significant if the p-value is  $>0.05$ .

## Results

Phytochemical screening of *Rhizophora apiculata* leaf extract confirmed the presence of flavonoids, alkaloids, sterols, tannins, saponins, and phenols (Table 1).

Table 2 shows that the average diameter of growth inhibition in the negative control group was 0 mm, in the positive control group was 20.50 mm, in the 40% concentration group was 11.75 mm, in the 60% concentration was 12.50 mm, in the 80% concentration was 13.50 mm, and in the 100% concentration was 15 mm.

The average diameter of growth inhibition

**Table 1 Phytochemical Screening Result of Mangrove Leaf Extract**

Phytochemical Test	Result
Flavonoid	Positive
Alkaloid	Positive
Sterol	Positive
Tannin	Positive
Saponin	Positive
Phenol	Positive

in the negative control group was 0 mm, in the positive control group was 20.50 mm, in the 40% concentration group was 11.75 mm, in the 60% concentration was 12.50 mm, in the 80% concentration was 13.50 mm, and in the 100% concentration was 15 mm. In the Kruskal Wallis test, a p-value was obtained at 0.002 (p-value $<0.05$ ), and there were differences in the diameter of the inhibition zone between treatment groups. Then, the Mann-Whitney test was conducted to determine which groups had different inhibition zones.

Table 3 shows that the inhibition zone of

**Table 2 Inhibitory Zone of Mangrove Leaf Extract Against *Salmonella typhi***

Repetition	Diameter of Inhibition of the Growth of <i>Salmonella typhi</i> (mm)						p-value	
	Concentration of Mangrove Leaf Extract ( <i>Rhizophora apiculata</i> )			Control				
	40%	60%	80%	100%	Positive	Negative		
1	10	11	11	13	21	0		
2	11	11	13	14	20	0		
3	13	14	14	16	20	0	0.002*	
4	13	14	16	17	21	0		
Mean	11.75	12.50	13.50	15.00	20.50	0		

Kruskal-Wallis test, \*significant difference (p<0.05)

**Table 3 Significant Differences Among All Groups**

Group	Control -	Control +	40%	60%	80%	100%
Control -						
Control +	0.013*					
40%	0.013*	0.019*				
60%	0.013*	0.018*	0.369			
80%	0.014*	0.019*	0.180	0.544		
100%	0.014*	0.019*	0.038*	0.137	0.304	

The mean values of the groups were significantly different; \*significant different (p<0.005)

the negative control group had a significant difference from the inhibition zone of the positive group, the 40%, 60%, 80%, and 100% groups. The inhibitory zone of the 40% group had no significant difference with 60% and 80% but had significant differences with 100%. The inhibitory zone of the 60% group had no significant difference between 80% and 100%, and the inhibitory zone of the 80% group had no significant difference with 100%.

## Discussion

The mangrove leaves in this study were extracted using the maceration method by soaking the samples using an organic solvent at room temperature. This method is known to be very profitable in isolating bioactive compounds from natural materials. Immersing the sample makes the cell walls and cell membranes break down due to the presence of the difference in pressure inside and outside the cell. Therefore, secondary metabolites in the cytoplasm are dissolved in the organic solvent used, and compound extraction will be perfect according to the length of sample immersion.<sup>14</sup> The extract used to test the antibacterial activity of mangrove leaves at concentrations of 40%, 60%, 80%, and 100% was dissolved using Dimethyl Sulfoxide (DMSO) solvent. DMSO is a solvent that can dissolve almost all polar and non-polar compounds. In addition, DMSO does not inhibit bacterial growth, so it will not interfere with the results of observations of antibacterial activity tests.<sup>15</sup>

Phytochemical tests are qualitative tests that aim to determine the bioactive components contained in a material. The phytochemical test in this study showed positive results in the flavonoids, alkaloids, sterols, tannins, saponins, and phenols. The results of several previous studies on phytochemical screening of mangrove leaf extracts were in line with this study, stating that positive mangrove leaf extracts contain flavonoids, alkaloids, sterols, tannins, saponins, and phenols.<sup>10,16</sup> Such compounds are known to interfere with bacterial systems, providing a bacteriostatic effect. Prior studies have also confirmed the antibacterial potential of mangrove extracts against *Staphylococcus aureus* and *Escherichia coli*, supporting the broad-spectrum activity of mangrove-derived compounds.<sup>7,17,18</sup> Previous research concluded the potential of mangrove leaf extract as an antibacterial for gram-positive and gram-negative bacteria.

Chloramphenicol was used as a positive

control. This antibiotic acts as a bacteriostatic agent by inhibiting protein synthesis through interference with peptidyl transferase on the 50S ribosomal subunit.<sup>19</sup> In this study, chloramphenicol produced a mean inhibition zone of 20.50 mm against *S. typhi*, which according to the National Committee for Clinical and Laboratory Standards (NCCLS), falls within the sensitive category for Enterobacteriaceae (>18 mm).<sup>20</sup>

In this study, the antibacterial activity of mangrove leaf extract was determined against the growth of *Salmonella typhi* based on the diameter of the clear zone produced. The antibacterial activity of mangrove leaf extract was found in all test groups, and the greatest inhibitory power was found in the concentration of 100%. The data analysis shows a difference in inhibitory power between the chloramphenicol group and the mangrove leaf extract group with concentrations of 40%, 60%, 80%, and 100%. This shows that although mangrove leaf extract can inhibit the growth of *Salmonella typhi* bacteria, its effectiveness is not as good as chloramphenicol. This could be due to the antibacterial effect of mangrove leaf extract being lower than the antibiotic chloramphenicol. Still, it could also be due to the lack of absorption of the mangrove leaf extract soak into the test blank disk or the lack of antibacterial compounds extracted from the mangrove leaf sample, which can cause a decrease in the antibacterial effect. In conclusion, *R. apiculata* leaf extract exhibits antibacterial activity against *S. typhi*, with maximal inhibition at 100% concentration. Although its activity was less than chloramphenicol, the extract demonstrates potential as a natural antibacterial agent and may serve as a complementary or alternative therapy, particularly in the context of rising antimicrobial resistance.

## References

1. Genilar LA, Kurniawaty E, Mokhtar RA, Audah KA. Mangroves and their medicinal benefit: a mini review. Ann RSCB. 2021;25(4):695-709.
2. Wardina MA, Mustofa S, Malarangeng| AFTA Review Article: Potensi *Rhizophora apiculata* Sebagai Fitofarmaka. Medula. 2023;13(2): 137-46.
3. Mutik MS, Sibero MT, Widianingsih W, Subagiyo S, Pribadi R, Haryanti D, et al. Kandungan senyawa bioaktif dan aktivitas

- biologis ekstrak daun *Rhizophora apiculata* asal perairan Teluk Awur, Jepara. *J Kelaut Trop.* 2022;25(3):378–90.
4. Li Y, Kong D, Fu Y, Sussman MR, Wu H. The effect of developmental and environmental factors on secondary metabolites in medicinal plants. *Plant Physiol Biochem.* 2020;148:80–89. doi:10.1016/j.plaphy.2020.01.006
  5. Widiani DY, Aliyah SD, Awwalia EF, Al Husen IM, Komarudin P. Antibacterial test of *Rhizophora apiculata* extract originated from Mangrove Wonorejo Surabaya against *Staphylococcus aureus* and *Escherichia coli*. *J Marine Resources Coastal Management.* 2023;4(1):6–10.
  6. Acharya S, Jali P, Pradhan M, Pradhan C, Mohapatra PK. Antimicrobial and antioxidant property of a true mangrove *rhizophora apiculata* Bl. *Chem Biodivers.* 2023;20(9):e202201144. doi:10.1002/cbdv.202201144
  7. Marchello CS, Hong CY, Crump JA. Global typhoid fever incidence: A systematic review and meta-analysis. *Clin Infect Dis.* 2019;68(Suppl2):S105–S116. doi:10.1093/cid/ciy1094
  8. Ferrari RG, Rosario DKA, Cunha-Neto A, Mano SB, Figueiredo EES, Conte-Junior CA. Worldwide epidemiology of *Salmonella* serovars in animal-based foods: A meta-analysis. *Appl Environ Microbiol.* 2019;85(14):e00591–19. doi:10.1128/AEM.00591-19
  9. Hancuh M, Walldorf J, Minta AA, et al. Typhoid fever surveillance, incidence estimates, and progress toward typhoid conjugate vaccine introduction—worldwide, 2018–2022. *MMWR Morb Mortal Wkly Rep.* 2023;72(7):171–6. doi:10.15585/mmwr.mm7207a2
  10. Hancuh M, Walldorf J, Minta AA, Tevi-Benissan C, Christian KA, Nedelev Y. Typhoid fever infection – Antibiotic resistance and vaccination strategies: A narrative review. *Travel Medicine and Infectious Disease.* 2021;40(101946):2–15
  11. Kuehn R, Stoesser N, Eyre D, Darton TC, Basnyat B, Parry CM. Treatment of enteric fever (typhoid and paratyphoid fever) with cephalosporins. *Cochrane Database Syst Rev.* 2022;11(11):CD010452. doi:10.1002/14651858.CD010452.pub3
  12. Terreni M, Taccani M, Pernolato M. New antibiotics for multidrug-resistant bacterial strains: latest research developments and future perspectives. *Molecules.* 2021;26(9):2671. doi:10.3390/molecules26092671
  13. Alhaddad ZA, Tanod WA, Wahyudi D. Bioaktivitas antibakteri dari ekstrak daun mangrove *avicennia sp.* *J Kelaut Indones J Mar Sci Technol.* 2019;12(1):12–22
  14. Keerthi RR, Baskar K, Mavishna M, Johnson A. Antibacterial and antioxidant activity of mangrove plant (*Avicennia Marina*) extract against some specific oral pathogens. *Int J Health Sci.* 2022;6(3):1348–55. doi:10.53730/ijhs.v6nS3.5562
  15. Akasia AI, Nurweda Putra IDN, Giri Putra IN. Skrining fitokimia ekstrak daun mangrove *rhizophora mucronata* dan *rhizophora apiculata* yang dikoleksi dari Kawasan Mangrove Desa Tuban, Bali. *J Mar Res Technol.* 2021;4(1):16–22.
  16. Masuet-Aumatell C, Atouguia J. Typhoid fever infection - Antibiotic resistance and vaccination strategies: A narrative review. *Travel Med Infect Dis.* 2021;40:101946. doi:10.1016/j.tmaid.2020.101946
  17. Arifin MH, Yacoeb AM, Abdullah A, Riyadi PH. Drying method comparison of black mangrove leaves (*Rhizophora mucronata*) for an antioxidant activity assay. *Food Res.* 2023;7(Suppl3):67–75. doi:10.26656/fr.2017.7(S3).095
  18. Balouiri M, Sadiki M, Ibnsouda SK. Methods for in vitro evaluating antimicrobial activity: A review. *J Pharm Anal.* 2016;6(2):71–9. doi:10.1016/j.jpha.2015.11.005
  19. Eswaraiah G, Peele AK, Krupanidhi S, Kumar RB, Venkateswaru TC. Studies on phytochemical, antioxidant, antimicrobial analysis and separation of bioactive leads of leaf extract from the selected mangroves. *J King Saud Univ Sci.* 2020;32(1):842–7. doi:10.1016/j.jksus.2018.11.014
  20. Summer K, Browne J, Hollanders M, Benkendorff K. Out of control: The need for standardised solvent approaches and data reporting in antibiofilm assays incorporating dimethyl-sulfoxide (DMSO). *Biofilm.* 2022;4:100081. doi:10.1016/j.biofil.2022.100081
  21. Karundeng EDB, Hanizar E, Sari DNR. Potensi Ekstrak Daun *Rhizophora mucronata* Sebagai Antibakteri pada *Staphylococcus aureus*. *Biosapphire J Biol dan Divers.* 2022;1(1):10–18.
  22. Andriani S, Putri A, Khairani IA, et al. Aktivitas antibakteri ekstrak daun mangrove terhadap bakteri *Escherichia coli*. *J Sci Med Lab.* 2023;1(1):14–22.

23. Hafizhah R, Muthmainah N, Biworo A. Literature review: pola kepekaan *salmonella typhi* terhadap antibiotik. Homeostasis. 2021;4(3):773–84.
24. Cooper CR. Antimicrobial agent disk susceptibility table. Microbiology laboratory. [Internet] 2019 [cited 2024 September 12]. Available from: <http://crcooper01.people.yzu.edu/microlab/ast-chart.pdf>

## Family Support and Medication Adherence in Patients in Prolanis Program

Zahratul Aini,<sup>1</sup> Hijra Novia Suardi,<sup>2</sup> Fitria Meutia Dewi,<sup>3</sup> Tilaili Ibrahim,<sup>3</sup> Ika Waraztuty,<sup>3</sup> Vera Dewi Mulia<sup>4</sup>

<sup>1</sup>Department of Family Medicine, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

<sup>2</sup>Department of Pharmacology, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

<sup>3</sup>Medical Studies Program, Faculty of Medicine, Universitas Syiah Kuala Banda Aceh, Indonesia

<sup>4</sup>Department of Pathological Anatomy, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

### Abstract

The Chronic Disease Management Program, or *Program Pengelolaan Penyakit Kronis* (Prolanis), is a disease management program designed for individuals with chronic illnesses. It aims to maintain health and improve quality of life. The success of Prolanis depends not only on patient adherence to medication but also on family involvement as the primary source of support. This study aimed to examine the relationship between family support and medication adherence among Prolanis patients at Batoh Public Health Center, Banda Aceh, Indonesia. An observational analytic study with a cross-sectional design was conducted using consecutive sampling of 74 Prolanis participants. Data were collected through guided interviews. Among the participants, 33 individuals (44.5%) exhibited low medication adherence, while 41 individuals (55.5%) demonstrated high adherence. Additionally, 8 participants (10.8%) reported poor family support, whereas 66 participants (89.2%) received good family support. Data analysis using the chi-square test revealed a significant relationship ( $p=0.009$ ) between family support and medication adherence. Therefore, it can be concluded that family support is significantly associated with medication adherence in Prolanis patients. Families are the main supporters in maintaining the health of their family members, with an important role in encouraging, supporting, and supervising patients' treatment. Good support and constant encouragement and attention can increase patients' confidence, which in turn will affect their adherence to treatment.

**Keywords:** Chronic disease, family support, medication adherence, prolanis

### Introduction

Chronic diseases are a major threat to global population health. In 2010, 67% of deaths worldwide were due to chronic diseases and this increased to 74% in 2019.<sup>1</sup> Improving health outcomes requires not only curative but also promotive and preventive strategies. In 2014, the Indonesian government, through the National Health Insurance Agency (*BPJS Kesehatan*), collaborated with healthcare facilities to establish the Chronic Disease Management Program (*Program Pengelolaan Penyakit Kronis*; Prolanis).

Prolanis a program aimed at maintaining

the health withchronic disease, particularly Hypertension & Type 2 Diabetes Mellitus. The goal is to improve their quality of life through the provision of healthcare services and an integrated approach involving participants, healthcare facilities, and BPJS Kesehatan. The monthly activities conducted under Prolanis include several components. First medical consultations, where Prolanis participants schedule joint consultation sessions with the managing health facility. Second, group exercise sessions conducted regularly. Third, routine visits to check blood sugar and routine blood checks. In addition, there reminder activities using an SMS gateway system to motivate participants to attend regular visits to the healthcare facility. Another activity is home visits, in which healthcare providers visit the homes of Prolanis participants to provide information and education on personal and environmental health

### Corresponding Author:

Zahratul Aini,  
 Department of Family Medicine, Faculty of Medicine,  
 Universitas Syiah Kuala, Banda Aceh, Indonesia  
 Email: dr.zahratulaini@usk.ac.id

for participants and their families.<sup>5,7</sup>

In a study conducted by Muhammad Nur Sidiq with the title "The Effect of Prolanis exercise on Blood Pressure of Hypertensive Patients at Purwodiningratan Health Center, Surakarta City" with the results of research showing the effect of Prolanis exercise on blood pressure of hypertensive patients, where blood pressure decreased by 7 mmHg after doing Prolanis exercise 4 times. Program effectiveness is a way to measure the extent to which the program can run in order to achieve the goals that have been set before. Program effectiveness can be determined by comparing program objectives with program outputs. Muhammad Nur Sidiq's research showed that one of the Prolanis programs, namely Prolanis exercise, was effective enough to reduce blood pressure in hypertensive patients.<sup>8</sup> This program strives to achieve an optimal quality of life, emphasizing satisfaction, improved well-being, disease prevention, as well as cost-effective and efficient healthcare services for chronic disease patients.<sup>5</sup>

The success of Prolanis depends not only on program design but also on patient engagement and family involvement. Family support plays a crucial role in patient health by providing emotional encouragement, instrumental assistance, information, and supervision.<sup>6</sup> Family support is support provided to patients in terms of emotional support, informational support, instrumental support and assessment support. Family support can be provided through the participation and active role of the family in providing support to patients in overcoming worries and emotional burdens and the family has an important role in the success of patients in their treatment.

Based on Ginting's research<sup>9</sup> on factors influencing the utilization of the Prolanis Program at Puskesmas Darussalam Medan shows that the variables of knowledge and family support have a significant relationship with the utilization of the Prolanis program. In Abdullah's research<sup>10</sup> mentioned that the factors causing the decline in the number of visits by Prolanis program participants at Puskesmas Minasa Upa Makassar City showed that there was a significant relationship between knowledge, family support, and the role of officers on the utilization of chronic disease management programs.<sup>10</sup> The role of family, compared to professional intervention, is important as a caregiver, often including the closest individual with the most attentive nature and supportive contribution in addressing the health issues of patients.<sup>11</sup>

In the context of chronic diseases, caregiver is responsible for supervising medication intake, promoting regular check-ups, and ensuring adherence to medical recommendations.<sup>12</sup> This vigilant supervision not only expedites recovery but also curtails medication disruptions, promptly addresses medication side effects, and prevents resistance development.<sup>13</sup>

Previous investigations showed a relationship between family support and medication adherence in diabetic individual.<sup>14</sup> However, while this relationship has been well-documented in the context of diabetes, there remains a significant gap in understanding how family support influences medication adherence among patients enrolled in the Prolanis in Banda Aceh. Family support is very helpful for the success of patient treatment by always reminding patients to take medicine, gaining a deep understanding of the patient's illness, providing care starting from the problem of the disease suffered or psychological problems, and encouraging patients to remain active in treatment and caring for patients if they experience side effects from the drugs they take.<sup>15</sup>

There has been no research on the relationship between family support and medication adherence in Prolanis patients in Banda Aceh. Therefore, this investigation uniquely focuses on a specific and densely populated area, which is Batoh Health Center, with population of 26,119 residents, including 103 registered Prolanis patients.<sup>16</sup> Furthermore, the health center is led by a family physician (Sp. KKLP) and supported by qualified medical staff. By targeting this population, the study aims to determine the relationship between family support and medication adherence in Prolanis patients at the Batoh Health Center.

## Methods

This study employed an observational analytic design with a cross-sectional approach to analyze the relationship between family support and medication adherence among patients with chronic diseases. The research was conducted at the Batoh Community Health Center, Banda Aceh, where the Prolanis program is actively implemented. Data collection was carried out from September to October 2022.

Participants were selected using non-probability consecutive sampling. This involves including subjects who meet the research criteria into the study until a certain time period

is reached, ensuring that the required sample size is achieved. Initially, the population under examination consisted of 103 individuals, from which 29 were excluded for not meeting the inclusion criteria. The minimum required sample size of 51 was calculated using Cochran's formula for finite populations, assuming a 95% confidence level and a 5% margin of error.

The participants in this study were patients registered in the Prolanis program at the Batoh Community Health Center. They were individuals who actively participated in the program, meaning they regularly attended Prolanis activities and consultations related to their illness. Participation was also based on their willingness to be involved as respondents in the study. In addition, all selected patients were those who lived with their families.

Eligible participants were Prolanis patients who actively attended program activities, lived with their families, and agreed to participate. Patients with functional grade 5 (fully dependent on others for self-care), as well as those unable to communicate or complete the questionnaire due to cognitive or physical impairment, were excluded. Functional grade was determined based on the patient's level of independence, ranging from grade 1 (independent) to grade 5 (fully dependent). The functional grade classification is based on the patient's level of independence. Grade 1 represents patients who are able to perform physical activities as they did before the illness. Grade 2 includes patients who are able to perform self-care and light work both inside and outside the home. Grade 3 refers to patients who can perform self-care but are unable to do light work. Grade 4 is assigned to patients who are mostly inactive and require assistance with daily activities. Finally, Grade 5 includes patients who are fully dependent on others for self-care.

Data collected included demographic characteristics such as age, sex, education level, duration of Prolanis participation, and disease diagnosis. Family support was assessed using a validated questionnaire that measures two domains: instrumental support (12 items) and emotional support (13 items). Responses to the questionnaire are determined using a Likert scale, with respondent answers rated from very positive to very negative on a scale of 1 to 3 (never, rarely, often). The highest possible score is 75, and the lowest is 25. To determine the cut-off point for family support, a normality test using the Kolmogorov-Smirnov method was conducted because the sample size was greater than 50. The results indicated a non-normal distribution, so

the cut-off point was set using the median value. The median value was 70, thus scores below 70 are considered poor, and scores of 70 or above are considered good.

Medication adherence was assessed using the Indonesian version of the 8-item Morisky Medication Adherence Scale (MMAS-8),<sup>18,19,20</sup> a widely validated tool developed by Dr. Donald E. Morisky. The MMAS-8 has been used in various countries, including Iran, Malaysia, Spain, and China, and has been translated into Indonesian.

**Table 1 Characteristics of Prolanis Participants at Batoh Health Center (n=74)**

Characteristic	Frequency (n)	Percentage (%)
Age (years)		
<45	6	8.1
45-54	15	20.3
55-65	39	52.7
66-74	12	16.2
75-90	2	2.7
Gender		
Male	9	12.2
Female	65	87.8
Highest Education Level		
No Schooling	1	1.3
Elementary	8	10.8
School Graduate		
Junior High School	19	25.7
Graduate		
High School	35	47.3
Graduate		
College Graduate	11	14.9
Duration of Prolanis Participation		
<1 year	20	27
1-3 years	21	28.4
>3 years	33	44.6
Disease Diagnosis		
Diabetes mellitus	34	35.1
Hypertension	42	43.3
Diabetes mellitus and hypertension	12	12.4
Dyslipidemia	9	9.2

MMAS-8 consists of 7 items answered with a yes or no and 1 item with a 5-point Likert scale.

Reliability and validity test results show that the Indonesian version of the 8-item MMAS is valid and reliable and can be used as an instrument to measure the level of patient

compliance.<sup>20,21</sup> The results of the psychometric properties reliability test and validity test show that the Indonesian version of the MMAS-8 has good reliability and validity with the results of internal consistency reliability assessed using Cronbach's alpha coefficient is 0.824 and the

**Table 2 Distribution of Family Support Questionnaire Responses (n=74)**

Question	Never		Seldom		Often	
	n	(%)	n	(%)	n	(%)
<b>Instrumental Support</b>						
Reminds me to take medication when I forget	1	(1.4)	0	(0)	73	(98.6)
Procures medication for me when I cannot do it myself	1	(1.4)	3	(4)	70	(94.6)
Provides medication in a container when I cannot afford it	1	(1.4)	2	(2.7)	71	(95.9)
Accompanying me when taking Medication	2	(2.7)	17	(23)	55	(74.3)
Helps read the dosage when I cannot do it myself	1	(1.4)	0	(0)	73	(98.6)
Describing how to take medication when I cannot do it myself	1	(1.4)	1	(1.4)	72	(97.2)
Informing me about the benefits and risks of non-adherence to medication	1	(1.4)	3	(4)	70	(94.6)
Assisting in facilitating medication when I cannot afford it	1	(1.4)	2	(2.7)	71	(95.9)
Providing transportation for medical appointments if I cannot come on my own	1	(1.4)	1	(1.4)	72	(97.2)
Taking me for check-ups	1	(1.4)	4	(5.4)	69	(93.2)
Providing transportation even for short distances if I cannot manage	2	(2.7)	2	(2.7)	70	(94.6)
Motivating me to recover and adhere to medication	1	(1.4)	2	(2.7)	71	(95.9)
<b>Emotional Support</b>						
Covering expenses when I cannot afford it	1	(1.4)	0	(0)	73	(98.6)
Being there when I feel lonely	3	(4.1)	4	(5.4)	67	(90.5)
Being there when I feel alone	0	(0)	8	(10.8)	66	(89.2)
Being there when needed	0	(0)	6	(8.1)	68	(91.9)
Showing love	0	(0)	3	(4.1)	71	(95.9)
Giving attention	1	(1.4)	3	(4)	70	(94.6)
Cares for me	0	(0)	1	(1.4)	73	(98.6)
Willing to listen to my complaints	1	(1.4)	10	(13.5)	63	(85.1)
Meets and talks when I need them	0	(0)	2	(2.7)	72	(97.3)
Offering advice when I face problems	0	(0)	11	(14.9)	63	(85.1)
Provides encouragement when I am desperate	3	(4.1)	2	(2.7)	69	(93.2)
Reminds me to surrender and be grateful to God	1	(1.4)	3	(4)	70	(94.6)
Meets my food and drink needs at home	0	0 (0)	1	(1.4)	73	(98.6)

test-retest reliability using Spearman's rank correlation is 0.881.

Descriptive statistics (mean, standard deviation, frequency, and percentage) were used to describe respondent characteristics and study variables. The relationship between family support and medication adherence was analyzed using the Chi-square test and logistic regression, with significance set at  $p<0.05$ . Results are presented in tables for clarity.

Ethical approval for the study was obtained from the Health Research Ethics Committee, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh (No. 030/EA/FK/2022). Written informed consent was obtained from all participants, and confidentiality and anonymity were maintained.

## Results

A total of 74 Prolanis participants at Batoh Health Center were included in this study. The majority were aged 55–65 years (52.7%), female (87.8%), and high school graduates (47.3%). Most had participated in Prolanis for more than three years (44.6%). Hypertension (43.3%) was the most common diagnosis, followed by diabetes mellitus (35.1%), combined hypertension and diabetes mellitus (12.4%), and dyslipidemia (9.2%) (Table 1).

Table 2 shows the study revealed that almost all respondents received support from their families, both instrumentally and emotionally.

"Reminding me to take medication when I forgot" (98.6%) and "Helping read the dosage when I cannot do it myself" (98.6%) had the highest percentages among instrumental support, indicating strong family involvement in ensuring medication adherence. Meanwhile, "Accompanying me when taking medication" had the lowest percentage (74.3%), suggesting that while family support is present, physical accompaniment during medication intake might not always be prioritized.

In terms of emotional support, "Covering expenses when I cannot afford it" (98.6%) and "Being there when I feel alone" (91.6%) were among the most frequently received supports, highlighting the family's role in financial and emotional well-being. On the other hand, "Offering advice when I face problems" (83.1%) had a relatively lower percentage, implying that while emotional presence is strong, advisory support may vary depending on individual family dynamics.

In Table 3, The majority of participants demonstrated good medication adherence, with most reporting that they had taken their medication the previous day and had not skipped doses in the past two weeks. However, nearly half admitted to occasionally forgetting to take their medication. A smaller percentage of respondents had stopped or reduced medication without consulting a doctor, particularly in the absence of symptoms. Additionally, a few participants found it difficult to remember all their medications or had trouble following their treatment plan.

**Table 3 Distribution of Medication Adherence Questionnaire Responses**

Question	Yes		No	
	n	(%)	n	(%)
Do you sometimes forget to take your medication?	35	(47.5)	39	(52.7)
In the past two weeks, have there been days when you did not take your medication?	18	(24.4)	56	(75.6)
Have you ever reduced or stopped taking medication without informing the doctor because you felt worse when taking it?	5	(6.8)	69	(93.2)
When traveling or leaving home, do you sometimes forget to bring your medications?	22	(29.8)	52	(70.2)
Did you take your medication yesterday?	71	(96)	2	(4)
Have you ever stopped taking medication when there were no symptoms?	24	(32.5)	50	(67.5)
Have you ever had trouble with your treatment plan?	7	(9.5)	67	(90.5)
Do you often find it difficult to remember to take all your medications?	5	(6.8)	69	(93.5)

**Table 4 Distribution of Family Support (n=74)**

Family Support	Frequency	Percentage (%)
Poor	8	10.8
Good	66	89.2

**Table 5 Distribution of Medication Adherence Frequency**

Medication Adherence	Frequency (n=74)	Percentage (%)
Low	33	44.5
High	41	55.5

**Table 6 Relationship between Family Support and Medication Adherence (n=74)**

Family Support	Medication Adherence				Total	p-value	95% CI			
	Low		High							
	n	%	n	%						
Poor	7	87.5	1	12.5	8	100	0.027 1.25–92.7			
Good	26	39.4	40	60.6	66	100				

Table 4 presents the distribution of family support among the participants, with nearly 90% of respondents reporting adequate assistance from their families. Only a small proportion of participants experienced poor family support, highlighting the overall strong role of families in patient care and medication adherence.

Table 5 presents the distribution of medication adherence among the participants. More than half of participants (55.5%) demonstrated high medication adherence, whereas 44.5% showed low adherence. These findings suggest that although the majority of patients adhere to their prescribed medication regimens, a significant subset may benefit from targeted interventions to enhance adherence.

According to Table 6, the analysis indicates a significant association between family support and medication adherence. Patients who received good family support were more likely to exhibit high adherence compared to those with poor support. The statistical test yielded a p-value of 0.027, suggesting that this relationship is unlikely to be due to chance. The confidence interval (CI: 1.25–92.7) further reinforces this finding, highlighting the substantial impact of family support on adherence behavior.

## Discussion

In this study, most Prolanis patients received strong family support, which played a crucial role in promoting well-being. Good family support was associated with improved health maintenance, reduced illness, and a better quality

of life for elderly patients.<sup>23,24</sup> Families provided instrumental support, such as reminding patients to take medication, reading dosages when necessary, and accompanying them during medication administration. In contrast, some families also provide emotional support such as covering expenses, providing care, and meeting food and drink needs, and others listened to complaints and offered advice on problems. In the context of elderly, understanding the experiences faced was crucial, and family members often served as empathetic listeners, fulfilling the needs. Family support significantly contributes to building self-confidence and providing motivation.<sup>23</sup> Therefore, accompanying elderly patients, listening to their concerns, and offering advice, are essential components helping to foster a supportive environment.<sup>22,19</sup>

The attitude of family members, specifically spouses, in promoting, supporting, and monitoring patients determined the decision to either discontinue or continue medication. Persistent family encouragement and attention could boost the confidence of patients, influencing medication adherence.<sup>26</sup> This was consistent with the findings of this study, in which 40 participants with good family support demonstrated high adherence.

Overall, the majority of Prolanis patients had high medication adherence, consistent with findings by Aulina and Siyam<sup>26</sup> who reported similar results at Bandarharjo Health Center. Medication adherence significantly impacted medication success, with non-adherence posing risks such as blood pressure control disruption, medication failure, and potentially fatal side

effects. Additionally, patient adherence included compliance with medication recommendations related to timing, dosage, and frequency.<sup>25</sup> In this study, the most common reason for low adherence was forgetfulness, particularly when patients traveled without their medications or discontinued use when symptoms were absent.. Medication adherence is crucial for achieving treatment goals and preventing complications, where the right medication tends to promote recovery. This is particularly applicable to patients on long-term medication, which may last for a lifetime.

The result in this study shows a relationship between family support and medication adherence in Prolanis patients. Patients with poor family support had a significantly greater chance of experiencing low adherence compared to those with strong family support. However, a small number of individuals with limited family support still demonstrated high adherence, indicating that other factors may also influence adherence levels. The results of this study are in line with research conducted by Widyaningrum et al (2019) which found that out of 137 respondents, many had good family support, with high medication adherence observed in a majority of them<sup>28</sup> and research by Mulidan et al.<sup>29</sup> also stated that one of the factors influencing patient compliance with taking medication is family support.

The role of family in patient care is emphasized by Friedman, who described the family as the primary support system for individuals with health problems. This is in line with the perspective of Friedman emphasizing that the family serves as the primary support system for individuals facing health issues. Compared to medical professionals, the most suitable caregiver is family members due to being the closest to patients and mostly available when needed.<sup>10</sup> A caregiver assists in overseeing medication adherence, ensuring quick recovery, timely medication intake, and prevention of medication disruptions and resistance.<sup>12,13</sup> The results were consistent with Widyaningrum et al.<sup>28</sup> where good family support among participants led to high medication adherence, fostering a sense of love, encouragement, value, and support for patients, particularly elderly individuals suffering from chronic diseases. Similarly, Purnawinadi<sup>17</sup> also reported that family support, love, care, and respect for other members help reduce the burden of chronic illness.

The collected data showed that although

family members supported patients in participating in Prolanis, there was limited attention to medication adherence at home). Similarly, the role of the family in medication adherence for Tuberculosis patients, as in Arifal et al,<sup>30</sup> indicated that overcoming non-adherence in tuberculosis patients requires the family's role as a supervisor of medication intake. Only a few actively engaged in overseeing medication intake, primarily assisting with medication acquisition once a month or during supply exhaustion. Additionally, family members mostly accompanied patients to receive healthcare services without staying during medical appointments and consultations with the doctor, leading to missed educational opportunities provided by professionals. This lack of exposure to necessary information negatively impacted adherence behaviors.

Contrasting evidence was reported by Hanum et al.<sup>15</sup> who found no significant association between family support and medication adherence ( $p=0.785$ ). This discrepancy might be attributed to several factors, including variations in research locations, sample characteristics, and the methodological approach used. Differences in population demographics, healthcare settings, and cultural contexts could also contribute to contrasting findings. These factors highlight the complexity of researching the relationship between family support and medication adherence, suggesting the need for further exploration in diverse settings.

This study has several limitations. First, the cross-sectional design limits causal interpretations of the relationship between family support and medication adherence. Additionally, self-reported adherence may be subject to recall bias. Furthermore, researchers did not intervene directly with family members of PROLANIS participants, limiting the ability to fully explore the causes of low adherence despite good family support. Future research should consider longitudinal studies and objective measures of adherence.

The findings demonstrate a significant relationship between family support and medication adherence among Prolanis patients. Both instrumental supports such as reminding patients to take medication, reading dosages, and accompanying them during medication administration and emotional support such as providing care, listening to complaints, and offering advice play a crucial role in improving patients' adherence to treatment.

Patients with good family support were more

likely to have high medication adherence, while those with poor support had a greater risk of non-adherence. Additionally, families act as supervisors in the treatment process, ensuring that patients follow their therapy correctly to prevent complications.

However, while families support patients' participation in the Prolanis program, attention to medication adherence at home remains limited. Many family members assist in obtaining medication but are less involved in daily monitoring. Therefore, further interventions that engage families in medication adherence education are necessary to enhance the effectiveness of long-term therapy.

Healthcare providers should actively involve families in supporting medication adherence by educating them on the importance of reminders, supervision, and emotional encouragement. Family members should be integrated into medical consultations and chronic disease programs like Prolanis to enhance their role in patient care. Strengthening communication between healthcare providers and families through regular follow-ups and counseling can further improve adherence. Additionally, future research should explore family-based interventions and their long-term effects on medication adherence to develop more effective support strategies.

## References

1. Kementerian Kesehatan RI. Laporan Nasional Riskesdas 2018. Vol 1. Jakarta: Kementerian Kesehatan RI; 2019. p. 1.
2. Hidayat R, Agnesia Y. Faktor risiko hipertensi pada masyarakat di Desa Pulau Jambu UPTD Blud Kecamatan Kuok Kabupaten Kampar. *Jurnal Ners*. 2021;5(1):8-19.
3. Mohammed Nawi A, Mohammad Z, Jetly K, Abd Razak MA, Ramli NS, Wan Ibadullah WAH, et al. The prevalence and risk factors of hypertension among the urban population in Southeast Asian Countries: a systematic review and meta-analysis. *Int J Hypertens*. 2021;2021:6657003. doi:10.1155/2021/6657003.
4. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract*. 2019;157:107843. doi:10.1016/j.diabres.2019.107843
5. Purnamasari AT, Ningrum HD. Implementasi program pengelolaan penyakit kronis (Prolanis) di masa pandemi COVID-19 pada FKTP di Kota Malang. *J Kebijak Kesehat Indones*. 2023;12(2):84-96.
6. Fatimah E, Cusmarih C. Pengaruh tingkat pengetahuan, motivasi, dukungan keluarga terhadap kepatuhan minum obat pasien hipertensi Di Ruang An-Nas 1 Di RSIIJ Pondok Kopi. *Malahayati Nurs Journal*. 2022;4(3):720-32.
7. Pramana GA, Dianingati RS, Saputri NE. Faktor-faktor yang mempengaruhi kepatuhan minum obat pasien hipertensi peserta Prolanis di Puskesmas Pringapus Kabupaten Semarang. *Indones J Pharm Nat Prod*. 2019;2(1):52-8. doi:10.35473/ijpnp.v2i1.196
8. Sidiq MN, Widodo A. Pengaruh senam Prolanis terhadap tekanan darah pasien hipertensi di Puskesmas Purwodiningratana Kota Surakarta [dissertation]. Surakarta: Universitas Muhammadiyah Surakarta; 2019.
9. Ginting R, Hutagalung PGJ, Hartono H, Manalu P. Faktor-faktor yang mempengaruhi pemanfaatan Program Pengelolaan Penyakit Kronis (Prolanis) pada lansia di Puskesmas Darussalam Medan. *J Prima Med Sci*. 2020;2(1):24-31.
10. Abdullah, Stajar E, Kadir A. Faktor penyebab terjadinya penurunan jumlah kunjungan peserta Program Pengelolaan Penyakit Kronis (Prolanis) di Puskesmas Minasa Upa Kota Makassar. *J Ilm Kesehat Diagn*. 2017;11(4):382-7.
11. Mahali F. Eksplorasi pengalaman keluarga dalam perawatan pasien skizofrenia di Kalimantan Barat. *Tanjungpura J Nurs Pract Educ*. 2019;1(1):1-17.
12. Aris AA, Nurafifah D, Sagita N. Hubungan peran keluarga sebagai pengawas menelan obat (PMO) dan persepsi pasien dengan kepatuhan minum obat penderita TBC di Puskesmas Deket Kabupaten Lamongan tahun 2020. *J Kesehat*. 2021;10(1):1-13.
13. Yuliani NN, Maria I, Andre LT, Saal N. Peran pengawas minum obat terhadap keberhasilan pengobatan tuberculosis dengan strategi DOTS di Puskesmas Oebobo Kota Kupang. *Jurnal Inovasi Kebijakan*. 2019;4(2):31-41.
14. Ratnawati D, Wahyudi CT, Zetira G. Dukungan keluarga berpengaruh kualitas hidup pada lansia dengan diagnosa diabetes melitus.

- Jurnal Ilmiah Ilmu Keperawatan Indonesia. 2019;9(2):586-7.
- 15. Hanum S, Puerti NR, Marlinda M, Yasir Y. Hubungan antara pengetahuan, motivasi, dan dukungan keluarga dengan kepatuhan minum obat pada penderita hipertensi Di Puskesmas Peukan Bada Kabupaten Aceh Besar. *Jurnal Kesehatan Terpadu (Integrated Health Journal)*. 2019;10(1):30-5.
  - 16. Badan Pusat Statistik Kota Banda Aceh. Kecamatan Lueng Bata dalam angka 2018. Banda Aceh: Badan Pusat Statistik; 2018.
  - 17. Purnawinadi IG, Lintang IJ. Hubungan dukungan keluarga dengan kepatuhan minum obat pasien hipertensi. *Jurnal Skolastik Keperawatan*. 2020;6(1):35-41.
  - 18. Riani DA, Putri LR. Validasi 8-item Morisky Medication Adherence Scale versi Indonesia pada pasien hipertensi dewasa di Puskesmas Kabupaten Sleman dan Kota Yogyakarta [master's thesis]. Yogyakarta: Universitas Gadjah Mada; 201.
  - 19. Rosa F, Fujiati II. Hubungan Dukungan keluarga terhadap kepatuhan minum obat anti tuberkulosis (OAT) di UPT Puskesmas Teladan. *Jurnal Ilmiah Maksitek*. 2020;5(4):63-71.
  - 20. Riani DA, Putri LR. Gambaran kepatuhan minum obat pada pasien hipertensi dewasa di Puskesmas Kabupaten Sleman dan Kota Yogyakarta. *Jurnal Penelitian Multidisiplin*. 2023;1(4):310-20.
  - 21. Oktaviani F, Putri LR. Hubungan karakteristik pasien dibaetes mellitus tipe 2 terhadap kepatuhan penggunaan obat antidiabetes pada pasien diabetes melitus tipe 2 di Puskesmas Kota Batam. *Jurnal Kesehatan Pharmasi*. 2022;4(1):74-80.
  - 22. Ariana R, Sari CWM, Kurniawan T. Perception of prolanis participants about chronic disease management program activities (PROLANIS) in the Primary Health Service Universitas Padjadjaran. *Nurse Line Journal*. 2020;4(2):103.
  - 23. Yuziani Y, Sofia R. Correlation between chronic disease management program (prolanis) activities and health status of hypertension patients at Muara Satu community health center, Lhokseumawe city. *Jurnal Kedokteran Syiah Kuala*. 2023;23(2):261-8.
  - 24. Putri Wiraini T, Zukhra RM, Hasneli Y. Hubungan Dukungan Keluarga Dengan Kualitas Hidup Lansia Pada Masa COVID-19. *Health Care: Jurnal Kesehatan*. 2021;10(1):44-53.
  - 25. Bulu A, Wahyuni TD, Sutriningsih A. Hubungan antara tingkat kepatuhan minum obat dengan kadar gula darah pada pasien diabetes melitus tipe II. *J Ilm Keperawatan*. 2019;4(1):181-9.
  - 26. Chen X, Du L, Wu R, Xu J, Ji H, Zhang Y, et al. The effects of family, society and national policy support on treatment adherence among newly diagnosed tuberculosis patients: a cross-sectional study. *BMC Infect Dis*. 2020;20(1):623. doi:10.1186/s12879-020-05354-3.
  - 27. Lestari NF, Sawitri E, Fitriany E. Kepatuhan minum obat dan indeks massa tubuh berhubungan dengan tekanan darah pasien hipertensi prolanis di Puskesmas Segiri Kota Samarinda. *Jurnal Medika:Karya Ilmiah Kesehatan*. 2022;7(1):1-10.
  - 28. Widyaningrum D, Retnaningsih D, Tamrin. Hubungan dukungan keluarga dengan kepatuhan minum obat pada lansia penderita hipertensi. *Jurnal Ilmu Keperawatan Komunitas*. 2019;2(2):21-6.
  - 29. Mulidan M, Dedi D, Muhammad Khadafi, Dukungan keluarga berhubungan dengan kepatuhan minum obat pada pasien tuberkulosis paru. *Jurnal Penelitian Perawat Profesional*. 2021;3(3):579-80.
  - 30. Arifal A, Dian N, Novi S. Hubungan peran keluarga sebagai pengawas Menelan Obat (PMO) dan persepsi pasien dengan kepatuhan minum obat penderita TBC di Puskemas Deket Kabupaten Lamongan Tahun 2020. *Jurnal Kesehatan*. 2021;10(1):1-13.

## Preventing the Incidence of Severe Preeclampsia by Maintaining an Ideal Body Weight During Pregnancy

Emi Ferawati,<sup>1,2</sup> Hushat Pitalianto,<sup>3</sup> Widya Sepalanita<sup>1</sup>

<sup>1</sup>Polytechnic of Health Ministry of Health Republic of Indonesia Banten, Serang, Indonesia

<sup>2</sup>Postgraduated of Master Program in Midwifery, Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia

<sup>3</sup>Dr. Dradjat Prawiranegara General Hospital, Serang, Indonesia

### Abstract

Preeclampsia is a pregnancy-specific disease potentially leading to complications, morbidity, and mortality. In general, obesity may cause preeclampsia through several common mechanisms. This study aimed to examine the association between obesity and the incidence of severe preeclampsia (SP) at Dr. Dradjat Prawiranegara General Hospital, Serang, Indonesia. A retrospective cohort design was used and the sample comprised of 168 parturients (84 SP and 84 non-SP subjects). Sample selection was consecutively conducted from June to November 2023, while data were analyzed using the Chi-Square test and multivariable analysis with multiple logistic regression. There was a statistically significant relationship between nutritional status and obesity in participants with SP history ( $p<0.05$ ). Obese women had a 2.96 times higher risk of developing SP compared to non-obese. Additionally, the study found that multigravidae ( $\geq G2$ ) had a 2.19 times higher risk of suffering from SP compared to primigravidae (G1) ( $p=0.019$ ). Furthermore, women who only completed  $\leq$  junior high school education had a 2.14 times higher risk of suffering from SP compared to those who completed  $\geq$  high school ( $p=0.060$ ). In conclusion, women in delivery who suffered from obesity have a 2.68 times greater risk of suffering SP than non-obese, as evident from both bivariable and multivariable analyses.

**Keywords:** Body mass index, obesity, parity, severe preeclampsia, uteroplacental insufficiency

### Introduction

Hypertension is a common condition affecting 10% of pregnancies worldwide, including 3-5% of all pregnancies that experience preeclampsia complications.<sup>1</sup> In general, preeclampsia is one pregnancy-specific disease that causes complications, morbidity, and mortality,<sup>2</sup> usually during  $\geq 20$  weeks of gestation age.<sup>3</sup> It is characterized by hypertension, extremities edema, and proteinuria.<sup>4</sup> The various serious complications, include severe preeclampsia (SP), which is defined as preeclampsia with systolic  $\geq 160$  mm Hg or diastolic  $\geq 110$  mm Hg at least 4 hours apart on the 2 occasions. Other complications include liver or renal dysfunction, thrombocytopenia, pulmonary

edema, and central nervous system disorders.<sup>2</sup> It also significantly contributes to fetal-related complications associated with prematurity, fetal distress, growth restriction, intrauterine fetal death (IUFD), as well as increased mortality rates.<sup>3</sup>

According to the World Health Organization (WHO), SP occurs in  $\pm 2$ -10% of pregnancies worldwide, with 1.8-16.7% of the incidents in developing countries, and 0.4% in developed countries.<sup>5</sup> Obesity is considered one of the risk factors and the association can be explained through several common mechanisms.<sup>6,7</sup> Furthermore, SP, similar to obesity, is related to an increased risk of maternal cardiovascular diseases.<sup>1,4</sup>

Obesity, according to the WHO is defined as an abnormal or excessive fat accumulation that poses a harmful health risk,<sup>8</sup> indicated by body mass index (BMI) of 30 or greater.<sup>9</sup> It is a global public health issue with high rates in both developed and developing countries. About one-third of U.S adults suffer from obesity,<sup>4</sup> and in 2022,

### Corresponding Author:

Emi Ferawati,  
 Polytechnic of Health Ministry of Health Republic of  
 Indonesia Banten, Serang, Indonesia  
 Email: ferawati80@gmail.com

WHO reported the obesity pandemic in Europe as one implication of the COVID-19 pandemic, with 60% of European citizens being reportedly overweight or obese.<sup>10</sup> Furthermore, obesity is related to various comorbidities, including SP during pregnancy,<sup>4</sup> diabetes, and cardiovascular disease.<sup>8</sup> Nutritional risk factor differentiation plays a role in the SP provenance. Excessive weight gain during pregnancy or pre-pregnancy, related to insulin resistance, hyperinsulinism, and maternal systemic inflammation, is proposed as one of the pathophysiologies that leads to endothelial dysfunction, hypertension, proteinuria, thrombotic and multi-organ failure.<sup>4</sup>

Modest weight reduction  $\geq 5\text{--}10\%$ , can improve health status outcomes. Many people struggle to maintain weight loss, although strategies such as increased frequency of consultation can improve the success of body weight reduction.<sup>8</sup> Given the strong association between obesity and preeclampsia, this study aimed to evaluate the impact of obesity on the incidence of severe preeclampsia.

## Methods

This was a retrospective cohort study conducted to examine the impact of obesity in both SP and non-SP subjects at Dr. Dradjat Prawiranegara General Hospital Serang, Banten, Indonesia from June to November 2023. The population comprised all parturients who registered at Dr. Dradjat Prawiranegara General Hospital, for six months in 2023. Inclusion criteria for SP subjects include parturients who suffered from SP both in early-onset and late-onset SP, maternal age 18–35 years old,  $\geq 24$  weeks gestational age, singleton fetus, all types of labor either spontaneously or terminated pregnancy, presence of body weight data before pregnancy in medical register data/books/pregnancies notebooks. Meanwhile, inclusion criteria for non-SP subjects include parturients with normal delivery, maternal age 18–35 years old,  $\geq 24$  weeks gestational age, singleton fetus, all types of labor either spontaneously or terminated pregnancies, presence of body weight data before pregnancy or in the first-trimester in medical register data/books/pregnancy notebooks.

Exclusion criteria were maternal age  $<18$  or  $>35$  years old,  $<24$  weeks gestational age, multiple fetuses, and maternal pregnancy with complications, such as Diabetes Mellitus (DM), systemic diseases, or chronic hypertension. Dropout criteria include incomplete data, and

having no available body weight data before pregnancy in medical register data/book/pregnancy notebooks.

The sample size was calculated based on the Lemeshow formula. Consequently, the sample size was 74 for SP subjects and 74 non-SP subjects, each added with 10 subjects to anticipate dropout. Therefore, the total number of samples consecutively selected for both groups was 168.

The data used comprised both primary and secondary, collected through patients medical records or anamnesis according to the sample criteria. The instrument used in this study was the checklist, while the collected data were analyzed descriptively and analytically. Data analysis used the Chi-Square test and multivariable analysis with multiple logistic regression. This study received approval from the Health Research Ethics Committee, Polytechnic of the Health Ministry of Health of the Republic of Indonesia Tanjungkarang, Bandar Lampung, Indonesia (No. 355/KEPK-TJK/V/2023).

## Results

This study examined the impact of obesity on SP among 84 delivery women with SP and 84 non-SP women. Other variables studied apart from obesity were BMI, maternal and gestational age, as well as parity, education, and occupation, with the complete results presented in Table 1. Table 1 shows that most of the subjects had maternal age  $<30$  years, with a lower proportion in SP subjects vs non-SP (60.7% vs. 66.7%). Gestational age was mostly in the normal range between 37–42 weeks, and lower in the SP vs non-SP subjects (76.2% vs 84.5%). A significant proportion had parity status found in multigravidae vs primigravidae, with higher value in the SP vs non-SP subjects (64.3% vs 54.2%). In terms of education, the subjects mostly graduated from high school, with a lower proportion in SP vs non-SP (73.8% vs 79.8%). Regarding occupation, the majority were unemployed (housewives), with a higher proportion in SP vs non-SP subjects (100% vs 92.9%). Late-onset was higher than early-onset (76.2% vs 23.8%) and a significant proportion had protein ++ level (58.3%). Based on the results, characteristics that showed a relationship with SP incidence were parity ( $p=0.013$ ) and occupation ( $p=0.028$ ).

Delivery women who suffered SP consist of 20 subjects (23.8%) in the early-onset category and 64 (76.2%) in the late-onset. The relationship

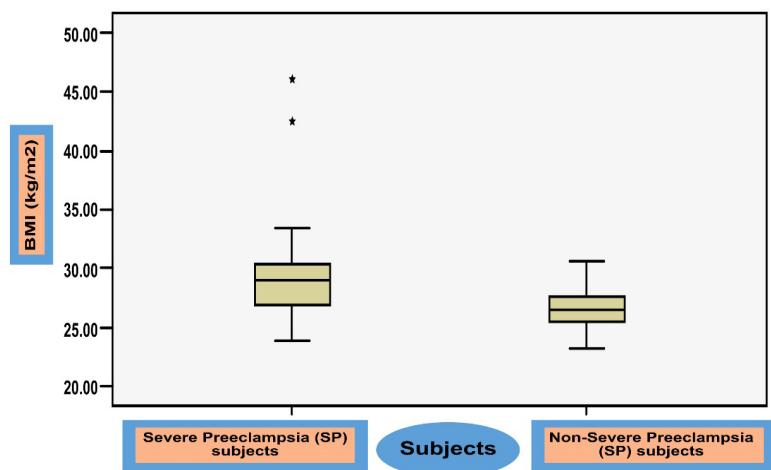
**Table 1 Characteristics of Severe Preeclampsia and Non-Severe Preeclampsia Subjects**

Characteristics	Severe Preeclampsia (SP) (n=84)	Non Severe Preeclampsia (n=84)	p-value
Maternal age (year)			
18-29	51 (60.7%)	56 (66.7%)	
30-35	33 (39.3%)	28 (33.3%)	
Average (SD)	27.3 (5.2)	26.0 (5.1)	
Gestation Age (week) :			0.422
<37	20 (23.8%)	13 (15.5%)	
37-42	64 (76.2%)	71 (84.5%)	
Average (SD)	37.4 (3.7)	38.3 (2.2)	
Parity:			0.174
G1	30 (35.7%)	46 (54.8%)	
≥G2	54 (64.3%)	38 (45.2%)	
Education :			
≤Primary High School	22 (26.2%)	14 (16.7%)	
High School	62 (73.8%)	67 (79.8%)	0.013
Academic/University	0	3 (3.6%)	
Occupation:			0.083
Working	0	6 (7.1%)	
Unemployed/Housewife	84 (100%)	78 (92.9%)	
Category of SP			
Early-onset SP	20 (23.8%)	-	
Late-onset SP	64 (76.2%)	-	0.028**
Protein :			
+1	26 (31.0%)	-	
+2	49 (58.3%)	-	
+3	9 (10.7%)	-	

**Table 2 Relationship between Nutritional Status with Severe Preeclampsia Incidence**

Nutritional Status (BMI, kg/m <sup>2</sup> )	Group		p-value	OR (95% CI)
	SP Subjects (n=84)	Non-SP Subjects (n = 84)		
18.5-<23	1 (1.2%)	0	0.008	
23.0-<25	4 (4.8%)	13 (15.5%)		
25.0-<30	55 (65.5%)	61 (72.6%)		1.0
≥30	24 (28.6%)	10 (11.9%)		2.93 (0.90-9.52)
Average (SD)	29.06 (3.56)	26.88 (1.97)		7.80 (2.04-29.84)
Median	28.89	26.52	<0.001**	
Range	21.08-46.02	23.23-31.87		
≥30 (obesity)	24 (28.6%)	10 (11.9%)	0.007	2.96 (1.31-6.67)
<30 (non obesity)	60 (71.4%)	74 (88.1%)		

Note: Chi-square test; \*\* Mann-Whitney test; OR (95% CI): Odds Ratio and 95% Confidence Interval



**Figure 1 Comparison of Body Mass Index (BMI) between Delivery Women with Severe and Non-Severe Preeclampsia**

between nutritional status and obesity with SP history was not statistically significant ( $p>0.05$ ).

Obesity showed a statistically significant relationship with delivery women who suffered SP incidence ( $p<0.05$ ). The risk of developing SP was 2.96 times greater among delivery women with obesity.

Multivariable analysis between obesity and characteristics of SP was analyzed by multiple logistic regression. The calculation comprised variables that had  $p$ -values  $p<0.25$  from bivariable results namely parity, education, gestational age, occupation, and obesity. Calculation results with backward methods obtained a significant final model as shown in Table 4.

Multivariable logistic regression (Table 4) showed that multigravidae ( $\geq G2$ ) had a 2.19-fold higher risk of SP compared to primigravidae ( $p=0.019$ ), and women with  $\leq$  junior high school education had a 2.14-fold higher risk compared to those with higher education, although this was marginally significant ( $p=0.060$ ). Obesity remained a significant independent risk factor, with a 2.68-fold higher risk of SP compared to non-obese women ( $p=0.021$ ).

## Discussion

This study found that multigravida women

**Table 3 Description of Nutritional Status in Severe Preeclampsia Case**

Nutritional Status (BMI, kg/m <sup>2</sup> )	Severe Preeclampsia Category		p-value
	Early-onset SP (n=20)	Late-onset SP (n=64)	
18.5-<23	0	1 (1.6%)	0.097
23.0-<25	3 (15.0%)	1 (1.6%)	
25.0-<30	12 (60.0%)	43 (67.2%)	
$\geq 30$	5 (25.0%)	19 (29.7%)	
$\geq 30$ (obesity)	5 (25.0%)	19 (29.7%)	0.685
<30 (non obesity)	15 (75.0%)	45 (70.3%)	

Note: \*) Chi-Square Test

**Table 4** Multiple Logistic Regression Analysis of Various Factors Associated with Severe Preeclampsia Incidence among Delivery Women (Final Model)

Variable	Coefficient B	SE (B)	p-value	OR <sub>adj</sub> (CI 95%)
Parity ( $\geq$ G2)	0.784	0.333	0.019	2.19 (1.14–4.20)
Education (Primary High school)	0.763	0.406	0.060	2.14 (0.97–4.75)
Obesity	0.985	0.425	0.021	2.68 (1.16–6.16)

Note: OR Adj (CI 95%): Odds Ratio Adjusted and 95% Confident Interval

and unemployed/housewives had significantly higher risks of severe preeclampsia (SP), along with obesity as an independent predictor.). This study produced results different from the theory stating that SP mostly occurs in primigravida, due to the maternal first exposure to fetal trophoblast. The parity status found in multigravida vs primigravida was higher in the SP subjects vs non-SP (64.3% v.s. 54.2%). Similar results were found in other studies conducted at Dr. M. Soewandhi Hospital, Dr. Soetomo, and Haji Hospital, as well as some community health centers in Surabaya, Indonesia, on early detection score of SP risk. One of the significant factors of SP risks is a history of multigravida, which is usually present as hypertension worsened by pregnancy. SP is generally found among multigravida mothers who have experienced vascular diseases including DM, chronic hypertension, or systematic diseases, which also may occur due to high parity. The incidence, according to the parity, mostly occurs in multigravida (64.5%) and primigravida (35.5%). Furthermore, a significant correlation was found between the parity and the SP incidence (OR=2.464). Multigravida mothers have a two-time higher risk of suffering from SP than primigravida.<sup>11</sup>

The results also showed that the majority of the subjects were unemployed (housewives), with a higher proportion in SP vs non-SP (100% vs 92.9% with  $p=0.028$ ). Similar results were found in a previous population-based study in Canadian hospitals (except Quebec) on the incidence and risk factors for SP, elevated liver enzymes, hemolysis, and low platelet count syndrome, as well as eclampsia at preterm and term gestation. It was a retrospective, population-based cohort study of all women with a singleton delivery from 2012 to 2016 ( $n=1,078,323$ ). The results showed that the rates of SP ( $n=2533$ ), regardless of gestational age and socioeconomic status were inversely associated.<sup>2</sup>

Table 2 shows that delivery women who

suffered SP consisted of 20 subjects (23.8%) in the early-onset SP category and 64 (76.2%) in the late-onset. The relationship between nutritional status and obesity with SP history was not statistically significant ( $p>0.05$ ). The result is similar to the theory stating that dietary intake of proper foods and nutrients can prevent and reduce the risk of SP, while also improving the outcomes. Excessive body weight gain is associated with SP risk, which is usually related to fluid retention. High dietary fibers such as fruits, and vegetables, can reduce the risk, while adherence to Western diet styles may increase the risk. Other nutrients, that may improve hypertension, such as sodium or salt, have little to no effect on the risk. In this case, there is a possibility that each person has individual differences in the dietary intake of foods and nutrients.<sup>12</sup> Based on the results, obesity had a statistically significant relationship ( $p<0.05$ ) with SP. Delivery women with obesity had a 2.96 times greater risk of developing SP compared to normal.

This study produced results similar to the theory stating that obesity during pregnancy is directly related to obstetric complications including SP<sup>13</sup> as well as a mediation analysis conducted in Paris, France, on maternal obesity and SP among immigrant women. Pre-pregnancy obesity mediates the association between maternal place of birth and SP in the PreCARE cohort among pregnant women ( $n=9,579$ ). About 95 women (0.99%) suffered SP, including 47.6% non-European immigrants, 16.3% born in Sub-Saharan Africa, and 12.6% obese ( $BMI \geq 30 \text{ kg/m}^2$ ). Women suffering from SP were higher in Sub-Saharan Africa ( $p=0.023$ ) and among the obese population ( $p=0.048$ ). Sub-Saharan African women had more risk of SP vs European-born women (aOR 2.53, 95% CI 1.39–4.58) and the obesity-mediated indirect effect was 18% of the total risk (aOR 1.18, 95% CI 1.03–1.35). In conclusion, Sub-Saharan African immigrant women have a two-fold higher risk of developing

SP than European-born women, one-fifth of which is mediated by pre-pregnancy obesity.<sup>14</sup>

Another study on SP prevalence and pregnancy outcomes in Sweden and China reported obesity as a significant risk factor. The condition was found as a stronger risk factor in China than in Sweden with (OR 5.12; 95% CI, 3.82–6.86 vs OR, 3.49; 95% CI, 3.31–3.67).<sup>15</sup>

Based on the results in Tables 3 and 4, the multivariable analysis between obesity and characteristics of SP were analyzed using multiple logistic regression. The calculation comprised variables that had p-values  $p<0.25$  from bivariable results namely parity, education, gestational age, occupation, and obesity.

Delivery women who were multigravidae ( $\geq G2$ ) had a 2.19 times greater risk of suffering SP compared to primigravidae (G1) with a p-value of 0.019. Similar results were found in a previous study conducted in Surabaya, Indonesia, on early detection score of SP risk. The incidence, according to the parity, mostly occurs in multigravida (64.5%) and primigravida (35.5%). This shows that there is a significant correlation between parity and SP incidence in pregnant women with (OR=2.464). In other words, multigravidae has twice a greater risk of suffering SP than primigravidae.<sup>11</sup>

This study showed that women who graduated from primary high school had a 2.14 times greater risk of suffering SP compared to those who graduated from  $\geq$ high school, with p 0.060 (Table 4). Similar results were obtained in a previous study conducted in Pakistan on SP incidence as well as maternal and neonatal outcomes with associated risk factors. The prospective study examined 142 patients with gestational hypertension and SP during two years. The results showed 8.67% cases of gestational hypertension and 3% of SP. Most of the preeclamptic women were in lower socioeconomic levels (44.4%) and had low educational levels (81.1%). The incidence of SP is related to good nutrition and proper diet, awareness, as well as low economic status.<sup>5</sup>

Another study in Turkey examined the effect of an education and counseling program on maternal neonatal outcomes in pregnant women at risk of SP. It was a randomized controlled trial design study and was conducted among 132 pregnant women attending an antenatal clinic for routine care. The results found a significant correlation between healthy lifestyle behaviors related to education and counseling with SP ( $p<0.008$ ). Patient education and counseling can prevent nearly half of the most harmful

outcomes<sup>16</sup> as shown in Table 4.

SP, defined as preeclampsia with systolic  $\geq 160$  mmHg or diastolic  $\geq 110$  mmHg, commonly develops after 20 weeks of pregnancy. It is evidenced by maternal organ or uteroplacental insufficiency, including renal or liver dysfunction, pulmonary edema, thrombocytopenia, and disturbances of the central nervous system.<sup>1</sup>

<sup>2</sup> Furthermore, the WHO defines obesity as an abnormal or excessive fat accumulation that can increase health risk,<sup>8</sup> indicated by BMI of 30 or greater.<sup>9,17</sup> Pre-pregnancy BMI can be classified based on body weight into several categories namely underweight (BMI  $<18.5$  kg/m<sup>2</sup>), normal weight (BMI 18.5–24.9 kg/m<sup>2</sup>), obesity (BMI 25–29.9 kg/m<sup>2</sup>), and obese classes I, II, III (BMI  $>30$  kg/m<sup>2</sup>). Although both are pregnancy high-risk factors, women who suffer obesity have statistically significantly higher complications than underweight women.<sup>17</sup> The adjusted risk of suffering SP is two times higher for overweight women (BMI of 26 kg/m<sup>2</sup>), and almost three times for obese women (BMI of 30 kg/m<sup>2</sup>).<sup>4</sup>

The results are based on the pathophysiology that SP has complexity and is not clearly understood yet. It is associated with abnormal placentation, systemic inflammation, and oxidative stress. Appropriate remodeling failure of the spiral arteries causes abnormal placentation, placental blood circulation resistance, and hypo-perfusion of the placenta. SP causes chronic placental ischemia, decreases blood circulation to the developing fetus, fetal hypoxia, and harmful adverse outcomes.<sup>1</sup> Pathological results are often present before the clinical onset, while endothelial and vascular abnormalities are responsible for the characteristic vasoconstriction.<sup>4</sup>

Nutritional risk factor differences such as deficiency of protein, calcium, essential fatty acids, and vitamins, have been shown to play a role in the SP provenance. In addition, excessive weight gain during pregnancy or a pre-pregnancy state of obesity and overweight, related to insulin resistance, hyperinsulinism, and maternal systemic inflammation, are proposed as one of the pathophysiology that leads to endothelial dysfunction, hypertension, proteinuria, thrombotic and multi-organ failure. These conditions increase future risk of cardiovascular disease as well as maternal mortality and morbidity.<sup>4</sup>

By carrying out early assessment of health risks, as well as providing support, motivation, prompt knowledge, and treatment tools, health practitioners can assist patients to achieve

optimal weight loss and health status.<sup>8</sup> Expert nutritionist advice is required throughout the pregnancy period. Current recommendations include restricting calories up to 1200 kcal/day, routine walking or physical exercise in the third trimester, and administering 150 mg aspirin to all women with  $BMI >35 \text{ kg/m}^2$ .<sup>17</sup>

In conclusion, multigravida status, low education, and obesity were identified as significant risk factors for SP. These findings underscore the importance of early risk stratification, patient education, and weight management interventions before and during pregnancy to reduce the burden of SP and its complications.

### Acknowledgment

The authors thank the Polytechnic of Health Ministry of Health Republic of Indonesia Banten, Serang, Indonesia, for assistance and support. This research was funded by DIPA Polytechnic of Health Ministry of Health Republic of Indonesia Banten (No: HK.02.03/XXX.II/5576/2023 for beginner research scheme through Simlitabkes application).

### References

1. Fox R, Kitt J, Leeson P, Aye CYL, Lewandowski AJ. Preeclampsia: risk factors, diagnosis, management, and the cardiovascular impact on the offspring. *J Clin Med* 2019;8(1625):1-22.
2. Lisonkova S, Bone JN, Muraca GM, Razaz N, Wang LQ, Sabr Y, et al. Incidence and risk factors for severe preeclampsia, hemolysis, elevated liver enzymes, and low platelet count syndrome, and eclampsia at preterm and term gestation: a population-based study. *Am J Obstet Gynecol*. 2021;225(538):1-19. doi:10.1016/j.ajog.2021.04.261
3. Ferawati E, Kuswandi K, Karmila N. Impact of severe preeclampsia on the incidence of low-birth-weight babies. *MKB*. 2023;55(4):227-31.
4. Lopez-Jaramillo P, Barajas J, Rueda-Quijano SM, Lopez-Lopez C, Felix C. Obesity and preeclampsia: common pathophysiological mechanisms. *Front Physiol*. 2018;9:1838. doi:10.3389/fphys.2018.01838.
5. Khan B, Yar RA, Khakwani Ak, Karim S, Ali HA. Preeclampsia Incidence and Its Maternal and Neonatal Outcomes With Associated Risk Factors. *Cureus*. 2022;14(11):1-9.
6. Spradley FT, Palei AC, Granger JP. Increased risk for the development of preeclampsia in obese pregnancies: weighing in on the mechanisms. *Am J Physiol Regul Integr Comp Physiol*. 2015;309(11):R1326-43. doi:10.1152/ajpregu.00178.2015
7. Jasovic-Siveska E. Obesity as risk factor for preeclampsia. *EC Gynaecol*. 2014;1(1):3-6.
8. Fruh SM. Obesity: risk factors, complications, and strategies for sustainable long-term weight management. *J Am Assoc Nurse Pract*. 2017;29(S1):S3-14. doi:10.1002/2327-6924.12510.
9. González-Plaza E, Bellarta J, Martínez-Verdú MÁ, Arranz Á, Luján-Barroso L, Seguranyes G. Pre-pregnancy overweight and obesity prevalence and relation to maternal and perinatal outcomes. *Enferm Clín*. 2022;32:S23-30.
10. Boutari C, Mantzoros CS. A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on. *Metabolism*. 2022;133:155217. doi:10.1016/j.metabol.2022.155217.
11. Dhiana S, Budi S, Santi M, Ernawati, Intim C. Early Detection Score of Preeclampsia Risk. *Indian J Forensic Med Toxicol* 2019;13(4):1717-21.
12. Esquivel MK. Nutritional Status and Nutrients Related to Pre-Eclampsia Risk. *Am J Lifestyle Med*. 2022;17(1):41-45. doi:10.1177/15598276221129841.
13. Abraham T, Romani AMP. The Relationship between Obesity and Pre-Eclampsia: Incidental Risks and Identification of Potential Biomarkers for Pre-Eclampsia. *Cells*. 2022;11(9):1548. doi:10.3390/cells11091548
14. Siddiqui A, Deneux-Tharaux C, Luton D, Schmitz T, Mandelbrot L, Estellat C, et al. Maternal obesity and severe pre-eclampsia among immigrant women: a mediation analysis. *Sci Rep*. 2020;10(1):5215. doi:10.1038/s41598-020-62032-9.
15. Yang Y, Le Ray I, Zhu J, Zhang J, Hua J, Reilly M. Preeclampsia Prevalence, Risk Factors, and Pregnancy Outcomes in Sweden and China. *JAMA Netw Open*. 2021;4(5):e218401. doi:10.1001/jamanetworkopen.2021.8401
16. Ugurlu M, Yayan T, Karasahin KE. The effect of an education and counseling program on maternal/neonatal outcomes in pregnant women at risk of preeclampsia. *P R*

- Health Sci J. 2021;40(3):127-35.
17. Khadilkar SS. Obesity in Pregnancy: Obstetrician's Obstacle. J Obstet Gynaecol India. 2019;69(3):197-202. doi:10.1007/s13224-019-01235-1

## Functional Outcome of Biportal Endoscopy Spine Surgery for Lumbar Disc Herniation Diseases

Ajid Risdianto,<sup>1,2</sup> Happy Kurnia,<sup>2</sup> Krisna Tsaniadi,<sup>2</sup> Dody Priambada,<sup>2</sup> Eri Andar,<sup>2</sup> Zaenal Muttaqien,<sup>2</sup> Yuriz Bakthiar,<sup>2</sup> M. Thohar Arifin<sup>2</sup>

<sup>1</sup>Doctoral Study Program at Medical Science and Health Science, Universitas Diponegoro, Indonesia

<sup>2</sup>Department of Neurosurgery, Faculty of Medicine Universitas Diponegoro/Dr. Kariadi Hospital Semarang, Indonesia

### Abstract

Biportal endoscopic spine surgery (BESS) is an innovative, minimally invasive technique to treat lumbar disc herniation (LDH). BESS provides superior surgical visualization with minimal tissue dissection. However, its application requires a thorough understanding of endoscopic anatomy and adaptation of endoscopy equipment, which are key factors in achieving optimal functional outcomes post-surgery. This study aimed to evaluate the functional outcomes and complications of BESS performed on 49 patients between 2020 and 2022 at Dr. Kariadi Hospital, Semarang, Indonesia. The majority of patients (53%) had herniation at the L4-5 level, followed by L5-S1. Pain assessment using the Visual Analog Scale (VAS) demonstrated a significant reduction in pain, from 4.26 to 1.5, post-surgery. Functional outcomes, as evaluated using MacNab's Criteria, revealed that 93.8% of patients achieved a satisfactory condition, with 36.7% reporting no pain and 57.1% experiencing occasional pain that did not affect their daily activities. Complications were minimal, with two cases of dural tears and intraoperative bleeding. The study concludes that BESS is a safe and effective procedure for LDH, resulting in significant pain relief and functional improvement, although certain technical challenges persist.

**Keywords:** Biportal endoscopy, lumbar disc herniation, MacNab scale score, visual analog scale

### Introduction

Lumbar disc herniation (LDH) is a leading cause of lower back pain and sciatica, affecting millions of people worldwide.<sup>1</sup> Traditional open spine surgeries, though effective in addressing LDH, are often associated with significant drawbacks, including extensive soft tissue damage, prolonged recovery periods, and higher risks of complications such as dural tears and infection.<sup>2</sup> These limitations underscore the need for more refined, minimally invasive approaches to spine surgery.<sup>2</sup>

In recent years, the development of endoscopic spine surgery (ESS) has emerged as a promising solution to these issues.<sup>3</sup> Techniques such as full-endoscopic discectomy and percutaneous endoscopic lumbar discectomy have shown

improved outcomes with less tissue damage, shorter hospital stays, and faster recovery times.<sup>4</sup> Among these advancements, biportal endoscopic spine surgery (BESS) has gained traction for its unique approach, which involves two independent portals, offering enhanced visualization and maneuverability around neural structures.<sup>5</sup> Despite these benefits, BESS presents technical challenges, such as limited working space and the steep learning curve required to achieve proficiency.<sup>6</sup>

This study evaluates the functional outcomes and complications of BESS in the treatment of LDH, based on clinical data from 49 patients who underwent the procedure at Dr. Kariadi Hospital, Semarang, between 2020 and 2022. By focusing on pain reduction and functional recovery, this study seeks to provide further insights into the efficacy and safety of BESS for treating lumbar disc herniation, offering a clearer understanding of its advantages and limitations.

The primary objectives of this research are to assess functional outcomes using MacNab's Criteria, evaluate pain reduction through

### Corresponding Author:

Ajid Risdianto  
 Division of Neurospine Surgery Department of  
 Neurosurgery, Faculty of Medicine, Universitas Diponegoro/  
 Kariadi Hospital, Semarang, Indonesia  
 Email: ajidrisdianto@lecturer.undip.ac.id

the Visual Analog Scale (VAS), and identify complications associated with the Biportal Endoscopic Spine Surgery (BESS) technique. The findings aim to inform future advancements in minimally invasive spine surgery and enhance patient care.

The novelty of this study lies in providing new clinical data on the use of BESS for treating Lumbar Disc Herniation (LDH), specifically from a cohort of patients treated at Kariadi Hospital.

## Methods

This study was conducted as an observational analysis of 49 patients diagnosed with lumbar disc herniation (LDH) and treated with biportal endoscopic spine surgery (BESS) at Dr. Kariadi Hospital, Semarang, between 2020 and 2022. Ethical approval was obtained from the Health Research Ethics Committee of Dr. Kariadi Hospital (approval number 2019-852). Written informed consent was obtained from all patients. Patients were eligible for inclusion if: 1) had a prolapsed lumbar disc with unilateral radiculopathy; 2) tested positive for the straight leg raise (SLR) or femoral stretch test; 3) had magnetic resonance imaging (MRI) confirming a single nerve root lesion; and 4) had undergone at least six weeks of conservative therapy, including bed rest, activity modification, physiotherapy, and medication, with persistent symptoms.

Exclusion criteria were: 1) multilevel disc prolapse or root involvement; 2) diagnosis of cauda equina syndrome; 3) discrepancy between clinical and radiological findings. All patients underwent BESS discectomy under general anesthesia. BESS involves two independent portals: one for the endoscope and another for surgical instruments. The procedure was performed using a saline irrigation system to maintain clear visualization. A combination of endoscopic instruments was used to perform the discectomy and decompress the affected nerve root.

Pain was evaluated using the Visual Analog Scale (VAS) both preoperatively and postoperatively. Pain and functional outcomes were assessed at a postoperative follow-up period of 1 months, which allowed for an early evaluation of surgical success and complication rates. However, longer-term follow-up is recommended in future studies to evaluate the durability of these outcomes. Functional outcomes were assessed postoperatively using MacNab's Criteria, classifying patients into

one of four categories: 1) Excellent (no pain, unrestricted activity), 2) Good (occasional pain, no interference with activities), 3) Fair (improved but with intermittent pain that interferes with work or leisure), 4) Poor (no improvement or worsened condition).

Statistical analysis was performed using SPSS software. Pre- and postoperative VAS scores were compared with the Student's t-test, with  $p<0.05$  considered statistically significant.

## Results

A total 49 patients were included in this study, the majority of whom were women (51%), with a mean age of 46.7 years. The most frequently herniated vertebral segments were L4-5 (53.1%), followed by L5-S1 (32.7%) and L3-4 (14.3%). The majority of herniations occurred on the left side (77.6%) (Table 1).

Evaluation of the pain carried out before and after the BESS procedure showed a significant decrease ( $p<0.001$ ) from a mean of 4.26 to 1.5 (Table 2). There was a substantial decrease in the VAS pain scale between pre-operative and post-operative BESS.

Further subgroup analysis was conducted to compare VAS score improvements across different herniation levels. Patients with L4-5 herniation exhibited the most significant mean VAS reduction (from 4.3 to 1.3), followed by those with L5-S1 (from 4.2 to 1.6), and L3-4 (from 4.1 to 1.8). Although all groups showed improvement, the L4-5 group demonstrated the

**Table 1 Demographic and Lumbar Disc Herniation Characteristics**

Demographic and Characteristics	n (%)	Mean (min-max)
Gender		
Male	24 (49)	-
Female	25 (51)	
Age		46.7 (18-65)
Level of vertebrae		
Lumbar 3-4	7 (14.3)	
Lumbar 4-5	26 (53.1)	
Lumbar 5-Sacral 1	16 (32.7)	
Location		
Left side	38 (77.6)	
Right side	11 (22.4)	

**Table 2 Pain Evaluation Pre- and Post-Surgery**

Variable	Mean
VAS Pre-surgery	4.26
VAS Post-surgery	1.5
p-value	<0.001

greatest overall pain reduction.

Additionally, a comparison based on herniation side showed that left-sided herniations (n=38) experienced a VAS reduction from 4.25 to 1.4, while right-sided herniations (n=11) showed a reduction from 4.27 to 1.7. Though both groups experienced statistically significant improvements, patients with left-sided herniations showed slightly better outcomes.

Table 3 shows an evaluation of functional outcomes after the BESS procedure based on MacNab criteria. The results showed that the majority of patients met criterion 2 (57.1%; occasional back pain or leg pain not interfering with the ability to perform regular work, or to enjoy leisure activity), followed by criterion 1 (36.7%; no pain, no restriction of activity) and criterion 3 (6.4%; improved functional capacity but handicapped by intermittent pain of sufficient severity to curtail or modify work or leisure activities).

## Discussion

This study evaluated the functional outcomes and complications associated with biportal endoscopic spine surgery (BESS) for lumbar disc herniation (LDH). A total of 49 patients who underwent BESS were analyzed, with a focus on patient demographics, pain reduction, and functional outcomes.

The majority of patients in this study were women (51%) with a mean age of 46.7 years. This aligns with other studies that suggest women are slightly more prone to LDH, where women accounted for 52.6% of LDH cases.<sup>7</sup> The most common herniation site was at the L4-L5 vertebrae (53.1%), followed by L5-S1 (32.7%). These findings are consistent with the global pattern of lumbar disc herniation, which predominantly affects the L4-L5 and L5-S1 levels due to the higher mechanical stress these segments endure. Sedighi et al. also reported similar distributions of herniation sites in their

**Table 3 Functional Evaluation After BESS Surgery**

MacNab Criteria	n (%)
Criteria 1 (no pain, unrestricted activity)	18 (36.7)
Criteria 2 (occasional pain, no interference)	28 (57.1)
Criteria 3 (intermittent pain, activity limitation)	3 (6.4)

study.<sup>8,9</sup>

Pain outcomes demonstrated a significant reduction in mean VAS scores from 4.26 preoperatively to 1.5 postoperatively (p<0.001). Patients with L4-5 herniations showed the most substantial decrease in VAS scores, which may be attributed to the high prevalence of this level in the cohort and its relatively accessible anatomy during endoscopic procedures. The L3-4 group exhibited slightly less improvement, possibly due to more complex anatomical constraints or smaller sample size. Moreover, laterality seemed to influence outcomes. Left-sided herniations had a marginally greater VAS improvement than right-sided ones. While the clinical relevance remains to be fully clarified, this could be partially attributed to the surgeon's right-handedness, which might facilitate better access and control during decompression on one side. Future studies with detailed documentation of surgeon handedness and operative technique may help validate this observation.

A significant reduction in pain levels postoperatively as demonstrated in Table 2. The mean VAS score dropped from 4.26 preoperatively to 1.5 postoperatively, highlighting the effectiveness of BESS in relieving pain. This result is statistically significant (p < 0.001) and consistent with the findings of Kim et al., where patients reported significant pain relief after undergoing BESS.<sup>10</sup> The ability of BESS to reduce pain while minimizing soft tissue damage has made it an attractive option compared to traditional open surgery, which typically involves longer recovery times and more extensive postoperative pain.

Functional outcomes were measured using MacNab's Criteria, as shown in table 3. The majority of patients (57.1%) achieved MacNab Grade 2 (occasional pain, no significant

interference with daily activities), while 36.7% of patients were classified as Grade 1 (no pain, no restriction of activity). Only 6.4% fell into Grade 3 (improved but with intermittent pain affecting activities). These outcomes are consistent with previous study that reported 87% of patients treated with BESS achieved either excellent or good results according to MacNab's Criteria.<sup>11</sup>

The results of this study align closely with previous research on BESS and other minimally invasive spine surgery techniques. Similar positive outcomes in patients with spinal stenosis treated with BESS, with 81% achieving good or excellent results and significant improvements in functional outcomes after BESS procedures.<sup>12,13</sup> The reduction in postoperative pain and improved functionality found in this study further reinforce the growing body of evidence that BESS is an effective technique for the treatment of lumbar disc herniation.

However, while the outcomes are promising, the complication rate must also be considered. In this study, two cases of dural tears and intraoperative bleeding were reported, which corresponds to a 4% complication rate. This is in line with other studies such as those where dural tears and minor intraoperative bleeding were among the most commonly reported complications during BESS procedures.<sup>10,14</sup> Despite these complications, the minimally invasive nature of BESS offers a significant advantage over traditional open surgeries, which are often associated with higher rates of infection, blood loss, and prolonged recovery times.<sup>5</sup>

Another important consideration is the anatomical characteristics of the disc bulging itself. The size of the bulge may play a critical role in the likelihood of complications, such as dural tears and intraoperative bleeding, as observed in two cases in this study. Larger or more protrusive disc bulges can make surgical access more challenging, increase manipulation of neural structures, and thereby raise the risk of iatrogenic injury.

Additionally, the spatial relationship between the herniated disc and the adjacent nerve root deserves attention. Depending on whether the nerve root is displaced laterally, compressed centrally, or lies directly over the bulging disc, the complexity of the surgical procedure and the risk of complications may vary. Discussing these anatomical nuances could help in preoperative planning and in anticipating technical difficulties during BESS procedures.

A key strength of this study is the detailed

analysis of both pain reduction and functional recovery, which provides a comprehensive evaluation of the BESS technique. Additionally, the use of objective criteria such as the VAS for pain and MacNab's Criteria for functionality ensures that the outcomes are both measurable and comparable to previous research.

However, this study has several limitations. First, the sample size of 49 patients, while adequate for a preliminary analysis, is relatively small compared to larger studies. A larger patient population would allow for more generalizable conclusions. Additionally, the follow-up period was not extensive, limiting the ability to assess long-term outcomes and potential late complications. Future studies should aim for a longer follow-up to evaluate the durability of the surgical results over time. Finally, while this study highlights the efficacy of BESS, it does not address the steep learning curve associated with mastering the technique. Surgeons unfamiliar with BESS may experience higher complication rates until they achieve proficiency.

In conclusion, BESS is a highly effective and minimally invasive approach for treating lumbar disc herniation. Significant reductions in pain and improvements in functional outcomes were observed, with a relatively low complication rate. Despite the technical challenges and steep learning curve, BESS offers several advantages over conventional open spine surgeries, including reduced tissue damage, faster recovery, and lower complication rates. However, to enhance the understanding and safety of the procedure, future studies should incorporate additional findings such as the size and anatomical positioning of the disc bulge, as well as the spatial relationship of the nerve root to the herniated disc. These factors may have critical implications for complication risks and surgical strategy, and their inclusion could greatly benefit preoperative planning and overall outcomes in BESS.

## References

1. Greenberg MS. Handbook of neurosurgery. 6th ed. New York: Thieme; 2006.
2. Kang KB, Shin YS, Seo EM. Endoscopic Spinal Surgery (BESS and UESS) versus microscopic surgery in lumbar spinal stenosis: systematic review and meta-analysis. Global Spine J. 2022;12(8):1943-55. doi:10.1177/21925682221083271
3. Kwon H, Park JY. The role and future of endoscopic spine surgery: a narrative

- review. *Neurospine*. 2023;20(1):43–55. doi:10.14245/ns.2346236.118
- 4. Han H, Song Y, Li Y, Zhou H, Fu Y, Li J. Short-term clinical efficacy and safety of unilateral biportal endoscopic transforaminal lumbar interbody fusion versus minimally invasive transforaminal lumbar interbody fusion in the treatment of lumbar degenerative diseases: a systematic review and meta-analysis. *J Orthop Surg Res*. 2023;18(1):656. doi: 10.1186/s13018-023-04138-0
  - 5. Awuah WA, Adebusoye FT, Alshareefy Y, Cheng Ng J, Tomas Ferreira AL, Abdus Salam AL, et al. Biportal endoscopic surgery for lumbar spine herniated discs: a narrative review of its clinical application and outcomes. *Annals Medicine Surgery*. 2023;85(8):3965–73. doi: 10.1097/ms9.0000000000001053
  - 6. Choi CM. Biportal endoscopic spine surgery (Bess): Considering merits and pitfalls. *J Spine Surg*. 2020;6(2):457–65. doi: 10.21037/jss.2019.09.29
  - 7. Azharuddin A, Aryandono T, Magetsari R, Dwiprahasto I. Predictors of the conservative management outcomes in patients with lumbar herniated nucleus pulposus: A prospective study in Indonesia. *Asian J Surg*. 2022;45(1):277–83. doi:10.1016/j.asjsur.2021.05.015
  - 8. Sedighi M, Haghnegahdar A. Lumbar disk herniation surgery: outcome and predictors. *Global Spine J*. 2014;4(4):233–43. doi:10.1055/s-0034-1390010
  - 9. Battié MC, Videman T, Parent E. Lumbar disc degeneration. *Spine (Phila Pa 1976)*. 2004;29(23):2679–90. doi:10.1097/01.brs.0000146457.83240.eb
  - 10. Kim JE, Choi DJ. Unilateral biportal endoscopic decompression by 30° endoscopy in lumbar spinal stenosis: Technical note and preliminary report. *J Orthop*. 2018;15(2):366–71. doi:10.1016/j.jor.2018.01.039
  - 11. Soliman HM. Irrigation endoscopic decompressive laminotomy. A new endoscopic approach for spinal stenosis decompression. *Spine J*. 2015;15(10):2282–9. doi:10.1016/j.spinee.2015.07.009
  - 12. Kim HS, You JD, Ju C Il. Predictive scoring and risk factors of early recurrence after percutaneous endoscopic lumbar discectomy. *Biomed Res Int*. 2019;2019(13):9–12. doi:10.1155/2019/6492675
  - 13. Eum JH, Heo DH, Son SK, Park CK. Percutaneous biportal endoscopic decompression for lumbar spinal stenosis: A technical note and preliminary clinical results. *J Neurosurg Spine*. 2016;24(4):602–7. doi:10.3171/2015.7.SPINE15304
  - 14. Choi DJ, Kim JE. Efficacy of biportal endoscopic spine surgery for lumbar spinal stenosis. *CiOS Clinics in Orthopedic Surgery*. 2019;11(1):82–8. doi:10.4055/cios.2019.11.1.82

## Home Environmental Hazard as Extrinsic Factors For Falls Among Community-Dwelling Elderly

Sharon Gondodiputro,<sup>1</sup> Farhan Bariq Safnul,<sup>2</sup> Indah Amelia<sup>1</sup>

<sup>1</sup>Departement of Public Health, Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia

<sup>2</sup>Faculty of Medicine Universitas Padjadjaran, Bandung Indonesia

### Abstract

Falls among the elderly are a major concern in both clinical practice and public health. Studies have shown that falls occur more frequently at home than outside home. This study aimed to identify the areas and types of home environmental hazards present in the residences elderly individuals. A quantitative descriptive study was conducted from April to May 2024 across six primary healthcare centers in Bandung, West Java, Indonesia, selected from having the highest number of elderly patients. A total of 100 elderly respondents were recruited using a multistage purposive convenience sampling method. Data collection was carried out using an instrument consisting of two parts: the first part focused on respondent characteristics and the second part on home environmental hazards. The study variables were respondent characteristics and environmental hazards in the terrace, living room, stairs, bedroom, bathroom, kitchen, and garage. Data were analyzed using Microsoft Excel software and presented in tabular form. Results showed that all areas of the home posed potential hazards, with the presence of scattered items on the floor as the commonly identified risk. In specific areas such as the kitchen, high shelves were found, and in the bathroom, there were slippery floors, squat toilets, absence of handrails, and inward-opening bathroom door. Home can be a source of environmental hazards that increase the fall risk among the elderly. It is essential to provide the elderly with adequate information on these risk to encourage preventive actions and, where necessary, home modifications that improve safety and reduce the risk of falls.

**Keywords:** Elderly, extrinsic factors, fall, home environmental hazards

### Introduction

Falls are a significant public health issue among older adults. Each year, approximately 28–35% of individuals aged 65 and older experience a fall, with this figure rising to 32–42% for those over the age of 70.<sup>1</sup> The prevalence of falls varies across countries. In the Region of the Americas, data showed that the proportion of older adults falling each year spans from 21.6% in Barbados to 34% in Chile (average 27.9%).<sup>1,2</sup> In the South-East Asia Region, studies indicate that the annual fall rate among older adults ranges from 6–31% in China and approximately 20% in Japan.<sup>1,3</sup> A study in Korea revealed 5.9% to 25.1% of community-dwelling elderly Koreans experience falls annually.<sup>4</sup> The incidence of falls in Indonesia is increasing. A report based on the Indonesia

Family Life Survey (IFLS-5) from year 2014–2015 found that 12.8% of individuals experienced one or more fall-related injuries within the previous two years, with a higher prevalence among women (14.0%) compared to men (11.5%). Of these, 7.6% reported a single fall, while 5.2% experienced multiple fall-related injuries during the same period.<sup>3</sup> In 2018, the incidence varied from 25.4% among community-dwelling older adults to 32.7% among institutionalized older adults.<sup>5</sup>

Falls and the resulting injuries are significant public health issues that frequently demand medical attention.<sup>1</sup> Falls and fall-related injuries represent a significant healthcare concern due to their link with morbidity, disability, hospitalization, institutionalization, and mortality.<sup>6</sup> In Australia, Canada, and the United Kingdom, hospital admission rates due to falls among individuals aged 60 and older range from 1.6 to 3.0 per 10,000 population. Meanwhile, fall-related injuries leading to emergency department visits in the same age group are higher, with

### Corresponding Author:

Sharon Gondodiputro  
Departement of Public Health, Faculty of Medicine  
Universitas Padjadjaran, Bandung, Indonesia  
Email: sharon@unpad.ac.id

rates of 5.5 to 8.9 per 10,000 population in both Western Australia and the United Kingdom. According to the World Health Organization, falls result in 20–30% of mild to severe injuries. The primary reasons for fall-related hospital admissions include hip fractures, traumatic brain injuries, and upper limb injuries. As age and frailty increase, older individuals who suffer fall-related injuries are more likely to remain hospitalized for the remainder of their lives.<sup>1,7</sup>

Falls contribute to 40% of all injury-related deaths, with rates vary by country and population group. In the United States, the fall fatality rate for individuals aged 65 and older is 36.8 per 100,000 population (46.2 for men and 31.1 for women). In Canada, the mortality rate for the same age group is 9.4 per 10,000 population. In Finland, for those aged 50 and older, the mortality rate is 55.4 per 100,000 population for men and 43.1 for women.<sup>1</sup> Furthermore, falls can lead to post-fall syndrome, characterized by dependence, loss of autonomy, confusion, immobility, and depression, ultimately resulting in further limitations in daily activities.<sup>1</sup>

A fall is a symptom rather than a condition itself and is often caused by an interaction of multifactorial factors or risks. Fall risk is described as an unforeseen incident where an individual ends up on the ground, floor, or a lower surface.<sup>8</sup> These falls risk encompass intrinsic, situational, and extrinsic factors.<sup>7,8</sup> Intrinsic factors contributing to age-related functional decline include medical conditions and adverse drug reactions.<sup>7</sup> Frequent health conditions, including muscle weakness, vertigo, gait and balance difficulties, visual and hearing impairments, cognitive and sensory deficits, orthostatic hypotension, diabetes, and osteoporosis, play a major role in contributing to falls.<sup>5,9,10</sup> Numerous studies have identified a link between certain medications and an increased risk of falls in older adults, particularly psychotropic drugs like hypnotics, sedatives, antipsychotics, and antidepressants, which may lead to sedation, balance issues, and impaired coordination. Cardiovascular drugs, including diuretics and beta-blockers, may worsen orthostatic hypotension, further raising the risk of falls. Antihistamines and anticholinergic medications can impair cognitive function and cause blurred vision, increasing the likelihood of falling.<sup>9,10</sup> Situational factors are those related to activities being performed, such as walking and talking at the same time, getting distracted by multitasking, rushing to the bathroom, or running to answer a phone call.<sup>7</sup> Extrinsic factors

contributing to falls include environmental hazards,<sup>7</sup> unsuitable footwear and clothing, as well as improper walking aids or assistive devices.<sup>11</sup> The extent to which environmental factors influence the risk of falls among older adults remains unclear. According to a systematic review by Kim, Do, and Yim in 2022, environmental factors contribute to more than 20%–22% of falls in the older adult population.<sup>12</sup>

A significant majority of fall-related emergency department visits (71.6%) were due to falls occurring indoors.<sup>13,14</sup> The majority of fall incidents occur at home and in its surroundings.<sup>13,15</sup> Environmental hazards in elderly homes include uneven flooring, unsecured carpets in the kitchen and bedroom, and a shower area not separated from the toilet. Other factors contributing to falls among the elderly include inadequate lighting in the living room, bathroom, bedroom, and parking garage, as well as clutter and obstacles like wires in the living room and parking area. Additionally, poorly maintained staircases with uneven step heights or slippery surfaces further increase the risk of falls.<sup>16</sup>

Bandung Municipality, the capital of West Java Province, has one of the largest populations of older adults in Indonesia. The presence of environmental hazards in the elderly's residences has not yet been known since studies of the home environmental hazards in elderly residences as a risk factor for falls in Bandung has not yet been conducted. Therefore, a study was carried out to examine the home environmental hazards in the homes of elderly residents in Bandung. The aim of this study was to identify the areas within the residences and the types of environmental hazards that serve as risk factors for falls among the elderly.

## Methods

A descriptive quantitative study was conducted in Bandung Municipality, West Java, Indonesia, from April to May 2024. This location was selected because Bandung is one of the cities in Indonesia with the largest elderly population. The study employed a multistage purposive convenience sampling technique. The municipality was divided into six regions, and one region with the highest elderly population was chosen from each region. Within these regions, there were 2–3 Primary Health Centers (*Puskesmas*). The *Puskesmas* with the highest number of elderly individuals in each regions

was selected for the study, resulting in a total of six *Puskesmas*. The minimum sample size based on the calculation for descriptive categorical data was 100 participants. Each *Puskesmas* had a different number of samples, determined by the proportion of its elderly population. Participants were recruited from the selected *Puskesmas* based on the following inclusion criteria: age  $\geq 60$  years, seeking treatment or consultation at the *Puskesmas*, male or female, not living in an institution, and if there were multiple elderly individuals living in the same household, only one was chosen to participate as a respondent. Elderly individuals who were not at home during the visit, unwilling to participate, or did not complete the study process were excluded.

The prospective respondents were elderly patients who were present at the *Puskesmas* at the time of data collection, and if they met the inclusion criteria, the researcher provided information about the study and requested their willingness to be visited at home. If the respondents understood and agreed to participate, they signed an informed consent form, and the researcher, together with the selected respondents, arranged a schedule for the home visit.

Data collection was carried out using an instrument. The development of the instrument to assess the home environment hazards in each room was adapted from the American Association of Retired Persons (AARP) Home Fit Guide, which categorizes elderly homes by room, several statements from HOMEFAST for the observed items, as well as findings from several related publications. The instrument consisted of two sections. The first section of the instrument gathered information on respondent characteristics, such as age (60–70, 70–80,  $\geq 80$  years), gender (male, female), education level (no education, elementary school, junior high school, senior high school, higher education), occupation (working, not working), health status (hypertension, diabetes mellitus, or other conditions), and medications used. It also included details of the areas in the home (terrace, living room, stairs, kitchen, bathroom, bedroom, garage), home ownership (owned, rented, or other), length of stay at the current residence (< one year, one to five years,  $>$  five years), household companions (none, family, others), total number of floors (single floor, multiple floors), and the floor level of the bedroom. The second section collected data on the environmental hazards present in various areas of the home: on the terrace (7 items), living room (6 items), stairs

(7 items), kitchen (5 items), bathroom (7 items), bedroom (9 items), and garage (3 items).

Data were collected through direct observation and interviews during home visits. During the home visits, the researcher conducted observations to identify potential hazards present in each household area, including the terrace, living room, stairs, bedroom, bathroom, kitchen, and garage. Data processing and analysis were performed using Microsoft Excel software. The study was approved by the Health Research Ethics Committee of the National Eye Center Cicendo Hospital in Bandung, with approval number DP.04.03/D.XXIV.16/4311/2024.

## Results

The study discovered that the number of female elderly nearly doubled the number of male elderly. The majority of elderly were between 60 and 70 years old. A large proportion had low levels of education, though 13 had higher education. Most elderly were unemployed. Many reported having hypertension and diabetes mellitus, while a smaller group had a history of asthma. Commonly used medications included amlodipine, an antihypertensive drug, and metformin, an antidiabetic drug. Additionally, a smaller subset of elderly used other antihypertensive and antidiabetic drugs, as well as anticoagulants and anti-arrhythmic medications, often in combination with amlodipine or metformin (Table 1).

Most participants lived in their own homes, had resided there for more than five years, and lived with family members. However, some elderly rented their homes and lived alone. The majority of homes were two-story houses, however most elderly having their bedrooms on the first floor. All residences were equipped with bathrooms. The study revealed that one elderly did not have a private bedroom. (Table 1).

The study identified environmental hazards in every part of the residence, some of which could be harmful and posed potential fall risks for the elderly. Table 2 outlines the most frequently observed hazards in different areas of the home. Clutter with items was recognized as a significant hazard in several spaces, including the terrace, living room, and garage. In the bathroom, the lack of a handrail near the toilet was a prominent hazard. Another notable observation was that bedroom doors opened inward, which could pose additional risks.

Cluttered furniture and items, slippery mats

**Table 1 Respondent Characteristics**

Characteristics (n = 100)	n	Percentage (%)
Age (years)		
60-70	70	70.0
71-80	24	24.0
>8	6	6.0
Gender		
Male	39	39.0
Female	61	61.0
Education		
No education	1	1.0
Elementary School	34	34.0
Junior High School	28	28.0
Senior High School	24	24.0
Higher Education	13	13.0
Occupation		
Yes	14	14.0
No	86	86.0
Chronic Diseases		
None	12	12.0
Hypertension	58	58.0
Diabetes Mellitus	15	15.0
Hypertension and Diabetes Mellitus	12	12.0
Asthma	1	1.0
Hypertension or Diabetes Mellitus and Asthma	2	2.0
Medication Used (n=88)		
Amlodipin	59	64.1
Metformin	19	20.7
Candesartan	4	4.3
Ascardia	2	2.2
Others (Bisoprolol, Nifedipin, Ascarbose)	8	8.7
Ownership		
Owned by her/himself	77	77.0
Rent	17	17.0
Others	6	6.0
Length of stay at the current residence		
<one year	1	1.0
one to five years	2	2.0
>five years	97	97.0
Areas in the home		
Terrace	75	75.0
Living room	91	91.0
Stairs	64	64.0
Kitchen	95	95.0
Bathroom	100	100.0
Bedroom	99	99.0
Garage	25	25.0

**Table 1 Continued**

Characteristics (n = 100)	n	Percentage (%)
Total number of floors		
One	36	36.0
Two	63	63.0
More than two	1	1.0
The floor level of the elderly's bedroom:		
First floor	99	99.0
Second floor	1	1.0

**Table 2 Frequent Environmental Hazards In Elderly Homes**

Area	Home Environmental Hazards	Percentage (%)
Terrace	Clutters with items	84.0
Living room	Clutters with items or furniture	94.6
Stairs	The step width is less than 30 cm.	95.3
Kitchen	Kitchen items were stored on high shelves.	63.2
Bathroom	No handrail	94.0
Bedroom	The bedroom door opens inward.	72.7
Garage	Clutters with items	88.0

or floors, uneven surfaces or steps, and poor lighting were common hazards found in nearly all areas of the home. An intriguing observation from this study was the presence of pets, such as cats or dogs, both indoors and outdoors (Table 3). Another notable finding was that terraces are frequently used as parking areas, mainly for two-wheeled vehicles. Additionally, steps connecting the terrace to the living room were a safety concern (Figure 1). The discovery of an LPG gas cylinder in the kitchen raises additional

concerns. This study showed that 64% of homes had stairs, with many having step dimensions that failed to meet safety standards. Moreover, some stairs were equipped with a handrail on only one side (64.1%), while others lack handrails entirely (37.5%).

In this study, the kitchen, as the main cooking area, was found to have cooking items stored at high positions (Figure 1). To access these items, individuals had to fully extend their arms, stand on tiptoes, or used a chair. The bathroom,

**Figure 1 Front Terrace, Bathroom/Toilet, and Kitchen**

**Table 3 Environmental Hazards in Elderly Homes by Area**

Environmental Hazards	n	Percentage (%)
Front terrace (n=75)		
Slippery doormat	44	58.7
Slippery floor	22	29.3
Uneven floor	32	42.7
Terrace cluttered with items	63	84.0
Parked vehicles	27	36.0
Presence of steps/outdoor stairs leading to the terrace	51	68.0
Presence of pets	10	13.3
Living room (n=92)		
Need/have to walk around furniture to pass through the room	14	15.2
Presence of a carpet	36	39.1
Cluttered with items or furniture	87	94.6
Items scattered on the floor	45	48.9
Poor lighting/dark	4	4.3
Presence of pets	9	9.8
Indoor Stairs (n=64)		
Cluttered with items on the steps	25	39.1
Damaged or uneven steps	13	29.3
Poor lighting/dark	35	54.7
No handrails on the stairs	24	37.5
Step width less than 30 cm	61	95.3
Step height greater than 20 cm	50	78.1
Handrails only on one side of the stairs	41	64.1
Kitchen (n=95)		
Kitchen items were stored on high shelves	60	63.2
Using a stool to reach kitchen items	18	18.9
Low lighting/dark	4	4.2
Presence of pets	8	8.4
LPG Gas cylinder for cooking	83	87.4
Bathroom (n=100)		
Slippery floor	54	54.0
No handrails/support bars in the bathroom	94	94.0
Wet floor	61	61.0
Squat toilet	60	60.0
Cluttered with items	48	48.0
Bathroom door swung inwards	82	82.0
Poor lighting/dark	2	2.0
Bedroom (n=99)		
Poor lighting/dark	2	2.1
Area less than 9 m <sup>2</sup>	63	63.6
Items scattered on the floor	46	46.4
Cables crossing the middle of the bedroom	2	2.1
Slippery carpet	67	67.6
Bedroom door swung inwards	72	72.7
Uneven floor	3	3.3
Slippery floor	33	33.3
Presence of pets	8	8.8

**Table 3 Continued**

Environmental Hazards	n	Percentage (%)
Garage (n=25)		
Uneven floor	15	60.0
Slippery floor	2	8.0
Cluttered with items	22	88.0

a frequently used space for the elderly, also contained various hazards. These included the absence of handrails near the toilet, limited space that restricted movement, and the frequent presence of wet floors. Additionally, inward-opening bathroom doors, a common feature in Indonesian homes, were identified as a potential issue for future safety concerns.

The bedroom, where elderly spent most of their time, was found to be particularly hazardous. Risks included cramped spaces, cluttered or scattered items, carpets, slippery floors, cables crossing the room, and inward-opening doors (Table 3).

## Discussion

Studies on home environmental hazards among the elderly in Indonesia remain limited. Home environmental hazards are one of the risk factors for falls in the elderly. A study conducted in the United States discovered that most emergency department visits due to falls among community-dwelling elderly took place at home.<sup>13</sup> A similar finding was reported in a study conducted in Yogyakarta, Indonesia, which found that elderly individuals who had experienced falls most often fell at home.<sup>16</sup> The majority of older adults fall due to slipping, tripping, and stumbling.<sup>7</sup> Every area in the home can contribute to fall risk. A study revealed that the primary locations where elderly individuals most frequently fall, in order, were the bedroom, stairs, and bathroom.<sup>13</sup> Another study found different results, indicating that the primary locations where elderly individuals most frequently fall, in order, were the bathroom, kitchen, bedroom, and living room.<sup>17</sup> The specific areas in the house where falls occur vary across studies, as they are influenced by the home's condition and other contributing factors. This study discovered that every area, such as the front terrace, living room, bedroom, indoors/outdoors stairs, kitchen, bathroom, and garage, in elderly's homes contain potential risks for falls. In general, a significant fall risk for the elderly is the presence of excessive

clutters obstructing their pathways, which was observed in nearly all areas of their homes, including indoor stairs and the bathroom. This condition makes it challenging for the elderly to move from the front terrace to various areas inside the house, increasing the risk of tripping or stumbling over object. A similar finding was also observed in a study conducted in Australia, where only 32% of elderly homes were found to have home clutters free.<sup>18</sup>

Elderly homes with outdoors and indoors stairs can be a risk to fall. A study found that both indoor and outdoor stairs contribute to the risk of falling in the elderly, with non-safe stairs significantly affecting the fall rate.<sup>19</sup> This study discovered that more than 50% elderly's home had outdoors stairs. These stairs were always used by the elderly when entering or leaving the house. These stairs can pose a fall risk due to their uneven surfaces. Indoor stairs are also found in elderly homes, however, nearly all elderly individuals have their bedrooms on the first floor, with only one home where the elderly person's bedroom is on the second floor. This arrangement is highly beneficial, as it prevents the elderly from having to frequently use the stairs to reach their bedroom. This is especially important considering that many staircases do not meet safety standards, such as having step widths of less than 30 cm, step heights exceeding 20 cm, poor lighting, and excessive clutter.

Carpets or indoor/outdoor mats, especially slippery ones, can cause elderly individuals to slip and fall.<sup>7</sup> This study revealed that carpets were present in certain areas of the home, such as the front terrace, the living room and bedroom. Based on the results of the study, it is recommended that elderly individuals should choose carpets or indoors/outdoors mats that are attached to the floor to prevent slipping.

The kitchen is an area of the home commonly used by the elderly. This study discovered that cooking items were often stored in high shelves, a finding supported by Kim.<sup>20</sup> Reaching for items in high shelves can cause balance issues, leading to falls in the elderly.

Most fall incidents in bathroom/toilets are

linked to the fact that this is where individuals exercise the most independence and are often alone due to the need for privacy. A study revealed that, among all areas in a home, the bathroom/toilets poses the highest fall risk for elderly.<sup>18,19</sup> Elderly individuals often fall due to wet, slippery, and unclean bathroom conditions, as well as the absence of handrails or support bars.<sup>21</sup> These problems are poorly understood in Vietnam. A cross-sectional study was performed at seven hospitals in Thai Binh province, Vietnam, to investigate the individual and environmental factors associated with recurrent falls among elderly patients hospitalized due to fall injuries in Vietnam. A history of recurrent falls within the last 12 months, sociodemographic, health, and clinical characteristics, as well as environmental conditions, were obtained via self-reported interviews. Multivariate logistic and Poisson regression models were used to identify associated factors. Overall, the mean fall episodes in the last 12 months were 1.8 (Standard deviation-SD = 1.2). This study yielded similar findings, revealing that most bathrooms/toilets in elderly homes had slippery, wet floors and lacked essential safety features such as handrails or support bars. Slippery bathroom floors or unsecured mats can heighten the risk of falls for older adults. A floor can become slippery if non-slip resistant materials are exposed to water, cleaning agents, or other substances that compromise their slip resistance.<sup>22</sup> As such, the best bathroom flooring should feature a dry surface, a non-slip surface, and mats that are securely attached, if present. Additionally, many of these homes had squat toilets and doors swung inwards which can further increase the risk of falls. Squat-style toilets have been widely used since ancient times in various Asian regions, including India, Japan, China, and Indonesia. As a result, they are commonly referred to as 'Asian-style toilets' or 'Eastern-style toilets'.<sup>23</sup> The use of squat toilets is often considered more hygienic than sitting toilets, as the body does not come into direct contact with the toilet surface, which may serve as a potential source of germ contamination. Moreover, squat toilets are perceived to be healthier, as the squatting posture during defecation aligns more closely with the natural ergonomics of the human body. However, such perceptions are largely shaped by cultural norms.<sup>23</sup> Toileting includes squatting, standing, and using the hands and arms. Both activities demand strong body coordination, balance, and sensory abilities.<sup>24</sup> Squat toilets can pose physical challenges for certain populations.

For elderly, the act of squatting and standing may lead to increased risk of falls. Therefore, it is recommended that squat toilets intended for older adults be equipped with handrails or other assistive devices to enhance safety and accessibility.<sup>18</sup> Inward-swinging bathroom/toilet doors can present significant barriers for elderly, particularly when space is limited and caregiver assistance is required to enter the bathroom. This design also poses substantial difficulties for older adults who use wheelchairs.<sup>25</sup> Moreover, inward-swinging doors could pose a hazard in case of an emergency,<sup>18</sup> because the door cannot be opened due to being blocked by the elderly person's body.

This study has several limitations. Firstly, the respondents were only selected from those who visited the *Puskesmas*, which may not provide a comprehensive representation of elderly individuals in the community. Future study should include elderly individuals from the community. Secondly, the study focused solely on the extrinsic factors contributing to fall risk and did not gather information on whether participants had experienced falls previously or the specific locations where these falls occurred. Therefore, additional studies are necessary to explore the relationship between hazards in the home environment and fall incidents, as well as to determine the most frequent fall locations in elderly households. Despite these limitations, the study successfully identified various areas and items in the homes of elderly individuals that contribute to fall hazards.

In conclusion, every area of the home may contain potential hazards that increase the risk of falls in elderly individuals. Common problems include excessive clutter, unsafe stairs, high kitchen shelves, slippery floor coverings, squat toilets without handrails, and bathrooms lacking safety features. Preventive strategies should focus on identifying hazards and implementing simple modifications to improve safety in the home environment.

## References

1. World Health Organization. WHO Global report on falls prevention in older age. WHO. Geneva: WHO; 2007. p. 1-2.
2. Salari N, Darvishi N, Ahmadipanah M, Shohaimi S, Mohammadi M. Global prevalence of falls in the older adults: a comprehensive systematic review and meta-analysis. J Orthop Surg Res. 2022;17(1):1-

- 13.
3. Pengpid S, Peltzer K. Prevalence and risk factors associated with injurious falls among community-dwelling older adults in Indonesia. *Curr Gerontol Geriatr Res.* 2018;2018:5964305. doi:10.1155/2018/59.
  4. Kim T, Choi SD, Xiong S. Epidemiology of fall and its socioeconomic risk factors in community-dwelling Korean elderly. *PLoS One.* 2020;15(6):6–10. doi:10.1371/journal.pone.0234787
  5. Susilowati IH, Nugraha S, Sabarinah S, Peltzer K, Pengpid S, Hasiholan BP. Prevalence and risk factors associated with falls among community-dwelling and institutionalized older adults in Indonesia. *Malaysian Fam Physician.* 2020;15(1):30–8.
  6. Montero-Odasso M, Van Der Velde N, Martin FC, Petrovic M, Tan MP, Ryg J, et al. World guidelines for falls prevention and management for older adults: a global initiative. 2022;51(9):afac205. doi:10.1093/ageing/afac205
  7. Vaishya R, Vaish A. Falls in older adults are serious. *Indian J Orthop.* 2020;54(1):69–74.
  8. Iamtrakul P, Chayphong S, Jomnonkwa S, Ratanavaraha V. The association of falls risk in older adults and their living environment: A case study of rural area, Thailand. *Sustainability.* 2021;13(0):1–16.
  9. Sharif SI, Al-Harbi AB, Al-Shihabi AM, Al-Daour DS, Sharif RS. Falls in the elderly: Assessment of prevalence and risk factors. *Pharm Pract (Granada).* 2018;16(3):1–7.
  10. Amatullah Y, Sastradimaja SB, Dwipa L. Intrinsic risk factors of falls in elderly. *Althea Med J.* 2016;3(3):334–9.
  11. Muladi A, Sutrisni ST, Lestari S, Suminar S. Tingkat keamanan lingkungan terhadap risiko jatuh pada lansia di Panti Werdha Dharma Bhakti Surakarta. *Khatulistiwa Nurs J.* 2023;5(1):18–25.
  12. Kim B, Do K, Yim J. Environmental factors influencing the prevalence of falls in South Korea. *Phys Ther Rehabil Sci.* 2022;11(1):66–77. doi: 10.14474/ptrs.2022.11.1.66
  13. Moreland BL, Kakara R, Haddad YK, Shakya I, Bergen G. A descriptive analysis of location of older adult falls that resulted in emergency department visits in the United States, 2015. *Am J Lifestyle Med.* 2021;15(6):590–7. doi:10.1177/1559827620942187
  14. Bleijlevens MHC, Diederiks JPM, Hendriks MRC, Van Haastregt JCM, Crebolder HFJM, Van Eijk JT. Relationship between location and activity in injurious falls: An exploratory study. *BMC Geriatr.* 2010;10(40):1–9. doi:10.1186/1471-2318-10-40
  15. Zhang L, Ding Z, Qiu L, Li A. Falls and risk factors of falls for urban and rural community-dwelling older adults in China. *BMC Geriatr.* 2019;19(1):1–17. doi:10.1186/s12877-019-1391-9
  16. Sabatini SN, Tambunan L, Kusuma HE. Elderly house environmental fall risk factors in Yogyakarta. In: *Proceedings of the 11th ISAIA, Sept 20-23, Miyagi, Japan.* 2016. p. 485–8.
  17. Lök N, Akin B. Domestic environmental risk factors associated with falling in elderly. *Iran J Public Health.* 2013;42(2):120–8.
  18. Aclan R, George S, Laver K. Common home hazards among healthy older aged adults and potential modifications required for age-friendly housing. *Aust Occup Ther J.* 2024;71(2):213–25.
  19. Mahmoodabad SSM, Zareipour M, Askarishahi M, Beigomi A. Effect of the living environment on falls among the elderly in Urmia. *Maced J Med Sci.* 2018;6(11):2233–8. doi:10.3889/oamjms.2018.434
  20. Kim D. Understanding how older adults negotiate environmental hazards in their home. *J Aging Environ.* 2022;36(2):173–93. doi: 10.1080/26892618.2021.1918814
  21. Vu HM, Nguyen LH, Nguyen HLT, Vu GT, Nguyen CT, Hoang TN, et al. Individual and environmental factors associated with recurrent falls in elderly patients hospitalized after falls. *Int J Environ Res Public Health.* 2020;17(2441):1–10. doi:10.3390/ijerph17072441
  22. Afifi M, Al-Hussein M, Bouferguene A. Geriatric bathroom design to minimize risk of falling for older adults- A systematic review. *Eur Geriatr Med.* 2015;6(6):598–603. doi:10.1016/j.eurger.2015.08.010
  23. Martosenjoyo T. Budaya bertoilet: duduk atau jongkok? *Etnosia J Etnogr Indones.* 2016;1(1):1–15. doi:10.31947/etnosia.v1i1.1800.
  24. Liu C, Fong JH, Hoh JWT, Wu H, Dong Y, Gu D, et al. Bathing and toileting difficulties of older adults in rural China: the role of environment. *BMC Geriatr.* 2020;20(1):1–9. doi:10.1186/s12877-020-01919-8
  25. Nurwulan NR. Bathroom design for enhanced comfort in Indonesian older adults and the disabled community. *Sci Eng Heal Stud.* 2024;18:1–10.

## Skinfold Thickness and Mid-upper Arm Circumference in Pediatric Patients with Chronic Kidney Disease

Siti Saqinah Suriadiredja,<sup>1</sup> Ahmedz Widiasta,<sup>2</sup> Rini Rossanti<sup>2</sup>

<sup>1</sup>Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia

<sup>2</sup>Department of Child Health, Faculty of Medicine Universitas Padjadjaran  
 Dr Hasan Sadikin General Hospital, Bandung, Indonesia

### Abstract

Chronic kidney disease (CKD) can impair the kidneys' capacity to manage nutrition, and any nutritional imbalances in CKD may affect the disease's progression. This study evaluated triceps skinfold (TSF) thickness and mid-upper arm circumference (MUAC) as indicators of nutritional status in children with early- and late-stage CKD at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. A descriptive cross-sectional design was used with secondary data from the nephrology division registry collected between August 2021 and August 2022. Data analysis was conducted with Microsoft Excel. The study involved 65 participants, with 32 in the early stage and 33 in the late stage. For early-stage patients, the average TSF was 13.75 mm and the MUAC was 12 cm, while, the average TSF and MUAC in the late stage were 11.39 mm and 11.70 cm, respectively. Based on TSF percentiles, most patients fell within the normal range, whereas MUAC measurements indicated that the majority were below normal. In terms of %TSF, most early-stage patients had above-average values, whereas late-stage patients were below average. All MUAC measurements indicated below-average values for both stages. Overall, TSF percentiles suggested that most patients had adequate nutritional status; however, %TSF revealed excess adiposity in early-stage patients and deficits in late-stage patients. MUAC consistently indicated deficits across both groups.

**Keywords:** Chronic kidney disease, mid-upper arm circumference, nutritional status, pediatric, skinfold thickness

### Introduction

Chronic kidney disease (CKD) is a common kidney disorder. According to Kidney Disease: Improving Global Outcomes (KDIGO), CKD is defined as structural or functional kidney abnormalities lasting more than three months, with health implications, such as decreased glomerular filtration rate (GFR) and/or markers of kidney damage. CKD can then be divided into five stages based on the GFR.<sup>1</sup> In children, CKD is more common due to congenital kidney and urinary tract abnormalities. These causes will then lead to damage to the kidneys. How the kidney responds to the damage will affect the course of the disease.<sup>2</sup> Damage to the kidneys lead to a significantly kidney function deterioration. One of them is the function of the kidneys as a

regulator of nutrition in the body.<sup>3</sup> The presence of nutritional disorders in patients with CKD is also a multifactorial matter. This nutritional disorder can occur through several mechanisms: metabolic disorders, chronic inflammation, nutritional and appetite imbalances, disruption of normal microbiota, gastroparesis, dialysis, and oxidative stress.<sup>3</sup>

Protein-energy wasting (PEW) is the most common nutritional disorder in children with CKD. For children with CKD, this nutritional disorder is, of course, very detrimental. Given that children are very dependent on nutrition for growth and development. In addition, poor nutrition is also associated with a decrease in the quality of life of sufferers.<sup>3</sup> Therefore, it is crucial always to pay attention to the nutritional status of children with CKD.

The severity of CKD is also associated with sarcopenia, which increases the risk of cardiovascular complications. Sarcopenia is preceded by anorexia, which mainly occurs in patient undergoing kidney replacement therapy (KRT) for a long time.<sup>4</sup> Children with

### Corresponding Author:

Ahmedz Widiasta  
 Department of Child Health, Faculty of Medicine Universitas Padjadjaran/Dr Hasan Sadikin General Hospital, Bandung, Indonesia  
 Email: ahmedzwidiasta@gmail.com

This is an Open Access article licensed under the Creative Commons Attribution-NonCommercial 4.0 International License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original author and source are properly cited.

sarcopenia may appear cachectic, with reduced subcutaneous fat and diminished muscle mass.

Recommended assessments of nutritional status in CKD include weight, height, triceps and subscapular skinfold thickness, and arm and calf circumferences.<sup>5</sup> This study focused on triceps skinfold (TSF) thickness and mid-upper arm circumference (MUAC) as key indicators of nutritional status.

The objective of this study was to evaluate TSF thickness and MUAC in pediatric patients with early- and late-stage CKD, as these measurements reflect nutritional status. The findings are expected to raise awareness of nutritional deficits in pediatric CKD, contribute to strategies for preventing malnutrition-related cardiovascular complications, and support improvements in the quality of care for children with end-stage kidney disease at Dr. Hasan Sadikin General Hospital, Indonesia.

## Methods

This descriptive cross-sectional study used secondary data from the nephrology division patient registry at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, collected between August 2021 and August 2022. The study included patient data from individuals aged 3 months to 17 years and 364 days. The inclusion criteria were all patients diagnosed with chronic kidney disease (CKD) during the study period. The exclusion criteria were patients with special needs, where accurate measurements could not be taken, and patients with deformities in both arms.

Patients were classified by CKD stage according to glomerular filtration rate (GFR, mL/min/1.73 m<sup>2</sup>): stage 1 ( $\geq 90$ ), stage 2 (60–89), stage 3a (45–59), stage 3b (30–44), stage 4 (15–29), and stage 5 ( $\leq 15$ ). These stages are then grouped into the early stage, which consists of stages 1–3b, and the late stage, which consists of stages 4–5. The GFR was calculated using the formula for pediatric patients based on the KDIGO,  $GFR=41.3 \times (\text{height in meters}/\text{Serum Creatinine in mg/dL})$ .

The anthropometric measurements evaluated in this study included triceps skinfold (TSF), percentage of triceps skinfold (% TSF), mid-upper arm circumference (MUAC), percentage of mid-upper arm circumference (% MUAC), mid-upper arm muscle circumference (MAMC), and mid-upper arm muscle area (MMA).

TSF and MUAC were interpreted using WHO

percentiles for children aged 0–5 years and CDC percentiles for children  $>5$  years. Measurements were categorized as below the 5th percentile (reduced), between the 5th and 95th percentiles (normal), or above the 95th percentile (excess). To calculate and interpret the %TSF and the %MUAC, the TSF and the MUAC were first located in the WHO percentile tables for ages 0–5 years old and CDC for children above 5 years old. The percentages of each were calculated with the following formulas: % TSF=[(TSF actual)/(TSF 50<sup>th</sup> percentile)] $\times 100$ , MUAC=[MUAC actual/(MUAC 50<sup>th</sup> percentile)] $\times 100$ .

%TSF values  $>110\%$  indicated adipose tissue excess, while values  $<90\%$  indicated deficit. %MUAC values  $>110\%$  indicated muscle tissue excess, while values  $<90\%$  indicated deficit. The MMA was calculated with the formula: MMA=[MUAC [mm]–( $\pi \times \text{TSF}$ )] $\times 4\pi$ . It is then interpreted according to the Frisancho percentile tables, average muscle tissue if it is above the 15<sup>th</sup> percentile, mild to moderate depletion of muscle tissue if it is at the 5<sup>th</sup> to 15<sup>th</sup> percentile, and severe depletion of muscle tissue if it is below the 5<sup>th</sup> percentile.

The mid-upper arm muscle circumference (MAMC) was calculated using the formula: MAMC=[MUAC–( $\pi \times \text{TSF}$ )]. The result was then interpreted according to the Frisancho percentile tables, with a reduced muscle area indicated if there was more than a 10% reduction relative to the 50th percentile of the reference population.

The study was approved by the Health Research Ethics Committee of the Faculty of Medicine Universitas Padjadjaran (approval number: 1156/UN6.KEP/EC/2022).

## Results

A total of 65 pediatric patients with CKD met the inclusion criteria. Patient characteristics are summarized in Table 1. Among the 65 patients, the majority were male (52.3%) and adolescent (60%). The youngest patient was 2 years and 8 months old, while the oldest was 17 years and 8 months old. Regarding disease stage, 32 patients (45.7%) were in the early stage, and 33 patients (50.8%) were in the late stage. The mean TSF for early-stage patients was 13.75 mm, and the mean MUAC was 12 cm, whereas for late-stage patients, the mean TSF was 11.39 mm and the mean MUAC was 11.70 cm.

In the early stage, half (50%) were male, most were in stage 1 (59.4%), and adolescent age (43.8%). The most common complications

**Table 1 Characteristics of The Patients in Early and Late Stage**

Variable	Early Stage	Late Stage
	n=32	n=33
Sex, n (%)		
Male	16 (50)	18 (54.5)
Female	16 (50)	15 (45.4)
Age, n (%)		
29 days–1 year	-	-
2–5 years	8 (25)	3 (9.1)
6–10 years	10 (31.25)	5 (15.2)
11–18 years	14 (43.75)	25 (75.8)
Triceps skinfold thickness (mm)	13.75 (1.17)	11.39 (2.)
Mid-upper arm circumference (cm)	12 (2.17)	11.70 (2.0)
Blood pressure		
Systolic blood pressure (mmHg), mean (SD)	105.31 (13.23)	123.03 (24.8)
Diastolic blood pressure (mmHg), mean (SD)	69.68 (11.52)	78.79 (14.9)
Laboratorium results, mean (SD)		
Hemoglobin (g/dL)	12.15 (2.46)	8.28 (2.1)
Serum ureum (mg/dL)	39.62 (39.10)	156.36 (88.2)
Serum creatinine (mg/dL)	0.65 (0.42)	7.05 (5.5)
Serum sodium (mEq/L)	136.66 (2.60)	134.83 (4.4)
Serum potassium (mEq/L)	3.94 (0.52)	4.63 (1.4)
Ion calcium (mg/dL)	4.90 (0.37)	4.83 (0.9)
Serum phosphorus (mg/dL)	3.52 (0.00)	3.67 (1.7)
Serum albumin (g/dL)	2.96 (1.43)	3.07 (0.9)
Complication, n (%)		
Hypertension	7 (21.88)	17 (51.5)
Anemia	2 (6.25)	14 (42.4)
Urinary tract infection	1 (3.13)	8 (24.2)
Infection	1 (3.13)	2 (6.1)
Hypoalbuminemia	5 (15.63)	3 (9.1)
Hypokalemia	1 (3.13)	3 (9.1)
Hyponatremia	-	5 (15.2)
Hyperkalemia	-	3 (9.1)
Hyperphosphatemia	-	1 (3.0)
Hypomagnesemia	-	1 (3.0)
Malnutrition	2 (6.25)	10 (30.3)
Marasmus	-	2 (6.1)
Heart failure	-	1 (3.0)

encountered in this stage were hypertension (21.9%) and hypoalbuminemia (15.6%). The mean for triceps skinfold thickness was 13.75 mm with most of the patients (81.3%) at the 5<sup>th</sup>-95<sup>th</sup> percentile (good), and for mid-upper arm circumference was 12 cm with most of the patients (90.6%) at <5th percentile (reduced).

As for other measurements, most of the patients have excess adipose tissue (62.5%) according to their %TSF, severe muscle tissue deficit (96.9%) according to their %MUAC, and all (100%) had severe depletion of muscle mass according to their MMA and MAMC.

In the late stage, most patients were

**Table 2 Measurement Results in the Early and Late Stages**

Variable	Early Stage n=32	Late Stage n=33
	n (%)	n (%)
Triceps skinfold thickness (mm)		
<5 <sup>th</sup> percentile	-	5 (15.2)
5 <sup>th</sup> -95 <sup>th</sup> percentile	26 (81.2)	27 (81.8)
>95 <sup>th</sup> percentile	6 (18.8)	1 (3.0)
%TSF		
Severe deficit of adipose tissue (<70%)	2 (6.3)	10 (30.3)
Moderate deficit of adipose tissue (70-80%)	3 (9.4)	0
Mild deficit of adipose tissue (80-90%)	4 (12.5)	10 (30.3)
Average adipose tissue (90-110%)	3 (9.4)	5 (15.2)
Excess of adipose tissue (>110%)	20 (62.5)	8 (24.2)
Mid-upper arm circumference (cm)		
<5 <sup>th</sup> percentile	29 (90.6)	31 (93.9)
5 <sup>th</sup> -95 <sup>th</sup> percentile	3 (9.4)	2 (6.1)
>95 <sup>th</sup> percentile	-	-
%MUAC		
Severe deficit of muscle tissue (<70%)	31 (96.9)	31 (93.9)
Moderate deficit of muscle tissue (70-80%)	0	0
Mild deficit of muscle tissue (80-90%)	1 (3.1)	1 (3.0)
Average muscle tissue (90-110%)	0	1 (3.0)
Excess of muscle tissue	0	0
MMA (mm <sup>2</sup> )		
Severe depletion of muscle mass (<5 <sup>th</sup> percentile)	32 (100)	33 (100)
Moderate depletion of muscle mass (5 <sup>th</sup> -15 <sup>th</sup> percentile)	-	-
Average muscle mass (>15 <sup>th</sup> percentile)	-	-
MAMC (mm)		
Reduced muscle mass (>10% reduction in relation to 50th percentile of reference population))	32 (100)	33 (100)

male (54.5%), in stage 5 (66.7%), and in the adolescent age group (75.8%). The most common complications encountered in this stage were hypertension (51.5%) and anemia (42.4%). The mean for triceps skinfold thickness was 11.33 mm with most of the patients (81.8%) were at the 5<sup>th</sup>-95<sup>th</sup> percentile (good), and for mid-upper arm circumference was 11.70 cm with most of the patients (93.9%) at <5th percentile (reduced). As for other measurements, most of the patients had mild and severe depletion of adipose tissue (30.3%, each) according to their %TSF, severe muscle tissue deficit (93.9%) according to their

%MUAC, and all (100%) had severe depletion of muscle mass according to their MMA and MAMC.

## Discussion

Muscle wasting in CKD is a crucial consequence of undernutrition, which is characterized by reduced muscle mass.<sup>6</sup> It is also one of the signs of protein-energy wasting (PEW).<sup>7</sup> Saenz-Pardo-Reyes et al. claim that %MUAC can also be used to evaluate MUAC readings.<sup>8</sup> In addition, MUAC can also be derived into mid-arm muscle area

(MMA), which estimates the area of the arm's muscle portion excluding the bone. It has been discovered that MMA can be a reliable substitute for adult muscle mass and may be investigated as a standalone evaluation tool for muscle wasting or as a risk factor for PEW in children with CKD.<sup>8</sup> In the present study, decreased muscle mass was observed in both early and late stages. Similar findings were reported by Yilmaz et al. and Oladele et al., who demonstrated lower MUAC values in CKD patients.<sup>9,10</sup> Muscle loss associated with CKD can be caused by a disturbed balance between the catabolic and anabolic mechanisms that regulate muscle homeostasis. Dysregulated protein metabolism (increased protein breakdown and decreased protein synthesis) and impaired muscle regeneration are the fundamental underlying biochemical mechanisms that limit muscle growth and turnover.<sup>11</sup>

Increased protein breakdown can be caused by the activation of the ubiquitin (Ub)-proteasome system (UPS), caspase-3, and autophagy by lysosome. While the decrease in protein synthesis can be caused by metabolic acidosis, upregulated pro-inflammatory cytokine expression, and anorexia-mediated malnutrition. These elements are all linked to the regulation of the IGF-1-PI3K-Akt signaling pathway, which inhibits mTOR and protein synthesis and speeds up proteolysis, causing muscle atrophy.<sup>4,11</sup>

When evaluated using triceps skinfold percentiles, most patients in both early and late stages were within the 5th–95th percentile, consistent with findings from Lotfy et al., who reported normal TSF values in hemodialysis patients.<sup>12</sup> However, based on %TSF, most patients in the late stage had a deficit of adipose tissue. This is linear with the study conducted by Saenz-Pardo-Reyes et al., where most of the patients who underwent hemodialysis had a deficit of adipose tissue.<sup>8</sup> The differences between the interpretation of the measurements might be due to the wide range of the percentile. There is also a concern about TSF as one of the methods of measurement. According to Canpolat et al.,<sup>13</sup> there is debate over whether TSF accurately assesses the amount of body fat in children with CKD due to substantial inter-observer variability and differences in the regional distribution of muscle and fat in CKD patients, even though lower TSF values have previously been seen in children with CKD.

Hypertension was the most common complication in both stages. This is consistent with findings by VanDeVoorde et al.,<sup>14</sup> who

reported that hypertension can appear early in CKD, often remaining undetected and contributing to progression. Several mechanisms can cause hypertension in pediatric CKD. A key role is probably played by the renin-angiotensin-aldosterone system being activated. Children with CKD may have altered renin levels, given their degree of hypertension and fluid status, even though plasma renin levels may not be overtly increased. Other than the renin-angiotensin-aldosterone system, the other mechanisms are sodium and water retention, increased sympathetic tone, endothelial factors, secondary hyperparathyroidism, and drug-induced hypertension.

In early-stage patients, hypoalbuminemia was the second most common complication. In contrast, Schmidt et al. In early-stage patients, hypoalbuminemia was the second most common complication. Dahal et al.<sup>15,16</sup> reported that hypoalbuminemia may occur across all stages of CKD, while Schmidt et al.<sup>17</sup> observed a progressive decline in albumin levels in advanced stages. Hypoalbuminemia in CKD is associated with inflammation and inadequate protein and caloric intake, and is defined as serum albumin <3.5 g/dL (35 g/L).<sup>1</sup>

In late-stage patients, anemia was the second most common complication, consistent with findings by Masalskienė et al.<sup>18</sup> Anemia in CKD may result from chronic inflammation, iron deficiency, the effect of uremia on red blood cell membranes, and diminished erythropoietin production.<sup>19</sup> The North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) cohort further demonstrated that anemia prevalence increases with CKD severity, with rates of 73% at stage 3, 87% at stage 4, and >93% at stage 5.<sup>20</sup> Chronic inflammation, iron deficiency, the effect of uremia on red blood cell membranes, and or diminished erythropoietin production may all play a role in anemia in chronic kidney disease.<sup>21</sup> As for the definition of anemia, KDIGO defines anemia in children with CKD as: When the Hb concentration is less than 13.0 g/dL (130 g/l) in men and 12.0 g/dL (120 g/l) in females above 15 years old, when the Hb concentration is less than 11.0 g/dL (110 g/l) in children aged 0.5 to 5, 11.50 g/dL (115 g/l) in children aged 5 to 12, and 12.0 g/dL (120 g/l) in children aged 12 to 15.<sup>1</sup>

In this study, another complication found in the late stage was malnutrition. This finding is linear with a study by Tutupoho et al.,<sup>21</sup> where malnutrition correlates with declining GFR. Malnutrition has a complicated and multifaceted

pathological etiology. In addition to decreased appetite and nutritional intake, children with chronic kidney disease also experienced hormonal imbalances, metabolic imbalances, inflammation, increased catabolism, decreased anabolism, and dialysis-related abnormalities.

Beside malnutrition, there are various terms that have been used to describe nutritional issues in CKD, including sarcopenia, and cachexia.<sup>7</sup> It is stated in a study conducted by Oliveira et al., that according to the clinical consensus, reduced muscle mass appears to be the most reliable indicator of PEW in CKD and emphasizes this in the diagnostic criteria for cachexia as well.<sup>7</sup> According to the Society for Cachexia and Wasting Disorders (SCWD), cachexia is a complex metabolic syndrome linked to an underlying illness and marked by loss of muscle, with or without loss of fat. Cachexia has been described as a severe form of protein-energy waste common in people with chronic illnesses like CKD and has been linked to morbidity and quality of life in this population. The SCWD proposed the definition of cachexia as a weight reduction of 5% or more over a period of 12 months or a body mass index (BMI)  $<20 \text{ kg/m}^2$ . Additionally, three of the following five requirements must be met: impaired muscle strength, fatigue, anorexia, reduced fat-free muscle mass, and abnormal biochemistry (including elevated C-reactive protein (CRP) or interleukin-6 (IL-6), anemia, and hypoalbuminemia).<sup>7</sup>

The International Society of Renal Nutrition and Metabolism (ISRNM) define PEW as a condition of nutritional and metabolic abnormalities in individuals with chronic kidney disease (CKD) characterized by simultaneous loss of systemic body protein and energy storage, which ultimately results in cachexia. PEW wasting is diagnosed if three characteristics are present (low serum albumin, transthyretin, or cholesterol), reduced body mass, and reduced muscle mass (muscle wasting or sarcopenia, reduced midarm muscle circumference).<sup>7</sup>

In pediatric CKD, the criteria for diagnosing PEW consists of low BMI (below 5<sup>th</sup> percentile or below 1.64 Z-score for height-age and sex at entry into CKD), unintentional weight loss (decrease in BMI of 10% or more for height-age and sex percentile between the first and second annual visits from an initial BMI for height-age and sex percentile of below 80<sup>th</sup> percentile), decreased MUAC (below 5<sup>th</sup> percentile for height-age and sex at entry into CKD or a decrease in MUAC for height-age and sex percentile of 10%

or more between the first and second annual visits), serum albumin below 3.8 g/dL, serum cholesterol below 100 mg/dL, serum transferrin below 140 mg/dL, reduced appetite, and poor growth (below 3<sup>rd</sup> percentile of for height-age and sex or poor growth velocity (a decrease in height for age and sex percentile of 10% or more between the first and second annual visits). As for diagnosing kidney disease-related syndromes, at least three of the four criteria (body mass, muscle mass, biochemistry, and food intake) must be met.<sup>7</sup>

According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia is a syndrome marked by a generalized loss of skeletal muscle mass and strength that occurs over time and carries a risk of negative consequences like physical disability, diminished quality of life, and even death. Diagnostic criteria for sarcopenia are reduced muscle mass, low muscle strength, or poor physical performance.<sup>7</sup> Nutritional status is a crucial prognostic factor in pediatric CKD, associated with hospitalization, mortality, and quality of life, as emphasized by Zhang et al.<sup>3</sup>

Several limitations should be acknowledged. First, incomplete registry data limited the analysis and may affect generalizability. Additionally, the study did not account for factors such as economic status or racial/ethnic differences, which could influence nutritional status and disease outcomes. Second, only one measurement of skinfold thickness was taken, which limits the comprehensiveness of the assessment. Third, this study provides only an overview of the differences in skinfold thickness and mid-upper arm circumference between early- and late-stage CKD patients, without exploring potential correlations between these measures and other clinical outcomes.

In conclusion, most patients in the early and late stages demonstrated adequate nutritional status when assessed solely by triceps skinfold thickness percentile. However, based on the %TSF, most patients in the early stage have excess adipose tissue whereas most patients in the late stage have deficit values. For all measurements of mid-upper arm circumference, both the early and late stages had deficit values. Future research that investigates the correlation between anthropometric measurements and clinical outcomes in pediatric CKD patients could provide more valuable insights into the impact of malnutrition on disease progression.

## References

1. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024;105(4):A1. doi:10.1016/s0085-2538(24)00110-8
2. Schnaper HW. Pathophysiology of progressive renal disease in children. In: *Pediatric Nephrology*. 7th ed. Berlin: Springer; 2015. p. 2171-2206. doi:10.1007/978-3-662-43596-0\_58
3. Zhang H, Tao Y, Wang Z, Lu J, Bhatt GC. Evaluation of nutritional status and prognostic impact assessed by the prognostic nutritional index in children with chronic kidney disease. *Medicine (Baltimore)*. 2019;98(34):e16713. doi:10.1097/MD.00000000000016713
4. Souza VA, Oliveira D, Mansur HN, Fernandes NM, Bastos MG. Sarcopenia in chronic kidney disease. *J Bras Nefrol.* 2015;37(1):98-105. doi:10.5935/0101-2800.20150014
5. Burrowes JD, Kovesdy CP. Nutrition in Kidney Disease. 3rd ed. Cham: Humana Press; 2020. doi:10.1007/978-3-030-44858-5
6. Iyengar A. Nutrition assessment tools in children with chronic kidney disease. *Asian J Pediatr Nephrol.* 2022;5(1):7. doi:10.4103/ajpn.ajpn\_8\_22
7. Oliveira EA, Cheung WW, Toma KG, Mak RH. Muscle wasting in chronic kidney disease. *Pediatr Nephrol.* 2018;33(5):789-98. doi:10.1007/s00467-017-3684-6
8. Saenz-Pardo-Reyes E, Housni FE, López-Espinoza A, Moreno AGM, Padilla Galindo MR. Evaluation of nutritional status in patients with end-stage renal disease in hemodialysis using principal component analysis. *Prog Nutr.* 2020;22(1):96-105. doi:10.23751/pn.v22i1.7944
9. Yilmaz D, Sönmez F, Karakaş S, Yavaşcan Ö, Aksu N, Ömürlü IK, et al. Evaluation of nutritional status in children during predialysis, or treated by peritoneal dialysis or hemodialysis. *J Trop Pediatr.* 2016;62(3):178-84. doi:10.1093/tropej/fmv094
10. Oladele CO, Unuigbe E, Chukwuonye II, Obi EC, Ohagwu KA, Oladele G, et al. Assessment of nutritional status in patients with chronic kidney disease in Nigeria. *Saudi J Kidney Dis Transpl.* 2021;32(2):445-54. doi:10.4103/1319-2442.335457
11. Cheng TC, Huang SH, Kao CL, Hsu PC. Muscle wasting in chronic kidney disease: mechanism and clinical implications—a narrative review. *Int J Mol Sci.* 2022;23(11):6047. doi:10.3390/ijms23116047
12. Lotfy HM, Sabry SM, Ghobrial EE, Abed SA. The effect of regular hemodialysis on the nutritional status of children with end-stage renal disease. *Saudi J Kidney Dis Transpl.* 2015;26(2):263-70.
13. Canpolat N, Sever L, Agbas A, Tasdemir M, Oruc C, Ekmekci OB, et al. Leptin and ghrelin in chronic kidney disease: their associations with protein-energy wasting. *Pediatr Nephrol.* 2018;33(11):2113-22. doi:10.1007/s00467-018-4002-7
14. VanDeVoorde RG, Mitsnefes MM. Hypertension and CKD. *Adv Chronic Kidney Dis.* 2011;18(5):355-61. doi:10.1053/j.ackd.2011.03.003
15. Schmidt R. Prevalence and predictive value of hypoalbuminemia in Appalachians with chronic kidney disease. *World J Nephrol Urol.* 2012;1(1):27-32. doi:10.4021/wjnu3e
16. Dahal K, Baral A, Sah KK, Shrestha JR, Niraula A, Hada R. Cardiovascular risk factors in predialysis chronic kidney disease patients of Nepal. *J Adv Intern Med.* 2020;9(2):47-53. doi:10.3126/jaim.v9i2.32813
17. Kisic B, Miric D, Dragojevic I, Rasic J, Popovic L. Role of myeloperoxidase in patients with chronic kidney disease. *Oxid Med Cell Longev.* 2016;2016:1069743. doi:10.1155/2016/1069743
18. Masalskienė J, Rudaitis Š, Vitkevič R, Čerkauskienė R, Dobilienė D, Jankauskienė A. Epidemiology of chronic kidney disease in children: a report from Lithuania. *Medicina (Kaunas).* 2021;57(2):112. doi:10.3390/medicina57020112
19. Atkinson MA, Warady BA. Anemia in chronic kidney disease. *Pediatr Nephrol.* 2018;33(2):227-38. doi:10.1007/s00467-017-3663-y
20. Kalpatthi R, Atkinson MA, Warady BA. Special populations with anemia: anemia in the pediatric patient. In: *Management of Anemia*. Cham: Springer; 2018. p. 199-218. doi:10.1007/978-1-4939-7360-6\_12
21. Tutupoho RV, Asmaningsih N, Prasetyo RV. Association of malnutrition with renal function in children with kidney disease. *GSC Biol Pharm Sci.* 2021;17(3):100-6. doi:10.30574/gscbps.2021.17.3.0354

## Comparison of Sensitivity and Specificity between B.I.L.E. Criteria and Tokyo Guidelines 2018 (TG18) for Diagnosing Acute Cholangitis

**Nugroho Rizki Pratomo, Reno Rudiman, Bambang Am Am Setya Sulthana**

Department of Surgery, Faculty of Medicine Universitas Padjadjaran  
 Dr. Hasan Sadikin General Hospital Bandung, Indonesia

### Abstract

Acute cholangitis is an inflammatory condition of the biliary system due to bacterial infection associated with biliary stasis or obstruction. Diagnosis is made using the Tokyo Guidelines 2018 (TG18) criteria. The biliary imaging abnormality, inflammatory test abnormality, liver test abnormality, and exclusion of cholecystitis/pancreatitis (B.I.L.E.) criteria are relatively new, with limited studies evaluating their sensitivity, specificity, and validation. This study aimed to compare the sensitivity and specificity of B.I.L.E. and TG18 criteria for the diagnosis of acute cholangitis. This is an observational analytic study with prospective cohort design during May 2023–May 2024. Data were obtained from patients who came to the Emergency Department of Dr. Hasan Sadikin General Hospital Bandung, Indonesia, with clinical symptoms of fever and jaundice, suspected of acute cholangitis. There were 95 subjects in this study. Based on B.I.L.E. criteria, 57 (60%) patients were categorized as high probability and 38 (40%) patients were categorized as unlikely acute cholangitis, while the TG18 criteria resulted in 61 (64.2%) patients classified as definite and 34 (35.8%) patients classified as suspected acute cholangitis. The sensitivity of the B.I.L.E. criteria was 92.1%, with a specificity of 94.73%. Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of B.I.L.E. criteria were 92.1% and 94.73%, respectively. In contrast, the sensitivity and specificity of TG18 criteria in this study were 82.35% and 83.6%, respectively. The PPV of TG18 reached 73.68% while the NPV of TG18 reached 89.47%. In conclusion, B.I.L.E. criteria have higher sensitivity and specificity than TG18 criteria in diagnosing acute cholangitis patients.

**Keywords:** Acute Cholangitis, B.I.L.E. Criteria, Diagnostic, TG18 Criteria

### Introduction

Acute cholangitis is a severe condition caused by obstruction of the bile ducts, resulting in bile stasis and subsequent infection. The causes of bile duct obstruction vary, ranging from benign conditions such as choledocholithiasis to malignant causes. Obstruction in the bile ducts increases pressure within the biliary system, which in turn leads to reflux into the venous and lymphatic systems due to the absence of a basal membrane between the sinusoids and the small bile ducts. Microorganisms or endotoxins from infected bile can then enter systemic circulation, triggering systemic inflammation that, if untreated, may progress to septic shock and death. Accurate diagnosis and timely

intervention are therefore critical to improving outcomes.<sup>1</sup>

Asymptomatic gallstones affect approximately 1–2% of the population, and 1–3% may experience mild symptoms.<sup>2</sup> These cases may progress to serious complications, including acute cholangitis, acute cholecystitis, severe jaundice, or pancreatitis. Without prompt antibiotic therapy and biliary drainage, acute cholangitis carries a high mortality rate. Endoscopic retrograde cholangiopancreatography (ERCP) is the most common method of biliary drainage and decompression, and meta-analyses indicate that early intervention reduces mortality. However, ERCP carries a complication rate of about 10%, with mortality between 0.33% and 1%. Early complications include acute pancreatitis, bleeding, sepsis, and perforation, while later complications may involve recurrent pain and jaundice.<sup>3,4</sup>

Charcot's triad has historically been used for diagnosis but it exhibits low sensitivity, ranging from 21.2% to 70%. Recognizing

#### Corresponding Author:

Nugroho Rizki Pratomo  
 Department of Surgery, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital Bandung, Indonesia  
 Email: nugrohorizkipratomo@gmail.com

these limitations, the Tokyo Guidelines 2007 (TG07) were introduced as a global standard for diagnosing and grading the severity of acute cholangitis. However, subsequent revisions, including the Tokyo Guidelines 2013 (TG13), aimed at improving sensitivity but failed to enhance specificity. The definitions in the Tokyo Guidelines 2018 (TG18) are similar to TG13, focusing on diagnosing cholangitis based on biliary infection, with less emphasis on non-infectious causes. This gap in specificity poses a significant concern, as a highly specific diagnostic tool is essential to avoid unnecessary interventions like ERCP, which carries a risk of complications such as pancreatitis, bleeding, and perforation.<sup>5</sup>

In 2021, the American Society for Gastrointestinal Endoscopy (ASGE) introduced the biliary imaging abnormality, inflammatory test abnormality, liver test abnormality, and exclusion of cholecystitis/pancreatitis (B.I.L.E.) criteria to improve diagnostic accuracy. Four criteria biliary abnormalities or intervention, raised inflammatory markers, abnormal liver function tests, and exclusion of cholecystitis and acute pancreatitis are used to identify people who have a high risk of developing acute cholangitis. Studies assessing the B.I.L.E. criteria's sensitivity, specificity, and general validity are still few, nonetheless. Additionally, the B.I.L.E. criteria had a higher sensitivity in identifying acute cholangitis, fewer needless ERCP treatments, and less post-ERCP sequelae than TG18, while requiring more sophisticated diagnostic tests.<sup>6</sup> The limited evidence base for the B.I.L.E. criteria create uncertainty regarding which diagnostic tool provides greater accuracy and reliability for clinical decision-making. In particular, evidence is needed to clarify whether the B.I.L.E. criteria can truly outperform TG18 in balancing sensitivity and specificity while minimizing unnecessary invasive interventions. To address this gap, this study aims to compare the diagnostic performance of the B.I.L.E. and TG18 criteria in patients with suspected acute cholangitis at Dr. Hasan Sadikin General Hospital, Bandung.

## Methods

This research uses a prospective cohort design and observational analysis. Patients with fever and jaundice who were suspected of having acute cholangitis and who visited the emergency room at Dr. Hasan Sadikin General Hospital Bandung,

Indonesia between May 2023 and May 2024 provided the study's data.

The inclusion criteria were: (1) patients presenting with clinical symptoms suggestive of acute cholangitis, which may be caused by factors such as stones or tumors; (2) patients who underwent relevant diagnostic evaluations; (3) patients with post-hepatic jaundice accompanied by clinical symptoms of fever; and (4) patients aged 18 years and older. The exclusion criteria were: (1) patients diagnosed with cholecystitis and/or acute pancreatitis; (2) patients whose diagnostic tests did not meet the criteria set by the B.I.L.E. or Tokyo Guidelines 2018; and (3) patients with pre-hepatic or intra-hepatic jaundice. The sample size for this study was calculated using the sample size formula for diagnostic test research, resulting in a total of 95 study subjects. The sampling method used was consecutive sampling, in which subjects were selected consecutively based on the order in which they met the inclusion criteria until the predetermined minimum sample size was achieved.

Descriptive analysis was used to present categorical data such as age, gender, symptoms of fever, jaundice, lab results, and imaging findings. The study focused on determining the sensitivity and specificity of the B.I.L.E. and TG18 criteria for diagnosing acute cholangitis, with statistical analysis conducted using contingency coefficient computations. The r-value was used to categorize correlation strength, with a  $p < 0.05$  signifying significant findings. The correlations ranged from extremely strong to very weak. The ROC curve was used to examine sensitivity and specificity at various cutoff points in order to forecast the diagnosis of acute cholangitis.

The accuracy of the diagnostic criteria was assessed by testing the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The Health Research Ethics Committee of Universitas Padjadjaran granted ethical permission for the research under registration number DP.04.03/D.XIV.6.5/266/2024.

## Results

A total of 95 subjects met the inclusion criteria and did not meet the exclusion criteria, with the data presented in Table 1.

This table provides a summary of characteristics for a sample size of 95 individuals, divided into different categories along with their

**Table 1 Characteristics of Subjects**

Characteristics	n=95	%
Age (years)		
18-21	0	0
21-30	0	0
31-40	0	0
41-50	30	31.5
51-60	53	55.8
61-70	12	12.7
Sex		
Male	54	56.8
Female	41	43.2
Diagnosis of Acute Cholangitis		
Yes	57	60.0
No	38	40.0
ERCP		
Yes	17	17.9
No	78	82.1
B.I.L.E. Criteria		
Unlikely	38	40.0
High probability	57	60.0
TG18 Criteria		
Suspected: 1 item A + 1 item B/C	34	35.8
Definite: 1 item A, 1 item B, and 1 item C	61	64.2

respective counts (n) and percentages (%). Each category summarizes patient demographics and diagnostic criteria. The sample includes slightly more males (56.8%) than females (43.2%). There were no subjects aged over 18 and under 40 years, nor those aged over 70 years. This age distribution suggests that acute cholangitis or the need for diagnosis likely occurs more commonly in older adults, particularly those aged 50 and above. The majority of patients (55.8%) are in the 51-60 age group, followed by 31.5% in the 41-50 age group, and 12.7% in the 61-70 age group. About 60% of the patients are diagnosed with acute cholangitis, while 40% are not. The TG18 criteria further classify patients into "suspected" 35.8% and "definite" 64.2%. Based on the B.I.L.E. criteria, 40% of patients are deemed "unlikely" while 60% are considered to have a "high probability" of having acute cholangitis. Approximately, only 17.9% of the patients underwent an ERCP.

According to the B.I.L.E. criteria (Table 2), the majority of patients had biliary imaging abnormalities (81.1%), abnormal inflammatory markers (78.9%), and abnormal liver tests (100%). Cholecystitis or pancreatitis was excluded in 92.6% of patients. Based on TG18 criteria (Table 3), most patients presented with inflammatory evidence (90.5%), jaundice (96.8%), and abnormal liver function tests (100%). Imaging findings were also common, with 77.9% showing bile duct dilatation and 92.6% showing other imaging evidence such as

**Table 2 Characteristics based on B.I.L.E. criteria**

B.I.L.E. Criteria	n=95	%
Biliary imaging abnormalities (duct dilation >6 mm, strictures, choledocholithiasis) and/or interventions within the past 30 days (ERCP, percutaneous biliary drainage, or biliary surgical procedures).		
Yes	77	81.1
No	18	18.9
Abnormal inflammatory test results, such as body temperature >100.4°F (38°C), leukocytosis (WBC >12), leukopenia (WBC <4), or bandemia (>10% bands).		
Yes	75	78.9
No	20	21.1
Abnormal liver tests (total bilirubin above normal, aspartate aminotransferase, alanine aminotransferase, or alkaline phosphatase).		
Yes	95	100
No	0	0
Exclusion of cholecystitis and acute pancreatitis		
Yes	88	92.6
No	7	7.4

**Table 3 Characteristics based on TG18 Criteria**

TG18 Criteria	n=95	%
A-1 Fever > 38°C		
Yes	9	9.5
No	86	90.5
A-2 Inflammatory evidence		
- WBC <4,000 or > 10,000 /uL		
- CRP ≥1 mg/dL		
Yes	86	90.5
No	9	9.5
B-1 Jaundice		
- T-Bil ≥2 (mg/dL)		
Yes	92	96.8
No	3	3.2
B-2 Abnormal liver function test		
- AST/ALT, ALP/GGT > 1.5 x STD		
Yes	95	100
No	0	0
C-1 Dilatation of bile system		
Yes	74	77.9
No	21	22.1
C-2 Other imaging evidence (stricture, stone, stenosis, etc)		
Yes	88	92.6
No	7	7.4

strictures or stones. The diagnostic performance of both criteria was assessed (Table 4). TG18 showed a significant association with the diagnosis of acute cholangitis ( $p<0.001$ ), with a strong correlation ( $r=0.868$ ). Similarly, the B.I.L.E. criteria demonstrated a significant association ( $p<0.001$ ) and a good correlation ( $r=0.645$ ).

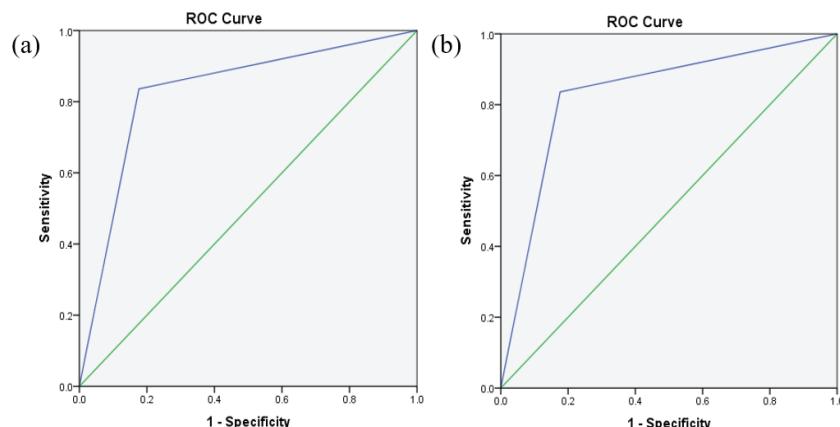
The ROC curve analysis (Figure 1, Table 5) demonstrated excellent diagnostic performance for both scoring systems. The B.I.L.E. criteria showed a higher AUROC (0.934, 95% CI: 0.874–0.994) compared to TG18 (0.830, 95% CI: 0.738–0.992), indicating superior accuracy in diagnosing acute cholangitis.

Further analysis of diagnostic performance (Table 6) revealed that the B.I.L.E. criteria had higher sensitivity (92.1%) and specificity (94.7%) compared to TG18 (sensitivity 82.4%, specificity 83.6%). The positive and negative predictive values were also superior for the B.I.L.E. criteria (92.1% and 94.7%, respectively).

## Discussion

This study found that the B.I.L.E. criteria demonstrated higher sensitivity (92.1%) and specificity (94.7%) compared to the Tokyo Guidelines 2018 (TG18), which showed sensitivity of 82.3% and specificity of 83.6%. These results indicate that the B.I.L.E. criteria may serve as a more accurate diagnostic tool for acute cholangitis in clinical practice.

The superior performance of the B.I.L.E.

**Figure 1 ROC Curve Analysis Of Acute Cholangitis from (a) B.I.L.E. criteria and (b) TG18**

**Table 4 TG18 and B.I.L.E Criteria in Diagnosing Acute Cholangitis**

Diagnosis	B.I.L.E. Criteria		p-value	r
	Not Acute Cholangitis	Acute Cholangitis		
TG 18 criteria				
Suspected	28 (29.5%)	6 (6.3%)	<0.001	0.645
Definite	10 (10.5%)	51 (53.7%)		
B.I.L.E criteria				
Unlikely	35 (36.8%)	3 (3.2%)	<0.001	0.868
High Probability	3 (3.2 %)	54 (56.8%)		

**Table 5 Results of the Area Under the ROC Curve of Binary Logistic Regression**

Diagnostic Criteria	AUROC	p-value	95%CI	
			Lower bound	Upper bound
B.I.L.E.	0.934	0.000	0.874	0.994
TG18	0.830	0.000	0.738	0.992

\*AUROC: Area under the Receiver Operating Characteristic (ROC) curve; 95% CI (Confidence Interval); TG18: Tokyo Guidelines 18

**Table 6 Sensitivity, specificity, PPV, and NPV**

Diagnostic Criteria	Sensitivity	Specificity	PPV	NPV
B.I.L.E. (High probability)	92.10	94.73	92.10	94.73
TG18 (Definite: 1 item A, 1 item B, dan 1 item C)	82.35	83.60	73.68	89.47

\*95% CI (Confidence Interval); PPV: Positive Predictive Value; NPV: Negative Predictive Value; TG18: Tokyo Guidelines 18

criteria may be explained by its comprehensive approach, which incorporates biliary imaging abnormalities, inflammatory markers, and liver function tests, while also excluding differential diagnoses such as acute cholecystitis and pancreatitis. This multimodal assessment increases diagnostic precision and helps reduce false positives, thereby lowering the likelihood of unnecessary ERCP procedures. In contrast, TG18 relies more heavily on clinical and laboratory features that are less specific for cholangitis, which may account for its lower diagnostic accuracy.

This study findings are consistent with prior studies. Buxbaum et al.<sup>13</sup> reported that the B.I.L.E. criteria could reduce unnecessary ERCPs and post-ERCP complications. Similarly, Gravito-Soares et al.<sup>11</sup> highlighted variability in the diagnostic accuracy of TG18, while Sperna Weiland et al. reported lower specificity, supporting the need for improved criteria. Hudgi et al.<sup>2</sup> also demonstrated inconsistencies in TG18 performance across different populations. These

differences suggest that although TG18 remains widely adopted, its diagnostic reliability may vary depending on patient characteristics and clinical settings.

From a clinical perspective, the use of B.I.L.E. criteria have important implications. More accurate diagnosis allows physicians to promptly identify true cases of acute cholangitis, initiate appropriate treatment, and avoid invasive procedures in patients who do not require them. This is particularly significant given the risks associated with ERCP, including pancreatitis, bleeding, sepsis, and perforation. By minimizing unnecessary interventions, the B.I.L.E. criteria have the potential to improve both patient outcomes and healthcare resource efficiency.

Despite these promising findings, this study has several limitations. First, the research was conducted at a single center with a relatively small sample size, which may limit generalizability. Second, the study focused only on diagnostic accuracy and did not assess the severity grading of cholangitis or patient outcomes, both of which

are essential for comprehensive management. Third, as the B.I.L.E. criteria are still relatively new, further multicenter validation with larger cohorts is needed to strengthen the evidence for their use in daily clinical practice.

In conclusion, this study demonstrates that the B.I.L.E. criteria outperform TG18 in sensitivity and specificity for diagnosing acute cholangitis. While our findings support the potential of B.I.L.E. as a more reliable diagnostic tool, further research is required to confirm its validity across different clinical contexts and to explore its impact on patient outcomes.

## References

1. Kiriyama S, Kozaka K, Takada T, Kiriyama S, Kozaka K, Takada T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). *J Hepatobiliary Pancreat Sci.* 2018;25(1):17-30. doi:10.1002/jhbp.512
2. Hudgi A, Cartelle AL, Ahmed A, Alkaddour A, Palacio C, Vega KJ, et al. Tokyo Guidelines (TG18) for Acute cholangitis provide improved specificity and accuracy compared to fellow assessment. *Cureus.* 2022;14(7):e27527. doi:10.7759/cureus.27527
3. An Z, Braseth AL, Sahar N. Acute cholangitis: causes, diagnosis, and management. *Gastroenterol Clin North Am.* 2021;50(2):403-14. doi:10.1016/j.gtc.2021.02.005
4. Iqbal U, Khara HS, Hu Y, Khan MA, Ovalle A, Siddique O, et al. Emergent versus urgent ERCP in acute cholangitis: a systematic review and meta-analysis. *Gastrointest Endosc.* 2020;91(4):753-60.e4. doi:10.1016/j.gie.2019.09.040
5. Sperna Weiland CJ, Busch CBE, Bhalla A, Bruno MJ, Fockens P, van Hooft JE, et al. Performance of diagnostic tools for acute cholangitis in patients with suspected biliary obstruction. *J Hepatobiliary Pancreat Sci.* 2022;29(4):479-86. doi:10.1002/jhbp.1096
6. Jena A, Singh AK. BILE criteria: Is it too early, or a stage is set?. *Gastrointest Endosc.* 2021;94(5):1016-17. doi:10.1016/j.gie.2021.06.005
7. Ahmed M. Acute cholangitis-an update. *World J Gastrointest Pathophysiol.* 2018;9(1):1-7. doi:10.4291/wjgp.v9.i1.1
8. Lu ZQ, Zhang HY, Su CF, Xing YY, Wang GX, Li CS. Optimal timing of biliary drainage based on the severity of acute cholangitis: A single-center retrospective cohort study. *World J Gastroenterol.* 2022;28(29):3934-45. doi:10.3748/wjg.v28.i29.3934.
9. Mohammad Alizadeh AH. Cholangitis: Diagnosis, Treatment and Prognosis. *J Clin Transl Hepatol.* 2017;5(4):404-13. doi:10.14218/JCTH.2017.00028
10. Mukai S, Itoi T, Tsuchiya T, Ishii K, Tanaka R, Tonozuka R, et al. Urgent and emergency endoscopic retrograde cholangiopancreatography for gallstone-induced acute cholangitis and pancreatitis. *Dig Endosc.* 2023;35(1):47-57. doi:10.1111/den.14379
11. Gravito-Soares E, Gravito-Soares M, Gomes D, Almeida N, Tomé L. Clinical applicability of Tokyo guidelines 2018/2013 in diagnosis and severity evaluation of acute cholangitis and determination of a new severity model. *Scand J Gastroenterol.* 2018;53(3):329-34. doi:10.1080/00365521.2018.1430255
12. Pak M, Lindseth G. Risk factors for cholelithiasis. *Gastroenterol Nurs.* 2016;39(4):297-309. doi:10.1097/SGA.0000000000000235
13. Buxbaum J, Qumseya B, Wani S. Toward an evidence-based approach for cholangitis diagnosis. *Gastrointest Endosc.* 2021;94(2):297-302.e2. doi:10.1016/j.gie.2021.04.016

## Closure Techniques and Postoperative Outcomes of Major Lower Limb Amputation in Acute Limb Ischemia

Reza Khadafy, Putie Hapsari, Hafidh Seno Radi Utomo

Department of Surgery Faculty of Medicine, Universitas Padjadjaran  
 Dr. Hasan Sadikin General Hospital Bandung, Indonesia

### Abstract

Amputation, derived from the Latin "amputare," refers to the removal of a body part covered by skin, often necessitated by acute limb ischemia (ALI). Effective wound closure is critical for minimizing complications, length of stay, costs, and the risk of re-amputation. This study compared postoperative outcomes of major lower limb amputation in ALI patients with primary versus delayed wound closure. A descriptive analytic study was conducted at Dr. Hasan Sadikin Hospital, Bandung, Indonesia, from January 2020 to December 2023, analyzing medical records of 46 patients aged 19–85 years, with a predominance of female patients. Thrombosis was the leading cause of ALI (76.1%), and hypertension was the most frequent comorbidity. Significant differences were observed in stump complications and revision surgery rates between primary and delayed wound closure groups ( $p<0.05$ ), while length of stay and mortality did not show statistically significant differences. In conclusion, the study highlights a significant relationship between different wound closure methods and complications, suggesting that choice of closure technique may influence the postoperative outcomes in ALI patients.

**Keywords:** Acute limb ischemia (ALI), delayed wound closure, major amputation, primary wound closure

### Introduction

Amputation, derived from the Latin word *amputare* (to cut), is defined as the removal of part or all of a body part covered by skin. Amputation involves the process of removing a limb or its part by cutting through one or more bones. Lower limb amputation, defined as the surgical removal of part or all of a limb, remains a major global health concern. Peripheral artery disease (PAD) is the leading cause, followed by trauma, infection, and malignancy. Epidemiological data show that trauma predominates in younger populations and in developing countries, whereas PAD is increasingly responsible for amputations in older adults. Common comorbidities such as hypertension and sepsis further complicate the clinical course and may adversely affect outcomes. Despite advances in surgical techniques and perioperative care, the incidence of lower limb amputation remains substantial, highlighting the need for preventive

strategies and comprehensive postoperative management. For upper limb amputations, trauma is the primary cause, accounting for 80% of all amputations.<sup>1</sup> It usually occurs in men aged 15 to 45 years. The second most common causes are cancer/tumors and complications from vascular diseases.

Amputation has significant economic, social, and psychological impacts. Upper limb amputation cases have a higher level of disability compared to lower limb amputations. Different levels of amputation result in varying quality of life outcomes. The more distal the level of amputation, the lower the patient's morbidity rate. It is estimated that 185,000 people undergo amputation in the United States each year, with 45 percent caused by trauma. Other causes include diabetes, vascular diseases, and malignancies. In many low- and middle-income countries, trauma is the leading mechanism for limb amputation. In Indonesia, general epidemiological data on amputation is not yet available; a recent study at RSCM reported that out of 111 DM patients hospitalized due to diabetic foot problems, 35% underwent amputation.<sup>4-7</sup>

Several factors are considered in determining the level of amputation, including local infection at the amputation site, systemic infection,

### Corresponding Author:

Reza Khadafy

Department of Surgery, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital Bandung, Indonesia  
 Email: reza.parenrengi@gmail.com

contamination of the wound, and the extent of tissue damage around the wound. Therefore, in the management process, a surgeon may choose between two types of techniques for wound closure after amputation: primary wound closure and delayed wound closure. Delayed closure is sometimes preferred over primary closure to reduce the risk of surgical wound infection. In primary closure, the skin is sutured immediately after surgery, whereas in delayed closure, the incision is left open and sutured after 2-5 days.<sup>2,3,8,9</sup>

Amputation with wound closure requires timely intervention to save the life of the patient or prevent life-threatening systemic complications. Moreover, choosing the appropriate wound closure method can reduce complications in amputation cases, length of hospital stays, treatment costs, or the need for re-amputation at a higher level.<sup>6,10</sup>

Meanwhile, at Dr. Hasan Sadikin General Hospital (RSHS), amputation management and wound closure procedures are performed quite frequently. However, precise data on the number and characteristics of patients have never been published, nor has any research been conducted. Furthermore, data on postoperative outcomes comparing primary versus delayed closure have not been found in the Indonesian or West Java population. Therefore, this study aims to evaluate the postoperative outcomes of patients with acute limb ischemia (ALI) undergoing major lower limb amputation, with a focus on differences between primary and delayed wound closure at RSHS.

## Methods

This analytical study employed a retrospective, cross-sectional design, with data collected between January 2020 and December 2023. The inclusion criteria were: (1) patients with ALI who underwent major lower limb amputation at RSHS between January 2020 and December 2023; and (2) complete medical records covering all amputations at or proximal to the ankle, including supporting data as required by the variables (including identity, examination findings, supporting examinations, risk factor history, surgical reports). The exclusion criteria were: (1) incomplete medical records that do not meet the required variables; (2) patients under the age of 18 at the time of amputation; and (3) patients who underwent amputation at other hospitals and came to RSHS for follow-

up or complication management. Patients were categorized into two groups: (1) patients who underwent amputation with primary wound closure (immediately after amputation); and (2) patients who underwent amputation with delayed wound closure (2-5 days after amputation).

Based on the unpaired comparative analysis formula, the minimum required sample size was 23 patients per group, for a total of 46 patients. Secondary data from medical records served as the primary study instrument, recorded by attending physicians during patient care. This study has obtained ethical approval from the Health Research Ethics Committee of Dr. Hasan Sadikin Hospital Bandung (approval number DP.04.03/D.XIV.6.5/345/2024).

Descriptive analysis was performed to summarize patient characteristics. Categorical variables were presented as frequency (n) and percentage (%), while continuous variables were expressed as median (range). A comparative test will be conducted to examine differences between the two groups. Statistical analysis will begin with a comparison test of the characteristics. Statistical analysis for categorical data will be tested using the Chi-square test if the Chi-square assumptions are met; otherwise, Fisher's exact will be used for 2x2 tables and Kolmogorov-Smirnov tests for tables other than 2x2. Binary logistic regression was applied when potential confounders were identified. Statistical significance was set at  $p \leq 0.05$ . Data were analyzed using SPSS version 25.0 for Windows.

## Results

This study examines differences in postoperative infection rates, length of stay, and the need for revision surgery based on wound closure techniques, as well as the influence of factors such as age and comorbidities (diabetes, hypertension, sepsis, heart dysfunction, and exposure to COVID-19 cases) on these outcomes. The data analyzed include demographic and clinical information from 46 patients, divided into two groups: those who underwent primary wound closure and those with delayed closure, with ages ranging from 19 to 85 years. Patient characteristics are summarized in Table 1.

Since the data were not normally distributed, a non-parametric test such as the Mann-Whitney U test was used. A p-value of 0.276 was greater than 0.05, which means there was no statistically

**Table 1 Subject Characteristics**

Variable	Total (n=46)	Group I (primary closure)	Group II (delayed closure)	p-value
Age	57 (22-28)	59 (25-88)	55 (23-86)	0.178
Gender				
Male	19 (41.3%)	10 (43.5%)	9 (39.1%)	0.118
Female	27 (58.7%)	13 (56.5%)	14 (60.9%)	
Cause of ALI				
Trombosis	35 (76.1%)	18 (78.3%)	17 (73.9%)	0.256
Emboli	11 (23.9%)	5 (21.7%)	6 (26.1%)	
Comorbid				
Diabetes mellitus	8 (17.4%)	5 (21.7%)	3 (13%)	
Hypertension	35 (76.1%)	18 (78.3%)	17 (73.9%)	
Sepsis	21 (45.7%)	14 (60.9%)	7 (30.4%)	0.231
Heart problem	14 (30.4%)	8 (34.8%)	6 (26.1%)	
COVID-19	8 (17.4%)	3 (13%)	5 (21.7%)	
Amputation Duration				
<48 hours	4 (8.7%)	2 (8.7%)	2 (8.7%)	
48 hours-1 weeks	39 (84.8%)	19 (82.6%)	20 (87%)	0.123
>1week	3 (6.5%)	2 (8.7%)	1 (4.3%)	

significant difference in the length of stay between Group I and II. The difference between these two groups was not statistically significant at the 5% significance level ( $p=0.276$ ). Therefore, it can be concluded that there was no significant

difference in the length of stay between Group I and II.

The analysis of revision surgery showed a significant difference based on the type of procedure ( $p=0.016$ ). Based on cross-tabulation

**Table 2 Association between Wound Closure Type and Main Outcomes**

Variables	Total Data (n=46)	Group I (primary closure)	Group II (delayed closure)	p-value
Duration of stay				
Mean ± SD	17.15	20.96	13.35	
Median	12.50	13.00	12.00	0.276*
Range	66	66	37	
Stump complication				
Yes	16 (34.8%)	12 (52.2%)	4 (17.4%)	0.013**
No	30 (65.2%)	11 (47.8%)	19 (82.6%)	
Mortality				
Lives	17 (37%)	9 (39.2%)	8 (34.8%)	0.760**
Death	29 (63%)	14 (60.8%)	15 (65.2%)	
Amputation Stump Revision				
Yes	11 (23.9%)	9 (39.1%)	2 (8.7%)	
No	35 (76.1%)	14 (60.9%)	21 (91.3%)	0.016**

\*Mann-Whitney U Test; \*\*Chi-Square Test

**Table 3 Postoperative Outcomes of Major Amputation in Acute Limb Ischemia**

Variable	Odds Ratio (Exp(B))	95% CI for Exp(B)	p-value
Stump operation complication	5.182	(1.35–19.84)	0.017
Amputation revision	6.750	(1.30–35.10)	0.025
Mortality	1.205	(0.38–3.85)	0.760
Length of stay	1.105	(0.18–2.85)	0.840

results, primary wound closure (group I) was associated with higher rates of infection ( $p=0.013$ ). Also, patients in Group I showed a higher rate of revision surgery compared to Group II.

No significant difference was found between the type of procedure ( $p=0.760$ ) and the mortality rate. Statistical test results showed that the difference in mortality between primary and delayed wound closure groups was not statistically significant, so it can be concluded that the type of procedure does not have a substantial impact on patient mortality.

Normality tests for variables such as surgical wound infection, stump revision, and mortality were conducted using the Shapiro-Wilk test due to the sample size being less than 50, which showed that the data were not normally distributed.

The analysis results highlighted several key findings. First, there was a significant multivariate effect of the procedure type (primary vs. delayed) on overall postoperative outcomes ( $p=0.024$ ). Second, further univariate analysis revealed that the procedure type significantly affected postoperative stump complications ( $p=0.032$ ) and revision surgery rates ( $p=0.006$ ).

Among comorbidities, diabetes was significantly associated with revision surgery ( $p=0.028$ ), though not with infection rates. Sepsis showed a significant overall effect ( $p=0.004$ ), but no specific association with individual outcomes. Age, hypertension, heart disease, and COVID-19 exposure were not significantly associated with postoperative outcomes.

## Discussion

This study compared postoperative complications of primary versus delayed wound closure in patients undergoing major lower limb amputation for acute limb ischemia (ALI), with particular focus on surgical site infections (SSIs), revision surgery, length of stay, and

mortality. Patient-related factors such as age and comorbidities were also evaluated.

Key findings include a statistically significant difference in infection rates between the two groups. Group I (primary closure) had a higher risk of complications compared to Group II (delayed closure), as supported by Chi-square tests ( $p=0.013$ ) and binary logistic regression (odds ratio=5.182). The higher rate of stump complications in Group I may be attributed to higher prevalence of risk factors such as sepsis and diabetes within this group. Multivariate analysis confirmed that treatment group, sepsis, and diabetes were significant predictors of postoperative complications.

These results are consistent with previous studies. Silva et al. reported that delayed closure reduced infection risk in patients with non-traumatic causes of amputation, particularly those prone to impaired wound healing, such as ALI patients.<sup>11</sup> Katiyar et al. reported that in-hospital infections were detected in 23.3% of cases with primary closure and 27.3% of cases with delayed closure, although this difference was not statistically significant. However, it should be noted that the study conducted by Katiyar et al. focused on subjects with a trauma mechanism, such as injuries from a train collision.<sup>9</sup> The reduced infection rate in delayed closure may be attributed to the strategy of leaving the wound temporarily open, which reduces the chance of infection by preventing bacteria from being trapped under the closed skin flap.<sup>10,12,13</sup>

This study found that patients in the delayed closure group required more revision surgeries compared to the primary closure group. Katiyar et al.<sup>9</sup> found additional surgical procedures such as debridement and amputation revision after stump complications were not statistically significant (20% vs 15.2%;  $p=0.4$ ). Similarly, the need for amputation revision was also not statistically different (10% vs 12%;  $p=0.1$ ). The need for additional surgery in the delayed closure group may be related to the nature of the procedure itself, where the initial surgery

is followed by secondary surgery to close the wound. While this approach helps to reduce infection, it also increases the overall number of surgical interventions, potentially increasing morbidity.<sup>6,8,9,14</sup>

This study found no statistically significant difference in the length of hospital stay between the two groups, although the trend showed a longer hospital stay for the delayed closure group. This is in line with the findings of Silva et al.<sup>11</sup> who also noted a longer hospital stay for delayed closure (25 vs 16 days, although not statistically significant), possibly due to the need for a second surgery. Katiyar et al.<sup>9</sup> also found no statistically significant difference in the length of hospital stay between the groups (10.3 vs 11 days;  $p = 0.78$ ). Although the length of hospital stay was not significantly different, the financial implications of additional surgeries and longer hospital stays need to be considered, especially in hospitals with limited resources.<sup>9,15,16</sup>

This study found no significant difference in mortality rates between the two groups, despite differences in infection and revision rates. This suggests that while the choice of wound closure technique may affect immediate postoperative complications such as infection and the need for further surgery, they may not have a significant impact on overall survival. However, the study by Silva et al.<sup>11</sup> found a lower perioperative mortality rate in patients who underwent delayed wound closure 10.9% vs. primary 20.7%, ( $p=0.0247$ ) and a lower 30-day mortality rate (12.2% vs. primary 23.8%,  $p=0.022$ ) despite more cases with Rutherford grades 5 and 6, diabetes, and infection..

The findings of this study have important implications for clinical practice. The higher infection rate associated with primary closure, coupled with the increased need for revision surgery with delayed closure, suggests that the choice of wound closure technique should be tailored to the patient's specific condition. For patients at high risk of infection, such as those with severe ALI or multiple comorbidities, delayed closure may be preferable despite the need for additional surgery. Conversely, in patients who require minimal surgical intervention, primary closure may be considered, with careful monitoring for possible infection.<sup>15-18</sup>

This study has limitations. The relatively small sample size ( $n=46$ ) limits generalizability, and the retrospective, single-center design carries potential for selection bias. Lack of randomization between groups may also confound results, while unmeasured variables

such as severity of ischemia, preoperative optimization, and variations in surgical expertise could influence outcomes. Finally, variations in surgical expertise were not considered, which could significantly impact the results. To enhance the applicability of findings, future multicenter, randomized controlled trials with larger sample sizes and longer follow-up periods are recommended.

In conclusion, the study highlights a significant relationship between wound closure method and complications, suggesting that choice of closure technique can impact postoperative outcomes in ALI patients. While delayed closure may reduce the risk of postoperative infection, this technique also comes with its own challenges, including the need for additional surgery and the possibility of longer hospitalization. Further studies with larger sample sizes and more diverse patient populations are needed to refine these findings and optimize postoperative care in patients undergoing major lower limb amputation due to ALI.

## References

1. Ramirez C, Menaker J, Falcone RE. Traumatic amputations. *Curr Trauma Rep.* 2017;3(3):192-7. doi:10.1007/s40719-017-0089-1
2. Pomares G, Coudane H, Dap F, Dautel G. Epidemiology of traumatic upper limb amputations. *Orthop Traumatol Surg Res.* 2018;104(2):273-6. doi:10.1016/j.otsr.2017.12.014
3. Grudziak J, Mukuzunga C, Melhado C, Young S, Banza L, Cairns B. Etiology of major limb amputations at a tertiary care centre in Malawi. *Malawi Med J.* 2019;31(4):244-8. doi:10.4314/mmj.v31i4.5
4. Sitompul Y, Budiman B, Soebardi S, Abdullah M. Profil pasien kaki diabetes yang menjalani reamputasi di Rumah Sakit Cipto Mangunkusumo Tahun 2008-2012. *J Penyakit Dalam Indones.* 2015;2(1):9.
5. Cerqueira L de O, Duarte EG, Barros AL de S, Cerqueira JR, de Araújo WJB. WiFi classification: the Society for Vascular Surgery lower extremity threatened limb classification system, a literature review. *Malawi Med J.* 2019;31(4):244-8. doi:10.4314/mmj.v31i4.5
6. Perng C-K, Chou H-Y, Chiu Y-J. Identifying major predictors of lower-extremity amputation in patients with diabetic foot

- ulcers. *J Chinese Med Assoc.* 2021;84(3):285–9.
7. Oktalia AW, Retnaningrum YR, Khotimah S. Hubungan antara penyakit arteri perifer dan kadar Hba1c dengan tindakan amputasi ekstremitas pada pasien ulkus kaki diabetik di RSUD Abdul Wahab Sjahranie Samarinda. *J Sains dan Kesehat.* 2021;3(5):715–21.
8. Tofigh AM, Family S. Primary versus delayed primary skin closure in operated patients due to perforated peptic ulcer disease: a randomized controlled clinical trial. *Langenbecks Arch Surg.* 2022;407(4):1471–8. doi:10.1007/s00423-021-02405-4
9. Katiyar AK, Agarwal H, Priyadarshini P, Kumar A, Kumar S, Gupta A, et al. Primary vs delayed primary closure in patients undergoing lower limb amputation following trauma: A randomised control study. *Int Wound J.* 2020;17(2):419–28. doi:10.1111/iwj.13288
10. Barnes JA, Eid MA, Creager MA, Goodney PP. Epidemiology and risk of amputation in patients with diabetes mellitus and peripheral artery disease. *Arterioscler Thromb Vasc Biol.* 2020;40(8):1808–17. doi:10.1161/ATVBAHA.120.314595
11. Silva LR, Fernandes GM, Morales NU, Sobreira ML, Moura R, Bertanha M, et al. Results of one-stage or staged amputations of lower limbs consequent to critical limb ischemia and infection. *Ann Vasc Surg.* 2018;46:218–25. doi:10.1016/j.avsg.2017.06.144
12. Kumar GK, Souza CD, Diaz EA. Incidence and causes of lower-limb amputations in a tertiary care center: Evaluation of the medical records in a period of 2 years. *Int J Surg Sci.* 2018;2(3):16–9.
13. Rankin IA, Nguyen T-T, McMenemy L, Clasper JC, Masouros SD. The injury mechanism of traumatic amputation. *Front Bioeng Biotechnol.* 2021;9:665248. doi:10.3389/fbioe.2021.665248
14. Ali Y, Halvorson J, Nunn A, Miller P. Delayed closure is associated with decreased infection rate in amputations after trauma. *Am Surg.* 2019;85(5):501–4.
15. Shaw J, Challa S, Conway D, Liu M, Haonga B, Eliezer E, et al. Quality of life and complications in lower limb amputees in Tanzania: results from a pilot study. *Lancet Glob Health.* 2018;6(Suppl 1):S18. doi:10.1016/S2214-109X(18)30156-4.
16. Kumar N, Jaiswal P, Muni S, Pankaj D, Bhushan V, Raj A, et al. Comparative study on the outcome of primary skin closure versus delayed primary skin closure in case of emergency laparotomies. *Int J Health Sci (Qassim).* 2022;6(S1):3712–22. doi:10.53730/ijhs.v6nS1.5607
17. Agha R Al, Muneer H, Alqaseer A, Ismaeel T, Badr O. Major lower limb amputation: Causes, characteristics and complications. *Bahrain Med Bull.* 2017;39(3):159–61.
18. Chahrour MA, Habib JR, El Moheb MN, Cherfan P, Mahmoud D, El Rahyel A, et al. Incidence and predictors of surgical site infection complications in diabetic patients undergoing lower limb amputation. *Ann Vasc Surg.* 2022;81:343–50.
19. Essien SK, Zucker-Levin A. Comorbidity and risk factors of subsequent lower extremity amputation in patients diagnosed with diabetes in Saskatchewan, Canada. *Chronic Illn.* 2023;19(4):779–90. doi:10.1177/17423953221137891

## **Tension Band Wiring for Chronic Acromioclavicular Joint Dislocations Rockwood Type III/ISAKOS Type IIIB**

**Subhan Thaib, Setiyo Ramdani**

Division of Orthopaedic and Traumatology, Department of Surgery, Faculty of Medicine Universitas Syiah Kuala  
Zainoel Abidin General Hospital, Banda Aceh, Indonesia

### **Abstract**

Acromioclavicular joint (ACJ) dislocations account for 10% of shoulder injuries, with Rockwood type III being the most common. Despite its prevalence, there is no consensus regarding a gold standard surgical treatment for chronic ACJ dislocations. Patients often delay seeking medical attention during the chronic phase, during which soft tissue healing capacity significantly declines. A 30-year-old male presented with persistent shoulder pain and restricted elevation two months after a motorcycle accident. The patient initially sought alternative treatment, later developed chronic pain and an inability to elevate the shoulder. Physical and radiograph examinations revealed a Rockwood type III ACJ dislocation. After treatment with the tension band wiring (TBW) technique, functional outcomes were assessed using the Disabilities of The Arm, Shoulder and Hand (DASH) and Constant scores. The Constant score improved from 61 to 92 and while the DASH score decreased from 45 to 5 in 3 months and 2 weeks post-operation. International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS) subdivided Rockwood Type III injuries into IIIA (stable) and IIIB (unstable), with type IIIB requiring surgical treatment. Several studies suggested that mechanical stabilization with biological augmentation is sufficient in neglected cases. However, this technique is expensive and required specialized skill and expertise in shoulder arthroscopy. To overcome this challenge, TBW has emerged as a cost-effective and straightforward surgical technique that enables faster rehabilitation and provides a stable, pain-free shoulder without postoperative complications. It may serve as a viable treatment option, particularly in resource-limited or rural settings.

**Keywords:** Acromioclavicular joint, rockwood, tension band wiring

### **Introduction**

Acromioclavicular joint (ACJ) dislocations represent approximately 10% of all shoulder injuries in the urban population, with an incidence of 2.0 per 10,000 persons per year. Male sex and younger age groups are recognized risk factors.<sup>1</sup> Several studies have shown that Rockwood type III is the most common presentation, and the predominant trauma mechanism comprises a direct force to the superior acromion while the shoulder is in an adducted position. In addition, patients rarely consult medical professionals during the chronic stage of the condition.<sup>2</sup> Based on the time of occurrence, ACJ dislocations are considered acute when occurring within 3 weeks

of the accident and chronic when persisting for 6 or more weeks after the accident. Acute ACJ dislocations of less than 3 weeks after trauma are believed to have a potential for spontaneous biological healing due to the early inflammatory phase. Meanwhile, the healing potential in chronic ACJ slowly decreases over time, and coracoclavicular ligament reconstruction (Weaver-Dunn, autograft/allograft, synthetic ligament) is believed to be the main surgical technique option.<sup>3</sup> However, this technique is expensive and requires specialized skill and expertise in shoulder arthroscopy. There is also no consensus regarding a gold-standard surgical treatment for chronic cases.<sup>1</sup>

Long-term outcomes of the tension band wiring (TBW) technique have been reported. Lateur G described favorable results after 12 years and 6 months of follow-up in a patient with acute Rockwood type IV/VI ACJ dislocation, without recurrence.<sup>4</sup> Similarly, Venkatesh V reported satisfactory Constant scores in acute

---

#### **Corresponding Author:**

Setiyo Ramdani  
Division of Orthopaedic and Traumatology Department  
of Surgery, Faculty of Medicine Universitas Syiah Kuala  
Zainoel Abidin General Hospital, Banda Aceh, Indonesia  
Email: setiyoramdany@gmail.com

Rockwood type II and III dislocations treated with TBW, although implant migration and subsequent hardware removal were noted as potential complications.<sup>5</sup> In this case, a patient with chronic ACJ dislocations Rockwood type III/ISAKOS type IIIB was presented and successfully treated using the TBW technique. The use of this technique with K-wires is a cost-effective and simple surgical procedure, allowing faster rehabilitation and a stable and pain-free shoulder without any post-operative complications. Several studies have also reported that it is cost-effective and can easily be implemented in rural areas.

### Case

A 30-year-old right-handed male, married and employed as a chef (65 kg, 174 cm), presented on February 5, 2024, with pain in the right shoulder following a motorcycle accident sustained 2 months earlier. The patient had fell onto the right side, striking the shoulder against the roadside. This patient sought an alternative treatment, which led to chronic pain and the inability to elevate the right shoulder. Daily occupational activities involving cooking and recreational sports such as football and basketball were restricted.

Physical examination revealed that there was a prominence on the right distal clavicle and

tenderness on palpation. A deformity was found on the right side of the back as a lateral winging of the scapulae, and the range of motion of the right shoulder was limited due to pain and resistance. Abduction was restricted to <90° (Figure 1). Neurovascular examination was normal.

Diagnosis of ACJ dislocation was based on clinical history, physical examination, and radiographic findings. The patient was diagnosed with chronic ACJ Rockwood type III/ISAKOS type IIIB, based on the epidemiology in which type III was the most common presentation and male gender of a younger age group was a risk factor.<sup>1,6</sup> In this case report, the patient complained of pain in all areas of the right shoulder extending to the cervical spine with VAS 3, which matched the symptoms of chronic cases.<sup>6,7</sup> Due to inflammation and distal clavicle dislocation, physical examination revealed tenderness on palpation and prominence at the ACJ area, there is minimal AC joint movement on palpation. Right shoulder abduction was below 90° due to pain and resistance, which led to abnormal SHR (Scapulo Humeral Rhythm). The SHR refers to the coordinated movement of the humerus, scapula, and clavicle to achieve full abduction or elevation. The rhythm can be divided into three different phases during abduction. The first phase is a setting phase of the scapula, wherein the first 30° of abduction, the scapula shows minimal movement, while the clavicle elevates between 0-5° at the SC and AC joint. After the first 30° of



**Figure 1 Clinical Image Before Surgery Showing Inability to Elevate the Right Shoulder Above 90°**



**Figure 2 AP X-ray of Right Shoulder Before Surgical Treatment, ACJ Rockwood Type III**

abduction, the humerus and the scapula move in a ratio of 2:1. For the second phase, the humerus abducts 40°, while the scapula laterally rotates 20° with minimal protraction or elevation. The clavicle elevates 15° because of scapular rotation and begins to rotate posteriorly. In the third phase, the humerus abducts 60° and laterally rotates 90° to avoid impingement between the greater tuberosity of the humerus and the acromion process, while the scapula

laterally rotates another 40° and begins to elevate. The clavicle rotates 30–50° posteriorly and elevates another 15°. In reality, this is only a 5–8° rotation relative to the acromion because of a scapular rotation. The total amount of 60° lateral rotation of the scapula during phases two and three is made possible by 20° of motion at the AC joint and 40° of movement at the SC joint. It is important to observe the scapulohumeral rhythm through the ascending as well as the



**Figure 3 AP Radiograph of the Left Shoulder Showing Normal ACJ Alignment**



**Figure 4** Intraoperative Image Showing Anatomical Reduction of the AC Joint With Tension Band Wiring

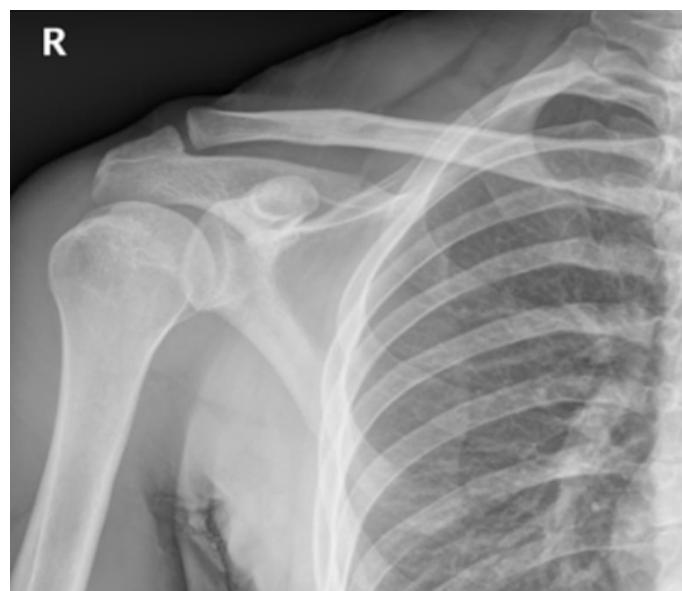


**Figure 5** AP X-ray After Surgical Treatment with TBW Technique

descending phase because weakness of muscles that control the scapula is more evident in the descending phase and a jump of the scapula may occur if control is lost.<sup>7</sup> According to previous studies, abnormal SHR and asymmetry were signs of conoid ligament injuries.<sup>8</sup> The functional outcome of the patient before the operation was assessed by the DASH (Disabilities of The Arm, Shoulder, and Hand) score and Constant score, each was 61 and 45, respectively. Neurovascular examination was normal, as shown in Figure 1.

In Figure 2, the patient's radiograph examination (AP view) revealed a disruption of the ACJ with 25 to 100% vertical displacement. Figure 3, shown AP view of normal left shoulder. Consequently, the patient was diagnosed with ACJ dislocations Rockwood Type III /ISAKOS Type IIIB.

Tension band wiring (TBW) was performed to stabilize the acromioclavicular joint (ACJ). Figure 4 demonstrates anatomical reduction of the ACJ, and the postoperative AP view radiograph (Figure 5) shows satisfactory correction





**Figure 6 AP X-Ray and Clinical Picture After Hardware (TBW) Removal**

following fixation. The patient was discharged on postoperative day 3, and sutures were removed on day 12. During the first 12 days, the upper limb was immobilized with an arm pouch, permitting only active and passive movements of the elbow. The patient was instructed to refrain from elevating the upper limb above the horizontal until the tension band was removed at 12 weeks after operation. No rehabilitation therapy was provided after surgery. Passive movements were started simultaneously as patient tolerated. Active movements were begun at 21 days and full range of movement were started after 3 weeks.

Follow-up evaluation was performed after hardware removal at 12 weeks. The AP radiograph at that time (Figure 6) demonstrated restoration of the coracoclavicular distance to normal. Scar tissue covered the postoperative wound, and functional outcomes were markedly improved, with the DASH score decreasing from 45 to 5 and the Constant score increasing from 61 to 92. No complications were observed, and the patient achieved a satisfactory range of motion. Written informed consent was obtained from the patient for both the surgical treatment and the publication of this case report, including the accompanying images. No personal identifying information is disclosed in this article.

## Discussion

A case of chronic acromioclavicular joint (ACJ) dislocation Rockwood type III/ISAKOS type IIIB

was diagnosed at Dr. Zainoel Abidin Hospital, Aceh, Indonesia. In this case, starting from the results of the anamnesis, physical examination, and supporting examinations carried out, so that the diagnosis of chronic ACJ dislocations Rockwood type III/ISAKOS type IIIB could be established. This diagnosis was made based on the history of the symptoms that he felt chronic pain and could not elevate his shoulder since 2 month after being on motorcycle accident. The delay in seeking medical care, due to prior use of alternative treatment, contributed to the rarity of this case.

ACJ dislocations are classified using radiographic and clinical examination into six types according to Rockwood. Type I was presented with AC ligament sprain, type II with complete AC tear with the CC intact, type III with AC and CC ligament tears and  $\leq 100\%$  superior displacement, type IV was grade III with posterior displacement and  $\leq 300\%$  superior displacement, in type V there was a 100 to 300% vertical displacement and type VI was grade III with inferior displacement.<sup>6</sup>

The ACJ is a diarthrodial joint formed by the lateral end of the clavicle articulating with the acromion process of the scapula. This plane synovial joint allows only gliding movement, achieved through a combination of translation, elevation, and rotation. Biomechanically, an articular movement was restrained, guided, and supported by static ligamentous stabilizers along with dynamic muscular stabilizers. Static stabilizers are supported by acromioclavicular (AC) ligament as horizontal

stabilizers, coracoacromial (CA) ligament and coracoclavicular ligament as vertical stabilizers. CC ligament had a primary function in vertical stabilizers and consisted of conoid ligament and trapezoid ligament. Dynamic stability was supported by the muscle that was attached to the clavicle, such as *m. pectoralis major*, *m. sternocleidomastoideus*, *m. trapezius* and *m. deltoideus*. The primary functions of the ACJ included allowing an additional range of motion to the scapula on the thorax, assisting in shoulder flexion and abduction, and transmission of forces from the upper extremity to the axial skeleton.<sup>6</sup> A direct force to the superior acromion, when the shoulder was in an adducted position, was the most common trauma mechanism on ACJ. In addition, ACJ dislocations were classified using radiographs and clinical examination into 6 different types according to Rockwood.<sup>1</sup> Recommendations for the management of these injuries were typically non-surgical for types 1 and 2, surgical for types 4 to 6, and controversial for type 3.<sup>2</sup> Experts noted that based on the time of occurrence, ACJ dislocations were acute when it occurred up to 3 weeks after the accident and chronic when it occurred 6 or more weeks after the accident.<sup>8</sup> Chronic instability is often associated with pain throughout the shoulder, extending posteriorly, and results from compensatory abnormal scapular movement and overuse of the periscapular muscles.<sup>1,2</sup>

According to previous studies, there were more than 160 ACJ reconstruction techniques. Generally, these techniques differentiate into 4 groups, namely ACJ stabilization technique (K-wiring, hook plate, tension band wiring), Coracoclavicular stabilization (CC ligament reparation, Bosworth screw, suture button, loop with button), excision on the lateral end of the clavicle with or without ligament reconstruction, and the last technique was weaver-dunn. The last 2 techniques were often used in chronic ACJ.<sup>9</sup> All of these surgical techniques aimed to restore anatomy and biomechanics, minimize deformity of the ACJ, and decrease the pain symptom in patients.<sup>6</sup> Until the present, there was no consensus regarding a gold standard surgical treatment due to the lack of studies and each surgical technique had its risks and benefits.<sup>2</sup>

Diagnosis of ACJ dislocations was obtained from a comprehensive anamnesis, physical examination, and radiograph. On anamnesis, the patient could normally describe an anterosuperior shoulder pain located over the ACJ, which was worse with elevation of the affected limb above 90° or upon laying on the

affected shoulder.<sup>6</sup> In a chronic case, the patient felt the pain extend into the cervical spine and all sides of the shoulder. Objective examination revealed bruising, swelling, or deformity of the ACJ, depending on the severity of the injuries. Patients was diagnosed holding their upper extremity in an adducted position with the acromion depressed, which could cause apparent elevation of the clavicle. In addition, the patients also showed tenderness over the ACJ on palpation and could have a reduced active and passive range of movements due to the pain. Special tests were used to aid in the diagnosis of ACJ dislocations and reduce the need for costly investigations and imaging procedures, including the Cross-body test (with 77% sensitivity), active compression test (with 95% specificity), horizontal translation test to assess an anteroposterior translation, O'brien test (with 16% sensitivity and 90% specificity) and Scapulohumeral Rhythm (SHR) observation to assess horizontal and rotational stability. Radiograph evaluation of the ACJ can be assed with anteroposterior (AP), lateral, and axial views. A Zanca view and an anteroposterior view were a specialized projection of the ACJ, which could be opted to observe when there was a vertical displacement of the ACJ.<sup>6,10</sup> Anteropsterior view was applied in this case to obtained patient diagnosis.

The complication of ACJ dislocations was an unstable distal clavicle which could lead to scapular dyskinesis (malposition and abnormal movement of scapula) and when left untreated it could cause a scapular malposition, inferior medial border prominence, coracoid pain, and malposition, as well as dyskinesis of scapular movement, also referred to as SICK scapula syndrome. In higher-grade ACJ dislocations, such as Rockwood type III-VI, there was a possibility of complications such as plexus brachialis injuries and intra-articular SLAP lesions.<sup>11</sup> ACJ dislocations Rockwood types I and II were generally treated conservatively with a shoulder sling for 2 weeks, an anti-inflammation drug followed by rehabilitation.<sup>12</sup> The type III treatment was still being debated, the International Society of Arthroscopy, Knee Surgery, and Orthopaedic Sports Medicine (ISAKOS) Upper Extremity Committee, in 2014, further subdivided Rockwood type III injuries into IIIA (stable) and IIIB (unstable) depending on the residual stability of the ACJ. Type IIIA could be treated with conservative measures, while type IIIB needed surgical treatment. However, recently, the treatment of grade III dislocation

was based on the surgeon's preference as well as the patient's age and activity level.<sup>12</sup> Surgery was also an option for patients whose ACJ was still painful 7 days after the injuries (VAS>7) and whose clinical function had not improved.<sup>16</sup> ACJ dislocations Rockwood type IV to VI required surgical treatment in general as an accurate anatomical reduction was a prerequisite to a good functional outcome, and it minimized the risk of scapular dyskinesis.<sup>17</sup> Acute ACJ dislocations less than 3 weeks after trauma were believed to exhibit the potential of spontaneous biological healing due to the early inflammatory phase, while the healing potential in chronic ACJ slowly decreased over time. Therefore, coracoclavicular ligament reconstruction (Weaver-Dunn, autograft/allograft, synthetic ligament) was believed to be the main surgical technique option in chronic cases.<sup>3</sup>

Tension band wiring technique was applied on this patient and 3 months after the primary operation and 2 weeks after hardware removal, the patient's functional outcome was reassessed by DASH score which revealed a significant improvement to 92 while the Constant score significantly decreased to 5. In addition, there were no complications and the patient regained a functional range of motion. TBW gave an excellent clinical result on this patient. TBW was a simple, less time-consuming surgical technique that allowed faster rehabilitation in active patients to achieve a stable and pain-free shoulder. According to a study by Muthukumar K, ACJ dislocations were treated with TBW, and the functional outcome was subsequently assessed with the Constant and DASH scores, which showed good functional clinical results.<sup>18</sup> In another study by Venkatesh V, acute ACJ dislocations type II and type III revealed a good constant score although there was a risk of implant migration and a secondary operation for hardware removal was needed.<sup>5</sup>

Functional assessment with DASH score and Constant score used questionnaires to assess functional limitations and were made sensitive to the patient's upper extremity symptoms. An excellent DASH score was in the range of 0 to 5 and a very good Constant score was in the range of 86 to 100.<sup>16,17</sup>

The TBW procedure was performed under general anesthesia through a 6 cm superior longitudinal incision placed perpendicular to the ACJ. The delto-trapezial fascia and muscle were split longitudinally. The Acromioclavicular joint and Coracoclavicular joint was left in place and go forward to reduce the ACJ, a tension band

wiring with 2 different 2.5 mm cross K-wires from the lateral acromion edge into the clavicle and a 1.5 mm steel wire in a figure of eight configuration was performed, to ensure that it reached the farthest side and improved pull-out strength to maintain reduction. To prevent a proximal K-wire migration, the lateral pin ends were bent. The correct K-wire and ACJ positions were confirmed by an intraoperative radiographic examination.<sup>17</sup> Immobilization was accomplished with a sling for 2 weeks, and an elevation of more than 90° was prohibited until after hardware removal on the secondary operation. The implant removal was performed three months after the initial procedure, TBW technique allowing the acromioclavicular joint (ACJ) to return to its anatomical position. This facilitated the biological soft tissues healing of the acromioclavicular and coracoclavicular ligaments and restoring their integrity. The patient was able to return to work two weeks after the hardware removal and didn't feel any pain with full range of movement on his right shoulder. This technique was selected because it allowed faster rehabilitation and the patient could resume work early. After surgical reconstruction, the ACJ dislocation recurrence rate ranged between 20% and 30% or even higher.<sup>1</sup> Lateur G who evaluated long-term outcomes of TBW for 12 years and 6 months on a patient with acute ACJ dislocations Rockwood type IV/VI, revealed a satisfying clinical outcome without any recurrence.<sup>4</sup> This patient showed the same result, where at the final evaluation, was able to perform daily activities without any pain in the shoulder.

Tension band wiring (TBW) was the treatment of choice for chronic ACJ dislocation Rockwood type III/ISAKOS type IIIB, providing excellent clinical results. This technique is simple, less time-consuming, and allows faster rehabilitation in young and active patients, leading to a stable and pain-free shoulder without postoperative complications. TBW is also cost-effective, making it suitable for use in rural areas. Moreover, it is effective in repairing the delto-trapezial muscles, fascia, and acromioclavicular ligaments, which play a crucial role in maintaining both horizontal and vertical stability of the clavicle. Overall, TBW demonstrated favorable clinical outcomes in this case..

This study has several limitations. First, being a single case, it may not represent other types of acromioclavicular dislocation (Types I, II, IV, V, and VI). Second, the short follow-up period constrains the ability to generalize the findings.

Further research with a larger cohort and longer follow-up is needed to validate these results.

## References

1. Nordin JS, Olsson O, Lunsjö K. Acromioclavicular joint dislocations: incidence, injury profile, and patient characteristics from a prospective case series. *JSES Int.* 2020;4(2):246-50. doi:10.1016/j.jseint.2020.01.012
2. Chernchujit B, Artha A. High grade acromioclavicular injury: Comparison of arthroscopic assisted acromioclavicular joint fixation and anatomic acromioclavicular joint reconstruction. *J Orthop.* 2020;22:151-7. doi:10.1016/j.jor.2020.04.007
3. Ozan F, Gök S, Okur KT, Altun İ, Kahraman M, Günay AE, et al. Midterm Results of Tension Band Wiring Technique for Acute Rockwood Type III Acromioclavicular Joint Dislocation. *Cureus.* 2020;12(12):1-7. doi:10.7759/cureus.12203
4. Lateur G, Boudissa M, Rubens-Duval B, Mader R, Rouchy RC, Pailhé R, et al. Long-term outcomes of tension band wiring with a single K-wire in Rockwood type IV/V acute acromio-clavicular dislocations: 25 cases. *Orthop Traumatol Surg Res.* 2016;102(5):589-93. doi:10.1016/j.otsr.2016.02.016.
5. Sunil S, Venkatesh V. Management of type 2 & type 3 acromio-clavicular joint injuries by principles of tension band wiring. *Indian J Orthop Surg.* 2020;6(3):175-81.
6. Maher N, Holdsworth J, Fogerty SJ. Acromioclavicular joint injuries: a review of pathoanatomy, assessment and current management approaches. *Orthopaedics and Trauma.* 2023;37(5):285-9.
7. Ranne JO, Kainonen TU, Lehtinen JT, Kanto KJ, Väistämäki HA, Kukkonen MK, et al. Arthroscopic coracoclavicular ligament reconstruction of chronic acromioclavicular dislocations using autogenous semitendinosus graft: a two-year follow-up study of 58 patients. *Arthrosc Sports Med Rehabil.* 2020;2(1):e7-e15. doi:10.1016/j.asmr.2019.10.002.
8. Martetschläger F, Kraus N, Scheibel M, Streich J, Venjakob A, Maier D. Diagnostik und Therapie der akuten Luxation des Acromioclaviculargelenks. *Deutsches Arzteblatt International.* 2019;116(6):89-95.
9. Jambukeswaran PST, Senthilnathan A, Prabhakar R. Comparison Between Two Surgical Techniques: Acromioclavicular Tension Band Wiring and Acromioclavicular Screw Fixation in Acromioclavicular Dislocations. *J Int Modn. Res. Revs.* 2016;4(11):1388-91
10. Thompson JC. *Netter atlas of human anatomy.* 8th ed. Philadelphia: Saunders; 2022.
11. Apley AG, Solomon L. *System of orthopaedics and trauma.* 10th ed. New York: Taylor & Francis Group; 2018.
12. Via RG, Bosco F, Giustra F, Lavia AD, Artiaco S, Risitano S, et al. Acute rockwood type III ACJ dislocation: Conservative vs surgical approach. A systematic review and meta-analysis of current concepts in literature. *Injury.* 2022;53(10):3094-3101. doi:10.1016/j.injury.2022.07.050.
13. Saade F, Carminati F, Bouteille C, Lustig JP, El Rifaï S, Boyer E, et al. Acromioclavicular joint separation: Retrospective study of non-operative and surgical treatment in 38 patients with grade III or higher injuries and a minimum follow-up of 1 year. *Orthop Traumatol Surg Res.* 2023;109(4):103405. doi:10.1016/j.otsr.2022.103405
14. Barth J, Duparc F, Andrieu K, Duport M, Toussaint B, Bertiaux S, et al. Is coracoclavicular stabilisation alone sufficient for the endoscopic treatment of severe acromioclavicular joint dislocation (Rockwood types III, IV, and V)? *Orthop Traumatol Surg Res.* 2015;101(8 Suppl):S297-S303. doi:10.1016/j.otsr.2015.09.003.
15. Muthukumar K, Jambukeswaran P, Sathish Kumar T. Is tension band wiring a gold standard method in management of acromioclavicular injuries: a prospective study. *Nat J Clin Orthop.* 2017;1(2):5-9.
16. Sumarwoto T, Hadinoto SA, Pradhana AI. Functional outcome by evaluation of DASH score on drop hand patient treated with Jones' tendon transfer: a retrospective study. *Joints.* 2020;10(2):39-45.
17. Ziegler P, Kühle L, Stöckle U, Wintermeyer E, Stollhof EL, Ihle C, et al. Evaluation of the Constant score: which is the method to assess the objective strength?. *BMC Musculoskelet Disord.* 2019;20(1):403. doi:10.1186/s12891-019-2795-6