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EDITORIAL

RESEARCH ARTICLE

Research Article

Relationship between Physical Activity of Pregnant Women in the Third Trimester of Pregnancy with Preterm Birth Using Kaiser Physical Activity Survey (KPAS) Questionnaire

Hubungan antara Aktivitas Fisik Perempuan Hamil pada Trimester Ketiga Kehamilan dengan Persalinan Prematur Menggunakan Kuesioner Kaiser Physical Activity Survey (KPAS)

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Abstract

Objective: To examine the relationship between the intensity of physical activity of pregnant women with preterm birth and to know the relationship between types of physical activity of pregnant women with preterm birth.

Methods: This research was a case-control study that was conducted at Dr. Cipto Magunkusumo Hospital and Karawang Hospital in January 2017 to June 2017 with KPAS questionnaire which was divided into two groups, preterm birth and term birth. The sample size was 127 subjects for each group. The analysis was done by multivariate analysis of the etiologic concept.

Results: In term birth, the most frequent physical activity intensities were: moderate intensity (64.6%, n = 82), light intensity (22%, n = 28), and vigorous intensity (13.4%, n = 17). In preterm birth, the most frequent physical activity intensities were: light intensity (40.1%, n = 51), vigorous intensity (33.9%, n = 43), and moderate intensity (26%, n = 33). Adjusted OR of preterm birth in light intensity versus moderate intensity was OR 5.32 (95% CI, 2.80-10.13; p = < 0.001). While adjusted OR of preterm birth in vigorous intensity compared with moderate intensity was OR 6.29 (95% CI, 3.28-13.46; p = < 0.001). Work and sport have a significant association with preterm birth with OR 3.19 (95% CI, 1.62 - 6.28; p = 0.001) and OR 1.85 (95% CI,1.11 - 3.09; p= 0.017). Occupational conditions are also associated with preterm birth, including: weight lifting with OR 5.16 (95% CI, 1.10-24.08, p = 0.021), walking with OR 3.57 (95% CI, 1.61-7.92, p = 0.001), sitting with OR 2.79 (95% CI, 1.23-6.31, p = 0.011), and standing with OR 3.04 (95% CI, 1.40-6.59; p = 0.003).

Conclusion: There is a significant relationship between the intensity of physical activity and type of physical activity in pregnant women with preterm birth.

[Indones J Obstet Gynecol 2018; 6-4: 203-208]

Keywords: intensity of physical activity, KPAS, physical activity, preterm labour

Abstrak

***Tujuan**: Mengetahui hubungan antara intensitas aktivitas fisik perempuan hamil dengan persalinan prematur dan mengetahui hubungan antara jenis aktivitas fisik perempuan hamil dengan persalinan prematur.*

***Metode**: Penelitian ini merupakan penelitian kasus kontrol yang dilakukan di RS Dr. Cipto Magunkusumo dan RS Karawang pada bulan Januari 2017 hingga Juni 2017 dengan kuesioner KPAS yang dikelompokkan menjadi dua, yaitu persalinan prematur dan persalinan cukup bulan. Jumlah sampel adalah 127 subjek untuk masing-masing kelompok. Analisis dilakukan dengan analisis multivariat konsep etiologik.*

***Hasil**: Pada persalinan cukup bulan, secara berurutan intensitas aktivitas fisik yang paling banyak dilakukan, antara lain : intensitas sedang (64,6%, n= 82), intensitas ringan (22 %, n = 28), dan intensitas berat (13,4 %, n = 17). Pada persalinan prematur, secara berurutan intensitas aktivitas fisik yang paling banyak dilakukan, antara lain: intensitas ringan (40,1 %, n = 51), intensitas berat (33,9 %, n = 43), dan intensitas sedang (26%, n = 33). Hubungan antara intensitas aktivitas fisik ringan dibandingkan intensitas sedang untuk persalinan prematur memiliki OR 5,32 (IK 95% 2,80-10,13; p = < 0,001). Sedangkan hubungan antara intensitas aktivitas fisik berat dibandingkan intensitas sedang untuk persalinan prematur memiliki OR 6,29 (IK 95% 3,28-13,46; p = < 0,001). Pekerjaan dan olahraga memiliki hubungan bermakna dengan persalinan prematur dengan OR 3,19 (IK 95% 1,62 - 6,28; p = 0,001) dan OR 1,85 (IK 95% 1,11 - 3,09; p= 0,017). Kondisi pekerjaan juga berhubungan dengan persalinan prematur, antara lain : angkat berat (OR 5,16; IK 95% 1,10-24,08; p = 0,021), berjalan (OR 3,57; IK 95% 1,61-7,92; p = 0,001), duduk (OR 2,79; IK 95% 1,23-6,31; p = 0,011), dan berdiri (OR 3,04; IK 95% 1,40-6,59; p = 0,003).*

***Kesimpulan**: Terdapat hubungan yang bermakna antara intensitas aktivitas fisik dan jenis aktivitas fisik pada perempuan hamil dengan persalinan prematur.*

[Maj Obstet Ginekol Indones 2018; 6-4: 203-208]

***Kata kunci**: aktivitas fisik, intensitas aktivitas fisik, KPAS, persalinan prematur*

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INTRODUCTION

Preterm birth has become a global problem, and over 60% of preterm birth occur in Africa and South Asia. Currently, Indonesia is in the fifth rank after India, China, Nigeria, and Pakistan.[1,2] In Indonesia, preterm birth is a national problem that causes neonatal deaths more than 70% without congenital abnormalities, and until this time, preterm birth is still being the first cause of neonatal death.[1,2] Now, physical activity start to become a consideration as a risk factor of preterm birth due to its capability to be modified. The hypothesis that physical activity can lead to preterm birth is from the change in blood flow at the time of physical activity which causes the disturbance of O2, CO2, and transplacental nutrients transport thus increasing the risk of preterm birth.[3-7] However, in other studies it was found that exercise would stimulate placenta cell proliferation and increase the volume of vascular villi, thereby increasing the transfer of oxygen and nutrients through the placenta and the baby.[8,9] Study on the relationship between types of physical activity with preterm birth has been widely done. Physical activity in women includes household activities, occupation, active living habits, and exercise. To date, there are only a few studies about the relationship between the total physical activity of pregnant women with preterm birth and it still could not be concluded whether there was a relationship between physical activity and preterm birth.[4,10] One cause that made the relationship between total physical activity and preterm birth still could not be concluded was the use of various methods in measuring physical activity.[4,11]

The purpose of this study was to determine the relationship between physical activity intensity with preterm birth and to determine the relationship between physical activity type with preterm birth by using validated questionnaire: Kaiser Physical Activity Survey (KPAS)

METHODS

This study was case control with 127 subjects for each group which performed at Dr. Cipto Mangunkusumo Hospital (RSCM) and Karawang hospital from January 2017 to June 2017.

Sampling in this study was conducted with convenient sampling. Information was obtained by interviews that were taken from patients who entered into case groups and control groups. Case group was patient who underwent preterm birth at Dr. Cipto Mangunkusumo Hospital (RSCM) and RS Karawang from January 2017 to June 2017 who had met the inclusion criteria and did not fall into the exclusion criteria. Information from both groups was taken as long as the patient was still in the hospital until the number of sample targets was fulfilled. Information was obtained by conducting interviews using written questions which were contained in the KPAS questionnaire. Information on physical activity based on the questionnaire is the physical activity that was performed by pregnant women in the third trimester.

Inclusion criteria in this study include: women who conduct preterm birth (third trimester) in Dr. Cipto Mangunkusumo hospital and Karawang hospital period January 2017 to June 2017; willing to follow the study and fill out the completeness of informed consent.

Exclusion criteria in this study include : vaginal bleeding in second trimester and third trimester confirmed by history taking with a history of vaginal bleeding in 2nd and 3rd trimester that occurred more than one time; cervical incompetence based on history taking and or ultrasound examination and from anamnesis is obtained from the history of the outcome of conception in the second trimester without any pain, and or there is an ultrasound examination which shows the cervical abnormalities and or amnion bag funneling; multiple pregnancies which was confirmed based on patient's medical history after she had both in current pregnancy; the history of abortion in this pregnancy which was confirmed by history taking; sudden onset of trauma which was confirmed by history taking; hypertension, diabetes mellitus, preeclampsia.

The KPAS Questionnaire

The KPAS questionnaire had been validated in 54 female samples at Baystate Medical Center using a seven-day accelerometer measurement. The coefficient correlation used to measure reproducibility in KPAS has ranged between r = 0.76 to 0.86 and Spearman's correlation coefficient between KPAS and 3 published cutting points for the accelerometer classification is ranged from r = 0.49 to 0.59.

Statistical Analysis

Statistical analysis was performed by using SPSS 20® software for the Windows® operating system. The analysis was done by multivariate analysis of the etiologic concept.

RESULTS

Characteristics of the subjects are presented in Table 1. In term birth, physical activity with moderate intensity is the highest level of physical activity intensity (64.6%, n=82), followed by physical activity with moderate intensity (22%, n=28), and the last was physical activity with vigorous intensity (13.4%, n=17). However, different result was found in preterm birth. In preterm birth, physical activity with light intensity was the most common physical intensity (40.2%, n=51), followed by physical activity with vigorous intensity (33.9%, n=43), and the last is physical activity with moderate intensity (26%, n=33).

Table 1. Subject's Characteristics

Variable	Preterm birth		p	or	95% CI	
	+ n (%)	- n (%)			Min	Max
Physical activity intensity			<0.001			
Light	51 (40.1)	28 (22.0)	<0.001	4.53	2.45	8.36
Moderate	33 (26.0)	82 (64.6)	Comparison			
Vigorous	43 (33.9)	17 (13.4)	<0.001	6.29	3.15	12.55
Education			0.002			
Elementary school	17 (13.4)	6 (4.7)	0.443	5.67	0.43	74.38
Junior high school	72 (56.7)	56 (44.1)	0.840	2.57	0.23	29.08
Senior high school	37 (29.1)	63 (49.6)	1.000	1.18	0.10	13.40
Bachelor	1 (0.8)	2 (1.6)	Comparison			
Age						
≤ 35 years old	68 (53.5)	78 (61.4)	0.253	0.72	0.44	1.19
> 35 years old	59 (46.5)	49 (38.6)	Comparison			
Vaginal discharge						
Yes	68 (53.5)	42 (33.1)	0.002	2.33	1.40	3.88
No	59 (46.5)	85 (66.9)	Comparison			
Parity						
Multiparity	89 (70.1)	76 (59.8)	0.115	1.572	0.94	2.64
Nulliparity	38 (29.9)	51 (40.2)	Comparison			
Closed pregnancy distance						
Yes	60 (47.2)	42 (33.1)	0.030	1.81	1.09	3.01
No	67 (52.8)	85 (66.9)	Comparison			
History of preterm birth						
Yes	57 (44.9)	45 (35.4)	0.159	1.48	0.90	2.46
No	70 (55.1)	82 (64.6)	Comparison			
Smoke						
Yes	21 (16.5)	20 (15.7)	1.000	1.06	0.54	2.07
No	106 (83.5)	107 (84.3)	Comparison			
Alcohol						
Yes	1 (0.8)	0 (0.0)	1.000	-		
No	126 (99.2)	127 (100.0)	Comparison			

Table 2 shows the relationship between physical activity intensity and preterm birth by controlling confounding variables which were: education level, vaginal discharge, parity, close pregnancy distance, and history of preterm birth. Physical activity with light intensity has OR 5.32 (95% CI, 2.80-10.13; p= < 0.001). Compared with moderate intensity. While physical activity with vigorous intensity has OR 6.65 (95% CI, 3.28-13.46; p = < 0.001) compared with moderate intensity.

Table 3 shows the relationship between physical activity type and preterm labor. Adjusted OR of working in preterm birth was 3.19 (95% CI, 1.62-6.28; p = 0.001) and adjusted OR of exercise in preterm birth was 1.85 (95% CI, 1.11-3.09; p = 0.017). Working condition was also associated with preterm birth, including: weight lifting (OR 5.16, 95% CI,1.10-24.08; p= 0.021), walking (OR 3.57; 95% CI,1.61-7.92; p = 0.001), sitting (OR 2.79; 95% CI, 1.23-6.31; p = 0.011), and standing (OR 3.04; 95% CI,1.40-6.59; p = 0.003).

Table 2. Relationship between Physical Activity Intensity with Preterm Birth

	Preterm birth		Unadjusted			Adjusted		
	Positive n (%)	**Negative n (%)**	**p**	**or**	**CI 95%**	**p**	**or**	**CI 95%**
Physical activity intensity			<0.001			<0.001		
Light	51 (40.2)	28 (22.0)	<0.001	4.53	2.45-8.36	<0.001	5.32	2.80-10.13
Moderate	33 (26.0)	82 (64.6)				Comparison		
Vigorous	43 (33.9)	17 (13.4)	<0.001	6.29	3.15-12.55	<0.001	6.65	3.28-13.46

Table 3. Relationship between Physical Activity Intensity with Preterm Birth

Variable	Preterm birth		p	or	95% CI	
	+ n(%)	**- n(%)**			**Min**	**Max**
Working						
Yes	36 (28.3)	14 (11.0)	0.001	3.19	1.62	6.28
No	91 (71.7)	113 (89.0)				
Exercise						
No	88 (68.2)	67 (53.6)	0.017	1.85	1.11	3.09
Yes	41 (31.8)	58 (46.4)				
Working condition Weightlifting						
Always-often	10 (7.8)	2 (1.6)	0.021	5.16	1.10	24.08
Never-seldom	119 (92.2)	123 (98.4)				
Walking						
Always-often	28 (21.7)	9 (7.2)	0.001	3.57	1.61	7.92
Never-seldom	101 (78.3)	116 (92.8)				
Sitting						
Always-often	23 (17.8)	9 (7.2)	0.011	2.79	1.23	6.31
Never-seldom	106 (82.2)	116 (92.8)				
Standing						
Always-often	27 (20.9)	10 (8.0)	0.003	3.04	1.40	6.59
Never-seldom	102 (79.1)	115 (92)				

DISCUSSION

In preterm birth, physical activity with light intensity was the most common physical intensity that was done by pregnant woman (40.2 %, n = 51), followed by vigorous intensity (33.9 %, n = 43), and the last was physical activity with moderate intensity (26 %, n = 33). The results of this study were different from previous studies that most pregnant women would reduce their physical activity. In this study, the most frequent intensity level of physical activity was physical activity with moderate intensity, and vigorous intensity which was 78% of all term birth and subjects who performed moderate intensity and vigorous intensity in preterm birth were 59.9%.

Based on the previous study it was found that only 15% of pregnant women who fulfill the recommendations of physical activity in pregnant women based on ACOG (2002).[2] In addition, a study which was conducted by Bisson et al (2017) showed that there was a decrease in the intensity of physical activity of pregnant women starting from the first trimester to third-trimester pregnancy.[12] In addition, in a study which was conducted by Santos et al. (2014) found that pregnant women who had no activity during pregnancy ranged from 64.5% to 91.5% and tended to increase in the third trimester of pregnancy.[13] Similarly, Pereira et al. (2007) showed that the prevalence of inactive pregnant women increased from 12.6% at the time before pregnancy to 21.6% in the second trimester and did not change until 6 months after delivery.[14] Based on the previous study, it could be seen that there were differences between the results of this study with research that was conducted previously. These differences can be influenced by differences in nutrients before pregnancy, socio-economic environment, and socio-cultural environment.[15]

In this study, we found that adjusted OR of light intensity of physical activity in preterm birth was 5.32 (95% CI, 2.80 - 10.13; p = <0.001) compared with moderate-intensity physical activity for preterm birth. The light intensity of physical activity was associated with preterm birth was caused by the association between light physical activity with gestational diabetes mellitus and preeclampsia which could lead to placental insufficiency and increased inflammatory cytokines leading to preterm birth.[13,16]

Adjusted OR of physical activity with severe intensity in preterm birth was 6.65 (95% CI, 3.28-13.46; p = <0.001) compared with moderate-intensity physical activity for preterm birth. This may be due to other confounding factors, such as nutrient status, and body weight that has not been controlled in this study. Therefore, further research is needed by controlling for confounding factors which were nutrition, and body weight.[17,18]

The strengths of the present study include: This study was conducted by using multivariate analysis so that confounding variables and interaction variables that may be associated with preterm birth can be controlled; this research used case-control as study design; this study used a validated KPAS questionnaire. Our study also has limitations, which in this study there was a possibility of overestimation of the intensity of physical activity, although the questionnaires used have used a validated questionnaire using accelerometry. To improve the accuracy in assessing the intensity of physical activity in pregnant women, the future study can be done accelerometry to know the intensity of physical activity accurately.

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Research Article

The Prevalence and Outcome of Teenage Pregnancies at a Tertiary Care Teaching Hospital

Prevalensi dan Luaran Kehamilan Remaja pada Rumah Sakit Pendidikan Tersier

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Abstract

Objective: To examine the prevalence as well as the maternal and perinatal outcome of teenage pregnancies.

Methods: For analyzing the prevalence of the teenage mothers, we used cross-sectional study design by evaluating the medical records of all pregnant mothers who went to the obstetric clinic of Dr.Cipto Mangunkusumo Hospital, Jakarta, Indonesia, during January 2014 until December 2016. For the outcome of the teenage mothers, we used retrospective study design by analysing medical records of teenage mothers who had delivery at the delivery ward of Dr. Cipto Mangunkusumo Hospital during January 2014 until December 2016. We compared their outcomes to outcomes of pregnant women aged 20 to 30 years old delivered at the same hospital in the same period. Maternal outcomes that were measured include preeclampsia, methods of delivery, anaemia, and postpartum haemorrhage, as well as perinatal outcomes including preterm delivery, and low birthweight.

Results: Among 3.578 out patients at Obstetric Clinic, RSUPN Dr. Cipto Mangunkusumo, we got 503 pregnant subjects, 16 (3.2%) were teenagers. Among 520 subjects who had delivery, 78 (15%) subjects were ≤ 19 years old. Teenage pregnancy was significantly associated with anemia ($p < 0.05$, adjusted OR = 2,08) and low birthweight ($p < 0.05$, adjusted OR = 1.83). Teenage pregnancy was not significantly associated with preeclampsia, methods of delivery, postpartum haemorrhage, and preterm delivery.

Conclusion: The prevalence of teenage pregnancy at Dr. Cipto Mangunkusumo Hospital was 3.2%, and teenage mothers who had delivery was 15%. Teenage mothers are at increased risk of anaemia and delivering low birth weight babies.

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Keywords: maternal outcome, perinatal outcome, prevalence, teenage pregnancies

Abstrak

***Tujuan**: Untuk mengetahui prevalensi kehamilan remaja serta luarannya.*

***Metode**: Untuk menganalisis prevalensi ibu remaja, kami menggunakan desain studi potong lintang dengan mengevaluasi rekam medis dari seluruh ibu hamil yang berobat ke klinik obstetri RSUPN Dr. Cipto Mangunkusumo pada periode Januari 2014 sampai Desember 2016. Pada luaran ibu hamil, kami menggunakan desain studi retrospektif dengan menganalisis rekam medis ibu remaja yang bersalin di RSUPN Dr. Cipto Mangunkusumo pada periode yang sama. Luaran ibu remaja dibandingkan dengan ibu yang bersalin berusia 20-30 tahun. Luaran ibu yang kami ukur meliputi preeklamsia, metode persalinan, anemia, perdarahan pascapersalinan, sedangkan luaran perinatal yang kami ukur meliputi kelahiran prematur dan BBLR.*

***Hasil**: Dari seluruh 3.578 pasien di Poliklinik Obstetri RSUPN Dr. Cipto Mangunkusumo, diperoleh 503 subjek yang hamil, sebanyak 16 (3,2%) subjek adalah remaja. Dari seluruh 520 subjek yang bersalin, 78 (15%) subjek adalah remaja. Kehamilan remaja berhubungan signifikan dengan anemia ($p < 0,05$, adjusted OR = 2,08) dan BBLR ($p < 0,05$, adjusted OR = 1,83). Kehamilan remaja tidak berhubungan signifikan dengan preeklamsia, metode persalinan, perdarahan pascapersalinan, dan kelahiran prematur.*

***Kesimpulan**: Prevalensi kehamilan remaja di RSUPN Dr. Cipto Mangunkusumo adalah 3,2% dan persalinan remaja di RSUPN Dr. Cipto Mangunkusumo adalah 15%. Ibu remaja berada pada peningkatan risiko anemia dan melahirkan bayi BBLR.*

[Maj Obstet Ginekol Indones 2018; 6-4: 209-212]

***Kata kunci**: kehamilan remaja, luaran ibu, luaran perinatal, prevalensi*

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INTRODUCTION

Teenage pregnancy, an important public health burden worldwide, is defined as a pregnancy occurring in females aged 10-19 years. Approximately, 11% of births worldwide are to teenagers aged 15-19 years, and more than 90% of these births occur in low- and middle-income countries. Moreover, the majority of teenage mothers are unmarried, and numerous teenage pregnancies are unplanned. Teenage pregnancy is associated with increased risk of poor maternal and fetal complications, including preterm birth, low birth weight, preterm premature rupture of

membranes (PPROM), preeclampsia, low Apgar scores, and perinatal mortality. However, previous studies have produced contradictory findings regarding whether the adverse pregnancy outcomes among teenage mothers are caused by their biological immaturity or poor socio-environmental factors.[1-3] To this date, studies regarding the complications of teenage pregnancy in Jakarta, Indonesia, are scarce. This study is aimed to investigate the prevalence as well as the maternal and perinatal outcome of teenage pregnancies.

METHODS

For analysing the prevalence of the teenage mothers, we used cross-sectional study design by evaluating the medical records of all pregnant mothers who went to the Women's Health clinic of Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, during the period between January 2014 and December 2016. For the outcome of the teenage mothers, we used retrospective study design by analysing medical records of teenage mothers who had delivery at the delivery ward of Dr. Cipto Mangunkusumo Hospital during January 2014 until December 2016. We compared their outcomes to outcomes of pregnant women aged 20 to 30 years old delivered at the same hospital in the same period. Maternal outcomes that were measured include preeclampsia, methods of delivery, anaemia, and postpartum haemorrhage, as well as perinatal outcomes including preterm delivery and low birthweight.

RESULTS

A total of 503 subjects were recruited for this study. The prevalence of teenage pregnancy was 3.2%. For the prospective study, a total of 520 subjects were included. Of these subjects, 78 (15%) were teenage mothers (≤ 19 years old). Demographic characteristics of the subjects who delivered are presented in Table 1.

Table 1. Demographic Characteristics of Subjects who Delivered

		n (mean/ range)
Mean age		24 (14 - 30)
Age category	Teenagers	78 (15.0)
	Adults	442 (85.0)
Marital age	<20 yo	233 (45.2)
	>20 yo	282 (54.8)
Education	Elementary high school	10 (1.9)
	Junior high school	84 (16.2)
	High school	426 (81.9)
Marital status	Married	515 (99.0)
	Unmarried	5 (1.0)
Employment	Employed	43 (8.3)
	Unemployed	477 (91.7)
Contraceptive methods	Yes	106 (20.4)
	No	414 (79.6)
Delivery methods	Vaginal delivery	228 (43.8)
	Vacuum-assisted delivery	10 (1.9)
	Forceps-assisted delivery	14 (2.7)
	Cesarean section	268 (51.5)
Antenatal care visits attendance	Yes	517 (99.4)
	No	3 (0.6)
Parity	Nulliparous	195 (37.5)
	Multiparous	325 (62.5)
Delivery methods	Spontaneous	228 (43.8)
	Nonspontaneous	292 (56.2)
Anemia	Yes	109 (21.0)
	No	411 (79.0)
Preterm birth	Yes	216 (41.5)
	No	304 (58.5)
Low birthweight	Yes	196 (37.7)
	No	324 (62.3)
Postpartum haemorrhage	Yes	31 (6.0)
	No	489 (94.0)
Preeclampsia	Yes	86 (16.5)
	No	434 (83.5)

In this study, we found significant association between teenage pregnancy and anemia as well as low birthweight. The association between teenage pregnancy and fetomaternal outcomes is presented in Table 2.

Table 2. Association between Teenage Pregnancy and Fetomaternal Outcomes

	Teenage (n = 78)	Adults (n = 442)	p value	Adjusted OR (95% CI)
Preeclampsia	11 (14.1%)	67 (15.2%)	0.530	1.08 (0.51-2.29)
Anemia	25 (32.1%)	52 (11.8%)	0.007	2.08 (1.22-3.54)
Nonspontaneous delivery methods	36 (46.2%)	256 (57.9%)	0.924	1.03 (0.60-1.76)
Preterm delivery	44 (56.4%)	172 (38.8%)	0.148	1.48 (0.87-2.53)
Low birthweight	42 (53.8%)	154 (34.8%)	0.026	1.83 (1.08-3.13)
Postpartum hemorrhage	0 (0%)	31 (73,8%)	0.016	-

DISCUSSION

In this study, the prevalence of teenage pregnancy was 3.2%. This number is lower compared to those in Indonesia, Malaysia, and Thailand, which were amounted to 4.8%, 0.6%, and 4.1%, respectively.[4] This might be due to better socioeconomic status as well as the education levels in Jakarta, compared to other cities in Indonesia. According to the Indonesian Basic Health Research (Riskesdas) 2013, 2.6% female aged 10-54 years married below the age of 15 years. Moreover, 23.9% of women married at the age of 15-19 years.[5]

The incidence of adolescents who gave birth at Dr. Cipto Mangunkusumo Hospital was 15%. This number is significantly higher compared to the teenage pregnancy prevalence at the same hospital. This might occurs because Dr. Cipto Mangunkusumo hospital is a tertiary care center; thus, pregnant teenagers are often referred to this hospital, despite attending another hospital for routine antenatal care.

Preeclampsia, which occurs in 2-8% of all pregnancies, is a specific multisystemic and multifactorial condition in pregnancy that increases the mortality and morbidity of the mother as well as the fetus. The risk factors include younger age, nulliparity, and obesity.[6] A previous study suggested that folic acid supplementation in early pregnancy may decrease the risk of developing preeclampsia, particularly in those with body mass index below 25 kg/m^2.[7] In this study, we did not find significant association between teenage pregnancy and preeclampsia ($p > 0.05$, adjusted OR = 1.08). This is similar to a previous study conducted by Socolov et al. which found no significant differences in pregnancy comorbidity, chronic hypertension, gestational hypertension, preeclampsia, and eclampsia, between teenage and adult mothers.[8] Torvie et al., Traisrisilps et al., Dedecker et al., Gortzak-Uzan et al., and Gupta et al. also found similar findings.[9-13]

Anaemia is a common complication in teenage pregnancy.[14] Chahande et al. reported that 72.6% of pregnant teenagers had anaemia.[15] Osbourne et al. found significant increment in the incidence of anemia in teenage pregnancy compared to those aged 20-24 years (11.1% vs 5.2%, $p < 0.001$). In our study, we found significant association between teenage pregnancy and anaemia ($p < 0.007$, adjusted OR = 2.08). This is similar to a case-control study conducted by Akadiri et al., which found that the incidence of anaemia was significantly higher in teenage mothers.[16] This might happened due to suboptimal nutritional status at the onset of pregnancy. Other two studies also found significant increment of anaemia in teenage mothers.[17,18]

We did not find significant association between teenage pregnancy and delivery method ($p > 0.05$, adjusted OR = 1.03). Several studies found an increased risk of cesarean section in teenage pregnancy. This differs from three studies which found that teenage pregnancy was not significantly associated with increased cesarean section rate.[19-21] Yadav et al. found decreased section rate in teenage pregnancy. In that study, there was a high incidence of prevalence, which may be associated with successful vaginal delivery.[22]

We did not find significant association between teenage pregnancy and preterm birth. However, we found significant association between teenage pregnancy and low birthweight. Bukulmez and Deren found that teenage pregnancy was not an independent risk factor of preterm birth[23], while Tufail and Hasmi found that neonates born from teenage mothers had higher risk of intrauterine growth restriction (5.3% vs 0%, $p = 0.043$).[24] Mahfouz et al. suggested that teenage mothers did

not belong to the high-risk group if there was good quality antenatal care. The poor outcomes of teenage pregnancy might be caused by low socio-economic status, lack of reading interest, inadequate antenatal care, lack of social support, and low use of contraceptive method.[16]

We found statistically significant association between teenage pregnancy and postpartum haemorrhage ($p < 0.016$). However, no subject had postpartum haemorrhage in this study. Thus, it might be concluded that adult mothers are at higher risk of developing postpartum haemorrhage. Sgaili et al., Shah et al., Traisrisilp et al., and Leppalahti et al. did not find significant difference between teenage and adult mothers.[9-12]

Our limitations include lack of measurement of antenatal care attendance. We also used retrospective study design. Thus the reliability was lower compared to prospective study.

CONCLUSIONS

The prevalence of teenage pregnancy and teenage mothers who delivered at Dr. Cipto Mangunkusumo Hospital were 3.2% and 15%, respectively. Teenage mothers are at an increased risk of developing anaemia and delivery low-birthweight babies.

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Research Article

Creatinine Clearance Levels are associated with the Incidence of Preeclampsia

Nilai Creatinine Clearance berhubungan dengan Insidensi Preeklamsia

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Abstract

Objective: To determine the correlation between creatinine clearance relationship with preeclampsia incidence.

Method: We used cross-sectional study design.

Results: Creatinine clearance examination conducted on 60 sample of pregnant women > 20 weeks, 30 normotensive samples and 30 preeclampsia samples. The obtained data analysed using SPSS software version 22.0 and discussed using the existing literature theory. Creatinine clearance average level in normotensive pregnancy 124.650 ± 14.3699ml/minutes/1.73m^2 and preeclampsia 74.003 ± 23.169ml/minutes/1.73m^2. After Mann-Whitney statistical test obtained p value = 0.000. From ROC curve analysis for creatinine clearance obtained sensitivity value 100% and specificity 99.53%.

Conclusion: There is a significant correlation between the creatinine clearance levels with preeclampsia.

[Indones J Obstet Gynecol 2018; 6-4: 213-217]

Keywords: creatinine clearance, normotensive, preeclampsia

Abstrak

***Tujuan**: Menentukan hubungan antara creatinine clearance dengan kejadian preeklamsia.*

***Metode**: Kami menggunakan desain studi potong lintang.*

***Hasil**: Dilakukan pemeriksaan creatinine clearance pada 60 sampel ibu hamil> 20 minggu, 30 sampel darah normal dan 30 sampel preeklamsia. Data yang diperoleh dianalisa dengan menggunakan software SPSS versi 22.0 dan dibahas dengan menggunakan teori literatur yang ada. Kadar rerata creatinine clearance pada kehamilan normotensi 124,650± 14,3699 ml/menit/1,73m^2 dan preeklamsia 74,003 ± 23,169 ml/menit/1,73m^2. Setelah uji statistik Mann-Whitney diperoleh nilai p = 0,000. Dari analisis kurva ROC untuk creatinine clearance diperoleh nilai sensitivitas 100% dan spesifisitas 99,53%.*

***Kesimpulan**: Ada hubungan yang signifikan antara creatinine clearance dengan kejadian preeklamsia.*

[Maj Obstet Ginekol Indones 2018; 6-4: 213-217]

***Kata kunci**: creatinine clearance, normotensi, preeklamsia*

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INTRODUCTION

Preeclampsia is a multiple organ disorder characterised by hypertension (blood pressure ≥ 140/90 mmHg) and proteinuria after 20 weeks of pregnancy. The clinical picture, preeclampsia occurs because the kidneys as the main target organ become endotheliosisglomerulus which led to a decrease in glomerular filtration rate.[1-4]

WHO estimates that preeclampsia cases seven times higher in developing countries than in developed countries. The preeclampsia prevalence in developed countries is 1.3% -6%, while in developing countries is 1.8% -18%. Preeclampsia is the second most common cause of maternal deaths in Indonesia after postpartum haemorrhage.[5]

The most often endothelial damage manifestations organ in preeclampsia is kidney. Preeclampsia causes 75% of acute kidney failure in pregnancy. Kidney function is an essential component in the pathophysiology of preeclampsia so that close monitoring of kidney function is vital to ensure timely delivery before serious kidney damage occurs.[1,2] Creatinine, urea, and uric acid are eliminated metabolite from the body through the kidney. Metabolite concentration measurement often used as kidney function indicator.[6-9]

Best calculation for glomerular filtration rate is by determining creatinine clearance. The creatinine cleanliness level in the blood plasma per unit, time used for filtration combination process and kidney glomerular secretion called creatinine clearance and a measure that can be observed from Glomerular Filtration Rate (GFR).[10-11]

Several studies have investigated the relationship of creatinine clearance with preeclampsia patients. Creatinine clearance in preeclamptic patients obtained significantly decreased compared with normotensive pregnancies. Creatinine clearance used to assess kidney glomerular function, it can be used as preeclampsia predictors. However, it still needs to be proven through studies. This is why the study was conducted.[8,9]

OBJECTIVE

To determine the correlation between creatinine clearance with the incidence of preeclampsia.

METHODS

We used cross-sectional study design to assess creatinine clearance relationship with the incidence of preeclampsia. Subjects were all pregnant women with normotensive and preeclampsia who went to the RSUP Prof. Dr. R. D. Kandou Manado and its affiliated hospital. Subjects consisted of two groups: 30 normotensive and 30 preeclampsia subjects. The inclusion criteria were 20 weeks' gestation women to term with preeclampsia, and willing to participate in research.

After anamnesis, physical examination, and signed informed consent, blood sampling performed. Serum creatinine levels in the blood sample examined in Laboratory RSUP Prof. Dr. R. D. Kandou Manado, then creatinine clearance calculated using the formula CKD-Epi = $141 \times \min (S_{cr}/K, 1)^{\alpha} \times \max (S_{cr}/K, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] $\times$ 1.159 [if black]. S_{cr}: serum creatinine (mg/dl), K: 0.7 (for women) and 0.9 (for men), A: -0.329 (for women) dan -0.411 (for men), Min: minimum of S_{cr} /Kor 1, Max: maximum fS_{cr} /Kor 1.

Data were analysed with the Mann-Whitney test to see whether there was relationship between creatinine clearance and preeclampsia. The data processed using Statistical Product and Service Solutions (SPSS) for Windows version 22.0.

RESULTS

A total of 60 subjects were recruited in this study. Subjects consisted of 30 normotensive and 30 preeclampsia subjects, all of which met the inclusion criteria and have signed the form of willingness to participate in this study. Characteristics of the subjects can be seen in Table 1.

Table 1. Characteristics of the Subjects

Characteristic	Normotensive		Preeclampsia	
	n	%	n	%
Age				
< 35 years	24	80	16	53.33
≥ 35 years	6	20	14	46.67
Parity				
Primiparas	15	50	13	43.33
Multiparas	15	50	17	56.67
Gestational Age				
> 20 - 28^{+6} weeks	-	0	-	0
29 - 36^{+6} weeks	3	10	8	26.67
> 37 weeks	27	90	22	73.33
Highest Education				
Bachelor (Sarjana)	1	3.33	-	0
Senior High School (SLTA)	13	43.33	14	46.67
Junior High School (SLTP)	12	40	11	36.67
Elementary School (SD)	4	13.33	5	16.67
Employment				
Civil Servants	1	3.33	1	3.33
Housewife	29	96.67	29	96.67

Table 2. The Creatinine Clearance of both Groups

Variable	Normotensive n=30	Preeclampsia n=30	p
Creatinine clearance (ml/minutes/1.73 m^2)			
Mean ± SD	124.650 ± 14.3699	74.003 ± 23.169	<0.001
Median	124.600	76.850	
Lowes Score	79.9	17.4	
Highest Score	154.2	112.3	

In this study, the normotensive group had higher mean creatinine clearance compared to the preeclampsia group (124.650 ± 14.3699 vs 74.003 ± 23.169, p < 0.001). The creatinine clearance of both groups is presented in Table 2.

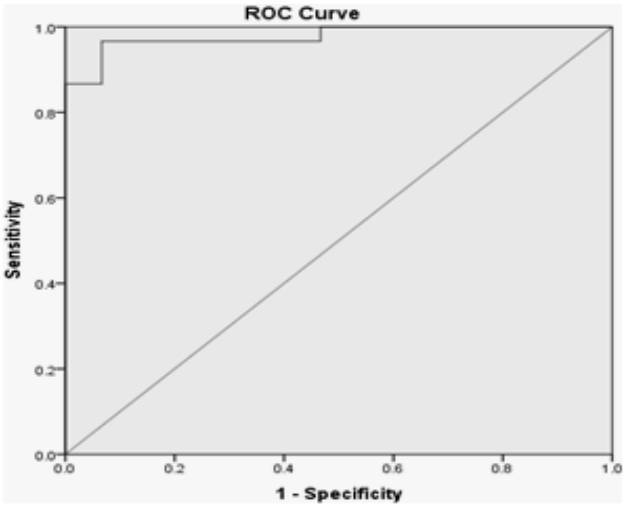

Figure 1. Graph of creatinine clearance variable distribution in preeclampsia and normotensive pregnancy group.

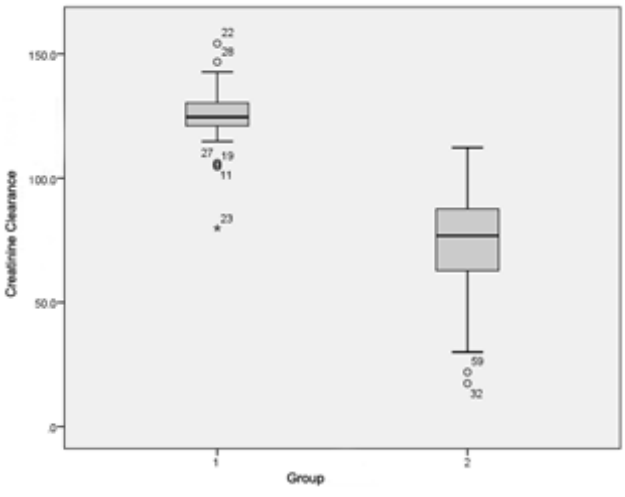

Figure 2. Graph of creatinine clearance ROC curve analysis.

ROC curve analysis creatinine clearance for normotensive patients, mild preeclampsia, and severe preeclampsia obtained the value of sensitivity 100% and specificity 99.53%.

Mann-Whitney test conducted to determine the relationship between Creatinine Clearance with preeclampsia. Statistical test showed that p = 0.000, which means that there is a significant relationship between creatinine clearance with preeclampsia.

DISCUSSION

This research aims to determine the existence of relationship between creatinine clearance with preeclampsia. This research on the relationship of creatinine clearance with preeclampsia is the first research conducted in RSUP Prof. Dr. R.D. Kandou Manado and network hospital.

Hypertension in pregnancy is one of the causes of maternal death. Preeclampsia is a secondary reduced perfusion organ pregnancy-specific syndrome to vasospasm and endothelial activation. Preeclampsia characterised by increased blood pressure accompanied by proteinuria in the pregnancy > 20 weeks. Pathogenesis basis of preeclampsia is maternal endothelial cell damage. Hypertension and proteinuria that dominate the clinical picture occur because kidney as the primary target organ experiences morphologic change characterised by endotheliosis at kidney glomerulus that will inhibit the filtration process. Numerous researches have reported that kidney function decreases in pregnancy with preeclampsia.[1,2,12]

In Table 1 shows that by age in normotensive, the vast majority were < 35 years as many as 24 peoples (80%) and the least were age ≥ 35 years as many as six peoples (20%). Whereas in preeclampsia the vast majority were age < 35 years as many as 16 people (53.33%), followed by age ≥ 35 years as many as 14 people (46.67%).

According to parity, in normotensive, normotensive as large as preeclampsia, i.e. 15 people (50%). Whereas in preeclampsia, the vast majority were multiparas by 17 peoples (56.67%) followed by primiparas 13 people (43.33).

Based on gestational age, in normotensive, the vast majority were in gestation > 37 weeks by 27 peoples (90%), followed by gestational age 29 - 36^{+6} weeks by 3 peoples (10%). Similarly, in a group of preeclampsia, the vast majority were in gestation > 37 weeks by 22 peoples (73.33%), followed by gestational age 29 - 36^{+6} weeks by 8 peoples (26.67%).

In the normotensive group, according to education characteristics, the vast majority were SLTA by 13 peoples (43.33%), followed by SLTP 12 peoples (40%), and SD 4 peoples (13.33%), and the least bachelor was by one people only (3.33%). Whereas in the preeclampsia group the vast majority were SLTA by 14 peoples (46.67%), followed by SLTP 11 peoples (36.67%), and SD 5 peoples (16.67%).

According to the employment characteristics in the normotensive group, the vast majority were housewife by 29 peoples (96.67%), followed by one civil servant (3.33%). In the preeclampsia group, the vast majority were housewives by 29 peoples (96.67%), followed by civil servant one people (3.33%).

In Table 2, we could see that based on creatinine clearance in normotensive has mean value 124.650, median value 124.600, and standard deviation 14.3699. In preeclampsia has mean value 74.003, median value 76.850, and standard deviation 23.1699. Mann-Whitney test analysis obtains a p value= 0.000. A p-value less than 0.05 indicates that there are significant differences between normotensive and preeclampsia based on creatinine clearance. These results are also consistent with a study conducted by Israa Jumaahin 2012 where there was significant difference of creatinine clearance value in preeclampsia compared with normotensive.[9]

In this research, ROC curve analysis for creatinine clearance obtained sensitivity value 100% and specificity 99.53%. Based on this sensitivity and specificity, showed that creatinine clearance is a good screening test for early detection of kidney disorder in patients with preeclampsia. Creatinine widely has been used to assess kidney function. Creatinine clearance sufficiently sensitive in assessing changes in glomerular filtration rate in the early stages of kidney disorder.[13]

The results of this research support the previous research by other researchers. A study conducted by Reuters in 2015 stated that there were significant differences of creatinine clearance in preeclampsia when compared with normotensive pregnancies, whereas in normotensive case obtained creatinine clearance as much as 132.70 ml/minutes/1.73 m^2 with standard deviation 11.0-15.6 and in preeclampsia 71.98 ml/minutes/ 1.73 m^2 with standard deviation 60-82.5 and p value< 0.05.[12]

There is also research conducted by Israa Jumaah in 2012 performed on 100 pregnant women, where 50 were pregnant women with normotensive and 50 other pregnant women with preeclampsia. From those researches concluded that creatinine clearance in preeclampsia women (103.6 ± 29.63 ml/minutes/1.73 m^2) significantly lower ($p < 0.05$) compared with normotensive pregnant women (125.30 ± 15.14 ml/minutes/ 1.73 m^2).[9]

The decrease of creatinine clearance in preeclampsia patients was due to morphological changes in kidney characterised by endotheliosis that will inhibit glomerular filtration so that in preeclampsia reduced glomerular filtration rate will happen. Starting with placental ischemia as result of placental implantation disorder that will lead to the release of a number of placental material into the maternal circulation including an increase in sFlt-1 (soluble fms-like tyrosine kinase), pro-inflammatory cytokines (TNFα and IL6), AT1-AA (Angiotensin II type 1 Receptor Autoantibodies and Thromboxane). These factors contribute to the endothelial activation resulting in maternal endothelial disorder and produce clinical findings such as hypertension and proteinuria. Proteinuria and hypertension dominate the clinical picture because the main target organ is the kidney. Thus, changes in kidney function is an important component in the pathophysiology of preeclampsia. With the presence of endothelial dysfunction would lead to a decrease in kidney function, resulting in a decrease in glomerular filtration rate.[14]

In this research, there was significant relationship between preeclampsia and creatinine clearance. This supported by several previous studies,

where creatinine clearance in preeclampsia significantly lower compared with normotensive pregnancies. Glomerular cell damage resulting increased in basement membrane permeability, thus lead to kidney filtration function disorder.[2] Clinically reduced kidney perfusion, and glomerular filtration rate is very important. This situation will be growing along with the getting worse disease. With the decrease in glomerular filtration rate eventually, plasma creatinine levels increase which means that creatinine clearance decreases because of the kidney is less able to filter creatinine of the blood.[8,15]

CONCLUSION

From this research, the mean of creatinine clearance in normotensive pregnancy group was 124.650 ml/minutes/1.73m^2, and preeclampsia 74.003 ml/minutes/1.73m^2. There was a significant relationship between creatinine clearance and preeclampsia. The mean rate of creatinine clearance in patients with preeclampsia was lower than normotensive.

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Research Article

Hypertriglyceridemia is Associated with the Incidence of Preeclampsia

Hipertrigliseridemia Berkaitan dengan Insidensi Preeklamsia

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Abstract

Objective: To investigate the correlation between lipid profile during the second trimester II pregnancy and the incidence of preeclampsia.

Methods: This Universitas prospective study was conducted at the Woman's Health Clinic of Hasanuddin Teaching Hospital, Department of Obstetrics and Gynecology of the Faculty of Medicine, and its affiliated hospital in Makassar city from March 2015 to March 2016.

Results: The examination of the lipid levels of 115 pregnant mothers, aged 24-28 weeks. The mothers were then observed whether they experienced preeclampsia up to the time they gave birth or not. In the end, eight subjects (6.9%) experienced preeclampsia, and 107 subjects (93.1%) have no preeclampsia. The statistical analyses used Fisher's Exact test and Mann Whitney test. The research results indicated that the mean value of the total cholesterol and Low-Density Lipoprotein (LDL) was higher in the preeclampsia group compared to the non-preeclampsia group: 267.37 ± 64.12 vs 238 ± 37.98; 177.38 ± 55.38 vs 157.24 ± 35.08 (p>0.05). The mean value of High-Density Lipoprotein (HDL) was lower in the preeclampsia group compared to the non-preeclampsia group: 64.75 ± 14.64 vs 67.86 ± 16.72 (p>0.05). The mean value of triglyceride in preeclampsia group was significantly higher (19.5%) compared to the non-preeclamptic group: 260.12 ± 58.86 vs 209.14 ± 65.10 (p=0.027).

Conclusion: The hypertriglyceridemia was correlated with the preeclampsia incidence.

[Indones J Obstet Gynecol 2018; 6-4: 218-221]

Keywords: lipid profile, preeclampsia, trimester II of pregnancy

Abstrak

***Tujuan**: Mengetahui hubungan antara profil lipid kehamilan trimester II dengan kejadian preeklamsia.*

***Metode**: Studi prospektif ini dilaksanakan di Poliklinik RS jejaring pendidikan Departemen Obstetri dan Ginekologi Fakulltas Kedokteran Universitas Hasanuddin dan Poliklinik Kesehatan Ibu dan Anak di beberapa Puskesmas Kota Makassar selama Maret 2015 sampai dengan Maret 2016.*

***Hasil**: Dari 115 ibu hamil dilakukan pemeriksaan kadar lipid, 115 ibu hamil pada usia kehamilan 24 - 28 minggu, kemudian diamati apakah subjek mengalami preeklamsia hingga proses persalinan. Terdapat delapan subjek (6,9%) berkembang menjadi preeklamsia dan 107 subjek tidak preeklamsia. Data dianalisis secara statistik dengan menggunakan uji Fisher's Exact dan uji Mann Whitney. Hasil penelitian menunjukkan bahwa nilai mean kolesterol total dan Low Density Lipoprotein (LDL) lebih tinggi pada kelompok preeklamsia dibandingkan kelompok tidak preeklamsia, yaitu 267,37 ± 64,12 : 238,01 ± 37,98; 177,38 ± 55,38 : 157,24 ± 35,08 (p>0,05). Nilai mean High Density Lipoprotein (HDL) lebih rendah pada kelompok preeklamsia dibandingkan tidak preeklamsia yaitu 64,75 ± 14,64 : 67,86 ± 16,72 (p>0,05). Nilai mean trigliserid daripada kelompok preeklamsia secara signifikan lebih tinggi 19,5% dibandingkan kelompok tidak preeklamsia, yaitu 260,12 ± 58,86 : 209,14 ± 65,10 (p=0,027).*

***Kesimpulan**: Hipertrigliseridemia berhubungan dengan kejadian preeklamsia.*

[Maj Obstet Ginekol Indones 2018; 6-4: 218-221]

***Kata kunci**: kehamilan trimester II, preeklamsia, profil lipid*

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INTRODUCTION

Hypertension in pregnancy plays a major role not only in improving maternal morbidity and mortality during pregnancy and childbirth but cause problems after delivery which cause the risk of cardiometabolic disease in the future. World Health Organization (WHO) estimates that cases of preeclampsia occurs seven times higher in developing countries than in developed countries and contribute maternal deaths due to its complications during pregnancy. The prevalence of preeclampsia in developed countries is 1.3% - 6%, while in developing countries is 1.8% - 18%. The incidence of preeclampsia in Indonesia itself is 128 273 / year (5.3%) and became one of the three causes of maternal mortality include haemorrhage (30%), eclampsia (25%) and infections (12%).[1]

Abnormal lipid metabolism had a significant impact on the pregnancy-induced pathogenesis of preeclampsia and associated with increased lipid peroxidation products that act as oxidative stress dysfunction endothelial.[2]

Results of a meta-analysis conducted by Gallos against 24 case-control studies and five cohort studies suggest a link between preeclampsia with triglyceridemia levels that precedes the occurrence of preeclampsia. In the study mentioned further research will be needed to define the prognostic accuracy test to identify women at risk, as well as whether the treatment lowers triglycerides can provide beneficial effects during pregnancy.[3]

Examination of biomarkers to predict pre-eclampsia developed at this time in addition to expensive, limited examination carried out on laboratory and specific regions. This research will conduct a cohort study that will look at the relationship between lipid profile in the second trimester and pregnant women with preeclampsia.

METHODS

This study is a prospective cohort study, consecutive random sampling. This research was conducted at the Dr. Wahidin Sudirohusodo teaching Hospital Department of Obstetrics and Gynecology, Universitas Hasanuddin Makassar and its network.

The inclusion criteria of this study were pregnant women who do the antenatal care in the second trimester of pregnancy (24-28 weeks), with a complete identity, has a phone number that can be contacted, volunteered to follow the research and planned deliveries in Makassar. Subjects will be excluded if she had a history of metabolic diseases such as diabetes mellitus, vascular disease and coronary heart disease, a blood sample lysis and the data is incomplete and does not follow the entire procedure. While the subject is considered to drop out if the pregnant women moved from Makassar or cannot be contacted or subject decided to stop participating in the study. Of the 115 subjects, obtained 8 (6.9%) of people who become preeclampsia serve as study groups, and 107 non-preeclampsia was used as a control group.

Three millilitres of venous blood of pregnant women who agreed to be the subject of research was taken and stored in tubes serum separator tube (SST), then the serum was examined on the same day. Serum lipid profile has been checked were total cholesterol, HDL, LDL and triglyceride using colourimetric, enzymatic through ROCHE / Hitachi system COBAS c. The concentration of lipid profile using milligrams per deciliter (mg/dl). Furthermore, the subjects were observed until delivery or until preeclampsia. Data analysis using the Fisher exact test and Mann Whitney's.

RESULTS

During the period of one year (March 2015 - March 2016), we obtained 128 second trimester pregnant women, gestational age range 24-28 weeks who were willing to be the subject of research. Of the 128 subjects, there were 13 subjects who lost through observation and only 115 subjects were followed until childbirth. Of the 115 subjects, we obtained 8 (6.9%) of people who become preeclampsia serve as the study group and 107 people who did not preeclampsia used as a control group.

Table 1. Characteristics of the Sample

Characteristics	Preeclamptic Group n=8 (%)	Non-Preeclamptic Group n=107 (%)	p-value
Age (years)			
< 20 and > 35	2 (25)	30 (28)	0.608
20-35	6 (75)	77 (72)	
Body Mass Index			
< 25	2 (25)	49 (45.8)	0.223
≥ 25	6 (75)	58 (54.2)	
Parity			
Primi / nulliparous	2 (25)	45 (42.1)	0.290
Multipara	6 (75)	62 (57.9)	

Fisher's Exact Test

Table 2. Lipid Levels in Pregnancy

Lipid levels (mg/dl)	Preeclamptic Group n=8	Non-Preeclamptic Group n=107	p-value
Total cholesterol	267.37 ± 64.12	238.01 ± 37.98	0.218
LDL	177.38 ± 55.38	157.24 ± 35.08	0.353
HDL	64.75 ± 14.64	67.86 ± 16.72	0.704
Triglycerides	260.12 ± 58.86	209.14 ± 65.10	0.027

Mann-Whitney Test

In table 1 we can see the tendency of preeclampsia occurs in the age group 20-35 years, body mass index greater than 25 kg/m^2 and multiparous. Characteristics of age, body mass index and parity (p> 0.05) were not statistically significant. The data showed homogeneous between groups of pre-eclampsia and non-preeclampsia group.

Table 2 shows the mean of each lipid in the preeclampsia and its counterpart. The increased levels of total cholesterol, LDL and HDL did not achieve a significant relationship between preeclampsia and non-preeclampsia group. There is a significant association between elevated levels of triglycerides of preeclampsia compared to the non-preeclampsia group with p = 0.027. The mean triglyceride levels of preeclampsia group 19.5% higher than its counterpart, whereas the mean value of total cholesterol and LDL respectively 12.3% and 11.3% higher, and the mean HDL levels 4.5% lower in the preeclampsia compared to the non-preeclamptic group. Compared with normal triglyceride levels in non-pregnant women (high levels of triglycerides <150 mg/dl) an increase of 42.3% was obtained among pregnant women.

DISCUSSION

This study shows an association between high levels of triglycerides in the second trimester of pregnancy and preeclampsia. The participation rate of the subjects in this study amounted to 89.8% with a total of 115 subjects. Of the 115 subjects who obtained 6.9% of subjects in the course of her pregnancy developed preeclampsia. It is concluded that there were 3.9% of cases the diagnosis of preeclampsia enforced of all pregnancies and is half of the cases are found in gestational hypertension.[4]

The incidence of preeclampsia is affected by parity, race/ethnicity, genetic predisposition, environment, socioeconomic and other factors. It is said the incidence of preeclampsia in nulliparous population ranged from 3 to 10%. In this study, two (4.3%) of 48 subjects nulliparous become preeclampsia.

Extremes of maternal age under 20 years and above 35 years increases the risk of preeclampsia.[5] In this study, 32 subjects are at the extreme age groups, and two of them suffered from preeclampsia, which is obtained statistically not significant results. Duckitt reported that the increase in preeclampsia increased almost two-fold in pregnant women aged 40 years or higher in primiparous and multiparous, while young age does not increase the risk of preeclampsia.[1,6]

Pregnancy causes changes in lipid profiles of different levels each trimester. Okojie et al. conducted a study involving 120 pregnant women, and they measured the total serum cholesterol, HDL, LDL and triglycerides in the first, second and third trimester compared with healthy women who were not pregnant. The result is an increase in total cholesterol, HDL, LDL and triglycerides were not significant in the first trimester but becomes significant in the second and third trimester compared to controls. Levels of lipid profile in second trimester described in Table 2, which found elevated levels of total cholesterol, LDL, HDL and triglycerides as much as 236.72 mg / dl, 156.64 mg / dl, 66.93 mg / dl and 207.93 mg / dl compared to the levels of healthy adult women who are not pregnant as much as <200 mg / dl, <100 mg / dl, 40-60 mg / dl and <150 mg / dl. It happens due to the increase of maternal fat metabolism is needed as an alternative to the energy needs of fetal development. In addition, lipids also caused hormonal changes among pregnant women (insulin resistance, progesterone, 17-β estradiol, Human Placental Lactogen), maternal factors that include the body mass index, weight gain during pregnancy, the nutritional

status of the mother, lipid levels before pregnancy and other medical problems having a significant effect on the metabolism of lipids and levels in plasma. It does not only have an impact on the pregnancy itself but a risk factor for atherosclerosis and cardiovascular disease in the future.[4,7,8]

Moningkey on nested control study involving 82 non-preeclamptic and 84 preeclamptic women were divided into 31 and 53 cases of early-onset and late-onset, respectively. Triglyceride level as risk factors that most contribute to the early and late onset of preeclampsia. The same results were obtained on systemic reviews conducted by Ray and Gallos, investigating the risk of preeclampsia with triglyceride levels of maternal included 24 case-control studies involving 2720 women and five prospective cohort studies involving 3147 women second trimester before the onset of preeclampsia, showed hypertriglyceridemia precede the onset of preeclampsia.[3,9,10] In this study, of 115 subjects of second-trimester pregnant women (gestational age 24-28 weeks), 8 (6.9%) subjects whose pregnancy develops into preeclampsia and its triglycerides were elevated significantly before the onset of preeclampsia ($p = 0.027$).

Pregnancy with hypertension and preeclampsia have a relationship with the occurrence of chronic hypertension and increased risk of cardiovascular disease in the future. This is because the metabolic abnormalities in pregnancies that include obesity, insulin resistance and abnormal lipid levels cause endothelial dysfunction and eventually preeclampsia. The underlying mechanisms are still further research. Early detection, control and handling is expected to positively affect the outcome of the pregnancy itself and lifestyle modifications for future cardiovascular health.[11]

CONCLUSIONS AND SUGGESTIONS

High levels of triglycerides in the second trimester of pregnancy is associated with the incidence preeclampsia. Examination of triglycerides can be considered as a basis of examination in the second trimester in order to see the likelihood of preeclampsia.

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Research Article

Demographic Characteristics of Mothers who Delivered Children with Birth Defects

Demografi Ibu yang Melahirkan Janin dengan Kelainan Bawaan

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Abstract

Objective: To determine the characteristics and background of mothers who delivered neonates with birth defects.

Methods: A retrospective study was used by evaluating the medical records of patients with birth defects in Dr. Cipto Mangunkusumo Hospital during the period between September 2014 to June 2016.

Results: A total of 67 (1.85%) out of 3,619 infants who were born in Dr. Cipto Mangunkusumo Hospital during the period between September 2014 and June 2016 had birth defects. Forty-seven (70.1%) mothers of the subjects irregularly attend antenatal care. The most frequent maternal comorbid disease in this study was asthma, which was found in 4 (5.97%) mothers of the subjects. 48 (58.7%) subjects had birth weight under 2500 g.

Conclusion: In this retrospective study, the main highlight is that 70.1% of the mothers who delivered neonates with birth defects did not attend antenatal care regularly. 58.7% of the neonates with birth defects had low birth weight. This study could be used as a base for further research investigating the role of antenatal care in early detection and/or the planning of delivery for babies with birth defects. Trends in babies with birth defects suggested that fetuses diagnosed with IUGR/SGA should be given special attention, as they were at increased risk for birth defects.

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Keywords: birth defect, maternal characteristics

Abstrak

***Tujuan**: Untuk mengetahui deskripsi/ciri-ciri dan latar belakang ibu yang melahirkan janin dengan kelainan bawaan.*

***Metode**: Studi retrospektif digunakan dengan menggunakan data sekunder rekam medis pasien dengan kelainan bawaan di Rumah Sakit Umum Pusat Nasional Dr. Cipto Mangunkusumo pada periode September 2014-Juni 2016.*

***Hasil**: Sejumlah 67 (1,85%) dari 3.619 neonatus didapatkan dengan kelainan bawaan di RSUPN Dr. Cipto Mangunkusumo pada periode September 2014-Juni 2016 . Sejumlah 47 (70,1%) ibu dari subjek tidak teratur dalam melakukan kunjungan antenatal care. Penyakit komorbid ibu yang paling banyak ditemukan dalam studi ini adalah asma, yang ditemukan dalam 4 (5,97%) subjek. 48 (58,7%) subjek memiliki berat lahir di bawah 2500 g.*

***Kesimpulan**: Pada studi retrospektif ini didapatkan 70,1% ibu yang melahirkan bayi dengan kelainan bawaan tidak melakukan kunjungan antenatal care. Didapatkan bahwa 58,7% bayi yang lahir dengan kelainan bawaan memiliki berat badan lahir rendah (BBLR). Studi ini dapat dijadikan sebagai landasan dilakukannya studi yang lebih besar untuk mengevaluasi peran antenatal care terhadap deteksi dini dan/atau perencanaan persalinan bayi dengan kelainan bawaan. Tren pada bayi dengan kelainan bawaan menunjukkan bahwa janin yang pada antenatal care didapatkan IUGR/SGA patut diperhatikan lebih untuk kecurigaan kemungkinan adanya kelainan bawaan.*

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***Kata kunci**: deskripsi ibu, kelainan bawaan*

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INTRODUCTION

Embryonic development is a complex process from the time of fertilisation to the formation of cells, tissues and organs. In early pregnancy, each body organ (system) has a critical period of organogenesis. Interference during this early pregnancy with intrinsic and extrinsic factors (i.e. parental and multifactorial effects) may lead to different types of birth defects.[1-3] Birth defects are one of the major causes of infant and child mortality, morbidity, and long-term disability.[4,5] The term 'birth defects; refer to any morphological, functional, behavioural, and metabolic defects that develop during the organogenesis period and present at birth or detected later in life.[2] Birth defects may be caused by genetic, chromosomal, environmental, and multifactorial effects, as well as micronutrient deficiencies or unknown etiological agents.[6,7]

Birth defects affect 3% of all neonates, cause 3.2 million birth defect-related disabilities, and result in 2.7 million infant deaths.[8] They have a significant effect on individuals, families, health-care systems and societies. Birth defects are particularly serious health burden in low- and middle-income countries, including Indonesia, due to consanguineous marriage, advanced maternal age, migration and poverty.

The magnitude of birth defects varies from country to country and from race/ethnicity, and about 40-60% of their causes are unknown.[9] According to the World Health Organization, approximately 3 million fetuses and infants are born each year with major malformations.[2]

Approximately 94% of infants born with birth defect were reported to come from the middle and low-income countries, and it also recorded 95% of the death of such children from birth defects.[10] The defects pose serious psychological stress or nursing mothers due to potential life-long disability.[11]

Studies describing maternal characteristics associated with birth defects have never been conducted in Indonesia. We aim to describe the characteristics of mothers who give birth to infants with birth defects.

METHODS

A retrospective study design was used by evaluating the medical records of patients with birth defects in Dr. Cipto Mangunkusumo Hospital during the period between September 2014 and June 2016. Inclusion criteria include subjects with spina bifida, anencephaly, meningo/encephalocele, congenital cataract, cleft palate, cleft lip, cleft lip and palate, hypospadias, epispadias, talipes, reduction deformity, atresia ani with/without fistula, omphalocele, gastroschisis, or conjoined twins.

RESULTS

Sixty-seven (1.85%) out of 3,619 neonates born at Dr. Cipto Mangunkusumo Hospital during the period between September 2014 and June 2016 had birth defects. Six (9%) mothers of the subjects were Javanese. Fifteen (22.39%) mothers of the subjects resided in East Jakarta. Forty-seven (70.1%) mothers of the subjects irregularly attend antenatal care. Demographic characteristics of the subjects are presented in Table 1.

Table 1. Demographic Characteristics of the Mothers of the Subject

Characteristic	n (total 67)	%
Maternal ethnic group		
Javanese	6	9
Sundanese	3	4.5
Betawi	1	1.5
Batak	1	1.5
Padang	1	1.5
Badui	1	1.5
Others	1	1.5
Unknown	53	79.1
Domicile		
Central Jakarta	5	7.46
East Jakarta	15	22.39
West Jakarta	6	8.96
North Jakarta	3	4.48
South Jakarta	5	7.46
Bekasi	12	17.91
Tangerang	4	5.97
Depok	5	7.46
Bogor	1	1.49
Other	1	1.49
Unknown	10	14.93
Education		
Undergraduate	2	3
D3	1	16.4
Senior High School	11	1.5
Junior High School	1	1.5
Elementary	1	1.5
Unknown	51	76.1
Regularity of Antenatal Care Visits		
Regular	8	12
Irregular	47	70.1
Unknow	12	17.9
Antenatal Care Location		
Dr. Cipto Mangunkusumo Hospital	6	9
Other than Dr. Cipto Mangunkusumo Hospital	49	73.1
Maternal Age		
≤ 35 y.o	49	73
> 35 y.o	18	27
Gravidity		
< 2	22	32.84

≥ 2	45	67.16
Types of delivery		
Caesarean section	42	63
Spontaneous	25	37
Gestational age		
< 37 weeks	40	60
≥ 37 weeks	27	40
Maternal comorbid disease		
Asthma	4	5.97
Diabetes	1	1.49
Graves'disease	2	2.99
Others*	4	5.97
Denied	43	64.18
Unknown	13	19.40

**Others = severe preeclampsia, primary infertility, thyroid carcinoma, uterine myoma*

In this study, the commonest birth defect was omphalocele (20.48%), followed by labiognatopalatochizis (9.64%), talipes (9.64%), and others consisting of anencephaly, atresia ani, as well as conjoined twins (8.43%). Defects related to gastrointestinal system (29.79%) were the commonest, followed by central nervous system (19.7%), and facial and oral malformations (13.64%). The occurrence of multiple organ defects was 18.18%. Forty-two (63%) mothers of the subjects underwent caesarean section. Forty (60%) mothers had gestational ages below 37 weeks. Four (5.97%) mothers of the subjects had asthma in this study.

The percentage of each birth defect based on organ system were respectively as follow. The percentage of defects related to central nervous system including anencephaly, encephalocele, meningoencephalocele, ventriculomegaly, and spina bifida was 38.89%, 5.56%, 16.67%, 5.56%, and 33.33%, respectively. The percentages of defects related to gastrointestinal system including omphalocele, gastroschisis, and atresia ani, were 60.71%, 14.29%, and 25%, respectively. Musculoskeletal defects including talipes, limb shortness, hypoplasia of the extremities, and amelia were 57.14%, 28.57%, 7.14%, and 7.14%, respectively. Genitourinary defect including hypospadias was 5.97%. The percentages of other birth defects consisting of congenital cataract and conjoined twins were 12.5% and 87.5%.

Table 2. The Distribution of Prenatal Ultrasound and Postpartum Findings

Conformity	n
Prenatal ultrasound findings matching postpartum findings	36
Prenatal ultrasound findings not matching postpartum findings	12
No prenatal ultrasound findings	19

Of 67 subjects, 19 were excluded due to the lack of ultrasound findings. Of 48 subjects, 36 (75%) of prenatal ultrasound findings were matching with postpartum findings.

Table 3. Demographic Characteristics of the Subjects

Characteristic	n	%
Sex (n=67)		
Male	32	47.7
Female	35	52.3
Birth weight/ g (n=46)		
2500	19	41.3
<2500	48	58.7

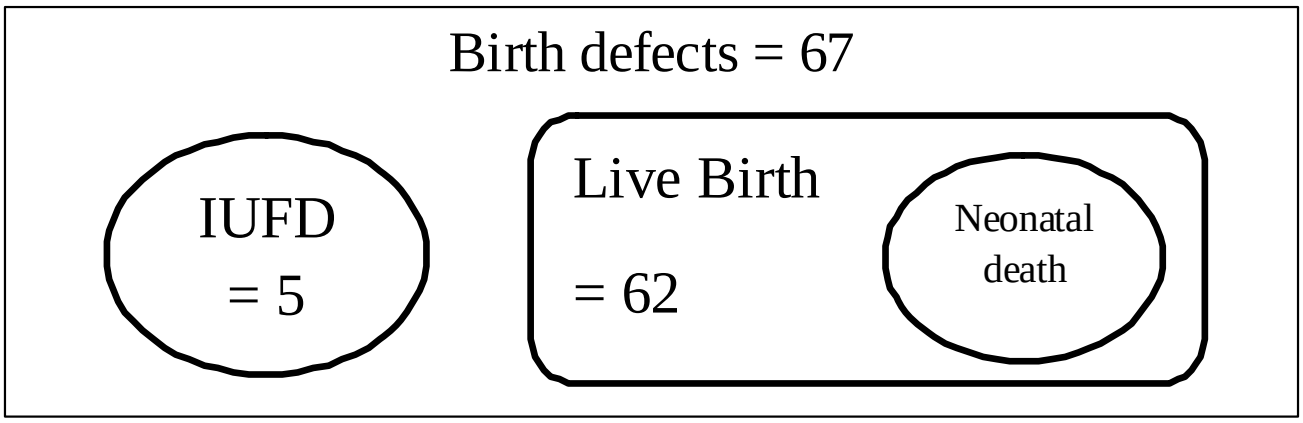

Figure1. The incidence of intrauterine fetal death (IUFD) and neonatal death.

The majority of the newborns were female (52.3%). 58.7% of the subjects had low birth weight (<2500 g). The mean birth weight of newborns was 2236.98 ± 792.92. The lowest and highest birth weights were 600 g and 3880 g, respectively. The incidence of intrauterine fetal death (IUFD) and neonatal death in their first 28 days of life were 7.46% and 32.8%, respectively (Figure 1).

DISCUSSION

Regularity of Antenatal Care Visits

Antenatal care is a crucial element for improving maternal and neonates health. Effective antenatal care improves maternal health through early detection, prevention as well as treatment of medical and obstetrical complications during pregnancy.[11] In this study, 40 (70.1%) mothers of the subjects irregularly attend antenatal care, which suggested that the regularity of antenatal care visits might be a key element in preventing birth defects. However, to our knowledge, studies investigating the association between regularity of antenatal care visits and the occurrence of birth defects have never been conducted. A possible explanation is that mothers who irregularly attend antenatal care have lower knowledge about the prevention of birth defects, which may lead to high incidence of birth defects. Further studies are required to investigate this association.

Maternal Educational Level

In this study, no direct association between maternal educational level and the occurrence of birth defects were found. This is in line with a previous study conducted by Bello et al[12] which revealed that the level of education had no significant relationship with their specific knowledge, knowledge in relation to risk factors and the overall knowledge about birth defect.

Maternal Age

In this study, maternal age above 35 years old had no direct association with the occurrence of birth defects. This is contrary to previous studies, which might be due to smaller population size. Hollier et al[13] concluded that increased maternal age was significantly associated with chromosomal aberrations, particularly aneuploidies. In addition, it has been reported that woman who were 25 years of age or older at delivery had significantly and progressively greater risk of having fetuses with non-chromosomal malformation compared to women aged 20-24 years. The National Center for Health Statistics[14] conducted a study about the effects of advanced maternal age on risks of congenital malformations. These data demonstrated a significant trend of increasing congenital heart disease with advancing maternal age. However, infants with chromosomal abnormalities were not considered separately in that study.

Gestational Age

In this study, 60% of the subjects had gestational age less than 37 weeks. This showed that the occurrence of birth defects is higher in the premature population. This finding is in line with several previous studies. In a population-based cohort study of 264,392 infants, 7,738 (2.93%) were identified as having birth defects. The study revealed that premature infants were more than two times as likely to develop birth defects (risk ratio [RR] = 2.43; 95% CI 2.30-2.56).[15]

Maternal Comorbid Disease

The most frequent maternal comorbid disease in this study was asthma (5.97%). This is in line with a previous study conducted by Blais et al[16], which found that maternal asthma was significantly associated with an increased risk of congenital malformation. This might be due to impaired fetal oxygenation and medications used to treat asthma. A systematic review and meta-analysis of 21 studies[17] found that maternal asthma was associated with a significantly increased risk of congenital malformations (RR 1.11, 95% CI 1.102-1.21).

Prenatal Ultrasound and Postpartum Findings

Prenatal ultrasound was established in Russia in 2000 as a routine method of screening for birth defects. The effectiveness of prenatal screening can be estimated by the prenatal detection rate, which represents the proportion of birth defects recognised before delivery.[20] The sensitivity and specificity of ultrasound were 39% and 99.9%, respectively. Several birth defects can be identified accurately based solely on prenatal findings. Exam-

ples include anencephaly, spina bifida, chromosomal abnormalities, and conjoined twins. However, not all birth defects can be identified accurately based solely on prenatal findings. The positive predictive value of prenatal ultrasound for congenital heart defects varies from 70% to 98%, depending on the type of ultrasound (four-chamber view alone, with outflow tract view, fetal echocardiography) and the specific cardiac defect.[18-21] In this study, 25% of the subjects' abnormalities were not identified accurately.

Birth Weight

In this study, the majority of the subjects had birth weight <2500 g. This finding is in line with previous studies. In a cohort of 307 fetuses with congenital heart diseases, 17 % were associated with a birth weight centile <10th when standard population centiles were used. The Baltimore-Washington Infant Study[22] suggested that, in infants with CHD, birth weight was significantly lower than the control population. Mili et al[23] found that low-birth-weight infants were at a 1.76-times higher risk of having birth defects than those weighing 2500 g to 3999 g.

Postnatal Treatment

Neonatal screening for birth defects may facilitate early detection, treatment and care. Neonatal screening programmes (physical examination of all neonates and screening for congenital hypothyroidism, phenylketonuria, sickle-cell disease and glucose-6-phosphate dehydrogenase deficiency) and training of primary health-care providers aids the diagnosis and appropriate referral for treatment of infants with birth defects. Physical examination of all neonates by trained primary health-care practitioners is feasible in most health care centre and allows the identification of numerous birth defects, including cardiovascular defects that are associated with a high risk of early mortality and referral.[8]

CONCLUSION

In this retrospective study, the main highlight is that 70.1% of the mothers who delivered neonates with birth defects did not attend antenatal care regularly. 58.7% of the neonates with birth defects had low birth weight. This study could be used as base for further research investigating about the role of antenatal care in early detection and/or the planning of delivery for babies with birth defects. Trends in babies with birth defects suggested that fetuses diagnosed with IUGR/SGA should be given special attention, as they were at increased risk for birth defects.

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Research Article

Lidocaine-Prilocaine Cream versus Lidocaine-HCL Injection for Pain Relief during Second Degree of Perineal Tear Suturing after Vaginal Delivery: A Comparative Study

Lidokain-Prilokain Topikal versus Injeksi Lidokain-HCL dalam Menghilangkan Nyeri Selama Penjahitan Luka Perineum Tingkat Dua Pascapersalinan Pervaginam: Sebuah Studi Komparatif

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Abstract

Objective: To compare the effectiveness of topically applied lidocaine-prilocaine cream with lidocaine-HCl injection in the reduction of pain during second degree of perineal tear suturing after vaginal delivery.

Methods: One hundred and twenty-four subjects with second degree of perineal tear after vaginal delivery were enrolled in this randomised clinical trial. Subjects were assigned randomly to have either application of lidocaine-prilocaine cream (n=62) or local injection of lidocaine-HCl (n=62) for anaesthetic during perineal suturing. Pain measured with visual analogue scale (VAS) for the first 5 minutes during the perineal suturing. Statistical analysis was performed by comparative analytic numerical unpaired with independent t-test between the two groups and significance was assessed at $p<0.05$. Data were presented as mean ± standard deviation (SD).

Results: There was no significant different of pain score between lidocaine-prilocaine cream and lidocaine-HCl injection group (5.66 ± 1.07 vs 5.56 ± 1.5; $p=0.473$).

Conclusion: Application of lidocaine-prilocaine cream as effective as injection of lidocaine-HCl for reducing pain during second degree of perineal tear suturing after vaginal delivery.

[Indones J Obstet Gynecol 2018; 6-4: 228-231]

Keywords: lidocaine-prilocaine cream, lidocaine-HCl injection, pain, perineal suturing, vaginal delivery

Abstrak

***Tujuan**: Untuk membandingkan efektivitas antara lidokain-prilokain topikal dan lidokain-HCl injeksi dalam mengurangi nyeri selama penjahitan luka perineum tingkat dua setelah persalinan normal.*

***Metode**: Seratus dua puluh empat perempuan dengan robekan perineum tingkat dua postpartum pervaginam mengikuti uji coba klinis secara acak ini. Enam puluh dua perempuan (n=62) menggunakan lidokain-prilokain topikal dan 62 perempuan lainnya (n=62) menggunakan injeksi lokal lidokain-HCl untuk anestesi selama penjahitan perineum. Nyeri diukur dengan visual analog scale (VAS) untuk 5 menit pertama selama penjahitan perineum. Analisis statistik dilakukan dengan uji numerik komparatif tidak berpasangan dengan uji t independen antara kedua kelompok dengan tingkat kemaknaan $p<0,05$. Data disajikan sebagai rerata ± standar deviasi (SD).*

***Hasil**: Tidak terdapat perbedaan signifikan skor nyeri antara kelompok lidokain-prilokain topikal dan kelompok injeksi lidokain-HCl ($5,66 \pm 1,07$ vs $5,56 \pm 1,5$; $p = 0,473$).*

***Kesimpulan**: Efektivitas lidokain-prilokain topikal untuk mengurangi nyeri sama dengan injeksi lidokain-HCl selama penjahitan robekan perineum tingkat dua postpartum pervaginam.*

[Maj Obstet Ginekol Indones 2018; 6-4: 228-231]

***Kata kunci**: lidokain-prilokain topical, lidokain-HCl injeksi, nyeri, penjahitan perineum, persalinan normal*

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INTRODUCTION

Approximately 75% of women post vaginal birth will have some degree of trauma to their labia, vaginal walls or perineum. The inadequate diagnosis and inappropriate management of the trauma are strongly associated with maternal morbidity. Perineal trauma is associated with significant short- and long-termmorbidity.[1] Perineal trauma can occur spontaneously or result from episiotomy. Perineal pain is reported to be the most severe in the immediate postnatal period.[2] Discomfort of perineal pain continues for up to two weeks postpartum in about 30% of women and 7% report pain at three months.[3]

More than 60% of labours are followed by rupture of the perineum which require suturing. Perineal tear is one of the birth trauma which the

main factor is perineal condition.[4] Rates of perineal trauma from episiotomy that require suturing between 44% and 79%.[5,6] A 2nd-degree perineal tear is defined as injury to perineum involving perineal muscles but not involving the anal sphincter.[7] Morbidity following perineal trauma has led to these arch of different interventions to be used during the second stage to reduce perineal trauma. Perineal injection with local anaesthetics is the most common technique to provide anaesthesia during perineal suturing. Another alternative technique to injectable anaesthetic is topical anaesthetic such as lidocaine-prilocaine cream. This anaesthetic is a mixture of 2.5% lidocaine and 2.5% prilocaine that is used widely as topical anaesthetic for pediatric, dermatologic, reconstructive, and gynecologic minor procedures. The advantages of this anaesthetic are locally effect without significant systemic absorption, ease of use, and transient side effects.[8]

Hence, this study was aimed to compare the effects of lidocaine-prilocaine cream and lidocaine-HCl injection on reduction of perineal pain during episiotomy repair after normal vaginal delivery.

METHODS

This randomised clinical trial was conducted at Dr. Wahidin Sudirohusodo Hospital and some of its affiliated hospitals between April and September 2016. The study protocol was approved by the Health Research Ethics Committee of Faculty of Medicine, Universitas Hasanuddin. Vaginally postpartum women with second degree of perineal tear were enrolled in this study. Written informed consent was obtained from all women who agreed to participate in the trial before study entry. Women were assigned randomly to have either local injection of lidocaine-HCl or application of lidocaine-prilocaine cream for pain relief during perineal suturing. Pain measured with visual analogue scale (VAS) for the first 5 minutes during the perineal suturing. Statistical analysis was performed by comparative analytic numerical unpaired with independent t-test between the two groups and significance was assessed at $p<0.05$. Data were presented as mean ± standard deviation (SD).

RESULTS

A total of 124 vaginal postpartum subjects were enrolled. Of these, 62 subjects were assigned to receive local anaesthesia with lidocaine-HCl injection, and 62 subjects had topical application of the lidocaine-prilocaine cream. The only significant difference of characteristics between both groups was BMI ($p<0.05$). The clinical characteristics of postpartum women are summarised in Table 1. Analysis of pain score during perineal suturing based on subject characteristics shows length of perineal suturing for longer than 15 minutes significantly different ($p=0.026$) between lidocaine-prilocaine cream and lidocaine-HCl injection (Table 2). Pain scores during perineal suturing are displayed in Table 3. There was no significant difference in pain score between both groups ($p>0.05$).

Table 1. Subject Characteristics

Characteristics	Lidocaine-prilocaine cream (n=62)	Lidocaine-HCl injection (n=62)	*p-value*
Age (years)	24.3 ± 3.6	24.6 ± 4.3	0.654
BMI (kg/m^2)	21.5 ± 1.9	22.3 ± 2.4	0.038
Length of the second stage of labour (minute)	31.2 ± 12.0	36.5 ± 20.6	0.089
Birth weight (gram)	3002.3 ± 339.6	2996.9 ± 348.2	0.931
Length of perineal suturing (minute)	15.1 ± 4.2	15.8 ± 5.1	0.401

Table 2. Comparison of Pain Score Based on the Characteristics between Lidocaine-Prilocaine Cream and Lidocaine-HCl injection

Characteristics	Lidocaine-prilocaine cream (n=62)	Lidocaine-HCl injection (n=62)	*p-value*
Age			
Low risk	5.66 ± 1.07	5.06 ± 1.49	0.535
High risk	0	4.5 ± 2.12	0
BMI (kg/m^2)			
Normal	5.68 ± 1.09	5.67 ± 1.5	0.699
Abnormal	5.33 ± 0.58	5 ± 1.41	0.655
Length of the second stage of labour (minute)			
< 60	5.66 ± 1.09	5.52 ± 1.49	0.386
≥ 60	5.67 ± 0.58	5.8 ± 1.62	1.000
Episiotomy			
Yes	5.59 ± 1.1	5.5 ± 1.61	0.426
No	6 ± 0.89	5.72 ± 1.23	0.558
Length of perineal suturing (minute)			
≤ 15	5.4 ± 0.74	5.73 ± 1.43	0.243
> 15	6 ± 1.33	5.32 ± 1.6	0.026

Table 3. Pain Score during Perineal Suturing

	Mean ± SD	*p-value*
Lidocaine-prilocaine cream (n=62)	5.66 ± 1.07	0.473
Lidocaine-HCl injection (n=62)	5.56 ± 1.5	

DISCUSSION

This study shows there is no significant difference between lidocaine-prilocaine cream and lidocaine-HCl injection in reducing pain during second degree of perineal tear suturing of vaginally postpartum suggest that the two anaesthetics had similar effects. Similar results were also reported by previous study that compared the same anaesthetic for perineal suturing with this study.[9] However, our findings are in disagreement with results from the study by Franchi et al. who observed lidocaine-prilocaine cream more effective in reducing pain compared to mepivacaine injection during perineal repair after delivery.[8]

Injection anaesthetics are most frequently used due to its safety, inexpensive, wide availability, and immediate effect. Insertion of the needle and injection of the anaesthetic into the skin, burning sensation during infusion, oedema, and risks of accidental intravascular administration are the side effects of this anaesthetic. Lidocaine-prilocaine cream releases two amide anaesthetic (2.5% lidocaine and 2.5% prilocaine) to the dermal layers before penetrating the smooth and striated muscle and the individual axons within the nerve. An inward flux of sodium ions through the nerve membranes inhibit nerve conduction to induce pain. Compared to the side effects of lidocaine injection, lidocaine-prilocaine cream generally mild and transient and no serious reactions that were reported.

Although this present study show lidocaine-prilocaine cream and lidocaine-HCl injection in terms of pain reduction, our results indicated that lidocaine-prilocaine cream as effective as lidocaine-HCl injection. Therefore, the lidocaine-prilocaine cream can be an alternative for lidocaine which has been routinely used for years during perineal tears repair and episiotomy. Finally, it has been stated that lidocaine-prilocaine cream can be an efficient alternative to the injectable analgesics used for local obstetric and gynecologic procedures.

CONCLUSION

In conclusion, this study has shown that application of lidocaine-prilocaine cream as effective as

injection of lidocaine-HCl for reducing pain during second degree of perineal tear suturing after vaginal delivery.

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Research Article

Identification of Microorganisms in Vaginal Swab and Peritoneal Fluid of Women with Endometriosis

Identifikasi Mikroorganisme pada Swab Vagina dan Cairan Peritoneum pada Wanita dengan Endometriosis

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Abstract

Objective: To discover the correlation between microorganisms found in vaginal swab culture and peritoneal fluid culture from laparoscopy in reproductive age women diagnosed with endometriosis.

Methods: This cross-sectional study was conducted in Bunda Hospital and YPK Hospital, Central Jakarta. Thirty-one subjects were included. Data were analysed using SPSS 20.0 for Windows. Bivariate analysis was used to identify the correlation between independent and dependent variables.

Results: From 31 subjects with mean age 34.42±5.056 years old, 87.1% were infertile. Vaginal swab culture was found positive in 83.9% subjects while peritoneal fluid culture was found positive only in 9.6% subjects. There was moderate correlation between chronic pelvic pain and positive vaginal swab culture (r=0.601; p=0.001), but weak correlation between Ca125 and vaginal swab culture (r=0.440; p=0.010). Peritoneal fluid culture had significant inverse correlation with left tubal patency (r=-0.346; p=0.047). There was weak correlation between vaginal swab culture and peritoneum fluid culture with correlation coefficient of 0.13.

Conclusion: Most bacteria found in vaginal swab culture and peritoneal fluid culture were the ones found in the gastrointestinal tract. However, vaginal swab and peritoneal fluid culture were not sufficient to prove the hypothesis that infection has a role in the pathogenesis of endometriosis. Therefore, advance examination such as LPS and PCR might be needed to be done in the future research with cohort study, to overcome the limitation of this study.

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Keywords: ascending bacterial contamination, culture, endometriosis vaginal swab, peritoneal fluid

Abstrak

***Tujuan**: Membuktikan adanya korelasi antara mikroorganisme yang ditemukan pada hasil kultur bilasan vagina dengan mikroorganisme yang ditemukan pada cairan peritoneum hasil laparoskopi perempuan usia reproduksi yang terdiagnosis endometriosis*

***Metode**: Penelitian ini menggunakan desain penelitian analitik potong lintang yang bertujuan untuk melihat adanya hubungan korelasi serta mengetahui tingkat korelasi antara mikroorganisme kultur bilasan vagina dengan mikroorganisme pada cairan peritoneum pasien endometriosis.*

***Hasil**: Hasil kultur bilasan vagina dari 31 subjek penelitian yang diteliti, mikroorganisme terbanyak adalah Enterococcus faecalis (32,3%), Eschericia coli (29,1%), dengan 16,1 % dengan hasil kultur negatif. Sedangkan dari hasil kultur bilasan peritoneum terdapat 3 subjek (9,6%) dengan hasil positif yaitu dengan jenis bakteri Eschericia coli, Enterococcus faecalis, dan Pseudomonas. Terdapat korelasi lemah antara hasil kultur bilasan vagina dengan kultur bilasan peritoneum (r 0,13). Terdapat korelasi sedang antara kultur positif bilasan vagina dengan nyeri pelvik kronis, korelasi lemah antara kultur positif bilasan vagina dengan nilai Ca 125, dan korelasi lemah antara kultur positif cairan peritoneum dengan tuba kiri yang non paten.*

***Kesimpulan**: Sebagian besar bakteri dari bilasan vagina dan bilasan peritoneum pada pasien endometriosis memiliki hasil bakteri dari organ pencernaan. Terdapat korelasi lemah antara hasil kultur bilasan vagina dengan kultur bilasan peritoneum pada pasien endometriosis.*

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***Kata kunci**: bilasan vagina, cairan peritoneum, endometriosis, kontaminasi bakteri asenden, kultur*

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INTRODUCTION

Endometriosis is an abnormal growth of endometrium, consists of glandular epithelium and stroma, outside the uterus.[1] This gynecological condition occurs in 7-10% reproductive age women.[2] In 2009, a study in Jakarta reported that endometriosis is found in 64.6% infertility cases.[3] Endometriosis symptoms such as chronic pelvic pain, dysmenorrhea, dyspareunia, irregular bleeding, gastrointestinal symptoms, fatigue/ anemia can be disturbing.[4] Endometriosis can be found in many organs, with the highest prevalence is in uterus, ovarium, or pelvic peritoneum.[5] It is known that in endometriosis there is an imbalance

of cell proliferation and apoptosis with chronic inflammation process during its course.[6] However, the exact cause and mechanisms in endometriosis have not been understood completely.

There are several hypotheses to its pathogenesis, such as transplantation of uterine endometrium to another site by retrograde menstruation (Sampson's transplantation theory), coelomic metaplasia theory, and mullerian ducts remnant.[4] The several factors contributing to endometriosis growth are hormones, genetics, inflammation, and infection initiation. High endotoxin concentration in menstrual fluid and peritoneal fluid is possibly happened because of ascending bacterial contamination, such as Escherichia coli. This hypothesis expected to be involved in peritoneal endometriosis growth.[4] Lipopolysaccharide (LPS) from Gram-negative bacteria acts as inflammatory mediator that promotes endometrium stromal cell proliferation and invasion through cyclooxygenase 2 (COX 2) and prostaglandin E2 (PGE_2) regulation. PGE_2 affects bacterial growth directly and indirectly.[5,6] Women's lower reproductive tract exposed to many microorganisms allows ascending infection to the upper reproductive tract, leading to endotoxin accumulation in menstrual and peritoneal fluid causing inflammation and growth of endometriosis.[7,8]

Eventhough many literatures discussing infection role in the pathogenesis of endometriosis, the research has not been proven. This study was conducted to discover the correlation between microorganisms found in vaginal swab culture and peritoneal fluid culture from laparoscopy in reproductive age women diagnosed with endometriosis, in order to examine the possibility of contamination and ascending infection as a trigger in inflammatory cascade in endometriosis cases.

METHODS

This cross-sectional study was conducted at Bunda Hospital and YPK Hospital, Central Jakarta, Indonesia. A total of 31 subjects were included and obtained by consecutive sampling. Subjects included were reproductive age women (18-40 years old), diagnosed with endometriosis based on history, physical examination, and USG, agreed to laparoscopic procedure for diagnostic/therapeutic including obtaining peritoneal fluid, agreed to vaginal examination and vaginal swab sampling, agreed to join this research by filling the informed consent forms. Women with vaginal bleeding of unknown cause, suspected with tubal and ovarium abscess from history, physical examination, and further diagnostic procedures, done vaginal douching in the later five days or routinely, and whose peritoneal fluid was contaminated with blood at laparoscopic procedure, were excluded. Subjects suspected endometriosis that could not be found during laparoscopic procedure was dropped out.

Data were analysed using SPSS 20.0 for Windows. Univariate analysis was used to describe characteristics of the subjects. Data normality test continued with bivariate analysis by Spearman test was used to find correlation between independent and dependent variable. Statistical significance defined in two methods: correlation coefficient greater than r table or p-value <0.05.

RESULTS

A total of 31 subjects were included in this study with their mean age is 34.42±5.056 years old. Table 1 described clinical and demographic characteristic of the subjects.

Table 1. Clinical Characteristics

Characteristics	n (%)	
	Yes	No
Infertility	27 (87.1)	4 (12.9)
Use of contraception/hormonal therapy	3 (9.7)	27 (90.3)
Leucorrhea	5 (16.1)	26 (83.9)
Dysmenorrhea	18 (58.1)	13 (41.9)
Chronic pelvic pain	2 (6.4)	29 (93.6)

Characteristics	n (%)	
	Yes	No
Dyspareunia	3 (9.7)	28 (90.3)
Cervical motion tenderness	0 (0)	31 (100)
Rectovaginal nodule	0 (0)	31 (100)
Parametrium pain	0 (0)	31 (100)
Cyst	26 (83.9)	5 (16.1)
Unilateral;	16 (51.6);	
Size (mm, median [range])	20 (10-85)	
Bilateral;	10 (32.2);	
Size (mm, median [range])	46 (30-80)	
Tubal patency		
Left	14 (45.2)	17 (54.8)
Right	15 (48.4)	16 (51.6)
Hb (mean [SD])		12.40 (1.443)
Leukocyte (mean [SD])		7445.5 (1783.4)
Thrombocyte (mean [SD])		322910 (86996.2)
Ca125 (median [range])		24 (7-136.4)
Endometriosis classification		
AFS 1 (mild)		8 (25.8)
AFS 2 (moderate)		5 (16.1)
AFS 3 (severe)		7 (22.6)
AFS 4 (very severe)		11 (35.5)

Based on vaginal swab culture, five samples (16.1%) were negative, while the 83.9% were positive for bacteria, with Enterococcus faecalis in 10 samples (32.3%) was the most common, followed by E.coli in 9 samples (29.1%). Other bacteria found were Staphylococcus haemolyticus, actinobacter, enterobacter, Staphylococcus epidermidis, Streptococcus agalactiae, and trichomonas. Culture of peritoneal fluid revealed 28 samples (90.4%) are negative, the rest three samples (9.6%) were contained with e.coli, enterococcus faecalis, Pseudomonas. Table 2 below showed the microorganisms obtained in culture of vaginal swab and peritoneal fluid, also with the endometriosis classification.

Table 2. Microorganisms Obtained in Culture and Classification of Endometriosis

Vaginal Swab Culture	Peritoneal Fluid Culture	Classification of Endometriosis
Enterococcus faecalis	-	4
Staphylococcus haemoliticus	-	1
Enterococcus faecalis	-	1
Enterobacter	-	4
E. coli	-	4
Trichomonas	-	3
E. coli	-	1
E. coli	-	4
Enterococcus faecalis	-	3

Vaginal Swab Culture	Peritoneal Fluid Culture	Classification of Endometriosis
Enterococcus faecalis	Enterococcus faecalis	4
E. coli	Pseudomonas	4
Staphylococcus haemoliticus	-	3
-	-	4
Enterococcus faecalis	-	2
Enterococcus faecalis	-	1
Enterococcus faecalis	-	1
-	-	4
Streptococcus agalactiae	-	1
Enterococcus faecalis	-	4
Actinobacter	-	2
Enterococcus faecalis	-	2
E. Coli	-	2
E. Coli	-	2
Streptococcus agalactiae	-	3
Enterococcus faecalis	-	3
E. Coli	-	1
Staphyloccocus epidermidis	-	4
Enterococcus faecalis	-	1
-	-	4
E. coli	E. coli	3
-	-	3

Correlation between characteristics of the subjects and findings of vaginal swab and peritoneal fluid culture was obtained with bivariate nonparametric correlation test. Nominal data in subjects characteristic were analysed using Pearson test to obtain Phi coefficient, while ordinal or numeric data using point-biserial coefficient test.

Table 3. Correlation between Subjects Characteristics and Culture Results

Characteristics	Vaginal Swab Culture		Peritoneum Fluid Culture	
	r	p	r	p
Age	-0.019	0.916	0.069	0.702
Infertility	-0.157	0.367	0.117	0.500
Use of contraception/hormonal therapy	0.134	0.443	-0.100	0.566
Leucorrhea	0.179	0.305	0.160	0.357
Dysmenorrhea	-0.046	0.790	0.077	0.658
Chronic pelvic pain	**0.601**	**0.001**	-0.080	0.645
Dyspareunia	-0.160	0.357	-0.100	0.566
Cervical motion tenderness	-	-	-	-
Rectovaginal nodule	-	-	-	-
Parametrium pain	-	-	-	-

Characteristics	Vaginal Swab Culture		Peritoneum Fluid Culture	
	r	p	r	p
Cyst	-0.179	0.305	0.134	0.443
Tubal patency				
Left	0.123	0.478	**-0.346**	**0.047**
Right	0.097	0.576	-0.326	0.061
Hb	0.178	0.321	-0.096	0.594
Leukocyte	0.122	0.500	-0.056	0.756
Thrombocyte	-0.134	0.458	0.305	0.084
Ca125	**0.440**	**0.010**	0.116	0.520
Classification of endometriosis	-0.253	0.155	0.258	0.146

There was moderate correlation between chronic pelvic pain and positive vaginal swab culture (r=0.601; p=0.001). Weak correlation showed between Ca125 and vaginal swab culture (r=0.440; p=0.010). Peritoneal fluid culture had inverse correlation with left tubal patency (r=-0.346; p=0.047) significantly, and right tubal patency (r=-0.326; p=0.061) insignificantly. Correlation between variables in this study, vaginal swab culture and peritoneum fluid culture, were obtained by inferential analysis using Lambda coefficient.

Table 4. Correlation between Vaginal Swab Culture and Peritoneum Fluid Culture

Variables	r	p
Lambda		
Vaginal swab culture as dependent variable	0.130	0.049
Peritoneum fluid culture as dependent variable	0	0

Table 4 above showed that there was a weak correlation between vaginal swab culture and peritoneum fluid culture with correlation coefficient of 0.13.

DISCUSSION

Infertility is more common in women with endometriosis. As much as 25-50% of infertile women have endometriosis and 30-50% women having endometriosis are infertile. This study found that there are 87.1% of women having endometriosis were infertile. It can be explained by mechanisms, such as pelvic anatomy abnormality, endocrine system and ovulation abnormality, altered peritoneal function, also cell-mediated alteration in endometrial hormone and function. Pelvic or tubal adhesion obstructs released oocyte from ovarium and transport ovum because of blocked tubal patency. Women having endometriosis have more inflammatory mediators such as active macrophages, prostaglandin, IL-1, TNF, and protease in the peritoneal fluid.[9]

Lower reproductive tract infection increases the risk of endometriosis, especially inflammation of the cervix, vagina, and vulva.[10] Ascending migration of untreated infection leads to endometritis and subclinical pelvic inflammatory disease which are risk factors of endometriosis. Normal flora in the vagina is predominantly Lactobacillus. Alteration in vaginal pH and vaginal flora increases the risk of lower reproductive tract infection. Women with bacterial vaginosis and nonspecific vaginitis have increasing opportunistic pathogens such as Staphylococci, enterococci, enterobacter, candida, peptostreptococci, peptococci, and predominantly anaerobic Gram-negative bacteria.[11] The growth of bacteria, often found in small amount, indicates dysbiosis which could be symptomatic or asymptomatic. Streptococci, staphylococci and E. coli have been known to cause invasive disease. S. agalactiae is also found invasive in postpartum women and neonates.[12]

Several characteristics of the subject correlated with positive vaginal swab culture or peritoneal swab culture. Moderate correlation between chronic pelvic pain and positive vaginal swab cul-

ture consistent with the theory that chronic pelvic pain is one of the symptoms of pelvic inflammatory disease.[13] Marker Ca125 was also examined in this study. Increased Ca125 in circulation could be normal in menstruation and pregnancy or a result of inflammatory reaction that changes endothelial permeability. In this study, higher Ca125 was found in positive vaginal swab culture. The weak correlation between Ca125 and vaginal swab culture can be explained by bacterial-induced inflammation process of gynaecology organs.[14,15] This study showed that peritoneal fluid culture had significant inverse correlation with left tubal patency. This might be due to different vascularisation and pelvic anatomy, in which pathologic symptoms are also found more common in the left side.[16,17] A study explained that slower drainage of left ovarium causes higher microorganisms on the left side.[18] As a result, positive peritoneal fluid culture was found higher in left tubal obstruction.

From total 31 subjects, only two of them had similarity in the result of vaginal swab culture and peritoneal fluid culture. This finding supported bacterial contamination hypothesis, which might be explained by ascending migration of bacteria. There was a hypothesis that intestinal microbes could also have a role in the pathogenesis of endometriosis, as this microbes act as the main regulator of inflammatory process outside the intestines.[18] However, there were possibilities explaining the positive results of the culture. Those bacteria could be normal flora or contamination while taking and processing the samples. Different normal flora from the vagina can be found in peritoneal fluid, such as anaerobic bacteria. The similar culture result in 2 subjects could also not correlate or have different genetic material.[19]

In this study, PCR for bacterial DNA was not performed. As a result, the correlation between bacteria found in vaginal swab culture and peritoneal fluid culture cannot be analysed. Negative cultures because of small concentration of bacteria might be detected positive by PCR and contain high endotoxin concentration.[7,19] Unfortunately, laboratory assay for LPS detection was also not performed, so we could not prove the bacterial contamination hypothesis and LPS relationship to culture findings.

CONCLUSION

Most of bacteria found in vaginal swab culture and peritoneal fluid culture were the ones found in gastrointestinal tract. There was moderate correlation between chronic pelvic pain and vaginal swab culture, weak correlation between Ca125 and vaginal swab culture, also between left tubal occlusion with peritoneal fluid culture. There was weak correlation between microorganisms found in vaginal swab culture and peritoneal fluid culture. However, vaginal swab and peritoneal fluid culture were not sufficient to prove the hypothesis that infection has a role in the pathogenesis of endometriosis. Therefore, advance examination such as LPS, PCR DNA might be needed to be done in the future research with cohort study, to overcome the limitation of this study.

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Research Article

The Effect of Pyridoxine on Prostaglandin Plasma Level in Patients with Primary Dysmenorrhea

Efek Pemberian Piridoksin terhadap Kadar Prostaglandin Plasma pada Pasien Dismenore Primer

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Abstract

Objective: To determine the effect of vitamin B6 (pyridoxine) to the levels of prostaglandins and intensity of pain in primary dysmenorrhea.

Methods: The levels of prostaglandin (PGF2α) in plasma measured by ELISA and pain intensity by verbal rating scales conducted on 35 women with primary dysmenorrhea (n=35) supplemented with vitamin B6 100mg for four days and controls with placebo (n=35).

Results: Prostaglandin levels decreased significantly after vitamin B6 supplementation (2212.9±1374.2 vs 1490.3±1119.0; p<0.05) followed by a significant reduction in pain intensity (4.29±0.7 vs 1.71±0.5; p<0.05) in the test group compared to control.

Conclusion: Due to vitamin B6 effects on decreasing prostaglandin levels and pain of primary dysmenorrhea, so that B6 vitamin can become the treatment for the primary dysmenorrhea.

[Indones J Obstet Gynecol 2018; 6-4: 239-242]

Keywords: primary dysmenorrhea, prostaglandin, pyridoxine

Abstrak

***Tujuan**: Untuk mengetahui pengaruh pemberian vitamin B6 (piridoksin) terhadap kadar prostaglandin dan intensitas nyeri pada dismenore primer.*

***Metode**: Pemeriksaan kadar prostaglandin (PGF2α) dengan ELISA dan pengukuran intensitas nyeri dengan verbal rating scales dilakukan pada 35 orang (n=35) wanita dengan dismenore primer yang mendapatkan vitamin B6 100mg selama 4 hari dan kontrol yang mendapatkan plasebo (n=35).*

***Hasil**: Kadar prostaglandin menurun bermakna setelah pemberian vitamin B6 (2212,9±1374,2 vs 1490,3±1119,0; p<0,05) disertai dengan penurunan intensitas nyeri yang bermakna (4,29±0,7 vs 1,71±0,5; p<0,05) pada kelompok uji dibandingkan kontrol.*

***Kesimpulan**: Vitamin B6 menurunkan kadar prostaglandin dan nyeri sehingga vitamin B6 dapat dipertimbangkan menjadi salah satu pengobatan dismenore primer.*

[Maj Obstet Ginekol Indones 2018; 6-4: 239-242]

***Kata kunci**: dismenore primer, piridoksin, prostaglandin*

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INTRODUCTION

Dysmenorrhea, abdomined pain during menstruation usually cramps and centred at the lower abdomen, is a common gynecologic disorder in reproductive-aged women. Various studies in different populations reported dysmenorrhoea prevalence range between 20%-94%[1-3]. Primary dysmenorrhea is painful spasm pain in the lower abdomen that occurs before and/or during menstruation without macroscopic pelvic pathology. The onset of pri-mary dysmenorrhea usually occurs in adolescents, on or shortly after menarche (6-24 months)[4,5].

Prostaglandins (PGF2α and PGE2) are involved in the pathogenesis of primary dysmenorrhea pain particularly PGF2α[6]. Elevated levels of PGE2 and PGF2α observed in primary dysmenorrhea which stimulates the myometrium resulting in increased contraction and uterine dysrhythmias leading to decreased blood flow to the uterus and ischemia[5-8].

Early management of primary dysmenorrhea is a non-steroidal anti-inflammatory pain medication (GAINS) that inhibits prostaglandin[9]. However, these drugs have side effects such as dyspepsia syndrome and peptic ulcer[5]. Dietary supplements such as vitamins (E, B1, B3, B6) is an alternative treatment for dysmenorrhea although it is not as widely studied[10]. Pyridoxine (vitamin B6) is a water-soluble vitamin and part of the B complex vitamin. Vitamin B6 can stimulate cell membranes in transferring magnesium and increase intracellu-

lar magnesium that plays a role in muscle relaxation. In addition, decreased levels of vitamin B6 in the blood resulted in the liver not being able to conjugate estrogen so that estrogen levels increased associated with complaints of menstrual pain[5,10,11]. This study aimed to determine the effect of vitamin B6 (pyridoxine) the levels of prostaglandins and pain in primary dysmenorrhea.

METHODS

This randomised pretest-posttest control group study was conducted on a student of the Faculty of Medicine, Universitas Hasanuddin Makassar with primary dysmenorrhea and met the study criteria from September to November 2016. All of the women who enrolled were fully informed about the study and gave their consent before enrollment. The study was approved by the Health Research Ethics Committee of Faculty of Medicine, University of Hasanuddin. Students received vitamin B6 (100 mg/day for four days) and placebo (control). Plasma prostaglandin level was measured by ELISA technique whereas the intensity of pain with Visual Analog Scale (VAS). An unpaired t-test was used to compare the effect of vitamin B6 and placebo in prostaglandin levels and menstrual pain. A p value of less than 0.05 was taken to be statistically significant. Results presented in mean ± SD.

RESULTS

This study examined prostaglandin levels and pain intensity in 35 people (n = 35) of women of reproductive age (test group) with primary dysmenorrhea who received vitamin B6 supplementation and placebo as control (n = 35). Characteristics of the study samples are shown in Table 1.

Table 1. Characteristics of Samples

Characteristics	Treatment group (n=35)	Controls (n=35)
Age (years)	18.9±0.85	18.2±0.67
Menarche (years)	12.8±0.77	12.7±0.70
BMI (kg/m^2)	20.3±2.12	20.7±1.94

Prostaglandin levels before administration were higher in the treatment group compared to placebo (2212.9±1374.2 pg/ml vs 1623.3±1111.7 pg/ml) but not significantly different (p>0.05). After administration, prostaglandin levels decreased in both groups (1490.3±1119.0 pg/ml vs 1613.9±1105.5 pg/ml). However, the differences between the two groups were not significant (p>0.05). The intensity of pain between the two groups was significantly differenced before and after administration of vitamin B6 and placebo (all p<0.05) (Table 2).

The effect of vitamin B6 and placebo on prostaglandin levels and pain intensity was also examined in this study. The results show that vitamin B6 decreased prostaglandin levels and pain intensity significantly compared to placebo (p=0.000) (Table 3).

Table 2. Effects of Vitamin E and Placebo on Prostaglandin Level and Pain

Administration	Prostaglandin level*		p	Pain score		p
	Treatment group (n=35)	Placebo (n=35)		Treatment group (n=35)	Placebo (n=35)	
before	2212.9±1374.2	1623.3±1111.7	0.053	4.29±0.7	3.80±0.8	0.011
after	1490.3±1119.0	1613.9±1105.5	0.643	1.71±0.5	3.66±0.8	0.000

** Mean ± SD pg/ml*

Table 3. Prostaglandin Level and Pain Intensity between Treatment Group and Placebo

Treatment	Prostaglandin level		*p*	Pain score		*p*
	before	after		before	after	
Vit. B6 (n=35)	2212.9±1374.2	1490.3±1119.0	0.000	4.29±0.7	1.71±0.5	0.000
Placebo (n=35)	1623.3±1111.7	1613.9±1105.5	0.295	3.8±0.8	3.6±0.8	0.257

DISCUSSION

Prostaglandins are lipid compounds from the enzymatic reaction of cyclooxygenase (COX) in arachidonic acid and specific prostanoid synthase enzymes. PGE2 and PGF2α are mainly synthesised in the reproductive system. Over expression of COX-2 in ectopic endometrial cells leads to high levels of PGE2, PGF2α and other specific prostaglandins in uterine tissues in women with menorrhagia, dysmenorrhea or endometriosis[12,13]. PGF2α primarily derived from COX-1 in the female reproductive system and plays an essential role in ovulation, luteolysis, uterine smooth muscle contraction and initiation of labour as well as pain[14].

The endometrium of the menstrual secretory phase contains an arachidonic acid compound which converted to PGF2α, PGE2, and leukotriene during menstruation. PGF2α always stimulates uterine contractions and as the major mediator for dysmenorrhea. PGF2α and PGE2 levels in the endometrium correlated with the severity of dysmenorrhea[9]. Primary dysmenorrhea is caused by spastic uterine hypercontractility. Higher levels of PGF2α and PGE2 are present in menstrual blood in women with dysmenorrhea compared to without dysmenorrhea[15]. PGF2α levels increased 4-fold in endometrium and plasma in women with dysmenorrhea compared to without dysmenorrhea[9] so that PGF2α is a smooth muscle stimulant and a strong vasoconstrictor[16]. The present study found that levels of prostaglandins in students with primary dysmenorrhea higher than control although the difference was not significant.

Primary dysmenorrhea occurs only in the ovulatory cycle in which the uterus is under the influence of progesterone while prostaglandin synthesis is associated with the ovarian function. Menstrual pain is caused by an imbalance in the control of the autonomic nervous system to the myometrium. Vitamin B6 acts as a regulator of several ion membrane transports that modulate hormonal function due to its ability to bind to the receptors of steroid hormones[17]. The nutritional status of vitamin B6 greatly influences and modulates selectively in the production of serotonin and γ-aminobutyric acid (GABA), a neurotransmitter that controls depression, perception and anxiety[18].

The prostaglandin level and pain intensity in this study decreased significantly after vitamin B6 administration despite the prostaglandin level of the test group did not differ significantly with the placebo group (control). A study by Proctor show vitamin B6 has better results in reducing menstrual pain compared to placebo[19]. Changes in the intensity of pain can be affected by hormone levels, nutritional status, stress, physiologic, exercise and diet[6].

CONCLUSION

In conclusion, vitamin B6 decrease prostaglandin and pain levels so vitamin B6 might consider as treatment for primary dysmenorrhea.

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Research Article

Relationship of Retinol Binding Protein Four Serum Level on Endometrial Hyperplasia and Endometrial Carcinoma

Hubungan Kadar Serum Retinol Binding Protein Empat pada Hiperplasia Endometrium dan Karsinoma Endometrium

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Abstract

Objective: To determine the relationship between elevated serum retinol-binding protein 4 with abnormal uterine bleeding.

Methods: This study was an observational quantitative with cross-sectional methods, with all women who had abnormal uterine bleeding caused either by endometrial carcinoma or endometrial hyperplasia at RSUP Prof. Dr. R.D. Kandou, and affiliation hospitals from November 2016 until April 2017. Data were analysed with SPSS version 2.0 to see the significance level.

Results: Of 26 research subjects, 23 subjects with endometrial hyperplasia and three subjects with endometrial carcinoma. From the total of 26 malignancy and hyperplasia diagnoses, 21 had IMT > 25, and 23 were diagnosed with Endometrial Hyperplasia and 3 Carcinoma Endometrium. 18 subjects had elevated serum RBP4 levels, with 15 people with endometrial hyperplasia and 3 with endometrial carcinoma. With the Fischer Exact test statistic, serum retinol binding protein 4 levels were found in both endometrial hyperplasia and endometrial carcinoma p = 1.00, meaning no significant difference for the occurrence of abnormal uterine bleeding.

Conclusion: There was no significant association between serum retinol binding protein 4 between endometrium carcinoma and endometrial hyperplasia.

[Indones J Obstet Gynecol 2018; 6-4: 243-247]

Keywords: abnormal uterine bleeding, endometrial carcinoma, endometrial hyperplasia, serum retinol binding protein 4

Abstrak

Tujuan: *Mengetahui adanya hubungan peningkatan kadar serum retinol binding protein 4 pada hyperplasia endometrium dengan karsinoma endometrium.*

Metode: *Penelitian ini adalah jenis kuantitatif observasional secara potong lintang, dengan semua perempuan yang mengalami perdarahan uterus abnormal yang disebabkan oleh hiperplasia endometrium atau karsinoma endometrium di Obstetri dan Ginekologi Rumah Sakit Umum Pusat (RSUP) Prof. Dr. R.D. Kandou, dan RS jejaring mulai November 2016 sampai April 2017. Data dianalisa dengan SPSS versi 2.0 untuk melihat tingkat kemaknaannya.*

Hasil: *Dari 26 subjek penelitian, 23 subjek dengan hiperplasia endometrium dan 3 subjek dengan karsinoma endometrium. Didapatkan data penelitian dari total keganasan diagnosa dan hiperplasia sejumlah 26 orang, sebanyak 21 orang memiliki IM T>25 dan sebanyak 23 orang didiagnosa dengan Hiperplasia Endometrium dan 3 orang karsinoma endometrium. Didapatkan sebanyak 18 subjek penelitian mengalami peningkatan kadar serum RBP 4, dengan 15 orang yang mengalami hiperplasia endometrium dan 3 orang dengan karsinoma endometrium. Dengan uji statistik Fischer Exact test, didapatkan kadar serum retinol binding protein 4 baik pada hiperplasia endometrium dengan karsinoma endometrium p=1.00, mengartikan tidak mempunyai perbedaan bermakna untuk terjadinya perdarahan uterus abnormal.*

Kesimpulan: *Tidak terdapat hubungan bermakna kadar serum retinol binding protein 4 antara karsinoma endometrium dengan hiperplasia endometrium.*

[Maj Obstet Ginekol Indones 2018; 6-4: 243-247]

Kata kunci: *hiperplasia endometrium, kadar serum retinol binding protein 4, karsinoma endometrium, perdarahan uterus abnormal*

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INTRODUCTION

In healthy women, the menstrual cycle and reproductive health depend on the balance between the hormones formed by the hypothalamus and the pituitary. The hypothalamus will produce gonadotropin-releasing hormone (GnRH), this hormone will control the release of hormones released by the pituitary luteinizing hormone (LH) and follicle stimulating hormone (FSH). FSH and LH play a role in follicular maturation, ovulation and corpus luteum formation and synthesis of sex steroids.[1]

In reproductive-aged women, the reproductive and endocrine organs are functioning perfectly, at the age of perimenarche the hypothalamic-pituitary and ovarian axis are immature while at perimenopause the organ function begins to decline. Based on nutritional status, women with a BMI> 25 have a higher risk of menstrual cycle disturbance than women with nutritional status <25.1

RBP 4 is identified as one molecule of adipose molecule derivatives that contributes to the cause of insulin resistance in obesity and type 2 diabetes mellitus. RBP will cloak directly on objects with obesity or glucose intolerance, type 2 diabetes or with risk factors for cardiovascular pathology disorders.[2]

RBP4 is a protein compound derived from the lipocalin group and is a carrier-specific protein for retinol (vitamin A alcohol) in the blood. This compound will deliver retinol from the storage of the liver and then distributed throughout the body tissues. In plasma, the RBP 4 complex will bind to the transthyretin complex and will be filtered by the renal glomerulus. Lack of this RBP will affect vitamin A levels and distribution to all cells.[2]

Based on the background of changes in estrogen levels in women with abnormal uterine bleeding (PUA), malignancy and endometrial hyperplasia in which estrogen levels will be affected by nutritional status which is a representation of adipose tissue it is necessary to do research on levels of Retinol Binding Protein 4 (RBP4) in patients Abnormal Uterine Bleeding (PUA) malignancy and endometrial hyperplasia to aid in more accurate diagnosis and management.

METHODS

This was a cross-sectional study, with all women who had abnormal uterine bleeding caused either by endometrial carcinoma or endometrial hyperplasia at RSUP Prof. Dr. R.D. Kandou, and affiliation hospitals from November 2016 until April 2017. Data were analysed With SPSS version 2.0 to see the significance level.

Data collection was performed by following steps: Patients who meet the inclusion criteria are given an explanation of the action to be performed and the patient signs the consent statement following the research provided. Subject of this research is anamnesis, physical examination and then recorded in research status. Venous blood taken for RBP4 was examined, then reversed slowly about 5-10 times. Immediately within 30 minutes, the sample was centrifuged at 1000 g at a speed of about 3000 rpm for 15 minutes then the serum obtained was stored in a refrigerator with a temperature of -200C and then sent to Jakarta by using Ice pack to maintain the storage temperature before the examination of RBP 4 in the Laboratory Prodia Jakarta. Examination of serum RBP 4 level was done by quantitative method, using ELISA method.

Table 1. Distribution of Research Subject Characteristic

Characteristic	BMI > 25		BMI < 25		total
	n	%	n	%	
Age					
> 40	18	81.81	4	18.18	22
< 40	3	75	1	25	4
Education					
Elementary	1	50	1	50	2
Junior high school	2	40	3	60	5
High school	15	93.75	1	6.25	16
Diploma	2	100	0	-	2
Bachelor	1	100	0	-	1
Occupation					
Civil	1	100	0	-	1
Private	20	92.64	5	7.35	25

Table 2. Difference of serum RBP4 between Endometrial Hyperplasia and Endometrial Carcinoma

	BMI > 25		**BMI < 25**			
	RBP 4 <26.800 ng/ml	**RBP 4 >26.800 ng/ml**	**RBP 4 <26.800 ng/ml**	**RBP 4 >26.800 ng/ml**		
Hyperplasia	3	15	3	2	23	p=1.00
Carcinoma	0	3	0	0	3	
	3	18	3	2	26	

RESULTS

From above data, it is found that the most age group obtained is at the age of 40 years (22 people) with 18 people have BMI >25. While the highest education status is high school with 15 subjects. A total of 20 subjects were private employees, and only one subject works as a civil servant.

Of the total 26 malignancy and hyperplasia diagnoses, 21 had a BMI of > 25 and 23 were diagnosed with Endometrial Hyperplasia and 3 Endometrial Carcinomas. 18 subjects had elevated serum RBP4 levels, with 15 people with endometrial hyperplasia and 3 with endometrial carcinoma.

DISCUSSION

RBP 4 is identified as one molecule of adipose molecule derivatives that contributes to causing insulin resistance in obesity and type 2 diabetes mellitus. RBP will correlate directly to objects with obesity or glucose intolerance, type 2 diabetes or with risk factors for cardiovascular pathology disorders.[2]

As a system for retinol transport, a specific protein retinol binding will be produced in the liver and will mobilise retinol from the liver as the primary storage area. Once excreted from the liver, the retinol binding protein complex will circulate in the blood further binding to the plasma transthyretin. When retinol has reached the target tissue, the bone-specific retinol-free protein will be rapidly catabolized and excreted in the kidneys. The turning point of biological retinol binding protein has a half-life of 11.5 hours in adult humans.[2]

In Table 1. Characteristics of the subjects are seen by age, occupation, education, BMI and basic aetiology of AUB-M. All samples were patients who had been diagnosed with AUB-M. In Table 1 it was found that the most age group obtained was at the age of 40 years (22 people) with 18 of them had IMT > 25. While the highest education status was high school with 15 samples. A total of 25 samples have private employment, and only one person works as a civil servant. According to Kovacs P. 2012. Endometrial bleeding will be more common at age ≥ 40 years than in women <40 years. Age 40 years is the beginning of perimenopausal age. Where at age 40 a woman will be more frequent to occur anovulation and based on it at age 40 menstrual cycle will be longer. In research in Australia, when the menstrual cycle has exceeded 42 days, menopause can be predicted to occur within 1 to 2 years. The duration of the follicular phase is the determinant of the length of the cycle. As discussed in the literature review, there are 2 estrogen receptors that simultaneously affect the body's estrogen levels. One of the estrogen receptors derived from the ovaries (E2 receptors) so that researchers need to choose the conditions in which E1 receptors (skin, fat, muscle, endometrium) can be assessed as a major factor in this study.[2-6]

In Table 2, the largest distribution of research samples obtained aetiology of endometrial hyperplasia and endometrial carcinoma is 26 people and of that 21 people have IMT > 25 and as many as 18 people have serum RBP 4 > 26.000. Adipose tissue is found on almost all body surfaces. Corrected directly with the surface area of the body which in this study is defined as the body mass index. Increasing IMT means that the broader the adipose network is owned by the individual. In the event of AUB-M with the aetiology of malignancy and hyperplasia has been explained and in the aetiology endometrial has been suspected one of the risk factors is the nutritional status, where will be directly related to endometrial status. Pathological nutrition status will affect the occurrence of metabolic syndrome. And this will affect the adipose network which will then affect

the level of an individual RBP. In endometrial hyperplasia with BMI < 25 serum RBP4 levels were found in 3 people with serum RBP 4 <26.800. Then at the RBP 4 level of endometrial hyperplasia patients with BMI > 25, there were three subjects with serum RBP 4 <26.800. This may be due to many things, where elevated serum RBP 4 levels are affected by various factors such as comorbidities, insulin sensitivity, dietary patterns, and other lab variables not examined in this study. The results of this study are consistent with those reported by Kovacs, P 2012, obesity, a risk factor often encountered in endometrial malignancies.[6-10]

Endometrial hyperplasia is a pathological condition in the endometrium in the form of increased proliferation of the endometrial glands resulting in changes in the ratio of glands and stroma, shape and size of the gland, the glandular structure increases to 2-3 layers and has the potential to be an atypical form of cells when there is no balance of inhibitors and the initiator of the proliferation of glandular cells.[9-11]

With the imbalance between estrogen and progesterone where there is a state of Unopposed Estrogen that will cause endometrial thickening. Estrogen hormones known to be produced in the ovaries are also produced on adipose tissue. Adipose tissue has been known as the organ that produces adipokine where one of the adipokines is RBP4. With increased adipose tissue will be associated with increased BMI.[1] In Table 3 the results of the Fischer exact test show p = 1.00. This means there is no significant difference between serum retinol binding levels of Protein 4 in endometrial hyperplasia and endometrial carcinoma. This may occur because in this study increased serum RBP 4 levels obtained as many as 17 people with both endometrial hyperplasia and endometrial carcinoma. Increased RBP 4 was associated with BMI levels > 25 in this study there were 21 people with BMI > 25. So that serum RBP 4 levels were > 50% increased by more than 26,800. So with the statistical test obtained p-value = 1.00. So it can be said there is no significant difference in serum RBP 4 levels between endometrial hyperplasia and endometrial carcinoma. While in BMI obtained in this study, showed that with total samples of hyperplasia and endometrial carcinoma with BMI > 25 were 21 people. Susanne et al. 2007, reported BMI associated with serum RBP 4 levels, the higher the BMI then serum RBP 4 levels will also increase. In several other studies have also been done to see the relationship between serum RBP4 and BMI levels. This is in line with the results obtained in this study where elevated serum RBP 4 levels in BMI > 25 as many as 18 people. In addition, there have been several studies linking RBP with insulin resistance wherein insulin resistance will be associated with Diabetes Mellitus type 2.[12-16]

This research has advantages and disadvantages, the limitations that will be able to influence the research results, such as the lack of research samples, RBP in normal BMI patients and not experiencing AUB-M, cannot control confounding variables such as, GDS, dietary patterns, unexamined FSH-LH, estrogen, HOMA-IR levels. Moreover, some other mediators whom other studies have suspected will affect the results of our research. While the advantages of this study were all those examined were patients with AUB with endometrial hyperplasia aetiology and endometrial carcinoma, also this study used data obtained by Anatomical Pathology and ultrasound. Another advantage is that all samples were taken from September 2016 to April 2017 so that it can be used as an overview of PUA events with the aetiology of malignancy and endometrial hyperplasia.[16-18]

CONCLUSION

There was a no correlation between serum RBP 4 between endometrial hyperplasia and endometrial carcinoma.

SUGGESTION

Further studies with larger sample size and better study design are required.

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Research Article

Effectiveness of Oral Misoprostol to Prevent Postcesarean Section Urinary Retention

Efektivitas Misoprostol Per-oral terhadap Perubahan Residu Urin sebagai Pencegahan Retensio Urin Pascaseksio Sesarea

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Abstract

Objective: To determine the effect of misoprostol on the incidence of urinary retention in post-cesarean section patients by measuring maternal residual urine volume 6 hours after catheter removal.

Methods: This was a single-blind randomized controlled trial, at Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Palembang Hospital from October 2016 to February 2017. Samples were patients who underwent cesarean section, either elective or emergencies treated at Department of Obstetrics and Gynecology Hospital, Dr. Mohammad Hoesin Palembang. Subjects were allocated into two groups: treatment group (receiving misoprostol) and placebo group. Urinary retention is diagnosed if post-voiding residual urine volume after Foley catheter removal was >200 ml. Statistical analysis was performed using SPSS 17.0

Results: There were no differences in mean time between of urination between control group (placebo) and 600μg oral misoprostol group. The average of urine volume and residual urine volume between control group (placebo) and 600μg oral misoprostol group was significantly different. 600μg misoprostol orally can increase the amount of urine and reduce the volume of urinary residue after cesarean section.

Conclusion: 600μg oral misoprostol can increase urine volume and reduce volume of residual urine post-cesarean section.

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Keywords: cesarean section, misoprostol, urinary retention

Abstrak

***Tujuan**: Untuk mengetahui pengaruh misoprostol terhadap kejadian retensi urin pada pasien operasi seksio sesarea dengan mengukur volume residu urin maternal 6 jam setelah kateter dilepaskan.*

***Metode**: Penelitian uji klinik acak berpembanding (Randomized Controlled Trial) secara single blind (tersamar tunggal) ini dilakukan di Departemen Obstetri dan Ginekologi RSUP Dr. Mohammad Hoesin Palembang mulai bulan Oktober 2016 sampai dengan Februari 2017. Sampel penelitian adalah semua pasien seksio sesarea, baik elektif maupun emergensi yang dirawat di Departemen Obstetri dan Ginekologi RSUP Dr. Mohammad Hoesin Palembang. Subjek dialokasikan menjadi 2 kelompok yaitu kelompok penanganan yang menerima misoprostol dan kelompok plasebo. Retensio urin didiagnosis jika volume residu urin pascaberkemih setelah kateter Foley dilepaskan >200 ml. Analisis statistik dilakukan dengan menggunakan SPSS 17.0*

***Hasil**: Tidak terdapat perbedaan rerata waktu urinasi antara kelompok kontrol (plasebo) dengan misoprostol peroral 600μg.Terdapat perbedaan rerata jumlah urin, dan volume residu urin antara kelompok kontrol (plasebo) dengan misoprostol peroral 600μg. Misoprostol per oral 600μg dapat meningkatkan jumlah urin dan mengurangi volume residu urin pascapersalinan seksio sesarea.*

***Kesimpulan**: Misoprostol per oral 600μg dapat meningkatkan jumlah urin dan mengurangi volume residu urin pascapersalinan seksio sesarea*

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***Kata kunci**: misoprostol, retensio urin, seksio sesarea*

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INTRODUCTION

Postpartum urinary retention (PUR) is an obstetric case that is often encountered in clinical practice. The reported PUR prevalence varies from 1.7 to 17.9% focusing on PUR after vaginal delivery. Groutz et al. studied 125 women with postpartum voiding difficulties, as many as 38% of maternal women with the aid of vacuum instrumentation, 27% with spontaneous labour, and 15% with cesarean section.[1,2]

According to Weissman, factors including episiotomy, birth trauma, and severe perineal lacerations are not sufficient enough to induce PUR. On the contrary, there is some evidence to indicate the strong correlation between cesarean section and

PUR incidence. Kermans et al. stated the prevalence of post-cesarean section PUR is higher than vaginal delivery (2.1% vs 3.2%). Intraoperative bladder manipulation is thought to be the cause of weak detrusor muscle contractions. Patients terminated abdominally tend to be unable to empty the bladder due to inadequate contraction of detrusor muscles postoperative; patients are also reluctant to contract the abdominal wall to start urinary expenditure. Epidural anaesthesia may also decrease or exclude sensations of urgency from the need for urination during labour and the postpartum period.[3-7]

Inaccuracies or delays in diagnosis and management of PUR can cause excessive distension of the bladder, detrusor muscle damage, and increase risk of urinary tract infections, long-term voiding dysfunction and renal injury.[3]

Prostaglandin (PGS) is essential to improve detrusor muscle contraction. Misoprostol is an analogue of prostaglandin E1 (PGE1) synthetic. It has various advantages, including relatively affordable price, widely available, has long half-life, and stable at room temperature. Kelly et al. reported that within three months of therapy using oral PGS analogue 600 mg per day, 56% of patients reported improvement of interstitial cystitis symptoms, especially voiding disturbance due to pain and urine retention.[8-10]

Until today, effectiveness of misoprostol in preventing and overcoming urinary retention after cesarean section at Dr Mohammad Hoesin Palembang has not been studied. Therefore, this study aimed to determine the effect of misoprostol on the incidence of urinary retention in patients with cesarean section by measuring maternal residual urine volume 6 hours after catheter removal.

METHODS

This single-blind randomised controlled trial was conducted at the Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Palembang Hospital in October 2016 until February 2017.

Samples were all patients underwent elective and emergency cesarean sections, treated in Department of Obstetrics and Gynecology, Dr. Mohammad Hoesin Palembang Hospital. Inclusion criteria were patients undergoing cesarean sections at Dr. Mohammad Hoesin Palembang hospital by lower uterine segment incision, with regional anaesthesia, and those willing to participate in this research and signed informed consent. On the contrary, patients with urinary tract infections, having previous voiding problems prior to caesarean section, patients with severe preeclampsia, diabetes mellitus, renal dysfunction, and indications of cesarean section; those with prolonged labor, history of cesarean section, polyhydramnios, multiple pregnancies, and induction of labor with misoprostol were excluded from the study. Patient who has a habit or a history of smoking and alcohol consumption were also excluded from the study.

Patients were dropped out from the analysis if experiencing allergic or hypersensitivity during administration of misoprostol and suffered from urosepsis. Based on samples calculation, 15 samples were needed in each group. Sample was chosen by simple random sampling.

All post-cesarean patients who were treated at Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Palembang Hospital and met the inclusion criteria were asked to sign the informed consent, subjects then being matched based on age, parity, and gestational age. Simple random sampling was applicated to allocate subjects who received misoprostol and placebo. Sample did not know in which treatment group the belonged to.

Treatment group received 600 mcg misoprostol per day, administered orally after the patient completed a cesarean section. It was divided into three doses; 200 mcg orally after cesarean section, 200 mcg orally within 8 hours after the first dose, 200 mcg in 8 hours after administration of the second dose. Control group received a placebo in the form of three tablets of starch material. Placebo tablet was administered the same way as misoprostol. Foley catheter installed for 24 hours in post-cesarean section patients. After 24 hours post-surgery, catheter was removed, and patient was asked to urinate. Time interval between urination and time of catheter removal was then recorded. Patient was asked to collect urine in a bottles and researcher would measure the amount of urine volume in the bottle using a measuring cup. After the first voiding (after Foley catheter was removed), residual urine volume was measured by catheter. Catheterization was done using 16F Foley catheter as soon as voiding. Urine residues was collected in urine bag to measure urine volume. If the residual urine volume was >200 ml,

patient could be diagnosed with urinary retention after cesarean section. If the patient was not able to urinate spontaneously 6 hours after Foley catheter was removed, patient could be diagnosed with urinary retention after cesarean section. Patients underwent catheterisation and urine volume was measured.

Data was collected using forms previously provided, and then it was analysed using X^2 test for dichotomous variables and t tests for continuous variables. To determine the significance of differences between residual urine volume between misoprostol group and placebo group, data tes normality was performed with Shapiro Wilk test. If data were normally distributed, the unpaired t-test would be used. If data were not normally distributed, non-parametric Mann-Whitney test would be used. Differences were considered significant if $p < 0.05$. All data were analysed using SPSS version 18.

RESULTS

Population of this study were 30 pregnant women who underwent cesarean section and met inclusion and exclusion criteria. 15 women were located in the treatment group and 15 women as control in the placebo group. After follow-up, no research subject was dropped out or withdrawal from this study. Mean of urination time between control and treatment group was not significantly different (p = 0.589) (Table 1).

Table1. Comparison of Oral Misoprostol 600 μg and Placebo Group Based on Urination time

Variable	600 μg Oral Misoprostol	Placebo	p*
Time (Hour)	2.467 ± 0.972	2.667 ± 1.029	0.589*

**Independent T test, p = 0.05*

Mean urine volume between control group (placebo) and treatment group was significantly different (p = 0.029) (Table 2). Mean of urine volume was higher in treatment group.

Table 2. Comparison of 600 μg Oral Misoprostol and Placebo Group Based on Urine Volume

Variable	600 μg Oral Misoprostol	Placebo	p*
Urinary Volume (cc)	425.33 ± 71.20	320.00 ± 157.21	0.029*

**Independent T-test, p = 0.05*

Mean of residual urine volume between control group (placebo) and treatment group was significantly different (p = 0.001) (Table 3). Mean of residual urine volume was lower in treatment group.

Table 3. Comparison of 600 μg Oral Misoprostol and Placebo Group Based on Residual Urine Volume

Variable	600 μg Oral Misoprostol	Placebo	p*
Urinary Volume Residue (cc)	112.67 ± 28.59	147.33 ± 24.33	0.001*

**Independent T-test, p = 0.05*

DISCUSSION

Urinary retention after cesarean section is the inability to urinate 6 hours after Foley catheter removal or the volume of residual urine is > 200 ml. There are two parameters to diagnose urinary retention in this study including urination time, interpreting the time interval since Foley catheter removal until the patient can void spontaneously and residual volume, which is the amount of residual urine post spontaneous urination, as measured by catheterisation methods.

Before treatment, the characteristics of research subjects were statistically researched, the results of which, age (p = 0.407), body mass index (p = 0.489), and parity (p = 0.244) between the two groups did not differ significantly. It confirms that the differential effectiveness of 600μg oral misoprostol with placebo in preventing the occurrence of postpartum urinary retention is not influenced by demographic characteristics.

This study also showed there are no differences between the mean time urination between the control group (placebo) and misoprostol orally 600 μg (p = 0.589), in which both the misoprostol group and placebo, all pregnant women after cesarean section were able to urinate 6 hours after the catheter Foley released. The results of this study differs from the research conducted by Azami and Gatut in 2013 which showed differences between the mean time urination between the control group (placebo) with 600μg oral misoprostol (p = 0.010). PGS role in relaxation-contraction and sensitivity to stimuli urinary bladder has been widely studied, PGS released during or immediately after the occurrence of bladder distention, and PGS also regulates smooth muscle contraction and modulates neuronal transmission in urinary tract.[11,12]

Therefore, it can be concluded that misoprostol can increase sensitivity to stimuli urinary bladder, that is distended bladder with urine, and accelerates urination time in the study samples.

The was no difference of urination time in both study groups (misoprostol vs placebo), this might be caused by several factors, such as, the whole research samples were from pregnancies with no disorders that affect micturition (examples: UTI, cystitis, neurological disorders, prolonged labor, renal dysfunction, preeclampsia, smoking, alcohol, etc.) so that the samples were all under normal urination condition.

Intraoperative bladder manipulation occurred minimally. It was mentioned earlier that one of the exclusion criteria for the study was pregnancies with complication, so the cesarean section operation may take place smoothly without any difficulty that may involve manipulation of bladder.

Fluid intake in this study could not be controlled by the researcher. It is known that fluid intake pre-operative or post-operative determines urine production which then would affect the urination time. However, the calculation of urine time of all samples were after catheter removal, which means all samples at the beginning of the calculation of urination time had an empty bladder.

Both groups were installed foley catheters until 24 hours post-operative. A study conducted by T Mohammad Rizki in 2009 showed a significant association between the length of catheter insertion with urinary retention, where the faster the settled catheter was removed, the incidence of urinary retention was increased by $p = 0.038$ ($p < 0.05$).

A small amount of samples. A study with 30 samples, with each group of 15 samples, may be less representative of the population, so no time difference in urination was found. This is one of the weaknesses of the study, so it is expected that in the next study should involve a larger sample size.

Prevention of urinary retention in obstetric cases can be done in several ways, among others, by overcoming postpartum pain, by installing a Foley catheter for 24 hours or by administration of PGS. The release of PGS by the bladder can be stimulated by a variety of factors, including neuropeptides (substance P, neurokinin A), and inflammatory factor (bradykinin), which causes vesicular contractions and facilitates urinary reflex.[4]

In this study statistical analysis showed that there was a difference in the mean number of urine volume between the control group (placebo) with 600 μg oral misoprostol, in which the urine volume of group who received 600 μg peroral misoprostol was more than the group who received placebo. The results of this study were slightly different from the Azami and Gatut research in 2013 where the results showed no difference in the mean volume of urine between the control group (placebo) with 600 μg per oral misoprostol ($p = 0.051$). However, the same result was found the amount of urine volume in the misoprostol group was higher than those of the placebo group. This difference is probably due to the research of Azami and Gatut route of misoprostol was suppository. After oral administration, the half-life of misoprostol ranges from 20 to 40 minutes, then decreases rapidly within 120 minutes and remains low whereas at rectal administration is less than 20 minutes.[8,12]

Another possible cause is the uncontrollable fluid intake in this study as discussed earlier. After oral administration, misoprostol is faster and almost entirely absorbed by the gastrointestinal tract, plasma peak levels are achieved in 30 minutes, while the half-life ranges from 20-40 minutes, then decreases rapidly within 120 minutes and remains low. Misoprostol plays a role in opening Ca2 + ion channels so that extracellular Ca2 + ions can enter easily into intracellular and bind to calmodulin. This bond further activates the formation of MLC kinase which facilitates the formation of P-myosin. P-myosin will bind to actin causing contraction of detrusor muscle. Detrusor muscle contractions will trigger the function of the bladder to return to normal.[9]

In addition to urinary and urine volume time, another parameter for assessing postpartum urinary retention is the volume of urine residue > 200 ml. With statistical analysis, this study showed that there was a difference in mean residual urine volume between the control group (placebo) and 600 μg oral misoprostol, in which the volume of urine residues of the group receiving peripheral misoprostol was 600 μg less than those receiving placebo, but no residual volume was found > 200 ml in both misoprostol and placebo groups.

The results of this study were not much different from the research done by Azami and Gatut in 2013 where the results showed that there was a difference of average urine volume between the control group (placebo) and 600 μg ($p < 0.001$) oral misoprostol, whereas the volume of urine residues of the group receiving 600 μg oral misoprostol less than those receiving placebo and no residual volume > 200 ml was found in either the misoprostol or placebo group.[12]

So it can be concluded that in this study 600μg oral misoprostol can increase the amount of urine volume and reduce the volume of residual urine after cesarean section.

The majority side effect of misoprostol in this study (20% of 15 samples) was shivering. These findings are consistent with the study of Azami and Gatut (2003) who found 38% of shivering incidents. Other adverse effects were diarrhoea, Wagner (1985) has documented adverse drug events of oral route misoprostol in the gastrointestinal tract and suggested that rectal route delivery is safer to prevent the adverse effects of misoprostol in the gastrointestinal tract. Other possible causes of diarrhoea in this study include electrolyte imbalances, gastroenteritis-associated diseases that may be suffered by the patient and undetected during the study.

The results of the fisher exacts analysis found no significant association between the types of intervention and the incidence of drug side effects, suggesting that the adverse effects of drugs on the study could be "brutal" and not necessarily caused by misoprostol. The patient's subjectivity bias for shivering perception can disrupt the analysis of drug side effects, and this bias is difficult to control. A larger sample size is needed to determine if side effects do occur, and what are the side effects that may result from misoprostol administration.

Some disadvantages in this study besides the small number of samples is not to include patients with PUR (+). All samples did not experience PUR, and the effectiveness analysis of misoprostol was done on non PUR samples. Secondly, no misoprostol was administered in different doses, so this study could not determine the best dose of misoprostol for PUR handling, as well as the possible toxic effects based on misoprostol dosage. Further research is expected to include post-cesarean serum PUR population with larger sample quantities and provide varying doses of misoprostol intervention.

CONCLUSION

There is no difference in mean time of urination between the control group (placebo) with 600μg oral misoprostol. There is an average difference in the amount of urine volume, and the volume of residual urine between the control group (placebo) with 600μg oral misoprostol. 600μg oral misoprostol can increase the amount of urine and reduce the volume of urinary residue after cesarean section.

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Research Article

Conformity of Human Papillomavirus between Self-examination of Vaginal Fluid and Cervical Specimen with Fluid-Based Cytology in Precancerous Lesions

Tingkat Kesesuaian Human Papillomavirus antara Pemeriksaan Cairan Vagina secara Mandiri dan Spesimen Serviks dengan Sitologi Berbasis Cairan pada Lesi Prakanker

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Abstract

Objective: To determine the conformity of human papillomavirus between self-examination of vaginal specimen and cervical specimen with fluid-based cytology in precancerous lesions.

Methods: A cross-sectional study performed on cervical and vaginal fluid from 90 pre-cancerous lesions patients from April to September 2016. Cytological examination performed with self-examination and liquid-based cytology technique. HPV genotyping performed with PCR technique. Data were analysed with SPSS.

Results: Most of the women aged >35 years (89%), 78% (71/90) multiparity and 74.4% (67/90) do not know about HPV screening. High-risk type found in both vaginal and cervical fluid was type 16, 18, 33 and 45 whereas type 35 found only in vaginal fluid. The most prevalent high-risk HPV for both specimens were type 16 and 18. HPV type 42 and 53 were the low-risk HPV found in the vaginal and cervical specimens (table 2). Cohen's kappa for inter-test agreement shows a strong correlation (r=0.864).

Conclusion: The HPV self-examination method can be used as a primary examination of cervical cancer lesions detection in addition to fluid-based cytology with the similar results.

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Keywords: cervical cancer, fluid-based cytology, human papillomavirus, self-examination

Abstrak

Tujuan: *Untuk mengetahui tingkat kesesuaian antara pemeriksaan HPV mandiri dari spesimen vagina dan hasil pemeriksaan sitologi berbasis cairan dari spesimen serviks.*

Metode: *Penelitian cross-sectional dilakukan pada cairan serviks dan vagina dari 90 pasien lesi pra-kanker pada April sampai September 2016. Pemeriksaan sitologi dilakukan dengan pemeriksaan diri dan teknik sitologi berbasis cairan. Pemeriksaan genotip HPV dilakukan dengan teknik PCR. Data dianalisis dengan SPSS.*

Hasil: *Sebagian besar perempuan dalam penelitian ini berusia >35 tahun (89%), 78% (71/90) multiparitas dan 74,4% (67/90) tidak mengetahui tentang skrining HPV. Tipe HPV risiko tinggi yang ditemukan pada cairan vagina dan serviks adalah tipe 16, 18, 33 dan 45 sedangkan tipe 35 hanya ditemukan pada cairan vagina. Tipe HPV risiko tinggi yang dominan untuk kedua spesimen adalah tipe 16 dan 18. HPV tipe 42 dan 53 adalah HPV risiko rendah yang ditemukan pada baik spesimen vagina maupun serviks. Kappa Cohen untuk tingkat kesesuaian antara pemeriksaan mandiri dan sitologi berbasis cairan menunjukkan korelasi kuat (r = 0,864).*

Kesimpulan: *Metode pemeriksaan HPV secara mandiri sendiri dapat digunakan sebagai pemeriksaan primer deteksi lesi kanker serviks selain sitologi berbasis cairan dengan hasil yang sama.*

[Maj Obstet Ginekol Indones 2018; 6-4: 253-256]

Kata kunci: *human papillomavirus, kanker serviks, pemeriksaan mandiri, sitologi berbasis cairan*

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INTRODUCTION

Cervical cancer is the third most common cancer and the fourth leading cause of cancer in the world. It is estimated that 530,000 women diagnosed with cancer and 275.000 of them died in 2008 around the world.[1,2] The development of cervical cancer is very difference between developed countries and developing countries. Globally, there were approximately 85% of cases and 88% of deaths from cervical cancer in developing countries.[3] In countries that do not have a good screening program, most of the cervical cancer patients came at an advanced stage, and in an incurable stage.[4] It is estimated that 50-80% of sexually active women will be infected with HPV in their life, and 80% will be free of infection within 2 years and will not cause cancer.[4,5] Cervical cancer is the only cancer that can be detected early

and inhibit its development.

The most important thing in HPV examination is the accuracy and level of conformity of examination results. There are currently several types of methods for detecting HPV infections in the genital tracts such as conventional Pap smears, visual inspection with acetic acid (IVA), HPV DNA testing with cervical smears and tests of vaginal swabs.[6] This study aimed to determine conformity of human papillomavirus between self-examination of vaginal fluid and cervical specimen with fluid-based cytology in precancerous lesions.

METHODS

This cross-sectional study was performed on cervical and vaginal fluid from 90 pre-cancerous lesions patients from April to September 2016 at Dr. Wahidin Sudirohusodo Hospital and its affiliated hospitals in Department of Obstetrics and Gynecology, Faculty of Medicine Universitas Hasanuddin. Cytological sampling performed with self-examination and liquid-based cytology technique. HPV genotyping performed with PCR technique (primer system MY09-MY11 (MY09/11) WI LTS-06 method) at the *Kalbe Genomics* (KalGen) *Laboratory* Jakarta Indonesia. Data were analysed with SPSS. This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Hasanuddin.

RESULTS

In the present study, self-examination and liquid-based HPV cytology were performed on 90 patients with precancerous lesions. Most of the women aged >35 years (89%), 78% (71/90) multiparity and 74.4% (67/90) do not know about HPV screening (Table 1).

Table 1. Samples Characteristic

Characteristic (n=90)	n	%
Age (years)		
20-34	10	11.1
>35	80	88.9
Parity		
Nulliparity	19	21.1
Multiparity	71	78.9
Knowledge about HPV screening test		
No	67	74.4
Conventional pap smear	23	25.6

High risk and low-risk HPV types were found both in the vagina and the cervix. High-risk type found in both specimens were type 16, 18, 33 and 45 whereas type 35 found only in vaginal fluid. The most prevalent high-risk HPV for both specimens were type 16 and 18. HPV type 42 and 53 were the low-risk HPV found in the vaginal and cervical specimens (Table 2). Cohen's kappa for inter-test agreement was 0.864 (Table 3).

Table 2. HPV Type in Vaginal and Cervical Specimen

HPV	Vagina		Cervix		Vagina and cervix	
	n	%	n	%	n	%
			High risk			
16	31	34.4	30	33.3	30	33.3
18	22	24.4	30	33.3	21	23.3
33	3	3.3	2	2.2	2	2.2
45	7	7.8	6	6.7	6	6.7
35	1	1.1	-	-	-	-
			Low risk			
42	9	10	9	10	8	8.9
53	7	7.8	6	6.7	6	6.7

Table 3. Concordance of HPV Type between HPV Self-sampling and Liquid-based Cytology

HPV self-sampling	Liquid-based cytology		Total	r	p
	High-risk HPV (n)	Low-risk HPV (n)			
High-risk HPV	49	5	54	0.864	0.000
Low-risk HPV	1	35	36		

DISCUSSION

Age is a major factor in HPV infection in cervical cancer. The prevalence of women aged 20s infected with high and low-risk HPV between 20%-40%.[7] The study also found that the highest HPV type 16 infection occurs at age 25-40 years compared to HPV type 18 for the same age group then the risk of infection decreases with age.[8,9] Women aged >35 years with pre-cancerous lesions in the present study higher than women aged 20-34 years with the same diagnosis. A study by Sanner et al., found that 40% of women who do not participate in the screening programs in Sweden prefer to perform self HPV examination making this examination could reduce the incidence of cervical cancer by 25-50% in postmenopausal women.[10]

We included sexually active women aged 20-55 years in our study. Sexually active young women would have a positive HPV test result, and 20s was the limit age for cervical cancer screening based on the pathogenesis of the disease. However, high-risk HPV type 16/18 decreases with age at diagnosis. Approximately 70% of young women newly infected with HPV and infection clearance occurs after 12 months whereas the age of 55 years decreased the effectiveness of cytological examination is known to decline in the elderly age group. A Randomized Trial in Screening to Improve Cytology (ARTISTIC) also found that the prevalence of HPV decreased 40% in age 20-24 years, 12% (35-39 years), and 7% (>50 years). Abnormal biopsy examination represents CIN 1 and CIN 2/3. These criteria based on the manifestation of low-grade histological changes (CIN 1) in new high-risk HPV infection. This change is usually temporary, while in CIN 2/3 acts as a precursor of cervical cancer. High-grade CIN 2/3 lesions along with risk factors will increase the incidence of persistent high-risk HPV infection whereas the latest pap smear examination (last for three months) and histopathology are the last diagnostic and the gold standard for the whole examination. This examination directly impact on the results of diagnostic tests performed.[6,11-13]

Various methods for detecting and determining the type of HPV DNA have been widely introduced. The most commonly used inspection methods are hybrid capture 2 (HC2) and PCR. In this study, we used PCR GMP 09/11 method. The use of PCR methods has been shown to have higher sensitivity to detect high-risk HPV than HC2. According to one RCT result, the GPM 09/11 amplification method shows very low sensitivity (49%).[14] Therefore, the use of similar methods is likely to lead to low levels of audit sensitivity.

By comparing the health cost effects of some cervical cancer screening strategies, a positive HPV test will be followed by cytologic examination. The combination of cytologic and HPV examinations simultaneously shows that the use of HPV DNA testing as a single primary screening tool or in combination with cytology provides more cost-effectiveness than primary screening with cytology, as it may extend the screening interval.[15] Based on the Canadian Cervical Cancer Screening Trial comparing the performance of human papillomavirus (HPV) testing and Papanicolaou cytology in 10.154 samples found that the sensitivity for both tests, when used at the same time, was 100% and the specificity was 92.5%.[16] Further research by synergising the existing inspection modalities will improve diagnostic ability, so the accuracy and precision of the tool can be as expected. Improving the validity of the tool, to obtain the lowest possible false negative value will provide hope for clinicians to detect earlier an illness, so treatment and treatment can be given at an earlier stage and improve the prognosis of the disease.

The accuracy level of conformity with the results of this examination kappa test indicates that 0.864 results are obtained which means that 86.4% of results between self-examination and liquid-based cytology have very strong correlation. In a previous study assessing the sensitivity and specificity of diagnostic tests for independent HPV examination in detecting HPV in high-grade precursor lesions and cervical cancer showed sensitivity 56% and specificity 98%. The results showed that the examination was only able to detect 56% of the abnormal group, and if the negative results of this examination 98% ensure the absence of disease. The study had negative predictive value of this examination for only 68% and positive predictive value of 96%. Based on these results, it can be said that self-examination has the ability to ensure the positive results of 96%, but the use of examination tools as an early detection tool requires high negative false results. The accuracy of this diagnostic test is 79%. These results indicate that 79% of the results of the tests performed have the conformity of the results with the standard of all samples. Briefly stated that if a person is diagnosed negatively with HPV self-examination, then the

possibility to get negative results in the pathological findings is 98%.

CONCLUSION

The degree of conformity of HPV vaginal self-examination and cervical fluid-based cytology in pre-cancerous lesions has suitability with very strong categories so that the HPV self-examination method can be used as a primary examination of cervical cancer lesions detection in addition to fluid-based cytology with the similar results.

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Research Article

Post-operative Recovery Assessment of Urinary Tract Dysfunction Following Radical Hysterectomy for Cervical Cancer Patients

Kajian Pemulihan Fungsi Berkemih pada Pasien Kanker Serviks Pascahisterektomi Radikal

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Abstract

Objective: To assess the length of recovery phase in urinary tract dysfunction following radical hysterectomy for cervical cancer patients in Dr. Cipto Mangunkusumo Hospital.

Methods: This survey study was conducted at Dr. Cipto Mangunkusumo Hospital from September 2016 to May 2017. Subjects were cervical cancer patients from stage IA2 to IIA2 who underwent radical hysterectomy. A suprapubic catheter (SPC) was inserted to observe the urine production after the procedure. Patients were then directed for bladder training protocol involving clamping and opening SPC. Sensation of bladder fullness followed by spontaneous micturition was recorded. Measurement of post-voiding residual (PVR) urine volume after spontaneous micturition until less than 100 ml was considered as the resolution of urinary tract dysfunction. The average days of every achieved phase were then calculated.

Results: Twenty-nine subjects underwent radical hysterectomy during the observation period. However, only 21 subjects continued the bladder training protocol and recorded for the recovery phases. The average time needed to obtain sensation of bladder fullness and spontaneous micturition was 7.57 ± 4.78 days (median 5 days, minimum 3 days, maximum 22 days) and 8 ± 5.21 days (median 6 days, minimum 3 days, maximum 23 days). The objective PVR urine became less than 100 ml was obtained after 21.42 ± 18 days (median 18 days, minimum 7 days, maximum 74 days).

Conclusion: Following radical hysterectomy, recording the recovery phase of urinary tract dysfunction is essential to ensure complete resolution. Complete resolution of the urinary dysfunction is achieved after 21.42 ± 18 days in average (median 18 days, minimum 7 days, maximum 74 days).

[Indones J Obstet Gynecol 2018; 6-4: 257-260]

Keywords: cervical cancer, post-voiding residual volume, radical hysterectomy, urinary tract dysfunction

Abstrak

***Tujuan**: Menilai masa pemulihan disfungsi saluran kemih setelah histerektomi radikal pada pasien kanker serviks di RSUPN Dr. Cipto Mangunkusumo.*

***Metode**: Studi survei dilakukan di RSUPN Dr. Cipto Mangunkusumo dari September 2016 hingga Mei 2017. Subjek penelitian terdiri atas pasien kanker serviks stadium IA2 hingga IIA2 yang menjalani histerektomi radikal. Kateter suprapubik (SPC) digunakan sebagai alat untuk memantau produksi urin pascaoperasi. Pasien diinstruksikan untuk mengikuti protocol bladder training yaitu melalui prosedur menutup, dan membuka kateter. Rasa sensasi ingin berkemih dan berkemih spontan. Pengukuran residu volume urin pascaberkemih di bawah 100 ml dianggap merupakan indikator pemulihan disfungsi saluran kemih. Rata-rata hari dari tiap fase kemudian dihitung.*

***Hasil**: Dua puluh sembilan subjek didapatkan selama penelitian. Namun, hanya 21 subjek yang dapat mengikuti protocol bladder training dan dicatat perkembangan pemulihannya. Rata-rata hari yang diperlukan untuk merasakan sensasi berkemih dan berkemih spontan adalah 7,57 ± 4.78 hari (median 5 hari, minimum 3 hari, dan maksimum 22 hari) dan 8±5.21 hari. (median 6 hari, minimum 3 hari dan maksimum 23 hari) Rata-rata hari untuk mencapai residu urin di bawah 100 ml adalah 21.42 ± 18 (median 18 hari, minimum 7 hari, dan maksimum 74 hari).*

***Kesimpulan**: Setelah prosedur histerektomi radikal, pencatatan masa pemulihan penting untuk dipantau untuk memastikan pemulihan lengkap. Rata-rata hari yang diperlukan untuk pemulihan adalah 21,42 ± 18 hari (median 18 hari, minimum 7 hari, dan maksimum 74 hari).*

[Maj Obstet Ginekol Indones 2018; 6-4: 257-260]

***Kata kunci**: disfungsi saluran kemih, histerektomi radikal, kanker serviks, volume residu pascaberkemih*

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INTRODUCTION

Cervical cancer is the third most common female cancer occurs in Indonesia following breast and colorectal cancer.[1] To date, the treatment of cervical cancer is still limited to specific surgery (radical hysterectomy), radiotherapy, chemotherapy and chemoradiation. The 5-year survival rate for both radiotherapy and radical hysterectomy reach up to 85%, but the after-effect of each treatment is different.[2]

Radical hysterectomy procedure for cervical cancer affects the urinary tract in short and long-

term. Long-term effects occur approximately in 8-80% of the population according to the institution.[3] The most common one is voiding dysfunction.[4] Study conducted in Thailand showed 25.1% of the patients in early stage who underwent radical hysterectomy had symptomatic bladder dysfunctions such as incomplete bladder emptying, urgency, nocturia, terminal dribbling, frequency and micturition pain.[5]

Short-term effects occur in lower urinary tract such as loss of bladder sensation, inability to void and vesicoureteral reflex. In three months evaluation after the procedure, some of the patients showed several symptomatic bladder dysfunctions such as frequency, urgency, while the other side showed diminished bladder sensation, voided by abdominal straining, urine retention, mild stress incontinence and difficulty in initiating micturition with suprapubic catheter inserted for 35-39 days.[6]

In two weeks of observation, all the patient who underwent radical hysterectomy showed voiding sensation dysfunction and 68% had residual urine in their bladder.[7] There is still no adequate data for the incidence of bladder dysfunction globally. These urine dysfunctions lasted for one to six months in 13% of the patients, while the other 3% lasted for more than six months.[8] Shingo Fuji et al. showed 92% of the patients would have the sensation of bladder fullness, and only 71% obtained the satisfaction of micturition 14-days after surgery. These were objectively evaluated by measuring post void urine residual volume under 50 ml only in 46% of patients 14-days after surgery.[9]

Obstetric and Gynecologic Department Oncologic Division in Dr. Cipto Mangunkusumo Hospital has been doing radical hysterectomy procedures for cervical cancer patients for years. However, until today, the study for evaluating the after effects from the procedure, the recovery phase and the therapies is still limited.

OBJECTIVES

This study is aimed to observe the recovery phase of the urinary tract dysfunctions following radical hysterectomy in cervical cancer patients in Dr. Cipto Mangunkusumo Hospital. We also want to observe the period needed to achieve full bladder sensation, spontaneous micturition and to have post-void residual volume below 100 ml in cervical cancer following radical hysterectomy procedures in Dr. Cipto Mangunkusumo Hospital.

METHODS

This study is a cross-sectional study conducted in 7 months (September 2016 - May 2017) in Dr. Cipto Mangunkusumo Hospital, Jakarta. The subjects were cervical cancer patients stage IA2, IB1, IB2, IIA1 and IIA2 who underwent radical hysterectomy, did not have any urinary tract dysfunctions, not under any urinary tract treatments such as alpha-blockers, never had any surgeries involving urinary tracts, not in the radiotherapy nor chemotherapy before radical hysterectomy, did not have vesicovaginal and retrovaginal fistules after surgery, did not use indwelling Foley catheter in the bladder training.

Subjects were collected from elective radical hysterectomy surgery patients until fulfilled the minimum sample of 21 subjects (as calculated previously), then they were followed for the urinary tract functions after the procedure. The subjects who fulfilled the criteria were asked for the availability for observation (informed consent). The data were collected from the history taking, physical examinations and the medical record. Suprapubic catheter was inserted to monitor the urine production after the surgery. The patients were instructed to clamp and open the catheter according to the bladder training protocol. The training started on the third to eighth-day post operation or when the patients start to feel the full bladder sensation. The bladder training was guided by the nurses assisted and accompanied by the family members. The catheter was clamped at 06.00 am will be opened periodically every 4 hours in exact time (10.00, 14.00, 18.00 and 22.00). The catheter will remain open from 22.00 to 06.00 in the night. Every spontaneous micturition, the urine would be collected and measured, then the patient or the family member recorded the volume in the bladder diary given by the nurse. Following the spontaneous micturition, the suprapubic catheter would be kept open for 5 minutes, and the residual urine would flow through the suprapubic catheter, and the residual urine volume would be then recorded also in the bladder diary. If there were no sensation to micturate until 4 hours, the clamp would be opened on the exact time given (10.00, 14.00, 18.00 and 22.00) for 5 minutes, and then the volume was recorded.

The time needed to achieve full bladder sensation and spontaneous micturition were then observed. Post-voiding residual urine volume below 100 ml considered to be the objective indicator for recovery of urinary tract dysfunctions. Data were then analyzed by SPSS for Mac vers. 20.0. Data with normal distribution were reported as mean and standard deviation, while the abnormal data distribution would be reported as median with minimum and maximum value.

RESULT

Twenty-seven subjects enrolled in this study. Six subjects were excluded from this study due to ureter malinjury and vesicovaginal fistula, detached suprapubic catheter or false-route in early placement, and consideration of surgical operator to use foleycatheter for bladder function monitoring.

Subject Characteristic

Eleven subjects were under laparotomy radical hysterectomy, while another 10 subjects were under laparoscopy. Most subjects (6 subjects, 23.8%) are in the range 40-44 years old and suffer from cervical cancer stage IB1 (7 subjects, 30.4%). No subjects are in stage IA2. Distribution of age is normal according to Shapiro-Wilk Test. Distribution of days needed to achieve full bladder sensation, spontaneous micturition, and residual urine below 100ml are not normal (Table 1).

Table 1. Subject Characteristic According to Age and Cervical Cancer Stage

Age (year)	(%)
30 - 34	1 (4.8)
35 - 39	4 (19)
40 - 44	5 (23.8)
45 - 49	3 (14.3)
50 - 54	2 (9.5)
55 - 59	3 (14.3)
> 60	3 (14.3)
Stage	
IA2	0 (0)
IB1	7 (33.3)
IB2	4 (19)
IIA1	5 (23.8)
IIA2	5 (23.8)

Overview of Postoperative Bladder Dysfunction Recovery

During bladder function monitoring, bladder training was started on postoperative day 3 until postoperative day (POD) 8 depended on the surgeon's decision. In study of Fujii et al., Foley catheters were withdrawn on POD 9. No single agreement or pilot study is explaining the most proper time to withdraw the Foley catheter and start the bladder training.[9]

In this study, POD 14 and 21 were used to evaluate the bladder function in accordance to Fujii et al. study.[9] The earliest micturition sensation was achieved on POD 3 during postoperative monitoring of bladder function recovery. The longest period needed to achieve sensation was POD 22. Earliest spontaneous micturition was achieved on POD 3, and the longest was on POD 23. The earliest days needed to achieve residual urine below 100ml was 7 days post operation while the longest was on POD 36.

On POD 21, only 13 subjects (61.9%) were already achieved residual urine below 100ml. The average days needed to achieved residual urine below 100ml is 21.43 ± 8 days (median 7 days). See Table 2.

Table 2. Bladder Dysfunction Recovery Overview

	Full bladder sensation	Spontaneous micturition	Residual urine <100ml
Post Operative Day 14	90.4% (19/21)	85.7% (18/21)	38.1% (8/21)
Post Operative Day 21	95.2% (20/21)	95.2% (20/21)	61.9% (13/21)
Average (days)	7.57 ± 4.78	8 ± 5.21	21.42 ± 18
Median (days)	5	6	18
Minimum (days)	3	3	7
Maximum (days)	22	23	74

On POD 14, 90.4% subjects (19 subjects) have already felt full bladder sensation, and 85.7% subjects (18 subjects) have already achieved spontaneous micturition.This data are not much different from Fujii et al. study which 91.7% subjects have felt full bladder sensation and 45.8% subjects objectively achieved residual urine below 100ml. Fujii et al. did not evaluate spontaneous micturition in subjects.

On POD 21, 95.2% subjects (20 subjects) felt full bladder sensation and achieved spontaneous micturition. This data is not much different from Fuji et al. study which all of the subjects (24 subjects)

are no longer suffered from bladder dysfunction on POD 21.[9]

The outcome difference between this study and Fujii et al. study mainly due to radical hysterectomy technique performed. In Fujii et al., nerve-sparing radical hysterectomy were applied to all subjects, while in this study, we did not differentiate between laparotomy and laparoscopy technique nor nerve sparing and non-nerve sparing technique. This could be one of weakness in this study where variables influencing were not analyzed.

Many studies have reported urinary tract dysfunction after radical hysterectomy. Voiding dysfunction is most problems reported. Buchsbaum et al. reported urinary retention in 10%-60% post radical hysterectomy patients. It used to be treated with intermittent catheterization.[10] This voiding dysfunction is persistent in 5% and becomes long-term bladder dysfunction. There is no clear definition between short term and long term bladder dysfunction.[6,11]

Even though there is no clear definition of bladder dysfunction after radical hysterectomy, this study is aimed to know the recovery period of short-term bladder dysfunction. The main purpose is giving clearer information to cervical cancer patients who undergo radical hysterectomy about the procedure and also the side effects. In daily practice, radical hysterectomy will affect the urinary function and increasing probability of Foley catheter placement in the long run. Decreasing total bladder capacity and worsening residual urine volume.[11] Therefore, it is crucial to be acquainted with the average recovery period of bladder dysfunction after radical hysterectomy. On final point, the data can be used to form guidelines in managing bladder dysfunction after radical hysterectomy especially when further intervention is needed.

It is important to consider the education level of each patient, especially in recording bladder diary. The accuracy of residual urine measurement can be doubted if the patient never empties the urine bag after every micturition process. It is best anticipated to ask one of the family members to assist the monitoring process.

CONCLUSION

In this study, the average days to achieve full bladder sensation in Dr. Cipto Mangunkusumo Hospital was 7.57 (median 5 days). The spontaneous micturition was achieved after 8 days on average (median 6 days). Residual urine under 100ml was achieved after 21.42 days on average (median 18 days). This overview of bladder dysfunction recovery is essential in giving patient education. Each patient should know that radical hysterectomy produces bladder dysfunction and the recovery will take an exact period of time. Continuous and repeated education is important for patient, family, medic and paramedic staffs especially in recording the bladder diary.

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Literature Review

How to Recognize, Prevent and Address Complications of Laparoscopic Gynecologic Surgery

Mengenali, Mencegah dan Mengatasi Komplikasi Operasi Ginekologi Laparoskopi

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Abstract

Objective: To highlight the needs of awareness on recognising, prevent and address complications in laparoscopic gynecologic surgery.

Methods: Literature review.

Discussion: The complications of laparoscopic gynecologic surgery mainly can be classified as complications related to anaesthesia, entry technique, electrosurgical, postoperative and visceral due to surgical procedure it self. Lam proposed a 6 phase-based classification of laparoscopic surgery complications; patient identification, anaesthesia and positioning, abdominal entry and port placement, surgery, postoperative recovery and counselling. The aim of this classification is to promote a culture risk management to improve patient safety and outcome. Every phase above should be able to assessed, analysed and executed properly to prevent complications.

Conclusion: Complication in operative laparoscopy is generally minor and can be handled successfully. However, although very rare, major complications are detrimental to the patient. It also becomes heavy burden for the surgeons. Preventive measures should be implemented not only by the operator but also the anaesthesiologist, and theatre practitioners. Systematic drills, which regularly rehearsed is essential in order to maintain team proficiencies.

[Indones J Obstet Gynecol 2018; 6-4: 261-266]

Keywords: complications, gynecologic laparoscopy, operative laparoscopy

Abstrak

***Tujuan**: Untuk menekankan pentingnya mengenali, mencegah dan mengatasi secara dini komplikasi operasi laparoskopi ginekologi.*

***Metode**: Kajian pustaka.*

***Diskusi**: Komplikasi operasi ginekologi laparoskopi dapat diklasifikasikan menjadi komplikasi yang berhubungan dengan anestesi, teknik masuknya trokar utama, terkait elektro surgikal, komplikasi pascaoperasi dan komplikasi visera (pembuluh darah, usus, cedera traktus urinarius) terkait tindakan operasi itu sendiri. Lam mengusulkan suatu klasifikasi berbasis fase, antara lain, identifikasi pasien, anestesi dan posisi pasien, akses masuk abdomen dan penempatan trokar, terkait operasi, pemulihan pascaoperasi dan konseling. Tujuan dari klasifikasi ini adalah untuk meningkatkan budaya sadar risiko, guna meningkatkan keselamatan pasien. Setiap tahap harus dapat dilaksanakan, dinilai dan dianalisis dengan baik untuk mencegah terjadinya komplikasi.*

***Kesimpulan**: Komplikasi pada operasi ginekologi laparoskopi umumnya ringan dan dapat ditangani dengan baik. Walaupun jarang terjadi, komplikasi berat umumnya sangat merugikan pasien dan menjadi beban operator. Langkah-langkah pencegahan ini harus dilaksanakan oleh operator, tim anestesi serta seluruh tim kamar operasi. Simulasi harus dilaksanakan, guna mempertahankan ke-cakapan tim.*

[Maj Obstet Ginekol Indones 2018; 6-4: 261-266]

***Kata kunci**: komplikasi, laparoskopi ginekologi, laparoskopi operatif*

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INTRODUCTION

Laparoscopic surgery has been widely used by various fields of medical science; one that rapidly developed is gynecologic surgery area. Worldwide, laparoscopic gynecologic surgery performed with an increasingly complex variety of indications. At present, sophisticated laparoscopic procedures such as laparoscopic hysterectomy, myomectomy, sacrocolpoplexy, and pelvic lymph node dissection have become daily routine operations.[1]

Although the benefits of laparoscopic gynecologic surgery have been recognised for the last decades, the range of complications of this procedure has not been highlighted. Risk of complications increases with the complexity of the surgical procedure and strongly influenced by the experience of the surgeon. Prevention of complications of laparoscopic gynecologic surgery should be started by raising awareness and take necessary precautions to ensure safety. Review of complications rate worldwide shown in Table 1.[2-4]

Table 1. Review of Laparoscopic Surgery Complications Worldwide[2-4]

Author	Country	Number of sample	Mortality	Overall Rate	Conversion to Laparotomy
Bateman[2]	USA	2.324		8.6/1000	
Jansen[2]	Netherland	25.764	8/100,000	5.7/1000	3.3/1000
Harkki[2]	Finland	32.205		4/1000	
Chapron[2]	France	29.966	3.3/100,000	4.6/1000	3.2/1000
Miranda[2]	United Kingdom	2.140	0	7.9/1000	
Min Sun Kyung[3]	Korea	2668	0	12.4/1000	0.4/1000
Putz[1]	Norway	2.308	0	28/1000 (intraoperative complications)	

Classifications of Complications

According to the type of laparoscopic procedure, laparoscopic surgeries were classified into four groups: diagnostic, minor, major and advanced laparoscopic surgery.[3] Type of procedure related to complications followed. The complications of laparoscopic gynecologic surgery mainly classified as complications related to anaesthesia, entry techniques, electrosurgical complications, visceral complications (vascular, bowel, urinary tract injury) and postoperative complications. This can be simplified as approach and technique related.

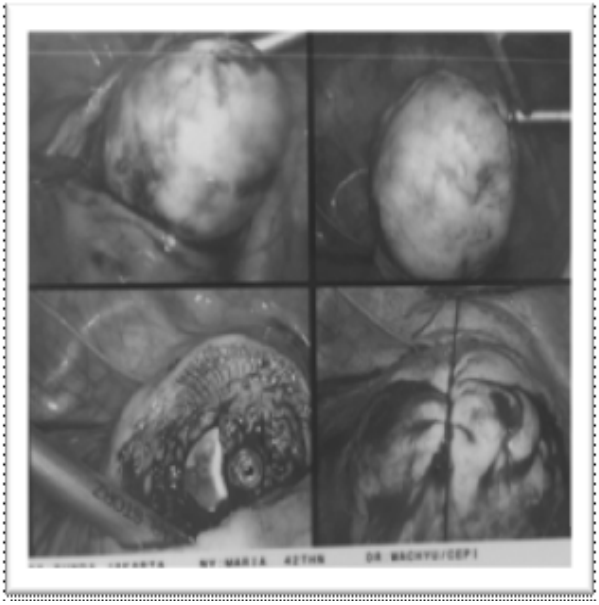

Figure 1. Appearance of uterine manipulator indicates that the intramural myoma reach the uterine cavity

In 2009, Lam proposed a phase-based classification of laparoscopic surgery complications. The aim of this classification is to promote a culture of risk management, based on strategies to improve patient safety and outcome. According to phases of laparoscopic surgery procedure, complications can occur in any of this 6 phases; phase I - patient identification, phase II - anaesthesia and positioning, phase III - abdominal entry and port placement, Phase IV - surgery, phase V - postoperative recovery, phase VI - counselling.[4] To prevent any complications either minor or major complications, every phase above should be able to be assessed, analyzed and executed properly.

Phase I - Patient identification

Pre-operative evaluation is mandatory before planning surgery. This step will provide valuable information in order to reduce both anaesthetic and surgical complications. Complete history, physical examinations together with laboratory/ radiology workup will help in illustrating steps that will be implemented. It must be ensured that the patient has neither absolute nor relative contraindications such as significant compromise on cardio-respiratory system/hemodynamic instability, severe intra-abdominal adhesions, advanced malignancy, pregnancy. Risk factors, such as obesity, a low body mass index (BMI), previous surgery, previous intra-abdominal infection, inflammatory bowel disease and any medical conditions, should be identified.[5]

Apart of patient peculiarity, other factors such as operator skills and training, equipment, the capability of operating theatre, hospital facility for post-operative care (ICU if necessary) and capability of theatre practitioners (scrub nurse, surgical assistant and theatre runner), should betaken under consideration before deciding any procedure. Prior plan of treatment (preoperative, intraoperative and also postoperative) should be carefully made to improve surgical outcomes.

Phase II - Anaesthesia and positioning

Most of the gynecologic laparoscopy surgeries are performed with the patient in the supine position with various modifications of the lithotomy position, with or without Trendelenburg positioning. The Trendelenburg position is used in these procedures to shift the abdominal viscera from the pelvis cranially to improve exposure.[5] This specific factor should be highlighted. Modified lithotomy position is associated with a particular risk of positioning injury. Incorrect positioning can lead to complications; which range from minor transient injuries to major permanent damage that caused long-term functional restrictions, secondary morbidity, or even death.[6]

Patients positioning and length of procedure has a significant impact on the patient's hemodynamic which eventually will impact anaesthesia. Optimal patient positioning should prevent pressure injuries (pressure ulcers), skin irritation, burns, nerve damage, circulatory problems and hypothermia.[6] Neurological injury alone can occur as a result of transection, compression, stretching or entrapment mechanism. Every hour in lithotomy position will increase the risk of lower limb neuropathy to 100 fold.[7]

Generally, the patient should initially be placed supine with arms tucked in by her sides on the operating table in a neutral position with the thumb pointing up.[8] Both legs are placed in lithotomy position supported by padded stirrups. The thigh positions should be parallel to the abdomen while the knee flexed to 90-120 degrees.[5,7] Hip flexion and hip abduction (measured from inner thigh to inner thigh) of less than 90 degrees and minimal external rotation of the hip.[7]

Besides patients positioning, laparoscopic surgery also presents unique anaesthetic challenges which differ from open surgery, such as the effects of pneumoperitoneum, extra peritoneal gas insufflations and venous gas embolism.[9]

Phase III - Abdominal entry and port placement

Abdominal entry and port placement have been recognised as one step that contributes on more than 50% serious laparoscopic complications.[4] The rates of life-threatening complications due to abdominal entry are relatively low, 0.4/1000 for iatrogenic gastrointestinal injuries and 0.2/1000 for major blood vessel injuries.[9] In a prospective multicenter observational study, Jansen et al. found that two deaths occurred in 25,764 procedures in one year period due to approach-related.[6] Therefore abdominal entry and port placement should not be underestimated.

Entry associated complications can occured as visceral or vessel injury.[8] Surgical complications associated with the entry to the peritoneal cavity include: damage to the anterior abdominal wall and major retroperitoneal vessels, damage to the bowel, extra peritoneal insufflation, herniation through port sites and failure to achieve access to the peritoneal cavity.[10]

Various techniques can be used on abdominal entry and port placement during laparoscopic gynecologic surgery, such as Closed (Veress needle) entry technique, Open (Hasson) entry technique, Direct Entry and Vision-Guided Direct Entry.[10] Each technique has its advantages and disadvantages. Many studies have compared each technique applied to various indications, however, based on currently available data, no abdominal entry method that considered superior over another and recommended as the standardised method.[9]

ISGE on 2016 suggest that safe and effective laparoscopic entry will be best served when the surgeon would use technique, entry position and type of instrumentation which he/she feels most comfortable for the majority of procedures. However if in particular circumstances, this chosen technique poses a major risk of complications, the operator should be willing to use an alternative technique/position/instrument that he/she has been adequately trained to use.[9]

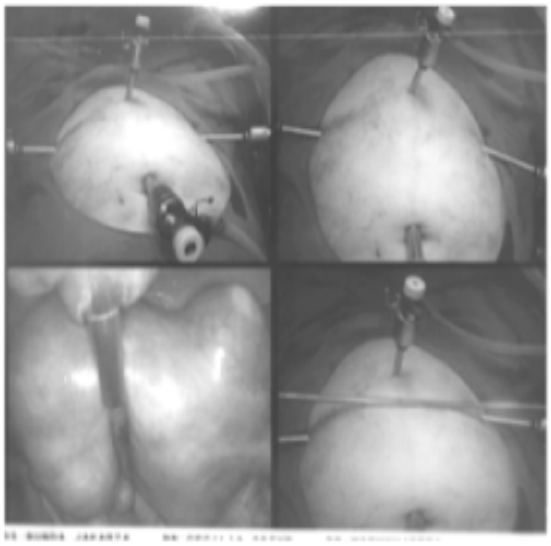

Figure 2. Position of main and associated trocar during abdominal entry.

Phase IV - Surgery

The rate of laparoscopic surgery complications after entry range between 0.1-8.3%.[8] Injury can occur as direct injuries to visceral organs, such as vascular injury, urinary tract injury and bowel injury, or as result of herniation through port sites (Richter's hernia), thermal injuries and also anastomotic leaks.[8,11] Major vascular injuries are the rarest[11], while most mortality caused by bowel injury (reported mortality rates up to 3.6%).[12] The major risk factor for bowel injury is adhesions from prior surgery.[11] Adhesiolysis is a challenging procedure and should only be performed by an experienced surgeon. In gynecological surgery, both laparoscopic and laparotomy, adhesions are reported as the major cause of complications.[12]

Specific complications need specific management. Complications to blood vessels likely occurred to inferior epigastric and iliac vessel. Uterine injuries which occur due to instrument manoeuvre can be managed with observation, pressure, sutures or diathermy. Bowel injury may be recognized be observation of faecal contents, faecal odour, diathermy burn or a hematoma visible on the bowel, postoperative abdominal pain, temperature, vomiting or peritonitis. General surgeon involvement is advised in managing these complications. Management may be with peritoneal lavage and broad-spectrum antibiotics, laparoscopy or laparotomy with or without bowel repair, resection or colostomy formation. Injury to inferior epigastric vessel controlled by pressure, the insertion of a catheter balloon tamponade, sutures or diathermy. Injury to iliac vessel need prompt control and repair, laparotomy and vascular surgeon input as generally appropriate.[5]

Injury to the urinary tract can happen to ureter or bladder. Ureteric injury management depends on time of presentation. Cystoscopy and pyelogram are helpful. Stenting and surgical repair with urology input may be required. Bladder injury can be recognised from visual inspection, hematuria, air in the catheter bag, urine leakage from trocar incision or oliguria. Cystogram is helpful in diagnosis. Urology input is advised. Nerve injury (Sciatic, perineal and brachial nerves implicated especially) usually transient and can be managed conservatively. Incisional hernia is uncommon and usually occurs with port sites >5mm and should be managed surgically.[5]

Laparoscopy is a mode of access with its strength and weakness. Regarding its superiority, it should be remembered that in some cases laparotomy is a better approach. Conversion from laparoscopy to laparotomy intra-operative should never be considered as a failure; it only replaces one possible legitimate approach with another. Not performing laparotomy where required can lead to unnecessary complications.[13]

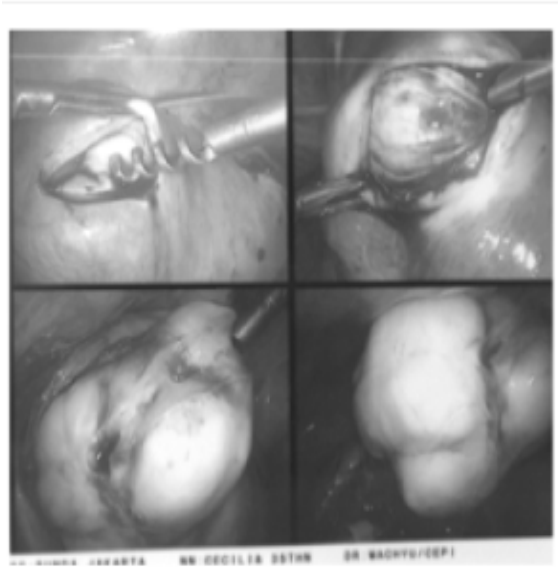

Figure 3. Aplication of myom-screw to big myoma is a crucial step.

Phase V - Postoperative recovery

Complications of surgery sometimes may not present until postoperative period, so that observation and follow up is always necessary. It is estimated that 26-95% of the injuries diagnosed during the postoperative period. Sign of complications can occur as early as 12 hours after surgery, and delayed symptoms likely occur until the first 14 days after surgery.[2,13] Key to minimised complication is by recognising symptoms as early as possible. Unrecognized injury and delayed diagnosis in the most dangerous postoperative complications. Any unusual sign or symptoms in post laparoscopy cases should be evaluated. Possible complications should be followed with full workup and treated immediately. In case a patient needs further surgical evaluation, sooner is better than later. Delays in treatment cause "complications of a complication".[2]

Phase VI - Counselling

Patient education is the key to managing complication in laparoscopic surgery. Early recognition of laparoscopic complications after operation requires patient education.[2] Physician should be aware that the patient does need to be treated not only medically, but also psychologically. Patient and family should be treated as partners and involved in the decision-making process.

Managing Complications

The most important steps in dealing with complications of laparoscopy are prevention and recognisiation of early warning signs of complications. Thus, any complication occurred can be minimised and addressed accordingly. This should be implemented in every phase of operative laparoscopy, ranging from preoperative to postoperative period.

Patient selections are needed to reduce the risk of complications. Predetermined systematic, safe and practised back up plans of action must be in place in the event that a complication occurs. Complications can also be reduced by experience and proper training. Proper training is required especially in dealing with surgical complications. Experienced and well-trained surgeon can face difficulties and complexity of cases better than poorly trained surgeons. There is no one best approach for all surgery. Surgeons should use the recommended technique which most comfortable and make it familiar. Switch to laparotomy should be implemented without any doubt when it is necessary. Good communication between the operator with the patient and family, anasthesiologist and theatre practitioners is crucial in generating a successful surgery. Together with good documentation that portrays a clear description of techniques utilised.

Guidelines and recommendations are necessary and should be developed to create preventive habitude in laparoscopic practice. However, it should be remembered that each centre has its characteristic (facility, society and cases specific) so that these guidelines should always be viewed as advice, instead of rules. Furthermore, it should be able to be adjusted with the peculiarity of each practice.

CONCLUSION

Complications in operative laparoscopy are generally minor and can be handled successfully. Although major complications are infrequent, the incidences of major complications are generally very detrimental to the patient and become a heavy burden for operators. These complications can be prevented by maximising patient selection, predetermined planed of surgery and anaesthesia, competent theatre practitioners (scrub nurse, surgical assistant and theatre runner), appropriate and ongoing training not only on surgical technique but also on mastering the instrument and energy sources available, excellent communication and documentation. These measures should be implemented not only by the operator but also the anesthesiologist and theatre practitioners.

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EDITORIAL

Born too Early, Where are We Now?

Hermanto T Joewono

The World Health Organization[1,2], AAP and ACOG[3] define preterm births as babies born alive before 37 completed weeks of pregnancy and WHO sub-categories based on gestational age: extremely preterm (< 28 weeks), very preterm (28 to 32 weeks) and moderate to late preterm (32 to 37 weeks). Other classification: spontaneous PTBs - due to preterm labour (40 - 50%) or preterm premature rupture of membranes (20 - 30%); and iatrogenic/ indicated: due to maternal or fetal issues that influence the health of the mother or fetus. Every year, 13 -15 million babies are born preterm, over 85% occur in Asia and Africa, and this number is rising. Across 184 countries, the rate of PTB ranges from 5% to 18% of babies born.[1,2] Preterm babies are the leading cause of death among children under five years of age, approximately one-third of all infant deaths in the United States or 1 million deaths every year, meaning every minute 2 babies die of PTBs. Since these deaths occur in infants supposed to live for 70 - 80 years, PTB represents one of the most important, if not the most important, the cause of years - of - life lost.[4] For the most part, these are healthy babies. Preterm babies also account for approximately 45% of children with cerebral palsy, 35% of children with vision impairment, and 25% of children with cognitive or hearing impairment.[4,5] There are many pathways from risk factors to the terminal cascade of events resulting in labour. Preterm labour likely occurs when local uterine factors prematurely stimulate this cascade, or suppressive factors that inhibit the cascade and maintain uterine quiescence are withdrawn prematurely. The four major factors leading to preterm labour are intrauterine infection, decidual haemorrhage, excessive uterine stretch, and maternal or fetal stress. Uteroplacental vascular insufficiency, exaggerated inflammatory response, hormonal factors, cervical insufficiency, and genetic predisposition also play a role.[6] Biological domain show different perspectives and may complement the theories on PTBs.[7-9]

In accordance to WHO ten main recommendations (and 17 additional sub-recommendations)[2] and Berghella optimism, interventions that can be suggested are, non medical: a statement of political will from the decision makers, developing community awareness, movement and national network for prevention PTBs (NNPPB) may be reasonable options (in accordance with Preterm Birth International Collaborative/PREBIC), before pregnancy: strengthening the family planning program to prevent adolescent pregnancy and avoiding too short or too long interpregnancy interval. Smoking and alcohol inhibitions, modify obesity and identify history preterm birth.[10-12] During the first trimester screening by ultrasound, lab markers and improve the scoring system to predict PTBs. During the third trimester: accurate identification of women in true preterm labour allows appropriate of further intervention: tocolysis is to allow antenatal corticosteroids. Neuroprotection by magnesium sulfate administration before 32 weeks of gestation.[13], after birth period: assessment of newborn by umbilical blood gas analysis, resuscitation by NRP method/algorithm, NICU preparation and admission if necessary, surfactant if appropriate and the more affordable method: Kangaroo care[2] and collaborative research between biologist and medicine to reveal pathophysiology of preterm labour and birth which in turn also reveal the physiologic mechanism of labour.

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