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Reproductive factors and risk of spontaneous abortion

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ABSTRACT

One of the causes of bleeding and infection in pregnant women is abortion-a failure reproduction. Spontaneous abortion is a pregnancy complication that can affect women both physically and psychologically. This research was purposed to find out the spontaneous abortion incidence, the relation of mother's age to the spontaneous abortion incidence by controlling the others risk factors such as the interval of the pregnancy, parity, and the usage of contraception. Type to the research is a case-control study where the number of subjects is 174 of pregnant women who have a spontaneous abortion as the case and who have no spontaneous abortion as the controlled group. The univariable used distribution of frequency, the analysis of bivariable used chi-square test, and the analysis of multivariable used multiple logistic regression analysis. The proportion of case group was The largest sample proportion in the case group for the age variable was at the age of 20-35 years (48.3%), pregnancy interval ≥2 years (56.9%), parity gave birth more than 4 times (62.1%), and use contraception (56.9%). Meanwhile, the control group for the variable age was at the age of 20-35 years (78.4%), pregnancy interval ≥2 years (79.3%), parity between 2-3 births (57.8%), and use contraception (73.6%). All variables were associated with the incidence of spontaneous abortion as follow age of mother <20 years old (p-value 0.000; OR 4.06; 95% CI 1.72-9.57), age of mother >35 years old (p-value 0.000; OR 3.61; 95% CI 1.17-11.07), pregnancy interval (p-value 0.002; OR 2.90; 95% CI 1.38-6.10), parity (p-value 0.013; OR 2.24; 95% CI 1.12-4.51), use of contraception (p-value 0.000; OR 3.43; 95% CI 1.59-7.34). The most dominant factor was mother age <20 years old (OR: 3.82; 95% CI 1.64-8.94). Mothers aged <20 years are at high risk for spontaneous abortion.

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INTRODUCTION

Pregnancy complications are problems or health problems that occur during pregnancy and can affect maternal morbidity. Bleeding is still the most reported symptom of pregnancy complications. There was an increase based on the Demography Survey and Indonesian Health (SDKI) from 3% to 5% in the SDKI in 2017 (1). One of the causes of bleeding and infection during pregnancy is abortion (2). Abortion, including spontaneous abortion, is an

accidental miscarriage before 20 weeks of gestation with a fetal weight <500 grams. Spontaneous abortion is a pregnancy complication that can affect a woman both physically and psychologically (3).

The pregnant women in the first trimester and the second one who experience abortus might cause heavy bleeding which leads to shock, perforation, infection, and damage the kidney function. It might happen if it is not handled carefully as soon as possible and would contribute to the number of the mother's mortality (4).

Around 10 to 20 % of pregnancy might be ended by spontaneous abortion. Spontaneous abortion is the condition where the fetus is out before the 20 weeks of pregnancy spontaneously. The bleeding was assumed as the menstrual blood which was happened due to the long cycle of a menstrual period. It is a clinical symptom that is not realized by most pregnant women that they were having a spontaneous abortion so that they ignored it. The number of this case might reach 50% if it is based on similar cases that happened before the normal menstrual cycle (5).

In Indonesia, there is no accurate and comprehensive data which is related to the abortion incidence toward pregnant women. Even if it exists, it is still very limited to a certain scope. Abortion becomes an important problem that has an important role in the increasing number of sick and mortality of the mother, especially unsafe abortion which is estimated 11% contribute to the mother's mortality in Indonesia (6).

From a normal pregnancy, there might be a possibility of complication that can threaten the pregnant women's life, it is estimated that 20% of pregnant women would experience the unpredicted complication. The complication that happened actually can be prevented by noticing all possibilities that become the risk factors of abortion, so it can be treated well (7). The risk of spontaneous abortion incidence in the first and second trimesters will increase regarding the mother's age. The abnormality factor on the mother chromosome with the older age is suspected as the cause of it. The mothers, whose age less than 20 years old has less than a 2% probability of experiencing abortion. The risk will increase up to 10% if the mother's age is more than 35 years old and increase more at the age over 45 years old, up to 50% (8).

Some researches which had been done in several hospitals in Denmark showed that there are several risk factors related to spontaneous abortion. They are malformed fetuses, mother's chronic diseases, abnormal womb, immunology factor, and infection. It is said that the age of a mother with an older father, obesity, smoking habit, alcohol dan caffeine addiction are also the risk factors toward spontaneous abortion. It is also found that the social and cultural factor such as low education, underweight and overweight, earlier menstrual phase, working habit, living environment, bad died and access to the health facility like poor pregnancy checking are the risk factors toward the incidence of spontaneous (8)

Although the cause of most miscarriages is unknown, they presumably result from a complex interplay between parental age, genetic, hormonal, immunological, and environmental factors (9). Genetic factors, including parental chromosomal rearrangements and abnormal embryonic genotypes or karyotypes, could underlie more than half of recurrent miscarriages. Maternal age is the strongest known risk factor. The risk of miscarriage is slightly elevated in the youngest mothers and then rises sharply in older mothers. There could be shared underlying risk factors for miscarriage and other adverse pregnancy outcomes. Several studies have looked at the association between the history of miscarriage and the future risk of other pregnancy complications (10)(11), but less is know about how complications might predict the future risk of miscarriage (12).

In the dr. Doris Sylanus Hospital Palangka Raya, in 2017, from 1800 patients who were treated in the Midwifery Room, experience a high number of spontaneous abortion incidence, that was 182 patients. This research was purposed to find out the spontaneous abortion incidence, the relation of mother's age to the spontaneous abortion incidence by

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controlling the others risk factors such as the interval of the pregnancy, parity, and the usage of contraception.

METHOD

This study used a case-control design consisting of patients who received services in 2018 in the midwifery room of the Regional Public Hospital of dr. Doris Sylvanus Palangka Raya. Subjects investigated 174 persons, 58 women diagnosed with s spontaneous abortion as case group, and 116 women who did not experience abortion incidence for the control group. Subjects were excluded if they had parity less than 2 or if medical record data were incomplete. Samples were selected by consecutive sampling. Data were collected using a checklist. Ethical approval was granted for the study by the Ethics Committee of the Palangka Raya Health Polytechnic Ministry of Health.

The independent variable in this study was the age of mothers, and the dependent variable was the abortion incidence, while the outer variable was the interval of pregnancy, the parity, and the use of contraception. Data analysis was completed in three stages. Univariable analysis was done to find a picture of data characteristic of each variable which was observed and presented descriptively using a table of frequency distribution. Analysis of bivariable was done to identify the relationship between the independent variable and the dependent variable, the outer variable and the dependent variable and the outer variable and the independent variable. Analysis of multivariable was done to find out the relationship among variables, in which see the relationship between the independent variable and the outer variable which were significant on the dependent variable.

The statistical test used was the chi-square test, because the variables tested categorical nature. The result was χ2 value, *p-value*. Exceptional for analysis of the relationship of the independent variable of the interval of pregnancy and the dependent variable of spontaneous abortion, it was calculated from the value of Odds Ratio (OR) and Confidence Interval (CI) which was 95%. Analysis of multivariate showed the effect of the independent variable on the dependent variable by controlling the other variables. The statistical test was a multiple logistic regression analysis. The test showed the value of OR as an approach to find the risk extent.

RESULTS

Analysis of invariable data aimed to picture the distribution of frequency of mothers who experienced spontaneous abortion incidence (case) and who did not experience spontaneous abortion incidence (control).

Table 1. Characteristic of study subject

Characteristic	Spontaneous abortion incidence					
	Cases		Control		Total	
	n=58		n=116		n=174	
	n	%	n	%	n	%
Mother age						
• <20 years old	20	34,5	16	13,8	36	20,7
• 20-35 years old	28	48,3	91	78,4	119	68,4
• >35 years old	10	17,2	9	7,8	19	10,9
Interval pregnancy						
• <2 years	25	43,1	24	20,7	49	28,2
• ≥2 years	33	56,9	92	79,3	125	71,8
Parity						
• ≥4	36	62,1	49	42,2	85	48,9
• 2-3	22	37,9	67	57,8	89	51,1
Used contraception						
• Not use contraception	25	43,1	21	18,1	46	26,4
• Use contraception	33	56,9	95	81,9	128	73,6

Table 1 showed the characteristic of the study subject of each variable, including the abortion incidence, the age of mothers, the interval of birth, the parity, and the use of contraception. The total sample obtained for this study was 174, including 58 (33.3%) mothers who experienced spontaneous abortion incidence as cases and 116 (66, 7%) mothers who did not experience spontaneous abortion incidence as controls. For most mother who were between 20–35 years old (68, 4%), it was showed that mothers did function of reproduction as it should be at that age, more than a half (71,8%) owned an interval pregnancy about 2 years and as seen from the parity side, most of them (51,1%) owned 2-3 parities and more than a half of them (73,6%) used contraception.

Table 2. Result of Analysis Reproductive Factors with Spontaneous Abortion

Variable	Spontaneous abortion incidence				χ^2	*p*	OR	*95%CI*
	Cases		Control					
	n	%	n	%				
Mother age								
• <20 years old	20	34,5	16	13,8	13,26	0,000	4,06	1,72-
• 20-35 years old	28	48,3	91	78,4			Ref	9,57
• >35 years old	10	17,2	9	7,8	6,9	0,000	3,61	1,17-11,07
Interval pregnancy								
• <2 years	35	43,1	24	20,7	9,60	0,002	2,90	1,38-
• ≥2 years	33	56,9	92	79,3				6,10
Parity								
• ≥4	36	62,1	49	42,2	6,08	0,013	2,24	1,12-
• 2-3	22	37,9	67	57,8				4,51
Used contraception								
• Not use contraception	25	43,1	21	18,1	12,43	0,000	3,43	1,59-7,34
• Use contraception	33	56,9	95	81,9				

Table 2. The result of the analysis of reproductive factors with spontaneous abortion showed the proportion of mothers who experienced spontaneous abortion incidence. Mothers who were before 20 years old were 34,5 % and mothers who were after 35 were 17,2%, while mothers who were 20-34 years old were 48,3%. The result of this bivariable analysis was OR value 4, 06 (95% CI= 1, 72-9, 57), and *the p-value* was 0,003 of mothers who were before 20 years old. In contrast, OR value was 3, 6 (95% *CI*= 1,17-11,06), and *p-value* was 0,008 of mothers who were after 35 years old. It was found that each OR value > 1 and interval of CI was not more than 1, as well as *p-value* <0,05, so the age variable of this study also a risk factor that contributed to spontaneous abortion incidence. It could be concluded that there was a significant relationship between the ages of mothers with spontaneous abortion incidence. OR value meant mothers who were before 20 years old had 4 times risk and mother who were after 35 years old had 3.6 times risk to experience spontaneous abortion incidence compared with who did not experience spontaneous abortion incidence. As seen in a group of age, it could be stated that mothers before 20 years old and after 35 years old were two groups that had risk to cause spontaneous abortion incidence compared to mothers between 20 – 34 years old.

It was found that the proportion of mothers with birth interval less than 2 years experienced spontaneous abortion incidence (43, 1%) was bigger than who did not experience spontaneous abortion incidence (20, 7%). After doing a bivariable analysis on the independent variable (the birth interval) and dependent variable (the spontaneous abortion incidence), it was found that OR value was 2, 90 (95% CI= 1, 38-6, 10) with *a* p-

value was 0, 0019. OR value described mothers with birth intervals less than 2 years had risk 2, 9 times bigger to experience spontaneous abortion incidence compared to those who did not experience spontaneous abortion incidence.

The proportion of spontaneous abortion incidence on mothers with parities ≥4 was (62,1%), while mothers with parities 2-3 were (37,9%). The result of bivariable analysis showed OR value was 2,24 (95% CI= 1,12-4,51) and *p*-value was 0,0136. OR value obtained meant mothers with parities ≥4 had risk 2, 24 times to experience spontaneous abortion incidence compared to mothers who did not experience spontaneous abortion incidence.

The proportion of spontaneous abortion on mothers who did not use contraception was 43, 1%, while on mothers who used contraception was 56, 9%. The result of statistical result on the bivariate analysis found the OR value was 3, 43 (95%CI=1, 59-7,34) and *p*-value was 0,0004, it could be stated that not using contraception was also a factor to experience spontaneous abortion incidence. There was a significant relationship between the use of contraception with spontaneous abortion incidence, mothers who did not use contraception had a risk 3-4 times bigger to experience spontaneous abortion incidence compared to those who did not experience spontaneous abortion incidence.

Tabel 3. Analysis of relationship between age of mothers and spontaneous abortion incidence by controlling the birth interval, the parity, and the use of contraception

Variable	Model 1	Model 2	Model 3	Model 4
	OR	OR	OR	OR
	95% *CI*	95% *CI*	95% *CI*	95% *CI*
Mother age				
• <20 years old	4,06	4,38	4,13	3,82
• 20-35 years old	(1,72-9,57)	(1,95-9,88)	(1,78-9,57)	(1,64-8,94)
• >35 years old				
	3,61	3,49	3,37	3,62
	(1,17-11,06)	(1,25-9,78)	(1,18-9,64)	(1,24-10,62)
Interval pregnancy				
• <2 years		3,08	2,89	2,97
• ≥2 years		(1,48-6,38)	(1,36-6,13)	(1,37-6,39)
Parity				
• ≥4			2,99	3,31
• 2-3			(1,40-6,38)	(1,12-4,76)
Used contraception				
• Not use contraception				3,00
• Use contraception				(1,39-6,48)
R^2	0,04	0,11	0,15	0,17
Deviance	212,21	196,63	188,23	182,94
N	174	174	174	174

Table 3. The result of this analysis showed that there was a significant relationship between age of mothers and incidence of spontaneous abortion after controlling variable of the birth interval, parity, and use of contraception simultaneously (for those who were before 20 years old with OR = 3,82; 95% CI=1,64-8,94 and those who were ≥35 years old with OR=3,62; 95% CI= 1,24-10,62). All of the variables included in each model had a significant relationship with spontaneous abortion incidence. The best model to do intervention was a model in which all significant variables were included, and its deviance value was smaller, as well as the coefficient determinant (R2) was bigger compared to the other models. With this consideration, the researcher tended to choose model 4 as the best model, because it was effective enough and parsimony, where it had the strength of high prediction on

abortion incidence and presence of variables, were good enough to explain important factors related to spontaneous abortion incidence.

DISCUSSION

Based on Tabel 2. the result of the analysis of the study showed that maternal age is a risk factor toward spontaneous abortion. This was in line with the result of the study conducted in dr. Soedjono Military Hospital Magelang said that women with unsafe childbearing age have a higher risk of pregnancy loss (13). Some studies also say that among some factors leading to spontaneous abortion, the number of cases where maternal age is the reason is on top. In women under the age of 20, the uterus muscles are not in their best condition to do their function; also, the hormone system, contractions, and the uterus itself do not yet have fine coordination. Another additional problem that needs to be concerned is the psychological conditions. Normally, women at these ages have unstable mental states in accepting and facing all stages during pregnancy; one of the causes is that the pregnancy is unprepared or, even worse, unwanted. Going through pregnancy at very young ages also tends in that the mothers have less care for any of their childbearing conditions (14)(15).

For women over the age of 35, the risk is more of the fertility decline; deterioration of health conditions due to the physiological state which is no longer at its best; and also the psychological matters. When a woman gets older than 35, one condition she has to face is that estrogen produced by the corpus luteum becomes inadequate which results in the inability to maintain the implantation (16) (4).

Furthermore, a uterus infection that causes embryo implantation failure and a possibility of chromosomal abnormality at the age of over 35 is also to blame for spontaneous abortion (17). Another study mentions that pregnancies at the age of 35 can highly be related to the occurrence of some medical conditions that can cause certain negative effects towards the mothers, such as diabetes mellitus, high blood pressure, and other diseases. The risk of incidence of trisomy disorders to occur also increases as the mother gets older(16)(15). Besides some medical conditions mentioned above, there are still other unidentified risk factors, which is mainly due to the lack of facility to evaluate specific causes of abortion in the first trimester of pregnancy (18).

Gaps between pregnancies in this study showed a certain correlation with spontaneous abortion. The study conducted at the hospital in Riau and the one in Magelang showed that the pregnancy gap of fewer than 2 years has a higher risk of spontaneous abortion or pregnancy loss; if a woman bears a child with an unsafe pregnancy gap, the risk of pregnancy loss to occur will be higher (17) (19). Small gaps between pregnancies increase the probability of spontaneous abortion which then plays a role in maternal morbidity and mortality rate. The importance of controlling ideal gaps between pregnancies and keep them being over 2 years is under consideration where female reproductive organs return to their prepregnant state, which then is known as puerperium or postpartum period. The period of 24 months is the least interval recommended to set gaps between pregnancies so that risks of pregnancies going wrong such as miscarriage, low birth weight (LBW) and short breastfeeding sessions can be prevented beforehand (18). Another research also says that controlling gaps between giving births is an important matter to discuss with partners before attempting the next pregnancy to get the best outcome (13). These small gaps are seen to associate with increased risks for adverse pregnancy outcomes as a result of maternal nutritional deficiencies, folic acid deficiencies, cervical insufficiency, vertically transmitted infections, and abnormal blood vessel remodeling on the endometrium that affect the pregnancy outcomes (20).

After delivery, the suggested interval before the next pregnancy is at least 24 months to decrease the risks that may occur to the mothers, perinatal period, and babies which surely have negative effects. This states that couples are highly recommended to delay their attempts to have another offspring until the second birthday of their latest child (21). The result of the study shows that the incidence of spontaneous abortion has a high rate in

parity of more than or equal to 4. This is in line with another study showing that this incidence increases on more parity. Parity is a risk factor for abortion. Researchers think that if the parity is more than or equal to 4, the period of nutrient depletion can be extended while the repletion gets shorter; therefore, this condition then will cut down the nutrition for the mother (22)

Abortion has a greater risk in cases when the gravida is less than 3. Gravidity history is associated with a condition when the function of the endometrium around corpus uteri starts deteriorating and vascularization starts to decrease which causes the area is no longer fertile and unprepared to bear the result of the conception. The conception outcome cannot go to the implantation process very well which then can lead to the conception failure in which some or the entire outcome is failed to conceive(23).

The risk-increasing rate of this aneuploid conception is a consequence of the long meiotic dormancy period on primary *oocyte* between the first meiotic prophase on the fifth month of fetal life until the formation of *oocyte* some decades later. On nullipara, the prolonged time as they wait for their first pregnancy refers to subfertility. Previous studies show that subfertility is one risk factor of abortion. On a group of women who have given birth, grand multipara occurs more to older women. It is known that grand multipara is also one risk factor of abortion (6).

From the use of contraception, this study showed that the incidence of spontaneous abortion occurs more in groups of women who used contraception. The failure of contraception used by fertile couples to delay, to make the gaps bigger, or to stop giving birth can bring unwanted pregnancy. The contraception that often causes failure is short-term contraception. The risk of short-term contraception failure (pills or condoms) is 4,55% per 100 participants per year. The use of contraception around the time of conception is one of the risk factors of spontaneous abortion. However, this study was not able to distinguish the type of contraception used as well as the regularity and accuracy of the use of the contraception itself, thus this study cannot conclude whether the failure is because of the wrong method or the users themselves who are at fault. The failure of contraception is associated with the incidence of abortion, but the research does not distinguish between spontaneous abortion and medical abortion (23).

Based on bivariate and multivariate analysis, it was shown that not using contraception is a risk factor of spontaneous abortion. The use of contraception is done for various reasons, such as to control the time, number, and gaps between pregnancies according to the parents' wishes. Some health risks or side effects that might occur to the women related to the use of this contraception such as high blood pressure, irregular menstruation, and headache are a few reasons why women decide not to use contraception (24). The value of R^2 which was obtained after controlling gaps between pregnancies, parity, and the use of contraception was 17%, meaning the fetal ages, as well as other variables only, explain 17% of the variability of spontaneous abortion. This shows that there are still more risk factors that influence the incidence of spontaneous abortion occurs which were not analyzed in this study.

CONCLUSION

The age of less than 20, which is too young, and of more than or equal to 35, which is too old, each has high risks of spontaneous abortion to occur. The one less than 20 has a risk of 4 times higher than the average, and the age of more than or equal to 35 has a risk of 3,6 times higher to experience spontaneous abortion than going the pregnancy without one. The number of women with gaps between pregnancies of less than 2 years is found more in groups experiencing spontaneous abortion than the ones who do not experience the loss. There is a correlation between pregnancy gaps with spontaneous abortion, women with gaps between pregnancies less than 2 years have a higher risk of 2,9 times to undergo spontaneous abortion rather than those who do not experience the loss. The incidence of spontaneous abortion increases as maternal parity does. Mothers with parity of more than

or equal to 4 have a risk of 2,2 times higher to undergo spontaneous abortion than do not experience one. The use of contraception is considered as one of the risk factors of spontaneous abortion, women who do not use contraception have a risk of 3,3 higher to undergo the spontaneous abortion than those who do not experience the loss. After controlling the gaps between pregnancies, parity, and the use of contraception, it was obtained that the result of analysis R^2 was 17 % which meant the gaps between pregnancies and other variables can only explain 17% variability of the incidence of spontaneous abortion. This shows that there are still more other factors that influence the incidence of spontaneous abortion which were not analyzed in this study.

In planning the pregnancy, women are better to bear children at the ages between 20-35 years old, with parity of no more than 4, using contraception to control the pregnancy gaps or control the births and if they want to attempt for another child, it is suggested that they wait until the age of latest offspring is more than 2 years old. The related government services like The Public Health Office and The National Population and Family Planning Board need to recommend good gaps between pregnancies when they deliver the counseling to fertile couples so that the pregnancies can go without problems, besides counseling or socialization regarding the use of contraception along with its side effects also needs to be performed, so that the mothers can use the contraception to control the pregnancy gaps without worries if the side effects come to the surface.

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