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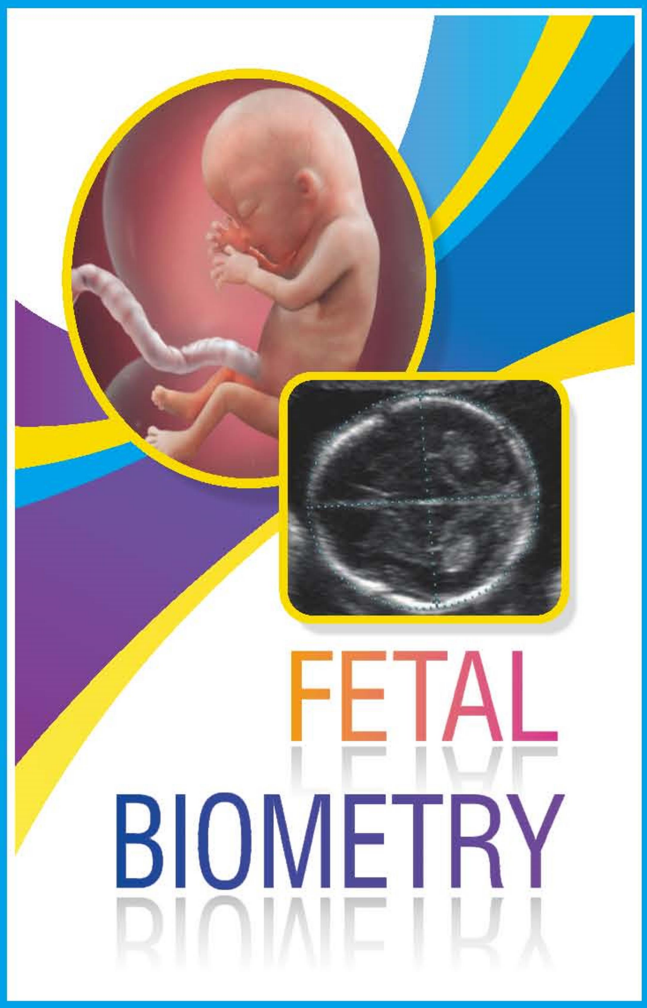

Editorial

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Case Report

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EDITORIAL

RESEARCH ARTICLE

CASE REPORT

Research Article

Factors Affecting the Development of Anxiety in Postmenopausal Women: A Cross-Sectional Study in Coastal Areas

Faktor-Faktor yang Mempengaruhi Terjadinya Kecemasan pada Perempuan Pascamenopause: Suatu Studi Potong Lintang di Daerah Pesisir

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Abstract

Objective: To analyze factors associated with anxiety in post-menopausal women.

Methods: This study was descriptive analytic with cross-sectional approach conducted in 228 postmenopausal women that aged 50-64 years old in coastal areas of Kendari City. Samples were taken by simple random sampling. The technique of collecting data used questionnaires and the Taylor Manifest Anxiety Scale (T-MAS). Data were analyzed using Chi-square test with a significance value $p \leq 0.05$.

Results: The results showed that 188 respondents (82.4%) had anxiety. Its most experienced anxiety was aged 50-54 years old (37.7%), low education (96.0%), as housewife (62.7%), low income (91.2%) and lived with a partner (54.4%). There was correlation between anxiety with age (p=0.016), education level (p = 0.009), income (p = 0.011), and residence status (p = 0.029). There was no correlation between anxiety with occupation (p = 0.351).

Conclusion: There was a correlation between anxiety in post-menopausal women in coastal areas with age, education level, income, and residence status.

[Indones J Obstet Gynecol 2018; 6-3: 133-136]

Keywords: age, anxiety, education level, income, postmenopausal women, residence status

Abstrak

***Tujuan**: Menganalisis faktor-faktor yang berhubungan dengan kecemasan pada perempuan pascamenopause.*

***Metode**: Penelitian ini merupakan penelitian deskriptif analitik dengan pendekatan potong lintang yang dilakukan pada 228 perempuan pascamenopause yang berusia 50-64 tahun yang tinggal di daerah pesisir Kota Kendari. Pengambilan sampel dilakukan secara simpel random sampling. Teknik pengumpulan data menggunakan kuesioner dan mengacu pada Taylor Manifest Anxiety Scale (T-MAS). Analisis data menggunakan uji Chi-square dengan tingkat kemaknaan p≤ 0,05.*

***Hasil**: Penelitian ini mendapatkan bahwa 188 responden (82,4%) mengalami kecemasan. Kecemasan terbanyak dialami oleh mereka yang berusia 50-54 tahun (37,7%), tingkat pendidikan rendah (96,0%), sebagai ibu rumah tangga (62,7%), berpenghasilan rendah (91,2%) dan tinggal bersama pasangannya (54,4%). Terdapat hubungan antara kecemasan dengan usia (p=0,016), tingkat pendidikan (p = 0,009), pendapatan (p = 0,011), dan status tinggal (p = 0,029). Tidak terdapat hubungan antara kecemasan dengan pekerjaan (p = 0,351).*

***Kesimpulan**: Terdapat hubungan antara kecemasan pada perempuan pascamenopause di daerah pesisir dengan usia, tingkat pendidikan, pendapatan, dan status tinggal.*

[Maj Obstet Ginekol Indones 2018; 6-3: 133-136]

***Kata kunci**: kecemasan, pendapatan, perempuan pascamenopause, status tinggal, tingkat pendidikan, usia*

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INTRODUCTION

Menopause is a natural process experienced by every woman. A number of symptoms can be found due to hormonal changes that occur during menopause, including psychiatric, somatovegetative, and urogenital symptoms.[1,2] Low steroid hormone concentrations during menopause are associated with memory impairment, lack of concentration, anxiety, depression, irritability, insomnia, and libido disorders. These symptoms can disrupt the quality of life of menopausal women.[3-5]

Although menopause is a natural process, some women have a lot of worries when entering the menopause. Psychiatric problems often experienced is anxiety. Anxious because of the feelings of old age, unattractive, worrying about sexual desire decreases and feels useless and does not produce anything.[6,7] Restlessness, irritability, depression, anxiety, and sleep disturbances are the most common complaints at the consultation to a doctor.[3]

Mild anxiety and stress vulnerability are common in the premenopausal period; while anxiety, depression, and irritability are more intense during perimenopause. Anxiety disorders tend to be more chronic compared to mood disorders (i.e., depression) in a woman suffering during the menopause.[3] Previous study has shown that 75% of menopausal women feel menopause as a problem or disorder, while the other 25% do not question it.[8] Anxiety in the face of menopause is associated with perceptions about menopause, that is positive perception hence lower level of mother's anxiety in the face of menopause.[9] Anxiety in the face of menopause is associated with level of knowledge, the less knowledge means that the increasing anxiety in the face of menopause.[10] The purpose of this study was to analyze the factors associated with anxiety in postmenopausal women in coastal areas.

METHODS

This study used cross-sectional approach on postmenopausal women in coastal area of Kendari City in December 2016. Samples were postmenopausal women aged 50-64 years old who meet inclusion and exclusion criteria.

Sampling was done by simple random sampling with a sample size of 228. Technique of collecting data used questionnaire and refer to Taylor Manifest Anxiety Scale (T-MAS), which contains physical, psychological, social and sexual aspects in marriage with ordinal measurement scales. Data were analyzed using Chi-square test with significance value $p \leq 0.05$.

RESULTS

The study was conducted on 228 participants. Table 1 demonstrates the demographic characteristic of participants. Most participants were aged 50-54 years old, low education level, as housewife, low income and live with a partner.

Table 1. Demographic Characteristic of the Subjects

Variables	n (%)
Age	
50-54	86 (37.7)
55-59	62 (27.2)
60-64	80 (35.1)
Level of education	
Low	219 (96.1)
High	9 (3.9)
Occupation	
Employees	85 (37.3)
Housewife	143 (62.7)
Income	
Low	208 (91.2)
Sufficient	20 (8.8)
Residence status	
With a partner	124 (54.4)
With family	104 (45.6)

Table 2 shows the distribution of anxiety in postmenopausal women in coastal areas. There were 82.5% postmenopausal women in coastal areas with anxiety.

Table 2. Distribution of Anxiety among the Subjects

Variables	n (%)
Anxiety	188 (82.5)
Nonanxiety	40 (17.5)

Table 3 shows correlation between some variable with anxiety in postmenopausal women in coastal areas. There was a significant correlation between anxiety with age (p=0.016), education level (p = 0.009), income (p = 0.011), and residence status (p = 0.029). There was no significant correlation between anxiety with occupation (p = 0.351).

Table 3. Correlation between some Variable with Anxiety in Postmenopausal Women in Coastal Areas

Variables	Anxiety n (%)	Non Anxiety n (%)	p-value
Age			
50-54	79 (34.6)	7 (3.1)	
55-59	47 (20.6)	15 (6.6)	0.016
60-64	62 (27.2)	18 (7.9)	

Variables	Anxiety n (%)	Non Anxiety n (%)	p-value
Education level			
Low	184 (80.7)	35 (15.3)	0.009
High	4 (1.8)	5 (2.2)	
Occupation			
Employees	67 (29.4)	18 (7.9)	0.351
Housewife	121 (53.1)	22 (9.6)	
Income			
Low	176 (77.2)	32 (14.0)	0.011
Sufficient	12 (5.3)	8 (3.5)	
Residence status			
With a partner	109 (47.8)	15 (6.6)	0.029
With family	79 (34.7)	25 (10.9)	

DISCUSSION

The largest group of postmenopausal women in coastal areas who experienced anxiety were those who aged 50-54 years old. The World Health Organization (WHO) indicates that menopause occurs at an average age of 45-55 years old around the world. Previous research has found that between the ages of 42 to 52 years, women with high levels of anxiety during premenopause continue to experience this during menopause.[3] Premenopausal woman with low anxiety levels can be more susceptible to increased levels of anxiety during and after menopause transition.[11] While other studies have found that postmenopausal women, aged between 45 and 55, have high levels of anxiety compared to premenopausal women between 35 and 45.[12]

This study found that there was correlation between anxiety in postmenopausal women with age. This is in contrast with previous study that found there was no correlation between age with anxiety in premenopausal and perimenopausal women.[8,13]

This study found that most of the anxiety occurred in the low education respondents. Previous study has found that there is a significant correlation between education levels with anxiety in premenopausal women. The higher education, the acceptance of information will be easier, able to think rationally and openly with new ideas. Acceptance of information and knowledge about menopause will support the readiness of facing menopause.[13] Anxiety in the face of menopause is not associated with education level. There is significant influence on knowledge and anxiety of perimenopausal women.[8,10]

The group with the most anxiety is housewives. Previous study found that there was a significant correlation between occupation and anxiety in premenopausal women.[13] There was no significant influence between occupation and anxiety in perimenopausal women.[8] The activities of women can affect the quality of life. Work is something done to earn a living or livelihood. There is an element of need in work. Anxiety in post-menopausal women may come from both of the work itself and the process leading to menopause.[8,13]

The study found that there was relationship between income with anxiety in postmenopausal women. The anxiety in postmenopausal woman will decrease if she has enough income. The ability to daily meet needs can affect quality of life. The ability to daily meet needs will reduce the complaints of menopausal women, who feel old and cannot do anything. This was not agreed with the previous study that there was no significant influence between economic conditions and anxiety in perimenopausal women.[8] Depression in postmenopausal women can be associated with socioeconomic statuses such as education and income.[6]

The study found that there was correlation between the residence status with anxiety in

postmenopausal women. There was a significant correlation between family social support with anxiety in the face of menopause.[13] Family support, both material and non-material assistance, causes the individual to feel cared for, valued, loved and accepted in the family. The older, the more changes that can make a woman feel anxious. Anxious because of the feelings of old age, unattractive, worrying about sexual desire decreases and feels useless and does not produce anything.[6,7] These conditions need a separate concern so that required understanding of the husband and children as members of the immediate family.[8]

Husband's support greatly affects women in the face of menopause. In this study, it was found that participants with the most anxiety were those living with a partner. Women will feel depressed because they lose her role as a woman in her old age. At that time a woman needs positive support such as helping with household chores. Good communication must be maintained in order to understand each other and find the best solution if it becomes a problem.

CONCLUSION

There is correlation between anxiety in postmenopausal women in coastal areas with age, education level, income and residence status. There is no correlation between anxiety in postmenopausal women in coastal areas with occupation.

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EDITORIAL

Fetal Biometry is a Prerequisite Part of Modern Antenatal Care

Azen Salim

Accurate gestational-age estimation, preferably by ultrasound measurement of fetal crown-rump length (CRL) before 14 weeks' gestation, is an important component of high-quality antenatal care.[1-3] Gestational age determination during the first trimester has a minimal deviation.

The most precise way to estimate gestational age is by measuring CRL between 8^{+0} and 14^{+0} weeks gestation. It is associated with a 95% prediction interval of 2.7 days.[4,5] The impact of this finding is very significant in deciding whether the gestation is preterm or term. Unnecessary complications which occur in preterm babies could be avoided, and intensive care observation of the newborn will be minimised. Accurate dating of gestational age also supports us for the preparation of a fetus whenever has to be delivered due to unexpected condition e.g. premature preterm rupture of the amniotic membrane.

In case of fetal death, long bone measurements will inform us when the fetus died. It is crucial, especially in monochorionic diamniotic twins pregnancy. Twin to twin transfusion syndrome with one co-twin death has a high risk of complication to the living co-twin. It depends on when such a tragedy occurs.[6] As we know, serious complications might influence the living co-twin.

Monitoring fetal growth and development longitudinally at second and third trimester as a follow up antenatal care is an essential integrated examination.[7,8] Following the growth curve, any deviation will be identified. The deviation might be smaller or larger the normal curve. Tracing the growth curve of fetuses gives us a valuable information about its well-being. Any jeopardy of the fetuses can be detected, any interventions if needed can be planned thoroughly.[9]

The measurement of each organ of the fetus can be plotted to its gestational age normal distribution curve or compared to each gestational age Z score. Deviation from its normal distribution curve or Z score may be identified, e.g. short limb, microcephaly, ventriculomegaly.[10] By collecting information from such fetuses, a differential diagnosis could be made, e.g. skeletal dysplasia, short limb syndrome. Measurements information will guide us to the specific diagnosis.

Thus, uniform and standardised measurement and protocol have to be created to achieve optimal results. Training and operator standardisation performance would be a success if right centre and trainer were available. Training and certification programs to achieve a favourable result performing fetal biometry is a prerequisite.[11,12]

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Research Article

Malondialdehyde Levels in Preeclampsia before and after Delivery

Kadar Malondialdehid pada Penderita Preeklamsia Berat sebelum dan sesudah Persalinan

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Abstract

Objective: Determine differences plasma levels MDA in preeclampsia before and 2 hours after delivery.

Methods: This was an analytic cross-sectional study. Subject consists of 23 pregnancies with preeclampsia, where 23 blood samples taken before delivery and 23 were taken 2 hours after delivery. This study was conducted from August 2016 until December 2016 at Department of Obstetrics and Gynecology Faculty of Medicine Universitas Sam Ratulangi / Prof. Dr. R. D. Kandou Hospital Manado and satellite hospital. Samples were taken from plasma and analysed using HPLC method at Prodia clinical laboratory.

Results: In patients with severe preeclampsia before delivery we found average value (1.4796 ± 0.40819 nmol/ml), minimum value (1.03 nmol/ml) and maximal value (2.77 nmol/ml) and 2 hours after delivery with average value (1.2470 ± 0.34324 nmol/ml), minimum value (0.91 nmol/ml), and maximum value (2.47 nmol/ml). by using Wilcoxon test, we found there were significant differences in plasma levels of MDA (p = 0.000).

Conclusion: This significant difference suggests that decreased plasma levels of MDA 2 hours after delivery and gives the sense that there is a relationship between oxidative stress of cells with severe preeclampsia before and shortly after delivery, that MDA is an indicator of oxidative stress.

[Indones J Obstet Gynecol 2018; 6-3: 143-148]

Keywords: malondialdehyde, oxidative stress, peroxidation lipid, preeclampsia

Abstrak

***Tujuan**: Menentukan perbedaan kadar plasma MDA pada preeklamsia sebelum dan 2 jam setelah persalinan.*

***Metode**: Penelitian ini merupakan penelitian potong lintang analitik. Subjek terdiri atas 23 kehamilan dengan preeklamsia, di mana 23 sampel darah diambil sebelum persalinan dan 23 sampel diambil 2 jam setelah persalinan. Penelitian ini dilakukan sejak Agustus 2016 sampai Desember 2016 di Bagian Obstetri dan Ginekologi Fakultas Kedokteran Universitas Sam Ratulangi / RSUP. Prof. Dr. R. D. Kandou Manado dan rumah sakit satelit. Sampel yang diambil dari plasma dan dianalisis menggunakan metode HPLC di laboratorium klinis Prodia.*

***Hasil**: Pada penderita preeklamsia berat sebelum persalinan kami menemukan rata-rata nilai (1,4796 ± 0,40819 nmol/ml), nilai minimum (1,03 nmol/ml) dan nilai maksimal (2,77 nmol/ml) dan 2 jam setelah persalinan dengan rata-rata nilai (1,2470 ± 0,34324 nmol/ml), nilai minimum (0,91 nmol/ml), dan nilai maksimum (2,47 nmol/ml). Dengan menggunakan uji non parametrik Wilcoxon, kami menemukan adanya perbedaan bermakna kadar plasma MDA sebelum dan 2 jam sesudah persalinan (p = 0,000).*

***Kesimpulan**: Perbedaan bermakna ini menunjukkan bahwa penurunan kadar plasma dari MDA 2 jam setelah melahirkan dan memberikan arti bahwa ada hubungan antara stres oksidatif sel dengan preeklamsia berat sebelum dan sesaat setelah persalinan, MDA merupakan indikator stres oksidatif.*

[Maj Obstet Ginekol Indones 2018; 6-3: 143-148]

***Kata kunci**: lipid peroksidase, malondialdehid, preeklamsia, stres oksidatif*

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INTRODUCTION

Preeclampsia is a disease characterized by increased blood pressure, proteinuria and oedema that occurs at age 20 weeks to 48 hours postpartum.[1-3] Preeclampsia is associated with the incidence and maternal and perinatal mortality rate both in the world and in Indonesia. Worldwide preeclampsia causes 50000-76000 maternal deaths and 900,000 causes perinatal deaths each year. According to WHO (World Health Organization). The incidence of preeclampsia in pregnancy is ± 5-10%, and became one of the three main causes of maternal mortality after bleeding and infection.[2,3] The incidence in Indonesia is 3.4 to 8.5% of all pregnancies and is still the number two cause of maternal and perinatal mortality rate highest (24%) after bleeding.[1,3]

To this date, even the theory of the etiology and pathogenesis of preeclampsia is still yet to be verified; thereby, preeclampsia is still described as

a "disease of theories".[4] One theory of the etiology of preeclampsia is currently an imbalance between the production of free radicals and antioxidant defense system causes oxidative stress (Hubel et al., 2006).[5] In conditions of oxidative stress, there will be increasing product of lipid peroxidation,[6] which is strongly suspected of instrumental cause endothelial function and the onset of clinical symptoms of preeclampsia.[6-8] Increased lipid peroxidation can be measured with various measurement markers lipid peroxidation in the blood, one using malondialdehyde (MDA),[9] which has been recognised as a clinical marker of lipid peroxidation.[10-12]

Currently, MDA is a marker of oxidative stress and lipid peroxidation in vivo the nicest and most stable, MDA have been found in almost all biological fluids, but the blood (plasma or serum) and urine is a sample of the most commonly used because it is most readily available, least invasive, and gives the same result accuracy and precision of the indices of oxidative stress (Nielson et al., 1997).[13] MDA is a marker of lipid peroxidation measurement of the most widely studied. MDA formed as a compound which is a secondary product or spoilage end of lipid peroxides in the body. Although various studies on the association of lipid peroxidation as a causative factor of preeclampsia has done a lot lately, but there is still disagreement about the increase in lipid peroxidation itself. Most studies of lipid peroxidation in preeclampsia, getting MDA levels were significantly higher in patients with preeclampsia and decreased after delivery. Several studies related, examines the MDA levels in patients with severe preeclampsia before and after delivery, and showed that MDA levels increased up to 24 hours after delivery and decreased significantly 48 hours after the delivery, (Kobe, et al, 2002).[14] (Kressig, et al., 2008) gain of 58 patients of which 20 patients and 38 controls weight preeclampsia found MDA levels at 24 hours after delivery, higher than the control group in patients preeclampsia.[15]

Measurement of markers of oxidative stress and lipid peroxidation is still an interesting study because it deals with prediction, risk, aetiology, and the intervention of preeclampsia. Research to see the differences in levels of MDA as a marker of lipid peroxidation in preeclampsia before and shortly after delivery is still rare in Indonesia, and has never worked at the Department of Obstetrics and Gynecology Faculty of Medicine Universitas Sam Ratulangi Prof. Dr. R. D. Kandou Hospital Manado, although the MDA until now has been recognized as a good clinical marker of lipid peroxidation in vivo.

OBJECTIVE

This study was conducted to determine the plasma levels of MDA in patients with preeclampsia before and shortly after delivery.

METHODS

This study was an analytic cross-sectional study with Wilcoxon test order to compare the plasma levels of MDA in preeclampsia before and 2 hours after delivery. This study was conducted and evaluated since August 2016 to December 2016 at Department of Obstetrics and Gynecology Faculty of Medicine Universitas Sam Ratulangi / Prof. Dr. R. D. Kandou Hospital Manado and satellite hospital in Manado to research subjects who meet the inclusion and exclusion criteria. Inclusion criteria were women with severe preeclampsia who will give birth, intra uterine fetal alive, willing to participate in the study by completing the informed consent form. Exclusion criteria were pregnant women with chronic hypertension, diabetes mellitus and refused to join the study. The subject of this study consisted of 23 pregnancy woman with preeclampsia. After anamnesis, physical examination and has signed informed consent, samples were taken from serum as much as 5 cc before and 2 hours after delivery, and put in a sterile sample container, centrifuged and stored in -20°C and then processed in Prodia Clinical Laboratory with HPLC (High-Performance Liquid Chromatography) analytic. This study also has been approved by the Integrated Health Research Unit of Prof. Dr. R. D. Kandou Hospital Manado. Data were analysed with SPSS version 22.0.

RESULTS

Table 1, shows that majority subject in woman with preeclampsia are most age ≥ 35 years old (12 patients, 52.18%), cases of gravidity 1 (12 patients, 52.18%), nullygravidity (12 patients, 52.18%), high school education (21 patients, 60.87%) and most jobs are housewife for (11 patients, 47.82%).

Table 1. Research Subject Characteristics

Characteristics	Severe Preeclampsia	
	n (23)	%
Age		
< 35 years	11	47.82
≥ 35 years	12	52.18
Gravidity		
1	12	52.18
2	4	17.39
3	3	13.04
4	1	4.35
5	3	13.04
Parity		
Nulligravida (0)	12	52.18
Primigravidity (1)	5	21.73
Multigravidity (2-4)	6	26.09
Abortion		
0	21	91.30
≥ 1x	2	8.70
Education		
Bachelor	4	17.40
High School	14	60.87
Junior High school	5	21.73
Occupation		
Government Employee	2	8.70
Student	3	13.04
House wife	11	47.82
Farmer	1	4.35
Privat Employee	6	26.09

Significant results were obtained between the systolic blood pressure in patients with severe preeclampsia before and 2 hours after delivery, with p = 0.000; and diastolic blood pressure in patients with severe preeclampsia before and 2 hours after delivery, with p = 0.008.

Table 2. Distribution of Variables Systolic and Diastolic Blood Pressure in Patients with Severe Preeclampsia before and 2 Hours after Delivery

Variable	Severe Preeclampsia		
	before delivery (n = 23)	two hours after delivery (n = 23)	p
Sistol (mmHg)	170.43 ± 8.779	155.22 ± 9.472	
Mean ± SD	160	0.000	
Minimum	190	140	
Maximum	105.22 ± 5.931	170	
Diastol (mmHg)	100		
Mean ± SD	100		0.008
Minimum	120	102.17 ± 4.217	
Maximum	110		

Table 3. Distribution of Variable Plasma Levels of MDA in Patients with Severe Preeclampsia before and 2 hours after Delivery

Variable	Severe Preeclampsia		
	before delivery (n = 23)	two hours after delivery (n = 23)	p
MDA (nmol/ml)			
Mean ± SD	1.4796 ± 0.40819		
Minimum	1.03 ± 0.91	1.2470 ± 0.34324	0.000
Maximum	2.77	2.47	

Significant results were obtained. Where the value of p = 0.000 for plasma levels of MDA in patients with severe preeclampsia before and 2 hours after delivery.

DISCUSSION

In this study based on the characteristics of the age (Table 1) distribution of the subjects obtained majority were age ≥ 35 years (12 patients, 52.18%). This is consistent with the literature that says that one of the risk factors of severe preeclampsia is age. Age over 35 years is vulnerable age for a pregnancy, because the physiological function of the organs of the body including the reproductive function begins to decline, in addition to the decrease in cardiac output induced contractions of the myocardium, coupled with other degenerative diseases can be debilitating condition of the mother, which can impair blood circulation of the mother to fetus.[2-4] These are the things that show that in women aged over 35 years is essentially a decline in physical conditions coupled with the burden of pregnancy can aggravate the risk factors of pathological conditions in pregnancy, including severe preeclampsia.[11]

The characteristics of parity, gravidity, and abortion (Table 1) is the most severe incident preeclampsia on nullipara (12 patients, 52.18%), and gravidity 1 (12 patients, 52.18%). This is consistent with the literature that explains that primigravid is one other risk factor for the occurrence of preeclampsia occurs preeclampsia.[4,15] In barriers trophoblast invasion into the decidua. As known trophoblast invasion is very important that decidua tissue becomes soft and loose, making it easier dilatation spiral arteries, if this does not happen, then the uteroplacental blood flow decreases, and there hypoxic and ischemic placenta.[6] During pregnancy, the placenta becomes the main source of oxidant and anti-oxidant synthesis endogen.[9,16] Decreased levels of antioxidants in the placenta may be one trigger of abortion, intrauterine growth and preeclampsia.[6,9,10] Data obtained from this study, (21 patients, 91.30%) samples not experiencing abortion.

Based on education and occupation characteristics (Table 1), most cases are high school (14 patients, 60.87%) and house wife (11 patients, 47.82%). It is different with some literature that explains that one of the causes of the high rate of maternal mortality caused by complications during pregnancy, childbirth and the puerperium, including severe preeclampsia. Influenced by education and occupations where there is a lack of knowledge about the whys and control of important complication before and after delivery in preeclampsia.[3,4]

In (Table 2), we found in the systolic blood pressure in patients with severe preeclampsia before delivery (170.43 ± 8.779 mmHg) and 2 hours after delivery (155.22 ± 9.472 mmHg), with p = 0.000; and diastolic blood pressure in patients with severe preeclampsia before delivery (105.22 ± 5.931 mmHg) and 2 hours after delivery (102.17 ± 4.217 mmHg), with p = 0.008. which means there were significant differences in the systolic and diastolic blood pressure before and 2 hours after delivery in severe preeclampsia. Increased systolic and diastolic blood pressure and correction proteinuria levels are an important consideration to determine prognosis in patients with preeclampsia/eclampsia.[1,2,17] (Llurba et al., 2004) suggests that 78 patients with severe preeclampsia as much as 33.4% showed an increase in blood pressure, mentions one theory that placental trigger preeclampsia, preeclampsia which will only happen if there is a placenta and improvement in the state began after the release placenta.[18] These results are supported by previous studies carried out by (Lumban Raja et al., 2013) which suggests that there was an increase systolic blood pressure at a time before and a decrease in systolic blood pressure after 24 hours of labor from 174.91 + 2.619 mmHg become 150.09 + 2.994 mmHg (p <0.001). Diastolic blood pressure also showed an increase before delivery and significantly decrease 24 hours after delivery from 107.27 mmHg become 93.36 mmHg (p <0.001). There are significant differences in systolic and diastolic blood pressure in preeclampsia before and after delivery.[19]

In the process of delivery, oxygenation comes from mother to fetus undergoing a process of oscillation, which causes unstable respiratory of the mother.[16] This instability caused by a weak period and shallow breathing during labor, where the conditions are like this will decrease the partial pressure CO2 in the arteries, when the uterus contracts, will cause changes in blood pressure in the blood vessels of the uterus, it is compounded by the response of pregnant women to pain and stress during birth, this response will lead to a state of

tissue hypoxia and ischemic tissue resulting in increased stress oxidative and produce free radicals that will influence the delivery process.[12] The lipid peroxide as oxidants or free radicals are highly toxic, will circulate throughout the body in the bloodstream and will damage the endothelial cell membrane, causing dysfunction endotel.[5] Been estimated previously that the release of certain factors from the placenta and increased resistance utero placental response to ischemia results in endothelial dysfunction in the maternal circulation (KM Sowinski, 2000).[20] Lipid peroxidation also induced in the placenta during pregnancy. The lipid peroxide generated from the trophoblast and villi chorealis be secreted into the mother's blood circulation, resulting in increased concentration in the mother's blood circulation which will cause an increase in plasma levels of MDA.[8,9] Previous studies provide data, plasma levels of MDA will decrease after delivery, (Nakai, et al, 2000) suggests these results show that the greatest possible placenta is a source of increased lipid peroxidation in pregnant women with preeclampsia, with the release of the placenta after delivery will provide an overview of the decrease in the levels of lipid peroxidation on the first day to the third day after delivery, there is no research has been conducted to assess the presence of lipid peroxide levels decrease shortly after delivery.[12]

In this study, we examined plasma levels of MDA in patients with severe preeclampsia before and 2 hours after delivery (Table 3), in patients with severe preeclampsia before delivery we found average value (1.4796 ± 0.40819 nmol/ml), minimum value (1.03 nmol/ml) and maximal value (2.77nmol/ml) and 2 hours after delivery with average value (1.2470 ± 0.34324 nmol/ml), minimum value (0.91 nmol/ml), and maximum value (2.47 nmol/ml) by using the non-parametric Wilcoxon test, we found there were significant differences in plasma levels of MDA (p = 0.000). This significant difference suggests that decreased plasma levels of 2 hours after delivery and gives the sense that there is a relationship between oxidative stress of cells with severe preeclampsia before and shortly after delivery.

This study has a relationship with some of the research that has been done before, where the research done by (Santoso et al, 2012) to get the plasma levels of MDA in patients with severe preeclampsia before delivery seem higher, and decreased after the 8th day after delivery with average levels of plasma MDA in pregnant women with severe preeclampsia amounted to 0.883 mol/ml, and amounted to 0.284 in women of severe preeclampsia 8th day after the delivery.[21] (Kressig et al., 2008) gain of 58 patients of which 20 patients severe preeclampsia and 38 controls found MDA levels at 24 hours after delivery, higher than the control group in severe preeclampsia.[15] (Kobe et al., 2002) suggests an increase in MDA levels were significantly non enzymatic accompanied by a decrease in antioxidants, such as Vitamin E, Vitamin C, and Vitamin-A in pregnant women who develop severe preeclampsia.[14] It may consider granting antioxidants in patients with severe preeclampsia, according to research conducted by (Roberts JM et al., 2010) that the provision of anti-oxidants such as vitamins A, B6, B12, C, E, FE, and folic acid, can lower blood pressure can reduce the risk of preeclampsia.[22]

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Research Article

Secretory Leukocyte Protease Inhibitor in Preterm Labor and Pregnancy

Secretory Leukocyte Protease Inhibitor pada Persalinan dan Kehamilan Prematur

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Abstract

Objective: To investigate the levels of secretory leukocyte protease inhibitor (SLPI) in women with preterm labor and pregnancy.

Methods: SLPI level examination conducted to 32 samples of pregnant women who meet the inclusion and exclusion criteria, consists of 16 preterm labor and 16 preterm pregnancy. Sample analysis carried out in Prodia Laboratory Jakarta. SLPI level examination used ELISA method. The obtained data processed by SPSS software version 20.0 and discussed with existing literature theory.

Results: Mean plasma SLPI level in patients with preterm labor is 30.319 ng/ml and median: 29.950 ng/ml with p value: 0.652, while the mean on preterm pregnancy is 45.975 ng/ml and median: 41.600 ng/ml with p value: 0.005.

Conclusion: There are significant differences of SLPI level between preterm labor and preterm pregnancy.

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Keywords: preterm labor, preterm pregnancy, SLPI

Abstrak

***Tujuan**: Untuk mengetahui kadar secretory leukocyte protease inhibitor (SLPI) pada persalinan dan kehamilan prematur.*

***Metode**: Dilakukan pemeriksaan kadar SLPI pada 32 sampel ibu hamil yang memenuhi kriteria inklusi dan eksklusi, terdiri dari 16 persalinan prematur dan 16 kehamilan prematur. Analisis sampel dilakukan di Laboratorium Prodia Jakarta. Pemeriksaan kadar SLPI menggunakan metode ELISA. Data yang diperoleh diolah dengan menggunakan perangkat lunak SPSS versi 20.0 dan dilakukan pembahasan menggunakan teori kepustakaan yang ada.*

***Hasil**: Rerata kadar SLPI plasma pada pasien persalinan prematur yaitu 30.319 ng/ml dan median : 29.950 ng/ml dengan p value: 0.652, sedangkan rerata pada kehamilan prematur yaitu : 45.975 ng/ml dan median : 41.600 ng/ml dengan p value: 0,005.*

***Kesimpulan**: Terdapat perbedaan kadar SLPI yang signifikan antara persalinan prematur dengan kehamilan prematur.*

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***Kata kunci**: kehamilan prematur, persalinan prematur, SLPI*

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INTRODUCTION

The main causes of infant morbidity and mortality are obstetrics and perinatology problem. It is close to preterm birth. 70% of neonatal morbidity and mortality are caused by prematurity. More than 65% of neonatal deaths occur in infants born preterm, with a mortality rate of 19,000 per year.[1,2] American College of Obstetrician and Gynecologist (ACOG) stated that the definition of preterm labor is labor that occurs before 37 weeks gestation or less than 259 days from the first day of the last menstrual period (LMP). Meanwhile, according to the World Health Organization (WHO), preterm birth is defined as birth that occurs before 37 weeks gestation, with intact fetal membrane.[3] In outline, preterm labor are classified into three major groups, there are: 25% of preterm labor occurs with indication of unstable condition of mother or fetal status. Preterm rupture of membranes cause 30% of preterm labor, whereas preterm labor that occurs spontaneously without prior rupture of membranes 40-50%, with half the cause is ascending infection on genital tract that causes intrauterine infection.[2,4]

Some literature states that infection and inflammation lead to more than 50% of preterm pregnancies.[5] Significant increase of inflammatory mediators will trigger a substance released as regulator of inflammatory response. Protease inhibitors act as inflammatory response regulator as well as inhibitors to the elastase products.[6] Secretory leukocyte protease inhibitor (SLPI) is the most potent protease inhibitor in inhibiting the

inflammatory process against Neutrophil Elastase (NE) that can cause the cervix to soften. Secretory leukocyte protease inhibitor excreted during pregnancy with the highest concentration found on the cervical mucus and serves as the main barrier to infection in the genital tract during pregnancy. SLPI secreted dominantly by the decidua, especially the parietal decidua and korio decidua. Lower levels secreted by the amnion and placenta.[7,8] Increasing concentrations of SLPI would form inflammatory interactions in maintaining a pregnancy and then limit it during delivery. Anti-microbiological effects caused by SLPI would protect the uterus during implantation and prevent infection during pregnancy.[3,5,7] Based on the function of SLPI above, research conducted with the aim to determine the concentration differences of SLPI in preterm labor and preterm pregnancy with intact membranes, and determine SLPI cutoff point to predict the preterm labor incidence.

METHOD

In this research, the design used was cross-sectional by comparing concentrations of Secretory Leukocyte Protease Inhibitor (SLPI) on research subjects serum, among preterm labor without preterm rupture of membranes and preterm pregnancy. This research conducted in Section / SMF Obstetrics and Gynecology Faculty of Medicine, Universitas Sam Ratulangi, Prof. Dr. R.D. Kandou Central General Hospital Manado and network hospitals Department of Obstetrics and Gynecology Faculty of Medicine Universitas Sam Ratulangi, began in September 2016 until the samples quantity fulfilled. The samples were pregnant women who experience preterm labor in the delivery room of RSUP Prof. Dr. R. D. Kandou Manado and network hospital that met the inclusion criteria. The control group was 20-36 weeks pregnant women who checkups in Obstetric Polyclinic RSUP Prof Dr. R.D. Kandou Manado and network hospital. Sample collected by consecutive sampling where every subject which met the research criteria included in the research up to a certain time until the number of samples fulfilled. The inclusion criteria were 20-36 weeks pregnant women based on the first day of the last menstrual period, active phase labor stage 1, live singleton pregnancies lies the head, intact membranes, no complications or obstetric complications, and patients willing to participate in research and signed an informed consent sheet. While exclusion criteria were pregnant women with preterm labor history in previous pregnancy, has systemic infection on the subject, there are congenital malformations in the fetus, and refused to follow the research.

The number of samples using single mean formula with reference to the SLPI concentration in women with intact membranes preterm labor i.e. 698 μg/l (ranges: 320-1054 μg/l; standard deviations assumption 250 μg/l).

$$n = \left(\frac{Z_\alpha^2 \sigma}{d^2} \right) = 15.4 = 16$$

n = number of samples = 15.4 = 16

Z_α = 1.96

σ = standard deviation = 250 μg/l

d = desired accuracy = 125 μg/l

So number of samples = 32 (each of the 16 women with intact membranes preterm labor 16 women with intact membranes term labor). The statistical test is t-test (independent samples; 2 mean difference), or equivalent non-parametric tests, i.e. the Mann-Whitney test. The cut-off point, sensitivity, and specificity will be determined using analysis of Receiver Operating Curve (ROC).

RESULT

A total 32 subjects consisting of 16 pregnant women who experienced preterm labor and 16 pregnant women with preterm pregnancy were recruited. Characteristics of the subjects are presented in Table 1.

Table 1. Characteristics Subject on Both Group Research

Characteristic	Preterm Labor		Preterm Pregnancy	
	n	%	n	%
Age				
≤ 24	7	43.75	5	31.25
25-34	7	43.75	5	31.25
>34	2	12.5	6	37.5
Parity				
0	3	18.75	5	31.25
1	5	31.25	4	25

2	5	31.25	4	25
3	1	6.25	1	6.25
4	2	12.5	2	12.5
Mass Body Index				
< 19.8	2	12.5	-	0
19.9 - 26	8	50	7	43.75
26.01 - 29.99	5	31.25	6	37.5
> 30	1	6.25	3	18.75
Antenatal Care				
< three times	7	43.75	6	37.5
≥ four times	9	56.25	10	62.5
Left Upper Arm Circumference				
≤ 23.5	2	12.5	2	12.5
> 23.5	14	87.5	14	87.5

From the above data obtained maternal age in the group of preterm labor <24 years as many as seven people (43.75%) and ages 25-34 years as many as seven people (43.75%). Whereas in the group of preterm pregnancy obtained age group <24 years as many as five people (31.25%), and ages 25-34 years as many as five people (31.25%). The highest Parity in the group preterm labor is parity 1 and 2 i.e. 5 people for each with a percentage 31.25%. While groups of preterm pregnancy who present in the obstetric polyclinic the majority were parity 0 as many as five people (31.25%). The body mass index in the group of preterm labor divided into four groups. The highest number was found in the body mass index between 19.9 to 26 as many as eight peoples (50%). Whereas in the group of preterm pregnancy that went to the obstetric polyclinic have highest body mass index from 19.9 to 26 as many as seven people (43.75%). Antenatal care visit in preterm labor group the most are ≥ four times as many as nine people (56.25%). Whereas in preterm pregnancy group most patients have antenatal care regularly, i.e., ten people (62.5%) do antenatal care ≥ four times. Left upper arm circumference measurements in preterm labor group most obtained > 23.5 cm as many as 14 people (87.5%). Whereas in the group of preterm pregnancy who present at the polyclinic obtained measurements of left upper arm circumference > 23.5 cm as many as 14 people (87.5%).

Table 2. Descriptive SLPI Distribution Level Data

Group	Preterm Labor	Preterm Pregnancy
Mean	45.975	30.319
Median	41.600	29.950
Interval for mean	41.198 - 50.752	27.794 - 32.844
Standard Deviation	8.9641	4.7389
Range	25.3	16.5

Table 3. SLPI Variable Normality Test (Shapiro Wilk Test)

Group	p-value
Preterm Labor	0.005
Preterm Pregnancy	0.652

From Table 2 obtained SLPI concentration ratio between preterm labor and preterm pregnancy. In preterm labor group, obtained mean value for SLPI concentration is 30.319 with standard deviation 4.7389, median 29.950, range 16.5 and the ranges obtained 27.794 - 32.844. In preterm pregnancy group obtained mean value for SLPI concentration 45.975 standard deviations 8.9641, median 41.600, range 25.3 and the range obtained between 41.198 - 50.752.

From the data Shapiro-Wilk normality test seen levels of secretory leukocyte protease inhibitor (SLPI) in preterm pregnancy group is not normally distributed (one of them p <0.05), so Mann-Whitney test will be conducted as non-parametric test.

Mann-Whitney non-parametric test showed that p = 0.000 which means that there are significant differences between SLPI level of preterm pregnancy and preterm labor. Conclusion SLPI levels and preterm labor correlate.

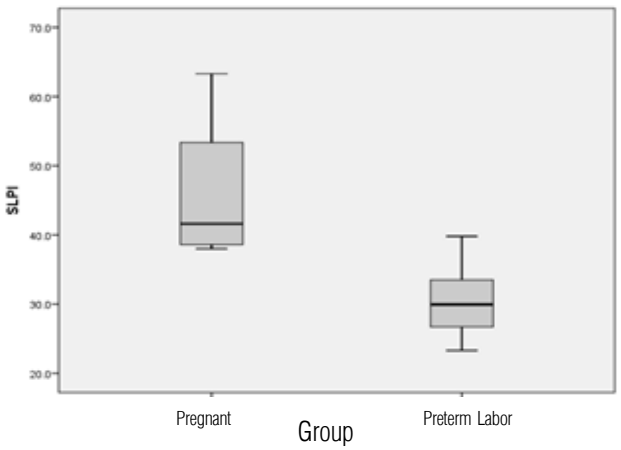

Figure 1. Graphs the Level of SLPI in Preterm Labor and Preterm Pregnancy

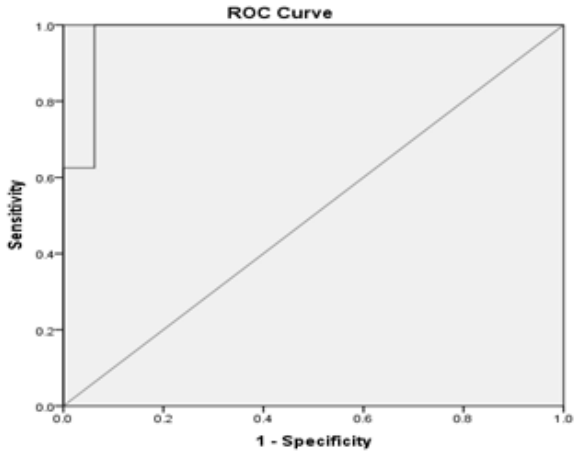

Figure 2. ROC (receiver operating characteristic) Cut off Point of SLPI.

From those data ROC (Receiver Operating Characteristic) curve made to determine the cut-off point of SLPI concentration, i.e., 37.9 ng/ml with sensitivity 100% and specificity 93.7%.

DISCUSSION

Some research says that many demographic factors that imply the risk of preterm labor threat. In term of epidemiology, there are several risk factors for preterm labor, which are[9-11]:

Idiopathic, Iatrogenic, such as aggravate circumstances to mother or fetus, Infections, both extra and intrauterine, multiple pregnancies, maternal factors: stress in mothers, cervical incompetence, disease in mothers, reproductive history: previous prematurity history, ruptured membranes history, abortion history, primipara, too close spaced pregnancies, low maternal weight gain during pregnancy, parity, sociodemographic: low socioeconomic, too young or too old age, race, marital status, unfavorable environmental factors, too heavy daily activities.

A prematurity history in the elderly will be a potentially important factor for the prematurity back in the offspring. Another meta-analysis also noted that prematurity history or intrauterine infection would cause carrier to cytokine inflammatory mediators, and its correlation with genotypic researched continuously.[4,12]

In this research, from the characteristic table showed that the incidence of preterm labor was highest at age less than 24 years and the age of 25-34 years. Too young or too old maternal age also a risk factor for preterm labor. Research in Sweden mentioned that the maternal age during pregnancy between 13-17 years of age increases the risk of preterm labor twice control age of 20-24 years. While on maternal age over 35 years increases the risk of preterm labor twice compared with control age of 20-30 years.[5] According to creasy, maternal age relationship to preterm labor is the younger the maternal age, the greater the risk preterm labor. Maternal age less than 20 years and maternal age over 40 years has a risk for preterm labor. Maternal age less than 18 years old have greater risk score than 20 years. The preterm labor incidence is much found at younger age due to such factors: socioeconomic, education, and lifestyle habits.[9,13]

Based on some research, preterm labor is more common in primipara. And some research also indicates the preterm labor risk increased in pregnancies of more than four.[6,7] In this research obtained highest preterm labor occurred in women with parity 1 and 2.[14] In the table of research subject characteristics, based on the body mass index obtained the highest number of preterm labor occurrences is 19.9 to 26 for eight patients. Cohen et al. mentioned significant relationship between low maternal body weight or low BMI during pregnancy with preterm labor incidence. Low maternal body weight or low BMI during pregnancy as well as poor nutrition also risk factor for preterm labor.[15,16] Some anthropometric examination can be used to determine the nutritional status of pregnant mother, one of which is by measuring Left Upper Arm Circumference (LUAC). Through this examination can predict mother experiencing Chronic Energy Deficiency (CED) if LUAC < 23.5 cm. Lack of energy has the risk to deliver a baby with low birth weight and increase the risk to preterm labor.[12,17] From the MUAC measurement characteristic table in this research, in preterm labor group obtained only two people with LILA measurement < 23.5 cm.

SLPI Concentration in Preterm Labor and Preterm Pregnancy

SLPI serves as a potent inhibitor and immunity in an inflammatory process, by reducing the inflammatory genes expression and reduce cells inflammatory accumulation, as well as contributing to the immunity balance. In broad outline, SLPI has anti-inflammatory activity, anti-virus, and anti-

bacterial.[18,19] SLPI concentration increased from the second trimester to the third trimester, although the concentration changes and activities at the labor onset has not been widely researched.[20-22] Denison et al. mentioned that SLPI in the amniotic fluid concentration continued to increase since the second trimester until term pregnancy, and at the labor onset. In the second trimester obtained SLPI concentration 24 ± three ng/ml, whereas the term pregnancy SLPI concentration is 751 ± 53 ng/ml. The highest concentration of SLPI obtained in term labor onset i.e. 3929 ± 107 ng/ml.[20]

Zhang et al., In their research mentioned that SLPI concentration in the amniotic fluid third trimester of pregnancy (802 ± 138 ng/ml) higher than SLPI concentration in the second trimester of pregnancy (106 ± 15 ng/ml) with the significance value $p < 0.0001$. Helmig et al., mentioned that in preterm pregnancy with preceded rupture membrane, has an SLPI concentration average value in amniotic fluid lower that intact membrane, i.e., 579 μg/l in rupture membrane pregnancy and 1038 μg/l in intact membrane pregnancy.[23] From some of conducted research, it can be concluded that the increased SLPI with age pregnancy serves to maintain the pregnancy of inflammatory process that can cause preterm labor. Several studies of the low concentration of SLPI in the amniotic fluid in preterm rupture case due to lower anti-protease activity, where in the protease has the ability in membrane degradation that can soften and ripen the cervix. SLPI concentration reduction will result in decreased in SLPI antimicrobial effect to the uterus, that can cause infection and lead to preterm labor.[24,25]

This is consistent with research conducted by Punchner et al. where SLPI concentration assessed in spontaneous preterm labor with prior rupture preterm labor. From these studies obtained low concentrations of SLPI in prior rupture preterm labor case. Theoretically can be explained that the low concentration of SLPI in rupture of membranes associated with the inflammatory process. In this research, research conducted on 16 patients with preterm pregnant mother compared with 16 patients mothers who experience preterm labor without ruptured membranes. Blood sampling performed on all samples and tested in the laboratory. Then conduct Mann - Whitney non-parametric test which showed that $p = 0.000$ which means obtained statistically significant difference of SLPI concentration values between groups of preterm labor and preterm pregnancy. So the results of this research can prove that low levels of SLPI is one of the preterm labor causes.

SLPI Cut Off Point

Some research that done previously stated, there is a tendency to lower concentration of SLPI in preterm labor case, by using amniotic fluid as SLPI concentration inspection material. However, some researchers got different SLPI concentration values and still have not found SLPI concentration cut off point to be used as a predictor of preterm labor without prior rupture. In this research, based on ROC curve obtained SLPI concentration cut off points mark of the preterm labor incidence is 37.9 ng/ml. If the SLPI concentration value ≤ 37.9 in women with a gestational age <37 weeks may lead to preterm labor with sensitivity 100% and specificity 93.7%. Expected the SLPI concentration assessment result in this research can serve as guidelines to predict preterm labor risk during antenatal as early detection.

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Research Article

Fetal Biometry Nomogram Based on Normal Population : an Observational Study

Nomogram Biometri Janin Berdasarkan Populasi Normal : Suatu Penelitian Observasional

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Abstract

Objective: To establish fetal biometry nomogram using percentile method based on normal population.

Methods: A descriptive retrospective study in order to establish fetal biometry nomogram using percentile method based on normal population. Four fetal biometry measurement (BPD, HC, AC and FL) was collected from ultrasonography examination result in Fetomaternal Division Ultrasound Unit - Anggrek Clinic and from medical record unit Dr. Cipto Mangunkusumo General Hospital, from January 2015 until April 2016. Data being documented using case report form and being tabulated using Microsoft Excell 2011 Version 14.7.0 (161029). All data were analyzed using SPSS 20.0 dan Matlab R2016a.

Results: There were 6169 pregnant women underwent fetal biometry ultrasound within January 2015 - April 2016. Based on inclusion criteria, 2798 (45%) were eligible as research sample distributed from 12 until 42 wga. Due to evenly distribution data, 2205 (78%) were distributed from 20 until 40 wga to develop fetal biometry nomogram. Most pregnant women were 28.9 years old (SD ± 5.74) in range of 21-30 (55%) years old. The youngest was 13 years old and the oldest was 45 years old. Four fetal biometry were collected and distributed evenly using percentile method to establish fetal biometry nomogram. As for estimated fetal weight curve was developed by Hadlock C formula. Each biometry was calculated the 10th, 50th and 90th centile curves according to gestational age. Thus, representing the fetal biometry and modified Hadlock C estimated fetal weight nomogram based on normal population in Jakarta.

Conclusion: Each biometry and modified Hadlock C estimated fetal weight were calculated in 10th, 50th and 90th centile curves according to gestational age represent fetal biometry nomogram based on normal population in Jakarta.

[Indones J Obstet Gynecol 2018; 6-3: 149-154]

Keywords: biometry, estimated fetal weight formula, nomogram

Abstrak

***Tujuan**: Untuk mendapatkan nomogram biometri janin dengan pendekatan persentil berdasarkan populasi normal.*

***Metode**: Penelitian ini merupakan penelitian deskriptif retrospektif untuk mendapatkan nomogram biometri janin dengan metode persentil pada populasi normal. Parameter biometri meliputi diameter biparietal (DBP), lingkar kepala (LK), lingkar perut (LP) dan panjang femur (PF). Data parameter biometri menggunakan data pemeriksaan USG di Divisi Fetomaternal-Klinik Anggrek dan data rekam medis RSUPN Dr. Cipto Mangunkusumo sepanjang Januari 2015 hingga April 2016. Data penelitian didokumentasikan pada formulir laporan kasus dan ditabulasi menggunakan software Microsoft Excell 2011 Version 14.7.0 (161029). Analisis data penelitian menggunakan SPSS 20.0 dan Matlab R2016a.*

***Hasil**: Dari total 6169 data perempuan hamil yang melakukan pemeriksaan ultrasonografi biometri janin sejak Januari 2015 hingga April 2016, didapatkan 2798 (45%) sampel data yang memenuhi kriteria inklusi penelitian. Data tersebut didistribusikan berdasarkan usia kehamilan dari usia kehamilan 12 minggu hingga 42 minggu. Normalitas sebaran data merupakan hal penting pada penelitian, sehingga dilakukan reduksi data agar mendapatkan sebaran normal untuk menghasilkan kurva dengan metode persentil. Hasil akhir didapatkan 2205 (78%) sampel data penelitian yang didistribusikan dari usia kehamilan 20 minggu hingga 40 minggu untuk mendapatkan nomogram biometri janin dengan metode persentil. Data demografi menunjukkan rerata usia ibu hamil 28.9 tahun (SD ± 5.74) dalam kelompok usia 21-30 tahun (55%). Usia ibu hamil termuda 13 tahun dan yang tertua 45 tahun. Data empat parameter biometri dikumpulkan dan didistribusikan merata menggunakan metode persentil untuk menghasilkan nomogram biometri janin. Pada penelitian dihasilkan pula nomogram taksiran berat janin yang dikembangkan dari rumus Hadlock C. Data tiap parameter biometri janin dikalkulasikan berdasarkan persentil 10, 50 dan 90 sesuai usia kehamilan. Nomogram biometri janin dan taksiran berat janin modifikasi Hadlock C yang dihasilkan merupakan gambaran nomogram berdasarkan populasi normal di Jakarta.*

***Kesimpulan**: Gambaran nomogram tiap parameter biometri dan nomogram taksiran berat janin modifikasi Hadlock C persentil 10, 50 dan 90 sesuai usia kehamilan merupakan representasi nomogram biometri janin berdasarkan populasi normal di Jakarta.*

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***Kata kunci**: biometri, formula taksiran berat janin, nomogram*

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INTRODUCTION

Fetal growth is complex interaction between maternal-fetal-placental factors and has become fetal wellbeing indicators throughout pregnancy.[1-3] Imbalance interaction between these factor will manifest into fetal growth disturbances, fetal growth restriction or macrosomia. Thus, high quality of ante natal care will detect normal or abnormal fetal growth.[4-7]

In order to improve maternal and neonatal health, including decrease perinatal death, high quality of ante natal care is a necessity. Not only by early detecting of high risk pregnancy, but also monitoring fetal growth. An accurate monitoring fetal growth will provide proper obstetric management.[1,4-6] Therefore, it will prevent under/over treatment, decrease morbidity and prevent mortalilty.[4-7]

There are two methods known for monitoring fetal growth, clinical examination (fundal height measurement) and imaging method (fetal biometry ultrasonography).[1,2,5,8] No significant differences in determining estimated fetal weight between clinical and imaging methods (64% VS 62.5%; $p > 0.2$).[1,9-12] Nevertheless, ultrasonography examination has become most obstetrician preferences due to its diagnostic values.[1,8,12,13] Not only for monitoring fetal growth, but also evaluating fetal development and evaluating cause of fetal growth disturbances.[2]

Obstetricians use various fetal biometry parameters in monitoring fetal growth, standard and advanced measurement. Standard fetal biometry measurement are biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL).[1,2,8] Advanced fetal biometry measurement commonly use for special purposes, such as evaluating cause of fetal growth disturbances, evaluating fetal development and evaluating fetal nutritional status.[1,2] Things to be concerned in monitoring fetal growth is fetal biometry parameters applied in estimating fetal weight formulas. It influences accuracy of estimated fetal weight result.[8,11,14-16]

There are two main concern in monitoring fetal growth, fetal biometry nomogram or curve and estimated fetal weight formulas being applied. Both are influencing examination result accuracy and in determining fetal growth disturbances.[3,6-8,15,17] Accuracy in evaluating fetal growth will increase if fetal biometry nomogram apply is based on local population.[3,6,7]

There is no publication on fetal biometry nomogram based on our local normal population. This study was conducted to establish fetal biometry nomogram based on Indonesia normal population.

METHODS

This was a descriptive retrospective study in order to establish fetal biometry nomogram based on normal population using percentile method. It was conducted in Fetomaternal Division Ultrasonography Unit - Anggrek Clinic and Medical Record Unit Dr. Cipto Mangunkusumo General Hospital, during January - September 2016.

Standard fetal biometry parameters measurement, including biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and fetal length (FL) was collected from ultrasonography examination result in Fetomaternal Division Ultrasound Unit - Anggrek Clinic and from medical record unit Dr. Cipto Mangunkusumo General Hospital, from January 2015 until April 2016.

Inclusion criteria in this study, including : pregnant women underwent ultrasound fetal biometry examination in Fetomaternal Division Ultrasound Unit-Anggrek Clinic towards January 2015 - April 2016; criteria for determining last menstrual period : Last menstrual period from regular cycle, duration 25 - 35 days. Last 3 months menstrual cycle was regular, fetal biometry ultrasound examination in 10 - 12 wga, serial ultrasound examination in Fetomaternal Division Ultrasound Unit-Anggrek Clinic Dr. Cipto Mangunkusumo General Hospital; Last menstrual period was determined by 2 out of 3 criteria; Ultrasound examination was conducted between 12 wga until 42 wga; Singleton intrauterine live fetus; Pregnancy without complications.

We emphasize our study in normal population. Therefor, there were some exclusion criteria in this study, including : pregnancy with obesity; pregnancy with malnutrition; pregnancy with infection and chronic infection; pregnancy with mild and severe anemia; pregnancy with metabolic disorders; multiple pregnancy; intrauterine fetal death; fetal anomaly (lethal and non lethal); pregnancy with preeclampsia/eclampsia; pregnancy with autoimmune disease; smoking and alcohol consumption.

All data being documented using case report form and being tabulated using Microsoft Excell 2011 Version 14.7.0 (161029). All data were analyzed using SPSS 20.0 and Matlab R2016a. This study was approved by Ethic Committee of Faculty of Medicine, Universitas Indonesia - Dr. Cipto Mangunkusumo General Hospital.

RESULT

Based on Fetomaternal Division-Anggrek Clinic documentation and medical record data, there were 6169 pregnant women underwent fetal biometry ultrasound examination from January 2015 until April 2016. There were 2798 samples met inclusion criteria varied from 12 wga until 42 wga.

Demographic characteristic was including patients age. Patients mean age underwent ultrasonography examination was 28.9 years old (SD±5.74) in range 21-30 years old (55%). The youngest patient is 13 years old and the oldest 45 years old. Patients demographic characteristic was shown in Table. 1.

Table 1. Demographic Characteristics of Research Subject

Variable (n = 2205)	Description
Age (Year)*	28.9 ± 5.74
Age Distribution**	
≤ 20	156 (7.1%)
21 - 30	1211 (55%)
31 - 40	784 (35.5%)
41 - 50	54 (2.4%)

**Numerical data evenly distributed were presented in mean±SD*
***Categorical data presented in n (%)*

Table 2. Fetal Biometry Parameters Characteristic

Biometry Parameters	Gestational Age	n	Mean ± SD	95% CI
Biparietal Diameter	20	59	47.37 ± 2.01	46.83 - 47.90
	24	67	59.40 ± 3.25	58.60 - 60.19
	28	111	71.36 ± 4.24	70.48 - 72.24
	32	146	80.63 ± 4.90	79.82 - 81.43
	36	150	88.96 ± 8.03	87.66 - 90.25
	40	127	93.40 ± 3.60	92.14 - 94.66
Head Circumference	20	59	173.35 ± 8.19	171.18 - 175.53
	24	67	219.06 ± 15.12	215.31 - 222.81
	28	111	258.76 ± 13.53	255.94 - 261.58
	32	146	288.25 ± 12.50	286.20 - 290.30
	36	150	315.62 ± 16.12	313.01 - 318.23
	40	127	325.35 ± 13.92	320.49 - 330.21
Abdominal Circumference	20	59	154.02 ± 9.43	151.54 - 156.50
	24	67	196.50 ± 10.819	193.84 - 199.16
	28	111	239.06 ± 13.504	236.21 - 241.90
	32	146	275.96 ± 15.89	273.35 - 278.57
	36	150	314.94 ± 18.32	311.97 - 317.91
	40	127	337.62 ± 17.28	331.59 - 343.65
Femur Length	20	59	32.78 ± 3.09	31.97 - 33.59
	24	67	43.12 ± 2.55	42.49 - 43.75
	28	111	52.25 ± 3.75	51.46 - 53.04
	32	146	59.98 ± 3.77	59.36 - 60.60
	36	150	68.59 ± 3.41	68.04 - 69.14
	40	127	73.05 ± 2.08	72.32 - 73.78

**Numerical data evenly distributed were presented in mean ± SD*

Main concern in this research is evenly distribution of data in order to establish nomogram with good precision. Therefor, we performed data reduction from total data met inclusion criteria. There were 2205 samples evenly distributed from 20 wga until 40 wga. Fetal biometry characteristic were shown in Table 2.

2205 data were then distributed using percentile method based on gestational age to establish fetal biometry nomogram based on normal population. Each fetal biometry parameters nomogram were compile in Figure 1.

In this study, we developed data to establish estimated fetal weight nomogram based on normal population in Jakarta. We used Hadlock C formula to establish estimated fetal weight nomogram based on normal population. Regression equation for each fetal biometry parameters were shown in Table 3.

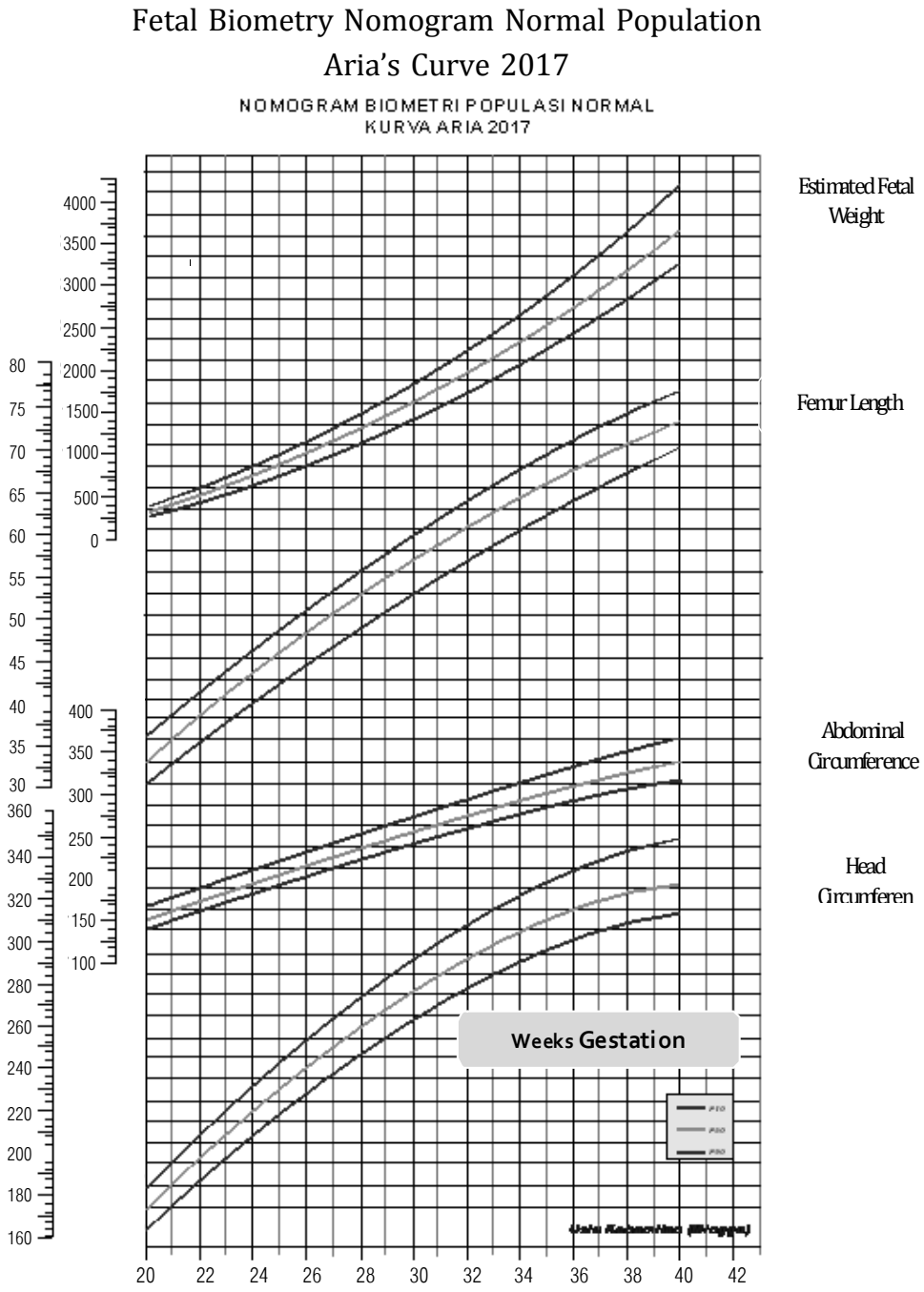

Figure 1. Fetal Biometry Nomogram Based on Normal Population

Table 3. Fetal Biometry Nomogram Regression Equation Based on Percentile

Biometry Parameters	Percentile	Regression Equation
Biparietal Diameter	P10	$y = -0.059066 \times X^2 + 5.8359 \times X + (-49.309)$
	P50	$y = -0.063745 \times X^2 + 6.1934 \times X + (-51.889)$
	P90	$y = -0.055744 \times X^2 + 5.7912 \times X + (-43.448)$
Head Circumference	P10	$y = -0.25332 \times X^2 + 22.604 \times X + (-189.49)$
	P50	$y = -0.26538 \times X^2 + 23.581 \times X + (-193.65)$
	P90	$y = -0.25735 \times X^2 + 23.711 \times X + (-190.2)$
Abdominal Circumference	P10	$y = -0.25332 \times X^2 + 22.604 \times X + (-189.49)$
	P50	$y = -0.14188 \times X^2 + 17.888 \times X + (-150.21)$
	P90	$y = -0.061531 \times X^2 + 13.583 \times X + (-79.216)$
Femur Length	P10	$y = -0.028433 \times X^2 + 3.7173 \times X + (-32.72)$
	P50	$y = -0.040289 \times X^2 + 4.4826 \times X + (-41.111)$
	P90	$y = -0.03635 \times X^2 + 4.263 \times X + (-35.188)$
Estimated Fetal Weight	P10	$y = (-152.15) + (17.54 \times X) + (-0.14 \times X^2)$
	P50	$y = (-150.21) + (17.89 \times X) + (-0.14 \times X^2)$
	P90	$y = (-79.21) + (13.58 \times X) + (-0.06 \times X^2)$

DISCUSSION

This is a descriptive retrospective study aimed to establish fetal biometry nomogram based on local normal population. By this means normal population in Jakarta. Selection of fetal biometry nomogram being applied influence evaluation accuracy in monitoring fetal growth. It is because race or ethnical characteristic between population are different.[18] Therefor, we recommend using fetal biometry nomogram based on our local normal population.[5,18-20]

There is limited publication related fetal biometry research in Asia, specially Indonesia. No publication on fetal biometry nomogram based on Indonesia normal population. Thus, nomograms result from this study represent fetal biometry nomogram based on normal population in Jakarta.

This nomogram can be compared with other nomogram resulted form others population, such as Tokyo's Curve, Korean's Curve, Pakistan's Curve and also International population resulted from Intergrowth project. Based on our observational, mean difference between our curve compare to Tokyo's Curve and Intergrowth project was 1-2 mm for each biometry. As for Korean's Curve and Pakistan's Curve, our curve was smaller with mean difference 3-4 mm. Factor influence the result was total samples being used in the research, such as Intergrowth project that use 13.000 samples.

Method used in this research has advantages and disadvantages. Retrospective method used in this research had some benefits, specially time period conducting research. It needed short period time rather than longitudinal method to get data distribution evenly. Nevertheless, disadvantages using this method were non optimal controlling confounding factors. It influences result accuracy. In this research, confounding factor were controlled by research operational definition and only researcher conduct the selection and data collection.

As comparison, longitudinal or cross-sectional method has its own advantages. Confounding factor for longitudinal method can be controlled optimally, thus given advantages for the result. Meanwhile, it is needed longer period of time to conduct the research in order to get data distribution evenly.[5,18,20] Due to retrospective method used in this research, fetal biometry nomogram resulted need to be validated in order to be generalized in Indonesian population.

This research has some weakness, including : Retrospective data. This influence data accuracy due to non optimal confounding factors control; Less demographic characteristic data. Due to limitation of medical record data, such as height, body weight, haemoglobin and socio-economic; Validation data is needed in order to generalized data to be applied for Indonesian population.

CONCLUSION

High quality of ante natal care is a necessity in order to improve maternal-neonatal health and decrease perinatal death. Thus, detection of high risk pregnancy during ante natal care, including fetal growth monitoring in detecting fetal growth disturbances. Each biometry and modified Hadlock C estimated fetal weight were distributed in 10th, 50th and 90th centile curves according to gestational age represent fetal biometry nomogram based on normal population in Jakarta.

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Research Article

Different Doses of Intraumbilical Oxytocin on the Third Stage of Labor

Berbagai Dosis Oksitosin Intraumbilikal pada Manajemen Aktif Kala III

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Abstract

Objective: To compare the dose of oxytocin injected intraumbilicall towards the duration of the third stage, blood loss volume, hemoglobin and hematocrit.

Methods: This study is a prospective randomised study with a control. The control group was given an intramuscular injection of 10 IU oxytocin. The intervention of the three groups intraumbilical oxytocin treatment dose of 10 IU, 20 IU and 30 IU diluted in 50 ml of normal saline solution and administered intraumbilically. The sample selection by purposive sampling and the distribution group based on systematic random sampling (10 samples each). Data were taken from the period April 2016-January 2017 with the inclusion and exclusion criteria. Data were analysed using Chi-square, T-test, ANOVA and Post hoc tests.

Results: Characteristics study for variables of age, occupation, parity, education, episiotomy and neonates weight showed homogeneous characteristics. The mean duration of the third stage for all groups was between 366.7 ± 159.0 seconds and 440.1 ± 244.99 seconds. While the average number of postpartum haemorrhage for all group 61.894 ± 226.3ml and 309.5 ± 110.26 ml. There were no differences in the dose of oxytocin on the duration of the third stage (p> 0.05) and the amount of bleeding (p> 0.005). There was a difference of haemoglobin between intervention group of oxytocin dose of 10 IU and 30 IU intraumbilical (p = 0.031). There was no difference between the mean hematocrit levels between the groups (p> 0.005).

Conclusion: There were no differences in the dose of oxytocin intraumbilical towards the duration of the third stage, the amount of bleeding and hematocrit levels. The decrease of haemoglobin greater in 30 IU intraumbilical significantly.

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Keywords: duration of the third stage, haemoglobin and hematocrit, oxytocin intraumbilical, the amount of bleeding

Abstrak

***Tujuan**: Membandingkan dosis injeksi oksitosin intraumbilikal terhadap lama kala III, jumlah perdarahan pascasalin, hemoglobin dan hematokrit.*

***Metode**: Penelitian ini merupakan uji klinis acak dengan pembanding. Kelompok kontrol diberikan injeksi oksitosin 10 IU intramuskular. Intervensi pada 3 kelompok yaitu kelompok perlakuan oksitosin intraumbilikal dosis 10 IU, 20 IU dan 30 IU yang dilarutkan dalam saline 0,9% sebanyak 50 ml yang diinjeksikan pada vena umbilikal. Pemilihan sampel secara purposive sampling dan pembagian kelompok berdasarkan sistematik random sampling (10 sampel tiap kelompok). Data diambil periode April 2016 - Januari 2017 dengan kriteria inklusi dan eksklusi. Data dianalisis dengan uji Chi square, uji T, Anova dan Post hoc test.*

***Hasil**: Karakteristik umum variabel usia, pekerjaan, paritas, pendidikan, episiotomi dan berat badan neonatus menunjukkan karakteristik homogen. Rerata lama kala III untuk semua kelompok adalah antara 366,7 ± 159,0 detik dan 440,1 ± 244,99 detik. Sedangkan rerata jumlah perdarahan pascasalin untuk semua kelompok 226,3 ± 61,894 ml dan 309,5 ± 110,26 ml. Tidak ada perbedaan dosis oksitosin terhadap lama kala III (p>0,05) dan jumlah perdarahan (p>0,005). Ada perbedaan rerata hemoglobin setelah intervensi oksitosin dosis 10 IU dan 30 IU intraumbilikal (p=0,031). Tidak terdapat perbedaan rerata kadar hematokrit antara semua kelompok (p>0,005).*

***Kesimpulan**: Tidak ada perbedaan dosis oksitosin intraumbilikal terhadap lama kala III, jumlah perdarahan dan kadar hematokrit. Ada perbedaan rerata hemoglobin setelah intervensi oksitosin dosis 10 IU dan 30 IU intraumbilikal.*

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***Kata kunci**: hemoglobin dan hematokrit, jumlah perdarahan, lama kala III, oksitosin intraumbilikal*

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INTRODUCTION

Postpartum haemorrhage (PPH) is a major cause of maternal mortality worldwide with an estimated mortality rate of 140,000 per years. The incidence of postpartum haemorrhage in developed countries is 5% of deliveries, while in developing countries is 28% of labour. The causes maternal mortality of postpartum haemorrhage are due to 80% uterine atony and 10% retained placenta. Most of these deaths occur within 4 hours after delivery, is a consequence of the third stage of labor.[1-3]

Indonesian Demographic Health Survey in 2012 showed the maternal mortality rate increased from

228 per 100,000 live births in 2007 to 359 per 100,000 live births in 2012.[2] The leading causes of maternal mortality in Indonesia is postpartum haemorrhage (28%), eclampsia (24%) and infections (11%). Postpartum haemorrhage is bleeding, or blood loss of more than 500 ml which occurred after the child is born either before, during, or after birth placenta.[2-4]

To prevent postpartum haemorrhages carried out active management of the third stage. Active management of the third stage consists of the injection of oxytocin 10 IU intramuscularly (IM), massage of uterine fundus and cord traction to accelerate the delivery of placenta by inducing uterine contractions.[4,5]

Oxytocin can be given intramuscularly or intraumbilically. The route of intraumbilical oxytocin will be distributed directly to the oxytocin receptors in the myometrium thereby the myometrium will contract better.[4,6,7] Result analysis showed that the active management of the third stage could reduce postpartum haemorrhage up to 58%.[6,7] Cochrane reviewed the active management of the third stage reduces the incidence of postpartum bleeding, shorten the third stage and the need for trasfusion.[4-6]

METHODS

This study was a randomised study with a control. Intervention in the three groups of intraumbilical oxytocin treatment with the dose of 10 IU, 20 IU and 30 IU diluted in normal saline 50 ml injected into the umbilical vein. The control group was given an intramuscular injection of 10 IU oxytocin. This research was conducted in the Department of Obstetrics and Gynecology Hospital Dr. Moh. Hoesin, Palembang. The research was conducted in April 2016 to January 2017. The study population was all pregnant women who gave birth in Department of Obstetrics and Gynecology Hospital. Dr. Mohammad Hoesin / Faculty of Medicine, Universitas Sriwijaya Palembang. The samples were all pregnant women who gave birth, qualified inclusion and exclusion criteria.

Sampling was done by purposive sampling and divided into control group and intervention group by systematic random sampling. Sample size calculations with Pocock formula. The number of samples obtained each study group were ten respondents. The inclusion criteria were pregnant women without complication (physiologically), premature rupture of membranes (PROM) <12 hours. Exclusion criteria of obesity with a body mass index (BMI) of 35 kg/m^2, abnormal uterine (eg, anatomical abnormalities, fibroids), a blood disorder in the mother (Von Willebrand disease, idiopathic thrombocytopenia purpura, disseminating intravascular coagulation (DIC)), placental abruption or placenta previa, multiple pregnancy, polyhydramnios, estimated fetal weight >3500g, hypertension or preeclampsia, history of PPH or retained placenta, a history cesarean section or laparotomy and fetal death.

Material

The materials were disposable syringes 50 ml Terumo, disposable syringe 3 ml ONEMED, oxytocin 10 IU (brand Syntocinon® produced by Novartis), saline solution 0.9% (manufactured by PT Widatra Bhakti), stopwatch Kadio KD-2005, glassware Pyrex, digital scales (brand Camry), sterile gauze and cloth mat or underpad COSMO Med.

Procedures

Subjects were randomised systematically by the arrival of the patient. The subject of the first sequence to 10 specified in the control group of 10 samples, and the subject of the order of 11 to 20 in the Intervention group 10 IU intraumbilical and so on until 40 samples. All samples were checked haemoglobin and hematocrit on admission and 2 hours after delivery.

The intervention group after delivered and clamped umbilical cord was first injected 10 IU oxytocin were diluted in 50 ml of normal saline solution to the umbilical vein with the distance of about 10 cm from the vulva. The second intervention group were injected 20 IU oxytocin were dissolved in 50 ml of normal saline solution. The third intervention group 30 IU oxytocin dissolved in 50 ml of normal saline solution. Then do massage cord proximally to the spread of oxytocin to the placental implantation site. The control group was injected 10 IU oxytocin intramuscular using a 3 ml disposable syringe lateral upper thigh.

The duration of the third stage is counted starting after birth neonates, injection of oxytocin IM or intraumbilical until the placenta is born with

a stopwatch. The amount of bleeding is calculated by measuring the blood by using a measuring cup, then under a cloth or gauze pad and used weighed. The difference in weight on a sterile pad (under-pad) and gauze before and after use was converted into ml (1 g = 1 ml), then weighed with scales Camry models NS.

Analysis and Interpretation

Data were analysed using Chi-square, T-test, ANOVA and Post hoc.

RESULT

Experimental research design with pre and post-test with control to compare the dose injection of oxytocin intraumbilical was conducted in April 2016 until January 2017 at the General Hospital Dr. Mohammad Hoesin Palembang. Total samples of 40 pregnant women who delivered and fulfilled the inclusion criteria. The amount of bleeding, duration of the third stage, haemoglobin and hematocrit each control group and the intervention will be assessed and compared.

Characteristics of Subjects

The range of respondents age was 14-45 years, and the largest age group was 20-35 years old as many as 32 samples (80%). The majority of respondents do not work or as housewives (92.5%). The majority of parity was primigravida (47.5%) with a high school education level was 80%. Majority of 60% respondents done episiotomy with the average birth weight of newborns in this study were 2949 ± 282.95 gram (Table 1).

Table 1. Characteristics of Subjects

Characteristics	**Oxytocin 10 IU intramuscular (%)**	**Oxytocin 10 IU intraumbilical (%)**	**Oxytocin 20 IU intraumbilical (%)**	**Oxytocin 30 IU intraumbilical (%)**	***Total***	***p-value***
Age (years old)*						
<20	1 (25)	1 (25)	1 (25)	1 (25)	4 (100)	0.254
20-35	8 (25)	9 (28.1)	7 (21.9)	8 (25)	32 (100)	
>35	1 (25)	0	2 (50)	1 (25)	4 (100)	
Address**						
Urban area	10 (31.3)	5 (15.6)	8 (25)	9 (28.1)	32 (100)	0.033
Rural area	0	5 (62.5)	2 (25)	1 (12.5)	8 (100)	
Occupation*						
Housewives	9 (24.3)	10 (27)	8 (21.6)	10 (27)	37 (100)	0.158
Private sector	1 (100)	0	0	0	1 (100)	
Teacher	0	0	2 (100)	0	2 (100)	
Parity*						
0	5 (26.3)	7 (36.8)	3 (13.8)	4 (21.1)	19 (100)	0.515
1	4 (36.4)	1 (9.1)	2 (18.2)	4 (36.4)	11 (100)	
2	1 (14.3)	2 (28.6)	3 (42.9)	1 (14.3)	7 (100)	
≥ 3	0	0	2 (66.6)	1 (33.4)	3 (100)	
Education*						
Elementary	0	0	2 (100)	0	2 (100)	0.061
Junior High	2 (100)	0	0	0	2 (100)	
Senior High	5 (15.6)	10 (31.2)	7 (21.9)	10 (31.2)	32 (100)	
D3/S1	3 (75)	0	1 (25)	0	4 (100)	
Episiotomy**						
Yes	6 (25)	8 (33.3)	4 (16.7)	6 (25)	24 (100)	0.343
No	4 (25)	2 (12.5)	6 (37.5)	4 (25)	16 (100)	
Birth weight neonates***	3.085 ± 316.27	2.860 ± 307	2.890 ± 261.19	2.960 ± 282		0.297

Duration of the third stage

The mean time of the third stage for all groups was between (366.7 ± 159.0 seconds) and (440.1 ± 244.99 seconds). Mann-Whitney test showed the distribution of data not normal, followed by a test of Kruskal Wallis. From the results of Kruskal Wallis showed there was no difference between all the intervention group (p = 0.492). It can be concluded that there was no difference in the duration of the third stage among the control group (oxytocin dose of 10 IU IM) with oxytocin intraumbilical all doses groups (Table 2).

The Blood Loss during The Third Stage

Post Hoc test results obtained probability between the control group (oxytocin dose of 10 IU IM) at a dose of 10 IU oxytocin group intraumbilical, a dose of 20 IU oxytocin intraumbilical, and a dose of 30 IU oxytocin intraumbilical (p>0.05). It can be concluded that there was no difference in the number of blood lossamong the control group (oxytocin dose of 10 IU IM) and intervention intraumbilicalgroups in all doses of oxytocin significantly.

Table 2. Comparison of Intraumbilical Oxytocin Dose in the Duration of the Third Stage between the Two Groups

Groups	Average ± SD	Groups	Average ± SD	p-value
Oxytocin dose 10 IU IM	401.4 ± 209.48	Oxytocin dose 10 IU Intraumbilical	366.7 ± 159.09	0.791
		Oxytocin dose 20 IU Intraumbilical	440.1 ± 244.99	0.384
		Oxytocin dose 30 IU Intraumbilical	384.7 ± 314.59	0.185
Oxytocin dose 10 IU Intraumbilical	366.7 ± 159.09	Oxytocin dose 20 IU Intraumbilical	440.1 ± 244.99	0.427
		Oxytocin dose 30 IU Intraumbilical	384.7 ± 314.59	0.570
Oxytocin dose 20 IU Intraumbilical	440.1 ± 244.99	Oxytocin dose 30 IU Intraumbilical	384.7 ± 314.59	0.096

Mann Whitney, Kruskal Wallis

Table 3. Comparison of Intraumbilical Oxytocin in Blood Loss, Haemoglobin and Hematocrits to All Groups.

Primary outcome	Oxytocin 10 IU intramuscular (Group 1)	Oxytocin 10 IU intramuscular (Group 2)	Oxytocin 20 IU intramuscular (Group 3)	Oxytocin 30 IU intramuscular (Group 4)
Blood loss, ml p value	309.5 ± 110.26 1 vs 2 = 0.051 1 vs 3 = 0.952 1 vs 4 = 0.407	226.3 ± 61.894 2 vs 3 = 0.058 2 vs 4 = 0.244	307.0 ± 86.929 3 vs 4 = 0.442	275.0 ± 101.57
Difference in haemoglobin level (g/dl) p value	0.27 ± 0.79 1 vs 2 = 0.840 1 vs 3 = 0.230 1 vs 4 = 0.256	0.35 ± 0.43 2 vs 3 = 0.315 2 vs 4 = 0.183	0.33 ± 0.72 3 vs 4 = 0.023	0.65 ± 0.75
Difference in hematocrit level (%) p value	0.60 ± 2.41 1 vs 2 = 0.628 1 vs 3 = 0.505 1 vs 4 = 0.278	1.50 ± 1.58 2 vs 3 = 0.855 2 vs 4 = 0.121	0.80 ± 1.99 3 vs 4 = 0.085	1.90 ± 2.51

Post Hoc test (LSD test), p=0.005
Mean ± SD

Comparison of Dose Oxytocin to Haemoglobin

Post Hoc test probability between the control group (oxytocin dose of 10 IU IM) at a dose of 10 IU oxytocin group intraumbilical, a dose of 20 IU oxytocin intraumbilical, and a dose of 30 IU oxytocin intraumbilical >0.05. There was no difference between the average amount of bleeding control (doses of 10 IU oxytocin IM) with all doses of oxytocin intraumbilical significantly. In addition, the results obtained probability value was 0.023 between the 20 and 30 IU oxytocin intraumbilical ($p<0.05$). There was difference haemoglobin level of 30 IU oxytocin group intraumbilical lower than the oxytocin group 20 IU intraumbilical.

Comparison of Dose Oxytocin to Hematocrit Levels

Post Hoc test results obtained probability between the positive control group (oxytocin dose of 10 IU IM) with all doses of oxytocin group intraumbilical ($p>0.05$). There was no difference of mean hematocrit levels among the control group with the intervention group intraumbilical all doses of oxytocin significantly.

DISCUSSION

General characteristics of Chakra research revealed no significant differences in age, education level and occupation of respondents.[9,10,12] In the study Movahed was no significant difference between the parity of the respondents ($p = 0.632$) with the characteristics of the respondents there are many primigravid (46%).[9,10,15]

Episiotomy was performed in 60% of respondents with average birth weight of newborns 2949 ± 282.95 grams. Research of Movahed were mean weight neonates 3303.8 ± 366.3. Statistically, there was no significant difference between the variables an episiotomy or not ($p = 0.244$) with weight neonates ($p = 0.782$).[11,12]

Based on the analysis there were no significant differences in age, occupation, parity, education, episiotomy and weight neonates. The variable addressed indicates significant value. Characteristics of research subjects, in general, have a homogenous result.

The longest duration of the third stage found in groups of 20 IU oxytocin intraumbilical dose and shortest found in the oxytocin group an intraumbilical dose of 10 IU. From the statistical analysis, Mann-Whitney and Kruskal Wallis test showed there was no difference duration of the third stage between groups ($p> 0.05$). The results of this study are supported by Movahed research conducted in 2012 showed a statistically significant in the oxytocin intraumbilical group could shorten the time of the third stage than the control group (4.2 ± 4:11 vs 4:52 ± 5:53 min; $p = 0.031$). Neither Puri study conducted in 2012 reported that oxytocin intraumbilical significant reduction in the duration of the third stage of labour at five study groups.[5,6,10]

Highest blood loss was found in the group of an intramuscular dose of 10 IU oxytocin, and the least amount of bleeding was found in the group intraumbilical dose of 10 IU oxytocin. Statistical analysis of Post Hoc showed there was no difference in the amount of bleeding between the groups ($p> 0.05$). Chakra obtained the cut-off point of bleeding in the third stage of 136 ml, effective when the third stage of bleeding is less than or equal to 136 ml. The effectiveness of bleeding in the third stage on the intraumbilical group by 55% higher compared to the intramuscular group is at 8.3%, a statistically significant correlation based on the amount of bleeding in the third stage ($p = 0.001$). Cochrane meta-analysis on 15 studies suggest a significant borderline; there were no differences in the duration of the third stage and the amount of bleeding between the groups with expectative management intraumbilical oxytocin, saline only, intramuscular oxytocin and prostaglandins. Controversial opinion on oxytocin intraumbilical various doses may provide clinical benefit in reducing the length of the third stage and the number of haemorrhage research of Weeks and G. Carroli.[8,9,13]

Statistical analysis showed there was no difference between the haemoglobin levels after intervention dose of 10 IU oxytocin and oxytocin IM dose of 20 IU intraumbilical. This means that the dose of 10 IU oxytocin and oxytocin IM dose of 20 IU intraumbilical effective to prevent a decrease in haemoglobin ($p<0.05$). While the intervention of oxytocin dose of 10 IU and 30 IU intraumbilical not effectively prevent a decrease in haemoglobin levels was statistically significant ($p>0.05$). These results indicate a dose of oxytocin intraumbilical

small and large are not effective to prevent a decrease in haemoglobin. Increasing doses of oxytocin intraumbilical more than 20 IU will lead to lower haemoglobin levels significant.

In addition to haemoglobin, changes in hematocrit levels were also assessed in this study. Statistical analysis showed that there was difference between the mean hematocrit levels after intervention dose of 10 IU oxytocin and oxytocin IM dose of 20 IU intraumbilical. A dose of 10 IU oxytocin and oxytocin IM dose of 20 IU intraumbilical effective to prevent a decrease in hematocrit ($p>0.05$). While the intervention group oxytocin dose of 10 IU and 30 IU intraumbilical not effectively prevent a decrease in hematocrit seen from a decrease in hematocrit levels were statistically significant ($p<0.05$). These results indicated a dose of oxytocin intraumbilical small and large were not effective to prevent a decrease in hematocrit. Increasing doses of oxytocin intraumbilical more than 20 IU would decrease hematocrit levels.[7,8,10]

The absence of a significant decrease in haemoglobin and hematocrit levels in the intervention group a dose of 10 IU oxytocin and oxytocin IM dose of 20 IU intraumbilical indicate that this intervention can prevent postpartum bleeding.[7,8,14,15]

Post hoc tests showed the effectiveness of all doses of oxytocin intraumbilical no different from the effectiveness of the control of oxytocin. However, the effectiveness of a dose of 30 IU oxytocin intraumbilical significantly different with a dose of 20 IU oxytocin intraumbilical. Haemoglobin and hematocrit levels after intervention intraumbilical dose of 30 IU oxytocin lower than the levels of haemoglobin and hematocrit after intervention intraumbilical dose of 20 IU oxytocin so that it can be concluded extra doses of oxytocin intraumbilical more than 20 IU would not prevent a decrease in haemoglobin levels and hematocrit.[7,8,15]

In theory, exposure to high doses of oxytocin cause desensitisation and down-regulation on the oxytocin receptor. Oxytocin receptors are a group of G protein-coupled receptors (GPCRs). Desensitization is a process that prevents overstimulation on cells through two mechanisms. First with the receptor phosphorylation inhibits the activation of protein G. Both with binding proteins, called arrestins, preventing activation of the G protein that did not happen with the oxytocin receptor binding.[13,15]

Research Anisodowleh comparing haemoglobin in the intervention group with oxytocin 10 IU dissolved in 20 ml saline compared with oxytocin 20 IU in a solution of Ringer's lactate 1 l at 100 ml/min intravenously, showed haemoglobin level was 12.45 ± 0.78 g/dl and 12.49 ± 0.85 g/dl ($p=0782$). Haemoglobin levels after 6 hours of labour are higher in the intervention group compared to the control group 12.32 ± 0.88 g/dl vs 11.58 ± 0.86 g/dl, but this difference was not significant ($p=0.23$). A decrease haemoglobin concentration from 1.96 g/dl to 1.2 g/dl in the intervention group and the control that shows a positive effect on injection of oxytocin intraumbilical. The differences are not significant due to the active management of the third stage in the two groups was performed using a uterotonic and standards procedure.[8,11,12]

Research Movahed et al. described the decrease of haemoglobin levels in the intervention group who received injections of oxytocin is intraumbilical not significantly different with the control group who received intravenous oxytocin ($p=0.228$). So that the injection of oxytocin intraumbilical concluded no benefit in preventing postpartum haemorrhage quantified grading Hb.[6,7,10]

Puri results explained the significant differences in levels of haemoglobin and hematocrit on four intervention groups and one control group. The concentration of 10 IU oxytocin increased in groups of 2 to 20 IU in group 3, further reduction of time in the third stage but the difference was not statistically significant. Oxytocin concentrations increased to 30 IU (or 0.06 IU/ml) in group 4 significantly reduced the volume of blood , and there were differences in haemoglobin concentration and hematocrit before and after childbirth.[6]

Limitations of this study were the small sample number and not blinded when the retrieval and analysis of data. Measurement of the amount of bleeding was based on the amount of bleeding that accommodated (underpad, gauze). It was subjective, not using the colourimetric technique, radiolabeled red blood cells, gravimetric or dye dilution method.

CONCLUSION

Oxytocin intraumbilical 10 IU reduced the duration of the third stage and blood loss. There were no differences in the duration of the third stage, volume blood loss and hematocrit level among the control group (oxytocin dose of 10 IU IM) with oxytocin intraumbilical all dose groups significantly. However, there was a difference between the mean haemoglobin levels of 20 and 30 IU oxytocin, whereby haemoglobin levels 30 IU oxytocin group intraumbilical lower than 20 IU oxytocin group intraumbilical.

SUGGESTION

Oxytocin intraumbilical10 IU could be an alternative in the active management of the third stage an action that was not invasive to the mother, easy, cheap and minimal side effects to prevent postpartum bleeding. The results are expected to be used as basic data for more advanced research, using the number of subjects a larger study and consider the factors that may be a bias in this study.

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Research Article

Basal Temperature, Cervical Mucous, and Both Combination as Diagnostic Tools to Detect Ovulation

Akurasi Suhu Basal Tubuh, Lendir Serviks, dan Kombinasi Keduanya sebagai Alat Pendeteksi Ovulasi

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Abstract

Objective: To make basal body temperature examination and cervical mucus as an alternative examination in detecting ovulation, especially in health facilities that do not have ultrasound.

Methods: This cross-sectional study was conducted at the outpatient clinic of RSUPN Dr. Cipto Mangunkusumo in the year 2016-2017. A total of 49 infertile female patients who had normal menstrual cycles were asked to participate and performed basal body temperature measurements, cervical mucus sampling and transvaginal ultrasound examination, the data are subsequently grouped into 3 Days Estimated Ovulation (DEO); DEO-2 days, DEO and DEO+ 2 days. Diagnostic tests were performed and accurate comparison between basal body temperature, cervical mucus and a combination of both were later assessed.

Results: The best accuracy was found on cervical mucus and combination of both with 65% in detecting ovulation, whilst the lowest was basal body temperature (59%) with sensitivity 46.7%, and specificity 78.9%. Cervical mucus in diagnosing ovulation has a sensitivity of 70% and specificity 57.8%. The combination of temperature-cervical mucus in diagnosing ovulation has sensitivity of 46.67% and specificity of 94.73%.

Conclusion: Cervical mucus examination has better accuracy compared with basal body temperature examination in detecting ovulation. Further research for validating these diagnostic tools to the wider community and not only in patients with infertility is needed.

[Indones J Obstet Gynecol 2018; 6-3: 162-166]

Keywords: basal body temperature, cervical mucus, infertility, ovulation detection, ultrasound

Abstrak

***Tujuan**: Untuk menjadikan pemeriksaan suhu basal tubuh dan lendir serviks sebagai pemeriksaan alternatif dalam menditeksi ovulasi terutama pada fasilitas kesehatan yang tidak mempunyai ultrasonografi.*

***Metode**: Penelitian potong lintang ini dilakukan di poliklinik RSUPN Dr. Cipto Mangunkusumo pada tahun 2016-2017. Sebanyak 49 pasien perempuan infertilitas yang mempunyai siklus menstruasi yang normal diminta untuk berpartisipasi dan dilakukan peng-ukuran suhu basal tubuh, pengambilan sampel lendir serviks dan pemeriksaan ultrasonografi transvaginal, data dikelompokkan menjadi 3 Hari Perkiraan Ovulasi (HPO) yaitu HPO-2, HPO dan HPO+2. Dilakukan uji diagnostik dan dilakukan perbandingan akurasi antara suhu basal tubuh, lendir serviks dan kombinasi keduanya.*

***Hasil**: Didapatkan hasil yang paling baik adalah akurasi lendir serviks dan kombinasi keduanya dengan hasil 65%. Dan yang paling rendah adalah suhu basal tubuh dengan hasil 59%. Dengan suhu basal tubuh dalam mendiagnosis ovulasi memiliki sensitivitas 46,7%, spesifisitas 78,9%, dan akurasi 59%. Lendir serviks dalam mendiagnosis ovulasi memiliki sensitivitas 70%, spesifisitas 57,8%, dan akurasi 65%. Kombinasi suhu-lendir serviks dalam mendiagnosis ovulasi memiliki sensitivitas 46,67%, spesifisitas 94,73%, dan akurasi 65%.*

***Kesimpulan**: Pemeriksaan lendir serviks memiliki akurasi yang lebih baik dibanding dengan pemeriksaan suhu basal tubuh dalam menditeksi ovulasi. Diperlukan penelitian mengenai validasi alat diagnostik ini pada masyarakat yang lebih luas dan bukan hanya pada kelompok yang mengalami infertilitas sehingga dapat diterapkan pada masyarakat umum.*

[Maj Obstet Ginekol Indones 2018; 6-3: 162-166]

***Kata kunci**: deteksi ovulasi, infertilitas, lendir serviks, suhu basal tubuh, ultrasonografi*

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INTRODUCTION

Infertility is one of disease problem raising awareness in developing countries. It causes both physical and psychosocial problem. The infertility prevalence in the world is estimated from 13 to 15%.[1] World Health Organization (WHO) stated that of 850 infertile couple, female, male factors, both of them contribute to 37%, 8%, and 35%; respectively. Meanwhile, the remaining (20%) is unexplained infertility. The most common female factors are ovulation abnormalities (25%), followed by endometriosis (15%), pelvic adhesion (12%), tubal occlusion (11%), other tubal problem (11%), and hyperprolactinemic (7%). Ovulation abnormalities can be caused by stress, polycystic

ovary syndrome (PCOS), hyperthyroid or hypothyroid, and others.[1]

To detect the ovulation incidence, there are several ways through indirectly methods such as calendar, hormonal assessment (LH, FSH, pregnanediol, glucuronic, estrone glucuronic, progesterone), basal temperature, cervical mucous. In addition, direct methods including ultrasound and laparoscopic are more accurate to detect it.[2-4]

The gold standard to detect ovulation is through ultrasound; however, there is another simple, cheap, and easy to use method to detect by herself, namely basal temperature assessment.[5-7] This examination is greatly influenced by hormonal change.[8] The increase of 0.2°C basal temperature occurs since the raise of progesterone level due to corpus luteum formation in ovulation.[7]

Meanwhile, another simple method to detect ovulation is through cervical mucous examination. This is widely used in natural contraception which shows highly reliable predictor.[9] Principally, low estrogen and high progesterone level approaching menstruation make cervical mucous become small amount, whitish colour, thick, and not elastic to hamper the sperm entering. On the high level of estrogen at ovulation, cervical mucous seems to be a lot, clearly colour, thin, and elastic to support sperm enter the uterine cavum; therefore, sperm is easier to fertilise ovum.[7]

Based on theory above, this study aims to assess the accuracy of basal temperature, cervical mucous, and both combination to detect ovulation. We hope that this study can become a solution to detect infertility in limited resources without ultrasound and especially for general practitioner in primary health centre.

METHODS

This cross-sectional study design was held out at gynecology polyclinic Dr. Cipto Mangunkusumo Hospital, Jakarta from December 2016 to April 2017. We recruited 18-38-year-old women, having regular menstruation cycle between 26 and 34 days since menarche or minimally in the last three cycle, normal body mass index (BMI), physically healthy, positive ovulation sign during sample taken, and willingness to participate to this study. For patients with sign and symptoms of PCOS (acne, hirsutism, oligomenorrhea, obesity) or positive finding of PCOS on ultrasound, abnormality in abdomen or ovary on ultrasound or evidence of endocrine disease or other disease influencing menstruation cycle were excluded. By calculating sample, the minimal subject was 46 women.

Flow of this study started from women fulfilling requirement would be counted for day estimated ovulation (DEO) through 14 days before next menstruation. Subjects were asked to assess the basal temperature in the morning before active during six consecutive days on the second day after the end of menstruation. Basal temperature in the morning would be recorded on DEO-2 days, DEO, and DEO+2 days by themselves using digital oral thermometer. Meanwhile, cervical mucous assessment would be determined by themselves and investigator by putting into four categories. Investigator took the sample at polyclinic Dr. Cipto Mangunkusumo hospital using speculum and taking cervical mucous to assess the amount of cervical mucous, Spinnbarkeit test, Ferning test, and Insler test. Besides, investigator performed ultrasound examination to monitor the follicle development up to rupture evidence.

The data were run into sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) analysis for each examination consisting of basal temperature, cervical mucous, and both combination by comparing with ultrasound. The ROC analysis by observing the area under curve (AUC) was analysed. We considered $p<0.05$ as significant value. This analysis was performed through Stata 12.0 for Windows©. This study has been approved by ethical committee in Dr. Cipto Mangunkusumo hospital/Faculty of Medicine Universitas Indonesia under number 994/UN2.F1/ETIK/2016.

RESULTS

There were 49 subjects recruiting to this study. Table 1 showed the demographic characteristics of participated subjects in this study.

Table 1. Demographic Characteristics of Subjects in this Study

Characteristics	n (%)
Age (y.o) (mean (SD))	29.51 (0.65)
Marital age (y.o) (median (min-max))	23 (18-33)
Menarche (y.o) (median (min-max))	12 (10-13)
Menstrual cycle (days) (median (min-max))	28 (27-34)
Body mass index (kg/m^2) (mean (SD))	21.87 (0.20)

Working	
Yes	25 (51%)
No	24 (49%)
Smoking	
Yes	8 (16.3%)
No	41 (83.7%)
Alcohol consumption	
Yes	3 (6.1%)
No	46 (93.9%)

On the basal temperature assessment, there were 18 subjects (36.7%) increasing ≥0.2°C or reaching nadir point; however, the other 31 subjects (63.3%) did not reach nadir point. Meanwhile, based on cervical mucous, there were no subjects approaching Insler score ≥10 and category 4 of Billing on DEO-2 days. There were 29 subjects (59.2%) having Insler score ≥10 and category 4 of Billing on DEO and all subjects (100%) showing Insler score ≥10 and category 4 of Billing on DEO+2 days.

Ultrasound examination showed that there were no subjects, 30 subjects (61.2%), and 49 subjects (100%) revealing ovulation sign on DEO-2 days, DEO, and DEO+2 days; respectively.

Table 2 pointed out the diagnostic test analysis of basal temperature compared with ultrasound as gold standard. The result showed the sensitivity, specificity, PPV, and NPV were 46.7%, 78.9%, 77.78%, and 48.38%; contributively. The positive possibility ratio of this examination was 2.21 and negative possibility of 0.42 with accuracy level reaching 59%.

Table 2. Diagnostic Test of Basal Temperature

		Ultrasound		Total
		+	-	
Basal Temperature	+	14	4	18
	-	16	15	31
Total		30	19	49

Table 3 showed the diagnostic test of cervical mucous compared with gold standard. Of the result, we obtained sensitivity of 70%, specificity of 57.8%, PPV of 72.4%, and NPV of 55%. Meanwhile, the positive and negative possibility ratio were 1.66 and 0.51; also the accuracy level was 65%.

Table 3. Diagnostic Test for Cervical Mucous

		Ultrasound		Total
		+	-	
Cervical mucous	+	21	8	29
	-	9	11	20
Total		30	19	49

Table 4 indicated the diagnostic test of combination between basal temperature and cervical mucous in detecting ovulation. The result showed the sensitivity, specificity, PPV, and NPV were 46.67%, 94.73%, 93.33%, and 52.94%; respectively. The positive possibility ratio of this examination was 8.86 and negative possibility of 0.56 with accuracy level approaching 65%.

Table 4. Diagnostic Test of Combination between Basal Temperature and Cervical Mucous

		Ultrasound		Total
		+	-	
Basal Temperature	+	14	1	15
and Cervical mucous	-	16	18	34
Total		30	19	49

On the discrimination test of these diagnostic tools to detect ovulation, we got that the combination of basal temperature and cervical mucous having the best area under the curve (AUC) (70.7%; 95% CI 56.3-85.1%; p=0.01). This value was better than the discrimination level showed by basal temperature of 62.8% (95% CI 47.7-80.2%; p=0.13) and cervical mucous of 63.9% (95% CI 46.9-78.7%; p=0.1)

DISCUSSION

Fitzgerald et al.[10] stated that the new pregnancy rate would decrease after 31 years old and their study was supported by George et al.[11] result. George concluded that women fecundity declined after 32 years old. Subjects in this study were still on reproductive age whereas most of them (55.1%) were less than 32 years old. Only one subject was 37 years old. In this study, there were 16.33% subjects smoking and 6.1% subjects having alcohol history. Based on systematic review and meta-analysis by Augood, et al[12], they stated that infertility risk raised on smoking women (OR 1.60; 95% CI 1.34-1.91); meanwhile, study by

Mikkelsen, et al[13] on alcoholic women, infertility risk was not influenced by alcohol drinking habit. Therefore, 16.3% subjects consuming alcohol in this study could impact to this study.

Basal temperature reflects the ovary cycle through the increase of 0.2-0.5% temperature (biphasic curve). It is caused by thermogenic effect of pregnanediol and lasted up to 14 days during luteal phase. The increase of temperature signs ovulation event.

In this study, the cervical mucous view was varied on the three day of sample taken. Cervical mucous can change on ovulation due to the drastic increase of estrogen approaching ovulation. Therefore, cervical mucous becomes a lot, thin, watery, alkali, acellular with fern, long spinnbarkeit, and acceptable for sperm. It can be recognised physically as watery and smooth sensation and clear mucous. All physical finding can be determined by Insler score and Billings category. Several literatures revealed that this method is reliable to be a diagnostic tool for detecting ovulation incidence.[14,15]

Sensitivity and specificity of basal temperature as ovulation diagnostic tools were 46.7% and 78.9% with 59% of accuracy. Compared with study by Guermandi et al.8, they obtained sensitivity of 77% and specificity of 33% with 74% of accuracy. The poor level of basal temperature sensitivity on this study was caused by ovulation was not always followed by the increase of temperature so that basal temperature could not be a reliable tool to detect the incidence of ovulation.

Variation of cervical mucous on each menstrual cycle makes this sign as predictor of ovulation. In this study, cervical mucous had sensitivity and specificity of 70% and 57.8% with accuracy reaching 65%. This assessment was cheap and not invasive so that this methods would be trained to young women hoping pregnancy. Some studies showed that this method was effective enough to detect ovulation. Alliende et al.[16] concluded that the comparison between cervical mucous and ultrasonography had sensitivity and specificity of 75.9% and 75.9%.

Combination of basal temperature and cervical mucous is a method effectively detecting ovulation and predicting fertility interval time. In this study, combination of both methods had sensitivity and specificity of 46.67% and 94.73% (65% of accuracy). Previous study by Frank-Hermann, et al.[17] concluded that this combination gave sensitivity of 89% to predict ovulation compared with ultrasound. This method became reference to avoid pregnancy with the successful rate reaching 0.3-0.5 or one unplanned pregnancy in 2 to 3 years. This combination revealed high specificity; therefore, one or both results indicated negative value, it meant there was negative result.

Of ROC curve, we obtained that combination between basal temperature and cervical mucous had the best area under curve (AUC) of 70.7% (95% CI 56.3-85.1%) followed by cervical mucous and basal temperature. Therefore, this combination of two parameters resulted better diagnostic tools to differ patients experiencing ovulation.

We recommended further investigation such as cervical mucous examination independently by women to recognise sign of ovulation and compared with gold standard tool (ultrasonography). In the end, we hope that Indonesian women can identify independently their fertility period.

CONCLUSION

Basal temperature can diagnose ovulation with sensitivity, specificity, and accuracy of 46.7%, 78.9%, and 59%; respectively. Meanwhile, cervical mucous has sensitivity of 70%, specificity of 57.8%, and accuracy of 65% to detect ovulation. Combination of both methods is capable of detecting ovulation with sensitivity, specificity, and accuracy of 46.67%, 94.73%, and 65%, respectively.

CONFLICT OF INTEREST

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Research Article

Rectovaginal Examination, Transvaginal Ultrasonography, and Magnetic Resonance Imaging as Diagnostic Tools for Identifying Deep Infiltrating Endometriosis Nodules

Rectovaginal Toucher, Ultrasonografi Transvaginal dan Magnetic Resonance Imaging sebagai Modalitas Penunjang Diagnosa Nodul Endometriosis Susukan Dalam

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Abstract

Objective: To investigate the comparison between rectovaginal examination (RVT), transvaginal ultrasonography (TVUS) and magnetic resonance imaging (MRI) as diagnostic tools for identifying various Deep Infiltrating Endometriosis (DIE).

Methods: Prospective longitudinal study was done involving 31 women referred for surgical management of DIE. Calculation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of RVT, TVUS and MRI for DIE were recorded.

Results: The mean age was 35.1 years. DIE were present in 95.45% of women which commonly located at uterosacral ligaments (58.33%), followed by rectovaginal (16,67%), rectosigmoid-colon (16.67%) and bladder-ureter (8.3%). TVUS had the best accuracy (RVT 50.24%; TVUS 88.85%; MRI 75.77%) among other diagnostic tools for nodules located at uterosacral ligaments (RVT 52.63%; TVUS 87%; MRI 40%) and rectovaginal (RVT 76.75%; TVUS 93.34%; MRI 80%), but it poorly identified nodules located at rectosigmoid (RVT 20%; TVUS 65.56%; MRI 88.75%) and bladder-ureteral area (RVT 50.44%; TVUS 87.66%; MRI 93.55%). RVT had good PPV (88.89%) but bad NPV (32.01%) profile, made it worth to be a screening diagnostic tool.

Conclusion: RVT was a good screening diagnostic tools as it could be done easily but was weak in diagnosing anterior DIE. TVUS gave a better diagnosis rates on DIE located at sacrouterina ligaments and rectovaginal area whereas MRI did better on bowel DIE (rectosigmoid-colon area) and urological DIE (bladder-ureteral area).

[Indones J Obstet Gynecol 2018; 6-3: 167-171]

Keywords: deep infiltrating endometriosis, magnetic resonance imaging, tranvaginal ultrasonography

Abstrak

***Tujuan**: Untuk mengetahui perbandingan rectovaginal toucher (RVT), USG transvaginal dan MRI sebagai penunjang diagnosis dalam mengidentifikasi Endometriosis Susukan Dalam (ESD).*

***Metode**: Sebuah studi prospektif longitudinal dengan 33 perempuan terlibat, perempuan dijadwalkan untuk menerima tindakan operasi untuk ESD. Sensitivitas, spesifisitas, nilai prediksi positif dan negatif serta akurasi dari RVT, USG dan MRI dinilai.*

***Hasil**: Rerata usia adalah 35,1 tahun. ESD ditemukan pada 95,45% perempuan, paling sering pada uterosacral ligaments (58,33%), disusul oleh rectovagina (16,67%), rectosigmoid-kolon (16,67%) dan bladder-ureter (8,3%). USG memiliki tingkat akurasi terbaik (RVT 50,24%; TVUS 88,85%; MRI 75,77%) dibandingkan modalitas diagnosa lainnya untuk nodul pada ligamentum uterosakral (RVT 52,63%; TVUS 87%; MRI 40%) dan rektovagina RVT 76,75%; TVUS 93,34%; MRI 80%), tetapi kurang baik dalam mendiagnosa nodul di rektosigmoid (RVT 20%; TVUS 65,56%; MRI 88,75%) dan area kandung kemih-ureter (RVT 50,44%; TVUS 87,66%; MRI 93,55%). RVT memiliki nilai prediksi positif yang baik (88,89%) namun nilai prediksi negatif yang rendah (32,01%), RVT dapat digunakan sebagai skreening awal diagnosa ESD.*

***Kesimpulan**: RVT dapat digunakan sebagai alat diagnosa awal karena dapat dilakukan secara mudah namun lemah dalam mendiagnosa ESD anterior. USG memberi gambaran yang baik dalam mendiagnosa ESD pada lokasi sakrouterina dan rektovagina, sedangkan MRI baik dalam mendiagnosa nodul endometriosis rektosigmoid dan kandung kemih-ureter.*

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***Kata kunci**: endometriosis susukan dalam, magnetic resonance imaging, transvaginal ultrasonography*

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INTRODUCTION

Deep Infiltrating Endometriosis (DIE) was a benign disease marked by the ectopic presence of endometrium deeper than 5 mm beneath the peritoneal surface, that infiltrated different pelvic location whether anteriorly or posteriorly.[1] It could be located anywhere including uterosacral ligaments, vagina, intestine, bladder or even ureter. As the DIE nodules were a major contribution to pain symptom for deep infiltrating endometriosis patients, radical surgical resection was the mainstay of treatment for this form of endometriosis. A proper diagnostic tools should be used in order to map the exact location of DIE

nodule, so in the time any surgical procedures occurred, all remaining nodules could be resected and complication could be avoided. Magnetic resonance imaging (MRI) and Transvaginal sonography (TVS) had been recommended for diagnosing and locating DIE. Bazot, et al[1-3] found that MRI provided a more reliable map of DIE than physical examination or TVS, but TVS and physical examination should remain the first-line technique examination, although normal finding did not rule out the diagnosis. In this study, we wanted to compare these three modalities in diagnosing DIE in various location including their strength and weakness as a consideration of their usage.

METHODS

Prospective longitudinal study was done on tertiary gynecology unit. Study was done by involving 31 women referred for surgical management of DIE between November 2015 until January 2017. All women underwent RVT and TVUS with/without additional MRI examination. Diagnostic criteria for RVT was identification of endometriotic nodules on palpation, whereas for both TVUS and MRI was based on visualization of hypointense/hypoechoic areas in specific location. Calculation of sensitivity, specificity, positive pre-dictive value (PPV), negative predictive value (NPV), and accuracy of RVT, TVUS and MRI for DIE on various sites were then recorded, with surgical/histological finding as the golden standard.

Rectovaginal Examination

Deep Infiltrating Endometriosis was diagnosed in a state when lesions were visualized on the posterior vaginal fornix during speculum insertion; or a nodule was detected on vaginal palpation examination, involving the vagina, torus uterinus, uterosacral ligaments, or pouch of Douglas; and a mass or infiltration was detected on rectal digital examination, involving the rectosigmoid colon.[1,2] All the examination were performed by experienced residents and gynecologist.

Transvaginal Ultrasonography

The TVS was performed with an GE Voluson E6 Ultrasound Machine. Each examination was interpreted directly by highly trained gynecologist sonographer with more than 10 years of experience in gynecologic imaging. DIE was diagnosed when a morphological criteria included abnormal hypoechoic linear thickening and nodules/masses with or without regular contours were found in at least one structure (uterosacral ligament, vagina, rectovaginal septum, rectosigmoid colon, or bladder).[2-4]

Figure 1. TVUS showed Deep Infiltrating Endometriosis infiltrated posteriorly until anterior rectum wall and rectovaginal

Magnetic Resonance Imaging

The MRI was done by opacification of the vagina and rectum with saline solution or sonographic jelly inside the vagina and the rectum to get better exposure of the anatomical space. No contrast was used. Each examination was interpreted by experienced radiologist. The diagnosis of DIE was based on the presence of morphologic abnormalities at posterior or anterior DIE sites. Uterosacral ligaments endometriosis was diag-nosed when a nodule was found at the site in a form of fibrotic thickening compared to the contralateral USL5. Rectovaginal septum endo-metriosis was diagnosed by a nodule passing through the lower border of the posterior cervix. Rectosigmoid colon endometriosis was diagnosed by diasapperance of the fat tissue plane and its replacement by a tissue mass.[5] Bladder and ureter endometriosis was diagnosed by appearance of nodule foci at the anatomical sites.[5]

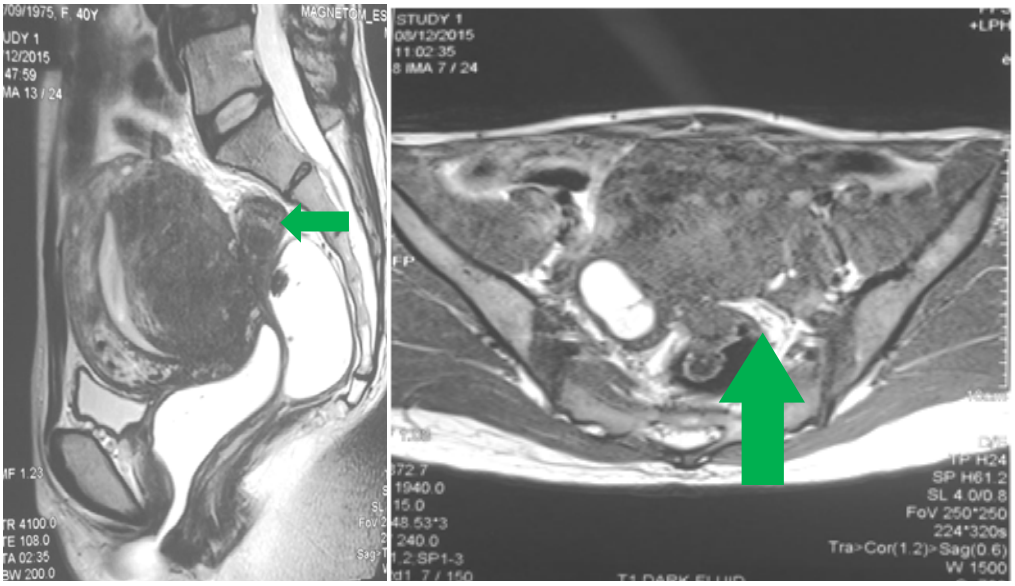

Figure 2. MRI showed adenomyosis in uterine posterior corpus, infiltrated posteriorly until anterior rectum wall into the lumen.

Surgical/Histological Finding (reference standard)

Laparoscopy was performed on every single patients include in this study. Surgical finding was based on masses visually found when the procedure occurred. All location of endometriosis were recorded on the surgical reports. Endometriosis was diagnosed histologically by the presence of ectopic endometrial tissue in a form of ectopic glands together with stroma.[6]

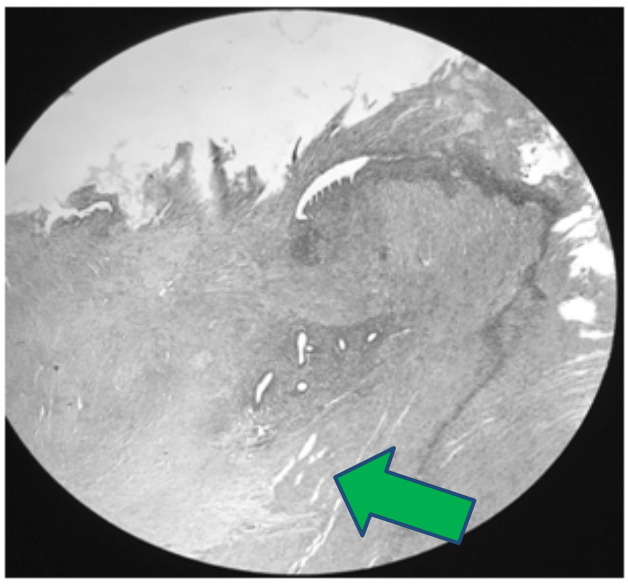

Figure 3. Histological finding of ectopic endometrial gland.

Statical Analysis

For each four location including uterosacral ligaments, rectovaginal, rectosigmoid and bladder-ureter were evaluated by comparing them with the standard reference (surgical/histological finding). The sensitivity, specificity, positive - negative predictive values, and accuracy of every modality were then recorded.

RESULT

The mean age of samples was 35.1 years. DIE distributed in different locations, but commonly found and uterosacral ligament (58.33%), whether on one side or both; followed by rectovaginal and rectosigmoid area (16.67%); lastly by bladder-ureter area (8.3%). Firstly, the overall sensitivity, specificity, positive - negative predictive values, and accuracy of every modality were recorded. The overall sensitivity of RVT, TVUS, MRI were 45.71%; 67.64%; 52.63% respectively. The overall specificity of RVT, TVUS, MRI were 50.44%; 88.03%; 95.22% respectively. The overall positive predictive value of RVT, TVUS, MRI were 88.89%; 88.46%; 83.33% respectively. The overall negative predictive value of RVT, TVUS, MRI were 32.01%; 78.88%; 85.44% respectively. The overall accuracy of RVT, TVUS, MRI were 50.24%; 88.85%; 75.77% respectively. Then, the sensitivity, specificity, PPV, NPV and accuracy on four location were recorded. Data can be seen on table 3.

Table 1. Distribution of DIE

Location	Responses	
	n	Percent
Uterosacral Ligament	14	58.33
Rectovaginal	4	16.67
Rectosigmoid Colon	4	16.67
Bladder - ureter	2	8.3

Table 2. Overall Sensitivity, Specificity, PPV, NPV and Accuracy of RVT, TVUS and MRI

	RVT %	TVUS %	MRI %
Sensitivity	45.71	67.64	52.63
Specificity	50.44	88.03	95.22
PPV	88.89	98.46	83.33
NPV	32.01	78.88	85.44
Accuracy	50.24	88.85	75.77

(0%), which means that if there was no nodule palpated at RVT examination doesn't mean that there will be no Deep Infiltrating Endometriosis. Moreover RVT can only access around vaginal and rectum part, so diagnosing Deep Infiltrating Endometriosis located at urological sites was nearly impossible. Patient with typical symptoms such as, severe dysmenorrhea, dysuria, dyschezia and dyspareunia, further examination using other diagnostic methods could be considered.

Transvaginal Ultrasonography (TVUS) was a good modality available for diagnosing deep infiltrating endometriosis as it gave a wide exposure of gynecological anatomy.[7-9] This study showed that for overall accuracy, TVUS still the best diagnostic methods (RVT 50.24%; TVUS 88.85%; MRI 75.77%). But as study went deeper, it show that TVUS was great at diagnosing DIE nodules located at uterosacral ligaments

Table 3. Sensitivity, Specificity, PPV, NPV and Accuracy of RVT, TVUS and MRI on Various Location

Location	Modality	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
	RVT	52.63	88	100	65	52.63
Uterosacral Ligaments	TVUS	73.68	99	93.33	90	87
	MRI	33.33	35	100	55	40
	RVT	55.55	80.01	71.42	76.75	76.75
Rectovaginal	TVUS	66.67	89.55	100	88.43	93.34
	MRI	50	100	100	80	80
	RVT	20	90	100	90	20
Rectosigmoid	TVUS	75	95	60	94	65.56
	MRI	100	100	66.67	100	88.75
	RVT	0	79.99	0	80.56	50.44
Bladder and Ureter	TVUS	33.3	88.87	44.5	92	87.66
	MRI	50	97.77	100	95.55	93.55

DISCUSSION

This study show that RVT, TVUS and MRI had their own roles in diagnosing Deep Infiltrating Endometriosis. RVT was a very simple examination that could be done easily in everyday practice. With high score of Positive Predictive Value (88.89%), shows that if the nodule was palpable during RVT examination, the chance Deep Infiltrating Endometriosis mass was high, but on the other hand RVT shows a very low Negative Predictive Value

(RVT 52.63%; TVUS 87%; MRI 40%) and rectovaginal. (RVT 76.75%; TVUS 93.34%; MRI 80%), but lack of strength at diagnosing rectosigmoid (RVT 20%; TVUS 65.56%; MRI 88.75%) and bladder-ureter DIE (RVT 50.44%; TVUS 87.66%; MRI 93.55%). But still TVUS gave better perception of DIE than RVT itself.

As stated on the previous line, Magnetic Resonance Imaging (MRI) provided better diagnostic rates on bowel (RVT 20%; TVUS 65.56%; MRI 88.87%) and urological (RVT 50.44%; TVUS

87.66%; MRI 93.55%) endometriosis. Bowel endometriosis was one of the most severe forms of DIE.[1] With accurate preoperative diagnosis, mapping of the nodule could be done, and best procedure could be performed. It was also crucial for informing women on the specific risks of surgery for example colorectal resection.[10] Various features of colorectal endometriosis can influence surgical management, such as the degree of rectal wall infiltration, the size of the rectal lesion, the distance from the anal margin and the possible association with other endometriotic lesions.[10] Although urological endometriosis cases were rare, only for about 1-2% of all endometriosis cases, the side effects occurred were devastating. Silent hydronephrosis or even silent loss of kidney secondary to urological endometriosis could happen whether in a form of blocking mass or ureter stricture mimicry.[11,12] MRI gave better mapping on both sites, providing better prognosis for bowel and urological DIE patients.

CONCLUSION

Early diagnosis of pelvic endometriosis, and especially DIE, even though was a major challenge, but it could help to avoid mutilating surgery, improved quality of life, and enhanced fertility.[12] RVT should be done in daily examination on endometriosis patient but weak in diagnosing anterior DIE. TVUS gave a better diagnosis rates on DIE located at sacrouterine ligaments and rectovaginal area whereas MRI did better on bowel DIE (rectosigmoid-colon area) and urological DIE (bladder-ureteral area).

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Research Article

Compatibility between Menstrual Pictogram Assessment and Haemoglobin Assessment in Abnormal Uterine Bleeding

Uji Kesesuian Pemeriksaan Piktogram Menstruasi dengan Pemeriksaan Hemoglobin pada Pasien Perdarahan Uterus Abnormal

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Abstract

Objective: To determine the amount of wasted blood and diagnosed AUB and determine amount of decrease in haemoglobin levels by adjusting the examination of menstrual pictogram with haemoglobin.

Methods: Diagnostic test was conducted in the Department Obstetrics and Gynecology Dr. Mohammad Hoesin/Faculty of Medicine Universitas Sriwijaya Palembang, start from January 2015 through January 2017. Sample was obtained from 39 patients with abnormal uterine bleeding who meet the inclusion and exclusion criteria. Frequency and distribution of data are described in tables and cross analyze (cut-off point) to find cut points difference menstrual pictogram and a decrease in haemoglobin levels using ROC curve. Accuracy is measured by the value of Kappa. Data analysis using SPSS version 21.

Results: From 39 samples that obtained, majority characteristics age > 35 years (59%), ideal BMI (59%) and multiparous (48.7%). From statistical analysis, there was significance association between haemoglobin measurement tools and menstrual pictogram (p = 0.063). Both measuring devices have compatibility in predicting the type of AUB (p = 0.047), with the degree of conformity is weak (Kappa = 0.232).

Conclusion: Accuracy of menstrual pictogram examination and haemoglobin has a weak degree of conformity, so menstrual pictogram examination can't be used to determine a decrease in haemoglobin levels. Menstrual pictogram menstruation only used as an evaluation of therapeutic response.

[Indones J Obstet Gynecol 2018; 6-3: 172-178]

Keywords: abnormal uterine bleeding, haemoglobin, menstrual pictogram

Abstrak

***Tujuan**: Untuk mengetahui jumlah darah yang terbuang dan dapat menegakkan suatu diagnosis PUA dan mengetahui jumlah penurunan kadar hemoglobin dengan cara menyesuaikan pemeriksaan piktogram dengan pemeriksaan hemoglobin.*

***Metode**: Uji diagnostik ini dilakukan di Departemen Obstetrik dan Ginekologi RSUP Dr. Mohammad Hoesin/Fakultas Kedokteran Universitas Sriwijaya Palembang mulai Januari 2015 sampai Januari 2017. Didapatkan sampel sebanyak 39 pasien perdarahan uterus abnormal yang memenuhi kriteria inklusi dan eksklusi. Frekuensi dan distribusi data dijelaskan dalam bentuk tabel dan dilakukan analisis titik potong (cut off point) untuk mengetahui titik potong selisih piktogram dan penurunan kadar hemoglobin menggunakan kurva ROC. Nilai akurasi diukur dengan nilai Kappa. Analisis data menggunakan SPSS versi 21.*

***Hasil**: Dari 39 sampel didapatkan mayoritas memiliki karakteristik berusia > 35 tahun (59%), IMT ideal (59%) dan multipara (48,7%). Dari analisa statistika adanya hubungan signifikan antara alat pengukuran hemoglobin dan piktogram (p = 0,063). Kedua alat ukur memiliki kesesuaian dalam memprediksi jenis PUA (p = 0,047), dengan derajat kesesuaian lemah (Kappa = 0,232).*

***Kesimpulan**: Akurasi pemeriksaan piktogram dan pemeriksaan hemoglobin memiliki kesesuaian lemah, sehingga pemeriksaan piktogram ini tidak dapat digunakan untuk mengetahui penurunan kadar hemoglobin. Piktogram menstruasi hanya dapat digunakan sebagai evaluasi respon terapi.*

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***Kata kunci**: hemoglobin, perdarahan uterus abnormal, piktogram menstruasi*

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INTRODUCTION

Abnormal uterine bleeding includes all of the menstrual abnormalities both in amount and duration. Clinical manifestations may be a lot or a little bleeding, elongated or irregular menstrual cycles. This terminology is replaced by the current menorrhagia, which is a lot menstrual bleeding or heavy menstrual bleeding (HMB) where the amount of bleeding of > 80 ml during the menstrual cycle and blood only contribute as much as 50%. While abnormal uterine bleeding caused by coagulopathy factors, local hemostasis disorders endometrium and ovulation disorders that were previously included in dysfunctional uterine bleeding (DUB).[1-3]

Based on the HIFERI consensus (2013) in Bogor, it has been agreed that the definition of normal menstruation is a physiological process which occurs bleeding, mucus and cellular debris from the uterus periodically at regular intervals that occurred since menarche to menopause with the exception of pregnancy and breastfeeding, which is the result of harmonic regulation of hormonal organs.[2,4,5]

Based on International Federation of Gynecology and Obstetrics (FIGO) there are nine major categories were prepared in accordance with the acronym "PALM-COEIN".The classification system is based on the consideration that a patient may have one or more factors causing abnormal uterine bleeding. With this approach, management for AUB patients can be more comprehensive.[1,2,6-9]

Management of abnormal uterine bleeding in general, doctor needs to take account into age, marital status, fertility, weight, type and duration of bleeding, underlying disease and prognosis.[10,11]

First treatment for abnormal uterine bleeding is stabilized the patient, cessation of bleeding using sex steroid hormones (estrogen, progestin and androgen), inhibitors of prostaglandin synthesis, antifibrinolytic and operative treatment.[3,4,7,10]

To determine the severity of bleeding in a clinical examination is often difficult. For example, some studies have reported a lack of correlation between the patient's perception of the amount of bleeding by the amount obtained from objective calculation. When the method of estimation is subjectively compared to the objective, 38-76% of women who suffer from menorrhagia obtained from objective estimation method. Many factors influence the patient's perception of the amount of bleeding, among others, menstruation duration, age, number of used pads, amount of blood loss and circumstances that may affect the amount of blood loss. Higham and Shaw stated that there's a relationship between height, age, parity and the amount of bleeding, but still needed an objective measurement.[12]

Another method to estimate the amount of blood loss can be done by estimating the amount and type of pads used by a woman during menstruation This chart is called the Pictorial Blood Assessment Chart (PBAC) was first introduced by Higham et al. in 1990 in the form of visual inspection with a value of scoring. Total score more than 100 points each menstrual cycle, meaning the loss of the amount of bleeding more than 80 ml. Validity of PBAC has been studied, debated and reported that the study had a 86% sensitivity and specificity of 89% and had been observed that 74% of anaemia caused by menorrhagia.[12-14]

Janssen et al. modify PBAC techniques to create a menstrual pictogram or scale of "bleeding" by calculating the number of millilitres of blood was found in sanitary napkins, tampons, blood clots and spots of blood on the underwear. Menstrual pictogram have a higher accuracy rate than the PBAC for every shape and size have different numbers of absorption pads. These menstrual pictograms were developed to create a simulation by performing dilutions balanced between blood whole blood and 0.9% saline solution and using "Kotex" branded pads, day and night type.[12,15,16]

Month: _____

	Pads			Tampons			Clots		Flooding	Score
Date	Light (1 pt each)	Medium (5 pts each)	Heavy (20 pts each)	Light (1 pt each)	Medium (5 pts each)	Heavy (10 pts each)	5 cent size (1 pt each)	50 cent size (5 pts each)	1 pt each episode	
1										
2										
3										
4										
5										
6										
7										
8										

PBAC Scoring System

Pads		
1 point	For each lightly stained pad	
5 points	For each moderately stained pad	
20 points	For each completely saturated pad	
Tampons		
1 point	For each lightly stained tampon	
5 points	For each moderately stained tampon	
10 points	For each completely saturated tampon	
Clots/Flooding		
1 point	For each small clot (Australian 5 cent coin)	
5 points	For each large clot (Australian 50 cent coin)	
5 points	For each episode of flooding	

Figure 1. Pictorial Blood Assessment Chart (PBAC)

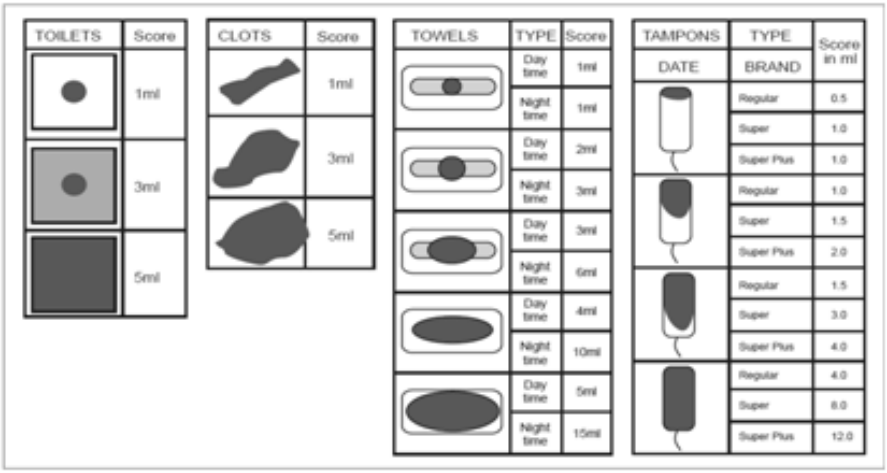

Figure 2. Menstrual Pictogram

METHODS

This study is a diagnostic test with an observational analytic design performed on 39 women with abnormal uterine bleeding. This research was conducted in Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Hospital, Palembang during January 2015 - January 2017. Inclusion criteria were patients diagnosed with AUB, not being pregnant, not undergoing treatment of infertility, and willing to participate in the study and signed informed consent.

Patients who refused to participate in the study, history of surgical uterine (<6 weeks), complication with other diseases (kidney, liver, hypertension, cancer, diabetes mellitus, ectopic pregnancy), hemodynamically unstable, were excluded from the study.

All patients who met the inclusion criteria then collected basic data including: identity, gestational age, parity, the first day of last menstrual period (LMP), reproductive status physical examination, gynecology and laboratory tests. Then patient is given a branded napkin "kotex" (day and night type) and was given a menstrual pictogram chart that has been taught how to fill it out and still be evaluated by researchers. After seven days (depending on the state of the patient) re-evaluation carried out by way of summing over the use of pads and a blood clot and conduct laboratory tests.

Data were analysed using SPSS software version 21.0; descriptive data will be analysed using Fisher exact test, the cut off point inspection of menstrual pictogram and haemoglobin will be displayed through the image of the curve Receiving operating characteristic (ROC), sensitivity, specificity, and to assess the degree of compliance with Kappa test.

RESULTS

The demographic characteristics of the study sample are presented in Table 1. Table 1 Based note that the majority of the sample has characteristic aged > 35 years (59%), ideal BMI (59%), multiparous (48.7%).

Table 1. Demographic Characteristics (n = 39)

Characteristics	n	%
Aged (year)		
< 25	3	7.7
25-35	13	33.3
> 35	23	59
	38.2 ± 1.107	
IMT		
< Underweight	4	10.3
Ideal	23	59
> Overweight	12	30.8
	22.5794 ± 3.51335	
Parity		
Nullipara	15	38.5
Primipara	5	12.8
Multipara	19	48.7
Diagnosis		
PUA ec PALM COEIN	39	100

Compliance Pictogram Assessment and Haemoglobin Assessment in AUB Patients

Table 2 showed no significant relationship between haemoglobin measurement tools and pictograms (p = 0.063). However, the second measuring instrument has its suitability in predicting the type of AUB (p = 0.047), with the degree of conformity is weak (Kappa 0.232).

Table 2. Compliance Pictogram Assessment and Haemoglobin

AUB	Hb≤1.35		Hb>1.35	
	n	%	n	%
Pictogram ≤ 678	3[a]	12.5	6[b]	35.29
Pictogram > 678	21[c]	87.5	9[d]	52.94
	24	100	17	100

Fisher exact test, p = 0.063
Kappa test = 0.232; p = 0.047

Table 2 shows as much as 65.4% (a + d) examination gives the same results (concordance). While as much as 122.79% (b + c) give different results (Discordant). Compliance of examination is not 65.4%, due to the conformity is bias. After correction of accidental factors, researchers obtained pure conformity (Kappa value) of 0.23158. Because the researchers wanted a minimum Kappa was 0.46, the examination pictogram with haemoglobin is weak, so these tests can not be used to determine a decrease in haemoglobin levels in AUB patients.

Analysis of Accuracy or Compliance Pictogram Examination with Haemoglobin

ROC analysis on Haemoglobin difference with AUB, Haemoglobin difference is not significant in predicting the occurrence AUB with p = 0.054. Difference in haemoglobin cannot be used as single predictor of AUB.

The cut off point difference in haemoglobin in AUB patients, where a decrease in haemoglobin of 1.35 able to predict AUB events with 0.818 sensitivity and specificity of 0.5.

ROC analysis a pictogram difference in the incidence of PUA, pictogram difference was not significant in predicting the occurrence AUB with p = 0.087. Pictograms difference can not be used as a predictor of AUB. The cut off point of difference pictograms in AUB patients, as the reduction of 678 pictograms able to predict AUB with specificity and sensitivity 0.394 and 0.667.

DISCUSSION

Abnormal uterine bleeding (AUB) is defined as an increase in menstrual frequency, duration or amount of blood loss. Abnormal uterine bleeding may be caused partly by the growth of neoplasms, hormone dysfunction, trauma, infection, coagulopathy, and complications of pregnancy.[7,17]

In this study, the largest age group is > 35 years (59%), followed by the age group 25-35 years (33.3%), then <25 years (7.7%). The incidence of AUB 19.1% of all visits for gynecological cases, about 10-30% women in reproductive age and over 50% of perimenopausal women (Haynes, 1977). Research conducted by Harlow et al. on menstrual cycle length, reveals that the number of population variability menstrual cycle length immediately after menarche and just before menopause. According to Jukic et al., age is a major factor that led to changes in the length of the menstrual cycle. Cycles will be shorter at the time between early menopause and then in the mid to late menopausal transition. Meanwhile, according to Deligeoroglou et al., in adolescence, prevalence is ~ 20%, the primary mechanism involved is anovulation, due to lack of maturation of the hypothalamic-pituitary-gonadal.[18-21]

In this study, incidence AUB affected most to the ideal BMI (59%), while IMT > average (30.8%). Results of this study is together with Beno et al., 2010, which found that there is a relationship between overweight and dysfunctional uterine bleeding (DUB) (p: 0.024), but after the test statistics, variable parity does not have a significant effect on the occurrence of DUB (p for bivariate and multivariate > 0.05).[22-25]

Most parities in this research were multiparas 19 (48.7%). Rifki et al. showed that of the 51 cases studied, parity observed in multiparous women with as many as 34 (66.67%). Ichimura et al., shows nullipara women have a high risk for the occurrence of uterine myoma, whereas multiparous women have decreased relative risk for the occurrence of uterine myoma. In multiparous with children, more than five are at risk only 0.2% for uterine myoma. According to Munro et al., 2011, endometrial polyp, are common benign lesions, asymptomatic pathogenesis, but can also contribute to a regular menstrual or abnormal uterine bleeding.[7,18]

Uterine adenomyosis usually occurs in older age compared with uterine myoma, which is between 40-50 years. The incidence is not related to parity. More than 80% of women with uterine adenomyosis have other pathological processes in the uterus; 50% of patients with uterine myoma, an estimated 11% with endometriosis cyst, and 7% of cases with polyps. Bird et al. reported on the case of uterine adenomyosis 51.2% of patients complained a lot of bleeding, 10.9% irregular bleeding, dysmenorrhea 28.3%, 2.2% and 23.9% asymptomatic postmenopausal bleeding.[7,18]

The incidence of uterine myoma in women is estimated 20-25%, up to 70-80% in studies using the histopathological examination and ultrasonography. Ichimura et al., ovarian hormone believed to stimulate uterine growth due to an increased incidence after menarche and pregnancy is greater tumour growth but decreases after menopause. Farrer-Brown et al. showed that the most important cause of bleeding is the presence of endometrial ectasiavenules. Myoma is in the myometrium causing obstruction and proximal venous congestion in the myometrial and endometrial. Vein thrombosis and shedding were aetiology of bleeding in the endometrium.[17,26,27]

Brech et al., suggests a correlation between the severity of bleeding manifestations with a surface area of the endometrial. Along with a surface area of endometrial bleeding, the endometrium trigger local hyperestrogenism conditions in the area immediately adjacent to submucousmyoma, endometrial hyperplasia and endometrial polyps will often be found.[27]

Coagulopathy terminology used for systemic hemostatic abnormalities associated with PUA. According to Munro et al., 13% of women with menstrual bleeding has many systemic hemostatic disorders, and the most common is von Willebrand disease. Ovulatory dysfunction usually occurs in adolescent women, women with polycystic ovarian syndrome, hyperprolactinemia, hypothyroidism, obesity, weight loss, anorexia, excessive exercise or in perimenopause. Usually irregular bleeding, prolonged or shorter cycle with minimal bleeding.[7]

Counting the number of sanitary products is accurate method to measure blood loss during menstruation and also establishes the diagnosis HMB. Barr and Janssen et al., comparing the levels of haemoglobin women with menstrual blood loss, measured by the alkaline hematin method as the gold standard, obtained anaemia by 74%, while, hematocrit, serum iron and protoporphyrin that is inversely proportional to the amount of menstrual blood loss. Burnet et al., (2010) inaccuracies haemoglobin level with alkaline hematin technique, the accuracy rate is only 17% of the 166 research subjects. Chudnoff et al., (2010) menstrual pictogram examination and haemoglobin (alkaline hematin) are not accurate, because the low value of scoring bleeding on pictogram, causing false negative or false positive. In this study, 3 false negatives (3/23; 13.0%) and 1 false positive (1/23; 7.7%) of the 166 research subjects.[28-31]

This study is a clinical trial to determine the suitability pictogram and haemoglobin examination by measuring the amount of bleeding seen from the use of pads and given the least reference menstrual pictogram research in Indonesia. In this study, the *gold standard* could not be determined, because the examination of pictogram and haemoglobin has low sensitivity and specificity as well as compliance so it can't be used as gold standard.

There are no studies that determine the AUB by a decrease in haemoglobin levels with pictogram, this is the first study that tried to find the cut off point decreasing in haemoglobin levels and a pictogram to uphold the AUB diagnosis. However, this study proved that the haemoglobin or pictogram give a weak predictive value, so we need further research is good with more samples or other laboratory assessment criteria.

From ROC assessment, we obtained haemoglobin decline in predicting the AUB at 0.750% (good), although it can't be used because of no significance ($p = 0.054$). This is due to a decrease in haemoglobin is determined by the amount of bleeding in patients with AUB, while bleeding on the AUB depend on the AUB degree itself. There are no studies that examined the sensitivity and specificity of haemoglobin or pictogram. The importance of this study is as long as there is no clear limit to determine a diagnosis and determine AUB by haemoglobin decreased levels of haemoglobin by the pictogram. Nevertheless, the authors recognize that there are still many shortcomings in this study. The big difference in the results may be caused by several factors that can lead to bias in the form of the number of small samples, the accuracy of which is

used at the time of haemoglobin, the assessment of blood on the pads and form blood clots, intravenous fluids, diet, blood transfusion, as well as the body's response to bleeding/anemia. Future research may use a larger number of samples that include AUB broad patient population to provide valid results.

CONCLUSION

We found weak significance conformity between pictogram inspection with haemoglobin examination. Menstrual pictogram is not a suitable method for predicting a decrease in haemoglobin in an AUB patient population.

RECOMMENDATION

Further research is needed regarding the accuracy of the menstrual pictogram examination and haemoglobin by increasing the number of population and sample a larger scale and bias control.

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Research Article

Changes in Cortisol Levels before and after Supportive Psychotherapy in Patients with Comorbid Cervical Cancer Distress with Depression Type

Perubahan Kadar Kortisol sebelum dan sesudah Psikoterapi Suportif pada Pasien Kanker Serviks dengan Komorbiditas Distres Tipe Depresi

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Abstract

Objective: To prove the success of supportive psychotherapy that was provided as a distress therapy on advanced cervical cancer. Knowing the prevalence of distress type of depression in patient with epithelial cervical cancer, proving the benefits of psychotherapy supportive for distress can decreasing cortisol level in cervical cancer patient, can assess distress thermometer score, HAM-D17 score and scoring incident predictors of distress with depression type.

Methods: There were 32 subjects from 71 advanced cervical cancer patients had mild-moderate depression. Then randomization blocking was performed to determine a subject who entered the treatment group (n = 16) who got supportive psychotherapy or control group who got common psychotherapy (n = 16). All of participants assessed the distress level with cortisol value, distress thermometer score, and HAM-D17 score before and after they got supportive psychotherapy.

Results: After the intervention of psychotherapy in the treatment group decreased HAM-D17 score, the average decline 7.53 (SB 3.34). The mean decreasing in the control group was 3.98 (SB 2.85). There is a significant difference in mean reduction in HAM-D17 scores on treatment and control groups with p = 0.003 (p <0.005). There was decreasing blood cortisol level in the treatment group amounted to 39.43, while the control group there was a drop of 1.59. The reduction of cortisol level in the treatment group and the control has a p-value 0.302. After got supportive psychotherapy, found a decreasing the average value of the thermometer distress in the treatment group 3.02 and the control group 2.51, with a p value more than 0.492.

Conclusion: There were 45% of cervical cancer patients in the clinic experiencing distress disorder with depressive type. The blood cortisol level could be decreased by giving supportive psychotherapy with a mean decrease of 39.43 nmol/l. There was a significant reduction in the level of depression (HAM-D17 score) of 7.53 points and distress thermometer impairment by 3 points after given supportive psychotherapy. Obtained scoring predictors for the occurrence of distress type of depression in patients with advanced cervical cancer with a sensitivity of 46.15% and a specificity of 89.47%.

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Keywords: cervical cancer, cortisol, distress, distress thermometer, HAM-D17 score

Abstrak

***Tujuan**: Untuk membuktikan keberhasilan psikoterapi suportif yang diberikan sebagai terapi distress pada kanker serviks stadium lanjut. Mengetahui prevalensi distress tipe depresi pada pasien kanker serviks epitelial, manfaat psikoterapi suportif terhadap distress pasien kanker serviks stadium lanjut dalam menurunkan kadar kortisol, nilai thermometer distress, nilai HAM-D17 dan scoring predictor terjadinya distress tipe depresi pada pasien kanker serviks stadium lanjut.*

***Metode**: Didapatkan 32 subjek penelitian dari 71 pasien kanker serviks stadium lanjut yang memenuhi kriteria inklusi (45%) yang mengalami distress sedang-berat tipe depresi ringan-sedang dan selanjutnya dilakukan randomisasi blok untuk menentukan subjek yang masuk kelompok perlakuan (n=16) dan kontrol (n=16). Sampel penelitian akan diberi penerangan terlebih dahulu dan bila sudah dapat dimengerti dan dipahami maka pasien diminta untuk menandatangani lembar persetujuan. Setelah pasien menyetujui untuk ikut serta dalam penelitian, selanjutnya pasien akan dinilai tingkat distress dengan kadar kortisol, nilai thermometer distress, dan nilai HAM-D17 sebelum dan sesudah psikoterapi suportif.*

***Hasil**: Setelah dilakukan intervensi psikoterapi pada kelompok perlakuan terjadi penurunan skor HAM-D17, rerata penurunannya 7,53 (SB 3,34). Rerata penurunan pada kelompok kontrol 3,98 (SB 2,85). Terdapat perbedaan yang bermakna penurunan rerata skor HAM-D17 kelompok perlakuan dan kontrol dengan nilai p=0,003 (p<0,005). Terdapat penurunan kadar kortisol darah pada kelompok perlakuan sebesar 39,43 sedangkan pada kelompok kontrol terdapat penurunan sebesar 1,59. Penurunan kadar kortisol pada kelompok perlakuan dan kontrol ini memiliki nilai p 0,302. Setelah diberikan psikoterapi suportif, didapatkan penurunan rerata nilai thermometer distress pada kelompok perlakuan sebesar 3,02 dan pada kelompok kontrol sebesar 2,51 dengan nilai p lebih dari 0,492.*

***Kesimpulan**: Terdapat 45% pasien kanker serviks di poliklinik yang mengalami gangguan distress tipe depresi yang bermakna, penurunan kadar kortisol darah sesudah diberikan psikoterapi suportif dengan rerata penurunan sebesar 39,43 nmol/l pada penderita kanker serviks yang mengalami distress tipe depresi, penurunan bermakna tingkat depresi (skor HAM-D17) sebesar 7,53 poin sesudah diberikan psikoterapi suportif pada penderita kanker serviks yang mengalami distress tipe depresi, penurunan nilai thermometer distress sebesar 3 poin sesudah diberikan psikoterapi suportif pada penderita kanker serviks yang mengalami distress tipe depresi dan didapatkan skoring prediktor terjadinya distress tipe depresi pada pasien kanker serviks stadium lanjut dengan sensitivitas 46,15% dan spesifisitas 89,47%.*

[Maj Obstet Ginekol Indones 2018; 6-3: 179-187]

***Kata kunci**: distress, kanker serviks, kortisol, skor HAM-D17, thermometer distress*

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INTRODUCTION

The majority of cancer patients experience distress condition caused by the cancer itself and treatment they are going through. Research shows 20-40% of cancer patients experience meaningful distress.[1] The prevalence of distress in gynecological cancer patients is around 30%. Research on patients being treated at the hospital showed a high incidence of either depression (20-45%) or delirium (increased from 15% to 75% due to the increasing severity of the disease).[1]

The most gynecological cancer in Indonesia is cervical cancer. Problems faced by patients ranging from cervical cancer-related disease such as vaginal bleeding, pelvic pain, smelly vaginal-discharge until sexual relationship problems which probably felt until died. All of these problems will lead to a meaningful distress of her life. Definition of distress in cancer patients is an uncomfortable multifactorial emotional experience that either comes from psychological problems or social/spiritual/religious problems that could interfere with their ability to face cancer, physical symptoms and the cancer therapy itself effectively (NCCN).[1,2] The use of the word distress selected by the NCCN aims to eliminate or reduce the stigma attached to such words like psychiatric, psychological, or emotional.[1,2] Screening and identification of psychological distress in the early presence of distress would make the management become more effective and therefore could improve the quality of cancer care management and improve the survival.[1,2] NCCN (*The National Comprehensive Cancer Network*) recommends distress screening to all cancer patients, psychosocial therapy integration and the development of a treatment plan with referral to the psychosocial management center if needed into a routine cancer therapy in all cancer patients.[1]

NCCN recommends the use of distress thermometer to identify the presence of distress. Distress thermometer is a tool similar to the initial screening scale of measurement for pain: a value of 0 (no distress) up to a value of 10 (the most severe distress). In this study, the results of measurements of the distress thermometer are grouped into three groups namely the values 1-3 as a group of mild distress, 4-6 as a moderate distress group and 7-10 as a severe distress group. The current use of the distress thermometer has been used widely in integration of psychiatric counseling and psychosocial therapies into a better comprehensive service or hospitality for cancer patients.[1,3]

In addition to assessing distress condition, there is laboratory examination of cortisol, which is often known as the *stress hormone* which is the organism's response to stress and anxiety/restlessness.[4] Cortisol is a hormone that is released through the glucocorticoid mechanism along the Hypothalamus-Pituitary-Adrenal (HPA) axis as a response to inflammation (Rhen and Cidlowski, 2005), stress and other stimulus (Chrousos and Gold, 2005) which roled as a regulator in important metabolic functions.[5] Dallman, Tsigos, Chrousus, et al conclude cortisol level influenced by circadian cycles (diurnal rhythm) with the highest level in the morning and continues to diminish throughout the afternoon and evening and reached a nadir when the middle of the night.[4,5] As a response of the body to face with the stress then the suprachiasmatic neurons in the hypothalamus secretes Corticotrophin-Releasing Hormone (CRH), which will further stimulate the secretion of Adreno-Corticotropic Hormone (ACTH) released from the pituitary which will eventually stimulate the adrenal cortex to release cortisol. Then negative feedback mechanism would happen by which cortisol would suppress the production of CRH and ACTH in hypothalamus and hypophysis. But in certain circumstances such as chronic inflammatory and cancer, found negative feedback is not well response so that diurnal cortisol rhythm disorder would happen.[6]

Zhang et al. declared glucocorticoid would stimulate gene expression of anti-apoptosis and act as antagonistic toward cytotoxic capability against epithelial cancer cells (solid tumors).[7] Volde and Conzen found cortisol/glucocorticoids would inhibit the process of apoptosis in breast, cervical and ovarian cancer cells.[6] In vitro model of ovarian cancer, cortisol can cause effects obtained by catecholamine; ability of tumor invasion (Nakane et al, 1990; Sood et al 2006), improved regulatory factors such as VEGF angiogenic-pro (Lutgendorf et al., 2003) and the expression of matrix metalloproteinase (Lutgendorf et al, 2008).[8,9] Abercrombie et al. discovered that breast cancer patients with more advanced stages would have higher average cortisol level than patients with earlier stage and Sephton et al. also discovered the existence of the curve cortisol more ramps.[8]

A research in the relationship of diurnal cortisol level and survival in epithelial ovarian cancer patients revealed that an increasing one standard deviation of the cortisol level is associated with an increased risk of death of 46% and at group that have higher level of cortisol have a survival average 3.3 years whereas in the group who have lower cortisol level have a survival average of 7.3 years. And that's the important rationale of why the psychotherapy becomes an important basis - because it attempts to decrease the cortisol level.

Stommel et al. reported cancer patients with a history of depression would have the risk of death 2, six times in the first 19 months after initial diagnosis of depression found. Faller et al. conducted a study on 103 cancer patients, demonstrated the state of depression that also related to decreased survival time. With regard to the potential direct impact on survival, the depression that arises would make a decrease in compliance against therapy, extended hospital care time, reduced the quality of life and ability to take care of themselves.[10]

While the definition of depression itself is a mood disorder characterized by the presence of abnormality in the mood, impaired psychomotor, impaired cognitive function and biorhythms disorders. Then to make diagnosis of depression using the diagnostic criteria for major depressive disorder based on DSM-V (Diagnostic and Statistical Manual of Mental Disorders Fifth edition) as a censorship.[10] RSCM used screening diagnosis of depression according to SCID (Structured Clinical Interview for DSM)-I Indonesian version January 2000 v1.01. And proceed using the Hamilton Psychiatric Rating Scale for Depression (HAM-D17) as a tool to ensure the diagnosis of depression, assessing the success of therapy and categorizing depression scale based on score/total value calculated. HAM-D17 scale is a scale often used in clinical research as a golden standard.

Other scales than HAM-D17 are Montgomery-Asberg Depression Rating Scale (MADRS), the Beck Depression Inventory (BDI), the Zunf Self-Depression Rating Scale, the Wechsler Depression Rating Scale, the Raskin Depression Rating Scale, and others.

METHOD

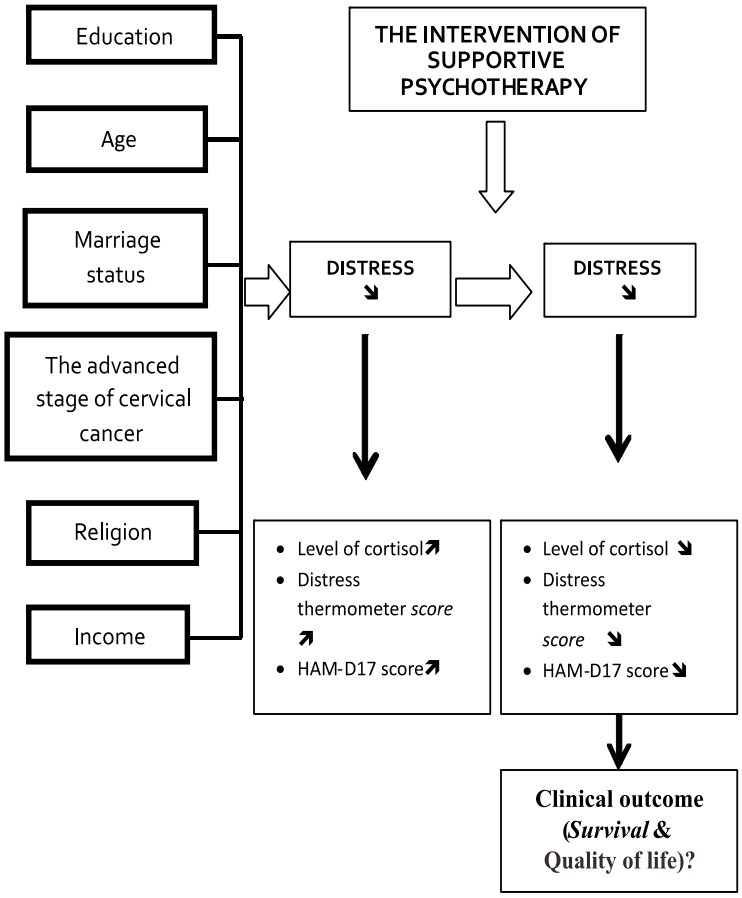
This study was a clinical trials/randomized experimentsubtle parallel design. The intervention group was invasive cervical cancer epithelial type advanced stage (IIB - IVB) who have experienced distress level of moderate to severe depression-type with mild-moderate who get special Psychotherapy/supportive Psychotherapy (Department of Psychiatry). The comparison group is invasive cervical cancer epithelial type advanced stage (IIB - IVB) who have experienced distress level of moderate to severe depression-type with mild-moderate who get Psychotherapy (Gynecologic Oncology Division). Determination of the distress level based distress thermometer which is determined by patients themselves with the explanation by Obstetrics and Gynecology doctor. In this study the results of measurements of the distress thermometer are grouped into three groups namely the values 1-3 as a group of mild distress, the values 4-6 as distress groups and the values 7-10 as heavy distress group. In addition to the distress thermometer also added a questionnaire in the form of a list of 35 problems to help patients identify their problem quickly into five different categories: practical daily life issues, family problems, emotional problems, spiritual/religious problems and physical problems. The assessment and determination of the type of depression and distress degree of depression were done by a psychiatry doctor. The diagnosis of depression screening used by RSCM is SCID (Structured Clinical Interview for DSM)-I version the language Indonesia January 2000 v1.01. Then proceed with using the Hamilton Psychiatric Rating Scale for Depression (HAM-D17) as a tool to ensure the diagnosis of depression, assessing the success of therapy and categorize the light weight depression based on score/total value that calculated. Category of the depression degree based on HAM-D17 is normal when the value 0-7; mild depression when the value 8-13; depression are when the value of 14-18; severe depression when the value of 19-22. Inspection and measurement of patient's blood cortisol level conducted by the Biochemistry Laboratory Medical Faculty, University of Indonesia in Jakarta. Then the General Psychotherapy conducted in Gynecologic Oncology Division Clinic and Special Psychotherapy conducted in the Adult Psychiatry Polyclinic Department of RSUPN Dr. Cipto Mangunkusumo. Determination of the sample is randomized in sealed envelope.

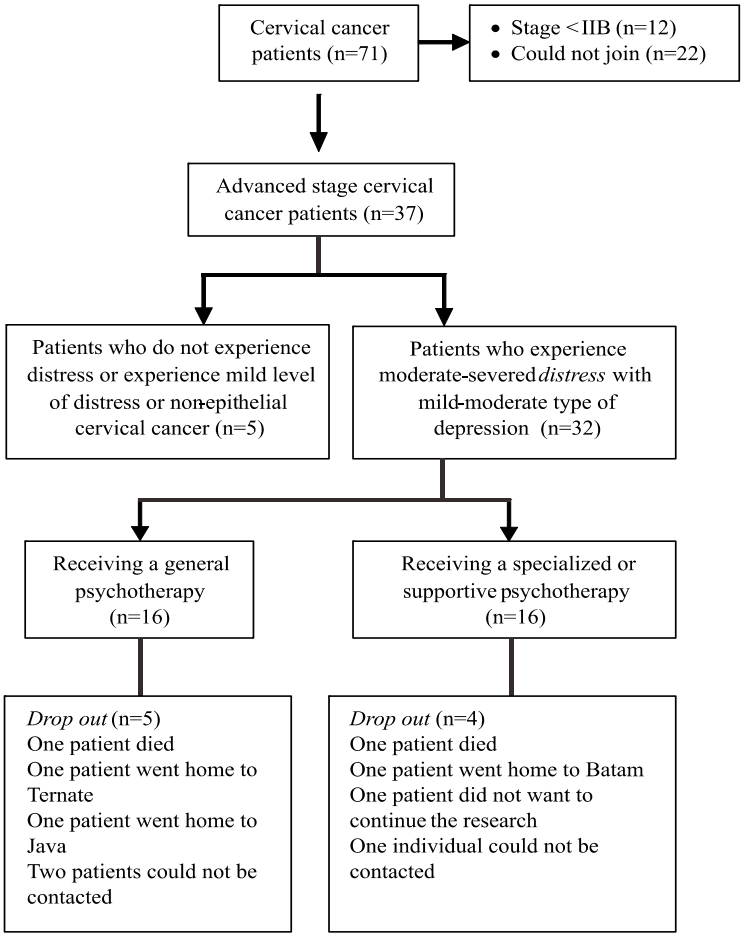
The inclusion criterion is cervical epithelial cancer patients with advanced stage (Stage IIB - IVB) who are willing to participate in as a subject of research. Whereas the exclusion criterions are neuroendocrine type of cervical cancer, cervical cancer in pregnancy and cervical cancer patients who experience severe depression type of distress.

Some of the variables examined in this research include independent variables such as; age, education, marital status, advanced stage of cervical cancer, religion, occupation, parity and ethnicity and dependent variables such as; cortisol level, distress thermometer score, and HAM-D17 score. The involvement of these variables can be seen from research concept framework chart below:

RESULTS AND DISCUSSION

Purposive sampling method had been conducted from 14th of June until 27th of October 2016 at RSCM Gynecologic Oncology Clinic. Obtained the number of cervical cancer patients based on staging; stage IB 8 pts, stage IIA4 pts, stage IIB20 pts,stage IIIA 3 pts, stage IIIB34 pts, stage IVA1 pts and stage IVB1 pts. The number of the subject of advanced cervical cancer stage that successfully screened are 37 people, five subjects do not include the inclusion criteria; 4 subjects of mild distress and one subject suffered neuroendocrine type of cervical cancer. Then 32 subjects fulfilled the inclusion criteria; patients with cervical cancer stage IIB to IVB with moderate to severe distress and fulfilled mild to moderate distress criteria. To determine the subject, it needs to conduct block randomization; the subject of the treatment group (n = 16) and controls (n = 16). During the research in five weeks, there were drop out in both groups. There were 5 patients from the control group (1 patient passed away, 1 patient back to Java, 1 patient back to Ternate and 2 patients could not be reached), meanwhile 4 patients from experiment/treatment group (1 patient passed away, 1 patient back to Batam, 1 patient did not want to continue the research, and 1 patient could not be reach). Imputation of data needed to be done to create better and valid statistic analysis and results in both groups. The flowchart below describes the research subjects :





Distribution of cervical cancer patients based on stage of cervical cancer, as many as 9 (35%) of people from the Group's treatment and 6 (40.0%) those of the control group was at stadium II B. as much as one (6.7%) people from the control group are at stage III A while on no treatment group (0.0%). Then the respondents who are at stage III B in group treatment as 6 (37.5%) of people and 8 (53.3%) those of the control group. There is no respondent at stage IVA experiment and control group.

While respondents who are at stage IV B only 1 (6.3%) people from the experiment group. Score the thermometer on the experiment group as well as score in the control group with the range of lowest value 5 and highest value 9, while the median value for distress thermometer was good in both groups. The value of p in the distribution stage of cancer, the distress thermometer score and HAM-D17 score entirely > 0.05, means a control and experiment group are homogenous. Similarly, the value of P for the variable age, education, religion, ethnicity and employment in both research groups is > 0.05, so it can be inferred that subject demographics research on experiment and control groups are homogeneous.

Analysis of the Changes in Blood Cortisol Levels Before and After Supportive Psychotherapy

The lives of cancer cells are very supported by micro-environment around the cancerous tissue. Cancer and their micro environment able to produce interleukin pro-inflammation-6 (IL-6) cytokines. IL-6 cytokines could trigger angiogenesis in cancer tissue micro environment, the growth and spreading of cancer cells. IL-6 cytokines could facilitate the work of IL-1 (interleukin-1) and TNF-α (Tumor Necrotizing Factor-α) in the hypothalamus then it can increase cortisol level in the blood.[5]

Chronic stress will disrupt along with the effect of increasing the final HPA T helper type 2 (Th2). Group T helper has special characteristics secreting cytokines lymphocytes and IFN-γ T, which is already known as prototypes cytokines Th1 and IL-5

as an indicator high polarized of Th2 cells, so it can be used to measure the level of each class T helper Immune Response.[11] Th-1 is needed for an effective antitumor immunity and reportedly is also connected to increased the disease-free survival and overall survival.[4,11]

Then we conduct psychotherapy which aims to lower cortisol level. Prospective clinical trial research that evaluates the benefits of the therapy group supportive-expressive (SEGT/supportive-expressive group therapy) on the survival of breast cancer patients who are already metastasize. Spiegel discovers the existence of benefits (positive effects) of psychotherapy in reducing growth/ progressiveness for breast cancer who do not have estrogen receptor, although there's no benefits on a group of patients that have estrogen receptors.[7] Fawzy et al to evaluate both the initial and long-term effects of a group who get a structured intervention for six weeks which includes education about health, increased ability to resolve problems and distress management techniques. Maligna Melanoma patients among obtained a clear intervention benefits including reduced significant psychological distress and immunological changes when compared to the control group. At further control six years later of these patients, found an increase in the risk of recurrence and mortality occurred more in the control group than the group of patients with psychosocial interventions have been performed.

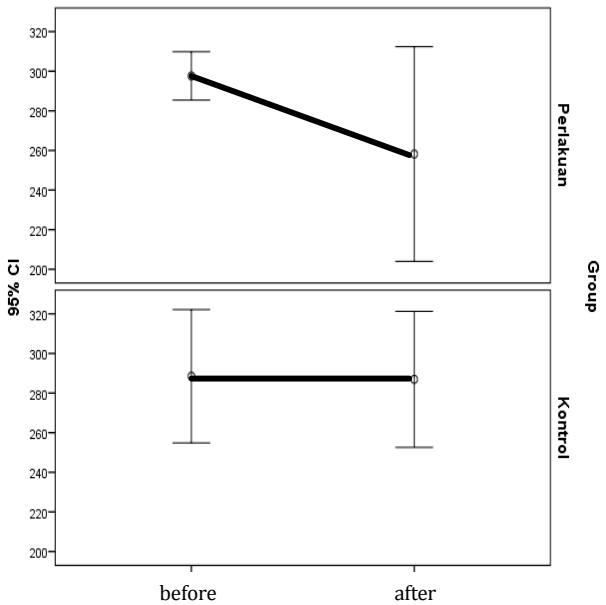


Figure 1. Blood Cortisol Level before and after Supportive Psychotherapy

From the results of cortisol in blood the whole subject of research, the median decrease in cortisol level obtained group treatment a lot more compared to the control group. There is blood cortisol level decrease in the treatment group of 39.43 whereas in the control group there was a decrease of 1.59 (p=0.302). This shows the importance of supportive psychotherapy in order to lower blood level of cortisol.

The psychotherapy conducted in this study only as much as five times. Whereas in previous research, psychotherapy is done as much as 6-10 times and get the resulting improvement in the mood and the immune system of the patient.[12] The least amount of meetings were given to patients due to the brevity of time research that resulted in a decrease in cortisol level in blood was not statistically significant. Another possible cause which made level of cortisol is not statistically significant was sampling time. The best time for taking samples of blood cortisol was in the afternoon-evening cortisol level when the respondents returned to basic level of cortisol which only associated with the disease.[4,5,11] Cortisol sampling performed when the respondents have arrived at RSCM after undergoing stressful conditions such as bogged down in a meaningful way to the Dr. Cipto Mangunkusumo Hospital.

Analysis of Changes of the Distress Thermometer before and after Supportive Psychotherapy

From the analysis results of thermometer score, obtained that the mean distress thermometer prior to psychotherapy in the treatment group was 6.12 (SB 1.67), whereas in control group was 6.44 (SB 1,32). After giving supportive psychotherapy, decreasing score happen in treatment group as average 3.4 and control group as 3.61 (p value > 0.492).

In addition to distress thermometer score, the study also unravels any problem encountered by respondents within the last week before measured the distress thermometer score. Researchers got the most problem complained that respondents from the control group were sad and painful feeling. While in the treatment group, the problems were obtained in the form of fear, anxiety, grief, worry, and pain. Almost all respondents revealed these problems diminished after got psychotherapy.

Analysis of the changes of HAM-D17 Score before and after Supportive Psychotherapy

After the intervention of psychotherapy in the treatment group, HAM-D17 score is decreased with average score 7.53 (SB 3.34). Whereas in the control group also decreased with the average score 3.98 (SB 2.85). This difference is statistically and clinically significant, which means a decrease in the average HAM-D17 score between the treatment group and the control group has a value of p = 0.003 (p < 0.005). Based on the analysis results of summary according to distress level experienced by 32 respondents obtained 13 people from the control group experienced mild depression and three people suffered moderate depression. While in the treatment group, ten people suffered mild depression and six people experience moderate depression.

Table 1. HAM-D17 Score before and after Supportive Psychotherapy

HAM D17	Group		p
	Treatment (n=16)	Control (n=16)	
First	13.63 (SB 2.92)	11.75 (SB2.72)	0.070
Second	6.10 (SB 2.60)	7.77 (SB 2.96)	0.100
The Delta	-7.53 (SB 3.34)	-3.98 (SB 2.85)	0.003

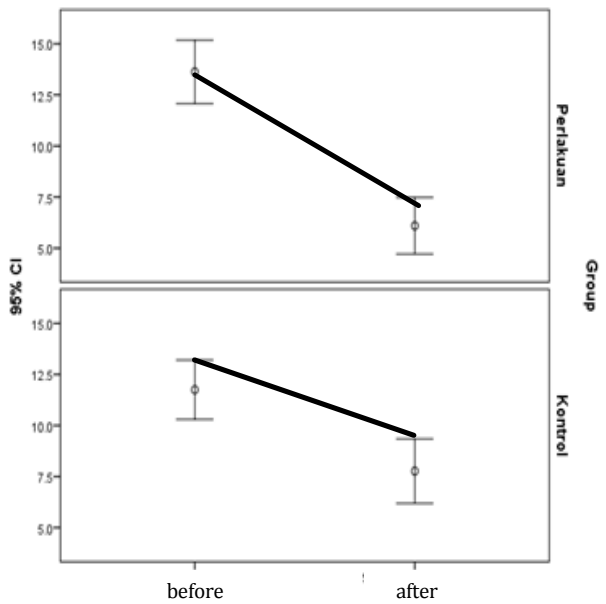


Figure 2. The Tendency of Decreasing Score HAM-D 17 before and after Supportive Psychotherapy

From the chart above, HAM-D17 score decreasing in treatment group seem steeper than in the control group and cortisol delta decreasing is statistically significant proven. This shows that supportive psychotherapy in advanced stage cervical cancer patients experienced mild and moderate depression disorders are very important. These results are in accordance with the results from various studies of supportive psychotherapy that psychotherapy is effective in lowering depression symptoms. As shown by the results of two meta-analyses done by Driessen et al. about the effectiveness of short-term psychodynamic psychotherapy. From 23 1,365 people, found a short-term dynamic psychotherapy more effective to decrease symptoms of depression. There was a lot of changes happened positively after therapy, and the results of the therapy remained until one year. When a comparison is done between techniques of psychotherapy and supportive expressive obtained there was no significant difference even though such therapy is given for three or 12 months.[13]

From research conducted by Cuijpers et al which compared 7 main types of psychosocial therapy for patients with mild to moderate depression that are cognitive behavioral therapy (CBT/Cognitive Behavioral Therapy), non supportive directive therapy, the activation behavior therapy, psychotherapy, dynamic problem solving therapy, interpersonal psychotherapy, and social skills training concluded that all of the psychosocial therapies have almost the same effectiveness, except interpersonal psychotherapy has slightly better effectiveness than the others while non supportive directive psychotherapy has a slightly lower effectiveness compared to others.[13] Research by Goodwin et al about the effectiveness of expressive supportive psychotherapy in patients who have experienced metastatic breast cancer concluded psychotherapy resulted in the improvement of psychological symptoms, decrease in pain, change in the form of mood as well as changes in the perception of pain.[11,14]

From the results of research by Carlson et al., psychosocial therapies that are obtained in the form of Mindfulness Base Cancer Recovery and supportive group therapy - expressive given in breast cancer patients could improve the level of stress, social support, quality of life and diurnal cortisol profile. And from research by Nelson et al., psychosocial therapy such as Psychosocial Telephone Counseling (PTC) on the cervical cancer

patients could significantly improve the quality of life and associated with the specific immune system changes mediated T helper cell group on cervical cancer patients. And finally, this condition resulted in improving and increasing life expectancy (survival rate).[11,14]

Scoring System Using Multiple Variables to Predict Depression Levels

Variables in the multivariate analysis at this stage are variable distress thermometer, cortisol, stage of cancer, marital status and parity. To find a point of intersection of these variables first performed bivariate analysis and continued to stage scoring.

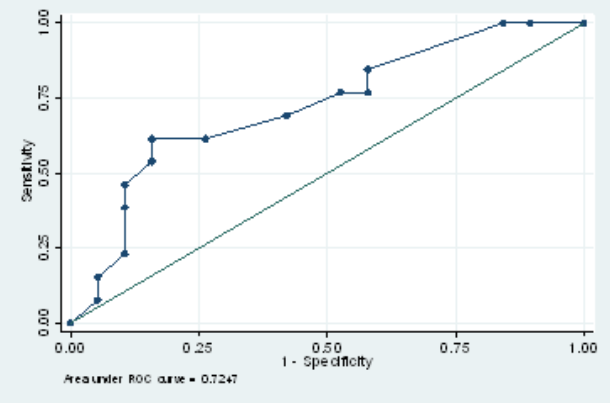


Figure 3. ROC of Variables in Predicting the Level of Depression

Table 2. The Final Model Results of Variable Predictor Scoring System for Depression

Variables	Koef (β)	SE	p	OR (IK 95%)	Score
Distress thermometer	1.021	0.996	0.305	2.776 (0.394-19.568)	10
Cancer stage	0.492	0.830	0.553	1.636 (0.322-8.318)	6
Cortisol	1.309	0.873	0.134	3.701 (0.669-20.471)	15
Status of marriage	0.612	0.906	0.499	1.844 (0.312-10.888)	7
Parity	1.132	0.970	0.243	3.103 (0.464-20.769)	12

Based on the table above, cut-off point curve, sensitivity, specificity and total score, the best cut point value for estimating the group of moderate depression in patients with epithelial cervical cancer is 32. Probability score of a patient experienced moderate depression can be seen in the table below.

Table 3. The Probability of a Predictor Score for Depression Level

Total score	Mild	Moderate	Probability
≥ 32	2	6	75.0%
< 32	17	7	29.2%

From the analysis above could be inferred the ROC (Receiving Operating characteristic Curve) below. Determination of the final scoring model could predict the level of depression in epithelial cervical cancer patients as much as 72.47% with sensitivity 46.15% and specificity 89.47%.

CONCLUSION

The prevalence of distress type depression in epithelial cervical cancer patients at RSCM as 45%. Supportive psychotherapy in treating distress epithelial cervical cancer patients could lower cortisol level and the score of the distress thermometer. And the supportive psychotherapy had also proven lowering the score of HAM-D17 (*p=0.003*). Supportive psychotherapy is very important in the treatment of cervical cancer patients who experienced distress type depression. Hopefully, the "team of Psycho-Oncology" or "Palliative care and pain management team" in RSCM would be formed so the cancer patients could be managed comprehensively.

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Research Article

Human Papilloma Virus-16 and 18 Infection and the Cervical Cytology Changes in Combined Hormonal Contraceptive Users

Infeksi Human Papilloma Virus Tipe 16 dan 18 dan Perubahan Sitologi Serviks pada Akseptor Kontrasepsi Hormonal Kombinasi

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Makassar

Abstract

Objective: To evaluate the correlation between HPV-16 and 18 infection and the cervical cytology changes among combination hormonal contraceptives users.

Methods: A cross-sectional study involved 40 women using combined hormonal contraceptive (oral or injection/DMPA contraceptive) and 40 women of non-hormonal contraceptive users was conducted in Dr. Wahidin Sudirohusodo hospital, some affiliated hospitals of Department of Obstetrics and Gynecology Faculty of Medicine, Universitas Hasanuddin and a private clinic in Makassar from November 2015 and April 2016. HPV 16 and 18 genotyping in cervix using PCR method and cervical cytology changes using liquid-based cytology (LBC) method were performed. HPV infection and cervical cytology changes were analysis based on Fisher's test and chi-square test.

Results: A significant difference found only in parity ($p<0.05$) between users and control of baseline characteristics. Neither users nor control were significantly associated with HPV-16 and 18 infection and changes in cervical cytology.

Conclusion: Combined hormonal contraceptives are not correlated with HPV-16 and 18 infection and changes in cervical cytology.

[Indones J Obstet Gynecol 2018; 6-3: 188-192]

Keywords: cervix, combined hormonal contraceptive, human papilloma virus

Abstrak

***Tujuan**: Untuk mengetahui hubungan antara HPV-16 dan 18 infeksi dan perubahan sitologi serviks pada akseptor kontrasepsi hormonal kombinasi.*

***Metode**: Penelitian potong lintang pada 40 perempuan akseptor kontrasepsi hormonal kombinasi (oral atau injeksi/DMPA kontrasepsi) dan 40 perempuan bukan akseptor kontrasepsi hormonal kombinasi dilakukan di rumah sakit Dr. Wahidin Sudirohusodo, beberapa rumah sakit afiliasi dari Departemen Obstetri dan Ginekologi Fakultas Kedokteran Universitas Hasanuddin dan klinik swasta di Makassar dari November 2015 dan April 2016. Pemeriksaan genotip HPV 16 dan 18 dari serviks dilakukan dengan metode PCR dan pemeriksaan sitologi serviks menggunakan metode sitologi berbasis cairan (liquid based cytology). Infeksi HPV dan perubahan sitologi serviks analisis dengan uji Fischer dan uji chi-square.*

***Hasil**: Perbedaan bermakna antara akseptor kontrasepsi hormonal kombinasi dan kontrol hanya terdapat pada paritas ($p<0,05$) pada karakteristik sampel penelitian. Baik akseptor kontrasepsi hormonal kombinasi maupun kontrol tidak berkorelasi bermakna dengan infeksi HPV-16 dan 18 dan perubahan sitologi pada serviks.*

***Kesimpulan**: Kontrasepsi hormonal kombinasi tidak berkorelasi dengan infeksi HPV-16 dan 18 dan perubahan sitologi pada serviks.*

[Maj Obstet Ginekol Indones 2018; 6-3: 188-192]

***Kata kunci**: human papilloma virus, kontrasepsi hormonal kombinasi, serviks*

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INTRODUCTION

Cervical cancer is the second most prevalent cancer among women worldwide and the main cause of death, especially in young women. Approximately 500,000 new cases registered each year out of which 250,000 cases are attributable deaths according to the World Health Organization (WHO) statistics.[1] Approximately 90% of the cervical cancer deaths are in developing countries compared to other regions.[2]

Human papilloma virus is a DNA virus that infected skin and mucous in the lower genital tract. Approximately 95% incidence of cervical carcinoma associated with oncogenic HPV types; HPV 16 and 18 are the most prominent oncogenic HPV types found for more than 62% in cervical carcinoma. In addition to HPV infection, the incidence of cervical carcinoma increase with sexual activity, parity, pregnancy, smoking and oral contraceptive use.[1]

Previous studies have shown that hormonal contraceptives use associated with HPV infection. Oral hormonal contraceptives use for more than six years associated with the prevalence of HPV infection in women aged 20-37 years in Thailand after controlling for sexual activity and cervical cytologic abnormalities. Current use of oral contraceptive also associated with HPV 16 and 18 seropositive.[3] A study has also found that current users of oral contraceptive had a lower risk of HPV infection compared to current users of injectables users.[4] Therefore, hormonal contraceptive use increased persistent HPV infection.[5]

Estrogen and progestin in combined hormonal contraceptive affect the cervical cytology. Oral contraceptive cause cervical hypertrophy, hypersecretion and proliferation of endocervical gland that results in increased cervical mucus secretion, mucous edematous and pseudodecidualization. These are due to gestagen that contained in birth control pills. In addition, gestagen also causes metaplasia and epithelial dysplasia in the epithelial of portio and endocervical mucous membranes.[6] Hormonal contraceptives maintained the columnar epithelial cells in the ectocervix and transformation zone (cervical ectopy). Cervical ectopy occurs when columnar epithelium found in the endocervical area extends out on to the ectocervix. Cervical ectopy is common in young women, pregnant women and hormonal contraceptive users. Some hypothesise that hormonal contraceptive users biologically more vulnerable to HPV infection than non-users.[5,7] Our study aimed to evaluate the correlation between HPV-16 and 18 infection and the cervical cytology changes among combination hormonal contraceptives users.

METHODS

This cross-sectional study involved combined hormonal contraceptive users (oral and injection/ DMPA contraceptive) in Dr. Wahidin Sudirohusodo hospital, some affiliated hospitals of Department of Obstetrics and Gynecology Faculty of Medicine, Universitas Hasanuddin and a private clinic in Makassar from November 2015 and April 2016. As controls, we enrolled women of non-hormonal contraceptive users. The inclusion criteria consisted of using combined hormonal contraceptives for at least 2 years, age of first sexual intercourse ≥20 years, history of normal delivery for four times maximum, one sexual partner, no smoking, alcohol and drugs, and not being treated with antibiotics. Exclusion criteria were non-users of combined hormonal contraceptives suffering from cervical carcinoma, having sexual intercourse within 3 days prior to the examination and menstruation. This study was approved by the Health Research Ethics Committee of Faculty of Medicine, Universitas Hasanuddin. All participants provided written informed consent prior to the start of the study. HPV 16 and 18 genotyping in cervix using PCR method and cervical cytology changes using liquid-based cytology (LBC) method.

A total 101 women were enrolled in this study. There were three women at enrollment who were excluded, and 18 women were drop out from this study. Therefore, 80 women (n=80) were eligible for analysis in this study. The statistical analysis was based on Fisher's test and chi-square test. A p-value less than 0.05 was considered statistically significant.

RESULTS

The study included 40 women using combined hormonal contraceptives, and 40 women do not use this contraceptives method as control. Women in users group were aged between 20 and 35 years (72.5%), high education (82.5%), age of first sexual intercourse between 20 and 29 years (100%), multiparity (70%) and more than 3 years of using this contraceptive method (67.5%) compared to control (65%; 97.5%; 90%; 47.5%; 42.5%; respectively). The only significant difference found in parity between users and control ($p<0.05$). Baseline characteristics of the women in this study are summarized in Table 1.

HPV 16 infection detected only in one user (2.55) than none in control otherwise in HPV 18 infection. There was no significant correlation ($p>0.05$) between HPV-16 and 18 infection and combined hormonal contraceptives (Table 2). Cervical cytology using LBC method show cervical changes in 24 (60%) of combined hormonal contraceptives users compared to 19 (47.5%) in control. There were no significant cervical cytology changes between users and control group (Table 3).

Table 1. Baseline Characteristics of Study Participants

Characteristics	Users (n=40)		Control (n =40)		*p*
	n	%	n	%	
Age (years)					
20 - 35	29	72.5	26	65	0.469
>35	11	27.5	14	35	
Education					
Low (<SMA)	7	17.5	1	2.5	0.057
High (>SMU)	33	82.5	39	97.5	
Occupation					
Working	20	50	28	70.0	0.068
Not working	20	50	12	30.0	
Age of first sexual intercourse (years)					
20 - 29	40	100	36	90	0.116
30 - 39	0	0	4	10	
Parity					
Nulli/Primipara	10	25	21	52.5	0.012
Multipara	30	75	19	47.5	
Duration of contraceptive use (years)					
≤ 3	13	32.5	23	57.5	0.235
> 3	27	67.5	17	42.5	

Table 2. HPV 16 and 18 Infections in the Cervix of Study Participants

Subjects	HPV 16				*p*	HPV 18				*p*
	Positive		Negative			Positive		Negative		
	n	%	n	%		n	%	n	%	
Users (n=40)	1	2.5	39	97.5	1.000	0	0	40	100	1.000
Control (n=40)	0	0	40	100		1	2.5	39	97.5	

Table 3. Cervical Cytology Results using Liquid-based Cytology (LBC) Method

Subjects	Changes in cervical cytology				*p*
	Positive		Negative		
	n	%	n	%	
Users (n=40)	24	60	16	40	0.26
Control (n=40)	19	47.5	21	52.5	

DISCUSSION

In the present study, we found that there was no significant difference of HPV types 16 and 18 infections between combined hormonal contraceptive users and control. This result similar to the study by Morgan et al. that follow up 1135 women (consists of 376 combined oral contraceptives users, 331 DMPA users and 428 non-contraceptive users) for 18 months. They found new HPV infection in 269 women and high-risk HPV infection in 157 women.[8] However, HPV infection and COCs was not statistically significant after adjusting for age, a number of sexual partners, bacterial

vaginosis and duration of the COCs and DMPA use. Study also that COCs was not associated with the risk of cervical infection whereas DMPA use significantly associated with the risk of cervical infection primarily by chlamydial and gonococcal infections[5] but in another study show that cervical carcinoma risk increases by up to four-fold in women positive for cervical HPV DNA after long-term use of oral contraceptives.[9] Study by Urban show that use of oral and of injectable hormonal contraceptives was associated with a transiently increased risk of breast and cervical cancer after using the contraceptives for 5 years but not differ significant.[10]

Although women are infected with HPV cervical, most do not develop into cervical cancer. Several factors are also involved in the development of cervical cancer. Exogenous or environmental factors such as the use of hormonal contraceptives, smoking, parity and infections along with sexually transmitted diseases; viral factors such as the specific type of infection, co-infection with other HPV types, variants of HPV, viral load and viral integration; and host factors include endogenous hormones, genetic factors and other factors related to the immune response.[11] The number of full-term pregnancies is associated with an increased risk of invasive cervical carcinoma after adjustment for the number of sexual partners and age at first intercourse.[12] The mechanisms which high parity increases the risk of cervical carcinoma is through the maintenance of the transformation zone on the ectocervix for many years in which may facilitate exposure to HPV. A previous study found that high parity increases the risk of squamous-cell carcinoma of the cervix among HPV-positive women.[13] This study finding multiparity significantly found difference between users and control.

HPV infects immature basal cells of the squamous epithelium in areas of the immature metaplastic squamous present at the squamo columnar junction. Cervix is a wide area with immature metaplastic squamous epithelium that is highly susceptible to HPV infection. HPV replication took place immature squamous cells results in koilocytotic atypiaconsists of atypic core and halo perinuclear cytoplasmic. Perinuclear halo show typical expression of active phase HPV infection in cervical cytology.[14] Therefore, other types of HPV infection may be present in the women cervix of the present study both combined hormonal contraceptive users and control.

Cervical cytology results show cervical changes both in users and control but the difference not statistically significant. This results similar to previous studies that found cervical histologically change due to combined hormonal contraceptives use. Effects of 17 β-estradiol from COCs causes progressive metaplasia in the transformation zone that leads to dysplasia in squamous epithelium.[15] These findings are in disagreement with results from the study by Syrjanen et al., found that COCs was not a significant predictor in women with cervical intraepithelial neoplasia (CIN) ⅔ or high-grade squamous intraepithelial lesion (HSIL) in women with positive and negative HPV infection. They also found that the disease with high-oncogenic risk HPV types infection is not correlated to contraception.[16] Most HPV infection is asymptomatic and does not change the cervical tissue; therefore, cervical changes could not be detected on Pap smear. Some studies found the majority of HPV infections will regress spontaneously within five years, but only a few women with high-risk HPV infection will develop into CIN ⅔ and will eventually cervical cancer.[17,18]

Estrogen increases expression of oncogenic proteins E6 and E7 in HPV as a major stimulant of cervical cancer.[19] Steroid hormones (estrogen and progesterone) play a role in the initiation and progression of cervical cancer through carcinogenesis. Lesions from HSIL develop into cervical carcinoma reported from women using estradiol.[15,20]

CONCLUSION

In conclusion, our study show there is no relationship between HPV 16/18 infection and cervical cytology changes among combined hormonal contraceptives users.

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Case Report

Vaginal Delivery in Placental Abruption

Persalinan Pervaginam pada Solusio Plasenta

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Abstract

Objective: To describe the case of vaginal delivery in placental abruption.

Methods: A case report

Results: In the case of placental abruption, we could perform vaginal delivery.

Conclusion: The treatment of placental abruption can be vaginally or by cesarean section depending on the severity of disease, gestational age, and state of the mother and fetus.

[Indones J Obstet Gynecol 2018; 6-3: 193-197]

Keywords: IUFD, placental abruption, vaginal delivery

Abstrak

***Tujuan**: Mendeskripsikan kasus persalinan pervaginam pada solusio plasenta.*

***Metode**: Laporan kasus.*

***Hasil**: Pada kasus solusio plasenta persalinan dapat dilakukan secara pervaginam.*

***Kesimpulan**: Penanganan terhadap solusio plasenta dapat secara pervaginam ataupun secara seksio sesarea bergantung dari berat ringannya penyakit, usia kehamilan, serta keadaan ibu dan janin.*

[Maj Obstet Ginekol Indones 2018; 6-3: 193-197]

***Kata kunci**: IUFD, persalinan pervaginam, solusio plasenta*

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INTRODUCTION

Placental abruption is the premature separation of the placenta from normal implantation in the uterus (uterine corpus) in the period more than 20 weeks of pregnancy and before the fetus delivery.[1,2] Placental contains many blood vessels that allow the delivery of nutrients from mother to fetus. If the placenta separates from the normal implantation, it'll cause great bleeding.[3-5]

The incidence of placental abruption range from 1% - 2% of all gestation.[1] Risk of maternal mortality estimated 0.5% - 5% and fetal mortality 20-40%. The incidence of abruption increases parallel to increase of gestation. Bleeding of placental abruption is actually more dangerous than placenta previa because on certain cases bleeding that looked out through the vagina is not comparable, it causes placental abruption is more dangerous because in such circumstances often approximate total blood that has come out is difficult to predict, because the fetus had died and the mother is in shock condition.[1,6-10]

The cause of placental abruption is not known with certainty, but in severe cases correlation with chronic vascular hypertension, 15.5% accompanied by preeclampsia. Other factors are thought to play a role as a cause of placental abruption is the high level of parity and rising age of the mother, in addition relation to chorioamnionitis, premature rupture of membranes, smoking, multiple gestation, low birth weight.[3,11,12]

Symptoms and signs of placental abruption are diverse, making it difficult to enforce the diagnosis quickly. The symptom can be found as a single symptom, but more often a combination of symptoms. Placental abruption is a disease of pregnancy relatively common and can seriously harm the condition of mother. A mother who had experienced placental abruption, have a higher risk of experiencing a recurrence in

subsequent pregnancies. Placental abruption also tends to make the morbidity and even mortality in the fetus.[3,13]

The management of placental abruption is termination of pregnancy to save the life of the fetus and delivery of the placenta in order to stop the bleeding. Mode of delivery in cases of placental abruption can be vaginally or by cesarean section depending on severity of the disease, the amount of bleeding, signs of spontaneous labor or not, gestational age, and signs of fetal distress. If the fetus is still alive and term infant, but there is no sign of vaginal delivery, generally we choose delivery via emergency cesarean section.[2] In a lot of bleeding immediately do resuscitation by administering blood transfusions and crystalloid fairly followed childbirth accelerated to control the bleeding and save the mother with a hope that a fetus can also be saved. Generally, the pregnancy is terminated by induction or stimulation of parturition in patients with mild or fetal death, or directly by caesarean section, in severe cases or fetal distress.[14,15]

CASE

Patient R, 19 years old come to the ER with referrals obstetric hemorrhage. Patients admitted to 8 months pregnant. The first day of the last menstrual period 29 November 2014, the estimated date of confinement 5 September 2015, the gestational age of 32-33 weeks and has 1 time ultrasound examination and said the fetus in good condition. Patient undergoing antenatal examination regularly by a midwife. The patient was bleeding from one day before admission, contraction since 1 day before admission, water broke and bloody show denied. Movement of the baby has been reduced since 1 day before admission. This was her first pregnancy. Patient has been married since one year ago, and has never used contraception. History of massage was denied.

Figure 1. IUFD

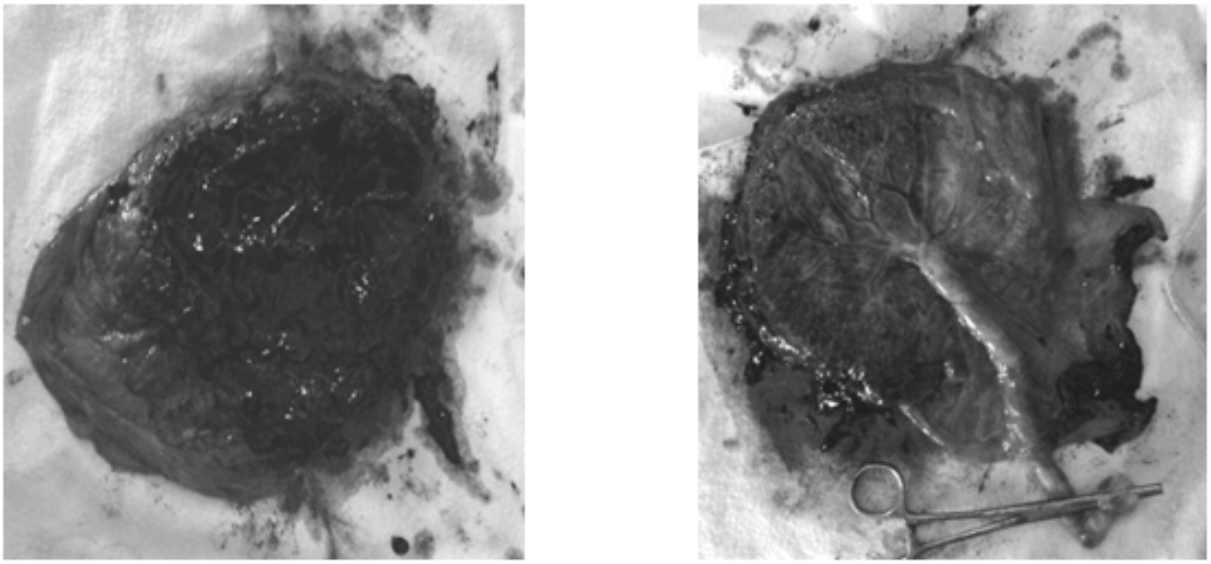

Figure 2. The placental maternal and fetal side view

On physical examination was found moderate condition, compos mentis, hemodynamically stable, blood pressure 120/80 mmHg, pulse 80 x/min, respiration rate 16 x/min, temperature 37°C, and found no abnormalities in generalist status. Height of the uterine fundus was found 30 cm, in the right location, irregular contraction, no fetal heart rate, vaginal toucher was found soft portio, thickness 1 cm, axial direction, opening 3 cm, head on Hodge I-II, amniotic fluid positive. Laboratory results were Hb 10.1 g/dl, Leukocytes 13,310/ul platelets 155.000/ul, rapid blood glucose 90 mg/dl. There was not found fetal heart rate from US examination, and there was a sign of abruption.

The patient was planned cervical ripening with misoprostol 25 mcg/6 hours, after 4 hours observation, it reached the 2nd stage of labour, later born baby boy weight 1700 grams, body length 42 cm, IUFD, placental ± 100%, grade III maceration. (Figure 1. and 2)

DISCUSSION

The pathophysiology of placental abruption is bleeding. It may occur in the blood vessels of the placenta or uterus that forms a hematoma in the decidua, thereby the placenta pressed and eventually released. If the bleeding is only slightly, small hematoma that would only urge the placental tissue, blood circulation between the uterus and the placenta has not been disturbed, signs and symptoms were not clear. Usually the bleeding will occur continuously as the uterine muscle that has been stretched by pregnancy is not able to continue to contract to stop the bleeding. As a consequence, retroplacentalhematoma will grow large, so that partially and finally all parts of the placenta separates from the uterine wall. Most blood will enter under the membranes and penetrate the membranes into the bag. (Figure 3).[3] However finally suspected abruption due to anaemia, tetanic contractions and ultrasound picture there were detatch.

The occurrence of placental abruption triggered by bleeding into the decidua basalis which is then split and improve thin layer attached to myometrium forming a hematoma decidua which causes the release, compression and eventual destruction of the placenta adjacent to the part. (Figure 4) Ruptured spiral decidua artery cause retroplacental hematoma which will have more bleeding, until the release of placental broader and reaches the edge of the placenta, because the uterus remains distention with their fetus, the uterus is unable to contract optimally to suppress the blood vessels. Furthermore, the blood that flows out can release the membranes. Placental abruption is the result of a process that started from a state that is capable of separating chorionic placental villi from implantation in basal decidua causing bleeding. Therefore pathophysiology relies on the etiology.[2]

The state of the fetus depends on the extent of the placenta detached from the uterine wall. When mostly or entirely apart, there will be anoxia resulting in fetal death. If a small portion is released, may not affect at all, or will result in fetal distress.

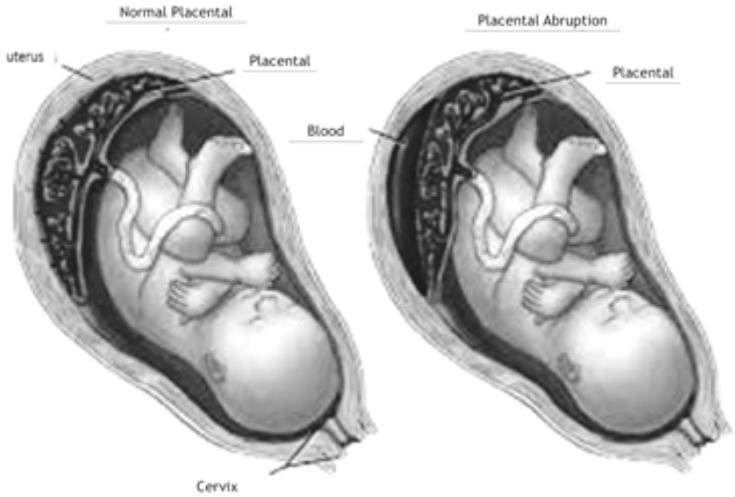

Figure 3. Differences in normal placental and placental abruption.

Time will determine the severity of blood clotting disorders, kidney disorders, and fetal status. The longer handling placental abruption, the more severe the complication.[3] In the case of fetal death in trimester 3 and immature cervix can be given misoprostol 25 ug vaginally every 6 hours or 25 mcg orally every 2 hours based on FIGO.[1,2,16]

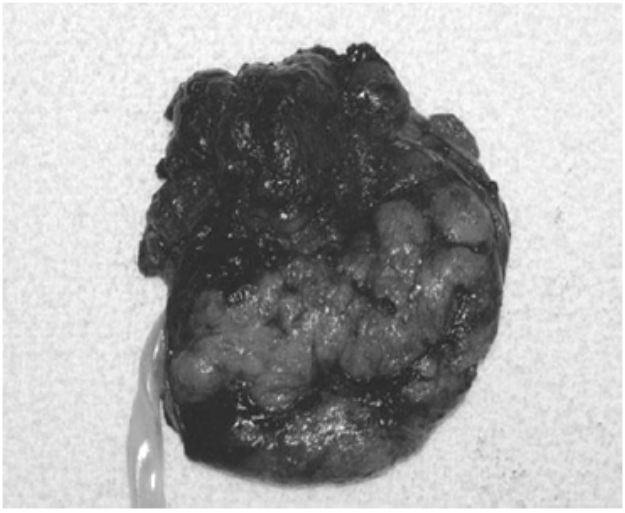

Figure 4. Overview of maternal placental abruption

In cases where there was a death of the fetus, we choose vaginal delivery unless there is heavy bleeding that is not resolved with many blood transfusions or other obstetric indications exist that require deliveries by cesarean section. Hemostatic on placental implantation site depends completely on the strength of contraction of the myometrium by pharmacologically or message that reinforced myometrial contractions and prevents heavy bleeding after childbirth although the state still coagulation disorders.[3]

Management abruption in a live fetus with the uterus rigid is by cesarean section but in the soft uterus may be considered to induce labor because of the possibility coagulopathy is low and the possibility of birth vaginally good, but when doing labor induction occurs hypertonus and the baby's heart rate is not good then you should followed by a cesarean section.[1]

According to the WHO guidelines in the event of severe haemorrhage with early signs of shock, we should take immediate delivery. If bleeding is severe with complete cervical dilation, vacuum extraction can be performed, and if the opening of the cervix is not yet complete, we can perform cesarean section. Meanwhile, when bleeding slightly depending the results of fetal heart rate, if the fetal heart rate normal, cesarean section can be performed. If the fetal heart rate absent and maternal blood pressure normal, vaginal delivery can be considered. When the fetal heart rate absent and the mother's blood pressure has a problem, we can break the membrane.[17]

In the above case for pregnant women with fetal IUFD, we planned to terminate the pregnancy by vaginal delivery with misoprostol.

CONCLUSION

The principle of mothers with placental abruption is to prevent maternal mortality, stop the source of the bleeding. Treatment of placental abruption varies according to case depending on the severity of disease, gestational age, as well as the state of the mother and fetus. If the fetus is still alive, term baby and there is no sign of vaginal delivery, then the selected delivery by cesarean section. While in patients with mild or fetus has died, the termination can be done by induction.

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