Editorial

Vaginal and Perineal Rejuvenation: Understanding Aesthetic Gynecology

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Aesthetic gynecology is a new surgical field that encompasses procedures designed to change aesthetic as well as functional aspects of women's genitalia following changes that may occur throughout childbirth, aging process, or purely for aesthetic concerns.[1] The definition of women's beauty and how it is perceived throughout the world have been influenced by an array of sociocultural views. Although the ideal aesthetic characteristics of female external genitalia still have to be defined, individual patient preferences must be taken into consideration for individualizing care and treatment; to the extent that patient-centered care is implemented thoroughly. The technique chosen should be specifically based on each patient's genital anatomy and applied with a realistic approach, to increase patient satisfaction and reduce the postoperative complication rates.[1] There are many physiological changes in a woman's life, such as giving birth to a child, weight changes, hormonal changes due to aging and menopause, all of which can change the elasticity of the vaginal canal, have an impact on the pelvic muscles, and reduce muscle tone on the vaginal wall. These conditions can lead to developmental disorders of a woman's urinary-genital system such as stress urinary incontinence, vaginal atrophy, vaginal dryness, and physiological stress that can affect a woman's quality of life, self-confidence, and the quality of her sexual life.

Various modalities are available to treat the above complaints which are included in the aesthetic gynecology category, starting from the invasive one, such as, labiaplasty, vaginoplasty, clitoral hoodectomy, hymenoplasty, labia major augmentation, and others, to the non-invasive category. such as, the use of energy-based devices, injecting filler substances, the use of physical devices, and administering topical hormonal gels or hormone replacement therapy (HRT) in the vagina.[1, 2] These two methods can also be combined to meet the patient's needs for achieving aesthetic genitalia. One of the most popular aesthetic gynecological procedures is vaginal rejuvenation, which sometimes includes rejuvenation of the perineum as well. Vaginal rejuvenation is a procedure whose main goal is to reduce the width of the vagina for functional and long-term health reasons. Currently, information about vaginal rejuvenation can be easily accessed and obtained, as a result, there is a significant increase in the demand for this vaginal rejuvenation procedure.

The surgical process of vaginal rejuvenation is known as vaginoplasty, which involves surgical techniques that range from tightening the vagina to correcting any damage or deformity found in the vagina. Vaginoplasty can result in muscle tightening not only at the vaginal introitus but up to the vaginal canal, where sometimes dissection is necessary to the levator and lateral muscles of the spine ischiadica. Vaginoplasty procedures also generally involve perineoplasty procedures, as they require realignment and strengthening of the perineal tissue as well. Complication rates of vaginoplasty range from 2 to 3.7%, which include dyspareunia, lack of lubrication, constipation, surgical wound infection, bleeding, suture rupture (usually in the perineum), pelvic floor pain for several weeks, and perforation of the rectal mucosa.[3] Apart from invasive procedures, there are also non-invasive procedures that can be offered to patients. The demand for non-invasive procedures with the aim of rejuvenating the vagina is found to be greatly increasing among the public. This procedure can include the application of energy-based devices, injection of certain substances such as fillers or Platelet Rich Plasma (PRP), and the use of physical devices.[4]

Aesthetic gynecology as a relatively new field within obstetrics and gynecology is now gaining momentum and has developed into one of the most desired procedure by women of all ages in elective surgery field. This field includes cosmetic procedures to improve the aesthetics of the vulvar and vaginal region as well as functional aspects of women's genitalia following the changes that may occur following childbirth and aging process. In addition to invasive methods, the use of energy-based devices has the potential to become the main therapy in the field of aesthetic gynecology, especially

vaginal rejuvenation. However, further research on a larger scale to support aesthetic gynecology procedures is needed to be done by professional institutions, in order to reach the standardization of treatment modalities.

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Research Article

Long-term Outcomes of Severe Preeclampsia Cases: Cross – Sectional Study

Keluaran Jangka Panjang Kasus Preeklamsia Berat: Studi Potong Lintang

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Abstract

Objective: to know the long term outcomes on severe preeclampsia mother by clinically and laboratory, and the long term outcome of the baby that she delivered.

Methods: This is a cross sectional study was conducted at Obstetrics Outpatient Clinic Dr. Cipto Mangunkusumo General Hospital (Cipto Mangunkusumo NCGH) on January–June 2017, of patients with previous severe preeclampsia that gave birth in Cipto Mangunkusumo NCGHon January 2014 – December 2016, and was descriptively analyze using SPSS Statistics 24.

Results: One hundred and twenty seven patients were studied, divided into 3 groups of post – delivery time which were 6 months, 12 months, and 24 months. The 6 months' group, mean of blood pressure were 147/92 mmHg (SD 38/SD 39), BMI 29 kg/m^2 (SD 6), CRP level 16.6 mg/l (0.3 – 42.60) and urine protein dipstick 1 (0 – 3). The 12 months' group, mean of blood pressure were 112/88 mmHg (SD 12/SD 24), BMI 21s kg/m^2 (SD 7), CRP level 12.7 mg/l (3.4 – 15.2) and urine protein dipstick 0 (0 – 3). The 24 months' group, mean blood pressure 154/95 mmHg (SD 45/SD 62), BMI 28.83 kg/m^2, CRP level 14,2 mg/l (SD 8.54) and urine protein dipstick 0 (0 – 3). Meanwhile, the long – term outcome of babies that 68% baby were born with preterm condition and mean birth weight were 1943 grams (SD 1245), the 5th minute Apgar score >7 were 63.78%, and only 44.88% baby had normal growth development.

Conclusion: It The long – term outcome patients with previous severe preeclampsia are blood pressure, BMI, and CRP level still high, and negative urine protein level until 2 years of post – delivery. The long – term outcome of the babies that delivered were on preterm condition and low birth weight, with less than 50% had normal growth and development.

Keywords: c–reactive protein, growth and development, proteinuria, post–delivery, severe preeclampsia.

Abstrak

Tujuan: *Untuk mengetahui keluaran jangka panjang pada pasien ibu PEB dari sudut klinis dan laboratoris, serta keluaran jangka panjang bayi yang dilahirkan.*

Metode: *Penelitian ini menggunakan desain potong lintang terhadap pasien riwayat PEB yang pernah melahirkan di RSUPN Dr. Cipto Mangunkusumo pada bulan Januari 2014–Desember 2016. Subjek diminta datang ke Poli Obstetri RSUPN Dr. Cipto Mangunkusumo pada Januari–Juni 2017 untuk dilakukan pemeriksaan klinis dan laboratoris (CRP dan protein urin), serta dilakukan analisa deskriptif menggunakan SPSS Statistik 24.*

Hasil: *Sebanyak 127 pasien yang diteliti terbagi dalam 3 kelompok yaitu pasien riwayat PEB setelah persalinan 6 bulan (kelompok I), 12 bulan (kelompok II), dan 24 bulan (kelompok III). Kelompok I didapatkan rerata tekanan darah (TD) 147/92 mmHg (SD 38/SD 39), IMT 29 kg/m^2 (SD 6), kadar CRP 16,6 mg/l (0,3 – 42,60) dan protein urin 1 (0 – 3). Kelompok II didapatkan rerata tekanan darah (TD) 112/88 mmHg (SD 12/SD 24), IMT 21 kg/m^2 (SD 7), kadar CRP 12,7 mg/l (3,4 – 15,2) dan protein urin 0 (0 – 3). Kelompok III rerata TD 154/95 mmHg (SD 45/SD 62), IMT 28,83 kg/m^2, dengan rerata kadar CRP 14,2 mg/l (SD 8,54) dan protein urin 0 (0 – 3). Sedangkan keluaran jangka panjang bayi yang dilahirkan bahwa 68% lahir dengan kondisi preterm dengan rerata berat lahir 1.943 gram (SD 1.245), nilai Apgar menit ke-5 >7 63,78%, dan hanya 44,88% tumbuh – kembang bayi normal.*

Kesimpulan: *Gambaran keluaran jangka panjang pasien riwayat PEB didapatkan tekanan darah, IMT dan kadar CRP masih tinggi, serta protein urin urin negatif setelah 2 tahun setelah persalinan. Keluaran jangka panjang bayi yang dilahirkan mayoritas kondisi preterm dan berat lahir rendah, dengan kurang dari 50% bayi tumbuh – kembang normal.*

Kata kunci: *c–reactive protein, preeklamsia berat, proteinuria, setelah persalinan, tumbuh kembang bayi.*

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INTRODUCTION

Preeclampsia has been one of the leading causes of maternal and perinatal morbidity and mortality and complicates 2-8% pregnancies worldwide.[1,2] Since 2013, the definition and diagnostic criteria for preeclampsia is upgraded and modernized by ACOG Task Force and removing proteinuria as an absolute criteria for diagnosing a preeclampsia. The latest guidelines from ACOG, preeclampsia is divided into 2 criteria with and without severe feature.[1]

Among several risk factors of preeclampsia, age > 35 years old and Body Mass Index > 30, are prone to have preeclampsia and preterm labor, also increasing cardiovascular disease and diabetes mellitus incidents in later days.[1-3] Short – term and long – term complication can also happen to preeclampsia patients and the baby delivered, that caused by endothelial dysfunction that led to blood flow uteroplacenter insufficiency.[1-3] Maternal complications are metabolic syndrome (obesity, chronic hypertension, cardiovascular disease, cerebrovascular disease, renal dysfunction) and risk of preeclampsia in the next pregnancy.[2,4-11] Meanwhile neonatal complications are metabolic syndrome and growth – development impairment (eg. cognitive function).[2,12,13]

CRP is one of systemic biomarker and acute phase protein that respond to inflammation, have been studied as predictive factor of complication of severe preeclampsia in pregnancy and outcome for maternal and neonatal in later days.[14-17] Many studies of CRP levels found increasing during pregnancy with preeclampsia.[17-19] One of the studies found that there is persistent increasing of high sensitivity – CRP (hsCRP) of 5 – 8 years after delivery in preeclampsia group than control group.[18] Others showed that meanwhile from 255 patients, 50 patients are having recurrence; with baseline CRP concentration between patients with preeclampsia recurrence and not having recurrence are almost the same, and not correlated with preeclampsia recurrence.[20]

Until today Indonesia do not have many studies about long term outcomes of severe preeclampsia cases, by clinical and laboratories. Due to this encourage us to study about long – term outcomes maternal and neonatal of severe preeclampsia from 6 months, 1 year, and 2 years after delivery.

The purpose of our study was to describe the long term outcomes on patients with history of severe preeclampsia by clinically and laboratories, and the long term outcomes of the baby she delivered.

METHODS

This was a cross – sectional study of patients with previous severe preeclampsia (using former diagnostic criteria for preeclampsia) that gave birth in Dr. Cipto Mangunkusumo NCGH in January 2014 – December 2016. Subjects were called to come to our Obstetrics Outpatient Clinic on January– June 2017 and get examined (physical and laboratories exams of CRP and urine dipstick). Subjects were consecutively – collected until all the samples needed were fulfilled, were grouped into 3 group time of delivery (6 months, 1 year, and 2 year). Inclusion criteria were patients post-delivery with history of preeclampsia, willing to join the study, reachable by phone and willing to come as scheduled, and live in Jakarta, Bogor, Depok, Tangerang, and Bekasi (Jabodetabek) area. Exclusion criteria were symptomatic infection disease (upper respiratory tract infection, reproduction tract infection, urinary tract infection), subjects were pregnant during contacted by phone, subjects refused to join the study, subjects were moved out of town, subjects were deceased, and subjects were unreachable by phone number in medical records. Drop out criteria were if during study subjects were symptomatic infected, known or diagnosed pregnant during visit, and not able to finish the study.

From medical records we found subjects' location and phone number, were contacted to visit our Obstetric Out clinic, given informed consent and early screening (exclusion criteria) verbally. During visit to out clinic, subjects will be asked for sign up the informed consent, done the physical exam and protein urine dipstick examination by nurse and doctors on duty, continued with CRP examination at Out clinic Laboratory. Data of subjects and her baby (before delivery) were collected from medical records. Patients then interviewed about latest condition of the baby in time of study (age, latest condition, and growth development). This study has passed the Ethical Approval Faculty of Medicine University of Indonesia. All data were descriptively analyzed with SPSS Statistics 24. Data with normal distribution, reported in means and standard deviation. Data with abnormal distribution, reported in median, minimum value, and maximum value.

RESULTS

We managed to get 765 subjects from medical records to be contacted. From those subjects, 184 subjects were able to be contacted, fulfilling the inclusion criteria, and willing to come to our hospital. As scheduled, only 130 subjects that able to come and following the study. During study, 3 subjects got into drop out criteria due to 2 subjects known to be pregnant by physical examination and 1 subject did not able to finish the study (not done the CRP examination).

Based on 127 datas of subjects collected, the mean age of patients when diagnosed with severe preeclampsia were 29 years old (SD 8.7),mean of BMI were 32.8 kg/m2 (SD 9.7) with 70% subjects were overweight – obesity, more than 50% gestational age were less than <37 weeks (61.42%), and almost all subjects were done the cesarean section (90.55%).Their blood pressure at first visit at that time were high (median 182/100 mmHg (abnormal distribution)), and urine protein were positive (median 1.5) (Table 1).

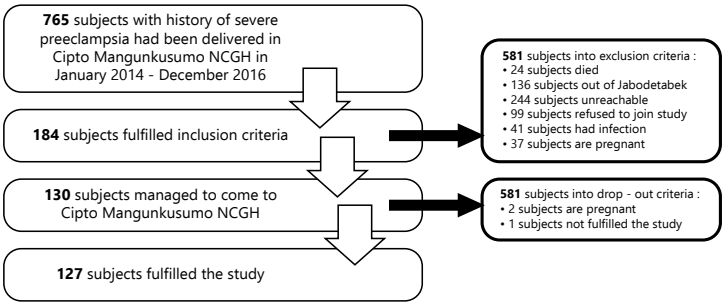

Figure1. Recruitement of subjects

Table1. Patients Characteristics

Variable	Mean (Standard Deviation)*	Median (Min – Max)**	n (%)
Age	29.3 (8.7)		
Parity		2 (1 – 5)	
Gestational age (weeks)	34.2 (6.3)		
< 37			78 (61.42)
37			49 (38.58)
Number of gestation (singleton/multiple)		1 (1 – 2)	
Mode of delivery			
Vaginal Delivery			10 (7.87)
Vacuum/Forceps Extraction			2 (1.57)
Cesarean section			115 (90.55)
Complication			
Yes			35 (27.56)
No			92 (72.44)
BMI first visit			
Underweight			2 (1.57)
Normoweight			36 (28.35)
Overweight – Obesity	32.8 (9.7)		89(70.08)
Systolic blood pressure first visit (diagnosed with severe preeclampsia)		182 (138 – 220)	
Diastolic blood pressure first visit (diagnosed with severe preeclampsia)		100 (80 – 145)	
Urine protein at first visit		1.50 (0 – 3)	

* Mean and standard deviation were used in normal distribution; ** Median and minimum/maximum value were used in abnormal distribution;*** n(%) was used in categoric value.

From 127 subjects collected, the mean of baby birth weight was 1943 grams (SD 1245), with 77.17% live at birth and 63.78% babies born with the fifth Apgar score were >7 (Table 2). The results from interviewing patients that 44.88% babies delivered were in normal growth and development, 32.28% their weights were under the normal curve, and 22.84% babies were died (including intrauterine fetal death, still birth, and perinatal mortality before 24 months of age).

Table 2. Children's Subjects Characteristics

Variable	Mean (Standard Deviation)*	Median (Min – Max)**	n (%)
Birth weight (grams)			
< 2500	1943 (1245)		96 (75.59)
2500 – 4000			29 (22.83)
> 4000			2 (1.57)
The fifth Apgar Score			
0 – 7		9 (0 – 10)	46 (36.22)
8 – 10			81 (63.78)
At birth condition			
Live			98 (77.17)
Died			29 (22.83)
Children growth – development			
Normal			57 (44.88)
Weight under curve			41 (32.28)
Died before age 24 months			29 (22.84)

* Mean and standard deviation were used in normal distribution; ** Median and minimum/maximum value were used in abnormal distribution; *** N(%) was used in categoric value.

From physical examination, we found that patients with history of severe preeclampsia their blood pressure and BMI are still high. Meanwhile, from laboratories examinations, that until 2 years after delivery the CRP level were also high (> 5 mg/l) and the urine protein were back to normal level (Table 3).

Table 3. Physical Examination Results

Physical Examination	Time of Study		
	6 months (n = 54)	12 months (n = 38)	24 months (n = 35)
Systolic Blood Pressure (Mean (Standard Deviation))	147 (38)	112 (12)	154 (45)
Diastolic Blood Pressure (Mean (Standard Deviation))	92 (39)	88 (24)	95 (62)
BMI(Mean (Standard Deviation))	29 (6)	21 (7)	34 (12)
CRP (Median (Min – Max))	16.6*(0.30 – 42.6)	12.7*(3.4 – 15.2)	14.2 (8.54)
Urine Protein(Median (Min – Max))*	1 (0 – 3)	0 (0 – 3)	0 (0 – 3)

* Abnormal distribution, reported in median and minimum/maximum value.

DISCUSSION

Our study had not been used the newest terminology for severe preeclampsia according to ACOG 2013 which is preeclampsia with severe feature. According to subjects characteristics, most patients of severe preeclampsia patients were in second pregnancy with gestational age less than 37 weeks (preterm pregnancy). This is because every case of severe preeclampsia had to be terminated after stabilization, except for the gestational age less than 34 weeks that given lung maturation before terminated.[1,2] Most patients came with very high blood pressure (median 182/100 mmHg) and obesity (mean BMI 30.51). During study, we found that blood pressure still high until 2 years after delivery and also BMI still high in 6 months and 2 years after delivery. Those could be influenced by factors such as lifestyles, physical activity, cholesterolemia, and nutrisional factors (eg. vitamin D). It is recommended that patients with history of preeclampsia in preterm pregnancy or with subsequent preeclampsia to have blood pressure, lipid profile, fasting blood glucose, and BMI examination every year, even though there is still limited evidence of accurate prediction of early onset preeclampsia to improve maternal and fetal outcome.[1-3,21] Studies have shown that cardiovascular disease is increasing in first pregnancy with severe preeclampsia, with

higher risk rate compare to risk rate of pregnancy with subsequent severe preeclampsia, preterm labor, or intrauterine growth restriction, thus similar to risk rate of obesity or smokers.[1,2,6] American Heart Association in 2019 is adding preeclampsia into one of the risk factors of short term and long term cardiovascular disease, and as a strong factor related to preterm labor.[3,6,7]

Severe preeclampsia is mostly happening during preterm pregnancy and resulting outcome of growth and development not optimal for children that have been delivered. It can be caused by any factors, exacerbated by lack of awareness of how important to do antenatal care with health care provider and lack of education and supervision of health care provider to every pregnant patients, especially pregnant patients with high blood pressure. Most infants had been delivered in preterm condition (61.42%), resulting low birth weight babies and extreme low birth eight babies(the lowest baby weight in this study was 340 grams). Even though 77.17% infants were born alive, but only 63.78% had 5th–minute Apgar Score > 7.It is due to most infants born with weight < 2500 gram (75.59%). WHO study in 2014 found that 30.89% preeclampsia patients had preterm labors and 9% had perinatal mortalities, meanwhile 39.84% eclampsia patients had preterm labors and 22.66% had perinatal mortalities.[22] During study, we found that 44.88% infants delivered are in healthy and normal growth – developmental state, 32.28% infants are still in below growth – developmental chart, and 22.84% infants are already died. Yet we still need to do further objective study of growth and development, especially infants with intrauterine growth restriction due to severe preeclampsia, eg. using Denver Charts, in collaboration with Social Pediatric Subdivision in Pediatric Department, measuring BMI and blood pressure, or vitamin D levels.[23-25] One of example was using Peabody Picture Vocabulary Test-Revised (PPVT-R) to assess verbal ability and Raven's Colored Progressive Matrices (CPM) to assess non – verbal ability of 10 years old children delivered from preeclamptia patients.[23]

Lots of studies of CRP had been done by cardiologists as measurement and marker of cardiovascular risks. CRP is a marker protein that sensitive to acute systemic inflammation, and considered related to cardiovascular risks in patients with history of preeclampsia.[14,15] CRP levels were not increasing in patients with history of preeclampsia in their next pregnancy and from 255 patients studied only 50 patients had subsequent preeclampsia with unsignificant difference of CRP levels between both groups.[18] From our study, we found that 6 months until 2 years after delivery are still high (>5mg/l), correspond to endothelial dysfunction in preeclampsia inducing inflammation process, thus increasing CRP level. We also concluded that preeclampsia are continuing disease causing complications, especially cardiovascular disease, and closed continuous observation to patients with history of preeclampsia are necessary. We also suggest to have further research with longer time of study groups and to learn changes in CRP levels that increased risk of subsequent preeclampsia in next pregnancy or cardiovascular diseases. From these further studies hopefully we may determine a baseline, specificity, and sensitivity of CRP levels for those risk factors. It will be one of consideration for these patients during antenatal care in her next pregnancy the needed to do CRP level measurement as early screening of preeclampsia and cardiovascular disease. Many factors may influence the increasing of CRP levels such as vitamin D levels, LDL levels, physical activities, lifestyles, and BMI. CRP levels are decreasing in patients with higher BMI but improvement of vitamin D levels and lifestyles, thus decreasing cardiovascular risks.[14,22] This study to be continued by considering those factors influencing CRP levels in longer time of study.

There are changes of urine protein results before and after delivery in this study, correspond to endothelial dysfunction in severe preeclampsia that cause changes in blood vessels reactivity, loss of vascular integrity, and coagulation cascade activation.[1-3,15] However in few studies, some HELLP syndromes and eclampsia cases had negative urine protein.[9,26] Our study is using dipstick urine protein which is qualitative examination that depend on urinary concentration with high false positive and false negative values.[1-3,9] We decided to use this tool because it is not expensive and not required certain skills.

The strength of our study is the numerous amounts and varieties of severe preeclampsia cases in Dr. Cipto Mangunkusumo NCGH supported with complete facilities, that this study could be done well in this education center. The weakness of our study are difficulties in gathering and contacting subjects due to lack of subjects's information in medical records (locations and

phone number) and their activities in time of study. Our study also did not have control group to be compared to, before and after delivery (clinically and laboratory), and between normal pregnancy and pregnancy with severe preeclampsia in the same time. Also we have limitations in performing laboratory examinations which influencing CRP levels, such as leucocytes, vitamin D, LDL levels, that we can not exclude sign of infection objectively and comprehensively. Thus this study could not determine the baseline, specificity, and sensitivity of CRP level as a marker for subsequent or worsening of severe preeclampsia in next pregnancy. We were using quantitative CRP examination in this study, furthermore we suggested to use hsCRP examination to have more specific results. This study were using descriptive cross sectional study design, so we were not able to have more accurate and systematic long term outcomes. Last condition of the babies delivered from the subjects were still subjectively and not specifically done, we suggested to use questionnaire about infants growth and development and factors influencing it, such as infant's BMI, growth and development pattern (eg. using Denver Charts), and infant nutritional status (eating habits, lifestyle, nutritional/diet measurements).

CONCLUSION

From this study we found that long term outcomes of blood pressure and BMI patients with history of severe preeclampsia are still high. CRP levels are also high even until 2 years after delivery, in contrary with urine protein had negative results in same time. Long – term outcomes of infants delivered from mother with history of severe preeclampsia are mostly in preterm labor condition and low birth weight, and less than 50% that have normal growth and developmental state until 24 months of age.

This study furthermore should be continued with prospective and analytical studythat able to study and determine CRP levels before and after pregnancy, even before the next pregnancy, to compare CRP levels in normal pregnancy and pregnancy with severe preeclampsia, with considering factors influencing the increasing of CRP levels. Further study will have better quality if infants from the subjects are also join the study to be examined objectively, in collaboration with Social Pediatric Subdivision in Pediatric Department.

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Research Article

Fetomaternal Outcomes in Term Labor with Pregnant Thrombocytopenia

Luaran Fetomaternal pada Ibu Hamil Aterm dengan Trombositopenia

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Abstract

Objective: To determine the relationship between term pregnant women and the incidence of post-partum haemorrhage, duration of healing of incision/perineorhaphy wounds, fetal thrombocytopenia, APGAR value and birth weight of infants in dr. Zainal Abidin Hospital Banda Aceh.

Methods: Design of research is observational analytic with a cross sectional approach. The research sample was taken by the total sampling method. The population in this study were all pregnant patients at term who came to the dr. Zainoel Abidin Hospital Banda Aceh and experienced thrombocytopenia 0at a predetermined time, met the inclusion and exclusion criteria. Analysis data with the Pearson correlation test formula to assess the strength of the relationship between two variables.

Results: Prevalence of aterm pregnant women with thrombocytopenia who visited and gave birth at Dr. Zainoel Abidin General Hospital during the study period was 1.62% from 1850 visited pregnant women. A total of 30 samples in this study, obtained a maternal outcome were postpartum haemorrhage as much as 60% (p-value 0.000). The duration of wound healing was 26.70%, (p-value 0.008). While the fetal outcomes were the incidence of neonatal thrombocytopenia 50% (p-value 0.000), nenonatal asphyxia with an APGAR value of 4-6 as much as 43.30% (p-value 0.003) and low birth weight of the baby at 36.70% (p-value 0.033). The five variables obtained a positive correlation with varying strengths of the relationship.

Conclusion: There is a close relationship between the incidence of thrombocytopenia at term pregnant women at delivery and fetomaternal outcomes in dr. Zainoel Abidin Hospital Banda Aceh.

Keywords: fetal outcome, maternal outcome, Score APGAR, thrombocytopenia.

Abstrak

Tujuan: *Untuk mengetahui hubungan ibu hamil aterm dengan kejadian perdarahan post-partum, lamanya penyembuhan luka insisi/perineorafi, trombositopenia janin, nilai APGAR dan berat badan lahir bayi di Rumah Sakit Umum dr. Zainal Abidin Banda Aceh.*

Metode: *Jenis penelitian ini adalah analitik observasional dengan pendekatan potong lintang. Sampel penelitian diambil dengan metode total Sampling. Populasi pada penelitian ini adalah semua pasien hamil aterm yang datang ke RSUD dr. Zainoel Abidin Banda Aceh dan mengalami trombositopenia pada rentang waktu yang telah ditentukan, memenuhi kriteria inklusi dan eksklusi. Analisa data dengan melakukan uji korelasi Pearson untuk menilai kekuatan hubungan dua variabel.*

Hasil: *Prevalensi ibu hamil aterm dengan trombositopenia pada penelitian adalah 1,62% dari 1850 ibu hamil yang berkunjung. Sebanyak 30 sampel pada penelitian didapatkan luaran maternal yaitu perdarahan postpartum sebanyak 60% (p-value 0,000). Lama penyembuhan luka didapatkan26,70%, (p-value 0,008). Sedangkan luaran fetal yaitu kejadian trombositopenia neonatus 50% (p-value 0,000), asifiksia nenonatus dengan nilai APGAR 4-6 sebanyak 43,30% (p-value 0,003) dan berat badan bayi lahir rendah 36,70% (p-value 0,033). Kelima variabel didapatkan korelasi positif dengan kekuatan hubungan yang bervariasi.*

Kesimpulan: *Terdapat hubungan erat antara kejadian trombositopenia ibu hamil aterm saat persalinan terhadap luaran fetomaternal di RSUD dr. Zainoel Abidin Banda Aceh.*

Kata kunci: *luaran fetal, luaran maternal, nilai APGAR, trombositopenia.*

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INTRODUCTION

Thrombocytopenia in pregnancy is a common hematological disorder that occurs during pregnancy. The prevalence of thrombocytopenia in pregnant women is 8-10% and complications in 7-8% of pregnancies. The American College of Obstetry and Gynecology about 75% of cases are caused by gestational thrombocytopenia; 15-20% metabolic disorders; 3-4% due to immunological processes; and the remainder 1-2% consists of rare constitutional thrombocytopenia, infection and malignancy.[1,2]

Hematological abnormalities that commonly occur during pregnancy are a benign process such as gestational thrombocytopenia. associated with systemic diseases such as preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), and acute fatty liver in pregnancy (AFLP). Furthermore, autoimmune diseases include systemic erythematous lupus (SLE), antiphospholipide syndrome (APS), thrombocytopenic purpura (PTT), hemolytic uremic syndrome (HUS), and idiopathic thrombocytopenia purpura (ITP) that are detected during pregnancy.[2-4]

Fifty five point one percent cases of mild thrombocytopenia because most of them are thrombocytopenia gestasional which usually causes mild to moderate thrombocytopenia.[3] Maternal complications that often occur are bleeding, that antepartum, intrapartum and postpartum haemorrhage. Pregnant women with thrombocytopenia have a greater risk of bleeding during and after delivery, especially if cesarean surgery or operative vaginal delivery is performed and during the puerperium.[5-7]

The major changes of hemostasis during normal pregnancy include increased concentrations of most clotting factors such as (thrombin, fibrinogen and fibrin), decreased concentrations of natural anticoagulants, and reduced fibrinolytic activity. These changes create a state of hypercoagulability, so that the incidence of thrombocytopenia can risk to bleeding complications during delivery.[8-10]

Maternal thrombocytopenia can cause fetomaternal outcomes in the form of postpartum haemorrhage, longer duration of surgical wound healing, hemoperitoneum events and the risk of relaparotomy. Whereas for fetuses, the assessment of thrombocytopenia used was fetal thrombocytopenia, birth weight, APGAR value, bleeding complications in the fetus and the number of platelets in the umbilical cord immediately after birth. This study aims to assess the relationship of thrombocytopenia at term pregnant women at delivery to fetomaternal outcomes.

METHODS

This research is an observational analytic study with cross sectional method, a research technique that analyzes the dependent and independent variables at the same time. This research was conducted at the dr. Zainoel Abidin General Hospital in Banda Aceh during January 2018 - December 2019. The population in this study were all term pregnant patients who gave birth with a total population of 1850 people, the prevalence of term pregnant women with thrombocytopenia who visited and gave birth during the study period is 1.62%.

The research sample was taken using the total sampling method. The total sample was 60 people and the sample in this study who met the inclusion and exclusion criteria was 30 samples of pregnant women at term with thrombocytopenia and 30 control samples. The inclusion criteria for the case group were term pregnant patients with thrombocytopenia diagnosed by obstetricians and gynecologists based on laboratory findings and pregnant women with gestational age 37 weeks 0 days to 41 weeks 6 days, while the exclusion criteria include case group patients with cases of postpartum haemorrhage other than thrombocytopenia and patients with a history of cytostatic drug use or chemotherapy. The control inclusion criteria in this study were uncomplicated term pregnant patients and live births from uncomplicated term pregnant women.

Data analysis in this study was conducted SPSS 26 both with univariate and bivariate analysis, namely to see the distribution of each variable and the relationship between independent factors and dependent factors using contingency coefficient test with a limit of significance. Pearson correlation used to determine whether there is a relationship between 2 variables, namely the independent variable and the dependent variable on an interval or ratio scale (parametric). The assumption in Pearson correlation, data must be normally distributed. Correlation can produce positive and negative.

This study has passed the ethical clearance of the Health Research Ethics Committee of the Faculty of Medicine, Universitas Syiah Kuala

dr. Zainoel Abidin Hospital number: 189/EA/FK-RSUDZA/2020.

RESULTS

The characteristics of the sample in this study showed that the most common age category was the 18–35-year-old with a total of 48 (80%) cases. In the parity characteristic, pregnant women with parity ≤ 3 children were the most frequently encountered group 50 (83.3%) cases, the gestational age group was mostly found at 39-40 weeks of age as many as 32 (53.3%) cases. In the category of BMI, the group with normal BMI was the group most frequently encountered 33 (55%) cases. In the occupational group, the majority of pregnant women were the IRT group most often found as many as 33 (55%) cases. In the education category, the majority of pregnant women have high school and elementary education 19 (31.7%) cases. The characteristics of pregnant women are shown in table 1.

Table 1. Characteristic Distribution of Term Pregnant Women

Characteristic	Term pregnant women n : 60	%
Age (y o)		
≤ 18	1	1.7
18 – 35	48	80
> 35	11	18.3
Parity (children)		
≤ 3	50	83.3
> 3	10	16.7
Gestational Age (weeks)		
37-38	28	46.7
39-40	32	53.3
BMI		
Underweight	2	3.3
Normoweight	33	55
Overweight	19	31,7
Obese	6	10
Occupation		
Housewife	33	55
Farmer	8	13.3
Entrepeneur	11	18.3
Government employee	8	13.3
Education		
Primary School	19	31.7
Middle School	14	23.3
High School	19	31,7
Bachelor's Degree	8	13.3

A distribution of pregnant at term with thrombocytopenia based on maternal outcomes was divided into 18 (60%) cases of postpartum haemorrhage with a p-value (0.000) and in the category of duration of wound healing, 8 (26.70%) cases were obtained with a p-value (0.008). Meanwhile, the fetal outcome was divided into 15 (50%) cases of neonatal thrombocytopenia with a p-value (0.000). In the category of nenonatus asphyxia, APGAR values of 4-6 were obtained as many as 13 (43.30%) cases with a p-value (0.003) and in the category of low birth weight babies occurred in 11 (36.70%) cases with a p-value (0.033).

Table 2. Distribution of Term Pregnant Women with Thrombocytopenia

Variable	Pregnant with thrombocytopenia (n:30)	(%)	Control Group (n:30)	(%)
Postpartum Haemorrhage				
Yes	18	60.00	4	13.30
No	12	40.00	26	86.70
Wound Healing duration				
Lengthened	8	26.70	0	0.00
Normal	22	73.30	30	100.00
APGAR Score				
4-6	13	43.30	2	6.70
7-10	17	56.70	28	93.30
Neonatal thrombocytopenia				
Yes	18	60.00	4	13.30
No	12	40.00	26	86.70
Birthweight (gr)				
< 2500	11	36.70	3	10.00
2500-4000	19	63.30	27	90.00

Bivariate Analysis

The assessment of the relationship between two variables to obtain a correlation value was carried out by statistical tests with bivariate analysis, namely to determine the relationship between the independent variable and the dependent variable. The statistical test used is the Chi Square test. With the degree of confidence (Confidence Interval) is 95% (alpha value (p-value = 0.05). The relationship of each variable between the independent factor and the dependent factor will be used the Pearson correlation coefficient test with a limit of significance.

Table 3. Correlation of Term Pregnant Women with Thrombocytopenia and Postpartum Haemorrhage

	Pregnant with thrombocytopenia	(%)	Control Group	(%)	*P-value*	Correlation coefficient (r)
Postpartum Haemorrhage						
Yes	18	36.7	4	13.3		
No	12	63.3	26	86.7	0.000	+0.462
Wound Healing duration						
Lengthened	8	26.7	0	0		
Normal	22	73.3	30	100	0.008	+0.733
APGAR Score						
4-6	13	43.3	2	6.7		
7-10	17	56.7	28	93.3	0.003	+0.607
Neonatal thrombocytopenia						
Yes	15	50	0	0		
No	15	50	30	100	0.000	+0.500
Birthweight (grams)						
< 2500	11	36.7	3	10		
2500-4000	19	63.3	27	90	0.030	+0.704

In this study, was found that the maternal outcome for postpartum haemorrhage was higher in women who experienced thrombocytopenia during term pregnancy with a distribution of up to 18 cases compared to pregnant women who did not experience thrombocytopenia during pregnancy. A correlation test was carried out and found a significant relationship between the incidence of postpartum haemorrhage in pregnant women at term who suffered from thrombocytopenia (p-value 0.000). The correlation coefficient value of +0.462 indicates a positive correlation with moderate strength between the incidence of postpartum haemorrhage in pregnant women at term who suffer from thrombocytopenia. We found that the maternal outcome for prolonging the healing period of the incision wound / perineorraphy in term pregnant women with thrombocytopenia was 8 cases (26.7%). There is a significant relationship between the lengthening of the incision wound healing period in pregnant women at term with thrombsytopenia (p-value 0.008) and a correlation value of +0.733 shows a positive correlation with a strong correlation strength.

The fetal outcome in term pregnant women with thrombocytopenia was found in 15 cases of neonatal thrombocytopenia (50%). There is a significant relationship between pregnant women at term who is suffering from thrombocytopenia and the occurrence of thrombocytopenia in neonates (p-value 0.000). The correlation coefficient value +0,500 means that there is a positive correlation between pregnant women at term thrombocytopenia and the incidence of thrombocytopenia in neonates with moderate correlation strength, fetal outcome in the form of neonatal asphyxia with an APGAR value of 4-6 was found in as many as 13 cases (43.3%). There is a significant relationship between pregnant women at term with thrombocytopenia and the occurrence of neonatal asphyxia with an APGAR score of 4-6 (p-value 0.003) with a correlation coefficient of +0.607. There was a positive correlation between pregnant women at term with thrombocytopenia and the incidence of neonatal asphyxia with moderate strength, while the outcome with birth weight <2500 grams was found in 11 cases (36.7%). There was a significant relationship between pregnant women at term with thrombocytopenia and the occurrence of asphyxia in neonates with birth weight <2500 grams (p-value 0.030). The correlation coefficient value is +0.704, there is a positive correlation between pregnant women at term thrombocytopenia and the incidence of birth weight <2500 grams with a strong association strength.

DISCUSSION

This study used an observational analytic method with cross sectional method by using a total sampling technique which was carried out at the dr. Zainoel Abidin Banda Aceh in a pregnant patient at term suffering from thrombocytopenia between January 2018 - December 2019. The total sample was selected based on inclusion and exclusion criteria, total 30 thrombocytopenia samples and 30 controls with various sample characteristics.

The prevalence of term pregnant women with thrombocytopenia who gave birth from January 2018 to December 2019 was a total population of

1850 people, using the prevalence rate formula (PR), the prevalence of term pregnant women with thrombocytopenia was 1.62%. The prevalence of thrombocytopenia in pregnant women is 8-10% and can cause complications occur in 7-8% of pregnancies, often detected in the third trimester of pregnancy.[5] Maternal thrombocytopenia is detected by complete blood count performed at antenatal examination.[5,7]

From the distribution of the characteristics of pregnant patients at term, we found that most of our population was aged 18-35 years, with a total of 48 (80%) cases. On the characteristics of maternal parity, parity ≤ 3 children was the group most frequently encountered, namely 50 (83.3%) cases, the gestational age group was mostly found at 39-40 weeks of age with as many as 32 (53.3%) cases. On the characteristics of BMI, the group with normal BMI was the group most frequently encountered, namely as many as 33 (55%) cases. In the occupational group, the majority of respondents were the most frequently encountered IRT groups, namely as many as 33 (55%) cases. Whereas in the educational characteristics the majority of respondents had high school and elementary education, namely 19 (31.7%) cases.

The study studied 1,079 antenatal cases studied, 95 of which found thrombocytopenia, giving a prevalence of 8.8%. Cases of mild thrombocytopenia were 74.7%, moderate thrombocytopenia was 17.9% and severe thrombocytopenia was 7.4%.[11] There was no significant difference in the distribution of cases and controls according to age (p-value 0.923), religion (p-value 0.947) and parity (p-value 0.068). In the postpartum period, thrombocytopenia persisted in 30% of medical thrombocytopenia and 5% in obstetric thrombocytopenia and there were no cases of gestational thrombocytopenia (p-value 0.001) Gestational thrombocytopenia the platelet count usually returns to normal within 6 weeks of delivery.[3,8,12] Thrombocytopenia in pregnant women is usually associated with adverse fetal, neonatal, or maternal effects, and special management is required other than regular monitoring. Vaginal delivery in these cases should be avoided so cesarean surgery may have to be chosen for obstetric reasons.[12-14]

Table 3 describes a significant relationship between postpartum haemorrhage and the incidence of thrombocytopenia in pregnant women, which shows a percentage of 36.7% with a value (p-value 0.000). This is consistent with research which says that a state of gestational thrombocytopenia or in those with a high risk for postpartum haemorrhage.[9,15,16] In a research was found that maternal complications with thrombocytopenia such as placental abruption (9.4%), postpartum haemorrhage (5.3%), episiotomy hematoma (2.5%), rectus sheath hematoma (1%) were more than in the control group because only 3% of cases had placenta.[17,18] abruption and 1.3% had postpartum haemorrhage in which none had an episiotomy or hematoma over the rectus abdominis muscle. Twenty patients required blood transfusions. However the need for blood transfusions was higher, (16.60%). Most women with ITP had uncomplicated pregnancies but an increased risk of PPH in women with ITP and a platelet count less than 150,000 / µl at birth.[19] Major changes in haemorrhage include increased concentrations of most clotting factors, decreased concentrations of some natural anticoagulants, and decreased fibrinolytic activity. These changes create a state of hypercoagulability, thereby reducing complications of labor bleeding.[20]

A significant relationship was also found between the incidence of thrombocytopenia in pregnant women with the length of incision healing / perineorrhaphy wounds where the percentage was 26.7% with a p-value of 0.008. A platelet count of 5000-10,000 / µL is needed to maintain the integrity of the vascular microcirculation to maintain the haemostasis process from the process of injury. Wound healing is a process involving cellular and biochemical responses both locally and systemically involving dynamic and complex processes of serial coordination including bleeding, coagulation, initiation of acute inflammatory response immediately after trauma.

CONCLUSION

In the maternal aspect, there is a moderate positive relationship between thrombocytopenia in pregnant women with post-partum haemorrhage and the duration of healing of incision wounds, caesarean section wounds and perineorrhaphy. In neonates, there is a moderate positive relationship between thrombocytopenia of pregnant women and neonatal thrombocytopenia. Meanwhile, with the APGAR score and the baby's birth weight, we found a strong positive correlation.

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CONFLICT of INTEREST

Author declare that there is no conflict of interests in this study.

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Research Article

Influence Total Hysterectomy against Function Sexual

Pengaruh Histerektomi Total dengan Fungsi Seksual

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Abstract

Objective: To determine whether there are differences the impact of total hysterectomy on sexual function between each woman. Women who perform total hysterectomy often experience fear of the negative effects of hysterectomy on their sexual function.

Methods: Randomized clinical trials have been conducted in outpatient clinic Obstetrics and Gynecological wards of Dr. Muhammad Hoesin General Hospital, Palembang from February to October 2020. There were 40 samples of women undergoing a total hysterectomy met the inclusion criteria. Sexual function before and after hysterectomy was analyzed with the Wilcoxon test. Data analysis using SPSS version 22.0.

Results: This study showed decreased of desire, decreased stimuli, decreased orgasm, increased lubrication, increased sexual satisfaction, and increased dyspareunia samples after a total hysterectomy. However, with statistical analysis obtained results there were no meaningful changes in sexual function of desire (p = 0.849), stimuli (p = 0.716), lubrication (p = 0.261), orgasm (p = 0.839), sexual satisfaction (p = 0.613) and dyspareunia (p = 0.510) after total hysterectomy.

Conclusion: It can be concluded that there is no significantly total hysterectomy effect on sexual function, based on FSFI (sexual desire, sexual arousal, lubrication, orgasm, sexual satisfaction, and pain.

Keywords: clinical trial, FSFI, hysterectomy, sexual function.

Abstrak

Tujuan: *Mengetahui adakah perbedaan dampak histerektomi total pada fungsi seksual antara setiap perempuan. Perempuan yang melakukan histerektomi total sering mengalami ketakutan akan efek negatif histerektomi pada fungsi seksualnya.*

Metode: *Telah dilakukan uji klinis secara acak di poliklinik rawat jalan bangsal Obstetri dan Ginekologi RSUP Dr. Muhammad Hoesin Palembang mulai bulan Februari sampai Oktober 2020. Sebanyak 40 sampel perempuan yang menjalani histerektomi total memenuhi kriteria inklusi. Fungsi seksual sebelum dan sesudah histerektomi dianalisis dengan uji Wilcoxon. Analisi data menggunakan SPSS versi 22.0.*

Hasil: *Penelitian ini menunjukkan penurunan hasrat, penurunan rangsangan, penurunan orgasme, peningkatan lubrikasi, peningkatan kepuasan seksual, dan peningkatan dispareunia setelah histerektomi total. Namun dengan analistik statistik didapatkan hasil tidak ada perubahan yang bermakna pada fungsi seksual yaitu hasrat (p=0,849), rangsangan (p=0,716), lubrikasi (p= 0,716), lubrikasi (p=0,261), orgasme (p=0,839), kepuasan seksual (p= 0,613), dan dispareunia (p= 0,510) setelah histerektomi total.*

Kesimpulan: *Dapat disimpulkan bahwa tidak ada pengaruh histerektomi total yang signifikan terhadap fungsi seksual berdasarkan FSFI (hasrat, seksual, gairah seksual, lubrikasi, orgasme, kepuasan seksual, dan nyeri.*

Kata kunci: *fungsi seksual, FSFI, histerektomi, uji klinis.*

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INTRODUCTION

Sexual function is the degree or degree of the entire normal sexual response cycle. The sexual desire (sexual desire) of men and women is the same, i.e. influenced by sex hormones, psychic factors, sexual stimuli received, and previous sexual experiences. When these factors are positive, the sexual drive appears well. [1.2] The sexual reaction cycle is divided into four phases according to Master and Johnson, namely: excitement phase, plateau phase, orgasm phase, and resolution phase.[3] Sexual responses in women can arise from things such as meaningful eyes, sweet and pleasant words, or a romantic atmosphere that arouses desire.[4]

A hysterectomy is the removal of the uterus through a surgical procedure that can be performed vaginally, abdominally, or laparoscopic. Total hysterectomy is the removal of the entire uterus and cervix, while subtotal hysterectomy is the removal of the uterine corpus only. In premenopausal patients, hysterectomy is most common in benign diseases, such as abnormal uterine bleeding, uterine fibroids, endometriosis, and chronic pelvic pain, abnormal utero defects, utero prolapse, and cancer; whereas in postmenopausal patients it is most often done in cases of pelvic organ prolapse.[5]

Hysterectomy has been widely studied to affect and cause changes in various phases of sexual activity, whether anatomical, hormonal, or psychological changes in women. The existence of various contradictions between the positive and negative impacts of total hysterectomy on the sexual function of patients, and the absence of research related to this in Palembang, became the background of research related to the effects of total hysterectomy on sexual function.

Female Sexual Function *Index* (FSFI) is a widely used assessment tool for female sexual function. The 19-point Questionnaire was designed to measure sexual function in women. FSFI assesses 6 domains of sexual function, including sexual desire, sexual arousal, lubrication, orgasm, sexual satisfaction, and pain (example: pain associated with vaginal penetration).[6] An FSFI cut point value of ≤ 26.55 as a diagnosis of sexual dysfunction in women.[7] Female Sexual Function Index (FSFI) has been reported as valid and reliable where the Cronbach alpha values in all six domains >0.82, and test-retest reliability over 2-4 weeks show high reliability in all domains (r = 0.79-0.86), as well as on total FSFI scores (r = 0.88). This reliability was proposed and has been confirmed in follow-up researches. Thus FSFI concluded reliable to discriminate between women with sexual dysfunction and women without sexual dysfunction in the entire domain or on a total score.

METHODS

This study was a Randomized clinical trial without comparison pre vs post-test in female patients who underwent total elective hysterectomy procedure in Obstetrics and Gynecology Department of RSUP Dr. Mohammad Hoesin Palembang to find out the outerness of postoperative sexual function compared to sexual function before surgery. The research was conducted from May to November 2020. The subject of this study was a woman who underwent a total hysterectomy. Obstetrics and Gynecology Department of RSUP Dr. Mohammad Hoesin Palembang Hospital during the research period, and met the research criteria (for matching).

The protocol of this research has been approved by ethics committee health research RSMH. The number of subjects is 40. Inclusion criteria consist of women aged 20-60 years, diagnosed with gynecological disorders and oncology indicated total hysterectomy, willing to do gynecological examinations and interviews before and after a total hysterectomy, willing to follow the research, and sign an informed consent sheet. Exclusion Criteria consists of women diagnosed with other diseases, whether metabolic, cardiovascular, hormonal, neurological, lung, paralysis or limb abnormalities, urinary tract infections, sexually transmitted infections, memory disorders, psychiatric disorders, women with poor family harmony, divorced (single), women with husbands who experience sexual dysfunction.

Drop out criteria consists of patients not having a total hysterectomy procedure, bleeding complications or postoperative infections, subjects unreachable or encountered for advanced data collection. The subject was selected purposive sampling according to the research criteria and accordingly diagnosed and decided to undergo a total hysterectomy (time of diagnosis). Every woman with gynecology and oncology patients at Obstetrics and Gynecology Department of RSUP Dr. Mohammad Hoesin Palembang Clinic who met the research criteria was explained the research conducted, for those

who agreed to participate in this study were asked to sign the informed consent sheet that had been provided for the research. All subjects performed anamnesis and routine gynecological examinations following standard procedures at Obstetrics and Gynecology Department of RSUP Dr. Mohammad Hoesin Palembang.

In each subject performed anamnesis, physical examination (vital sign, head to toe), anthropometric, gynecological examination (external examination and deep examination, or as indicated), and supporting examination (ultrasound and laboratory) following Obstetrics and Gynecology Department of RSUP Dr. Mohammad Hoesin Palembang therapy protocol. The diagnosis of the subject is documented. Subjects who fulfilled inclusion criteria were given informed consent by the researchers to follow the research.

The subjects who agreed to participate in the study were followed by filling out the Female Sexual Function Index (FSFI) questionnaire through a research-led interview. Follow up anamnesis clinical complaints, and fill out an FSFI questionnaire 6 months postoperative total hysterectomy performed back on each patients by researchers.

Total hysterectomy surgery was performed by consultant Obstetrics and Gynecology Department of RSUP Dr. Mohammad Hoesin Palembang. Diagnosis data, pre-questionnaire answers, and total post-hysterectomy are recaptured and tabulated in Microsoft excel 2003 for window data tables for later analysis using SPSS ver: 20.0. Data analysis is carried out according to data type and data dissemination type (Kolgomorov Smirnov test). Hi, Square/ Fisher's C-test is performed for nominal and categorical data. Paired sample T-test or Wilcoxon test was conducted at interval data, ROC (Receiver Operating Characteristic) test was conducted to assess the cut-off point of FSFI score in the sample, and regression logistics test was conducted to determine the risk factor of decrease or improvement of sexual function of women undergoing total hysterectomy. Results are presented in the form of tables and graphs to facilitate data reading and analysis of results with a confidence interval (CI) of 95%.

RESULTS

A total of 40 female subjects underwent total hysterectomy who met the research criteria. Examination of sexual function is assessed before and 6 months after hysterectomy. In this study, the average age of patients who performed hysterectomy totaled 45.55 ± 9.126 years with an age range of 32 to 60 years. The majority of subjects were housewives (85%) and married (100%).

Table 1. Demographic of Research Subjects

Characteristics	Amount	Percentage
Age		
Mean ± SD	45.55 ±9.126	
Median (MinMax)	44.5 (32-60)	
Job		
Housewives	34	85.0
Private Employees	1	2.5
Honorer	1	2.5
Retired	2	5.0
Students	2	5.0
Marital Status		
Married	40	100
Unmarried	0	0

The majority of subjects in this study were multipara (85.0%) with oncology diagnosis 57.5% and gynecological diagnosis 42.5%.

Table 2. The Efficacy of Total Hysterectomy on Sexual Function

Characteristics Sexual Function	Hysterectomy		*P-value*
	before	after	
Desire			
Mean ± SD	3.175 ±0.895	3.100 ±0.941	0.849*
Median (Min-Max)	3.6 (1.2- 5.4)	3.3 (1.2- 5.4)	
Stimulation			
Mean ± SD	3.728 ±1.399	3.720 ±1.400	0.716*
Median (Min-Max)	4.3 (0,0 – 5.4)	4.2 (0.0 – 5.4)	
Lubrication			
Mean ± SD	4.180 ±1.715	4.513 ±1.596	0.261*
Median (Min-Max)	4.8 (0.0 – 6.0)	4.95 (0.0 – 6.0)	
Orgasm			
Mean ± SD	4.080 ± 1.661	4.055 ± 1.700	0.839*
Median (Min-Max)	4.4 (0.0-6.0)	4.4 (0.0-6.0)	
Sexual satisfaction			
Mean ± SD	4.490 ±1.599	4.625 ±1.493	0.613*
Median (Min-Max)	4. 8 (0.8 – 6.0)	4, 8 (0.8 – 6.0)	
Sexual pain			
Mean ± SD	3.870 ±1.674	4.05 ±1.577	0.510*
Median (Min-Max)	4.0 (0.0 – 6.0)	4.2 (0.0 – 6.0)	

*Wilcoxon Test, p = 0.05

The study showed, there was a decrease in desire, increased stimuli, increased orgasm, increased lubrication, increased sexual satisfaction, and increased sexual pain of oncology subjects after a total hysterectomy. However, with statistical analysis obtained results there were no meaningful changes in sexual function of desire (p = 0.624), stimuli (p = 0.569), lubrication (p = 0.217), orgasm (p = 0.709), sexual satisfaction (p = 0.554) and sexual pain (p = 0.273).

Table 3. Comparison of Total Hysterectomy Effect on Sexual Function Based on Organs Removed

Characteristics Sexual Function	Removed Organs		*P-value*
	Uterus	Uterus + Ovaries	
Desire			
Mean ± SD	3.240 ±0.809	2.993 ±0.946	0.078*
Median (Min-Max)	3.6 (1.2- 4.2)	3.0 (1.2- 5.4)	
Stimulation			
Mean ± SD	3.660 ±1.231	3.600 ±1.362	0.09*
Median (Min-Max)	3.75 (1.2 – 5.4)	3.75 (0.0 – 5.4)	
Lubrication			
Mean ± SD	4.720 ±0.985	4.657 ±1.494	0.354*
Median (Min-Max)	5.1 (2.4 – 5.7)	5.1 (0.0 – 6.0)	
Orgasm			
Mean ± SD	4.040 ± 1.041	3,900 ± 1,685	0.167*
Median (Min-Max)	4.0 (2.8-5.6)	4.0 (0.0-6.0)	
Sexual satisfaction			
Mean ± SD	4.420 ±1.109	4.533 ±1.458	0.279*
Median (Min-Max)	4.5 (2.4 – 6.0)	4,8 (0,8 – 6,0)	
Sexual pain			
Mean ± SD	4,400 ±0.998	4,080 ±1.598	0.875*
Median (Min-Max)	4.6 (2.8 – 6.0)	4.2 (0.0 – 6.0)	

*Mann Whitney Test, p = 0.05

DISCUSSION

Hysterectomy is a surgical procedure that can be performed vaginally, abdominally, or laparoscopic. Total hysterectomy is the removal of the entire uterus and cervix, while subtotal hysterectomy is the removal of the uterine corpus only. In this study, women who underwent hysterectomy procedures were diagnosed with gynecological and oncological disorders (fibroma/ myoma, adenomyosis, endometriosis, cystic ovarian neoplasms, solid ovarian neoplasms, and cervical cancer).

A study conducted in the northern state of India found that hysterectomy is 7% among married women over the age of 15.[8] Another studies from the western state of India showed that 7-8% of rural women and 5% of urban women had undergone a hysterectomy at an average age of 37 years. In this study, the average age of subjects who performed total hysterectomy was approximately 45 years with a range of 32 to 60 years.

Previous studies which reported the average age of subjects who performed a total hysterectomy was approximately 45 years.[9] In this study obtained the average age of the subject of oncology patients who performed a total hysterectomy of 48.04 ± 10.53 years with an age range of 32 to 60 years. Similarly, the average age of gynecological patients who performed total hysterectomy was at 42.18 ± 5.43 years with an age range of 32 to 52 years.

This finding is in line with the study in 2018 that reported the same age average, in the study reported the average age of the sample who performed a total hysterectomy approximately 45 years with a range of 19 to 75 years.[10] The study found the majority of subjects in both diagnosis groups were housewives (78.3% and 94.1%) known to be married (100%). These results are no different from another research reported the majority of hysterectomy patients were housewives (73.2%) and married (90.2%).[11]

In a previous study involving 110 patients who performed hysterectomies, found that the majority of patients were married (95.37%). The percentage and likelihood of undergoing a hysterectomy are relatively high in women with high parity.[12,13] In this study, the majority of women who performed total hysterectomy were multipara (85%), only 2 people (5%) women who have not had children (nullipara) perform a total hysterectomy. Another study also received similar results, women who performed hysterectomy total majority had children 3 - 4 people (43.92%) and only 5.8% do not have children (nullipara). This is in line with the results of this study, the majority of subjects in both groups with gynecological diagnosis and oncology are multipara (82.6% and 88.2%). Similarly, research reported as many as 30.9% of women who performed hysterectomy had children 3-4 people.[14]

Sexual function is the degree or degree of the entire normal sexual response cycle. Due to sexual excitation, the body will experience a sexual reaction called a sexual reaction cycle. Sexual reactions occur not only in the genital

organs but also in other parts of the body. Psychically there is also a change.[15]

Based on analysis of this study, there were no significant changes in sexual function in the domain of desire (p = 0.624), stimuli (p = 0.569), lubrication (p = 0.217), orgasm (p = 0.709), sexual satisfaction (p = 0.554) and sexual pain (p = 0.273) in oncology patients after undergoing a total hysterectomy procedure. This finding is similar in patients with gynecological diagnosis, i.e. there is no meaningful change in sexual function in the domain of desire (p = 0.862), stimuli (p = 0.981), lubrication (p = 0.795), orgasm (p = 0.773), sexual satisfaction (p = 1.000) and sexual pain (p = 0.599).

Previous Research conducted found that there was a decrease in sexual desire in patients who underwent a radical hysterectomy after 12 months postoperatively. A study previously reported a decrease in sexual desire in patients undergoing radical hysterectomy after 12 months postoperatively. Decreased sexual desire after hysterectomy can occur due to a history of pre-operative low libido, besides, menopausal women surgically can increase the risk of hypoactive sexual desire disorder (HSDD) or lack of libido.[16] Also, changes in vaginal length become shorter after a hysterectomy procedure causing frequent trauma during intercourse that leads to poor quality of life. Some studies state that a penis size that is disproportionate to the size of the vagina will result in trauma during intercourse that causes dyspareunia.[17]

Another Research reported that the level of dyspareunia felt by the respondents of his research after a total hysterectomy procedure was mostly in the category of mild dyspareunia (64.5%). However, this level of mild dyspareunia occurred in both groups of subjects with sexual improvement (66.7%) and subjects felt there was a sexual decline (57.1%) and there is no relationship between dyspareunia and hysterectomy procedures. It's just that there remains a link between dyspareunia and sexual gratification.[17] Previous study that mentioned the absence of differences in sexual function after hysterectomy, where it is mentioned that the pain experienced during the 3 months in the study did not come from dyspareunia but other locations namely the area around the pelvis.[17]

In previous studies proposed an FSFI cut point value of <26.55 as a diagnosis of sexual dysfunction in women.[17] Based on the results of FSFI questionnaire calculations obtained assessment that before hysterectomy as many as 24 subjects suffered from sexual dysfunction and after hysterectomy still obtained 24 subjects suffering from sexual dysfunction. Another research found no significant difference between the frequency of sexual intercourse before and after hysterectomy. It relies on many anatomical and psychological factors such as emotional interactions between partners, the intimate closeness between partners, and quality of life and physical health.[18] Previous research also found no difference in FSFI scores before and after hysterectomy (p > 0.05). Similarly, research reported no difference in FSFI score before and after hysterectomy (p = 0.931).[18] This study also assessed changes in sexual function based on organs removed with the results that there was no change in sexual function to hysterectomy procedure with uterine removal only, but there were changes in sexual function in the form of decreased desire, decreased stimuli, decreased orgasm, increased lubrication, decreased sexual satisfaction and increased sexual pain after the total hysterectomy procedure with the removal of the uterus and ovaries.

In previous study which mentioned that hysterectomy and bilateral salpingo-oophorectomy performed for benign indications cause urinary tract disorders in the short term after surgery in sexually active and healthy women, resulting in sexual dysfunction and increased depression. However, age factors, educational status, employment also affect.[19] Another study also found that only a small number of women reported sexual dysfunction after a hysterectomy. Decreased sexual function is found in long-term follow-ups that may be caused by aging and bilateral salpingo-oophorectomy.[19]

It is known that premenopausal women who undergo hysterectomy accompanied by oophorectomy may experience menopausal symptoms, such as depression, volatile emotions, communication disorders, and low self-control, which can then affect sexual function, accelerate menopause time, and reduced elasticity of the vaginal mucosa, as well as shortening of the vaginal fornix. These changes cause pain and dryness of the cervical mucus during sexual activity. Decreased estrogen levels also result in decreased libido and sexual arousal. A study found that hormonal changes only occur in premenopausal women who undergo a total hysterectomy, whereas menopausal women do not experience this.[19] It is suspected that it is for

this reason that this study generally does not show any significant changes in sexual function due to the age of the majority of the study subjects who have begun to enter menopause. After a comparison based on the organs removed also, it was found that there was no significant difference in the influence of sexual function between hysterectomy procedures in uterine removal along with the removal of the uterus and ovaries. No significant difference in overall sexual function between post-hysterectomy women and healthy control.[19]

RESEARCH WEAKNESSES

The drawback of this study is the limited number of subjects and time. Some factors that were not explored in this study such as psychological factors, the quality of harmony in the household in addition to this study was not examined the length of the vagina because the length of the vagina also affects sexual satisfaction. This study also did not analyze the subject of oncology who received chemotherapy treatment. It can be added that another influencing factor is the bias of response to culture and norms in Indonesia, sexual problems are still considered taboo.

CONCLUSION

Scores of sexual function after total hysterectomy showed decreased desire, decreased stimuli, decreased orgasm, increased lubrication, increased sexual satisfaction, and increased sexual pain. Statically, there was no significant difference in the influence of sexual function between hysterectomy procedures in uterine removal alone and uterine and ovarian removal.

ADVICE

Other follow-up research on post-hysterectomy sexual function using more specific subject characteristics, using other hysterectomy surgical procedures techniques, measured the hormonal levels of the study subjects, or used long vaginal examinations of research subjects before and after hysterectomy.

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Research Article

Effect of Early versus Delayed Cord Clamping on Hematological Parameters of Term Neonates

Pengaruh Penjepitan Tali Pusat Dini Dibandingkan dengan Tertunda pada Parameter Hematologi Neonatus Aterm

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Abstract

Objective: To compare the bilirubin serum, hemoglobin, and hematocrit in term infants undergoing delayed cord clamping with early cord clamping after normal and caesarean delivery.

Methods: This is a prospective observational study. The neonates in which cord clamping was done within 15 seconds were considered in early cord clamping (ECC) group and where cord clamping was done after 1 minute was considered in delayed cord clamping (DCC) group. The PCV, Hb, serum bilirubin were observed after 48 hours in both the groups and compared.

Result: There was statistically significant difference in means of Hb level (p = 0.001) and PCV level (p = 0.001) between DCC and ECC group whereas no statistically significant difference was present in total serum bilirubin level (p = 0.359).

Conclusion: There was no significant increase in risk of polycythaemia and hyperbilirubinemia between delayed cord clamping and early cord clamping group rather has beneficial effects in increasing the hemoglobin and hematocrit in the infants.

Keywords: delayed cord clamping, early cord clamping, hematocrit, hemoglobin, serum bilirubin, hyperbilirubinemia.

Abstrak

Tujuan: *Untuk membandingkan serum bilirubin, hemoglobin, dan hematoklit pada bayi aterm yang dilakukan delayed cord clamping dan early cord clamping setelah persalinan normal dan seksio sesarea.*

Metode: *Studi ini merupakan studi prospektif. Neonatus yang dilakukan cord clamping dalam 15 detik dikelompokkan pada delayed cord clamping (DCC). PCV, Hb, bilirubin serum diobservasi dalam 48 jam pada kedua kelompok, kemudian dibandingkan.*

Hasil: *Terdapat perbedaan signifikan antara kadar Hb (p = 0,001) dan PCV (p = 0,0010 antara kelompok DCC dan ECC, sedangkan tidak terdapat perbedaan signifikan pada kadar bilirubin serum total (p = 0,3590.*

Kesimpulan: *Tidak terdapat peningkatan signifikan polisitemia dan hiperbilirubinemia antara DCC dan ECC.*

Kata kunci: *elayed cord clamping, early cord clapming, hematokrit, hemoglobin, serum bilirubin, hyperbilirubinemia.*

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INTRODUCTION

Delayed cord clamping (DCC) has proven to be beneficial in both term and preterm infants. According to ACOG committee opinion clamping of cord should be delayed at least 30 to 60 seconds in term and preterm infants except in cases where neonatal and maternal conditions necessitates urgent cord clamping.[1] Researches shows higher hemoglobin, haematocrit and increase in iron store in the newborns [2-4] and demonstrates lower rate of intraventicular hemorrhage in preterm infants [5,6].

In an Italian randomized controlled trial consisting of 132 new born shows increase in haematocrit and bilirubin level in DCC group.[7] Physiologic placental transfusion is increased by DCC and this increases 20-30% blood volume and 50% red cell volume in infants(2).AOGO committee opinion says there is small increase in bilirubin level in DCC cases which requires photo therapy[1]. Studies shows no increase in postpartum hemorrhage in delayed cord clamping.[8] The aim of this study is to determine the effect of delayed cord clamping on hematological parameter of term neonates.

METHODS

After getting ethical clearance (DMR/IMSSH/SOA/180274) this Prospective observational study was conducted in department of obstetrics and gynecology, IMS and SUM hospital between August 2019 – July 2020. Nonprobability convenient sampling was done. The labour patients admitted to the hospital meeting the following selection criteria were included in the study. The inclusion criteria's were gestational age between 37-42 weeks, expected birth weight > 2500gms, singleton birth, vertex presentation and good antenatal care and the exclusion criteria were mothers with haemorrhage, hemodynamic instability, preeclampsia or eclampsia, gestational diabetes mellitus, renal disease, cardiopathies or connective tissue diseases and foetal complications like Rh incompatibility, babies born asphyxiated, meconium-stained liquor, foetal congenital anomalies, malpresentation, nuchal cord and instrumental delivery.

The timing of cord clamping differs from surgeon to surgeon as there is no definite protocol in the hospital for the same. The timing of cord clamping was noted with the help of a stop watch by a single observer to avoid bias. Injection oxytocin 10 units in iv infusion was given to each mother after the delivery of the baby as per the hospital protocol. Usually, the babies are kept at the level of the introitus in normal delivery and also in cesarean delivery. According to the timing of umbilical cord clamping neonates were divided into 2 groups. The neonates in which cord clamping was done within 15 seconds were considered in the ECC group and neonates in which cord clamping was performed after 1 min of delivery were considered in DCC group. As per our hospital protocol the neonates were observed for 48 hours for the estimation of PCV, hemoglobin and serum bilirubin (total, direct, indirect bilirubin). PCV more than 65 was considered as polycythaemia, Hb level more than 11 was considered normal. Serum bilirubin level was plotted in the Bhutani chart to screen the high-risk cases. For the cases in the high-risk zone a repeat serum bilirubin was done after 4-8 hours and the value plotted in the American academy of paediatrics phototherapy guideline chart and phototherapy started if required. The neonates requiring phototherapy and their outcomes were observed.

The data collected were statistically analysed by using SPSS version 20. Mean ± standard deviation or rate (%) was used to express the results. Significance of the data was tested using ANOVA test. p value < 0.05 was considered statistically significant.

RESULTS

A total of 107 subjects were observed and analysed till discharge. Out of which 56 patients were in DCC group and 51 patients were in ECC group.

Table 1. Demography

Variables	DCC	ECC	*P-value*
Mean Age in Years	28.0 ± 4.929	29.06 ± 4.58	0.136
Primigravida	50	52.9	0.681
Multigravida	50	47.1	0.681
Mean gestational age in weeks	38.59 ± 1.05	38.68 ± 1.18	0.736
Cesarean section	51.8	58.8	0.318
Vaginal delivery	48.2	41.2	0.318
Mean Hb (gm%) of mother	11.78 ± 1.13	11.75 ± 1.09	0.874
Mean PCV (%) of mother	35.91 ± 3.43	36.14 ± 3.97	0.756

In Table 1 the demographic data are represented such as mean age of patients was 28.0 ± 4.929 years and 29.06 ± 4.58 years in the DCC and ECC group respectively which was statistically insignificant (p=0.136). In DCC group, 50% mothers were primigravida and 50% were multigravida, whereas in the ECC group primigravida was 52.9%and multigravida was 47.1%. The mean gestational age in DCC group was 38.59 ± 1.05 and 38.68 ± 1.18 weeks in ECC group (p = 0.736). 51.8% of patients underwent cesarean section and 48.2% underwent vaginal delivery in DCC group whereas 58.8% underwent LSCS and 41.2% underwent vaginal delivery in ECC Group. The mean Hb of the mother in DCC group was 11.78 ± 1.13 gm% and the mean Hb of mother in ECC group was 11.75gm% ± 1.09 while the mean PCV in DCC and ECC group was 35.91%± 3.43 and 36.14%± 3.97 respectively and the difference of mean Hb and mean PCV between both groups were not statistically significant. There was no significant demographic difference between both the groups.

Table 2. Distribution of Bilirubin of Neonate According to the Risk Category (Bhutani chart) and Phototherapy

Total bilirubin in neonate (mg/dl)	No of Cases	(%)	Mean (Total Bilirubin in mg/dl) ± SD	*P-value*	No of cases requiring photo therapy	(%)	*P-value*
DCC			12.36 ± 2.93	0.359	16	66.67	0.009
Low Risk (<11)	14	25.9					
Low Intermediate (11-13.2)	16	29.6					
High Intermediate (13.2-16)	21	38.9					
High (>16)	3	5.6					
Total	56	100					
ECC			11.82 ± 3.09		14	82.35	
Low Risk (<11)	21	41.2					
Low Intermediate (11-13.2)	15	29.2					
High Intermediate (13.2-16)	10	19.6					
High (>16)	5	9.8					
Total	51	100					

In the DCC group maximum number of neonates had total bilirubin between 13. 16 mg/dl, that accounts for 38.9% which falls under high intermediate risk group of Bhutani chart while in the ECC group total bilirubin of maximum neonates was less than 11mg/dl which accounts for 41.2% and they come under low-risk group of Bhutani chart. The mean of the total bilirubin in the DCC group was 12.36 ± 2.93 mg/dl and the mean total bilirubin of neonate in ECC group was 11.82 ± 3.09 (p= 0.359) mg/dl. 66.67% neonates received phototherapy in the DCC group and 82.35% neonates received phototherapy in the ECC group which was statistically significant (p=0.009).

Table 3. Statistical Representation of Different Groups

Groups		Range	Mean ± Standard Deviation	F-statistics	*P-value*
HB (gm%)	DCC	14.4-22.5	18.69±1.98	12.003	0.001*
	ECC	13.8 – 22.1	17.39 ± 1.88		
PCV (%)	DCC	41.4 – 66.0	53.35 ± 5.84	12.254	0.001*
	ECC	40.1 – 61.8	49.63 ± 5.07		
Total Bilirubin(mg/dl)	DCC	4.97 – 66.0	12.36 ± 2.93	0.851	0.359
	ECC	3.59 – 19.9	11.82 ± 3.09		

*Significant at 5% level of significance

The two-way ANOVA test showed statistically significant difference between the DCC and ECC group means of Hb Samples (F=12.003, p = 0.001). There is statistically significant difference between the DCC and ECC group means of PCV Samples (F=12.254, p = 0.001). There is no statistically significant difference between the DCC and ECC group means of total bilirubin samples (F=0.851, p = 0.359).

DISCUSSION

The aim of this study was to compare the hemoglobin, haematocrit and serum bilirubin levels between early and delayed cord clamping groups in term infants. In our study, in both the groups maximum mothers were within the age group of 25-30years. The mean ages were 28.17±4.929 and 29.17±4.58 years in the DCC and ECC group, respectively. There was no statistically significant difference in mean age between the two groups(p = 0.136). Mean maternal age was 26.27±4.59 and 26.17±4.38 years in ECC and DCC group respectively.[9] Mean maternal age of DCC group was 27.93±4.88 and ECC group it was 27.82±6.61. In both the studies the mean maternal age was similar to our studies.[10]

In this study the maximum number of patients delivered at 39-40 weeks period of gestation the mean gestational age at delivery being 38.59 weeks ± 1.05 in the DCC group and maximum number of patients were delivered at 38-39 weeks in the ECC group and the mean gestational age being 38.68 weeks ± 1.18 in the ECC group (p = 0.736) which was statistically insignificant.

In the present study we found that 50% are primigravida and 50% are multigravida in the DCC group whereas 52.9% are primigravida and 47.1% are multigravida in the ECC group. In our study in the DCC group 51.8% mothers delivered by cesarean section and 48.2% mothers delivered vaginally and in the ECC group 58.8% mothers delivered by cesarean section and 41.2% mothers delivered vaginally, the rate of cesarean section is higher in our hospital being a tertiary care centre and receiving complicated cases.

In this study in the DCC group the mean hemoglobin level of mothers was 11.78 gm% ± 1.13 and the mean Hb of mothers in ECC group was 11.75gm% ± 1.09 (p=0.874) which was statistically insignificant. In our study maximum number of mothers (55.4%) had hematocrit between 35-40% and the mean hematocrit being 35.91% ± 3.43 in the DCC group and maximum mothers (45.1%) in the ECC group had hematocrit between 35-40% and the mean hematocrit being 36.14% ± 3.97 (p=0.756) which is not statistically significant. This was similar to the mothers mean hematocrit in the third trimester was 36.8 ± 2.6% in the DCC group and 36.1± 2.6% in the ECC group (p= 0.08)which is also statistically insignificant.[11]

In the present study it is seen that in maximum number of neonates who underwent delayed cord clamping, the haemoglobin level was found to be between 19-22gm/dl (57.1%) and the mean hemoglobin being 18.69 ± 1.98 gm%. In the infants who underwent early cord clamping, maximum number of infants had hemoglobin between 15-18gm/dl (70.6%) and the mean hemoglobin being 17.39 ± 1.88 gm% (p=<0.001) which is statistically significant. This finding is similar to other [12,13]. Mean infant hemoglobin at 48hr after birth was 16.51±1.71 and 15.16±2.27 gm% respectively(p<0.001)[10].

Venous hematocrit was found to be higher in the delayed cord clamping group than in infants who had undergone early cord clamping after birth. The mean hematocrit in DCC was found to be 53.35 ± 5.84% and 49.63±5.07% in the ECC group and the difference was found to be statistically significant (p =<0.001). Polycythemia was seen only in one neonate who underwent DCC which was not statistically significant. This

did not result in any adverse outcome. Significant higher level of hematocrit [9]. A randomized controlled trial shows greater hematocrit level in delayed cord clamping group with statistical significance.[7] In a randomized trial demonstrates increase in mean hematocrit level significantly in DCC group.[14]

DCC helps in placental blood transfusion. So chance of hyperbilirubinemia is expected which has prevented many obstetrician to adopt DCC. In our study in the DCC group maximum number of neonates (38.9%) had serum bilirubin level within 13.2mg/dl – 16mg/dl. They were in high intermediate risk zone of Bhutani chart and it was seen that three infants had total bilirubin above 16mg/dl which made them fall under high-risk group of Bhutani chart. They were managed by phototherapy and none of the neonates required exchange transfusion. In ECC group maximum number of neonates (29.2%) had total bilirubin serum between 11-13.2mg/dl which were in the low intermediate category of Bhutani chart and surprisingly five infants had total bilirubin more than 16 mg/dl in the ECC group which came under high-risk group. The mean total bilirubin in the DCC group was found to be 12.36±2.93 mg/dl and 11.82±3.09 mg/dl in the ECC group, (p=0.359) which is not statistically significant. In our study 66.67% neonates received phototherapy in the delayed clamping group and 82.35% neonates received phototherapy for hyperbilirubinemia in the ECC group

Significant difference in neonatal polycythemia, hyperbilirubinemia or rate of phototherapy.[2] While increased rate of neonatal jaundice and polycythemia.[5] DCC has no significant effect on incidence of neonatal hyperbilirubinemia, or rate of phototherapy after cesarean delivery.15 Therefore we concluded that DCC improves the hematological outcome of the neonate without increasing the risk of polycythemia and hyperbilirubinemia. The limitation of our study is that this is a single centre study and only the immediate effect of DCC has been observed. Large multicentric studies with delayed effects of DCC should be carried out.

CONCLUSION

There is no significant increase risk of polycythemia between delayed cord clamping group and early cord clamping group. Delayed cord clamping is not associated with any harmful effects on new-born rather has beneficial effects in increasing in hemoglobin and hematocrit.

Both the groups maximum mothers were within the age group of 25-30 years. The mean ages were 28.17 ± 4.929 years and 29.17 ± 4.58 years in the DCC and ECC group respectively. There was no statistically significant difference in mean age between the two groups (p = 0.136)

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Research Article

Increased Knowledge and Attitudes of Preconception Care using the Dedi Torri Application

Peningkatan Pengetahuan dan Sikap Perawatan Prakonsepsi melalui Aplikasi Dedi Torri

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Abstract

Objective: To determine the increase in knowledge and attitude of preconception care through the application of DeDi torRi.

Methods: Uses pre-experiment using a one group pre-test and post-test design.

Results: Based on the paired t test in the first health education using the DeDi torRi application to the difference in knowledge obtained with a p value of 0.000 in attitudes with a p value of 0.000. Based on paired t test in the second health education using the DeDitorRi application to the difference of knowledge obtained with a p value of 0.000 and an attitude with a p value of 0.000.

Conclusion: Preconception care health education through DeDi torRi (application-based module) and education that is given repeatedly to reproductive age mothers can influence the increase in knowledge and attitude of preconception care.

Keywords: health education applications, preconception care, women of reproductive.

Abstrak

Tujuan: *Untuk mengetahui peningkatan pengetahuan dan sikap perawatan prakonsepsi melalui aplikasi DeDi torRi.*

Metode: *Pre-eksperimen dengan menggunakan rancangan one group pre-test dan post-test.*

Hasil: *Berdasarkan uji paired t test pada pendidikan kesehatan pertama menggunakan aplikasi DeDi torRi terhadap beda pengetahuan yang didapatkan dengan p value sebesar 0,000 pada sikap dengan p value 0,000. Berdasarkan uji paired t test pada pendidikan kesehatan kedua menggunakan aplikasi DeDi torRi terhadap beda pengetahuan yang didapatkan dengan p value sebesar 0,000 dan pada sikap dengan p value 0,000.*

Kesimpulan: *Pendidikan kesehatan menggunakan aplikasi DeDi torRi (aplikasi berbasis modul) efektif dalam meningkatkan pengetahuan dan sikap pada perempuan usia reproduktif terhadap perawatan prakonsepsi.*

Kata kunci: *aplikasi pendidikan kesehatan, perawatan prakonsepsi, perempuan usia reproduktif.*

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INTRODUCTION

Death of pregnant women is still a major problem throughout the world. Based on data from the World Health Organization (WHO) in 2013, maternal mortality rates (MMR) worldwide reached 289,000 per 100,000 live births and 99% occurred in developing countries (WHO, 2014). In Southeast Asia AKI reached 16,000 / 100,000 KH, Indonesia ranks in the top three reaching 190 / 100,000 live births after Timor Leste (270 / 100,000 live births) and Myanmar (200 / 100,000 live births).

The main causes of maternal death in Indonesia are the highest bleeding, hypertension in pregnancy, infection, prolonged labor, abortion, and others. Based on the results of the 2015 Intercensal Population Survey (SUPAS), MMR in Indonesia reached 305 per 100,000 live births. The maternal mortality rate due to hypertension is 27.1%, and deaths due to comorbidities such as cancer, heart disease and tuberculosis (TB) reach 40.8%[1].

The cause of infant death is birth premature, asphyxia and trauma, infections, congenital abnormalities and others[2]. In Yogyakarta the

number of maternal deaths was 34 with 34 cases in 2017. The cause of death in the perinatal group was intrauterine fetal death (IUFD), LBW and asphyxia. Gunung Kidul is the district with the most cases of maternal deaths, 12 cases[3].

Some of these risks require intervention in the preconception period [3]. The time to start services for pregnancy is not after but before conception [4]. The cause of maternal death can be prevented if there is adequate health / education and screening information before pregnancy [5]. Sustainable Development Goals (SDGs) targets reduce MMR to below 70 per 100,000 live births by 2030 [6].

Preconception care is a program launched by WHO in 2012 in Geneva that aims to reduce maternal, infant, disability and to reduce modifiable risk factors for non-communicable diseases. This program is implemented by all countries in the world, especially low and middle income countries commonly called Low and Middle Income Country (LMICs), one of which is Indonesia.

Women's low knowledge about preconception care results in women not utilizing health services before preparing for pregnancy[7]. The Centers for Disease Control and Prevention recommends that early detection and education be given to all men and women of reproductive age before conception to reduce risk.

Health education is the addition of one's knowledge and abilities through learning practice techniques or instruction in order to remember facts by encouraging self-direction and actively providing information[8]. Technology-based education is an innovative pathway for providing health information[9]. The use of cell phones can also be used to provide health education [10]. Mobile-based health applications or Mobile Health (mHealth) have a great opportunity as an effective public health improvement intervention. mHealth can also provide quality information at low and affordable costs, both in terms of users and health service providers[11]. Health interventions using cellular have a positive impact in efforts to prevent and improve health care [12].

The Gabby Preconception Care System is an innovation developed to support preconception care. Online interactive character animation (Gabby) is designed to identify and modify risks during the preconception. To be able to use Gabby, users can access it through the website and need the internet.

The Gabby system consists of screening women at risk during preconception, assessing readiness for behavior change based on their risk factors, educating them based on their risk factors and having a list of my health that can be read by health workers, users can write stories about their health problems that can read by other Gabby users.

Based on the available content, someone is encouraged to use Gabby every week and the material discussed is different for each interaction based on the risks discussed. Although there are many mHealth solutions related to pregnancy, mHealth solutions that focus on preconception care are still rare [13].

The difference with the DeDi torRi application (early detection of preconception risk factors) that will be developed by researchers is that this application consists of 4 features consisting of modules on preconception care, health problem handling modules, knowledge and attitude questionnaires and early detection of risk factors at a time preconception the final result of early detection is whether a woman is in the safe category or not when planning a pregnancy, this application is offline. But in the first phase of this study, the researcher wanted to find out the use of modules to increase knowledge and attitude of preconception care.

METHODS

Table 1. Distribution of Characteristics of Respondents

Characteristics of respondents	Total (n=40)	%
Age		
<35	24	60
≥35	16	40
	40	100
Education		
Low	21	52.5
High	19	47.5
	40	100
Employment		
Not work	38	95.0
Work	2	5,0
	40	100
Parity		
Primipara	13	32.5
Multipara	27	67.5
	40	100
Pregnancy history		
Have	5	12.5
don’t have	35	87.5
	40	100
Disease history		
have	4	10.0
don’t have	36	90.0
	40	100

Previous information about health checks before pregnancy	1	2.5
No	39	97.5
Yes	40	100

This research is a pre-experimental research using one group pre-test and post-test design. The population in this study were all women of reproductive age aged 15-49 who were in the working area of the Gunung Kidul district health office. The sample size is calculated using the Lemsehow formula and the total sample is 40.

The sampling technique used is non probability sampling using purposive sampling. The inclusion criteria in this study were women of reproductive age (15-49 years), at least mothers who had given birth once, mothers who lived in the working area of Wonosari I Puskesmas (Teguhan Hamlet, Wunung Village) in Gunung Kidul district, mothers who could read and write, mothers who can operate smartphones, can be invited to communicate well. Data were analyzed by paired t-test to find out the significance of Increased Knowledge and Attitudes of Preconception Care using the Dedi Torri Application. Data were processed with the help of Statistical Product and Service Solutions (SPSS) for Windows version 22.0.

RESULTS

Respondents in this study were mothers of reproductive age 15-49 years old who were in Wunung village, teguhan hamlet, the working area of Puskesmas Wonosari I and the number of samples were 40 people.

Based on table 1. In the age variable, the majority of respondents were at the age of <35 years, namely 24 people (60%). The characteristics of the latest education are the majority of those with low education (<SLTP) as many as 21 (52.5%). The characteristics of work are the majority of not working 38 people (95.0). The majority parity characteristics of multipara are 27 people (67.5%). Characteristics of previous pregnancy history, the majority did not have a history of previous pregnancy of 35 people (87.5%).

Characteristics of disease history, the majority do not have a history of disease 36 people (90%). Characteristics of previous information about treatment or medical examination before pregnancy, the majority had heard 39 people (97.5%).

Table 2. Distribution of Frequency of Pretest and Post-test I Knowledge of Preconception Care after the First Health Education and Second Health Education

Variable	Knowledge											
First Health Education and Second Health Education	Pretest				First Postest				Second Postest			
	Good		Less		Good		Less		Good		Less	
	n	%	n	%	n	%	n	%	n	%	n	%
	22	55.0	18	45.0	35	87.5	5	12.5	40	100	-	-

Based on table 2. pre-test and first post-test of knowledge in the first health education there was an increase in knowledge namely in the pre-test 18 respondents (45.0%) had less knowledge about preconception care in preparing for a safe and healthy pregnancy and the first post-test of respondents who low knowledge to 5 people (12.5%). First post test and second post test knowledge after the second health education an increase in knowledge that is in the first post test 5 people (12.5%) have less knowledge about preconception care in preparing for a safe and healthy pregnancy and in the post test second (after second health education) all respondents had good knowledge of preconception care in preparing for a safe and healthy pregnancy.

Table 3. Distribution of Pretest and Posttest Frequency Attitudes after the First Health Education

Variable	Attitude											
First Health Education and Second Health Education	Pretest				First Postest				Second Postest			
	Good		Less		Good		Less		Good		Less	
	n	%	n	%	n	%	n	%	n	%	n	%
	26	65.0	14	35.0	38	95.0	2	5.0	40	100	-	-

Table 4. Paired T Test Results Knowledge and Attitudes of Preconception Care in Reproductive Age Women in the First Health Education and Second Health Education

Variable	Pretest	First Post test	Second post test	Mean (95 % CI)	*P-value*
	Mean (SD)	**Mean (SD)**	**Mean (SD)**		
Knowledge	25.43 (4.867)	36.93 (0,917)	38.38 (0.490)	1.450 (1.170-1.730)	0.000
Attitude	54.20	56,85	58,83(1,509)	1.975(1.709-2.241)	0.000

Based on table 4. Knowledge statistical test shows that the first post test score is higher than the pre test that is 36.93. The difference in knowledge before and after the first health education is given is 11.50.

Attitude statistical test shows that the first post test is higher than the pre test that is 56.85. Difference in attitude before and after is 2.65. Statistical tests indicate p value = 0.000 (<0.05), so it can be concluded that health education using the DeDi torRi application can improve knowledge and attitudes towards preconception care in preparing for a safe and healthy pregnancy. The first and second post-test statistical tests had an increase of 38.38. Statistical tests show p value = 0.000 (<0.05), so it can be concluded that health education using the DeDi torRi application and repeated health education can increase knowledge of preconception care in preparing for a safe and healthy pregnancy.

Attitude statistical test shows that the first post test score is higher than the pre test that is 56.85. The difference before and after being given health education is 2.65. The first post-test and second post-test statistical tests were 58.83. Statistical tests show p-value = 0.000 (<0.05), so it can be concluded that health education using the DeDi torRi application and repeated health education can improve attitudes towards preconception care.

DISCUSSION

Effects of Health Education Using the DeDi torRi application on Knowledge Enhancement. The results in table 4 show that there is an influence of health education about preconception care with the application of DeDi torRi on increasing knowledge with a value of p = 0.000 <0.05.Based on the results of health education, health education using the DeDi torRi application can increase mothers' knowledge about preconception care. Modules as an effective health education to influence one's attitude. This media is also useful to increase the target's interest in forwarding messages to others [13].

The advantage of providing preconception health education through the DeDi torRi application is that this module is not made in book form but is made in the form of an application that is DeDi torRi installed on the respondent's smartphone, the application-based module (DeDi torRi) is offline so that it can be read over and over repeated by respondents in different times.

In addition, the application-based module that is provided is also accompanied by images that can describe the contents of the message and the language used is everyday language that is easy to understand. Android-based adolescent reproductive health education applications can increase understanding of adolescent reproductive health. [14]

The influence of health education using the DeDi torRi application to improve attitudes. The results of the study in table 4. show that there is an effect of health education on the improvement of respondents' attitudes about preconception care with a value of p = 0.000 <0.05. Health information in the form of application-based modules makes respondents tend to experience more positive behavioral changes.[15]

Because almost all women and men of reproductive age have access to the internet and or own a cellphone so that mobile health can play a role in providing information that can encourage awareness and ultimately support the implementation of preconception care [12].

Health education using mobile applications can improve nutrition and better lifestyle behaviors[16]. Changes in attitudes to respondents due to the addition of media in providing health education in the form of application-based modules making it possible for mothers to read it at home[17].

The results of this study are in line with the results, which states that mobile applications during pregnancy can increase maternal knowledge, behavior change and improve perinatal health[18]. Based on the research, which states that smartphone applications to promote lifestyles that focus on knowledge, attitudes, social support and apply effective self-regulation techniques to motivate workers with low

education [19].

Cellular health interventions have a positive impact on efforts to prevent and improve health care, such as HIV detection services for adolescents and reproductive-age populations and comprehensive health screening[11]. The application becomes a health promotion strategy and as a monitoring tool. The application can enable users to increase self-monitoring and increase awareness about health [20].

Based on the results , mobile applications that promote smoking cessation are well received by smokers who are hospitalized to give smokers an understanding of the effects of smoking [21].

The Smart Moms application was successful in increasing knowledge, attitudes and behavioral change interventions in the form of 18 modules which began at 13 weeks-24 weeks' gestation. Modules contain weight management treatments to encourage ideal body weight, self monitoring and healthy food recipes [22].

Effects of Health Education Provided Repeatedly Using the DeDi torRi application Towards Knowledge and Attitude Improvement

The average difference in the first pre-test and post-test in the first health education is 11.50 and the average difference in the post-test I post-test II in the second health education is 1.45 means that there is an increase in knowledge about preconception care. Difference in average attitude at the time of pre-test and post-test I 2.60 and the difference in post-test I post-test II that is 1.98 means that there is an increase in the attitude of preconception care.

The results of this study are consistent with the results, that reproductive health health education provided repeatedly is effective in increasing adolescent knowledge and attitudes about reproductive health [23].

CONCLUSION

Preconception care health education through DeDi torRi (application-based module) and education that is given repeatedly to reproductive age mothers can influence the increase in knowledge and attitude of preconception care. Health workers can consider methods of providing information or health education through an application-based module for mothers who are planning a pregnancy so that the pregnancy can run safely and healthily.

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Research Article

Return of Fertility after Discontinuation of Contraception According Type of Contraception, Duration of Use, Age and Body Mass Index

Kembalinya Kesuburan setelah Penghentian Alat Kontrasepsi Berdasarkan Jenis Kontrasepsi, Lama Pemakaian, Usia dan Indeks Massa Tubuh

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Abstract

Objective: To determine the relationship between the type of contraception, duration of use, BMI, and age on the return of fertility.

Methods: This was an analytic observational study with a cross-sectional design. The subjects in this study was 123 multigravida mothers who had met the inclusion criteria, namely with a history of regular intercourse and the exclusion criteria in this study were multigravida mothers with a history of abortion and failure of the family planning method. Data were collected by direct interviews and medical record data. Data were analyzed using Chi-square test and Logistic Regression test.

Result: The results of the Chi-square analysis showed a relationship between the type of contraception (p=0.001;OR=1.29) and age (p=0.031;OR=4.69) with the return of fertility. However, there was no correlation between the duration of use (p=0.964;OR=0.97) and BMI (p=0.246;OR=0.50) with the return of fertility. In the logistic regression test, there was no partial effect of the type of contraception (p=0.997;OR=0.22) and age (p=0.058;OR=0.01).

Conclusion: Based on the results of the analysis, it can be concluded that there is a relationship between the type of contraception and age with the return of fertility after family planning, where non-hormonal contraceptives and <30 years of age return to fertility faster, namely <1 year, but there is no relationship between duration of use and BMI with the return of fertility after family planning.

Keywords: contraception, family planning, fertility.

Abstrak

Tujuan: *Mengetahui hubungan jenis kontrasepsi, lama pemakaian, IMT, dan usia terhadap kembalinya kesuburan.*

Metode: *Penelitian ini merupakan penelitian observasional analitik dengan desain potong lintang. Subjek penelitian ini adalah ibu multigravida yang telah memenuhi kriteria inklusi yaitu dengan riwayat senggama teratur dan bersedia menjadi responden serta kriteria ekslusi dalam penelitian ini adalah ibu multigravida dengan riwayat abortus dan kegagalan metode KB. Besar subjek dalam penelitian ini sebanyak 123 orang. Pengambilan data dilakukan dengan wawancara langsung dan melihat data rekam medis. Analisis data dilakukan uji statistik Chi-square dan uji Regresi Logistik.*

Hasil: *Hasil analisis dengan Chi-square, menunjukan adanya hubungan jenis kontrasepsi (p = 0,001; OR = 1,29) dan usia (p=0,031; OR = 4,69) dengan kembalinya kesuburan. Namun, tidak terdapat hubungan lama pemakaian (p= 0,964; OR =0,97) dan IMT (p= 0,246; OR =0,50) dengan kembalinya kesuburan. Pada uji regresi logistik tidak terdapat pengaruh parsial dari jenis kontrasepsi (p=0,997; OR =0,22) dan usia (p=0,058; OR=0,01).*

Kesimpulan: *Berdasarkan hasil analisis yang dilakukan dapat disimpulkan terdapat hubungan jenis kontrasepsi dan usia dengan kembalinya kesuburan pasca KB, dimana pada jenis kontrasepsi non hormonal dan usia < 30 tahun lebih cepat kembali subur yaitu < 1 tahun, namun tidak terdapat hubungan lama pemakaian dan dengan kembalinya kesuburan pasca KB.*

Kata kunci: *keluarga berencana, kesuburan, kontrasepsi.*

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INTRODUCTION

The Family Planning Program is a government program in tackling population growth in Indonesia. This program aims to prevent or delay pregnancy. In the implementation of the Family Planning program, there are several methods used to prevent or delay pregnancy, namely the natural and modern family planning method using contraceptives[1]. The concern of women who use or are considering using contraceptives is the effect of contraception on future fertility because about 15% of couples of childbearing age experience infertility. Many women are concerned about the use of oral contraceptives which can cause fertility problems after discontinuation of use and believe that oral contraceptives can cause secondary amenorrhea associated with anovulation and reduced reproductive fertility. Post-pill amenorrhea is amenorrhea that occurs more than 1 year after discontinuation of combined oral contraceptives[2]. An important property that should be possessed by reversible contraceptives is that they do not affect future fertility. Delay and decreased fertility after discontinuation of contraception raises user dissatisfaction and reduces interest in using contraception[3].

Return to fertility after discontinuation of oral contraceptives has different effects between nulliparous and multigravida. In nulliparous, it reached 42 months, and in multigravida 30 months after discontinuation. The delayed infertility is due to the suppression of reproductive hormones in the hypothalamus and pituitary[4]. Return to fertility after discontinuation of Depo Medroxyprogesterone Acetate (DMPA) is thought to have a longer duration than other contraceptives[5]. Normally, fertility will return 4 months after using DMPA. Delayed return to fertility after using DMPA is not caused by damage or genetic abnormalities of the organ, but due to the continuous release of DMPA after injection[6]. After stopping contraception, fertility is not distrubed[7].

Lifestyle is a risk factor for infertility. Women who have a Body Mass Index (BMI) of more than 29 Kg / m^2 and less than 19 Kg / m^2, tend to take a longer time to get pregnant[8]. Obesity can impact the decreased ability to get pregnant. Obesity can affect the oocyte, endometrium, and embryo preimplantation[9]. Age can also affect the quality of the oocytes produced. The decrease in the number of follicles occurs with increasing age[10]. Female fertility decreases at the age of 32 years, greatly decrease after the age of 37 years[11].

The effectiveness of using oral contraceptives is very high when used regularly and correctly[12]. The effectiveness of injection contraception reaches 99% and in implant contraception the failure rate is 0.3%-1.0% per year[13]. In the use of non-hormonal contraceptives, it is known that the effectiveness is quite high when used correctly the use of IUD contraceptives the failure rate is 0.8 per 100 people each year[14]. The effectiveness of condoms is up to 98% when used correctly and consistently, while using condoms the effectiveness is 85%[1].

Until now, the use of hormonal contraceptives is more attractive to contraceptive acceptors because it is easier to use. Along with the increasing number of contraceptive users, the effect of contraception on fertility is still a concern for women of childbearing age. The ideal contraception is one with minimal side effects, high effectiveness, and rapid return to fertility[15]. From the description above, the return to fertility after discontinuation of contraception is a problem that needs attention. Previous research that has been conducted in Indonesia has compared types of injectable and oral contraceptives with the return to fertility after discontinuation. However, no research has been done on the factors of age and Body Mass Index (BMI) which can affect the return of fertility after using contraceptives. Therefore, the researchers wanted to know the relationship between the type of contraception, the length of time used, the age, and the Body Mass Index (BMI) on the return of fertility after family planning. By knowing the relationship between the type of contraception, the duration of use, age, and Body Mass Index (BMI) on the return of fertility, it is hoped that it can help consider the selection and placement of contraceptives.

METHODS

This study was an analytic observational study with a cross-sectional study design. This study was conducted by direct interviews with respondents and looking at medical record data. The data that has been obtained were analyzed using IBM SPSS Statistics for Windows version 25.0. This study was conducted in the Pakem Health Center working area in August - October 2020.

The subjects in this study were multigravida

pregnant woman at Pakem Health Center in Yogyakarta who met the inclusion criteria, namely post-family planning multigravida pregnant women with a history of regular intercourse and willing to be a respondent and meet the exclusion criteria, namely multigravida post-family planning mothers with a history of irregular intercourse, a history of abortion and pregnancy due to failure of the contraception method.

The subjects in this study were selected through a non-probability sampling method using a purposive sampling method. Data obtained by interviews and looking at medical record data. In this study, respondents were divided into two groups, namely being able to return to fertility in <1 year and ≥ 1 year. The data obtained were analyzed statistically using the chi-square test which aims to determine the relationship between the type of contraception, duration of use, age, and Body Mass Index (BMI) on the return of fertility.

RESULTS

Table 1. Characteristics of the Subjects and Univariate Analysis Table

Characteristics	Frequency	%
Type of Contraception		
Non Hormonal	40	32.5
Hormonal	83	67.5
Age (years)		
< 30	39	31.7
≥ 30	84	68.3
Education		
< High School	26	21.1
≥ High School	97	78.9
Body Mass Index (kg/m²)		
20 – 28	83	67.5
≤ 19 or ≥ 29	40	32.5
Duration of use (years)		
≤ 1	19	15.4
> 1	104	84.6
Return to fertility (years)		
≤ 1	104	84.6
> 1	19	15.4

Most of the subjects were ≥ 30 years old, most of the subjects' educational status was > Senior High School, most of the subjects used hormonal contraception, most of the subjects had a body mass of 20 Kg / m^2 - 28 Kg / m^2, most of the subjects used contraception> 1 year, and most of the subjects returned to fertile ≤ 1 year.

Table 2. Bivariate Analysis Table of Relationship Type of Contraception, Age, Duration of Use, and BMI to Return of Fertility

Variable	Return to Fertility				Total		OR	*P-value*
	≤ 1 years		≤ 1 years					
	N	%	N	%	N	%		
Type of Contraception							1.24	1.24
Non Hormonal	40	32.5	0	0.0	40	32.5		
Hormonal	64	52	19	15,4	83	67.5		
Age (years)							4.69	4.69
< 30	37	30.1	2	1,6	39	31,7		
≥ 30	67	54.5	17	13,8	84	68.3		
BMI (kg/m²)							0.50	0.50
20 – 28	68	55.3	15	12.2	83	67.5		
≤ 19 or ≥ 29	36	29.3	4	3,3	40	32.5		
Duration of use (years)							0.97	0.97
≤ 1	16	13.0	3	2.4	19	15.4		
> 1	88	71.5	16	13.0	104	84.6		

The results of the Chi-Square statistical test on the relationship between the type of contraception and the return of fertility, the p-value is 0.001 (p <0.05). The p-value <0.05 in the analysis test shows that the hypothesis is accepted and there is a significant relationship between the type of contraception and the return of fertility after family planning.

The results of the Chi-Square statistical test for the age variable with the return of fertility in Table 2 obtained a p-value of 0.031 (p <0.05). The analysis test shows that the hypothesis is accepted and there is a significant relationship between age and the return of fertility after family planning. Chi-Square statistical test for the variable Body Mass Index (BMI) with the return of post-birth control fertility, obtained a p-value of 0.246 (p> 0.05). The p value> 0.05 in the analysis test shows that the hypothesis is rejected, where there is no significant relationship

between Body Mass Index (BMI) and the return of fertility after family planning. In the statistical test, the correlation between the duration of using contraceptives and the return of fertility using Fisher's test was obtained a one-way significance value of 0.597 (p> 0.05). P value> 0.05, so there is no significant relationship between the duration of using contraceptives and the return of fertility.

Table 3. Multivariate Analysis Table of Relationship Age, Type of Contraception, and BMI to Return of Fertility

Variable	*P-value*	OR	B
Age (< 30 years)	0.058	0.01	-19.89
Type of Contraception (Non Hormonal)	0.997	0.22	-1.50
BMI (≤ 19 Kg/m^2 or ≥ 29 Kg/m^2)	0.529	1.49	0.40
Constant	0.035	0.29	-1.21

The results of the logistic regression test showed that the p-value for the variable age was 0.058, the p-value for the variable type of contraception was 0.997, and the p-value for the BMI variable was 0.529. From the results obtained, the variables age, type of contraception, and body mass index did not have a partial effect on the return of fertility. So it can be said that age (<30 years and ≥ 30 years) and the type of contraception (non-hormonal and hormonal) influence the return of fertility simultaneously, where the constant value (B = -1.21) shows if the age is <30 years with type non-hormonal contraception, it is possible to return to fertility ≤ 1 year. The value of B in the age variable (B = -19.89) shows that if the age is <30 years, the return of fertility is ≤ 1 year. The variable type of contraception (value B = -1.50) shows that when using non-hormonal contraceptives, the return of fertility is ≤ 1 year. Whereas the BMI variable (value B = 0.40) shows if BMI ≤ 19 Kg / m^2 or ≥ 29 Kg / m^2, then the return of fertility is> 1 year.

DISCUSSION

The results of the chi-square analysis regarding the relationship between the type of contraception and the return of fertility after birth control, the value of p = 0.001, p-value <0.05, indicates that there is a significant relationship between the type of contraception and the return of fertility. This research is in line differences in fertility restoration rates after family planning, The data show that the likelihood of getting pregnant is strongly influenced by the type of contraception. In this study it was shown that the rate of return to fertility after discontinuation of the IUD and oral contraceptives was shorter than that of implants and injections[7]. The bioavailability of oral contraceptives in the blood must be completely cleared to restore fertility after discontinuation of oral contraceptives. Link between impaired fertility and use of oral contraceptives is the use of high doses of oral contraceptive formulations. Thus, it can be concluded that the use of oral contraceptives can return to fertility more quickly since low dose contraception regimen is more frequently used nowadays [3,16]. This study is not in line which states that there is no significant effect of the type of contraception and the duration of contraception with the return of fertility[3].

In the study it is found that there was a significant relationship between age and the return of fertility after birth control with a p-value = 0.031. The age of users is related to the return of fertility because as a woman ages, the number of oocytes produced decreases, and the quality decreases[11]. Entering the age of 35, female fertility will decrease and decrease drastically at the age of 37 years.

Based on data analysis with chi-square, it was found that p-value = 0.246, p value> 0.05 in the analysis test showed that the hypothesis was rejected and the null hypothesis was accepted, namely there was no relationship between Body Mass Index (BMI) and the return of fertility after family planning. In infertile patients, AMH is positively correlated with BMI, especially in patients under 35 years of age, normal body weight, and normal ovarian reserve. Also, the appearance of excessive mild obesity appears to be associated with higher AMH values. This study is in correspondence which found no relationship between body mass index (BMI) and AMH serum level. This discrepancy in the results of these studies could be due to the heterogeneity of the populations analyzed[17]. On the other hand, where there is a relationship between body mass index (BMI) and female infertility. The function of the female reproductive organs is influenced by nutritional status, this is because to reach sexual maturity and increase fertility requires a good nutritional status[18].

In this study it is known that there was no significant relationship between the length of time using contraceptives and the return of fertility after family planning, where p-value = 0.964, p value> 0.05 in the analysis test showed that the hypothesis was rejected and the null hypothesis was accepted. The duration of contraceptive use does not affect the likelihood of becoming pregnant after contraception is stopped. Therefore, women do not need to be afraid of using contraceptives for a long time, because it will not affect fertility in the future[7]. Research related to the relationship between the length of time using DMPA injection contraceptive with the return of menstruation, where there was no relationship between the length of time using DMPA injection with the return of menstruation after cessation of use, the length of return of menstruation was influenced by several factors. There is no correlation between long-term use of injecting contraceptive of DMPA and reproductive reversibility[6]. In this study it was stated that there was an effect of the duration of IUD contraceptive use on the fertility of its users[5].

In table 3, the results of the analysis using logistic regression test, where the p-value of the age variable is 0.058 (p> 0.05), the p-value of the Contraception Type variable is 0.997 (p> 0.05) and the Body Mass Index variable p-value is 0.529 (p> 0.05) which means that age, type of contraception and Body Mass Index (BMI) do not have a partial effect on the return of fertility and the variables of age and type of contraception have a simultaneous effect. When using non-hormonal contraceptives and aged <30 years, fertility returns ≤ 1 year. Whereas at BMI ≤ 19 Kg / m^2 or ≥ 29 Kg / m^2, the possibility of returning to fertility is> 1 year.

CONCLUSIONS

Based on the research above, it can be concluded that there is a relationship between the type of contraception and age on the return to fertility after birth control where the non-hormonal contraceptives and age <30 years return to fertility (<1 year) . There is no significant relationship between the duration of contraceptive use and BMI with the return of fertility.

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Research Article

Risk of Malignancy Index 3 (RMI3) Performance as a Predictor Advanced Stage Epithelial Ovarian Carcinoma used for NACT

Perfoma Risk of Malignancy Index 3 (RMI3) sebagai Prediktor Karsinoma Ovarium Epithelial Stadium Lanjut untuk Pertimbangan Pemberian NACT

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Abstract

Objective: To find a non-invasive method in determining preoperative NACT administration. The method used is RMI 3 diagnostic scoring where this method can be used at the beginning of the examination and the results do not require a long time. assessed whether RMI3 performance can be used as a predictor of advanced epithelial ovarian carcinoma in the interest of NACT.

Methods: A cross-sectional study with samples of all patients suffering from ovarian cancer for the past 5 years, from January 2016 to January 2020 who had been diagnosed at the Gynecology Polyclinic using medical record data from the Gynecology Oncology Polyclinic and Anatomical Pathology Laboratory, RSUD dr. Saiful Anwar in the form of age, demographics, menopausal status, Ca125, ultrasound results. Data is processed using SPSS version 25.0.

Results: The number of initial samples of this study was 253 women, but after being included in the inclusion and exclusion criteria, there were 106 samples. After staging by an authorized clinician, there were 48 patients with early stage and 58 patients with advanced stage. Between the results of the RMI 3 score and the histopathological results on the ROC curve, it was found that the p-value was less than 0.05 ($p<0.05$) with an area of 0.945 and 95% CI of 0.907 - 0.982. P-value less than 0.05 indicates that the RMI3 score is very good for predicting advanced epithelial ovarian carcinoma. With a sensitivity value of 86% and a specificity of 83%, the cut of value RMI score 3 to be a predictor of advanced ovarian carcinoma is 888.3 and PPV 86.2%, NPV 83.3% and an accuracy value of 84.9%.

Conclusion: RMI 3 is very good to be used as a predictor of advanced ovarian carcinoma so that it is expected to be a reference for the administration of neoadjuvant chemotherapy in primary ovarian carcinoma which is predicted to be less likely to achieve optimal cytoreduction if surgery is performed to reduce the risk of mortality, morbidity and bad prognosis.

Keywords: advanced stage, diagnostic test, ovarian carcinoma, NACT, risk of malignancy index, RMI 3, USG.

Abstrak

Tujuan: Untuk mencari metode non invasive dalam penentuan pemberian NACT pre operatif. Metode yang digunakan adalah scoring diagnostic RMI 3 dimana metode ini bisa digunakan saat awal pemeriksan dan hasil nya tidak memerlukan waktu yang lama. menilai apakah performa RMI3 dapat digunakan sebagai prediktor karsinoma ovarium epitelial stadium lanjut dalam kepentingan pemberian NACT.

Metode: *Penelitian observasional analitik jenis studi retrospektif cross sectional dengan sampel semua pasien yang menderita kanker ovarium selama 5 tahun kebelakang yaitu dari bulan januari 2016 sampai dengan Januari 2020 yang telah didiagnosis di poli Ginekologi menggunakan data rekam medis poli Ginekologi Onkologi dan Laboratorium Patologi Anatomi RSUD dr. Saiful Anwar berupa usia, demografi, status menopause, Ca125, hasil USG. Data diproses menggunakan progam SPSS versi 25.0.*

Hasil: *Jumlah sampel awal penelitian ini adalah 253 perempuan, tetapi setelah dimasukan ke dalam kriteria inklusi dan eksklusi terisisa 106 sampel. Setelah di staging oleh klinisi yang berwenang, di dapat 48 pasien dengan stadium awal dan 58 pasien dengan stadium lanjut. Antara hasil skor RMI 3 dan hasil histopatologi pada kurva ROC didapatkan bahwa nilai p-value kurang dari 0,05 ($p<0.05$) dengan luas area sebesar 0,945 dan 95% CI sebesar 0,907 – 0,982. P-value kurang dari 0,05 menunjukkan bahwa skor RMI3 sangat baik untuk digunakan dalam memprediksi karsinoma ovarium epitelial stadium lanjut. Dengan nilai sensitifitas sebesar 86% dan spesifisitas sebesar 83% sehingga cut of value skor RMI 3 untuk menjadi prediktor karsinoma ovarium stadium lanjut adalah sebesar 888,3 dan PPV 86,2%, NPV 83,3% dan nilai akurasi sebesar 84,9%.*

Kesimpulan: *RMI 3 sangat baik untuk digunakan sebagai predictor karsinoma ovarium stadium lanjut sehingga diharapakan dapat menjadi acuan pemberian neoadjuvant kemoterapi pada karsinoma ovarium primer yang diprediksi kecil kemungkinannya mencapai sitoreduksi yang optimal bila dilakukan pembedahan untuk menurunkan risiko mortalitas, morbiditas dan prognostik yang kurang baik.*

Kata kunci: *karsinoma ovarium, risk of malignancy index, RMI 3, stadium lanjut, uji diagnostik, USG, NACT.*

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INTRODUCTION

Worldwide, ovarian cancer is the sixth most frequently diagnosed cancer. In the United States, ovarian cancer is the most common cancer of the four deadliest malignancies in women. The 5-year survival rate is relatively low overall in stages III and IV according to FIGO[1]. Ovarian cancer usually has few specific symptoms, more than 70% of patients are diagnosed at an advanced stage, with a 5-year survival rate of less than 30%. In contrast, 25% of patients diagnosed with stage I ovarian cancer have a 5-year survival rate of up to 90%[2].

The increasing morbidity, mortality and bad prognostic of debulking measures carried out in order to prove an ovarian carcinoma at an early stage is a dilemma, so that neoadjuvant chemotherapy is used in primary ovarian carcinoma which is predicted to be less likely to achieve optimal cytoreduction when surgery is performed[3]. So that it is necessary to give NACT before surgery, there is a dilemma if the clinician does not give NACT to patients with advanced stages, because patients with advanced cancer who have already had surgery have a high risk if the remaining residue is less than 1 to 2 cm[4].

Currently, the procedure for determining NACT is still based on two methods, ascites cytology and laparoscopy. And the requirement for giving NACT is to attach the results of the Anatomical Pathology laboratory. There are weaknesses of these two methods, the weakness of the ascites cytology method is its low validity, false negative value of 30%, for a false positive value of 6.38% even though the specificity value is high at 93% but the validity of this method is still classified as still weak because of the large percentage of patients who should have received NACT but were not given it [6]. The weakness of the second method, namely laparoscopy, is that it requires equipment technology and skilled operators. In terms of time, it is also a further weakness of this method, such as it takes a long time from the time the patient is examined, then scored, the laparoscopy process, waiting for histopathological results which is quite long[6]. So a non-invasive method with high accuracy is needed, the process is simple, the results can be obtained immediately in one examination.

The lack of early identification of precancerous lesions and the non-specificity of early symptoms lead to delays in diagnosis. When detected at an early stage, the disease is highly curable. Diagnosis during surgery is a more accurate opportunity to determine ovarian malignancy through histopathological examination of frozen section[7]. However, there is a dilemma if the clinician does not give NACT to patients with advanced stages. Because patients with advanced stage carcinoma who have already undergone surgery have a high risk such as the risk of morbidity, mortality and prognostic. If the remaining residue is less than 1 to 2 cm, is the bad prognosis.

Several examination formulas have been developed in various countries which are carried out in order to establish a preoperative diagnosis of ovarian cancer[8]. In addition to the Risk of malignancy index (RMI) there are many formulas for examining the suspicion of preoperative ovarian cancer such as (ROMA), (ROCA). Risk of Malignancy Index 3 (RMI3) is the result of the calculation of U x M x CA 125. Ultrasonography includes: multilocularity, dense area, bilaterality, ascites, and intra-abdominal metastases yielding one point each and postmenopausal status score M = 3; premenopausal status score M = 1. Serum CA 125 U/mL was entered directly into the equation[9].

Microscopic examination is important in predicting tumor appearance and determining the best therapeutic approach. Histopathological examination is still the gold standard for definitive diagnosis in cases of malignant ovarian tumors and is a requirement for NACT[10]. In the early stages, postoperative adjuvant chemotherapy is given to high-risk groups of patients. However, the data show that there are 60% of high-risk early-stage cancers that do not recur even without chemotherapy. Until now, there are still no accurate criteria or methods to determine which group of patients have a tendency to experience recurrence, so the management of high-risk early-stage cancer patients is entirely given chemotherapy. The ability to determine groups of patients who have a tendency to relapse will allow more selective therapy and will certainly reduce patient morbidity due to the cytotoxic side effects of chemotherapy[11].

Giving NACT requires accuracy from RMI which is considered capable of being a predictor and clinician's consideration in giving NACT. It is hoped that there will be no errors in the administration of NACT therapy, such as patients who should not require chemotherapy, but are given chemotherapy. Therefore, an ideal RMI3 value is needed for consideration of giving

NACT while taking into account the side effects of the chemotherapy. This is the first study to examine a preoperative non-invasive method for determining NACT administration to patients with advanced ovarian carcinoma.

METHODS

This is a cross-sectional study. In this study, the researchers tried to find the relationship between variables, namely by conducting an analysis of the data collected. This study was conducted in April 2021. The sample population is all populations suffering from ovarian malignancy in the oncology department of the Department of Obstetrics and Gynecology RSUD dr. Saiful Anwar Malang. The research sample was taken with a retrospective study, namely data collection from the medical record of patients suffering from ovarian malignancies for the last 5 years, from January 2016 until January 2020. Samples were also taken from the Anatomical Pathology Laboratory of RSUD dr. Saiful Anwar Malang. After all medical records of patients suffering from ovarian carcinoma were collected, a data collection sheet was made containing the necessary medical record data such as age, patient demographics, menopausal status, CA 125 levels, ultrasound results and histopathology results.

In this study, data analysis techniques were used to measure the accuracy of the Risk Malignancy Index 3 (RMI3), assessed by positive predictive value, negative predictive value, sensitivity, specificity and accuracy value. To determine the cut of value of RMI3 with histopathological appearance according to advanced stage ovarian carcinoma, the ROC curve was used. This statistical analysis uses SPSS version 25.0.

RESULTS

Based on data obtained from the polyclinic oncology and anatomic pathology laboratory for the previous 5 years, 253 patients had ovarian carcinoma. After all the medical records were searched, based on the inclusion and exclusion criteria, 106 samples were obtained. Then performed staging by oncology clinician, obstetrics and gynecology department of RSUD dr. Saiful Anwar, obtained as many as 48 samples suffering from early stages and 58 samples suffering from advanced stages. The following are the characteristics of this research sample:

Table 1. Characteristic Table

Characteristic	Epithelial ovarian carcinoma Stage		P-value
	Early (n = 48)	Advance (n = 58)	
Age (y o)	%	%	
20 - 30	4 (8.3)	1 (1.7)	0.008
31 - 40	7 (14.6)	6 (10.3)	
41 - 50	25 (52.1)	17 (29.3)	
51 - 60	9 (18.8)	26 (44.8)	
61 - 70	1 (2.1)	7 (12.1)	
71 - 80	2 (4.2)	1 (1.7)	
Education			
Elementary school	13 (27.1)	13 (22.4)	0.521
Junior high school	15 (31.3)	24 (41.4)	
Senior high school	19 (39.6)	21 (36.2)	
University	1 (2.1)	0 (0)	
Status			
Single	5 (10.4)	4 (6.9)	0.286
Married once	37 (77.1)	40 (69)	
Married more than once	6 (12.5)	14 (24.1)	
Parity			
Nuliparous	17 (35.4)	15 (25.9)	0.286
Multiparous	31 (64.6)	43 (74.1)	
Contraception			
Not Yet	9 (18.8)	10 (17.2)	0.840
Already	39 (81.3)	48 (82.8)	
BMI			
Underweight	18 (37.5)	33 (56.9)	0.110
Normal	23 (47.9)	21 (36.2)	
Overweight	7 (14.6)	4 (6.9)	
Family history of Gynecologic Cancer			
Denied	46 (95.8)	55 (94.8)	0.808
Be Found	2 (4.2)	3 (5.2)	
NACT			
Not Yet	42 (87.5)	31 (53.4)	0.000
Already	6 (12.5)	27 (46.6)	
Menstrual cycle			
Regular	44 (91.7)	56 (96.6)	0.279
Not Regular	4 (8.3)	2 (3.4)	

Based on the table regarding the characteristics of the study sample, it is shown that of the 48 early-stage patients the majority are 41-50 years old and the majority of 58 patients are 51-60 years old. By using Chi-Square t test, obtained p-value of 0.008 ($p<0.05$) indicating that there is a statistically significant age difference. This indicates that the age group of patients with advanced stage Epithelial Ovarian Carcinoma is older than the group of patients with early Epithelial Ovarian Carcinoma.

Based on the characteristics of education, it was shown that in the early-stage Epithelial Ovarian Carcinoma patient group, most of the patients had high school education, namely 19

(39.6%) and in the group of advanced Epithelial Ovarian Carcinoma patients with junior high school education, 24 (41.4%) patients. By using the Chi-Square test, a p-value of 0.521 (p>0.05) was obtained which explains that there is no difference in educational characteristics between the two groups of patients. Likewise, the characteristics of marital status, parity, family planning, BMI, Family History of Tumors, and menstrual cycles in both groups were relatively the same (p>0.05).

Table 2. Variabel Ultrasound

Variabel USG	Epithelial ovarian carcinoma Stage		*P-value*
	Early (n = 48)	Advance (n = 58)	
Asites	%	%	%
Not Found	36 (75)	18 (31)	0.000
Found	12 (25)	40 (69)	
Papil			
Not Found	33 (68.8)	26 (44.8)	0.014
Found	15 (31.3)	32 (55.2)	
Septa			
Not Found	18 (37.5)	24 (41.4)	0.684
Found	30 (62.5)	34 (58.6)	
Solid Part			
Not Found	21 (43.8)	11 (19)	0.006
Found	27 (56.3)	47 (81)	
Metastasis Intra Abdomen			
Not Found	48 (100)	51 (87.9)	0.013
Found	0 (0)	7 (12.1)	

Based on the characteristics of ascites and papillae, the p-value was less than 0.05 (p<0.05) which proves that there are differences in the characteristics of the two groups of patients. Patients with advanced epithelial ovarian carcinoma have more ascites and papillae than patients with early stage epithelial ovarian carcinoma.

Determination of cut off Value RMI 3 to predict the stage of Epithelial Ovarian Carcinoma Advanced stage can be measured using the ROC curve. The following is the ROC curve of the RMI3 score.

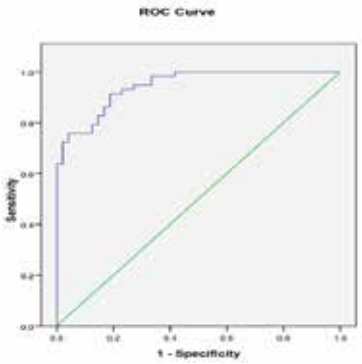

Figure 1. Curve ROC Skor RMI 3

Table 3. Area of the ROC Curve Score RMI 3

Variable	Area	*P-value*	95% CI
RMI 3	0.945	0.000	0.907 - 0.982

Based on table 3 above, the predicted results of the RMI3 score in predicting advanced-stage Epithelial Ovarian Carcinoma, obtained a p-value of less than 0.05 (p<0.05) with an area of 0.945 and 95% CI of 0.907 - 0.982. p-value less than 0.05 indicates that the RMI3 score is very good for predicting the stage of Epithelial Ovarian Carcinoma.

Table 4. Accuracy Comparison Value RMI 3

Score RMI 3	Result		Sensitifity (%)	Spesifity (%)	PPV (%)	NPV (%)	Accuracy (%)
	Early Stage	Advance Stage					
Cut Off Point = 789.45	%	%					
Early	39 (83)	8 (17)	86.2	81.3	84.7	83.0	84.0
Advance	9 (15.3)	50 (84.7)					
Cut Off Point = 888.3							
Early	40 (83.3)	8 (16.7)	86.2	83.3	86.2	83.3	84.9
Advance	8 (13.8)	50 (86.2)					
Cut Off Point = 969.3							
Early	40 (81.6)	9 (18.4)	84.5	83.3	86.0	81.6	84.0
Advance	8 (14)	49 (86)					
Cut Off Point = 1008							
Early	40 (80)	10 (20)	82.8	83.3	85.7	80.0	83.0
Advance	8 (14.3)	48 (85.7)					

Of the four cut off points, it is shown that RMI3 with a cut off point of 888.3 has the highest PPV, NPV, and accuracy values. From this test, it is proven that an RMI3 of 888.3 is more ideally used as a cut off point predictor of advanced stage Epithelial Ovarian Carcinoma.

The sensitivity and specificity of RMI3 score prediction for predicting advanced-stage Epithelial Ovarian Carcinoma is presented in the attachment. The following is a graph of the sensitivity and specificity of the RMI 3 score:

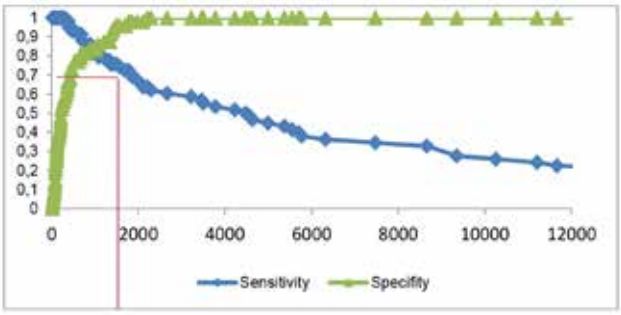

Figure 2. Sensitivity and Specificity Plot of RMI 3 Skor Score

Based on Figure 2, a plot between the sensitivity and specificity values of the RMI3 score is shown. As explained in the figure, it is shown that there is an intersection of the sensitivity and specificity values. This intersection shows the optimum value that can be used as a cut off value or limit in determining advanced-stage Epithelial Ovarian Carcinoma. The intersection point is obtained from the combination of the highest sensitivity and specificity values. Based on the sensitivity and specificity values in the appendix, it is shown that the highest combination of sensitivity and specificity values is located at the RMI 3 point of 888.3 where at that point the sensitivity value is 0.862 and specificity is 0.833. Thus, the cut of value for the RMI3 score to determine advanced-stage Epithelial Ovarian Carcinoma is 888.3.

The level of accuracy of RMI3 in predicting the stage of Epithelial Ovarian Carcinoma can be done by calculating the Positive Predictive Value (PPV), Negative Predictive Value (NPV) and the accuracy value. The PPV, NPV and accuracy values were calculated by comparing the predicted results of RMI3 with the results of histopathological examination. The following are the results of calculating the RMI3 accuracy level in predicting the stage of Epithelial Ovarian Carcinoma:

Table 4. RMI 3 Accuracy Rate as a Predictor of Advanced Stage Epithelial Ovarian Carcinoma

Score	Result		PPV (%)	NPV (%)	Accuracy
	Early Stage	Advance Stage			(%)
RMI 3	%	%			
Early	40 (83.3)	8 (13.8)	86.2	83.3	84,9
Advance	8 (16.7)	50 (86.2)			

Based on the results of the analysis using the contingency coefficient of the relationship between the RMI3 results and the histopathological results, the positive predictive value (PPV) was 86.2% and the negative predictive value was 83.3%. From the initial 48 patients with Epithelial Ovarian Carcinoma based on the results of histopathological examination, it turned out that there were 8 (16.7%) patients who were predicted to be in advanced stage. The NPV value of 83.3% indicates the RMI3 accuracy rate in predicting the early stage is 83.3%. The PPV value of 86.2% indicates the RMI3 accuracy rate in predicting advanced stages is 86.2%. Meanwhile, the accuracy value of RMI 3 is 84.9%.

DISCUSSION

Of the 106 women with ovarian carcinoma who were included in this retrospective study, it was shown that of the 48 early-stage patients the most were 41-50 years old and from 58 advanced-stage patients the most were 51-60 years old. The results obtained in this study are in line with Abdulrahman's retrospective study in Wales United Kingdom which said that the 51-60 age group had the highest incidence of ovarian malignancy[12]. A meta-analytical epidemiological study of 125 articles published in 1925-2018 stated that age On average, women with ovarian cancer are detected at the age of 50-79 years. Detection in the elderly shows the severity of the disease and the relatively lower survival rate[13].

This study revealed that patients with ovarian carcinoma who came to RSUD dr. Saiful Anwar Malang in January 2016 - January 2020 the highest proportion diagnosed with ovarian cancer was in the multiparous group, both in the early stage (64.6%) and advanced stage (74.1%). This study is inconsistent with several case-control studies which showed multiparous women

had a 30-60% lower risk of developing ovarian carcinoma. Increased parity is associated with a reduced risk of ovarian malignancy. Pregnancy is thought to reduce the risk of ovarian tumor malignancy by 19%[11].

The chance of ovarian cancer occurring in women who do not use contraception is higher. This study shows that women who have no history of contraceptive use are around 81.3% in the early stages and 82.8% in the advanced stages, this is due to the distribution of contraceptive use[14].

In this study, which used 106 samples of medical records of women with ovarian carcinoma, the results showed that the RMI score of 3 was very good for predicting advanced epithelial ovarian carcinoma with a p-value of less than 0.05 ($p<0.05$) with an area of of 0.945 and 95% CI of 0.907 - 0.982.

Determination of the Cut Off Value RMI 3 to predict the stage of Epithelial Ovarian Carcinoma Advanced stage can be measured using the ROC curve to see the sensitivity and specificity resulting from the prediction that is obtained at that point resulting in a sensitivity value of 86% and specificity of 83% so that the cut of value score RMI 3 to be a predictor of advanced ovarian carcinoma is 888.3. The level of accuracy of RMI 3 is shown by the PPV value of 86.2%, the NPV value of 83.3% and the accuracy value of 84.9%. In the study conducted by Tingulstad modified the RMI and defined RMI 3 and they observed that at the cut-off level of 200 the sensitivity and specificity were 71% and 92%[15].

This level of accuracy is in line with a study involving 548 female patients, they calculated an RMI with a cut-off point of 200, where there were sensitivity, specificity, PPV, and NPV of 81%, 85%, 48%, and 96%, respectively[16]. In another study, which used 100 female patients with ovarian carcinoma with a cut-off point of 200, the sensitivity, specificity, PPV, and NPV were 90%, 89%, 96%, and 78%, respectively[17].

In the study group, Aktürk stated that there were no statistically significant differences in identifying different malignancy risk indices between RMI 1, RMI 2, RMI 3 and RMI 4[18]. This study is also in line that the efficacy of RMI has been validated in a number of studies and has proven to be a simple, low-cost, and effective tool for triage management of ovarian carcinoma[19]. The sensitivity of RMI 3 indicates that it is able to label malignant tumors in high-risk cases, while its specificity demonstrated that he was able to label benign tumors as low-risk cases. It was the best result when all the parameters examined i.e. sensitivity, specificity, PPV, and NPV were high[20].

A definite or gold standard diagnosis of ovarian carcinoma can be established only after surgery. In order to detect the disease at a very early stage, several approaches have been used to triage women with suspected ovarian carcinoma. According to the referral guidelines, for women suspected of having ovarian carcinoma, patients were grouped according to menopausal status, CA 125 level more than 200 u/ml, presence of ascites, presence of intra-abdominal metastases (by ultrasound examination). With these indications, it can be referred to a gynecological oncologist because each of these parameters is significantly and independently associated with the possibility of ovarian malignancy. RMI based on menopausal status, CA125 levels, and ultrasound imaging is the most widely used preoperative method[18].

The results of this study indicate that women with an RMI 3 value limit of 888.3 have a risk of advanced ovarian malignancy, so that the lowest score of RMI 3 can be used as a reference for administering neoadjuvant therapy prior to diagnosis during surgery to prove histopathological results. This is in line with the research conducted by Petronella which said that women with an RMI value below 200 had a low risk of malignancy and therefore did not require surgery for histopathological examination of frozen section[21]. Although histopathological analysis is a useful method and reliable for determining the nature of ovarian tumors, there are still weaknesses, namely the prolongation of the operation time and the duration of anesthesia. This can really cause problems if the hospital does not have an anatomical pathology laboratory available, which will be time consuming and more expensive because of the transportation of specimens to the pathology laboratory center. In this study about 13% of patients with RMI values below 200 should be able to avoid excessive frozen section histopathological testing in cases of benign tumors [22]. The preoperative RMI score variable can be used as a reference for administering NACT and as part of the preoperative assessment. Consideration of the clinician must consider the advantages and disadvantages of giving chemotherapy, because of the many side effects of chemotherapy. So that there are no more mistakes in giving chemotherapy to ovarian carcinoma patients.

CONCLUSIONS

The results of this study indicate that the RMI3 score is very good to be used in predicting the stage of Epithelial Ovarian Carcinoma. The lowest value of RMI 3 that can be used as a reference limit to determine advanced stage Epithelial Ovarian Carcinoma is 888.3. It is hoped that this cut off value can be a reference for preoperative neoadjuvant therapy to avoid morbidity and mortality due to the high risk of surgery. And this non-invasive method can be a consideration for clinicians in determining the administration of NACT.

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Case Report

Pruritic Urticarial Papules and Plaques of Pregnancy (PUPPP)

Papula Urtikaria Pruritik dan Plak pada Kehamilan (PUPPP)

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Abstract

Objective: To report a rare case of pruritic urticarial papules and plaques of pregnancy (PUPPP) in multiparous woman and its literature review.

Methods: A case report with literature review.

Discussion: This article reports a multigravida woman, presented with aterm pregnancy with sign and symptoms of pruritic urticarial papules and plaques since the first trimester of pregnancy. This case supports the morphological variation of skin lesions in PUPPP, as the patient had lesions other than the characteristic urticarial papules and plaques, with hyperpigmentation skin changes. The management of this case include oral and topical corticosteroids, oral antihistamines and moisturizer is used to relieve pruritus and skin lesions.

Conclusion: PUPPP should be included in the differential diagnosis to differentiate this entity from other dermatoses associated with pregnancy, in order to provide appropriate treatment and reassurance.

Keywords: papules, plaques, pregnancy, pruritic, urticarial.

Abstrak

Tujuan: *Untuk melaporkan kasus langka mengenai papula urtikaria pruritik dan plak pada kehamilan (PUPPP) perempuan multipara, membahas literatur terkait pada PUPPP.*

Metode: *Laporan kasus dengan telaah literatur.*

Diskusi: *Melaporkan kasus perempuan multigravida, datang dalam usia kehamilan cukup bulan dengan tanda dan gejala papula, plak, urtikaria dan pruritus sejak trimester pertama kehamilan. Kasus ini mendukung variasi morfologi lesi kulit pada PUPPP, karena pasien memiliki lesi selain papula dan plak urtikaria yang khas, dengan perubahan kulit hiperpigmentasi. Penatalaksanaan kasus ini meliputi kortikosteroid oral dan topikal, antihistamin oral dan pelembap yang digunakan untuk meredakan pruritus dan lesi kulit.*

Kesimpulan: *PUPPP perlu dimasukkan dalam diagnosis banding untuk membedakan entitas ini dari penyakit kulit lain yang terkait dengan kehamilan, untuk memberikan pengobatan dan pelayanan yang tepat.*

Kata kunci: *kehamilan, papula, plak, pruritus, urtikaria.*

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INTRODUCTION

Physiological changes in pregnancy affects many organ systems, based on complex relation of endocrinologic, immunologic, metabolic and vascular, including dermatological changes. Some of dermatological changes give rise to skin disorder related to pregnancy.[1,2]

Pruritic Urticarial Papules and Plaques of Pregnancy (PUPPP), also known as polymorphic eruption of pregnancy is a benign, pruritic, inflammatory skin disorder, characterized by a polymorphous clinical presentation. PUPPP usually affects primigravida in their third trimester of pregnancy. The reported incidence of pruritic urticarial papules and plaques of pregnancy is 0.5% in single pregnancies, 2.9 to 16% in twin pregnancies and 14 to 17 % in triplet pregnancies.[3-5]

The cause of PUPPP remains unknown, there is association between PUPPP and significantly

increased maternal and fetal weight during the course of pregnancy, rapid abdominal distention leads to damage of the connective tissue, which then releases antigenic molecules, causing an inflammatory reaction.[6]

The primary symptom of PUPPP is pruritus. Clinical presentation constitutes intensely pruritic urticarial papules and plaques starting within adjacent to striae, sparing the periumbilical area. Later on, the lesions can spread to non-abdominal sites.[7] Approximately half of the patients later develop polymorphic skin lesions, such as urticarial papules and plaque (49%), eczematous lesions (22%), vesicles (17%), non-urticarial erythema (6%), and targetoid lesions (6%). Systemic symptoms are usually absent.[8]

There are no specific laboratory abnormalities and only nonspecific histopathology with a perivascular lymphohistiocytic infiltrate with some edema and eosinophils in the dermis.[4] Treatment of PUPPP is focused on the relief of pruritus. The most common agents used are antipruritic agents, skin emollients and topical corticosteroids. The maternal and fetal prognosis is unaffected.[9] We report a rare case of multigravida woman, with a history of pruritic erythematous papules and plaques in the first trimester of pregnancy.

CASE

A 37-year-old female, (gravida 3, para 2) at 38 weeks of gestation presented with signs and symptoms of pruritic erythematous papules and plaques since the first trimester starting on the lower abdomen. The rash spread to all extremities and the trunk; however, umbilicus, palms, and soles were spared. The patient also reported that the skin lesions found on her trunk and limbs were giving her insomnia due to continuous symptomatic outbreaks, predominantly including itchiness.

Physical examination revealed generalized discrete and confluent erythematous papules and plaques with hyperpigmentation skin changes on the trunk, abdomen and extremities (figure. 1). Direct immunofluorescent studies were all negative. Due to the diversity of skin manifestations, PUPPP was diagnosed.

Initial management include, systemic corticosteroids (methylprednisolone 8 mg twice a day) topical corticosteroids (mometasone furoate 0.1% twice a day), including oral anti histamine (cetirizine 10 mg daily) and moisturizer were prescribed. The patient had a good clinical response, symptoms was relief 4 weeks after delivery. She delivered a healthy, term, baby.

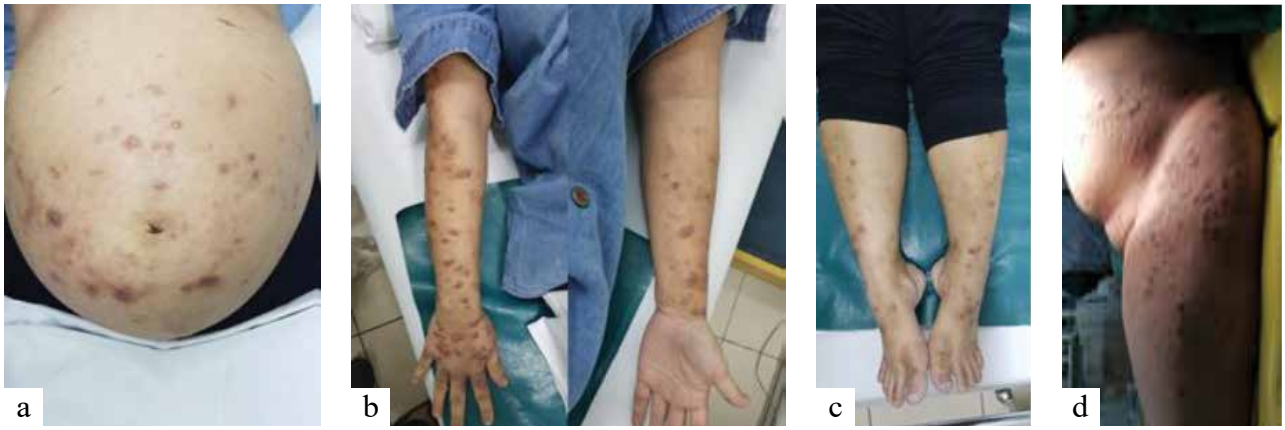

Figure 1. Generalized discrete and confluent erythematous papules and plaques on the abdomen (a) and extremities. Some tiny pustules and vesicles with hyperpigmentation skin changes on upper extremities (b) lower extremities (c) and thighs (d).

DISCUSSION

The patient in this case were presented itchiness with multiple lesions on the trunk, and extremities, with hyperpigmentation skin changes since the first trimester of pregnancy. The diagnosis of PUPPP can be made clinically in based on the appearance of the rash. Concerning PUPPP onset, there is different with previous studies, PUPPP mainly affected primigravida in the third trimester of pregnancy.[7] Multiple pruritic erythematous papules and plaques occurred after labor.[5] In our case affect patient with multigravida in the first trimester pregnancy. The reason for this incidence is not known but could be related to the population under study. Another reason may be under-diagnosis or under documentation.[10,11]

This case supports the morphological

variation of skin lesions in PUPPP, as the patient had lesions other than the characteristic urticarial papules and plaques, with hyperpigmentation skin changes.[11] Fifty seven patients with PUPPP and revealed various types of skin lesions.[8] Eighteen patients with the morphological variation of skin lesions in PUPPP, as six of the patients had lesions other than the characteristic urticarial papules and plaques. In addition to urticarial papules and plaques, five had additional findings, including papule vesicles (three cases), target-like lesions (one case), and eczematous lesions (one case) and, one case had papulovesicular lesions.[7] Concerning the distribution PUPPP in this case, characteristically involved the lower abdomen, and spread to the upper and lower extremities. Abdominal involvement with sparing of the umbilical region in PUPPP is an important feature in distinguishing PUPPP from other gestational dermatoses. Involvement of all the extremities occurred in this case as this pattern is rarely reported.[11]

The differential diagnosis of PUPPP include, pemphigoid gestation, and dermatitis. The most important diagnosis to exclude is pemphigoid gestation. As the clinical features can be overlap, histological and immunological studies are necessary to make the distinction between these two disorders. Although in pemphigoid gestation, lesions usually have an earlier onset during gestation, and often involve the umbilicus, along with positive immunofluorescence of perilesional skin.[3] Dermatitis in pregnancy usually occurs in patients with a personal or family history of atopy and is characterized by pruritic dermatitis lesions mainly on flexural areas.[11]

Our case didn't exam the histopathology. Even tough in general, histopathological findings of biopsies from skin lesion were essentially nonspecific, as previously described histological findings of PUPPP showed perivascular lymphohistiocytic infiltrate with some edema and eosinophils in the dermis.[5]

The management of this case include oral and topical corticosteroids, oral antihistamines and moisturizer is used to relieve pruritus and skin lesions. Topical corticosteroid substances such as mometasone can be regarded as safe during pregnancy, but large amounts of potent topical steroids over prolonged periods should probably be regarded similarly to systemic steroids.[12] Systemic corticosteroids, which are second line therapy may be required in this severe case. For systemic treatment during pregnancy prednisone, prednisolone, and methylprednisolone are regarded as safer than betamethasone, dexamethasone, cortisone, and hydrocortisone.[13] Three patients with PUPPP, all of whom were treated with autologous whole blood (AWB) injections. These cases demonstrate the usefulness and safety of AWB injections for treatment of patients with PUPPP during pregnancy and breastfeeding. The three patients were primigravida and AWB injection led to complete resolution of their symptoms, beginning within 2 days of the first injection. In our case, we didn't use AWB injections because the exact mechanism of action remains unclear, although it seems to affect immune function in experimental and clinical models.[4] Non pharmaceutical treatments such as moisturizer, oil baths and emollients should also be considered. While this provided symptomatic relief, the skin lesions resolved completely 1–4 weeks after delivery. [9,11]

CONCLUSION

Although PUPPP benign, discomfort skin lesions could affect the quality of life of patients during pregnancy and postnatal period. PUPPP should be included in the differential diagnosis to differentiate this entity from other dermatoses associated with pregnancy. Medicamentosa steroid and anti-pruritic agents could relief symptoms in order to provide appropriate treatment and reassurance.

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Literature Review

Nifedipine, Calcium Channel Blocker (Antihypertensive), as a Tocolytic to inhibit Premature Birth in Reducing the Risk of Neonatal Death in Childbirth: Meta-Analysis and Systematic Review of Large Clinical Trial

Nifedipine, Penghambat Kanal Kalsium (Antihipertensi), sebagai Tokolitik dalam Menghambat Kelahiran Prematur dalam Menurunkan Risiko Kematian Neonatus pada Persalinan: Meta-Analisis dan Telaah Sistematis dari Studi Besar Uji Klinis

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Abstract

Objective: To evaluate the role of nifedipine as a tocolytic agent.

Methods: Literature searches use medical search engines for example Pubmed, Google Scholar and Medical scientific journals, as like the American kind of Journal that is Learning Obstetrics and also learn about Gynecology. The literature used were published from 1986 to 2020. The main data extraction was in the form of an extended gestation period, divided into 48 hours, 7 days, and 37 weeks with data analysis using the RevMan 5.4 application.

Result: Twenty-four clinical trials were analyzed with total amount shown of 2,889 study subjects. The purpose of using kind of nifedipine to be such a tocolytic indicates no significant difference, within 48 hours or (RR 1.06; 95% CI, 0.99 - 1.13; p shown = 0.12), 7 days (RR 1.02; 95% CI, 0.95 - 1.09; p = 0.57), and up to 37 weeks (RR 1.22; 95% then CI, 0.96 - 1.54; p = 0.10) at the time it is compared with the group of control.

Conclusion: Administration of nifedipine as a tocolytic did not have a statistically significant difference, both in prolonging pregnancy and side effects for pregnant women and neonates compared to the control group.

Keywords: meta-analysis, nifedipine, preterm delivery, prolongation pregnancy, tocolytic.

Abstrak

Tujuan: *Untuk mengevaluasi peran nifedipin sebagai tokolitik.*

Metode: *Pencarian literatur menggunakan mesin pencari medis seperti Pubmed, Google Scholar dan jurnal ilmiah medis, seperti American Journal of Obstetrics and Gynecology. Literatur yang digunakan dalam rentang tahun 1986 - 2020. Kata kunci adalah ("pregnant woman" OR pregnancy) AND ("preterm birth" OR "preterm labor") AND nifedipine. Ekstraksi data utama berupa perpanjangan masa kehamilan, dibagi menjadi 48 jam, 7 hari, dan 37 minggu dengan analisis data menggunakan aplikasi RevMan 5.4*

Hasil: *Dua puluh empat uji klinis yang dianalisa dengan total 2,889 subjek penelitian. Penggunaan nifedipin sebagai tokolitik menunjukkan tidak ada sesuatu yang berbeda secara signifikan, dalam 48 jam (RR 1.06; 95% then CI, 0.99 - 1.13; p results = 0.12), 7 hari (RR shown 1.02; 95% then CI, 0.95 - 1.09; p = 0.57), dan sampai 37 minggu (RR 1.22; 95% CI, 0.96 - 1.54; p shown = 0.10) apabila dibandingkan dengan kelompok kontrol. Begitu pun dengan efek samping pada ibu hamil (RR 0.99; 95% CI, 0.74 - 1.31; p = 0.92) dan neonatus (RR 0.93; 95% of CI, 0.83 - 1.04; p shown = 0.21), ditemukan adanya kesamaan yang serupa pada grup atau golongan dalam kendali.*

Kesimpulan: *Pemberian nifedipin sebagai tokolitik tidak memiliki perbedaan yang signifikan secara statistik, baik dalam memperpanjang masa kehamilan maupun efek samping kepada ibu hamil dan neonatus dibandingkan dengan kelompok kontrol.*

Kata kunci: *kehamilan memanjang, kelahiran prematur, meta-analysis, nifedipin, tokolitik.*

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INTRODUCTION

Preterm birth is an issue of healthcare and social awareness which were claimed as the reason led of mortality rate in neonates around the world. They make it collected into upper rates kind of being neurodevelopmental in morbidity, then comes to sensorineural of impairments and also complications else.[1] Preterm of labor claimed it parturition which happenes at the time in 20 0/7 of weeks from gestation then 36 6/7 of weeks. It also get categorized becoming an early and also late of preterm. The meaning of early preterm claimed as the time that the baby get brought to the world in previous 33 weeks, then the late preterm happened the time a baby get brought to the world in 34 and also 36 weeks.[2,3]

Preterm birth interferes with normal maturation development of the organ systems, causing severe and prolonged side effects. It was found that it is easier and earlier for preterm-born to get high blood pressure, cardiac dysfunction, obstructive lung disease, elevation in blood glucose and mental state issues then those of the in-term population. Adverse health conditions can significantly effect on the welfare of individuals who were born prematurely from their childhood to adulthood.

Initiation of at the meaning given is complicated and incomprehensible. Felt Spontaneous onset of preterm labor coming from the rupture of membranes and or contractions definite explanation hasn't been founded, especially regarding the sequence and timing of events. There's still limited proof of the advantage of antenatal intervention, but using well-known risky categories of spontaneous from preterm delivery to elect between pregnant woman for getting more thorough interventions which should be targeted individually most matter compared to the perspective given from medical and also caregiving.[4,5] Indonesia was known to be registered some of countries which has the biggest preterm of giving birth in the year 2010.[6]

The condition defined the preterm of giving birth claimed as the main reason les to risk of neonatal death with giving it 35% %age of 3.1 million of death cases happened in a year as its total, and also are one of the cause behind under-5 mortality in worldwide after Pneumonia. While in high and also middle-income nations claimed that the condition of preterm birth causes the most factor of child death cases. Baby who born premature has bigger risk of dying because of other causes, mainly because of neonatal infections which predicted to be in 50% of neonatal deaths.[7] Preterm birth complications are the main reason led to mortality, whether being such neonatal period and also the global under-5 mortality.[8]

In Indonesia itself, the most factor led to neonatal deaths cases that occurred around year 2015 which prematurity which results (35.5 %),of asphyxia of having birth and also because of trauma (21.6 %) and for congenital anomalies (17.1%).[9] In 2019, neonatal mortality rate for Indonesia was 12.4 deaths cases each of 1,000 living births.[10]

Tocolysis is an obstetric procedure performed using method of giving medications in a purpose to get delaying the delivery of the fetus inside women who have premature contraction.[11,12]

The term of tocolysis is defined as a prolong of pregnancy between two until seven days and also acts more in making such an atmosphere happened in the uterus, in hope that it will decrease the fetal morbidity and mortality. The effectivity of tocolysis lies in its focus of delaying and weakening the uterine contraction. Myometrium as the smooth muscle in the uterus is it's pharmacological targets. Labor can start earlier regardless of the normal average gestation age is 40 weeks. It's believed that the sudden condition happen because a change of balance in proinflammatory and also in anti-inflammatory cytokines.[13]

Predisposition factor from preterm labor which are the infection, uterine happened to distention stress, complication in vascular and decidual senesence. Fetus has smaller chance of survival if the contractions begin too early. Calcium channel of blockers (Nifedipine) precisely go on T-type of calcium type of channels to prevent the contraction of uterus by prohibiting the way calcium goes to uterine smooth muscle.[11,12] Our main objective is evaluating the role of nifedipine as a tocolytic when compared to controls including side effects to pregnant women and neonates.

METHODS

Literature searches use medical search engines such as Pubmed, Google Scholar and Medical Scientific journals, for example the American of Journal which is learning Obstetrics and also learning Gynecology. The literature used ranges from 1986 to 2020. The key word are ("pregnant woman" OR pregnancy) AND ("preterm birth"

OR “preterm labor”) AND nifedipine. The main data extraction was in the form of an extended gestation period, divided into 48 hours, 7 days, and 37 weeks with data analysis using the RevMan 5.4 application. The inclusion criteria for the research subjects were pregnant women gets the risk of experiencing preterm labor with a gestational age range of 20 - 36 weeks. Using nifedipine as tocolytic and there is a control group, the research design is in the form of clinical trials, systematic reviews, and metanalysis.

RESULTS

Twenty-four clinical trials were analyzed with a total of 2,889 study subjects. The purpose of using nifedipine to be tocolytic which seem to have no significant difference, within 48 hours (RR 1.06; 95% CI, 0.99 - 1.13; p = 0.12) (figure 1), 7 days or the same with (RR 1.02; 95% CI, 0.95 - 1.09; p shown = 0.57) (figure 2), and comes around 37 weeks (RR 1.22; 95% CI, 0.96 - 1.54; p = 0.10) (figure 3) which was being compared with the group of control. Likewise with side effects in pregnant women (RR 0.99; 95% CI, 0.74 - 1.31; p = 0.92) and neonates (RR 0.93; 95% CI, 0.83 - 1.04; p shown = 0.21), there claimed not to have any difference with the group of control.

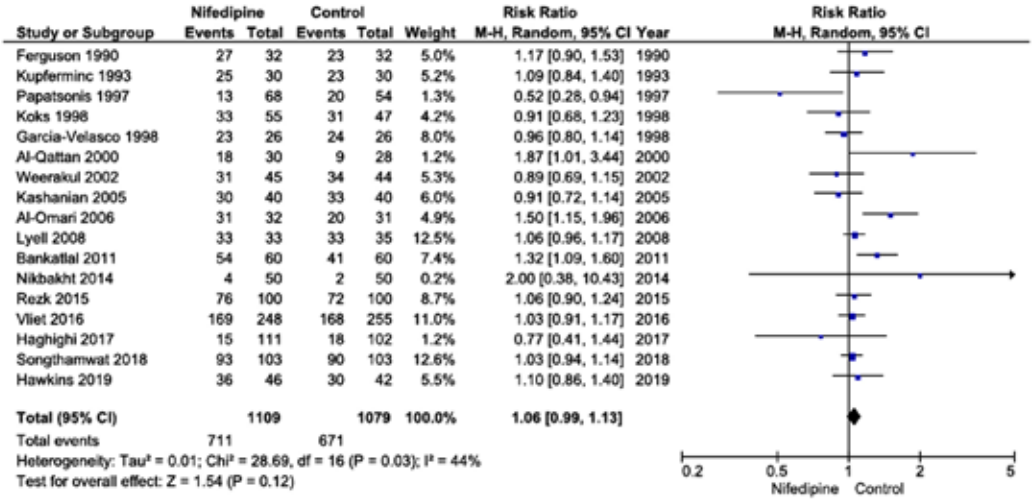

Figure 1. Forest plot showing the prolongation of Forest plot showing the prolongation of pregnancy up to 48 Hours

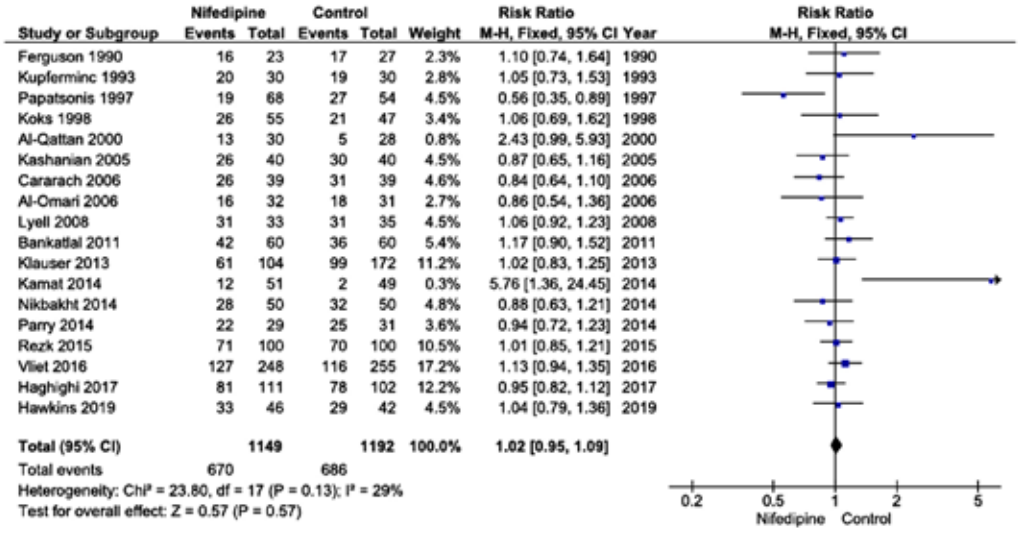

Figure 2. Forest plot showing the prolongation of pregnancy up to 7 days

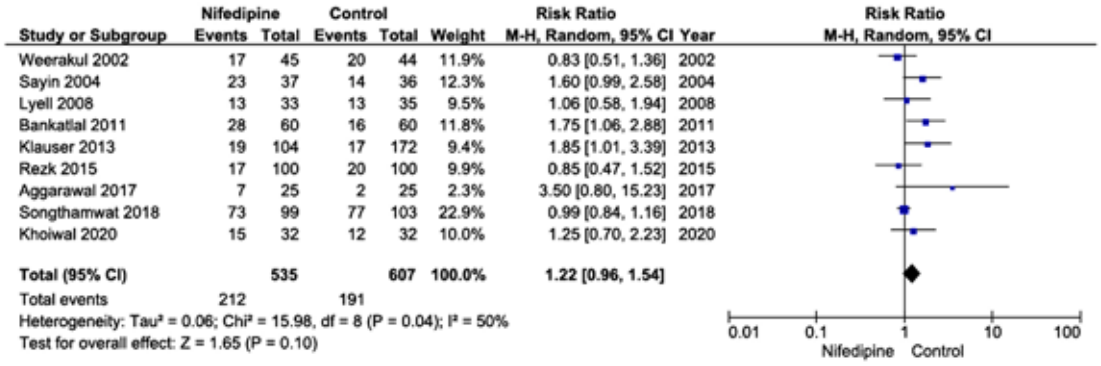

Figure 3. Forest plot showing the prolongation of pregnancy up to 37 weeks

DISCUSSION

Using meta-analysis in this study has the purpose to define it as based on two latest pre-existing meta analyzes. The two previous meta-analyzes examined the role of nifedipine as a tocolytic. Both in terms of effectiveness, or safety of pregnant women and their babies.

The first one showed that being compared to progesterone, nifedipine was better at prolonging pregnancy (RR 23.50; 95% CI, 18.40 - 28.60). However, there was no difference which the time it is compared with the placebo (RR 2.21; 95% CI, -3.63 - 8.05). For neonatal side effects, there was no difference with neonates weight (RR 5.58; 95% CI, -103.28 - 114.43).[14]

For a second meta-analysis, showed that when compared to atosiban nifedipine there claimed not to have any significant difference onto the prolongation period of having pregnancy to 48 hours or more. Both include the condition from having efficacy (RR 1.06; 95% CI, .92 - 1.22) and effectiveness (RR 0.93; 95% then CI, 0.84 - 1.03). The same thing happened in the extension of the gestation period to 7 days or more.[15]

There was no difference in maternal side effects (RR 0.47; 95% CI, .22 - 0.99, p = 0.05), palpitations (RR 0.37; 95% CI, 0.10 - 1.33, p = 0.13), hypotension (RR 0.30). ; 95% CI, 0.80 - 1.19, p = 0.09), vomiting (RR 1.55; 95% CI, 0.28 - 8.64, p = 0.62), nausea (RR 2.44; 95% CI, 0.13 - 46.73, p = 0.55). However, there were differences in tachycardia (RR 0.20; 95% CI, 0.05 - 0.74, p = 0.02).[16]

Likewise, there claimed not to have any significant difference of side effects for neonates alone with respect to respiratory failure (RR 0.79; 95% CI, 0.27 - 2.34, p = 0.67), intraventricular bleeding (RR 0.79; 95% CI, 0.26 - 2.41, p = 0.68), neonatal sepsis (RR 0.98; 95% CI, 0.60 - 1.60, p = 0.93), necrotizing enterocolitis (RR 1.75; 95% CI, 0.11-29.02, p = 0.69).[15]

Based on the results of several previous meta-analyzes, there is no difference between nifedipine as a tocolytic and others tocolytic as a control. The control group here was atosiban, indomethacin, MgSO4, progesterone, ritrodine, terbutaline, nicorandil, isoxsuprine, and placebo. Coming back from the term of Preterm Labor and also Birth guidelines which learnt from the National of Institute that learn about Health and also Care Excellence (NICE), nifedipine is still a recommendation in choosing tocolytics. This guide has been coming up in 2020.[16]

According to the National of Institute that learn about Health issues and also Care of Excellence (NICE), Nifedipine as a tocolytic offer to woman between 26^{0} and 33^{+6} weeks of having pregnancy those have such as intact of membranes and also being judged to be had kind of preterm labor.[16]

Calcium channel of blockers (CCBs) claimed as non- specific of soft muscle that is claimed to be relaxants, then predominantly is intended for the maintenance of hypertension and is claimed to get used in many doses to be a tocolytic for women in having kind of preterm labor.[17] Nifedipine is defined as dihydropyridine calcium channel of blocker that giving action onto L-type calcium of channels to get calcium influx moves to become myometrial of cells. Reducing Intracellular of calcium concentrations avoid the process of activating the myosin of light chain from kinase, and also the term thereby myometrium contraction.[18] Then, nifedipine gets contraindicating inside women whom have cardiac disease.[19]

The process of managing the condition of preterm labor defines are having rest in bed, adequate of having hydration, prophylactic cervical cerrclage and using tocolytic drugs.

Nevertheless the tocolytics haven't proofed to get improved the neonatal outcomes, it may deal with the delaying so antenatal of corticosteroid t administers or the mother being moved to a tertiary care facility.[16,20]

CONCLUSION

In our study, administration of nifedipine as a tocolytic did not have a statistically significant difference, both in prolonging pregnancy and side effects for pregnant women and neonates compared to the control group. We are looking forward for further study/research about nifedipine and other tocolytic agent in inhibiting Premature Birth in Reducing the Risk of Neonatal Death in Childbirth.

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