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Original Research

Relationship Between A Premature Rupture Of Membranes And The Increase Of Leucocyte Levels In Pregnant Women During COVID-19 Pandemic

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ABSTRACT

Background: *Premature Rupture of Membranes (PROM) is a condition in which the membranes rupture before women's delivery. The incidence of PROM in Indonesia is still quite high, around 4.5%-7.6% from all pregnancies. The incidence rate at DKI Jakarta in 2020 was 4.6% while at Pelni Hospital in the same year was 7.9%. The main cause of this incident was due to the occurrence of infection that spreads into the uterus and amniotic fluid as well as due to the inflammatory process. This causes arachidonic acid metabolism to be active so that the level of leucocytes in the blood being increase. The purpose of this study was to analyze the relationship between the incidence of PROM and leucocyte increasing levels at the Pelni Hospital during the COVID-19 pandemic in 2020.*

Methods: *The study had used analytic observational method with cross sectional approach. The number of samples were 97 people, done by simple random sampling technique, using Medical Records of respondents along year of 2020.*

Results: *Data showed the aged range of respondents were 20-35 years (79.4%); multigravida (53,6%); PROM (76.3%); respondents with method of delivery which done by cesarean section (71.1%); and respondents with PROM who experienced the increasing of leucocyte levels (80.4%). Results based on Chi-square test showed there was a relationship between PROM and increased leucocyte levels (p=0.036).*

Conclusion: *The relationship between PROM and the increasing of leucocyte levels to pregnant women at Pelni Hospital during COVID-19 pandemic in 2020 possibly caused by the presence of infections from ascending microorganisms.*

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INTRODUCTION

One of the direct causes of mortality and morbidity in pregnant women is obstetric complications and is still the biggest problem in developing countries (Abrar et al., 2017). According to survey data conducted in 2015, the Maternal Mortality Rate (MMR) in Indonesia is 305 per 100,000 (Kemenkes RI, 2018). The MMR value is an indication of the health and welfare status of a country (Shirin and Nahar, 2013). Obstetric complications that cause 80% of maternal deaths are severe bleeding after delivery, hypertension in pregnancy and infection (WHO, 2017). Infections that occur in pregnant women can cause premature rupture of membranes (PROM) (Kemenkes RI, 2018).

PROM is a condition in which the amniotic membrane ruptures before delivery occurs (Poerwoko., et al 2018) . Clinical symptoms that can be observed in PROM patients are sudden discharge of amniotic fluid from the vagina which is colorless and smells fishy. Based on the gestational age of the rupture of membranes, PROM can be classified into two groups, namely PROM at term and preterm (Hailemariam Segni, 2017).

Based on the survey, the incidence of pregnant women with PROM is still quite high at 5-10% of all pregnancies (WHO, 2017). According to the results of a 2016 study by the American College of Obstetricians and Gynecologists (ACOG) it is known that the incidence of PROM is 8% of all pregnancies, while the incidence of PROM in Indonesia is 4.5%-7.6% of all pregnancies (Panjaitan dan Tarigan, 2018). There are various factors that cause PROM, namely general factors caused by infection, heredity or obstetric factors due to overdistention (Manuaba, 2010). Infection is the most common cause of PROM which then spreads to the uterus and amniotic fluid resulting in an inflammatory process (Sohail, 2012).

If PROM is suspected, it is necessary to conduct an assessment of PROM in the form of anamnesis, physical examination, supporting examinations and conducting a culture examination if infection occurs (Manuaba, 2010). This culture examination can determine the pattern of bacteria and resistance in determining the selection of antibiotics for PROM patients and babies born if there are signs of infection. Signs of infection in the uterus are cloudy color of amniotic fluid, smelly amniotic fluid and mother's temperature >38°C (Prawiroharjo, 2008), and an increase in blood leukocyte levels >10,000/mm³.

Leukocytes play an important role in the immune system. The main function of these leukocytes is as protection or defense of the body to fight infection (Karolina et al., 2016). When microorganisms enter the body, they will cause leukocytes, which normally live in the lymph nodes, to circulate into the blood to defend the body from germs that cause the number of leukocytes to increase (Sherwood, 2016). In 2019 there was an outbreak that spread rapidly, namely coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) (Alfaraj et al., 2019).

Based on (Liu et al., 2020) that pregnant women are susceptible to SARS-CoV-2 infection which can increase the risk to pregnant women. Based on the above background, it is necessary to conduct research on the analysis of the relationship between the incidence of PROM with an increase in leucocyte levels which will be carried out at the Pelni Hospital during the COVID-19 pandemic in 2020 to increase knowledge of pregnant women's health and reduce mortality due to PROM in pregnant women.

MATERIALS AND METHOD

Instruments that used in this study is the medical records which seen in the period January-December 2020. The population in this study were all pregnant women >20 weeks at the Pelni Hospital Jakarta with a total population of 3,158 people. The sample in the study was seen according to the inclusion criteria, namely pregnant women who were recorded in the medical record, the exclusion criteria were the data was incomplete, there were other pregnancy complications (DM and hypertension) and the active phase at stage 1 so that a sample of 97 people was obtained by simple random sampling during the COVID-19 pandemic.

The independent variable in this study was premature rupture of membranes (PROM), while the dependent variable was an increase in leucocyte levels. The location of this research is at Pelni Pertamburan Hospital, West Jakarta with the time of conducting the research in May until June 2021. Data analyses in this study to see the relationship between the independent variable and the dependent variable using the chi-square test.

RESULTS

The characteristics of the sample in this study include the age of pregnant women, parity status, PROM classification, delivery method and leucocyte levels in pregnant women. The distribution of pregnant women at Pelni Pertamburan Hospital according to these characteristics is as follows:

Table 1. Characteristics of the Research Sample

Variable	Total (n=97)	Percentage (%)
Age		
<20 and >35 yo	20	20,6
20-35 yo	77	79,4
Gravida		
Primigravida	45	46,4
Multigravida	52	53,6
Classification of PROM		
PROM At term	74	76,3
PROM Preterm	23	23,7
Method of delivery		
Sectio caesarea (sc)	69	71,1
Normal	28	28,9
Increased leucocyte levels		
There is an increase in leucocyte levels (>10.000/mm³)	78	80,4
There is no increase in leucocyte levels (<10.000/mm³)	19	19,6

Table 1 showed the majority of pregnant women with PROM who are pregnant at the age of 20-35 years (79.4%), have multigravida status (53.6%), occur at gestational age >37 weeks or PROM At term (76.3%), sectio caesarea (71.1%) and there was an increase in leucocyte levels (80.4%).

Table 2. The relationship between a PROM and the rising of leucocyte levels at the Pelni Hospital in 2020

PROM	Rising of leucocyte levels		Total (%)	P-value
	There was an increase in leucocyte levels (>10.000 /mm³)	There was no increase in leucocyte levels (<10.000/mm³)		
PROM At term (37 - 40 weeks)	63 (85,1)	11 (14,9)	74 (100)	
PROM preterm (>20 - <37 weeks)	15 (65,2)	8 (34,8)	23 (100)	0,036
Total	78 (80,4)	19 (19,6)	97(100)	

Based on table 2, it can be seen that the p-value = 0.036 with asymp. sig < 0.05 which concluded that there was a significant relationship between PROM and leucocyte levels at Pelni Pertamburan Hospital in 2020.

DISCUSSION

The characteristics of the sample in this study can be seen in table 1. It is known that the majority of pregnant women who experience PROM at Pelni Hospital are pregnant at the age of 20-35 years which is included in the healthy reproductive age. This can occur due to various factors such as parity, fetal position abnormalities (Fitriyani et al., 2018), heredity, previous PROM history and genital infections (Hailemariam Segni, 2017) so that pregnant women who are classified as reproductive age are still at risk the occurrence of PROM.

This study is in line with research conducted by Ikrawanty (2019) which showed that the majority of pregnant women who experienced PROM occurred at the age of 20-35 years as many as 263 (95.6%) and as many as 12 (4.4%) pregnant women experienced PROM in Indonesia. age <20 and >35 years. However, the results of this study are not in accordance with the theory explained by Cunningham (2014) that pregnant women who are pregnant at the age of 20-35 years are the safest age to give birth to children because their reproductive organs are functioning optimally so that the risk of PROM is very small.

Based on the data obtained in table 1. pregnant women who experience PROM with multigravida status more than primigravida. This study is in line with previous research by Abrar et al (2017) that pregnant women with PROM occurred in primigravida as many as 113 people (45.6%) and multigravida as many as 135 people (54.4%). This could be due to trauma in a previous pregnancy and cause cervical insufficiency (Emechebe.,et al 2015). Cervical insufficiency is the term for the inability of the cervix to sustain the fetus without uterine contractions and dilatation.

This happens because of structural and functional damage (Wang et al., 2018). In addition, it is caused by damage to cervical tissue which allows the uterine floor muscles to stretch. As a result of this stretching can activate prostaglandin E2 and interleukin-8, that it can disrupt the balance of synthesis and degradation of the extracellular matrix, causing PROM (Merti, 2017).

These results are in accordance with the theory described by Prawirohardjo (2008)

pregnant women with PROM often occur in multigravida because in multigravida there is endometrial damage due to stretching, making it easier for infection to occur. This infection can originate from the vagina and cervix which will then occur in the biomechanical process of the amniotic membrane in the form of proteolytic and produce enzymes that can damage the enzyme itself so that damage to the extracellular matrix eventually occurs PROM (Cunningham, 2014).

Meanwhile, according to the theory of Nugroho (2012) explains that PROM is a rupture of the amniotic membrane which allows a direct relationship between the inside of the vagina and the external environment that facilitates infection. Whereas this amniotic membrane functions to limit and protect so that there is no direct contact with the outside environment so as to reduce infection. The longer the latent period, the higher the chance of infection in the uterus. The results of this study are in line with previous research by Widyana (2016) that pregnant women who experience PROM are mostly handled by SC around 58.8% and pregnant women with PROM are born normally around 41.2%.

Leucocytes are one of the components of blood cells that contain a nucleus and the number of leucocytes in the blood is around 5,000-9,000 cells/mm³ (Sutjahjo, 2016). Leukocytes have a function as the body's defense system that provides an immediate response when foreign objects enter the body (Cunningham, 2014). Leucocyte level is a value from laboratory examination to calculate the number of leucocytes in the blood with the aim of seeing whether infection and inflammation occur (Darmayani et al., 2018). If the leucocyte level is >10,000/mm³ in ul/blood, there is an increase in the leucocyte level (leucocytosis). Meanwhile, if the leucocyte level is <5,000/mm³ in ul/blood, there will be a decrease in the leucocyte level (leucopenia) (Pelni Hospital Referral Value).

Based on research data, it is known that pregnant women who experience PROM have more elevated levels of leucocytes. The results of this study are in accordance with the theory of Cunningham (2014) which states that an increase in leucocyte levels in PROM is caused by an infection. In pregnant women, there are physical and chemical changes in urine that encourage urinary tract infections (UTIs). If a UTI occurs in pregnant women, there is an increase in the incidence of PROM due to pathogenic bacteria that affect the amniotic membrane (Cunningham, 2014).

However, due to mechanical, hormonal and physiological changes during pregnancy, E. coli bacteria can ascend from the urinary tract and secrete phospholipase A2 and C that it can increase the concentration of arachidonic acid and can release PGE2 which functions to increase uterine myometrial contractions, interfere with the synthesis and degradation of the amniotic membrane and eventually PROM occurs (Cunningham, 2014). This study is in line with research conducted by Kurniawan (2020) which shows that the majority of pregnant women who experience PROM have an increase in leucocyte levels by 69.4% and a small proportion of pregnant women who experience PROM have no increase in leukocyte levels by 30.6%.

Based on the results of bivariate analysis, it is known that there is a significant relationship between PROM and an increase in leukocyte levels (p value = 0.036). This research is in line with the research that has been conducted by Widyana (2016), pregnant women who experience PROM have an increase in leucocyte levels. The results of this study are in accordance with research in China in 2016, that pregnant women who experience PROM have higher leukocyte levels (Wang et al., 2016). This occurs because the increase in leucocyte levels in pregnant women with PROM is

caused by an infection where these bacteria can spread to the uterus and amniotic fluid which then secretes enzymes that can degrade the extracellular matrix and significantly reduce the tensile strength and elasticity of the amniotic membrane (Negara et al, 2017).

Bacteria that spread to the body will activate the monocyte macrophage system which triggers an inflammatory reaction. Furthermore, it will increase arachidonic acid so that the leucocytes that normally live in the lymph nodes will circulate into the blood as a form of body defense from germs so that the number of leucocytes in the blood will be more than usual, resulting in an increase in leucocyte levels (Sherwood, 2016). In the era of the covid pandemic, the health of pregnant women needs to be considered, namely in the context of the potential impact of COVID-19 on pregnancy because inflammatory mediators related to COVID-19 have been associated with poor perinatal outcomes (Liu et al., 2020).

Based on the results of research conducted by the Spanish Obstetric Emergency Group, it was found that pregnant women who were exposed to COVID-19 had a higher risk of PROM at term and preterm. Therefore, the possibility can be used as a reason why in the era of the covid 19 pandemic, pregnant women who experienced PROM were very many, namely at the Pelni Hospital in 2020, there were more than 3000 patients experiencing PROM.

CONCLUSION

It was found that from 97 medical record data of pregnant women with PROM at Pelni Pertamburan Hospital, West Jakarta, 74 people (76.3%) occurred at gestational age > 37 weeks and 78 people (80.4%) of pregnant women with PROM experienced an increase in leucocyte levels. The relationship between PROM and the increasing of leucocyte levels to pregnant women at Pelni Hospital during COVID-19 pandemic in 2020 caused by the presence of infections from ascending microorganisms that spreads into the uterus and amniotic fluid as well as due to the inflammatory process. This causes arachidonic acid metabolism to be active so that the level of leukocytes in the blood being increases.

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