Continuity of Maternal and Baby Antenal Care (ANC) Services during the Pandemic

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Antenatal care is an essential part of pregnancy and is useful for detecting diseases and complications such as anemia, pre-eclampsia, gestational diabetes, asymptomatic urinary tract infections and stunted fetal growth. Pregnant women who do not receive antenatal care have a higher risk of maternal death, stillbirth, and other pregnancy complications such as viral infections.[1,2] Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), also called Coronavirus 2019 (Covid-19), was first discovered in December 2019 in Wuhan, China and is a widespread infection.[3] The gene that causes the Covid-19 disease has been dispersed globally, leading to a Covid-19 pandemic.[4] Pregnant women are considered a high risk group because they are more susceptible to the possible effects of COVID-19 during pregnancy, after pregnancy, and also on their neonates.[5]

Results of several systematic reviews and meta-analytic studies have reported that pregnant and recently pregnant women with COVID-19 tend to not have symptoms such as fever, dyspnea or myalgia but are more likely to be admitted to the intensive care unit compared to women of reproductive age who are not pregnant.[6] Preexisting maternal comorbidity such as chronic hypertension, diabetes, advanced maternal age, and high body mass index are risk factors that exacerbate COVID-19. Neonates of preterm pregnancies require further management in preterm neonate care facilities, as they at increased risk of death and being admitted to the intensive care unit.[6] Certain risk factors found in pregnancy, such as Pre-eclampsia, have been reported to worsen the condition of the mothers with COVID-19, however this requires further clinical evidence.[5]

Pregnant women during the COVID-19 pandemic are advised to continue routine antenatal care with some modifications, except for pregnant women who require independent isolation due to suspected or confirmed COVID-19. WHO issued a recommendation for low-risk pregnant women to receive at least 8 antenatal care. During the pandemic, direct physical antenatal consultations are carried out at least 6 times for low-risk pregnant women, but in high-risk cases the frequency of antenatal care is adjusted.[7] Several modifications are needed to provide adequate antenatal care to pregnant women carrying out social distancing and those who are suspected or confirmed to have COVID-19, with the aim of reducing transmission between pregnant women and medical staff.[2,7]

All pregnant women with a history of contact with confirmed COVID-19 individuals are monitored carefully, considering that some cases of COVID-19 are asymptomatic. Pregnant women with suspected or confirmed COVID-19 may not require hospitalization unless there is a significant health risk. Self-isolation to contain viral transmission is recommended, and can be carried out in health facilities, community facilities or at home, in accordance with current COVID-19 management pathways.[8] Supplementation of folic acid, calcium, vitamin D and micro nutrients is still given and adjusted to the needs of each pregnant woman. Provision of Iron tablets for pregnant women with suspected, probable or confirmed COVID-19 status is done with consideration of the treating doctor and the condition of the patient concerned. Antenatal care in the third trimester is performed to plan the location of the delivery. If the pregnancy is found to be high risk, a planned referral to the hospital can be arranged ahead of time.[7]

Should pregnant women be vaccinated? Pregnant women with COVID-19 have greater risk than women who are not pregnant. Vaccines, such as tetanus, pertussis and influenza, are safe to use during pregnancy.[9] Pregnant women should have access to vaccinations and be given the choice whether to have the vaccine after being educated about its benefits and risks. Current studies suggest that COVID-19 vaccination during the preconception period does not have a negative impact, although the number of observations were limited.[10] The European Society of Human Reproduction and Embryology (ESHRE) concluded that there is currently no information on the safety of different types of vaccines during pregnancy, and no recommendations can be made about which vaccine types are safest for men and women trying to conceive.[10]

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Research Article

Analysis of Antenatal Care Quality in Cases of Referred Pregnant Women in Emergency Rooms Based on MCH Book Records

Analisis Kualitas Asuhan Antenatal Berbasis Telaah Buku KIA pada Kasus Rujukan Ibu Hamil di Unit Gawat Darurat

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Abstract

Objective: To determine the quality of antenatal care received by pregnant women, and perceptions of pregnant women and antenatal care providers regarding antenatal care.

Methods: A quantitative and qualitative study of cases of referred pregnant women in the Emergency Room (ER) of Dr. Cipto Mangunkusumo Hospital (RSCM) from 2017–2018 was conducted. Quantitative data was obtained by assessing the overall completeness of filling in the Maternal Child Health (MCH) book used to report the antenatal care received by the subjects. The completeness of antenatal care in the health facility was obtained using a checklist. Qualitative data was obtained by interviewing pregnant women and antenatal care providers in health facilities.

Result: There were 1.442 cases of referred pregnant women in RSCM's ER for the year 2017–2018, of whom 820 possessed and could show their MCH Book. Pregnancy in adolescence below 20 years (9.1%) and pregnancy after age 35 (19.5%) were reported. Most pregnant women were well educated (74.3%), referred from hospital or clinic (57.6%), received antenatal care in a public health center (38.7%), were in labor (32%), and were in the third trimester of pregnancy (92%). All subjects presented an incomplete MCH book. Almost half had inadequate antenatal frequency (46%). The completeness of antenatal care components in health care was 90–100%. Qualitatively, the perceptions of mothers and antenatal care providers regarding quality of antenatal care, was inadequate.

Conclusions: The quality of antenatal care in the case of referred pregnant women at the RSCM's ER based on MCH Book records did not meet the required standard.

Keywords: antenatal care quality, MCH book.

Abstrak

Tujuan: *Menentukan kualitas asuhan antenatal pada kasus rujukan ibu hamil di IGD RSCM yang memiliki buku KIA, dan persepsi ibu hamil yang memiliki buku KIA dan tenaga kesehatan pemberi layanan kesehatan tentang asuhan antenatal.*

Metode: *Dilakukan studi kuantitatif dan kualitatif pada kasus rujukan ibu hamil di IGD RSCM yang memiliki buku KIA tahun 2017-2018. Pengambilan data kuantitatif dilakukan dengan telaah kelengkapan pengisian buku KIA secara umum, Kelengkapan komponen asuhan antenatal di fasilitas layanan kesehatan (fasyankes) asal asuhan antenatal didapatkan dari survei menggunakan daftar tilik. Pengambilan data kualitatif dilakukan dengan wawancara mengenai persepsi ibu hamil dan tenaga kesehatan pemberi pelayanan asuhan antenatal di fasyankes asal asuhan antenatal.*

Hasil: *Terdapat 1.442 kasus rujukan ibu hamil di IGD RSCM selama tahun 2017- 2018, 820 di antaranya memiliki dan dapat menunjukkan buku KIA. Terdapat subjek dengan usia kehamilan remaja di bawah 20 tahun (9,1%) dan usia diatas 35 tahun (19,5%). Sebagian besar ibu hamil yang dirujuk cukup berpendidikan (74,3%), dirujuk oleh RS atau klinik (57,6%) dan mendapat asuhan antenatal di puskesmas (38.7%), dalam status persalinan inpartu (32%), dengan usia kehamilan trimester III (92%). Semua subjek (100%) dinyatakan tidak lengkap dalam pengisian halaman di buku KIA. Hampir setengah subjek mempunyai jumlah kunjungan antenatal yang tidak ideal (46%). Kelengkapan komponen asuhan antenatal di fasyankes asal asuhan antenatal berkisar 90-100%. Secara kualitatif, didapatkan persepsi ibu hamil dan tenaga kesehatan pemberi asuhan antenatal, terhadap kualitas asuhan antenatal masih kurang tepat.*

Kesimpulan: *Kualitas asuhan antenatal pada kasus rujukan ibu hamil di IGD RSCM berdasar rekam Buku KIA belum memenuhi standar.*

Kata kunci: *buku KIA , kualitas asuhan antenatal.*

INTRODUCTION

Each year, approximately 303,000 women die from complicated pregnancy and delivery worldwide.[1] The World Health Organization (WHO) launched the Safe Motherhood Initiative to reduce maternal mortality, with high quality antenatal care as a critical element of the movement.[2] High quality antenatal care allows early detection and proper management of obstetric complications.[3,4] In Indonesia, the antenatal care service is facilitated through use of the MCH Handbook (Buku Kesehatan Ibu dan Anak). This book provides focused antenatal assessment written down as a guide for healthcare providers to assess pregnancy. It also provides a space specifically for writing down the results of assessments performed. Therefore, the maternal and child book not only reports the mother's health history throughout the pregnancy, but also provides an insight into what kind of antenatal service the mother has received.

Dr. Cipto Mangunkusumo Hospital is a tertiary referral hospital that receives referrals at a national level including cases of complicated pregnancy and delivery. According to the hospital's record, from a total number of 1204 obstetric cases referred to the Emergency Room (ER) in 2016, most were of severe morbidity, including 112 antepartum/postpartum hemorrhages, 401 premature rupture of membranes, 207 preterm labours, 31 infection in pregnancy, and 121 miscarriages. Most referred patients are reported to already have their pregnancies routinely checked by a doctor or midwife. This situation raises a question to the quality of antenatal care services, as complications are supposed to be detected and managed earlier during antenatal visits.[2] This study aims to assess the quality of antenatal care services received by pregnant women to provide a basis for the future establishment of improvement strategies.

METHODS

This is a descriptive study. Subjects were all pregnant women who had been referred to Dr. Cipto Mangunkusumo Hospital ER from 2017 to 2018. Quantitative data was obtained by assessing the overall completeness of filling in the MCH book (buku KIA) that reports the antenatal care received by the subjects. The completeness of antenatal care in the health facility was obtained using a checklist. Qualitative data was obtained by interviewing pregnant women referred to Dr. Cipto Mangunkusumo Hospital's ER for the year 2017–2018 and antenatal care providers in the health facility as a sub sample. The number of subjects interviewed was adjusted to allow for the amount of information obtained. In other words, the number was considered sufficient when data saturation from the interviews was reached, or when there was no new information obtained.

Assessment of the MCH books obtained information on the completeness of components in the book, as follows: family identity (page viii), mother's preparation for delivery (page 19), mother's pregnancy health status (page 20-23), mother's age, education, the referral health facility, name of health facility where the mother received antenatal care, and the diagnosis. For descriptive purposes, if any information was absent from the MCH book, the medical records at the health facilities were assessed.

RESULTS

There were 1442 pregnant women referred to Cipto Mangunkusumo Hospital's ER from 2017 to 2018. Those who could show their MCH books were eligible for inclusion in the study, which resulted in 820 women (57%) being included. There was 9.1% pregnancy among teenage women and 19.5% pregnancy for those over 35 years. The Indonesian Department of Health state that pregnancy for women below 20 years or above 35 years has greater risks of obstetric complications.[5] Age also significantly affects the mother's readiness to undergo antenatal assessments and to play her role as a mother.[6] Most subjects were senior high school graduates (74.3%). The higher a mother's education level, the more easily she can obtain and accept new information.[7,8] All subjects had their pregnancies checked by healthcare providers at least once. Most subjects were referred from hospital or clinic (58%). Almost all subjects were in the third trimester of pregnancy (92%), and 32% were in labour. This aligns with the theory that risks of peripartum complications increase during the 40th week of pregnancy and above.[9] Preeclampsia with severe features together with hypertension in pregnancy were the most common diagnoses made at the referring health facilities and Dr. Cipto Mangunkusumo Hospital (32% and 30%, respectively).

Nine healthcare facilities were visited, and antenatal care performed in these facilities was

assessed. Degree of completeness for antenatal care performed were 90–100%. Most antenatal care providers perform antenatal assessments according to the standard set by the Ministry of Health. All except one facility gave assurance that pregnant women were checked by a doctor and dentist at least once. In the one facility that does not, a visit to a doctor or dentist is only recommended if the pregnant woman has any complaints. In one Public Health Center (PHC), every pregnant woman was consulted by a psychiatrist for mental health screening and at the other PHC, pregnant women were provided with a swimming program and hypnobirthing. Every healthcare facility has three antenatal care report systems: MCH books, a Regional Health Information System Application (SIKDA), and a medical record or mother's form card from the PHC. Despite the adequate reporting system, the number of cases referred to higher level health facilities is high. All subjects (100%) presented incomplete MCH books. The extent of completeness for the MCH books is described in Table 1.

Table 1. Assessment of How Complete Items Regarding Mother's Preparation for Delivery are Filled (page 19 of MCH book) (n = 820)

Items	n	%
Mother's name		
Filled	730	(89)
Not filled	90	(11)
Address		
Filled	716	(87.3)
Not filled	104	(12.7)
Month and year of reporting		
Filled	589	(71.8)
Not filled	231	(28.2)
Delivery helper		
Filled	368	(44.9)
Not filled	452	(55.1)
Delivery budget		
Filled	198	(24.1)
Not filled	622	(75.9)
Transportation to healthcare facility		
Filled	194	(23.7)
Not filled	626	(76.3)
Post-delivery birth control		
Filled	340	(41.5)
Not filled	480	(58.5)
Blood donor (Blood type)		
Filled	205	(25)
Not filled	615	(75)
Documentation of immunization status		
Filled	514	(62.7)
Not filled	306	(37.3)
Husband/relative's signature		
Filled	258	(31.5)
Not filled	562	(68.5)
Midwife/doctor's signature		
Filled	278	(33.9)
Not filled	542	(66.1)
Patient's (mother's) signature		
Filled	257	(31.3)
Not filled	563	(68.7)

Interviews were performed with ten pregnant women and eleven antenatal care providers from nine healthcare facilities, from which obstetric cases in Dr. Cipto Mangunkusumo Hospital ER were referred. Only two out of ten subjects reported disappointment regarding the antenatal service they received. The rest had no complaints, although they were only told to read their MCH book and were never taught by healthcare providers how to use the book. Subjects were often not given the chance to ask questions about their pregnancy. Despite the high number of failures to detect complications earlier in antenatal visits, almost every subject reported their antenatal visits to be satisfactory. Subjects were satisfied after undergoing ultrasonography examination or being attended by midwives in a friendly manner. None of the subjects reported having their arm circumference measured, in contrast to antenatal care provider's statement about their antenatal care performance meeting the standard set by the Ministry of Health. Interiew results suggest that pregnant women's poor perception of high quality antenatal care accounts for the low quality of antenatal service they received.

Interviews with antenatal care providers reported that they regularly performed antenatal assessment according to the standard set by the Ministry of Health (the "10T" rule). Subjects reported spending approximately 20 minutes assessing a new patient and 10 minutes with a regular patient. There is some doubt over the credibility of this statement, considering if there are 30 patients in a day it is impossible to perform antenatal care consistent to the 10T rule within 10 minutes. It was found from both the referral letter from the referring healthcare facilities and the medical records in Cipto Mangunkusumo Hospital that preeclampsia is still the predominant diagnosis. Only two interviewees reported routinely checking whether the MCH book had been completely filled in. These findings suggest that antenatal care providers' perceptions about high quality antenatal care and consequently the quality of practiced antenatal care is lacking.

DISCUSSION

None of the women had their MCH books filled completely. In the page reporting mother's preparation for delivery (page 19), the most frequently completed item was mother's name (89%), whereas the least frequently completed

item was transportation to the healthcare facility (24%). In the page reporting mother's pregnancy health status (pages 20–22), the most frequently recorded item was date of assessment (99.4%), followed by mother's weight (98.7%) and blood pressure (98.7%), whereas the least frequently recorded item was blood type (25%). According to the Indonesian Basic Health Research (Riset Kesehatan Dasar) 2018, mother's weight measurement is the most frequently performed assessment, whereas height measurement is the least frequent.[10] In this study, mother's height measurement was the third least frequently reported physical assessment (23.3%) after blood type (73.6%) and arm circumference (24.4%). Some 54.75% of subjects did not have their MCH books filled by either general practitioner or obstetrician, suggesting that doctors' participation in completing MCH book is lacking. Every health care worker needs to participate optimally in reporting mothers' health assessments to support continuous evaluation of the risks of obstetric complications. The Indonesian Department of Health recommend that pregnant women receive an antenatal visit at least once in the first trimester, once in the second trimester, and twice in the third trimester. According to this standard, 373 subjects (46%) did not receive a sufficient number of antenatal checkups. It is important for pregnant women to have their pregnancy checked no less frequently than the minimum standard to assure the safety of the mother as well as the fetus during the pregnancy and later during delivery.[11]

Preeclampsia with severe features together with hypertension in pregnancy were the most common diagnoses made at both referring health facilities. The American College of Obstetricians and Gynecologists (2013) recommend screening for preeclampsia to be performed routinely during antenatal visits. This consists of cautious history taking to search for risk factors such as weight gain, administration of low dose aspirin (60–80 mg) and calcium supplements for patients at high risk.[12] Screening can also be supported by ultrasonography examination.[13]

Despite the adequate reporting system, the number of cases referred to a higher level of health facility was high. This suggests that without evaluating the practice of antenatal care, good reporting systems of assessment results will not improve the early detection of risks and medical complications. Without improvement in the quality of antenatal care, the number of patients referred to tertiary health care facilities such as Dr. Cipto Mangunkusumo Hospital will still be high.

CONCLUSION

All of the MCH books from the subjects in this study were incomplete. In addition, the frequency of antenatal visits of these pregnant women did not meet the WHO's recommendation. The results from assessment of the subject's MCH books suggest that the quality of antenatal care received by the subjects was relatively poor. All of the healthcare facilities reported that they were performing the antenatal care service according to the standard set by the Indonesian Ministry of Health, and they were scored 90%–100% when being assessed by the checklist, even though in reality it relevance to real practice is still questionable. The results of the interviews suggest that pregnant women and the antenatal care providers have poor perceptions about the quality of antenatal care.

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Research Article

Bax Expression of Throphoblast Cells did not Differ between Early and Late Onset Preeclampsia

Ekspresi Baks Sel Trofoblas tidak Berbeda antara Preeklamsia Awitan Dini dan Lanjut

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Abstract

Objective: To compare Bax protein expression in throphoblast cells of early and late onset PE.

Methods: A cross sectional study involving 36 cases of early onset PE and 36 cases of late onset PE was conducted. Bax protein expression was evaluated from sample of placental tissue collected from the study population and calculated using H-Score. Data on age, number of parity, gestational age, body mass index was collected from the medical records. Expression of Bax was compared using Mann-Whitney test.

Result: There was no difference in the clinical characteristics (age, number of parity, BMI, SBP, DBP, and MAP) between the two groups. There was no difference in the expression of Bax protein between the early and late onset PE (mean H-score early vs. late onset PE: 1.48 vs 1.46, p=0.814, Mann Whitney U test). Clinical characteristics of the study population also did not correlate with the Bax expression (R for number of parity: 0.052, age: 0.009, gestational age: -0.014, BMI: 0.063, all p values were >0.05, linear regresion).

Conclusions: There is no difference in the expression of Bax protein of throphoblast cells between early and late onset PE.

Keywords: apoptosis, BAX, early onset, late onset, preeclampsia.

Abstrak

Tujuan: Untuk membandingkan ekspresi protein Baks dalam sel trofoblas pada preeklamsia (PE) onset dini dan lambat.

Metode: Sebuah studi potong lintang yang melibatkan 36 kasus PE onset dini dan 36 kasus PE onset lambat dilakukan. Ekspresi protein Baks dievaluasi dari sampel jaringan plasenta yang dikumpulkan dari populasi studi dan dihitung menggunakan skor-H. Data usia, jumlah paritas, usia kehamilan, indeks massa tubuh dikumpulkan dari rekam medis. Ekspresi Baks dibandingkan menggunakan uji Mann-Whitney.

Hasil: Tidak terdapat perbedaan pada karakteristik klinis (usia, jumlah paritas, IMT, TDS, TDD, dan MAP) antara kedua kelompok. Tidak terdapat perbedaan dalam ekspresi protein Bax antara PE onset dini dan lambat (rata-rata H-skor PE onset dini dan lambat: 1.48 vs 1.46, p = 0.814, uji Mann Whitney U). Karakteristik klinis populasi studi juga tidak berkorelasi dengan ekspresi Bax (R untuk jumlah paritas: 0,052, usia: 0,009, usia kehamilan: -0,014, BMI: 0,063, nilai p dari semua variable tersebut adalah sebesar >0,05, dengan menggunakan regresi linier).

Kesimpulan: Tidak terdapat perbedaan dalam ekspresi protein Baks pada sel trofoblas antara PE onset dini dan lambat.

Kata kunci: dapoptosis, baks onset dini, onset lambat, preeklamsia.

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INTRODUCTION

Preeclampsia (PE) is a multisystem pathology of pregnancys characterized by the development of hypertension and its clinical consequences after 20 weeks of gestational age. PE is still notorious for its high maternal and perinatal mortality. PE is a direct cause of maternal mortality worldwide which associated with severe complications (i.e. intracerebral bleeding, pulmonary edema, heart and renal failure). The worldwide incidence of PE varies between 3-5%. Annualy, there were approximately 500,000 maternal and 900,000 perinatal deaths associated with PE in developing countries.[1-3] The annual incidence of PE in Indonesia is even higher, i.e. between 5-10%. Most importantly, the rate tends to increase year to year.

The exact mechanisms that underlie PE are still elusive. Hence, the treatment for PE is still mainly symptomatic. Several treatment modalities might reduce the risks for complication but the firm evidences assuring its safety for the mother and child are still lacking. Due to its elusive patho-mechanism, the effective prevention and treatment for PE is yet to be discovered. However, many experts believe that PE result from pathologic process that develops within the placenta. For example, the role of placental hypoxia that result from inadequate cytotrophoblasts invasion into the spiral arteries or inadequate spiral arterial remodeling that subsequently induce oxidative stress and endothelial dysfunction. The placenta in pregnancy with PE is suspected to be the source of oxidative stress and hence, the free radicals.[4] The apoptotic activity of the throphoblast may also play a crucial role in the development of PE, particularly the onset of development.

Therefore, this study is aimed to evaluate the expression of proapoptotic protein Bax within the throphoblast cells and compare it between early and late onset PE.

METHODS

This is a cross sectional study that involved singleton live pregnancy aged 20-40 weeks with early and late PE as case and control groups, respectively. The study was conducted at the Emergency Maternal Ward, Department of Obstetrics and Gynecology Dr. Sardjito General Hospital Yogyakarta from Mei 2020 to July 2020. The eligible subject who meet the inclusion criteria was recruited into the study population and a 3x3 cm placental tissue was sampled following delivery. Data were analyzed using SPSS for Windows version 24.

Bax protein expression was examined using immunohistochemistry. Bax protein expression was evaluated within the decidual thophoblast cells. HSCORE was calculated using the formula $\Sigma Pi \times (i+1)$, in which Pi was the percentage of positive cells, i was the intensity of staining with value 0 for negative staining, for weak staining, for moderate staining, and for strong staining. H-Score was evaluated by three independent observers who were not aware about the identity and diagnosis of the sample. Inter-observer validation was done using intra-class correlation (r). Data on age, gestational age, parity and BMI were obtained from the medical records. Age, gestational age, number of parity, BMI and H-Score were analyzed for their normality using Shappiro-Wilk test. Mann-Whitney test was utilized to determine the difference of Bax protein expression between early and late PE.

This study has been approved for ethical eligibility from the Research Ethics Committee of Medical Faculty of Universitas Gadjah Mada / Dr. Sardjito General Hospital Yogyakarta Protocol Number KE/0703/07/2020.

RESULTS

Table 1 summarizes the characteristics of the study population. There was no difference in the age, number of parity, BMI, SBP, DBP, and MAP between the two groups.

Table 1. Baseline Characteristics of the Study Population

Variables	Early onset PE	Late onset PE	P-value
	Mean ± SD	Mean ± SD	
Age (years)	30.3 ± 4.9	30.6 ± 6.9	0.473†
Number of parity	0.6 ± 0.7	0.7 ± 0.8	1.000†
Gestational age (weeks)	31.1 ± 2.2	37.2 ± 1.9	0.000†
BMI (kg/m2)	26.8 ± 4.7	27.6 ± 5.8	0.506*
Systolic BP (mmHg)	167.1 ± 20.2	166.4 ± 18.0	0.878*
Diastolic BP (mmHg)	99.7 ± 11.4	103.1 ± 12.4	1.000†
MAP (mmHg)	122.1 ± 12.9	124 ± 13.1	0.503*

*T-independent test, normally distributed data. † Mann-Whitney U test, non-normally distributed data.

Expression of Bax protein of throphoblast cells

Figure 1 represent Bax expression observed within the selected specimens. There was no difference in the expression of Bax protein between the early and late onset PE (Table 2). Clinical characterictis of the study population did not correlate with the Bax expression (Table 3).
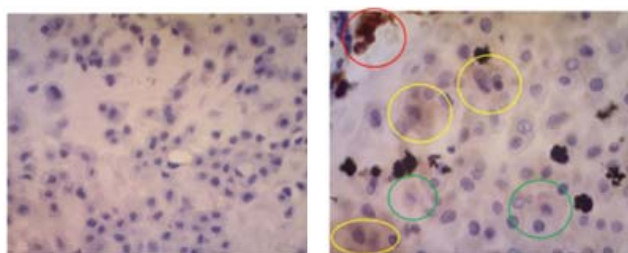
Figure 1. Left. No staining or negative staining. Right. Variable staining depicting strong (red circle), moderate (yellow circle), and weak staining (green circle). 400x magnification, light microscopy.

Table 2. Comparison of Bax Expression between Early and Late Onset PE.

PE	N	Mean H-Score	SD	P-value
Early	36	1.48	0.48	0.48
Late	36	1.46	0.46	0.46

Mann-Whitney U test

Table 3. Correlation between Baseline Characteristic and Bax Expression

Characteristic	R	P-value
Number of parity	0.052	0.332
Age	0.009	0.469
Gestational age	-0.014	0.453
BMI	0.063	0.299

DISCUSSION

PE can occur ealier in pregnancy (less than 34 weeks) and hence, called early-onset PE, or later than 34 weeks of pregnancy. The difference in the onset may be attributed to the difference in invasive capacity of cytotrophoblasts into the spiral arteries that begin in the first trimester (16-18 weeks). Late-onset PE is more common than the ealy-onset PE (2.7%-88% vs. 0.38% - 12%).[5] The influence of maternal age on the risk of PE is still controversial. In developed countries, advance maternal age (older than 35 years) has been associated with the increased risk of pregnancy complications such as abortion, fetal demise, gestational hypertension and PE).

In this study, the clinical characteristics did not differ between the two groups. Similar result also reported, in which there were no difference of mean age between early and late PE (30.3 ± 4.9 vs. 30.6 ± 6.9, p = 0.473).[6] Early onset PE tend to occur in older age group, while late onset PE was associated with chronic hypertension.[7] Low number of parity was associated with the earlier onset of PE, while multiparity was associated with the later onset of PE. Nulliparity has been cited as one the risk factors for the development of PE.[8], The risk for PE in nulliparas was 1.1 (0.73-1.66) but the association was not statistically significant (p = 0.657).[10] No significant association between number of parity and the risk of PE.[11] Our study also reporting similar result in which no significant difference in the number of parity between the two groups.

In this study, we demonstrate no difference in the expression of Bax protein between early and late onset PE. Similar result also demonstrated in which Bax expression did not differ between early and late onset PE. Immunohistochemistry offers significant advantage for Bax protein characterization since it can reflect the direct event of apoptosis in the placenta.[12] It is practically and ethically difficult to evaluate Bax protein expression on the placenta to predict the future emergence of preeclampsia. However, results from this study provide important information and serve as a basic theory to further evaluate the association of Bax levels in the placenta and the development of PE.

CONCLUSION

We conclude that the expression of Bax protein in the throphoblast cells did not differ between early and late onset PE. We recommend further study that use more accurate evaluation of Bax expression such as radioimmunoassay of Western ligand blotting.

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Polyglactin 910 (Vicryl Rapide) for Reducing Pain and Wounds Healing in Postpartum Perineum

Polyglactin 910 (Vicryl Rapide) untuk Mengurangi Nyeri dan Mempercepat Penyembuhan Luka pada Perineum Postpartum

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Abstract

Objective: The purpose of this study was to compare the use of polyglactin 910 (vicryrapide) and chromic catgut to perineal pain and healing wounds on postpartum.

Methods: This research is true experiment with a randomized controlled trial (RCT) and single-blind. The number of respondents pad this study of 40 respondents were divided into 20 respondents to the intervention group (vicrylrapide) and 20 respondents for the control group (chromic catgut). Data analysis using independent t-test.

Result: Statistical test results using independent t-test for pain showed p = 0.035 <0.05 and for wound healing showed p = 0.000 <0.05 of a second can mean the results are there differences in the use of threads polyglactin 910 (vicrylrapide) and chromic catgut thread to perineal pain and healing wounds in the mother postpartum perineum.

Conclusions: The use rapidevicryl thread to repair perineal perineum or stitches can reduce perineal pain and healing wounds better than the use of the chromic catgut thread.

Keywords: chromic catgut, pain, polyglactin 910, rapide vicryl, wound healing of the perineum.

Abstrak

Tujuan: *Untuk mengetahui perbandingan penggunaan polyglactin 910 (vicry rapide) dan chromic catgut terhadap nyeri dan penyembuhan luka perineum pada postpartum.*

Metode: *Penelitian ini merupakan penelitian true experiment dengan randomized controlled trial (RCT) dansingle blind. Jumlah responden pada penelitian ini sebanyak 40 responden yang di bagi menjadi 20 responden untuk kelompok intervensi (vicryl rapide) dan 20 responden untuk kelompok kontrol (chromic catgut). Analisis data menggunakan independent t-test.*

Hasil: *Uji statistik menggunakan t-test independent untuk nyeri didapatkan hasil p=0,035<0,05 dan untuk penyembuhan luka didapatkan hasil p=0,000<0,05 dari kedua hasil tersebut dapat diartikan ada perbedaan penggunaan benang polyglactin 910 (vicryl rapide) dan benang chromic catgut terhadap nyeri perineum dan penyembuhan luka perineum pada ibu postpartum.*

Kesimpulan: *TPenggunaan benang vicryl rapide untuk perbaikan perineum atau penjahitan luka perineum dapat mengurangi nyeri perineum dan penyembuhan luka yang lebih baik dibandingkan dengan penggunaan pada benang chromik catgut.*

Kata kunci: *chromik catgut, nyeri, penyembuhan luka perineum, polyglactin 910, vicryl rapide.*

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INTRODUCTION

Women who give birth vaginally will undergo perineal laceration / trauma well as spontaneous tearing during childbirth physiological or surgical incision (episiotomy). Spontaneous rupture perineum perineal injuries that occur due to certain reasons without tearing or deliberate action. These injuries occur during delivery and usually irregular[1]. Perieneum rupture is one of the trauma that often affects women during childbirth. Perineal trauma and perineal repair is associated with puerperal resulting in morbidity such as bleeding, infection, pain, urinary and faecal incontinence and sexual dysfunction[2]. Other factors that can increase morbidity Other types of materials or stitches are used during repair of perineal[3].

Suture material for perineal repair used can increase perineal pain in the short-term post-childbirth, thus required the use of suturing best to reduce perineal pain and repair of perineal trauma, so that will reduce the impact of short-term[4].

Suture material for perineal repair is often used is chromic catgut. Chromic catgut is yarn types absorption (absorption), have tensile strength 17-21 days, 90-110 days old absorption[5]. Other thread types that are rarely used is vicryl rapide is a type of yarn absorption (absorption), has a tensile strength of 10-14 days, 42 days longer absorption[6].

The use of suture materials are superior in addition to reducing perineal pain also can accelerate wound healing, such as research conducted by explains that the use of polyglactin 910 suture material (vicryl rapide) is an ideal suture material for perineal repair perineal pain that produces fewer and better wound healing compared to the use of chromic catgut suture material[3].

Based on the above researchers are searching for related to "Comparative Use of polyglactin 910 (Vicry Rapide) and Chromic catgut Against Pain and Wound Healing perineum on Postpartum"

METHODS

The research is true experiment (randomized controlled trial) with a single blinding technique. The population in this study were all postpartum mothers who birth at health centers and health centers Godean I Mlati II in Sleman. The sample in this study is a normal birth mothers who suffered wounds perineum and perineal suturing was done using 910 threads polyglactin (vicryl rapide) or chromic catgut. Sampling was done by consecutive sampling. The sample size in this study were 40 respondents (20 respondents intervention group, the control group of 20 respondents) with the inclusion criteria primigravida pregnant women who spontaneously vaginal delivery without complications or complications, Maternal with spontaneous rupture of 2nd degree perineal and given lidocaine when suturing and mothers who do not smoke. This study were followed up for 15 days to see perineal wound pain and wound healing of the perineum. Measuring tool to see perineal pain using the NRS and wound healing using REEDA.

RESULTS

This research was conducted in two health centers in Sleman namely Puskesmas Puskesmas Mlati Godean I and II. The number of samples in this study were 40 respondents (20 respondents 20 respondents intervention group and the control group).

Table 1. Characteristics of Research Subjects

characteristics of Respondents	Intervention group (N = 20), %	Control group (N = 20) %
Age (y.o)		
Not at risk		
20-35	19 (95.0)	19 (95.0)
Risk		
(<20 and> 35)	1 (5.0)	1 (5.0)
Total	20 (100)	20 (100)
Last hemoglobin		
Normal	18 (90.0)	16 (80.0)
mild anemia	2 (10.0)	4 (20.0)
Total	20 (100)	20 (100)
Techniques suturing		
simple interrupted	5 (25.0)	5 (25.0)
simple interrupted and		
simple continuous	15 (75.0)	15 (75.0)
Total	20 (100)	20 (100)
Personal hygiene		
SOP Godean I		
Community Health Center	10 (50.0)	10 (50.0)
SOP PHC Mlati II	10 (50.0)	10 (50.0)
Total	20 (100)	20 (100)

Table 2. The Mean Perineal Pain and Healing Wounds

Variables	Days to-	Group Intervention Average	Control Average
Wound pain perineum	1	4.15	5.30
	2	4.00	4.75
	3	3.55	4,05
	4	2.90	3.65
	5	2.55	3.10
	6	2.00	2.60
	7	1.65	2.40
	8	1.40	2.05
	9	1.15	1.50
	10	0.70	1.35
	11	0.50	1.15
	12	0.30	0.70
	13	0.15	0.35
	14	0.05	0.15
	15	0.05	0.15
Perineum Wound Healing	1	4.75	5.65
	3	1.65	2.30
	5	0.35	1.90
	7	0,00	1.75
	9	0.00	0.20
	11	0,00	0.00
	13	0.00	0.00
	15	0,00	0.00

Table 3. Comparison of Pain and Wound Healing Perineum Perineum

	Group Intervention mean ± SD	Control mean ± SD	Mean Difference	CI 95%	*P-value*
The perineum pain	25.10 ± 11.253	33.25 12,311	-8.150	-15.700 – 0.600	0.035
Perineum Wound Healing	6.75 ± 1.333	11.30 ± 1.455	-4.550	-5443 - 3.657	0.000

Results of research on Comparative Use of polyglactin 910 (Vicryl rapide) and Chromic catgut against Pain and Wound Healing perineum in Puskesmas Regency Sleman, it can be concluded use of polyglactin 910 (vicryl rapide) has a better effect on pain and wound healing of the perineum compared with the use of chromic catgut.

DISCUSSION

Based on the above table 1 showed that the characteristics of the respondents in the intervention group and controls by age in mind that almost all respondents are in the productive age and only 2 respondents who have a risky age. Respondents who experienced mild anemia in the intervention group as much as 2 respondents and in the control group as much

as 4 respondents. Sewing techniques used for engineering disconnected in the intervention group and by 5 respondents in the control group by 5 respondents in the two health centers had more frequent use sewing techniques baste and disconnected. Comparison of the appropriate personal hygiene at the health center respondents SOP intervention group and the control group is the same, each of the 20 respondents according to SOP I godean health centers and 20 health centers of respondents according to SOP Mlati II.

Based on Table 2 above showed a mean value of the highest perineal pain scores in the intervention group, namely on day 1 with a mean value of 4.15 and the lowest on day 14 with a mean value of 0.05, while the highest in the control group to-1 with a mean value of 5.30 and the lowest on day -14 with a mean value of 0.15.

The results mean value for perineal wound healing in the intervention group highest on day 1 with a mean value of 4.75 and the lowest at day-7 is 0.00. Whereas in the control group the highest average value on day 1 with a mean value of 5.65 and the lowest on day 11 with a mean value of 0.00.

Based on Table 3. The test results independent t-test can be concluded that perineal pain and healing wounds in the intervention group mean values of 25.10 and 6.75, whereas in the control group mean values of 33.25 and 11.30. The test results using statistical tests obtained independent t-test p-value <0.05, which means that there are differences in the use of threads polyglactin 910 (vicryl rapide) and chromic catgut thread to perineal pain and healing wounds in the mother postpartum perineum.

This is according to research conducted by explains that the use of suture material with *polyglactin* 910 (Vicryl rapide) superior than chromic catgut. *polyglactin* 910 (Vicryl rapide) can be absorbed naturally and may reduce pain compared with the use of chromic catgut sutures[7]. Also in line with research explained that the use of polyglactin 910 suture material (vicryl rapide) is an ideal suture material for perineal repair perineal pain that produces fewer and better wound healing compared to the use of chromic catgut suture material[8].

Explains that the use of thread vicryl rapide produces less pain and better wound healing (p <0.05 significant)[9]. In concluded that vicryl rapide better at reducing pain and wound healing in wound repair perineum.

Explained that the use of vicryl suture materials rapide there is a significant reduction in short-term pain[10]. The pain began to improve from the third day onwards, no experience moderate pain on day 7 and on day 15, no woman who complained of pain in the group vicryl rapide compared with chromic catgut were still experiencing mild pain on day 15. From day 7 onwards perception of pain was lower in the group vicryl rapide compared with chromic catgut

CONCLUSION

All in all, vicryl rapide thread to repair perineum or perineal wound suture is more effective to reduce perineal pain and has better perineal wound healing than chromic catgut thread. Health workers are suggested to choose the right material of thread in perineal repair in order to reduce pain and speed up the process of perineal wound healing in postpartum mothers with perineal rupture

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Research Article

Adiponection Serum Levels in Severe Preeclampsia

Kadar Adiponektin pada Pasien Preeklamsia Berat

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Abstract

Objective: To determine the difference adiponectin serum levels in pregnant patient with severe preeclampsia and normotency in Manado.

Methods: This study is a cross sectional study which the number of samples obtained was 52 samples in which the sample was divided into 26 pregnant samples with severe preeclampsia and 26 control samples. Samples were taken from Prof. dr. R. D. Kandou Manado Hospital and network hospitals around Manado within the inclusion and exclusion criteria. All patients were explained about the research procedure and singning the informed consent and take a blood sample by using the ELIZA method. After the data is collected, it is entered into the SPSS version 23.0 program for data analysis.

Result: There was a significant relationship between adiponection serum levels with the incidence of severe preeclampsia and normotency. But for body mass index variables there were no significant differences by using T test (independent sample) in each severe preeclampsia and normotency pregnancy group where p=0.903. Body mass index, height, weight, and weight gain during pregnancy showed that there is no difference between cases and controls (p>0.05) which means that body mass index is not related to the stete of the severe preeclampsia and normotency.

Conclusions: There was no relationship between BMI, age, parity, smoking, baby outcomes, delivery method and gestational age with the incidence of severe preeclampsia and normotency against adiponectin in this study.

Keywords: adiponectin, obstetrics, preeclampsia.

Abstrak

Tujuan: *Untuk mengetahui perbedaan kadar adiponektin serum pada pasien hamil preeklamsia berat dengan hamil normal di Kota Manado.*

Metode: *Studi ini merupakan studi potong lintang. Jumlah Sampel yang didapatkan sebesar 52 sampel dimana sampel dibagi menjadi 26 sampel hamil dengan preeklamsia berat dan 26 sampel kontrol. Sampel diambil dari RSUP Prof. dr. R. D. Kandou Manado dan rumah sakit jejaring sekitar manado yang memenuhi kriteria inklusi dan eksklusi. Semua pasien dijelaskan mengenai prosedur penelitian dan penandatanganan inform consent baru dilakukan pengambilan sampel darah untuk dilakukan pemeriksaan laboratorium dengan menggunakan metode ELISA. Setelah data dikumpulkan, maka dimasukkan ke dalam program SPSS versi 23.0 untuk data analisis.*

Hasil: *Perhitungan dengan menggunakan uji statistik Mann - Whitney menunjukkan bahwa terdapat perbedaan bermakna nilai rata-rata kadar adiponektin pada pasien hamil normal dengan pasien PEB (p = 0,000). Adanya hubungan bermakna kadar adiponektin dengan kejadian preeklamsia berat. Namun untuk variabel IMT yang dilakukan secara uji t (sampel independen) didapatkan kesimpulan tidak terdapat perbedaan bermakna pada masing-masing kelompok normotensi dan kelompok preeklamsia berat di mana p= 0,903, indeks massa tubuh, tinggi badan, berat badan, serta pertambahan berat badan selama kehamilan tidak berbeda antara kasus dan kontrol (p>0,5). Ini berarti bahwa IMT tidak berhubungan dengan keadaan terjadinya preeklamsia berat.*

Kesimpulan: *Tidak didapatkan hubungan antara IMT, usia, paritas, merokok, luaran bayi, cara persalinan dan usia kehamilan dengan kejadian preeklamsia berat dan normotensi terhadap adiponektin pada penelitian ini.*

Kata kunci: *adiponektin, obstetri, preeklamsia.*

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INTRODUCTION

Preeclampsia is a specific condition in pregnancy characterized by placental dysfunction and maternal response to systemic inflammation with endothelial activation and coagulation. Preeclampsia is a clinical syndrome where there is a decrease in organ perfusion due to vasospasm and endothelial activity characterized by hypertension, edema, and proteinuria that arise at gestational age above 20 weeks or immediately after delivery.[1,2] However, some other women show hypertension accompanied by other multisystem disorders that indicate a severe condition of preeclampsia even though the patient does not have a proteinuria. [3,4] Frequency of preeclampsia for each country varies due to many factors. In Indonesia is around 3-10% while in developing countries like the United Stated, it is reported that the incidence of preeclampsia is about 5% of all pregnancies. The World Health Organization (WHO) states that hypertension in pregnancy is a major cause of maternal and fetal mortality and morbidity. [3,5] About 50.000-70.000 deaths are reported due to preeclampsia. This disease occurs in 3-5% of pregnant women and is a major cause of death of pregnant women. The impact on pregnant women varies from severe hypertension, crisis hypertension, urgency, superimposed preeclampsia, HELLP syndrome, to eclampsia. Maternal Health shows that the incidence rate was 24.7% in 2011, 26.9% in 2012, and 27.1% in 2013 that effect for fetus such as premature birth, stunted fetal growth to fetal death. [2,6]

Treatment of severe preeclampsia is closely related to the use of antihypertensi. Calcium Channel Blocker acts on arteriolar smooth muscle and cause vasodilatation by inhibiting the entry of calcium into cell. Nifedipin is one of these classes of drugs that have been used since the last decade. The recommended dose is 10 mg orally can be repeated every 15-30 minutes, with a maximum dose of 30mg. Beside nifedipine, the drug used is also nicardipine which is a parenteral calcium that works reduce blood pressure in 20 minutes with 4-6 hours duration. Nicardipine more selectively in myocardial blood vessels, with lower side effect of tachycardia. Futhermore, Magnesium Sulfat prevent seizure in severe preeclampsia. The RCOG guidelines recommend loading magnesium sulphate 4gram for 5-10 minutes followed by a maintenance dose of 1-2 gram/hours for 24 hours postpartum or after the last seizure but monitoring of urine output, reflex of patella, frequency of breath and oxygen saturation.[7,8]

Severe Preeclampsia that is not resolved will have an impact on mother and baby. In the mother can occur brain haemorrhage which is the impact of cerebrovascular, neurological disorders, kidney and liver function, pulmonary edema, and blot clotting. While the fetus or baby can fetal growth restriction, preterm labor that can acute respiratory distress until death.[2,3,9]

Adiponectin is an important adipocytokine secreted mainly by fats that contain adipocytes and plays important role in glucose and lipid metabolism, inflammation and oxidative stress. Changes in adiponectin levels have been shown to directly affect lipid and glucose metabolism which further increase lipid synthesis, free faty acids, insulin resistance, obesity, cardiovascular disease, type 2 diabetes and inflammatory cytokines. It is a complex and actibe endocrine organ that plays an important role in regulating lipid and glucose. Adiponectin accounts for about 0.01% of all plasma protein (5-10^{m}g/ml).[4,5]

Adiponectin as an adipose tissue secretes various proteins into the circulation. These proteins are collectively called adipocytokines which are commonly referred to as adipokines. This adipokin consist of adiponectin, free faty acid (FFA), leptin, TNF-a, Plasminogen Activator Inhibitor-resistin, bone morphogenic protein, Insulin like growth factor, interleukin-I.[5,6] Adipose tissue is not only a place to store fat, but also an endoctine organ that plays an important role in the interaction of endocrine, metabolic, and inflammatory signals to regulate the body homeostatic energy. Increase adipose tissue will also be an increase in proinflammatory adipokines secretion along with a decrease in protective adiponectin secretion.

Pathophysiological of preeclampsia concepts related to atherosclerosis, endothelial dysfunction, insulin resistance, and inflammation. Many adipocyte hormones such as tumor necrosis factor, leptin, adiponectin, and interleukin 6 collectively called adiponectin that play an important role in the inflammatory and atherosclerotic processes. It is one of the many specific fatty tissue proteins and expressed and secreted from fat tissue.[4-6] In preeclampsia there is an immunological deficiency of trophoblast invasion into the spiral arteries which cause placental hypoperfusion and changes trigger activation of the vascular endothelium.

Experimental and clinical studies have stated that low plasma adiponectin levels are associated with metabolic factors associated with obesity and vascular disease both of which are risk factors for preeclampsia.

METHODS

This study is a cross sectional study to assess the comparison of adiponectin serum level in severe preeclampsia and normotency patients in Obstetrics and Gynecology.

The study was conducted at Prof. dr. R.D. Kandou Hospital Manado, Pancaran Kasih Hospital and Bhayangkara Hospital from Juli 2019 to December 2019.

The population in this study were all women who had clinical symptoms of severe preeclampsia at Prof. dr. R. D. Kandou Hospital and networking hospital in Manado. Samples were selected by history, physical examination and supporting examinations. Samples that met the inclusion criteria and had signed the consent form were included in the study. The sample used by consecutive sampling.

The inclusion criteria was patients with aterm pregnancy which have a high blood pressure and normotency and the ultrasonography study show intrauterine pregnancy in the fields of Obstetrics and Gynecology and willing to participate in research. The exclusion criteria was have a history of diabetes mellitus, cardiac or lung disease, malnutrition, HIV infection, refuse to participate in research, in medicine using antimicrobials, in treatment using immunosuppressants, fetal death, or preterm pregnancy.

The independent variable is severe preeclampsia and normotency patient and the dependent variable is adiponectin serum and body mass index.

Sampling was carried out at patient that met the inclusion criteria. Samples measured weight, height. After that the sample is taken blood sample from the vein about 5cc and has received an explanation and has signed a written statement of consent following the research that has been provided.

Sampling was carried out on blood sampling in patients and was sent to laboratory examination by using the ELIZA method. After the data is collected it is entered into the SPSS version 23.0 program for data anaylisis.

RESULTS

This research was conducted at Prof. dr. R.D. Kandou Hospital and networking hospital in Manado. The number of samples studied were 52 women who had clinical symptoms of severe preeclampsia and normotency in the field of Obstetrics and Gynecology who met the inclusion criteria.

Table 1 illustrates the distribution of research subjects based on age, gravidity, gestasional age, education, BMI, mode of delivery, the history of smoke, occupation.

The highest age distribution in the case of severe preeclampsia and normotency was in the reproductive age group of up to 20 years and below 35 years, 14 people and 15 people (53.8%, %7.6% p = 0,382). The results of the distribution of parity where multigravida were more dominant in the severe preeclampsia and normotency were 20 people and 18 people (77%, 69% p = 0.455). The results of the distribution of gestational age presentation in the severe preeclampsia group mostly >37 weeks-<40 weeks namely 16 people (61.5%) and for normotency patient were 20 people (77%)(p=0.542). The result of the distribution education levels group in severe preeclampsia mostly in primary and junior high school education which 13 people (50%) and normotency woman were 15 people (67%) (p= 0.324). Moreover, body mass index in the severe preeclampsia group mostly from the overweight and obesity groups of 19 people (75.1%) and normotency of 18 people (69.2%)(p = 0.451). The distribution result in group of severe preeclampsia and normotency that show the infant output is about >2500 gram-< 4000gram were 25 people (96.2%) and 24 patient (82,5%) (p-0.358). Futher more, the results of distribution mother delivery in normotency mostly by vaginal delivery 17 people (65.4%) neither in severe pregnancy by caesarean delivery with 21 people (80%) (p= 0.435) In the severe preeclampsia, 17 people (54.4%, p = 0.358) were smoke.

Table 2 illustrates the adiponectin serum in normotency and severe preeclampsia. In patient with normotency, adiponectin serum levels mean and standard deviation showed 4.423±1.08 while in severe preeclampsia adiponectin serum level meand and standard deviation showed 2.628±0.477. The calculation method using the Mann-Whitney statistical test showed that there were significant differences in the average

value of adiponectin serum level in severe preeclampsia (p=0.000). There was a significant relationship between adiponection serum levels with the incidence of severe preeclampsia and normotency.

Table 3 illustrates the distribution of body mass index variable and adiponectin serum in normotency and severe preeclampsia. grouping types of microorganisms. But for body mass index variables there were no significant differences by using T test (independent sample) in each severe preeclampsia and normotency pregnancy group where p=0.903. Body mass index, height, weight, and weight gain during pregnancy showed that there is no difference between cases and controls (p>0.05) which means that body mass index is not related to the state of the severe preeclampsia and normotency.

Table 1. Characteristics of Research subjects

Characteristics	Normotency		Severe Preeclampsia		P-value
	N	%	N	%	
Age (years)					0.382
<20	4	15.4	3	11.5	
>20 - <34	15	57.6	14	53.8	
≥35	7	27	9	34.7	
Paritas					0.455
Primigravida	8	31	6	23	
Multigravida	18	69	20	77	
Gestational age (week)					0.542
<37	0	0	0	0	
>37 - <40	20	77	16	61.5	
>40	6	23	10	38.5	
Education					0.324
Elementerary-Senior High School	15	57	13	50	
Senior High School	6	23	9	34.6	
Bachelor	5	20	4	15.4	
Body Mass Index					0.451
<18.5	0	0	0	0	
>18.5 - ≤25	8	30.8	7	26.9	
>25	18	69.2	19	73.1	
Delivery Method					0.435
Normal	17	65.4	5	20	
Cesarean Section	9	34.6	21	80	
History of Smoke					0.358
Never	8	30.8	9	34.6	
Smoker	18	69.2	17	65.4	
Fetal Weight (gram)					0.358
≤2500	0	0	2	7.7	
>2500 - <4000	25	96.2	24	92.3	
>4000	1	3.8	0	0	

Table 2. Adiponectin Serum in Normotency and Severe Preeclampsia

Variable	Normotency (n= 26)	Severe Preeclampsia (n=26)	P-value
Adiponectin Level (ng/ml)			
Mean	4.4238	2.6285	
Median	3.9350	2.72	0.000
Std Deviation	1.08555	0.477	
Minimun	3.37	1.74	
Maximum	7.05	3.40	

Table 3. Variable Distribution of Body Mass Index and Adiponectin Serum in Normotency and Severe Preeclampsia

Body Mass Index (BMI)		Adiponectin Serum		
		<3.58 ng/ml	3.58-9.66 ng/ml	>9.66ng/ml
Normotency	<18.5	0	0	0
	>18.5-<25	2	6	0
	>25 (overweight)	3	15	0
Severe Preeclampsia	<18.5	0	0	0
	>18.5-<25	7	0	0
	>25 (overweight)	19	0	0

	Grup	N	Mean	Std. Deviation
IMT	Normal	26	27.8473	4.62196
	PEB	26	27.6900	4.61608

DISCUSSION

In this study, 52 patients were eligible. All subjects of this study have met the inclusion criteria and exclusion criteria and have signed a form of willingness to be involved in this study.

In this study, sample characteristics were assessed from maternal age, education, occupation, and body mass index. In table 1, we can see a comparison of the characteristics of a sample of pregnancy with normotension and severe preeclampsia. The distribution of research subjects according to the age of group of mothers in the study was <20->35 years. The sample distribution in this study based on the age of the mother with the higher percentage in the age group of 20-35 years both in the normotension group of 15 people (57.6%) and the preeclampsia group of 14 people (53.8%). According to the theory that preeclampsia is more often found in the early and late reproductive age, namely in adolescents or over the age of >35 years, but in this study does not fit the theory of the causes of preeclampsia which cause a decrease in adiponectin levels. It is not in accordance with the theory of the factors causing the occurrence of preeclampsia in Prof. dr. R. D. Kandou Hospital and its surroundings based on the age group of 20-35 years.

The highest percentage of parity was multigravida in both normotension and severe preeclampsia groups, this is different from the theory that the frequency of preeclampsia is higher in primigravida compared to multigravida because the formation of antibody inhibitors (blocking antibodies) is not perfect against placental antigens so that arising from an immune response that does not benefit placental histocompability and increase the risk of preeclampsia. [10]

In this study an analysis show the relationship between serum levels of adiponectin in normotency and preeclampsia, in which there is a significant difference in the level of adiponectin with the average value of adiponectin levels obtained in the normotension group is 39.46 while in the preeclampsia group is 13.54 (p=0.00). This shows the relationship between adiponectin levels and the incidence of preeclampsia. An increased risk of preeclampsia has been noted to be related to several conditions related to insulin resistance, including gestational diabetes, maternal obesity, and excessive weight gain during pregnancy.[2]

The pathophysiology linking maternal obesity with pregnancy induced preeclampsia is an intensive subject of research with insulin resistance which plays an important role.[2,6] Although insulin resistance is increased in normal pregnancy activities to facilitate glucose transfer to the fetus and support the rapid growth of the fetus and placenta.

Research reports indicate that insulin signals and angiogenesis are closely related and irregularities in angiogenesis and insulin resistance can cause change in cellular critical function, endothelial cell injury, and consequently an increased risk for preeclampsia.

In this study table 3 shows that there is no relationship between the value of body mass index with the incidence of preeclampsia and the average body mass index in normotensive pregnancy is 27.84 and there is a decrease in the average body mass index value in the preeclampsia group 27.69 with a p-value 0.903. At the Hutzel-Wayne University Hospital in 22 normotensive pregnant women and 77 preeclampsia women showed that there was decrease in adiponectin levels with increasing maternal body mass index. Adiponectin levels in

the weight preeclampsia group with overweight and obesity (BMI>25kg/m2) were lower than the weight preeclampsia group with normal weight. Women with preeclampsia also had a higher BMI compared to normotensive control. This is because in obese there is an increase in inflammatory mediating factors such as IL6, C reactive peptide, TNF-alpha, and macrophages from the placenta which can cause dysfunction in the endothelial and vascular. But in this study, the adiponectin correlation test with BMI showed a weak correlation [5,6]

CONCLUSION

From the results of this study it was found that adiponectin levels in severe preeclampsia were significantly lower compared to normotensive pregnancy so it can be concluded that adiponectin levels were associated with the incidence of severe preeclampsia.

SUGGESTION

Further research to assess the relationship of adiponectin, preeclampsia, body mass index using a large sample and not only for aterm pregnancy but continue by examining the adiponectin levels in first/second trimester pregnant women as predictor of preeclampsia. Serum adiponectin examination can be considered as a marker for preeclampsia.

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Association of Husband Support and Postpartum Blues in Postpartum Women

Hubungan antara Dukungan Suami dan Gangguan Postpartum Blues pada Perempuan Pascamelahirkan

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Abstract

Objective: To determine the association of husband support and postpartum blues in postpartum women.

Methods: This was a cross-sectional study. Respondents are collected from postnatal women at the Pontianak St. Antonius Hospital, with random sampling. Retrieval of data use a research questionnaire. Data were analysed univariately and bivariate using the Chi-Square test method.

Result: Of the 96 respondents, 5.2% were <20 years old, 49% were in the 20-30 years age group, and 45.8% were> 30 years old . For parity data, 38.5% were primiparous women and 61.5% were multiparous women. As for employment status, 68.8% are in the unemployed group, and 31.2% are in the working group. 47.9% of respondents received inadequate husband support, and 52.1% respondents received adequate husband support. While 44.8% of respondents experienced postpartum blues, 55.2% did not. The results of the bivariate analysis showed a significant relationship between husband support and postpartum blues with p=0.042 and OR=2.331.

Conclusions: We found a significant relationship between husband support and postpartum blues disorder.

Keywords: family, husband support, postpartum blues.

Abstrak

Tujuan: Untuk mengetahui hubungan dukungan suami dengan gangguan postpartum blues pada perempuan pascamelahirkan.

Metode: Penelitian ini adalah penelitian analitik observasional dengan studi potong lintang, yang dilakukan di Rumah Sakit Santo Antonius Pontianak pada perempuan pascamelahirkan dengan metode pengambilan sampel acak sederhana. Dukungan suami diukur dengan menggunakan kuesioner Dukungan Suami dan PPB diukur dengan menggunakan kuesioner Edinburgh Postnatal Depression Scale (EPDS). Data dianalisis dengan menggunakan uji kai kuadrat.

Hasil: Dari 96 responden, sebanyak 5,2 % berada pada usia <20 tahun, 49% berada pada kelompok usia 20-30 tahun, dan 45.8% berada pada usia >30 tahun. Untuk data paritas, 38,5% adalah perempuan primipara dan 61,5% adalah perempuan multipara. Sementara untuk status pekerjaan, 68.8% adalah kelompok tidak bekerja dan 31,2% adalah kelompok bekerja. Responden yang mendapat tingkat dukungan suami yang kurang ada sebanyak 47,9% dan dukungan suami yang baik ada 52.1%. Responden yang mengalami PPB ada sebanyak 44,8% dan yang tidak mengalami PPB ada sebanyak 55,2%. Terdapat hubungan yang bermakna antara dukungan suami PPB dengan nilai p=0,042 dan OR sebesar 2,331.

Kesimpulan: Terdapat hubungan yang bermakna antara dukungan suami dan PPB.

Kata kunci: dukungan suami, gangguan postpartum blues, keluarga.

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INTRODUCTION

The period of pregnancy and birth (post-partum) is a dramatic episode for a woman, both from a biological, physical, and psychological point of view. Several adjustments are needed by women in dealing with these new activities and roles in the first weeks and months after giving birth. Some women manage to adjust well, but there are others who are unsuccessful and experience psychological disorders with a set of symptoms that researchers and clinicians confirm as Postpartum Blues (PPB) or Maternity Blues Disorder.[1]

When PPB is not handled properly, it will cause uncomfortable feelings for women who experience it, which also has a bad impact, especially for those closest to them, especially the relationship between husband and wife. Husband's support is the biggest factor in triggering PPB. This is because husband's support is an important coping strategy in times of stress and serves as a stress preventive strategy. [2]

Social support is physical and psychological comfort provided by friends or family members. Meanwhile, good social support has its own benefits for individuals who receive it. Particularly for pregnant women, good family support is proven to provide good pregnancy outcomes, such as babies with ideal weight and improved quality of pregnancy life itself. Research stated that pregnant women who receive adequate social support will improve their behavior in maintaining their health. [3] In contrast, women who do not get good social support are more likely to suffer from antenatal depression or other mood disorders.

The purpose of this study was to determine whether there is a relationship between husband's support and postpartum blues disorders in postpartum women at Santo Antonius Hospital, Pontianak. This study is expected to provide information for other researchers and to develop this research topic so that it can be widely used.

METHODS

This was a cross sectional study. Data were collected in June-August 2019. The target population in this study were all post-partum women at Santo Antonius Hospital, Pontianak. The research sample was 96 respondents, using simple random sampling method.

The dependent variable (dependent) from this study is postpartum blues disorder. The independent variable (independent) of this study is husband's support. The data was collected by the researcher by asking selected respondents to fill out the informed consent form, then the researcher and research assistant conducted interviews with the respondents using a husband's support questionnaire and the Edinburgh Postnatal Depression Scale (EPDS). The data is then processed and analyzed univariately and bivariately with the chi-square test.

RESULTS

Table 1. Subject Characteristics

Subject characteristic		n	%
Age (y o)	<20	5	5.2
	20-30	47	49.0
	>30	44	45.8
Parity	Primiparous	37	38.5
	Multiparous	59	61.5
Employment Status	Unemployed	66	68.8
	Employed	30	31.2

Interpretation : Most respondents are between the age of 20-30 years old, multiparous, and unemployed.

Table 2. Husband Support

Husband support	n	%
Poor	46	47.9
Good	50	52.1

Table 3. Postpartum Blues

Postpartum blues	n	%
Yes	43	44.8
No	53	55.2

Husband's Support and Postpartum Blues

Our study showed that there is a relationship between husband's support and PPB, meaning that postpartum women who have a poor level of husband's support will be more likely to experience PPB than post-partum women who have a good level of husband's support. In the postpartum group of women who experienced PPB, there were 26 women who received poor husband support (55.3%) and 17 women who experienced PPB and had a good husband's support level (34.7%). There were 21 women who did not experience PPB who had a poor level of husband support (44.7%). Meanwhile, there were 32 women who did not experience PPB and had a good level of husband's support (65.3%).

DISCUSSION

Subject characteristics data taken from this study are age, parity and work status of respondents. For age data, it was found that the largest number of respondents was in the 20-30 year age group as many as 47 people (49%). Meanwhile, for parity data, the largest group was respondents who had given birth before giving birth (multiparous) as many as 59 people (61.5%). As for work status, the group of respondents was dominated by the unemployed group as many as 66 people (68.8%).

If it is related to the age of the respondents in this study, the largest age group is young. From this study the age group that experienced the most PPB was the 20-30 year age group as many as 19 people from all the incidence (44.2%). Most women at a young age do not yet have qualified experience and mature mindset, so they do not understand the new role they will play as a mother. PPB affects as many of 13% of adult women[4] but also affects adolescent and younger mothers. There is evidence that the prevalence may be even higher in adolescents.[5,6]

Furthermore, the job characteristics of this study showed that most respondents do not work. The responsibility of being a parent is still believed to be the main responsibility of a mother. This thinking can influence a woman's decision, whether she wants to play a dual role as a working mother and woman, or if her child is the focus of her life. From this study, the unemployed women group was the dominant group who experienced PPB, as many as 31 people from all PPB incidents (72.1%). These results are also supported by research at the University of Nebraska regarding postpartum depression in 434 respondents, of the 97 women who experienced depression, 54% were in the unemployed group.[7]

From this study, the group of primiparous women (who gave birth for the first time) were dominant, which was 23 of the total incidence of PPB (53.5%). Regarding the characteristics of the number of children, primiparous women have a tendency to experience anxiety disorders compared to multiparous women because primiparous women have no experience of childbirth and caring for children, while multiparous women have previously had experience of childbirth and caring. for babies.

Based on data on husband's support, postpartum mothers who received good support from their husbands were higher than those who received support from their poor husbands. This can happen because pregnancy and childbirth are happy events that are seen as gifts for husband and wife.

The results showed that 50 respondents (52.1%) had good husband support and 46 respondents (47.9%) were less supported by their husbands. This result is also supported research at Puskesmas Gatak Sukoharjo where most of the data shows that husbands support themselves after giving birth, that husbands have attention and love for their wives, husbands feel responsible in carrying out the husband's role.[8] The amount of support from the environment, especially the husband given to the wife, is an important factor in influencing the wife so that there is no pressure to change roles after giving birth.[9]

Husband's support is influenced by various factors such as intimacy, self-esteem, and social skills. Husband's support is more influenced by intimacy than other aspects of social interaction, the more intimate a person is, the greater the support one gets. Based on the research data, it can be concluded that almost half of the incidence of PPB in post-partum mothers at Santo Antonius Hospital (44.8%). This result is consistent, which states that with support and a sense of satisfaction in marriage, a wife will be better able to cope with sadness or other emotional changes that she may experience during pregnancy and childbirth.[10]

CONCLUSION

The results of this study have generally answered questions about the relationship between husband support and postpartum blues in postpartum women. The results of this study indicate that there is a significant relationship between husband's support and PPB, with a value of p = 0.042 (p <0.05) and OR = 2.331. These results indicate that postpartum women who get a poor level of husband's support have a 2.331 times greater chance of experiencing postpartum blues than postpartum women who have a good level of husband's support.

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A Significant Increase in Maternal Blood Uric Acid Levels Accompanies the Severity of Hypertensive Disorders in Pregnancy

Peningkatan Signifikan Kadar Asam Urat Darah Ibu menyertai Keparahan Gangguan Hipertensi pada Kehamilan

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Abstract

Objective: To asses the relationship between maternal serum uric acid level and severity of hypertensive disorders in pregnancy and perinatal outcomes.

Methods: A cross sectional study was conducted at Persahabatan Hospital from January 2014 to December 2018. Subject were pregnant women with hypertensive disorder. Serum uric acid levels were taken from a venous blood sample at the time the patient came for delivery. The severity of hypertensive disorders in pregnancy were grouped into chronic hypertension, gestational hypertension, preeclampsia without severe feature, preeclampsia with severe feature, and preeclampsia with severe feature and organ involvement. The perinatal outcomes were the gestational age at birth, birth weight, and the first minute APGAR score. The relationship between maternal serum uric acid level and severity of hypertensive disorders in pregnancy and perinatal outcomes were analyzed using Mann Whitney and Kruskall Wallis test.

Result: A total of 704 out of 880 pregnant women with hypertensive disorder have met the criteria as research subjects. Maternal uric acid levels were found to increase significantly (p <0.001) with increasing severity of hypertensive disorders in pregnancy. Maternal who experienced preterm delivery had significantly higher blood uric acid levels (p <0.001) than those who experienced a term delivery. Maternal blood uric acid levels of infants with small birth weight for gestational age and first minute Apgar score <7 were slightly higher but not significant compared to maternal blood uric acid levels of normal birth weight infants and first minute Apgar score >7.

Conclusions: Maternal blood uric acid levels increased significantly accompanying the severity of hypertensive disorders in pregnancy. Blood uric acid levels tend to be higher in maternal who have poor perinatal outcomes.

Keywords: APGAR score, hypertensive disorders in pregnancy, preeclampsia, uric acid.

Abstrak

Tujuan: *Untuk menilai hubungan antara kadar asam urat serum ibu dan keparahan gangguan hipertensi pada kehamilan dan luaran perinatal.*

Metode: *Studi potong lintang dilakukan Rumah Sakit Persahabatan periode Januari 2014 sampai Desember 2018. Subjek penelitian adalah ibu hamil dengan gangguan hipertensi. Kadar asam urat darah diambil dari sampel darah vena pada saat ibu hamil datang untuk melahirkan. Tingkat keparahan gangguan hipertensi pada kehamilan dikelompokkan menjadi hipertensi kronik, hipertensi gestasional, preeklamsia tanpa gejala berat, preeklamsia dengan gejaka berat, dan preeklamsia dengan gejala berat dan keterlibatan organ. Luaran perinatal adalah usia kehamilan saat lahir, berat badan bayi lahir, dan skor APGAR menit pertama. Hubungan antara kadar asam urat darah ibu dan tingkat keparahan gangguan hipertensi pada kehamilan dan luaran perinatal dianalisis menggunakan uji Mann Whitney atau uji Kruskall Wallis.*

Hasil: *Sebanyak 704 dari 880 ibu hamil penderita hipertensi telah memenuhi kriteria sebagai subjek penelitian. Kadar asam urat darah ibu meningkat secara signifikan (p <0,001) dengan meningkatnya keparahan gangguan hipertensi pada kehamilan. Ibu yang melahirkan preterm memiliki kadar asam urat darah yang lebih tinggi secara bermakna (p < 0,001) dibandingkan ibu yang melahirkan aterm. Kadar asam urat darah ibu dari bayi dengan berat lahir kecil untuk usia kehamilan dan skor Apgar menit pertama < 7, sedikit lebih tinggi tetapi tidak signifikan, dibandingkan kadar asam urat darah ibu dari bayi berat lahir normal dan skor Apgar menit pertama pertama > 7.*

Kesimpulan: *Kadar asam urat darah ibu meningkat secara signifikan menyertai beratnya gangguan hipertensi pada kehamilan. Kadar asam urat darah cenderung lebih tinggi pada ibu yang memiliki luaran perinatal kurang baik.*

Kata kunci: *APGAR, asam urat, hipertensi dalam kehamilan, preeklamsia.*

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INTRODUCTION

Maternal mortality rate (MMR) is one of major health problems in Indonesia. In 2015, maternal mortality rate in Indonesia ranks among the highest among Southeast Asian countries at 305 per 100,000 live births.[1,2] This figure is still far from the Sustainable Development Goals target (SDG), which in 2030 expected that MMR in all countries will drop to under 70 per 100,000 live births.[3,4] The three main causes of maternal death are bleeding (30%), hypertension (25%), and infections (12%).[5] Among those three main causes, hypertension is one of the most difficult problems to undertake in pregnancy, causing maternal and neonatal morbidity. In fact, there are more than 60,000 maternal deaths worldwide each year due to hypertensive disorder in pregnancy.[6]

Based on guidelines from The American Congress of Obstetricians and Gynecologists (ACOG) in 2019, hypertensive disorders in pregnancy can be classified into; Hypertension in pregnancy; chronic hypertension, preeclampsia without severe disorders (preeclampsia without severe features), and preeclampsia with severe disorders (severe preeclampsia feature).[7] Preeclampsia appears at 20 weeks after gestation, characterized by hypertension accompanied by proteinuria.[8,9] There are many risk factors of hypertension in pregnancy, one of which is maternal serum uric acid level.[9]

Uric acid is a purine degradation product that is catalyzed by the enzyme xanthine dehydrogenase / xanthinoxidase (XDH / XO).[10] Previous studies reported a significant increase in uric acid levels in 16% of patients with hypertension in pregnancy and 75% of patients with preeclampsia.[11,12] Previous theory mentioned that elevated uric acid levels in the condition of preeclampsia is a secondary change caused by worsening of kidney function.[13] However, other studies have shown that worsening in preeclampsia is characterized by an increase in maternal uric acid blood levels.[14,15] Blood uric acid plays a role in the pathophysiology of preeclampsia through the process of inhibition of endothelial cell proliferation, trophoblast invasion, and inhibiting the release of nitric oxide (NO).[16] This results in blood vessels with large diameters that do not respond to smooth muscle thereby making inadequate oxygen and nutrient transport. Other studies have even shown that increased uric acid in patients with preeclampsia can be seen since the 10th week of gestation,

much earlier than the initial clinical symptoms shown by patients.[14] However, there has not been any study analyzing the outcome of mothers with hypertensive disorders having elevated uric acid level in Indonesia.

This study aims to asses the relationship between maternal serum uric acid level and severity of hypertensive disorders in pregnancy and perinatal outcomes.

METHODS

This is a cross sectional study determined to assess the relationship between maternal serum uric acid level and various maternal and perinatal complications. This study was performed in January 2011 to December 2018, at Persahabatan General Hospital, Jakarta, Indonesia. Subjects were all pregnant mothers with hypertensive disorders having delivery during the course of the study. Mothers with history of serum uric acid level elevation before pregnancy due to chronic diseases such as arthritis gout or renal disease were excluded from the study. The samples were recruited using total sampling method.

This study use 5% error bound and 95% confidence interval limit, power of the test considered to be 90%. The study was approved by the Research Ethics Committee, Faculty of Medicine, Universitas Indonesia with protocol number 17-03-0208 and Persahabatan General Hospital with ethical clearance number 09/KEPK-RSUPP/02/2018. All patients who were included in this study had given their informed consent prior to their inclusion in the study.

Collected data were then analyzed using SPSS for Macintosh ver. 20. Characteristics of patients in the form of sociodemographic and clinicopathologically are analyzed descriptively. Serum uric acid levels were taken from a venous blood sample at the time the patient came for delivery. The maternal outcome in this study was the degree of hypertension and grade of hypertension. Severity of hypertensive disorder was grouped into chronic hypertension, gestational hypertension, preeclampsia without severe feature, preeclampsia with severe feature, and preeclampsia with severe feature and organ involvement. Chronic hypertension was defined as hypertensive disorder history prior to pregnancy. Gestational hypertension was defined as blood pressure of more than 140/90 mmHg after 20 weeks of pregnancy without proteinuria or severe feature of preeclampsia. Preeclampsia without

severe feature was defined as blood pressure between 140/90 mmHg and 160/110 mmHg with proteinuria. Preeclampsia with severe feature was defined as blood pressure of more than 160/110 mmHg with proteinuria while preeclampsia with severe feature and organ involvement was defined as preeclampsia with or without proteinuria with either thrombocytopenia, liver dysfunction, renal insufficiency, pulmonary edema, new onset headache unresponsive to medication, or new onset visual disturbance. The infant outcomes in this study were gestational age at birth, infant birth weight according to the Lubchenco Curve and first minute APGAR score. The relationship between uric acid levels and various outcomes was questioned using the Kruskal Willis and Mann Whitney test.

RESULTS

A total of 704 subjects met the inclusion criteria and had been further analyzed. Clinical variables were analyzed for its distribution and presented accordingly. (Table 1)

Table 1. Clinical Characteristics of Subjects

Hypertensive Disorder	n (%)	Serum uric acid (mg/dL)
Chronic hypertension#	13 (1.8)	3.35 + 0.63
Gestational hypertension*	133 (18.9)	4.9 (3.2 – 8.0)
Preeclampsia without severe feature#	82 (11.6)	5.18 + 1.54
Preeclampsia with severe feature*	360 (51.1)	5.3 (2.2 – 9.8)
Preeclampsia with severe feature and organ involvement*	116 (16.5)	7.6 (2.7 – 16.0)

*#mean ± std deviation; *median (min – max)*

In order to determine the relationship between hypertensive disorder and serum uric acid level, hypertensive disorder categories suffered by patient was transformed into 3 different categories, namely 1) chronic hypertension and gestational hypertension, 2) preeclampsia without severe feature, and 3) preeclampsia with severe feature with/without organ involvement. The result can be found on Table 2

Table 2. Relationship between Hypertensive Disorder and Serum Uric Acid Level

Hypertensive Disorder	n (%)	Serum uric acid (mg/dL)	P-value
Chronic hypertension and gestational hypertension*	146 (20.7%)	4.8 (2.2 – 8.0)	
Preeclampsia without severe feature #	82 (11.6%)	5.18 + 1.54	< 0.001+
Preeclampsia with severe feature with/without organ involvement*	476 (67.7%)	5.7 (2.2 – 16.0)	

*#Mean ± std deviation; *median (min – max), +Kruskall Wallis test*

In order to determine the relationship between maternal serum uric acid level and perinatal outcome, Kruskal Willis analysis was done between preterm birth, birth weight, and APGAR score with maternal serum uric acid level. (Table 3)

Table 2. Relationship between Hypertensive Disorder and Serum Uric Acid Level

Category	n (%)	Maternal Serum Uric Acid (mg/dL)	P-value
Preterm Birth			
Aterm*	465 (66.01)	5.0 (2.2 – 9.8)	
Preterm*	239 (34.09)	6.3 (2.7 – 16)	< 0.001#
Birth Weight			
Normal*	619 (87.9)	5.4 (2.2 – 14.5)	
Small for Gestational Age*	85 (12.1)	5.6 (2.7 – 16.0)	0.169#
APGAR score			
> 7*	630 (89.5)	5.35 (2.2 – 14.5)	
< 7*	74 (10.5)#	6.0 (2.8 – 16.0)	0.06#

median (min – max), #Mann Whitney U test

Based on the analysis done, it was known that preterm birth babies tend to be born by mother with higher level of serum uric acid (p < 0.001). There was no relationship between maternal serum uric acid with birth weight and first minute APGAR Score (p > 0.05).

DISCUSSION

According to ACOG 2013 and 2019, hypertension disorders in pregnancy are divided into 4 groups, namely chronic hypertension, hypertension in pregnancy, preeclampsia without severe symptoms, and preeclampsia with severe symptoms.7 In this study, it was found that there was significant difference between groups (p<0.001). Studies have reported that increased maternal and perinatal complications were associated with higher maternal blood uric acid levels >6 mg / dL in preeclampsia patients.[10,11]

There are several studies assessing the pathophysiology behind increased severity of hypertensive disorders in pregnancy due to higher maternal uric acid level, namely endothelial dysfunction due to high oxidative stress, decreased NO levels suppressing the ability of vasodilation of blood vessels and increase vascular tone, especially placental vascularization, as well as increased vasopressor levels such as endothelin and thromboxane. One study has shown that administration of allopurinol in women with hypertensive disorders in pregnancy can reduce the incidence of endothelial dysfunction and improve vascular vasodilation.[13] Previous studies reported that condition of hypertension accompanied by hyperuricemia had the same risk of having preeclampsia compared to pregnant women with hypertension accompanied by proteinuria. In this study, it was not explained about the degree of hypertension in patients.[17]

Based on the analysis conducted in this study, maternal having preterm birth had higher level of serum uric acid (p <0.001). Previous studies suggested that hyperuricemia condition increases incidence of preterm birth, especially in patients with preeclampsia. However, the study also showed that patients with hyperuricemia without preeclampsia were more likely to have preterm births than patients with normal uric acid levels.13 Previous study also reported that increased maternal blood uric acid levels are associated with stunted fetal development and low birth weight babies.[18] Other studies in India show that 100% of patients with blood uric acid levels > 5.5 mg/dL during the last trimester of pregnancy have term infants with birth weights below 2500 grams.[19] However, it was known from this study that there was no relationship between serum uric acid level and birth weight or APGAR score.

CONCLUSIONS

Maternal blood uric acid levels increased significantly accompanying the severity of hypertensive disorders in pregnancy. Blood uric acid levels tend to be higher in maternal who have poor perinatal outcomes.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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Research Article

Efficacy of Channa Striata Extract Capsule (Vipalbumin®) for Serum Albumin Level and Wound Healing Postradical Hysterectomy in Cervical Cancer Patients

Efektivitas Konsumsi Kapsul Ekstrak Ikan Gabus terhadap Kadar Albumin Serum dan Penyembuhan Luka Pascahisterektomi Radikal Pasien Kanker Serviks

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Abstract

Objective: To determine the efficacy of Channa striata extract on serum albumin level and wound healing after radical hysterectomy in cervical cancer patients in Mohammad Hoesin Hospital Palembang.

Methods: A clinical trial was conducted in Mohammad Hoesin Hospital Palembang during period of January – September 2019. Samples were cervical cancer patients undergoing radical hysterectomy. Serum albumin level was measured before surgery, after surgery, and after the administration of *Channa striata* extract capsule. Efficacy of the supplement was analyzed with SPSS version 20 using paired t-test.

Result: Twenty-eight cervical cancer patients undergoing radical hysterectomy who fulfilled inclusion criteria were obtained. Majority of patients were aged between 40-49 years old (89.3%), normoweight (39.3%), and lived in rural area. Mean duration of surgery was 154.46 ± 40.47 minutes. Serum albumin level before surgery, after surgery and after the administration of Channa striatus extract were 3.4 ± 0.61 g/dL, 2.91 ± 0.42 g/dL, and 3.11 ± 0.49 g/dL, respectively. There was a statistically significant difference between serum albumin level before and after the surgery (p=0.000). However, no statistically significant difference was found between serum albumin level after surgery and after administration of Channa striata extract capsule (p=0.750).

Conclusions: There was no significant difference between serum albumin level after surgery and after administration of Channa striata extract capsule.

Keywords: cervical cancer , channa striatus extract , radical hysterectomy, serum albumin level.

Abstrak

Tujuan: *Untuk mengetahui efikasi ekstrak Channa striata terhadap kadar albumin serum dan penyembuhan luka pasca histerektomi radikal pada pasien kanker serviks di RS Mohammad Hoesin Palembang.*

Metode: *Uji klinis dilakukan di RS Mohammad Hoesin Palembang selama periode Januari – September 2019. Sampel adalah pasien kanker serviks yang menjalani histerektomi radikal. Kadar albumin serum diukur sebelum operasi, setelah operasi, dan setelah pemberian kapsul ekstrak Channa striata. Khasiat suplemen dianalisis dengan SPSS versi 20 menggunakan uji-t berpasangan.*

Hasil: *Didapatkan 28 pasien kanker serviks yang menjalani histerektomi radikal yang memenuhi kriteria inklusi. Mayoritas pasien berusia antara 40-49 tahun (89,3%), normoweight (39,3%), dan tinggal di daerah pedesaan. Durasi rata-rata operasi adalah 154,46 ± 40,47 menit. Kadar albumin serum sebelum operasi, setelah operasi dan setelah pemberian ekstrak Channa striatus berturut-turut adalah 3,4 ± 0,61 g/dL, 2,91 ± 0,42 g/dL, dan 3,11 ± 0,49 g/dL. Ada perbedaan yang signifikan secara statistik antara kadar albumin serum sebelum dan sesudah operasi (p=0,000). Namun, tidak ditemukan perbedaan yang signifikan secara statistik antara kadar albumin serum setelah operasi dan setelah pemberian kapsul ekstrak Channa striata (p=0,750).*

Kesimpulan: *Tidak terdapat perbedaan yang bermakna antara kadar albumin serum setelah pembedahan dan setelah pemberian kapsul ekstrak Channa striata.*

Kata kunci: *ekstrak Channa striatus, histerektomi radikal, kadar albumin serum, kanker serviks.*

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INTRODUCTION

Surgical wound is categorized into 4 classes, i.e. clean wound, clean-contaminated wound, contaminated wound and infected wound. Post-operative wound care will provide faster wound healing with better aesthetic and functional results. Patient's preoperative condition also plays role for wound healing, this include nutritional status, medical comorbidity and certain habits. Nutritional support and certain formula can modulate immune system and eventually will reduce postoperative complications and length of hospital stay.[1,2]

Preoperative serum albumin is one of the prognostic factors for postoperative complications and also associated with impaired nutritional status. The major physiological functions of serum albumin are the regulation of both plasma oncotic pressure and capillary membrane permeability, and ligand binding and transport. Therefore, low serum albumin must be corrected. [2-4]

Snake head fish *(Channa striata)* extract is a cheaper alternative for intravenous albumin. Several studies have been conducted to investigate efficacy of Channa striata extract in wound healing. However, there was no sufficient data to support the efficacy of *Channa striata* extract in post radical hysterectomy wound healing.[5]

The aim of this study is to assess the efficacy of *Channa striata* extract on serum albumin level and wound healing after gynecological surgery in RSUP Dr Moh Hoesin, Palembang.

METHODS

A clinical trial was performed in Dr. Mohammad Hoesin Hospital Palembang during period January – September 2019 using consecutive sampling method. Women with cervical cancer who had undergone radical hysterectomy in Dr. Mohammad Hoesin Hospital Palembang were included in this study. The inclusion criteria were women aged between 20 and 65 years old with postoperative serum albumin level less than 3.5 g/dL, had agreed to participate in the study and signed informed consent. Exclusion criteria were metabolic disorder such as diabetes mellitus and liver cirrhosis, patient with history of coagulopathy, hypersensitivity to or was contraindicated to receive albumin. All data were recorded and analyzed using SPSS ver 20.0

by paired t-test and multivariate binary logistic regression with 95% confidence intervals. The protocol of this study had been approved by Ethical Committee of Medical Faculty of Sriwijaya University and Dr. Mohammad Hoesin Hospital Palembang.

RESULTS

During the research period, 28 samples were included in this study. Mean age of the samples was 48.14 ± 8.09 year-old. Most samples were in the age group 40 – 49 year-old (n=25, 89.3%). Most patient lived in rural area (n=19, 67.9%). Detailed baseline characteristics was described in Table 1.

Table 1. Baseline Characteristics

Characteristics	n	%
age (year-old)		
mean ± SD	48.14 ± 8.09	
median (Min –Max)	48 (27 – 60)	
age (year-old)		
20 - 29	1	3.6
30 - 39	2	7.1
40 - 49	25	89.3
Educational background		
Elementary to junior high school	9	32.1
Senior high school or higher	19	67.9
Residence		
Urban area	9	32.1
Rural area	19	67.9
Bodyweight (kg)		
mean±SD	55.04±7.88	
median (min-max)	54.5 (35-73)	
Weight (m)		
mean±SD	1.53±0.47	
median (min-max)	1.53 (1.45-1.62)	
Body Mass Index (kg/m2)		
mean±SD	23.35±2.94	
median (min-max)	23.34 (15.55-29.99)	
Body Mass Index (kg/m2)		
Underweight	2	7.1
Normoweight	11	39.3
Overweight	7	25.0
Obese	8	28.6
Duration of surgery (minutes)		
mean±SD	154.46±40.47	
median (min-max)	150 (90-240)	
Duration of surgery (minutes)		
60 – 120	9	32.1
121 – 180	14	50.0
181 – 240	5	17.9

We measure serum albumin level at three points, before surgery, after surgery and after administration of Channa striata extract capsule (Vipalbumin®). Before surgery, serum albumin level was 3.4 ± 0.61g/dL (2.3-4.4 g/dL). Postoperative serum albumin level decreased to 2.91 ± 0.42 g/dL (2.2-3.5 g/dL). There were 92.9% (n=26) patients who showed a decrease of serum albumin level after surgery. There was a statistically significant difference between

serum albumin level before and after the surgery
(p=0.000)

Table 2. Comparison of Serum Albumin Level before and after Surgery

		Serum albumin level (g/dL)	*P-value*
Before surgery (3.4 ± 0.61)	After surgery	2.91 ± 0.42	0.000
	After administration of Vipalbumin®	3.11 ± 0.49	0.001

Wilcoxon Test, p = 0.05

After administration of Vipalbumin®, serum albumin level increased to 3.11 ± 0.49 g/dL (range 2.1-3.8 g/dL). There was a statistically significant difference between serum albumin level before surgery and after administration of Vipalbumin® (p=0.001).

Serum albumin level was compared before surgery and after administration of Vipalbumin®. Serum albumin level after surgery was 2.9 ± 0.42 and after administration of Vipalbumin® was 3.11 ± 0.49. There was no statistically significant difference between serum albumin level before surgery and after administration of Vipalbumin (p=0.750).

Table 3. Serum Albumin Level

Characteristic	Time		*P-value*
	after surgery	**after administration of Vipalbumin**	
Serum albumin level, mean ± SD, g/dL	2.91 ± 0.42	3.11 ± 0.49	0.750[a]

DISCUSSION

The oldest age was 60 year-old and the youngest was 27 year-old; the median was 48 year-old. This finding was consistent that reported incidence of cervical cancer was found highest in age range of 45-59 year old.[6]

Mean BMI was 23.34 kg/m2. Most patients were normoweight (39.3%). Based on Clark's study, BMI was correlated with cervical cancer prognosis. Extreme BMI (underweight, overweight and obesity) in cervical cancer patients was correlated with poor survival.[7]

Mean surgery duration was 154.46±4.6 minutes. Surgery can cause metabolic stress response and contribute to complications, healing time and length of hospital stay. There was negative correlation between serum albumin level before surgery and surgery duration.[8,9]

Preoperative serum albumin level mean was 3.4±0.61 with range 2.3-4.4 g/dL. After surgery, serum albumin level decrease to 2.91±0.42 with range 2.2-3.5 g/dL, most sample (n=26, 92.9%) experienced lower serum albumin level after the surgery. There was a statistically significant

difference between preoperative serum albumin level and postoperative serum albumin level (p=0.000). This result is consistent with their report.[8,10]

Serum albumin level after administration of snake head fish extract were increased (mean 3.11±0.49). There was no significant difference between serum albumin level after surgery and after administration of snake head fish extract (p=0.750). This finding is contradicted a significant difference between serum albumin level before and after administration of snake fish head in patients underwent emergency laparotomy. Study samples were patients with solid organ rupture and bowel perforation while our study samples were cervical cancer patients. Lower serum albumin level was found in cancer and cachexia cancer.[11,12]

CONCLUSION

There was no significant difference between serum albumin after surgery and after administration of Channa striata extract capsule.

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Research Article

The Role of Thrombocytosis as a Prognostic Factor for Epithelial Ovarian Cancer

Peran Trombositosis sebagai Faktor Prognostik pada Kanker Ovarium Jenis Epitelial

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Abstract

Objective: To determine whether thrombocytosis is a prognostic factor for epithelial ovarian cancer and its relationship with 3-year overall survival in epithelial ovarian cancer patients.

Methods: This study is a retrospective cohort study using medical record of patients with epithelial ovarian cancer registered in cancer registry of Oncology Division in Obstetrics and Gynecology Department, Dr. Cipto Mangunkusumo National General Hospital from January 2014 - July 2016. Data were collected when subjects were first until diseases outcomes identified in 3 years.

Result: Out of 220 subjects, 132 (60%) were patients with advanced stage epithelial ovarian cancer (stage II/III/IV). 94 (42.7%) subjects had thrombocytosis. Patients with advanced stage of disease had higher risk of having thrombocytosis than the ones with earlier stage (p=0.005; OR=2.329). Correlation between thrombocytosis and 3-year overall survival was known to be insignificant (p=0.555). There was shorter mean time survival between patients with thrombocytosis and the ones without but the there was no significant difference in hazard ratio between the two groups (p = 0.399).

Conclusions: Thrombocytosis is not a prognostic factor in patients with epithelial ovarian cancer. There is also no significant difference of 3-year overall survival between patients with or without thrombocytosis.

Keywords: epithelial ovarian carcinoma, prognosis, thrombocytosis.

Abstrak

Tujuan: *Membuktikan bahwa trombositosis sebagai faktor prognosis kesintasan pada pasien kanker ovarium jenis epitelial dan hubungannya terhadap kesintasan 3 tahun pasien kanker ovarium jenis epitelial.*

Metode: *Penelitian ini merupakan studi kohort retrospektif menggunakan data rekam medis pasien kanker ovarium epitelial yang terdaftar pada cancer registry Departemen Obstetri dan Ginekologi Divisi Onkologi Rumah Sakit Cipto Mangunkusumo pada tahun Januari 2014-Juli 2016. Pengamatan dilakukan saat subjek pertama kali didiagnosis akhir pengamatan selama 3 tahun.*

Hasil: *Didapatkan 220 subjek penelitian yang merupakan populasi terjangkau dan memenuhi kriteria inklusi dan eksklusi. Dari 220 subjek penelitian, 132 (60%) dari 220 subjek penelitian merupakan pasien dengan kanker ovarium stadium lanjut (Stadium II/III/IV). Trombositosis didapatkan pada 94 orang subjek penelitian (42,7%). Pasien dengan kanker stadium lanjut memiliki risiko trombositosis yang lebih tinggi dibandingkan subjek pada stadium awal (p=0,005;OR=2,329). Trombositosis secara statistik tidak bermakna pada kesintasan 3 tahun (p=0,555). Terdapat mean time survival yang lebih rendah pada pasien dengan trombositosis tetapi tidak ada perbedaan hazard ratio yang bermakna antara subjek dengan atau tanpa trombositosis (p=0,399).*

Kesimpulan: *Trombositosis bukan merupakan faktor prognostik pada pasien kanker ovarium jenis epitelial dan tidak terdapat hubungan antara trombositosis dan 3 tahun pada pasien dengan kanker ovarium jenis epitelial.*

Kata kunci: *karsinoma ovarium epitelial, prognosis, trombositosis.*

INTRODUCTION

Ovarian cancer is one of the most common cancers suffered by women along with breast, cervical, lung and rectal cancers. Epithelial ovarian cancer is the most deadly gynecological malignancy, representing 21,980 new cases in 2014 in the United States and about 14.270 (64.9%) of which outcome were death.[1] Only 30% of ovarian cancer patients can be diagnosed at an early stage, while the rest are already in an advanced stage.[2]

Cancer is a pathological condition that can be associated with thrombocytosis. This particular condition could be caused by the release of cytokines from several malignancies. Studies have shown that thrombocytosis in epithelial ovarian cancer is associated with increased levels of IL-6 in serum which will ultimately stimulate thrombopoiesis, therefore increasing thrombocyte production.[3] Platelets would influence natural evolution of cancer through several mechanisms, namely protection against tumor cells and simultaneously produce several Growth Factors (GF) and enzymes such as lysophosphatidic acid, Metalloproteinase Matrix (MMP), thymidine phosphorylase, and vascular endothelial growth factor (VEGF) which play a role in angiogenesis, invasion and metastasis of tumor cells.[4,5]

Thrombocytosis is associated with increased chance of recurrence for various cancer, including ovarian cancer (HR: 2.37; 95%CI: 1.82, 3.09).[6] Previous researched have also studied that there is a linear relationship between thrombocytosis, stage of cancer, and decreased survival in patients with ovarian cancer.[7] Growth factors and cytokines examination, while proven to be effective in determining the prognosis of cancer patients, remains to be costly for many countries, including Indonesia. Meanwhile, platelet examination is a routine blood test performed on patients, easy to do and relatively low cost compared to examination of growth factors and cytokines such as VEGF, PDGF and others.

This study aims to determine the relationship between thrombocytosis and 3-year survival of patients with epithelial ovarian cancer.

METHODS

An retrospective study was performed in National General Hospital Dr. Cipto Mangunkusumo on January 2014 to July 2019.

The study population were all epithelial ovarian cancer patients diagnosed between January 2014 and July 2016 and have completed appropriate treatment according to the procedure set. Patients with suspected sepsis, having another malignancy, or having incomplete medical record were excluded in this study. Consecutive sampling method was done in this study. Patients were then divided into thrombocytosis and non-thrombocytosis group. Thrombocytosis was defined as having thrombocyte in serum of more than 400.000 unit / dL. Baseline characteristics were analyzed and compared. Bivariate analysis between subjects' characteristics and thrombocytosis was done. Survival analysis using Kaplan-Meier was done to all subjects and overall survival between study groups were compared. Ethical clearance was issued from health research and ethical committee in Faculty of Medicine, Universitas Indonesia.

RESULTS

A total of 220 ovarian cancer patients had completed treatment in Dr. Cipto Mangunkusumo National General Hospital, therefore included in this study. Among those 220 subjects, 132 (60%) of whom were diagnosed with advanced ovarian cancer (stage II-IV), 94 (42.7%) of whom had thrombocytosis, 215 (97.7%) of whom had elevated CA-125 level, and 15 (6,8%) of whom died during the follow up period. Baseline characteristics of subjects can be found on Table 1.

**Table 1.** Baseline Characteristics of Subjects

Variables	Category	n	%
Age	≤ 50 years	97	44.1
	> 50 years	123	55.9
Thrombocytes	< 400.000 /dl	126	57.3
	≥ 400.000/dl	94	42.7
Stagimg	Early stage	88	40
	Advanced stage	132	60
	Stage II	35	15.9
	Stage III	77	35
	Stage IV	20	9.1
Histopathology	Serous	106	48.2
	Mucinous	42	19.1
	Endometrioid	23	10.5
	Clear Cell	47	21,4
	Transitional	2	0.9
Ascites	Not found	138	62.7
	Found	82	37.3
CA-125	< 35 IU/L	5	2.3
	≥ 35 IU/L	215	97.7
Tumor Residue	< 1cm	131	59.5
	≥ 1cm	89	40.5
3-years survival	Positive	205	93.2
	Negative	15	6.8

In order to determine the involvement of other variables in determining thrombocytosis level in ovarian cancer patients, bivariate analysis between groups was done. Result of bivariate analysis in this study can be found in Table 2.

Table 1. Baseline Characteristics of Subjects

Variable	Study Groups		P-value	RR	CI 95%
	Thrombocytosis (N = 29)	Non-Thrombocytosis (N = 61)			
Age (y.o)			0.013	0.66	0.49-0.90
> 50	43 (19.5)	80 (36,.4)			
< 50	51 (23.2)	46 (20.9)			
Ascites			< 0.001	1.86	1.38-2.50
Yes	50 (22.7)	32 (14.5)			
No	44 (20)	90 (42.7)			
CA-125			0.396	2.16	0.37-12.57
> 35 IU/L	93 (42.3)	122 (55.5)			
< 35 IU/L	1 (0.5)	4 (1.8)			
Stage			0.005	1.65	1.16-2.36
Advanced	67 (30.5)	65 (29.5)			
Early	27 (12.3)	61 (27.7)			
Residue (cm)			0.884	0.96	0.70-1.31
> 1	37 (16.8)	52 (23.6)			
< 1	57 (25.9)	74 (33.6)			

In order to compare overall survival rate of patients with and without thrombocytosis, survival analysis using Kaplan-Meier was done in this study. The Kaplan-Meier graph for this study can be found on figure 1.
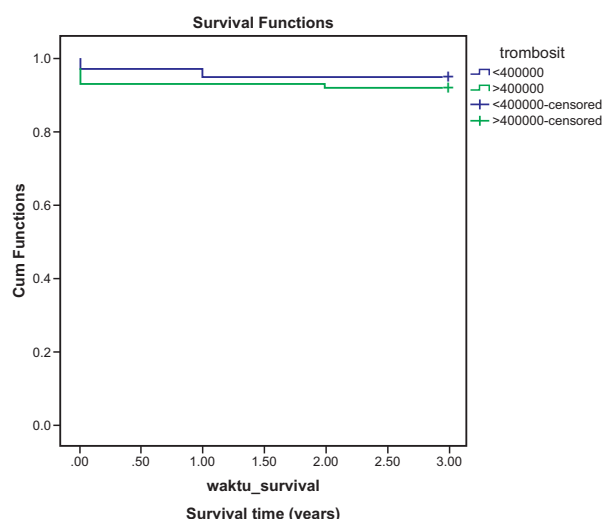
Figure 1. Kaplan-Meier Graph between Study Groups

In order to compare overall survival between groups, cox-regression analysis was done. It was found that there were no significant difference of survival time between study groups. (p = 0,555). The result of cox-regression analysis can be found on Table 3.

Table 3. Cox-regression Analysis of Study Groups

Variables	HR	P-value	95 % CI
Trombocyte level <400.000 /dl ≥ 400.000/dl	1.548	0.399	0.561-4.269

DISCUSSION

In this study, it was found that patients with advanced cancer had a higher risk for thrombocytosis (p = 0.005; OR = 2.329). These results are similar to previous studies such as studies.[3] In the mouse model, demonstrated an increase in hepatic thrombopoietin in response to excess tumor-derived interleukin-6 (IL-6) at higher tumor grading or advanced disease stage which then forms a positive feedback loop and promotes further tumor growth.[3]

Furthermore, thrombocytosis is known to have a relationship to overall survival (OS). In this study, researchers found that the presence or absence of thrombocytosis was not statistically significant in 3-years survival (p = 0.555). Further survival analysis showed a lower mean survival rate between the groups with thrombocytosis of 2.766 years compared to the group without thrombocytosis of 2.857 years. However, hazard analysis showed that thrombocytosis was not statistically significant to 3-years survival (p =

0.399). That thrombocytosis was not a significant prognostic factor in ovarian cancer patients.[8] The results found in the study showed that thrombocytosis had a stronger correlation with other patient characteristics such as ascites and other hematologic abnormalities, especially anemia.[8] Suggested that thrombocytosis was not a significant prognostic factor in patients with advanced stages. However, if the stage is stratified by early and advanced stages, thrombocytosis can be a significant prognostic factor in early stage patients.[6]

Differences in therapy given to patients with epithelial ovarian cancer in Indonesia can affect the prognosis and course of epithelial ovarian cancer, along with other influencing factors such as gene expression, chemotherapy response, and postoperative factors. Shown that different types of therapy given (p = 0.011), together with the stage of the disease, were significant prognostic factors for patient survival.[9] Although the difference in therapy is hypothesized to have an influence on overall survival, there are not many other studies that have discussed the difference in therapy for survival of patients with epithelial ovarian cancer, so further research is still needed.

CONCLUSION

Thrombocytosis was not a prognostic factor of epithelial ovarian cancer patients' survival. There were no significant difference of survival between epithelial ovarian cancer patients with and without thrombocytosis.

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Research Article

Role of TNF-α and Interleukin 6 Serum against Ovarian Reserve in Endometriosis Cysts

Peran TNF – α dan Interleukin 6 Serum terhadap Cadangan Ovarium pada Penderita Kista Endometriosis

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Abstract

Objective: To investigate the correlation between pro-inflammatory factors (TNF-α and IL-6) with ovarian reserve in patients with endometriosis cysts.

Methods: This is a cross sectional study. The number of samples is 25 people. Sampling technique consecutive sampling. The study began in June 2019 until the number of samples was fulfilled at the Obstetrics and Gynecology Polyclinic of the Dr. General Central Hospital M. Djamil Padang and at the Biomedical Laboratory of the Faculty of Medicine, Andalas University, Padang. To determine the correlation of TNF-α, IL-6, and AMH in patients with endometriosis cysts. Examination of TNF-α, IL-6, and AMH levels was carried out in a quantitative manner, using the ELISA method.

Result: The mean AMH level was 2 ± 0.40 pmol / L and TNF-α level was 11.16 ± 4.79 pg / ml. Correlation of AMH level with TNF-α indicates the value of $r = -0.049$ which has weak strength and negative pattern means that the higher the TNF-α level, the lower the AMH level. The analysis showed that there was no correlation between TNF-α levels and AMH levels in patients with endometriosis cysts ($p > 0.05$). Correlation of AMH levels with IL-6 shows the value of $r = 0.35$ which has moderate strength and positive pattern means that the higher the IL-6 level, the higher the AMH level. The analysis showed that there was no correlation between IL-6 levels and AMH levels in patients with endometriosis cysts ($p > 0.05$).

Conclusions: There is a negative correlation of TNF-α levels with AMH levels in patients with endometriosis cysts, namely the higher TNF-α levels, the lower AMH levels and there is a positive correlation of IL-6 levels with AMH levels in patients with endometriosis cysts. Where the higher levels of IL-6, the higher levels of AMH.

Keywords: AMH, endometriosis, TNF-α, IL-6.

Abstrak

Tujuan: *Mengetahui korelasi faktor pro inflamasi (TNF-α dan IL-6) dengan cadangan ovarium pada penderita kista endometriosis.*

Metode: *Penelitian ini merupakan penelitian analitik kuantitatif dengan desain studi potong lintang. Jumlah sampel sebanyak 25 orang. Teknik Pengambilan sampel consecutive sampling. Penelitian ini dimulai Juni 2019 sampai dengan jumlah sampel terpenuhi di Poliklinik Obstetri dan Ginekologi Rumah Sakit Umum Pusat Dr. M. Djamil Padang dan di Laboratorium Biomedik Fakultas Kedokteran Universitas Andalas Padang. Untuk mengetahui korelasi TNF-α, IL-6, dan AMH pada penderita kista endometriosis. Pemeriksaan kadar TNF-α, IL-6, dan AMH dilakukan dengan cara kuantitatif, menggunakan metode ELISA.*

Hasil: *Rerata kadar AMH adalah 2 ± 0.40 pmol/L dan kadar TNF-α 11.16 ± 4.79 pg/ml. Korelasi kadar AMH dengan TNF-α menunjukkan nilai $r = -0.049$ yang memiliki kekuatan lemah dan berpola negatif artinya semakin tinggi kadar TNF-α maka semakin rendah kadar AMH. Hasil analisis menunjukkan bahwa tidak terdapat korelasi antara kadar TNF-α dengan kadar AMH pada penderita kista endometriosis ($p > 0.05$). Korelasi kadar AMH dengan IL-6 menunjukkan nilai $r = 0.35$ yang memiliki kekuatan sedang dan berpola positif artinya semakin tinggi kadar IL-6 maka semakin tinggi kadar AMH. Hasil analisis menunjukkan bahwa tidak terdapat korelasi antara kadar IL-6 dengan kadar AMH pada penderita kista endometriosis ($p > 0.05$).*

Kesimpulan: *Terdapat korelasi negatif kadar TNF-α dengan kadar AMH pada penderita kista endometriosis, yaitu semakin tinggi kadar TNF-α maka semakin rendah kadar AMH dan terdapat korelasi positif kadar IL-6 dengan kadar AMH pada penderita kista endometriosis. Dimana semakin tinggi kadar IL-6 maka semakin tinggi kadar AMH.*

Kata kunci: *TNF-α, IL-6, AMH, endometriosis.*

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INTRODUCTION

Endometriosis is one of the common gynecological abnormalities suffered by women of reproductive age in which stromal and endometrial glands can be found outside the normal location. not yet known with certainty.1 However, some studies suggest that around 6-10% of women of childbearing age experience endometriosis with an average age of patients around 28 years.[1-2]

Endometriosis is a local pelvic inflammatory process with changes in the function of immune-related cells, so that the serum of women with endometriosis increases the number of active macrophages that secrete products such as growth factors and cytokines.[3] Cytokines produced include interleukin 6 (IL-6), vascular endothelial growth factor (VEGF), and tumor necrosis factor α (TNF-α). Interleukin 6 is considered to play a potential role in the growth and / or maintenance of ectopic endometrial tissue. Interleukin 6 is an inflammatory and immune regulator that modulates the secretion of other cytokines, promotes T-cell activation and B-cell differentiation, and inhibits the growth of various cells.[4] TNF increases in peritoneal and serum search for patients with endometriosis, and it is said that TNF is an essential factor of pathogenensis of endometriosis.[5] The importance of TNF in the pathogenesis of endometriosis is further supported by the proliferative effect of TNF observed in endometrial cells of women with endometriosis but not in cells of healthy controls.[6] Also, TNF in high concentrations appears to affect sperm motility in vitro and may have an embryotoxic effect.[7] These findings suggest that TNF may have an additional role in the development of infertility related to endometriosis.

Anti Müllerian Hormone (AMH) is specifically produced by granulosa cells of preantral follicles and antral follicles. AMH is relatively stable during the menstrual cycle in normoovulatory women. IL-1β, IL-6, and serum TNF-α levels were significantly higher in women with endometriosis compared with healthy women. in patients with endometriosis increased TNF-a correlates with poor oocyte quality due to damage in the luteal phase due to increased TNF-a. So in patients with endometriosis anovulation will occur.8 Chronic inflammation is a pathogenesis of endometriosis.

Several studies have shown that in endometriosis women there is an increase in the volume of peritonium fluid, as well as an increase in the concentration of prostagladins, proteases, cytokines including IL-1, IL6, MCP-1, and TNF-α, angigenic cytokines (IL-8) and VEGF produced by macrophages. Recent studies have found higher chemotactic activity in macrophages in the peritonium fluid.[9]

Increasing the number of macrophages can damage oocytes and zygocytes thereby disrupting the fertilization process. In addition, endometriotic cells and macrophages are both responsible for high levels of reactive oxygen and nitrogen which adversely affect sperm implantation. Experiments in mice by adding IL6 resulted in decreased embryonic development and decreased sperm motility. The above inflammatory state also has toxic effects on gametes and embryos and interferes with tubal motility.[10]

METHODS

This was a cross-sectional study. Subjects were patients suffering from endometriosis cysts who underwent surgery in the FER subsection of Dr. General's Central Hospital M. Djamil Padang who met the inclusion criteria, in June 2019. The inclusion criteria were women of reproductive age (18 - 35 years old) who were diagnosed with endometriosis cysts (grade III-IV) by ultrasound. Exclusion criteria are patients with acute inflammatory diseases such as: acute bronchitis, cough, influenza, skin lesions, acute appendicitis, dermatitis, tonsillitis, infectious meningitis, sinusitis, physical trauma, patients with chronic inflammation such as asthma, gastric ulcer, tuberculosis, rheumatoid arthritis, periodontitis, crohn's disease, sinusitis, active hepatitis, operative laparoscopic procedures on the ovary, hormonal therapy, ovarian removal laparotomy, patients with polycystic ovary syndrome, patients with congenital abnormalities in the ovary and patients who have undergone chemotherapy and radiotherapy . Examination of TNF-α, IL-6, and AMH levels was carried out in a quantitative manner, using the ELISA method. Data were analyzed by T-test to. Data were processed with the help of Statistical Product and Service Solutions (SPSS) for Windows version 22.0

RESULTS

Table 1. Subject Characteristic

Characteristics	f (%)	Mean ± SD
Age		29.40 ± 3.62
BMI		23.16 ± 2.51
Marriage history		
Married	23 (92)	
Single	2 (8)	
Infertile		
Yes	22 (88)	
No	3 (12)	
Cyst size > 3cm		
Yes	25 (100)	
No	0 (0)	
Kind of cyst		
Monolokulare	20 (80)	
Multilokulare	5 (20)	

Interpretation: The mean age of the respondents was 29.40 ± 3.62 years and BMI 23.16 ± 2.51. A total of 23 respondents (92%) were married, experienced infertility, namely 22 respondents (88%), all respondents (100%) had cyst sizes of more than 3 cm, and 20 respondents (80%) had monolokulare cyst types.

Tabel 2. Correlation of TNF-α Level dan AMH Level

Variable	Mean ± SD	r	*P-value*
AMH level	2 pmol/L ± 0.40	-0.049	0.82
TNF-α level	11.16 pg/ml ± 4.79		

Interpretation. The mean AMH level was 2 ± 0.40 pmol / L and the TNF-α level was 11.16 ± 4.79 pg / ml. Correlation of AMH level with TNF-α indicates the value of r = -0.049 which has weak strength and negative pattern means that the higher the TNF-α level, the lower the AMH level. The analysis showed that there was no correlation between TNF-α levels and AMH levels in patients with endometriosis cysts (p> 0.05).

Tabel 3. Correlation of IL-6 Levels and AMH Levels in Patients with Endometriosis Cysts

Variable	Mean ± SD	r	*P-value*
AMH level	2 pmol/L ± 0.40	0.35	0.09
IL-6 level	17.15 pg/ml ± 3.48		

Interpretation. The mean AMH level was 2 ± 0.40 pmol / L and the IL-6 level was 17.15 ± 3.48 pg / ml. Correlation of AMH levels with IL-6 shows the value of r = 0.35 which has moderate strength and positive pattern means that the higher the IL-6 level, the higher the AMH level. The analysis showed that there was no correlation between IL-6 levels and AMH levels in patients with endometriosis cysts (p> 0.05).

RESULTS

Endometriosis is a local pelvic inflammatory process with changes in the function of immune-related cells, so that the serum of women with endometriosis increases the number of active macrophages that secrete products such as growth factors and cytokines.[6] Cytokines produced include interleukin 6 (IL-6), Vascular Endothelial Growth Factor (VEGF), and tumor necrosis factor α (TNF-α).[11]

Interleukin 6 is considered to play a potential role in the growth and / or maintenance of ectopic endometrial tissue. Interleukin 6 is an inflammatory and immune regulator that modulates the secretion of other cytokines, promotes T-cell activation and B-cell differentiation, and inhibits the growth of various cells.[4] TNF increases in peritoneal and serum search for patients with endometriosis, and it is said that TNF is an essential factor of endometriosis pathogenensis.[12]

Until now, the exact mechanism of decreased ovarian reserve in patients with endometriosis cysts is still being debated. One important factor that occurs in endometriosis cysts is the presence of a chronic inflammatory process that involves an immunocellular mechanism and an increased apoptotic mechanism. It is suspected that the chronic inflammatory process that occurs in endometriosis cysts will cause damage to the follicles contained in the ovaries. Damage to the ovarian follicle, especially to the antral follicle, will cause a decrease in the number of follicles or ovarian reserves.[13] Women with endometriosis have a higher incidence of oocyte apoptosis, more cell cycle changes, and a higher incidence of oxidative stress than women with infertility caused by other pathologies such as the fallopian, male, and idiopathic factors. Patients with advanced stage endometriosis show a higher incidence of apoptosis in granulosa cells.[11]

Endometriosis contributes to low pregnancy rates, both in the normal ovulation cycle, as well as intrauterine insemination, in vitro fertilization, and embryo transfer. The fertility cycle rate (CFR) in endometriosis women is 2-10% and the prevalence of endometriosis is higher in infertile women than in fertile women. TNF-α values in follicular fluid correlate with poor oocyte quality[14]. Tumor necrosis factor α is secreted by activated macrophages, and has a strong inflammatory, cytotoxic and angiogenic

effect. High TNF concentrations also have an effect on sperm motility in vitro, and may have an embryotoxic effect, causing an infertility effect on endometriosis.[14] Other studies also propose several mechanisms for the emergence of fertility disorders in endometriosis including tubal-ovarian dysfunction (anatomic disorders in the ovaries and tubes), ovulation disorders, hyperprolactinemia, luteinizes un-ruptured follicles, abnormal follicular development, decreased follicular development, decreased estrogen production and increased estrogen production granulosa cell apoptosis), impaired immunity (anti - endometrial antibodies), abnormal peritonium environment (increased peritonium fluid and high cytokine concentrations and macrophage activation), dysregulation of endometrial function.[15]

IL-1β, IL-6, and serum TNF-α levels were significantly higher in women with endometriosis compared with healthy women, where TNF-α levels of 300 pg / ml could be used as initial screening values for endometriosis in adolescents (7a) and Gulden Halis added in their study that in endometriosis patients increased TNF-α correlated with poor oocyte quality due to damage in the luteal phase due to increased TNF-α. so in patients with endometriosis anovulation will occur.[16] TNF-α values in follicular fluid correlate with poor oocyte quality[17]. Tumor necrosis factor α is secreted by activated macrophages, and has a strong inflammatory, cytotoxic and angiogenic effect. High TNF concentrations also have an effect on sperm motility in vitro, and may have an embryotoxic effect, thereby causing an infertility effect on endometriosis.[18]

According to research that IL-6 and TNF- are good markers of endometriosis, in this study it is also mentioned that IL-6 and TNF can be used to distinguish between patients with or not suffering from endometriosis with a high level of sensitivity and high specificity. Hwu et al reported an association between endometrioma and serum AMH levels. in a retrospective study compared to 141 women with endometrioma, there was an increase in AMH in women with endometrioma. In addition, women with bilateral endometrioma had lower AMH levels compared to unilateral endometrioma.[19]

In a journal written, endometriosis patients, both eutopic and ectopic, are involved in increasing estrogen production. In addition, an increase and pro-inflammatory cytokines including IL-1β, TNF-α, IFN-γ and IL-17,

cyclooxygenase-2 (COX-2) and COX-2 will catalyze the synthesis of prostaglandin E2 (PGE2). Prostaglandin and cytokine production has been widely cited as a cause of infertility in women with endometriosis.[20] There were six biomarkers selected (plasma concentrations of IL-6, IL-8, TNF-α, high sensitivity C-reactive protein, and cancer antigens CA125 and CA19-9) during the secretory phase or during menstruation that can diagnose minimal-mild and moderate-severe endometriosis with high sensitivity and specificity.[21]

In a study conducted by Folconer et al, this study compared TNF-α levels with AMH concentrations, in patients with endometriosis there was an increase in TNF-a accompanied by a decrease in AMH concentrations which is a marker that there was a decrease in the number of eggs in endometriosis patients.[22] Research stated the relationship of TNF-α with oocyte quality, in patients with endometriosis an increase in TNF-α was correlated with poor oocyte quality due to damage in the luteal phase due to increased TNF-α, so that in endometriosis patients anovulation would occur.[23]

The results of this study showed that more than half of the respondents (92%) were married, 88% were infertile, all respondents had cyst sizes of more than 3 cm, and most (80%) types of monolokulare cysts. This study shows that there is no correlation between TNF-α levels and AMH levels. From the analysis it is known that TNF-α and AMH levels are negatively correlated where an increase in TNF-α is followed by a decrease in AMH levels. This is in line with research which states that there is no significant difference in TNF-α levels between patients with endometriosis and no endometriosis. Likewise with research where there are no differences TNF-α levels were significant between the group with endometriosis and the control group. From their results it was found that there were no cytokines which showed a significant correlation with the endometriosis phase.[24] The results of this study are in line which states that circulating IL-6 and TNF-α are influenced by exogenous hormones for ovarian stimulation. From this study it was concluded that there was no relationship between cytokine circulation with mild endometriosis.

CONCLUSIONS

There is a negative correlation of TNF-α levels with AMH levels in patients with endometriosis

cysts, namely the higher TNF-α levels, the lower AMH levels but there is a positive correlation of IL-6 levels with AMH levels in patients with endometriosis cysts. Where the higher levels of IL-6, the higher levels of AMH.

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Case Report

Role of Ambulatory Laparoscopy in Diagnosis of Ascites with Unknown Etiology

Peran Laparoskopi dalam Mendiagnosis Asites akibat Etiologi yang tidak Diketahui

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Abstract

Objective: To determine the evidence about timing and role of laparoscopy in ascites work-up.

Methods: : Case report

Case: A-26-year-old P2 woman went to our hospital with a history of vaginal delivery 22 days before admission. She also presented with massive ascites. No obstetric complication was found. Transvaginal ultrasound revealed normal postpartum uterus and ovaries, surrounded with ascites. Both the liver and kidneys were found normal on ultrasound. Abdominal CT scan with contrast showed massive ascites with thickened omentum. Ascites ADA (adenosine deaminase) was 36 IU/L. Diagnostic laparoscopy was performed, we found massive yellowish ascites, miliary whitish lesions and hyperaemic tubal enlargement with thickening of the peritoneum. Biopsy was taken, pathology examination showed the appearance of chronic salpingitis and granulomatous peritonitis, in accordance with tuberculosis peritonitis.

Conclusions: Laparoscopy should be the method of choice in diagnosing ascites with unknown etiology after inconclusive results of laboratory and radiological examination. Better visualization, typical appearance in peritoneal TB, chance to perform direct biopsy with lower risk of morbidity are the hallmarks of laparoscopy to be the method of choice to rule out the etiology of ascites.

Keywords: ascites, laparoscopy, peritoneal tuberculosis.

Abstrak

Tujuan: *Untuk mengetahui bukti tentang waktu dan peran laparoskopi dalam penegakan diagnosis asites.*

Metode: *Laporan kasus*

Kasus: *Seorang perempuan 26 tahun para 2 datang dengan riwayat persalinan pervaginam 22 hari lalu datang dengan asites masif. Tidak ada komplikasi obstetri yang ditemukan. Pemeriksaan ultrasonografi transvaginal memperlihatkan uterus dan ovarium normal sesuai postpartum dikelilingi dengan asites. Kedua hati dan ginjal dalam batas normal. CT scan abdomen dengan kontras memperlihatkan asites masif dengan penebalan omentum. ADA (adenosine deaminase) di cairan asites 36 IU/L. Kami memutuskan melakukan laparoskopi diagnostik dan biopsi. Kami menemukan asites masif berwarna kekuningan dan pembesaran tuba hiperemis dengan penebalan peritoneum. Pemeriksaan patologi memperlihatkan salpingitis kronik dan peritonitis granulomatosa sesuai dengan peritonitis TB.*

Kesimpulan: *Laparoskopi merupakan metode pilihan dalam mendiagnosis asites dengan etiologi yang tidak diketahui jika hasil laboratorium dan pemeriksaan radiologis meragukan. Visualisasi yang lebih baik, penampilan khas TB peritoneum, kesempatan untuk melakukan biopsi langsung dengan risiko morbiditas yang lebih rendah adalah ciri utama laparoskopi sebagai metode pilihan untuk mendiagnosis etiologi asites.*

Kata kunci: *asites, laparoskopi, tuberkulosis peritoneal.*

INTRODUCTION

Ascites is a pathological accumulation of fluid in the peritoneal cavity. It can be caused by several pathophysiology mechanism such as portal hypertension (75%), malignancy (10%), heart failure (3%), tuberculosis (TB) (1%), and pancreatitis (1%).[1] Diagnostic approach of patient with ascites consists of history, physical examination, blood test, abdominal ultrasound, ascitic fluid analysis through visual inspection, biochemical testing (serum ascites albumin gradient, total protein, amylase, triglycerides, adenosine deaminase (ADA), glucose and lactate dehydrogenase, urea and creatinine), and non-biochemical testing (polymorphonuclear leukocyte count, bacterial cultures, PCR bacterial DNA, cytology), also diagnostic laparoscopy.[2]

Diagnostic laparoscopy offers advantages of direct visualization of peritoneal cavity in combination with ability to obtain targeted biopsy for histological and microbiological studies. It is helpful to determine the diagnosis of peritoneal carcinomatosis, TB peritonitis, and other peritoneal or omental diseases such as mesothelioma and sclerosing peritonitis.[3] However, laparoscopy techniques are not absolutely risk free. It may be associated with injuries to bowel, solid organ, major blood vessels with failure rate up to 14% owing to adhesion of primary illness or former surgery.[4,5] Currently, laparoscopy has wide application and it has made a revolution in gastroenterology, gynecology, and urological surgeries. Therefore, this case report would like to highlight the ability of laparoscopy in unknown ascites origin which has been performed several laboratories work up.

CASE

A-26-year-old P2 woman came to hospital with a history of vaginal delivery 22 days before admission presenting with massive ascites, anemia (Hb 8.1 g/dL), and malnutrition. Patient complained of abdominal enlargement for 2 weeks. There was no history of hypertension in pregnancy, liver disease such as hepatitis B, chronic cough, bloody cough, night sweats or decrease of body weight. On physical examination, we found tachycardia with heart rate 120 bpm and normal body temperature. The body mass index (BMI) was 17.6 kg/m2 (underweight) with upper arm circumference was 20 cm. On physical examination, there was

shifting dullness suggesting massive ascites with bilateral non-pitting oedema. Obstetrical status was within normal limits.

Abdominal and vaginal ultrasound showed a postpartum uterus with a small amount of blood clot inside the cavity. There was ascites with fibrins surrounding the pelvic and abdominal cavity suggesting signs of infection (figure 1). Liver and both kidneys were normal. Laboratory examination revealed an increase of Ca-125 level (513.6 U/mL), negative result for HIV and HbsAg. The chest X-ray showed minimal left pleural effusion, infiltrate at supra-hilar and lower lobe of left lung suspected pneumonia. Abdominal CT scan with contrast presented hepatosplenomegaly, calcification lesion at anterior mesentery abdomen sized 0.9 cm suspected lymphadenopathy, and massive ascites with thickened omentum. We performed ascites puncture; coming out 2 litres of yellowish ascites and sent it for ascites analysis, cytology, acid fast and gram staining, and adenosine deaminase (ADA). Ascites analysis was considered as exudate with serum-ascites albumin gradient or gap (SAAG) 0.8. Result of cytology was mesothelial, macrophage, and leucocyte, no malignant tumour cell found. Acid fast bacilli and gram staining showed negative results and ADA was 36 IU/L (normal range <30 U/L).


Figure 1. Gynecological ultrasound of patients showing fibrin covered uterus

We decided to perform diagnostic laparoscopy and biopsy for histopathology. We found massive yellowish ascites (2300 mL), uterus was covered by fibrin, left tube was enlarged, and left ovary was normal. On the right tube, there were papules on surfaces; meanwhile, the right ovary was normal. We performed left salpingectomy and took histopathology specimen from peritoneal wall. We could not visualize the appendix and liver because there was adhesion between intestine and peritoneal wall (figure 2). Pathology anatomy result showed

chronic salpingitis and granulomatous peritonitis consistent with tuberculosis peritonitis (figure 3 and 4). Therefore, the final diagnosis was massive ascites due to peritoneal and salpingitis tuberculosis; the patient got nine months of anti-tuberculous drug.
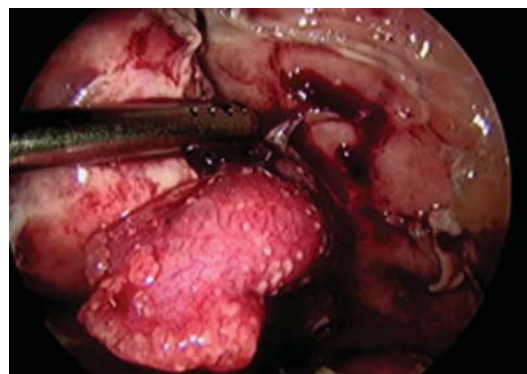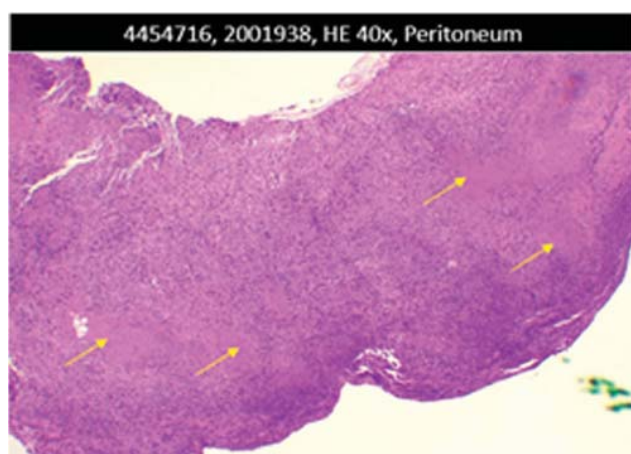

Figure 2. Laparoscopic finding: whitish and miliary nodules on left tube and peritoneal wall
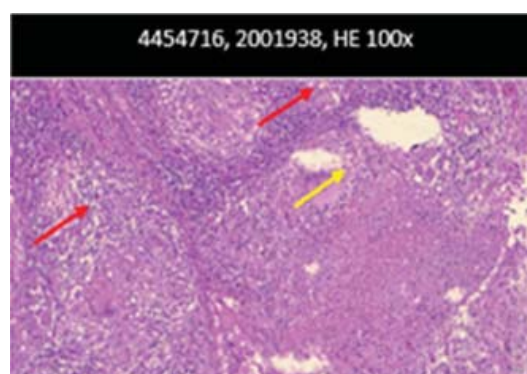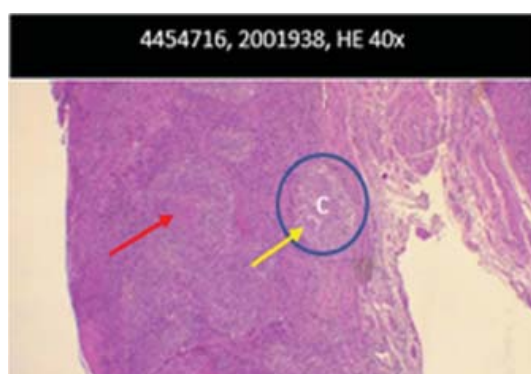
Figure 3. Histopathology from Fallopian tube specimens

Caseous necrosis (red arrow) was found as part of granuloma (blue circle). Granuloma was surrounded with rim of lymphocytes (yellow arrow) Caseous necrosis (yellow arrow) was found in many areas.

Figure 4. Histopathology of the peritoneum

Problem

In exudative ascites with unknown origin, how important is laparoscopy to differentiate peritoneal TB and other causes of ascites?

Searching strategy

To answer the clinical question, the search was conducted on Pubmed®, Cochrane Library®, Medline®, and Biomed Central®. In PubMed, the search included keywords using the MeSH, namely "Ascites" AND "Tuberculosis" AND "Laparoscopy". Meanwhile, in Cochrane, the MeSH descriptor consisted of "Ascites" AND "Laparoscopy" AND "Tuberculosis". The author used keywords of ascites AND laparoscopy AND tuberculosis both in Medline and Biomed Central. From the searching strategy above performed on March 19th 2020, there were 18, 0, 16, and 23 studies in Pubmed®, Cochrane Library®,

Medline®, and Biomed Central® database; respectively. The articles were screened using the criteria consisting of abstracts answering the clinical question, written in English language, full-text paper availability, and omitting all duplication papers. After screening, there were 4 articles appropriate to the inclusion criteria. Critical appraisal determining the validity, importance, and applicability (VIA) was conducted by 2 independent authors. The critical appraisal steps used in this article was written. The flowchart of searching strategy was shown at figure 4.[6-9]
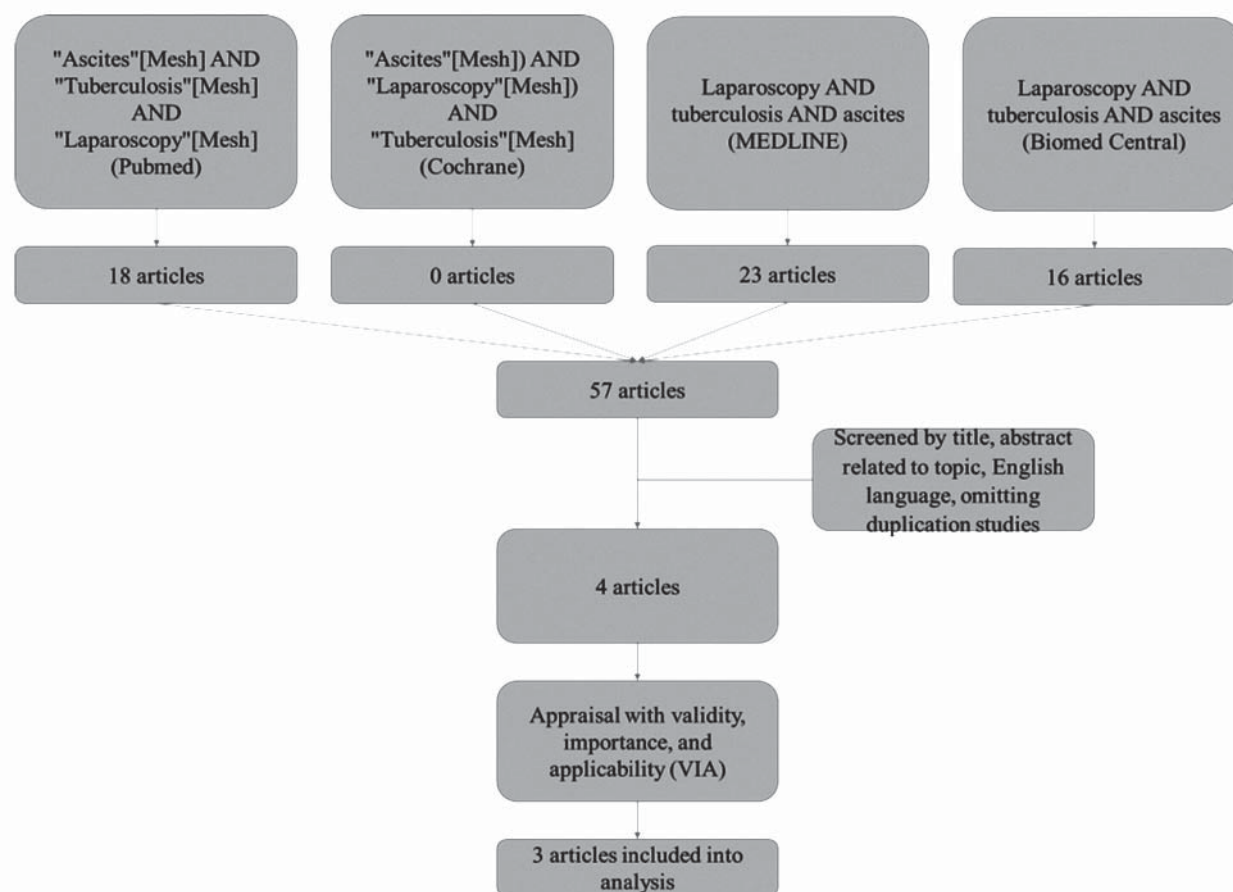
Searching Results

We conducted appraisal to 4 studies according to VIA criteria based on diagnostic study by Centre for Evidence-Based Medicine, University of Oxford, 2010. These consisted of two cross-sectional and two cohort studies. From diagnostic appraisal form, two studies did not show blind randomization and all studies did not validate in an independent group of patients. For importance, one study did not show the importance because only one case was performed laparoscopy.[7]

Other studies did not reveal the sensitivity and specificity of laparoscopy in peritoneal TB. They recruited samples starting from peritoneal TB patients presenting with ascites. They did not perform laparoscopy on peritoneal TB patients without ascites. Thus, there was only either positive rate or PPV of laparoscopy. For applicability, all studies can be applied in our patient because ambulatory laparoscopy for ascites work-up is available in our institution. Table 1 showed the result of appraisal diagnostic studies.

Table 1. Result of Diagnostic Appraisal Studies

| Study | Validity | | | | Importance | Available, affordable, accurate, and precise | Applicability Estimate patient's pre-test probability | Post-test probabilities affect management |
	Blind comparison	Appropriate spectrum of patient	Reference standard applied	Validated in an independent group of patients				
Demir K, et al	No	Yes	Yes	No	Positive rate of laparoscopy: 24/25 (96%)	Yes	Yes	Yes
Vardareli E, et al	Yes	Yes	Yes	No	N/A			
Bedioui H, et al	Yes	Yes	Yes	No	PPV of laparoscopy: 85%	Yes	Yes	Yes
Huang B, et al	No	Yes	Yes	No	Positive rate of laparoscopy: 43/51 (84.31%)	Yes	Yes	Yes

DISCUSSION

Ascites as an accumulation of fluids inside abdominal cavity is a sequelae of an illness which can come from local peritoneal or systemic disease.[10] Commonly, gradual painless accumulation of ascitic fluid is indicative of chronic benign condition while rapid accumulation and weight loss belong to malignant condition.[11] Routine laboratory test such as chemical examination of ascites fluid can help to diagnosis the original cause of ascites in most cases. Radiological tools are the last non-invasive way to determine etiology with limitations in some cases. In inconclusive laboratory and radiology tests, diagnostic laparoscopy with direct visualization of peritoneal cavity is mandatory to solve this problem and distinguish the origin of ascites.[12]

In our case, under laparoscopic view, there were papules on the surface of the right fallopian tube and adhesion between the peritoneal wall and intestine suspected to be peritoneal TB, confirmed with pathology examination. Peritoneal TB had an incidence of 0.5-1.5% and prevalence of 4-10% within cases of extra-pulmonary TB.[13] Most reported cases with peritoneal TB are frequently related with AIDS, liver cirrhosis, alcohol intake, poverty, and malnutrition.[14] The symptoms can be varied. The most common signs of peritoneal TB were abdominal mass (80.77%) followed by ascites (57.69%) and abdominal distention (57.69%)[15]. These signs were not specific and can be mimicking as occult malignancy or cirrhosis.[7]

Imaging techniques such as CT scan and MRI have limited efficacy to diagnosis peritoneal TB due to non-specific. CT scan may show generalized or localized ascites with thin mobile septa, thick omentum and peritoneum, lymphadenopathy, or thickened bowel. In our case, the abdominal CT revealed hepatosplenomegaly, calcification lesion at anterior mesentery abdomen sized 0.9 cm suspected lymphadenopathy, and massive ascites with omentum thickening. It is not specific as common findings of abdominal CT in peritoneal TB: smooth, strongly enhancing peritoneal thickening, a nodular or caked omentum, dense ascites, caseous nodes, soft tissue mesenteric, and omental infiltration.[16] Some studies supported PET-CT as non-invasive method to diagnose peritoneal TB, especially to differentiate with peritoneal carcinomatosis;[17,18] while others did not because of its high cost.[15,19] A study did a cost analysis of a peritoneal TB patients who underwent PET-CT scan had similar hospital expenses that performed surgery.[15]

Analysis of ascitic fluid is an important step in diagnosing ascites. In our case, the cytology, acid fast bacilli, and gram staining showed negative results. It raises the challenge for diagnostic difficulties due to the poor predictive value of those tests and low positive bacteriological rate on cytology which only 3% of positive results on direct examinations. Time needed for culture is more than two months for positive results in less than 35% of cases.[20] Polymerase chain reaction (PCR) of ascites for mycobacterium can be considered for diagnosis; however, it

is not widely available. PCR test could reach a sensitivity of 85% in smear-positive patients; however, it falls to 45% in negative smears.[20] Adenosine deaminase (ADA) as purine degrading enzyme is distributed in tissue and body fluid. It is necessary for T lymphocytes proliferation and differentiation as an immune cellular mechanism against M. Tuberculosis. Ascites ADA at cut-off level of 21.0 UI/L has the strongest factor to differentiate peritoneal TB and peritoneal carcinomatosis with good sensitivity, specificity, positive predictive value and negative predictive value (92.0%, 94.4%, 95.8%, 89.5%).[21] Another study stated that ascites ADA above 39 IU/L was reliable to diagnose peritoneal tuberculosis with 100% sensitivity and 97.2% specificity.[22] ADA in our study was 36 IU/L which meant approaching the cut off value of diagnosing peritoneal TB. In this circumstance, laparoscopy is needed to confirm the diagnosis.[23]

Laparoscopy is preferred over laparotomy due to its well-known minimal invasive advantages. It allows not only inspection of peritoneum, but also obtaining specimens for histology with lower risk of surgical morbidity.[15,24] Positive appearance of TB in 96% of cases[6]. This includes scattered or confluent multiple, whitish, miliary nodules (<5 mm) over the visceral and parietal peritoneum, adhesion, thickened and hyperemic peritoneum, and turbid ascites. Only one patient showed no signs of peritoneal TB despite histologic examination revealed it. In this study, no complications were found during and after laparoscopy. Reported 18 patients underwent image-guided percutaneous peritoneal biopsy (IGPB). This percutaneous biopsy has limited sensitivity as it is performed blindly, also tissue samples are usually small.[7]

In inconclusive ascites workup, laparoscopy and directed biopsy can establish the diagnosis in 80-95% of cases.[7,25] Studied 90 cases of isolated exudative ascites explored laparoscopically and found 59 cases of peritoneal TB8. The gross aspect of abdominal cavity at laparoscopy was typical in 90% of patients with confirmed tuberculosis. The PPV of TB by laparoscopy was 85%. The pathology examination of peritoneal biopsy to confirm the peritoneal tuberculosis was 58 out of 59 patients (98%). Peritoneal biopsy with laparoscopy is better because of direct visualization and higher quality of specimens obtained. Laparoscopy had lower risk of morbidity and zero mortality outside risk of anesthesia and surgery.[8,23]

As explained above, the standard of TB diagnosis worldwide is via culture of involved organism. However, this method has significant disadvantage that it consumes longer time to acquire the result. Another alternative tool includes the use of molecular diagnostic method such as PCR; nevertheless, it is not readily available, especially in rural area.[20] A different substitute is to assess peritoneal TB is to measure the level of ascites ADA. For own case, this method was still inconclusive because the cut off is 39 IU/L (100% sensitivity and 97.2% specificity).[22] Therefore, this case reported use of ambulatory laparoscopy as a choice to diagnose peritoneal TB.

CONCLUSION

Laparoscopy should be the method of choice in diagnosing ascites with unknown etiology after inconclusive results of laboratory and radiological examination. Better visualization, typical appearance in peritoneal TB, chance to perform direct biopsy with lower risk of morbidity are the hallmarks of laparoscopy to be the method of choice to rule out the etiology of ascites.

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Case Report

A large Parasitic Dermoid Cyst in the Pouch of Douglas: a Torsion Complication?

Kista demoid pada Pouch of Douglas: Apakah sebuah komplikasi torsio?

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Abstract

Objective: To identify the underlying etiology of dermoid cysts in the pouch of Douglas.

Methods: Case report.

Case: A 44-year-old woman presented to our clinic complaining of chronic, dull-aching lower abdominal pain of one-month duration. Pelvic ultrasound examination showed an eight-centimeter cystic appearing lesion in the right adnexa. Computed tomography (CT) suggested the diagnosis of dermoid cyst. Laparoscopy revealed a residual ovarian tissue on the right side and an eight-centimeter cystic mass occupying the pouch of Douglas. The entire specimen was removed en bloc through the umbilicus incision inside a bag with no spillage. Histopathologic examination confirmed the diagnosis of a mature cystic teratoma.

Conclusions: Parasitic dermoid cysts are extremely rare entity especially those located in the pouch of Douglas. Autoamputation and reimplantation is the most accepted etiology to explain this phenomenon.

Keywords: autoamputation, dermoid cyst, douglas, laparoscopy, mature cystic teratoma.

Abstrak

Tujuan: Untuk mengidentifikasi etiologi yang mendasari kista dermoid di kantong Douglas.

Metode: Laporan kasus

Kasus : Seorang perempuan 44 tahun datang ke klinik kami dengan keluhan nyeri perut bagian bawah yang kronis dan nyeri tumpul selama satu bulan. Pemeriksaan USG panggul menunjukkan lesi kistik delapan sentimeter yang muncul di adneksa kanan. Computed tomography (CT) menyarankan diagnosis kista dermoid. Laparoskopi mengungkapkan jaringan ovarium sisa di sisi kanan dan massa kistik delapan sentimeter menempati kantong Douglas. Seluruh spesimen dikeluarkan secara en bloc melalui sayatan umbilikus di dalam kantong tanpa tumpahan. Pemeriksaan histopatologi mengkonfirmasi diagnosis teratoma kistik matur.

Kesimpulan: Kista dermoid parasit adalah entitas yang sangat langka terutama yang terletak di kantong Douglas. Autoamputasi dan reimplantasi adalah etiologi yang paling diterima untuk menjelaskan fenomena ini.

Kata kunci: autoamputasi, douglas, kista dermoid, laparoskopi, teratoma kistik matur.

INTRODUCTION

Mature cystic teratomas also known as dermoid cysts are considered one of the most common ovarian germ cell neoplasms, with a reported incidence between 5% and 25% of all ovarian tumors.[1] However, parasitic dermoid cyst is considered a very rare entity with a cumulative incidence of 0.4% of all ovarian mature cystic teratomas.[2] The most common secondary site of implantation of parasitic dermoid cysts is reported to be the omentum due to its unique role as an intra-abdominal anti-inflammatory barrier.[3] Up to our knowledge only 20 cases of parasitic dermoid cysts have been reported to be found in the pouch of Douglas.[4–8] In this report we are presenting a rare case of parasitic mature cystic teratoma found in the pouch of Douglas in a 44-year-old woman, that was managed laparoscopically along with a literature review.

CASE

A 44-year-old woman, presented to our clinic complaining of chronic, dull-aching lower abdominal pain of one-month duration. she had no relevant medical or surgical history. Abdominal and pelvic examination were

unremarkable. Pelvic ultrasound examination showed eight-centimeter cystic lesion in the right adnexa. Computed tomography (CT) showed an eight cm right adnexal well defined oval shaped fat density thin walled multiseptated cystic lesion containing tubular structure, tufts of hair, calcific focus confirming the diagnosis of a dermoid cyst suggested to be originating from the right ovary. laboratory tests including the level of CA125 were all within normal range. Laparoscopy was performed and intraoperative findings Revealed a normal uterus, a 4 cm left para ovarian cyst, a residual tissue on the right side, which was connected to the right utero ovarian ligament and identified to be a remnant of the right ovary. It was slightly adherent along with the fallopian tube on the same side to an eight-centimeter, round, dark blue cystic mass occupying the pouch of Douglas (Figure.1).
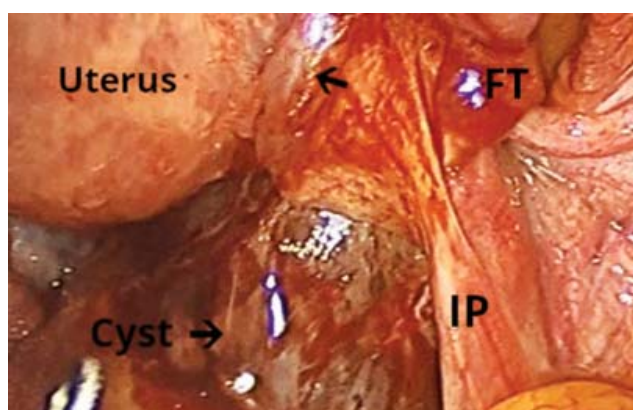
Figure 1. Laparoscopic view showing the cyst of around 8 cm occupying the pouch of Douglas. IP: indicates the infundibulopelvic ligament. FT: indicates the fimbria of the fallopian tube. Black arrow: indicates the residual ovarian tissue.

The mass was also adherent to the posterior uterine wall, the distal part of the sigmoid colon, and the rectum (Figure 2).
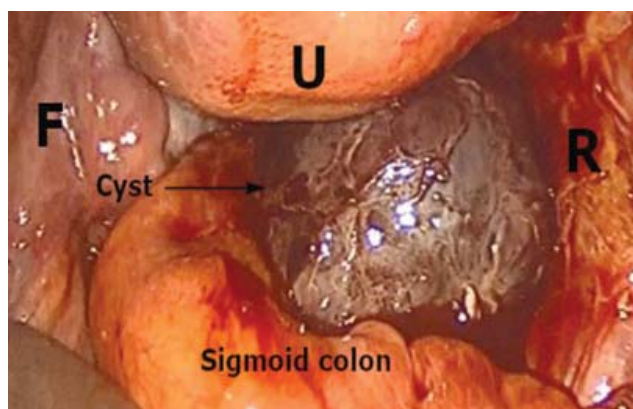
Figure 2. Laparoscopic view of the parasitic dermoid cyst showing it asan isolated mass, separate from the left adnexa and fallopian tube (F), adherent to the sigmoid colon, rectum (R), and the posterior uterine wall (U).

After adhesiolysis, the cystic mass was found to be completely isolated from both adnexa. There was no identifiable blood supply or a pedicle. The entire specimen was removed en bloc through the umbilicus incision without spillage using in-bag manual morcellation. The left para ovarian cyst was easily enucleated. The post-operative course was uneventful. The histopathological examination showed ovarian tissue surrounding a cystic lesion with widespread hemorrhagic necrosis with hair follicles and no evidence of malignant or immature components confirming the diagnosis of a strangulated dermoid cyst of the right ovary. The left para ovarian cyst was a benign mucinous cystadenoma.

DISCUSSION

Teratomas are tumors arising from pluripotent stem cells that have the capacity to differentiate into any of the three germ cell layers giving rise to many tissues such as hair, bone, muscle, and others.[9] Mature cystic teratomas almost exclusively contain adult or fetal tissues or both. In very rare exceptions embryonic structures may also be present. Therefore the most classical site of mature cystic teratomas is the ovaries.[10] Nevertheless, extragonadal teratomas have been reported to occur in various sites with a predominant arrangement toward the median and paramedian positions.[8,11] The exact etiology behind the development of extragonadal teratomas is poorly understood, however several theories have been proposed to explain this phenomenon. The first theory suggested the development of extragonadal teratoma from displaced primordial germ cells that might divert from their normal migratory path from the yolk sac toward the developing genital ridge.[9,11] Yet this theory is not applicable to our case due to the presence of ovarian tissue within the teratoma. The second theory puts forward the supernumerary or ectopic ovary as the origin of extragonadal teratoma which might be congenital or acquired after pelvic inflammatory disease or previous surgery.[7,11] The patient in our case had no previous surgical history and no renal anomalies were observed to explain any congenital abnormality related to the adnexa. The third and final theory is the most popular theory to explicit the presence of extragonadal teratomas in the abdominal cavity which assumes that the extragonadal teratoma is autoamputated

from an ovarian site and subsequently implanted in another extragonadal site.[11]

Theoretically autoamputation is considered a consequence of a previous torsion which is reported to be the most common complication an ovarian cystic tumor may endure.[1] The impairment of the blood supply will lead to venous and lymphatic congestion which will induce necrosis and atrophy in acute settings. On the other hand, if the torsion is subacute or chronic this will lead to the formation of collateral blood supply with the surrounding organs. In very rare cases the torsion may prompt the formation of parasitic cyst that is completely detached from its pedicle.[7,11] To determine the etiology clinically we depend on the state of the fallopian tube and the histopathology report that support the presence

of ovarian stromal tissue, since the actual moment of autoamputation is not inspected.[7] Whereas the most common site of parasitic dermoid cyst implantation is reported to be the omentum, the pouch of Douglas is considered to be a very rare site of implantation that needs to be further investigated.[8] Based on this, we performed a PubMed search using the following key words: "parasitic" or "extragonadal," "dermoid" or "teratoma," "cul-de-sac" or "Douglas" which brought forth 20 articles that we summarized in Table 1.[4–8] The patients age ranged from 18 to 83 years, with predominance toward childbearing and premenopausal age. Eleven patients out of 20 suffered from abdominal pain as a primary symptom. On the contrary, 5 patients were completely asymptomatic (Table 1).

Table 1: Summary of Mature Cystic Teratomas Found in the Pouch of Douglas

Author, Ref. number	year	age	symptom	Size (cm)	State of the ovaries	State of the fallopian tubes	histopathology	approach	etiology
Lefkowitch JH, [7]	1978	40	Urinary retention	11.5×9.5×7.5	Grossly normal	Not mentioned	MCT[a], no ovarian tissue	Laparotomy	Not specified
Turhan NO, [7]	2000	30	Yellow-green vaginal discharge	4.69×4.36×2.99	Both normal	Both normal	MCT, no ovarian tissue	Laparoscopy	Not specified
Chen HJ, [7]	2004	61	Lower abdominal pain	4.5×4	Rt. Ovarian cyst and atrophic Lt. ovary	Both normal	MCT, no ovarian tissue	Laparoscopy	Not specified
Kobayashi Y, [7]	2006	61	Asymptomatic	unknown	Both normal	Not mentioned	MCT, no ovarian tissue	laparotomy	Not specified
Kusaka M, [7]	2007	24	Sharp left lower quadrant pain	2×3.5×4	Lt. ovary not identified, uterus and Rt. Adnexa were normal	Left tube not identified	MCT, viable normal ovarian tissue detected	Laparoscopy	Auto-amputation
Khoo CK, [7]	2008	29	Bilateral lower abdominal pain	7.2×7.1×4.3	Rt. Ovarian dermoid cyst, normal Lt. ovary	Both normal	MCT, no ovarian tissue	Laparoscopy	Auto-amputation
Peitsidou A, [7]	2009	33	Admitted to the labor ward for cesarean section	8×5	Absent Rt. Ovary, normal Lt. ovary	Rt. Tube was blind ended, Lt. tube was normal	MCT, normal ovarian tissue detected	Laparotomy	Auto-amputation
Sinah R, [7]	2009	23	Abdominal pain	Largest is 4×3 in the pouch of Douglas	Normal Lt. ovary, underwent Rt. Oophorectomy	Not mentioned	MCT, no ovarian tissue	Laparoscopy	Recurrence after previous cystectomy
Bartlett CE, [7]	2009	29	Abdominal pain	6×8	small Rt ovary, normal left ovary	Dilated Rt. tube, normal Lt. tube	MCT, no ovarian tissue	laparoscopy	Auto-amputation
Bambao C, [7]	2010	50	asymptomatic	Not mentioned	Both atrophic	Not mentioned	MCT, no ovarian tissue	laparoscopy	Not specified
Matsushita H, [7]	2011	69	Lower abdominal pain	7	Atrophic Rt. ovary	Not mentioned	No ovarian tissue	laparotomy	Auto-amputation
Takeda A, [7]	2012	26	Positive urine pregnancy test, suspected ectopic pregnancy	2.9	Left ovarian dermoid cyst, normal right ovary	Both normal	Not mentioned	laparoscopy	Auto-amputation
Tokunaga M, [7]	2012	37	asymptomatic	6	Left adnexa removed due to previous immature teratoma, Rt. ovarian cyst	Rt. Tube normal	MCT, no ovarian tissue	laparoscopy	Not specified
Eda M, [7]	2012	83	Postmortem	8.1×7.4×6.1	Rt ovary intact, Lt ovary absent	Rt tube intact, Lt tube tapered.	MCT, no ovarian tissue	Anatomical dissection	Auto-amputation
Greene A, [12]	2014	48	Right sided flank pain	7.3×5	Rt ovary not found in normal anatomical position, Lt ovary normal	Rt. Hydrosalpinx, Lt. tube normal	MCT with viable ovarian tissue	laparoscopy	Auto-amputation
Kakuda M, [7]	2015	41	Abdominal pain	4	Small, defected Lt. ovary, normal Rt. ovary	Lt. tube was blind ended, normal Rt. Tube	MCT with ovarian stroma	laparoscopy	Auto-amputation
Ohshima K, [6]	2015	20	Lower abdominal pain	7×6.5×2.5	Both ovaries normal	Not mentioned	MCT, no ovarian tissue	laparoscopy	Displaced primordial germ cells
Jain P, [8]	2017	18	Abdominal pain	7×7	Both ovaries normal	Both tubes normal	MCT, no ovarian tissue	Laparoscopy converted to laparotomy	Not specified
John B, [4]	2017	32	asymptomatic	6	Lt. ovary not seen; Rt. Ovary normal	Distal portion of the Lt. tube was absent, normal Rt. Tube.	MCT, with ovarian tissue	laparoscopy	Auto-amputation
Sethi P, [5]	2019	40	Lower abdominal pain	15×15×10	Both ovaries normal	Not mentioned	MCT not arising from the ovaries	laparotomy	Displaced primordial germ cells

a Mature cystic teratoma

The state of the fallopian tubes and the histopathology report are both considered the pedestal of understanding and determining the underlying etiology. seven cases [4,7,12] manifested either fallopian tube abnormality or reported the presence of ovarian tissue microscopically, which strongly supports the theory of auto amputation among other proposed etiologies. We believe that the present case also demonstrates the autoamputation of a right ovarian teratoma depending on the macroscopic observation of the right ovary residuals and the presence of an isolated teratoma in the pouch of Douglas. Furthermore, the histopathology report confirmed the diagnosis of mature cystic teratoma and the presence of ovarian tissue which strongly supports the aforementioned theory. Regarding the approach, 13 cases were managed laparoscopically which is the recommended approach over laparotomy in such cases especially in premenopausal women.[11] The advantages of laparoscopy over laparotomy in managing benign adnexal tumors include better cosmetic results, less blood loss, less post-operative pain, decrease the need for analgesia, faster recovery, and shorter hospital stay. Therefore, the decision was made to perform laparoscopic removal of the cyst instead of laparotomy in our patient.

CONCLUSION

In Conclusion, parasitic dermoid cysts are extremely rare entity especially those located in the pouch of Douglas. Autoamputation and reimplantation is the most accepted etiology to explain this phenomenon. Concerning the management, laparoscopy is by far the gold standard approach for treating such cases.

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