17. RISK FACTORS FOR POSTPARTUM HEMORRHAGE

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RISK FACTORS FOR POSTPARTUM HEMORRHAGE CAUSED BY UTERINE ATONY

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Abstract

Pregnancy and childbirth are physiological processes experienced by women, but it does not rule out complications resulting in maternal death. One of the causes of maternal death is postpartum hemorrhage. Previous studies have found that postpartum hemorrhage is closely associated with uterine atony. This study aims to explore risk factors for postpartum hemorrhage caused by uterine atony. A case-control study design in Dr. Soetomo General-Academic Hospital. Patient medical records for a period of 2 years at the Dr. Academic General Hospital Soetomo Indonesia used and divided into case and control groups with a ratio of 1:2. Chi-square analyses odds ratios were calculated. A total of 32 patients with uterine atony and 64 medical records without uterine atony were studied. The results of statistical tests on several factors related to postpartum hemorrhage due to uterine atony showed that advanced maternal age (>35 years) (p= 0.763; 95% CI 0.474 – 2.768), grand multipara parity (p = 0.238; 95% CI 0.583-8.185), anemia with Hb <11 (p=0.027; OR=5.000. 95% CI 1.073–23.303), uterine overdistention including macrosomia, polyhydramnios, or gemelli (p=0.031; OR=2.647, 95% CI 1.081-6.482), accelerated labor (p=0.884, 95% CI 0.396-2.221, and previous history of postpartum hemorrhage (p=0.047; OR= 2.435, 95% CI 1.003 – 5.933). This case control study found that anemia, uterine overdistention, and a previous history of postpartum hemorrhage may increase the risk of postpartum hemorrhage due to uterine atony. Therefore, it is recommended to the public to increase awareness of the importance of early and regular pregnancy check-ups, especially in the management of anemia and to identify risk factors.

Keywords: *Postpartum hemorrhage, uterine atony, risk factors, maternal health*

Introduction

Pregnancy and childbirth are physiological processes experienced by women, but it does not rule out complications resulting in maternal death. According to WHO (2019), around 830 women die every day from preventable complications of pregnancy and childbirth, and 99% of maternal deaths occur in developing countries. One of the main causes of nearly 75% of maternal deaths in the world is hemorrhage, especially postpartum hemorrhage or known as Haemorrhagia Postpartum (HPP) [*WHO. 2019*] and it is estimated that one woman dies every 4 minutes due to this case [*Sebghati M, Chandraharan E., 2017*]. According to the Royal College of Obstetricians and Gynecologists (2016), primary postpartum hemorrhage is blood loss of 500 *ml* or more that occurs within 24 hours postpartum, with the category of 500-1000 *ml* being minor bleeding and more than 1000 *ml*

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being major bleeding. The most common cause of postpartum hemorrhage is uterine atony [*Nyfløt LT et al., 2017a*]. Postpartum hemorrhage is physiologically controlled by the contraction of the myometrial fibers surrounding the blood vessels that vascularize the placental implantation area, and uterine atony occurs when the myometrial fibers do not contract [*Lim PS, 2012*]].

Uterine atony is the cause of sever hemorrhage from the tone category in the most common cause of postpartum hemorrhage, which is 60%-80% of all postpartum hemorrhage cases [*Sebghati M, Chandraharan E., 2017*]. Uterine atony can specifically account for up to 80% of cases of postpartum hemorrhage [*Chauhan SP et al., 2006*]. The incidence of postpartum hemorrhage in developing countries is 50-60% higher than the incidence of uterine atony (23-24%) and retained placenta (16-17%). Uterine atony refers to inadequate uterine myometrial cells in response to endogenous oxytocin released during labor [*Gill P et al., 2021*]. In short, uterine atony can cause postpartum hemorrhage due to inadequate myometrial fibers surrounding the blood vessels that vascularize the placental implantation site. In this situation, the uterus is excessively distended, or the uterine activity is too weak, both of which are at risk for massive bleeding, leading to several complications [*Cunningham FG et al., 2012*].

The active role of the family and the community in regarding risk factors, disorders experienced by the mother during the pregnancy process, and early detection, fast and safe handling of complications by health workers can prevent and reduce the incidence of labor complications due to postpartum hemorrhage due to uterine atony. Wetta LA and coauthors stated several studies explaining the risk factors for uterine atony, including uterine overdistension (multiple pregnancies, polyhydramnios, fetal macrosomia), labor induction, uterine age, maternal age, parity, preeclampsia, and prolonged gestation [*Wetta LA et al., 2013*]. Therefore, the writer feels the need for research that analyzes the risk factors that can increase the incidence of uterine atony by studying medical records in Dr. Soetomo General Academic Hospital to provide a deeper understanding of the various risk factors that cause uterine atony in both the community and clinic areas to prevent an increase in morbidity and mortality due to moderate to severe postpartum hemorrhage.

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

RESEARCH METHOD

This study is a retrospective case-control study design in medical records. The population in this study included postpartum hemorrhage patients in Dr. Soetomo General Academic Hospital in the period 1 January 2018 – 31 December 2019. The sampling technique used in the study for the case group was a total sampling technique with a ratio of 1:2 to get a wider comparison of patients' medical records in the period 1 January 2018 – 31 December 2019 or until the data is met. The independent variables in this study were maternal age, parity, uterine overdistention, labor acceleration, anemia, and previous history of postpartum hemorrhage. The dependent variable in this study was postpartum hemorrhage with uterine atony in Dr. Soetomo General Academic Hospital. The instrument of this study used a case report form from secondary data from medical records of patients who met the inclusion criteria after obtaining ethical approval permits with the principles of anonymity and confidentiality. Furthermore, univariate and bivariate analysis was carried out using the chi-square correlation test and presented tabular form. The ethical considerations of this study were approved by the Ethics Committee at Dr. Soetomo General-Academic Hospital with number 0286/LOE/301.4.2/I/2021.

RESULTS AND DISCUSSION

The samples in this study were medical records from patients who experienced postpartum hemorrhage, divided into case groups and control groups. Case groups, namely medical records of patients who

TABLE 1.
Frequency Distribution of Occurrence Risk Factors for Postpartum Hemorrhage due to Uterine Atony

Variable	Postpartum Hemorrhage			
	Case		Control	
	n:32	%	n:64	%
1. Maternal Age				
< 20 years old	1	3.1	0	0
20-35 years old	19	59.4	42	65.6
> 35 years old	12	37.5	22	34.4
2. Parity				
Primipara	3	9.4	7	10.9
Multipara	24	75	52	81.3
Grandemultipara	5	15.6	5	7.8
3. Anemia				
< 11	30	93.8	48	75
≥ 11	2	6.2	16	25
4. Uterine Overdistention				
No	17	53.1	48	75
Macrosomia	8	25	6	9.4
Polyhydramnios	5	15.6	7	10.9
Gemelli	2	6.3	2	4.7
5. Acceleration of Labor				
No	19	59.4	37	57.8
Yes	13	40.6	27	42.2
6. Postpartum Hemorrhage History				
No	17	53.1	47	73.4
Yes	15	46.9	17	26.6

experienced postpartum hemorrhage due to uterine atony. Control groups, namely medical records of patients who experienced postpartum hemorrhage without uterine atony. In this univariate analysis section, the frequency distribution of the incidence of uterine atony, maternal age, total parity, anemia, uterine overdistention, labor acceleration, postpartum hemorrhage history will be presented.

Table 1 show the results of univariate analysis. Based on the results of the univariate analysis of this study, almost all research subjects were in the age group of 20-35 years, as many as 61 patients, with the proportions of each case group and control group being 31.1% and 68.9%, respectively. The age range at risk is at the age of <20 years and >35 years so that at the age of 20-35 years is a healthy reproductive age [*Wiknjosastro H et al., 2010*]. This is related to the number of parity, mostly in the multiparous group, namely 76 patients with a large percentage of 75% for the case group and 81.3% for the control group. The parity of a pregnant woman or giving birth is said to be at high risk based on obstetric complications, namely multipara and grand multipara [*Manuaba IAC et al., 1988*].

Based on previous research, anemia can increase the risk of postpartum hemorrhage [*Ramanathan G, Arulkumaran S, 2006*]. Postpartum hemorrhage accompanied by anemia is the cause of 40-43% of maternal deaths in Africa and Asia [*Frass KA, 2015*]. This is in line with the results of the frequency distribution of anemia in research subjects. Almost all research subjects experienced anemia with Hb <11, namely a total of 78 patients experienced postpartum hemorrhage, with a proportion of 30 patients experiencing uterine atony with a large percentage of 93.8%. Overdistention of the uterus can interfere with myometrial contractility after delivery and increase the incidence of uterine atony, occurring in at least 80% of cases of postpartum hemorrhage [*Bateman BT et al., 2010*]. One of the risk factors for this occurrence is uterine overdistention (polyhydramnios, macrosomia, and Gemelli) [*Blitz MJ et al., 2020*]. In the variable acceleration of labor, the results did not differ much between the case and control groups, with 40 patients experiencing accelerated labor. The incidence of difficult labor is unknown because there is no universal consensus on the definition of a delayed first stage of labor. The proportion of variables with a history of postpartum hemorrhage also showed that 17 patients did not have a history of postpartum hemorrhage by 53,1% in the case group, and 15 patients had a history of postpartum hemorhage by 46.9%.

In the maternal age variable, it is known that most of the case groups are in the productive age, namely 20-35 years, as many as 19, amounting to 59.4%. Followed by the age group >35 years as many as 12 patients at 37.5% and the last one at the age <20 years, namely one patient at 3.1%. In the number of parity variables, the case and control groups had not many different proportions. Most of them were in the multiparous group with 75% and 81.3%, respectively. Followed by grand multipara as much as 15.6% and 7.8% for the case and control groups, respectively. It was only found in

the case group in primiparas, which was 9.4%.

Anemia variable, almost all subjects in the case group experienced anemia with Hb <11 as many as 30 patients with a large presentation of 93.8%. The highest proportion with Hb <11 was also found in the control group, which was 75%. In the uterine overdistension variable, eight patients had macrosomia (25%), polyhydramnios in 5 patients (15.6%), and gemelli or twin pregnancy in 2 patients (6.3%). Acceleration of labor variable, the proportion of the case group and the control group, most of the research subjects did not experience accelerated labor with 59.4% for the case group and 57.8% for the control group.

The uterine overdistension variable was divided into four categories, namely macrosomia, polyhydramnios, gemelli, and not experiencing uterine overdistension. In the case group, 15 respondents experienced uterine overdistention with macrosomia there are 8 patients (25%), polyhydramnios there are 5 patients (15,6%), Gemelli there are 2 patients (6.3%), and 17 patients did not experience uterine overdistension. Patients (53.1%). In the control group, there were 48 respondents with 6 patients (9.4%) with macrosomia, 7 patients (10.9%) with polyhydramnios (20.9%), 2 patients (4.7%) with gemelli , and 48 patients who did not experience uterine overdistension. (75%). There was a history of postpartum hemorrhage in the case group and no history of postpartum hemorrhage with a percentage of 46.9% and 53.1%, respectively. Meanwhile, in the control group, the proportion of patients with a history of postpartum hemorrhage and no history of postpartum hemorrhage was 26.6% and 73.4%, respectively.

Bivariate analysis was used to determine the significance of the correlation between the dependent variable and the independent variable. This section describes the correlation between Maternal Age, Total Parity, Anemia, Uterine Overdistension, Accelerated Labor, History of Postpartum Hemorrhage with Postpartum Hemorrhage due to uterine atony. All variables in this study meet the data processing process with the chi-square test. The value of the significance of the correlation is indicated by the p-value <0.05. The following are

TABLE 2.

Correlation Between All Variables with Postpartum Hemorrhage Due to Uterine Atony

Variable		Case		Control		OR	95% CI	*p*-value
		n	%	n	%			
Maternal age	≤35	20	65.2	42	65.6	-	0.474-2.768	0.763
	>35	12	32	22	34.4			
	Total	32	100	64	100			
Parity	< 5	27	84.4	59	92.2	-	0.583-8.185	0.238
	≥ 5	5	15.6	5	7.8			
	Total	32	100	64	100			
Anemia	< 11	30	93.8	48	75	5.000	1.073-23.303	0.027
	≥ 11	2	6.2	16	25			
	Total	32	100	64	100			
Uterine Overdistention	No	17	53.1	48	75	2.647	1.081-6.482	0.031
	Yes	15	46.9	16	25			
	Total	32	100	64	100			
Acceleration of Labor	No	19	59.4	37	57.8	-	0.396-2.221	0.884
	Yes	13	40.6	27	42.2			
	Total	32	96	64	100			
Postpartum Hemorrhage History	No	17	53.1	47	73.4	2.435	1.003-5.933	0.047
	Yes	15	46.9	17	26.6			
	Total	32	100	64	100			

the results of the bivariate analysis. Table 2 showed the correlation between all variables with postpartum hemorrhage due to uterine atony.

Based on the table above, in the case group and control group in the Maternal Age Variable after recategorizing based on the theory which states that the factor for postpartum hemorrhage is an increase in maternal age, namely >35 years, mothers with age 35 have the highest proportion with a large percentage of 65,2% and 65,6%, respectively. This shows that only a small proportion of the case group is at an age at risk for postpartum hemorrhage due to uterine atony (>35), most of which are in healthy reproductive age, as many as 20 patients (6,2%). With a p-value of 0.763 (> 0.05), this result means no significant correlation between maternal age and postpartum hemorrhage. In the Total Parity variable, the category is divided into 2, namely <5 and 5. The division of this category refers to the theory that mothers with grandmultipara can increase the risk of obstetric complications neonatal. Perinatal mortality at this parity, almost all respondents in the case group and control group have parity <5 with a large percentage was 84.4% for the case group and 92.2% for the control group. With a p-value of 0.238 (> 0.05), this result means that there is no significant correlation between the amount of parity and postpartum hemorrhage. In the Anemia variable, it was found that most of the case groups and the control group had anemia with Hb <11 of 93.8% and 75%, respectively. With a p-value of 0.027 (<0.05) and an OR of 5.000 (95% CI 1.073-23.303). These results mean a significant correlation between anemia and postpartum hemorrhage. Pregnant women with anemia have a five times greater risk of uterine atony than pregnant women with Hb ≥ 11.

The uterine overdistension variable was re-categorized by combining macrosomia, polyhydramnios, and gemelli into one category and grouped into to 2, namely yes and no uterine overdistension in research subjects. The case group has a relatively small percentage difference, 53,1% for patients who do not experience uterine overdistension and 46.9% for patients who experience uterine overdistension. With a p value of 0.031 (<0.05) and an OR of 2.647 (95% CI 1.081-6.482). These results mean that there is a significant correlation between uterine overdistension and postpartum hemorrhage. Pregnant women with cases of macrosomia, polyhydramnios, and gemelli have a 2.647 times greater risk of uterine atony than women who do not experience uterine overdistension. In the variable acceleration of labor, the proportion of cases and controls was not much different, with a percentage result of 59.4% for patients who were not given oxytocin drip in the case group and 57.8% for patients who were not given oxytocin drip in the control group. With a p value of 0.884 (> 0.05), this result means that there is no significant correlation between accelerated labor and postpartum hemorrhage. In the variable history of postpartum hemorrhage, it was found that most of the case groups and the control group had no history of postpartum hemorrhage with a large percentage of 53.1% and 73,4%, respectively. With a p value of 0.047 (<0.05) and an OR of 2.435 (95% CI 1.003-5.933). These results indicate that pregnant women who have a history of previous postpartum hemorrhage have a 2.435 times greater risk than pregnant women who have no previous history of postpartum hemorrhage.

One of the risk factors associated with uterine atony is an increase in maternal age, namely age >35 years [*Moncrieff G.*, 2018]. This increase in age is related to maternal morbidity due to accompanying medical conditions such as increasing cases of hypertension and gestational diabetes [*Njoku CO et al., 2017*]. This study showed that maternal age in the range of 20-35 years had the highest proportion from the results of univariate analysis. The results of the bivariate analysis of this study showed that the incidence of uterine atony was most commonly found at the age of 35 years (65.2%). Statistically, there was no significant correlation between age and the incidence of uterine atony with a p-value of 0.763. Another study that is in line with the results of this study is the study conducted by Nyflot et al. (2017) in Scandinavia with a p-value of 0.101 [*Nyfløt LT et al., 2017b*]. The group of respondents >35 years of age was assessed to have no correlation with the

incidence of postpartum hemorrhage. Several studies that study the correlation between increasing maternal age and pregnancy complications are still contradictory. The cause of pregnancy complications is either increased maternal age or comorbidities [*Mills TA, Lavender T, 2014*].

Research conducted by Mgaya and coauthors stated that grande multipara was associated with an increased risk of maternal and neonatal complications such as malpresentation, meconium-mixed membranes, abnormal placental position, and low Apgar scores. Arterial narrowing and scar tissue from previous pregnancies in grand multiparous women are the causes of uterine atony [*Mgaya AH et al., 2013*]. This study showed that almost all samples of the case group had parity <5 with the proportion of 84.4% and p-value of 0.238. There was no significant correlation between parity and the incidence of postpartum hemorrhage due to uterine atony. There are studies in Uganda [*Ononge S et al., 2016*] and in Saudi Arabia [*Alsammani MA, Ahmed SR. 2012*] that aimed to determine the prevalence of grande multipara and associated risks found no significant difference between grande multipara and multiparous women in experiencing bleeding after labor.

Several studies link the risk of postpartum hemorrhage due to uterine atony with the degree of anemia and show a strong correlation. Previous studies have shown that severe anemia can impair myometrial contractility due to impaired hemoglobin and oxygen transport to the uterus, leading to tissue enzyme and cellular dysfunction [*Kavle JA et al., 2008*]. The results of this study indicate that anemia with Hb <11 has a significant correlation with the occurrence of postpartum hemorrhage due to uterine atony with a p-value of 0.027 and an OR of 5.0. The OR value in this study means that patients with anemia are five times more at risk of postpartum hemorrhage due to uterine atony than patients who are not anemic. The results of this study are in line with the results of research by Liu C and coauthors and Julizar M. and Sukandar H, their research also found that mothers with anemia were at risk for uterine atony compared to mothers who did not have anemia [*Julizar M, Sukandar H, 2019*; *Liu C et al., 2021*].

Ovedistention of the uterus occurs in pregnant women with macrosomia, polyhydramnios, and Gemelli. The stretching of the uterus can interfere with myometrial contractility after childbirth and increase the incidence of uterine atony [*Moncrieff G, 2018*]. There was a significant correlation between the dependent and independent variables in the uterine overdistention variable, indicated by a p-value of 0.031 and an OR of 2.647, which indicated that patients who had uterine overdistention had a 2.647 times greater risk than patients who did not experience uterine overdistention. The results of this study are in line with the research of Ononge S and coathors (2016) in Uganda showed that there was a correlation between the Gemelli variable and the macrosomia variable with the incidence of postpartum hemorrhage [*Ononge S,. et al., 2016*].

Macrosomia is recognized as a cause of fetal and maternal morbidity and mortality. Gemelli or multiple births can weaken uterine muscle contractions and retractions and increase the risk of postpartum hemorrhage [*Cunningham FG, 2005*]. The most common complications of polyhydramnios are a premature detachment of the placenta or placental abruption and uterine atony due to excessive stretching of the uterus, causing uterine dysfunction and postpartum hemorrhage [*Cunningham FG, 2012*].

Actions to accelerate labor are carried out in arrest of dilatation and arrest of descent due to poor contractions [*Cunningham FG, 2012*]. According to Rousseau A and Burguet A, using oxytocin during labor can cause hyperactivity of the uterus. Uterine hyperactivity includes abnormalities in the frequency of contractions (uterus contracts more than five times in 10 minutes), abnormalities in the duration of contractions (contraction duration >120 seconds). This uterine hyperactivity is related to the incidence of uterine atony as a cause of postpartum hemorrhage [*Rousseau A, Burguet A, 2017*]. Based on the data of this study, it was found that there was no significant correlation between the acceleration of labor and the incidence of uterine atony. The results of the chi-square test obtained a p-value of 0.884. The results of this study are in line with the research conducted by Sosa CG and coauthors (2011) in 19 maternity units in Latin

America which aim to determine the correlation between the use of oxytocin during the first and second stages of labor and the high incidence of postpartum hemorrhage in patients receiving active management of the third stage [*Sosa CG et al., 2011*]. In this study, it was found that there was no correlation between induction and acceleration of labor with the incidence of minor or major postpartum hemorrhage. However, it was unknown whether the dose used or the duration of exposure was unknown.

The theory explains that oxytocin during labor can cause desensitization of oxytocin receptors. The concentration of oxytocin receptors in the myometrium is significantly reduced and causes a loss of sensitivity of myocytes to stimulation of oxytocin. Desensitization of these receptors is the cause of uterine atony [*Rousseau A, Burguet A, 2017*]. Research results that are not in line with this theory can occur due to the limited sample that received accelerated labor with delivery in the case group.

A history of postpartum hemorrhage is a known risk factor for postpartum hemorrhage in subsequent pregnancies [*Kramer M S et al., 2013*]. Studies examining risk factors for postpartum hemorrhage have shown that women with previous postpartum hemorrhage have a 2 to 3 times higher risk for postpartum hemorrhage compared to those without such a history [*Oyelese YAC, Oyelese Y ACV, 2010*]. Based on Ford's JB and coauthors research results, A population-based study in New South Wales of 125.295 women reported a 15% risk of postpartum hemorrhage in women with one hemorrhage pregnancy and 27% in those with two previous hemorrhage pregnancies [*Ford JB et al., 2007*].

Based on the results of statistical tests, it was found that there was a correlation between postpartum hemorrhage and the incidence of uterine atony in with the proportion of the case group experiencing uterine atony, was 18.9%, the p-value was 0.047 with an OR of 2.435. This indicates that patients with a history of postpartum hemorrhage have a risk of 2.435 times than patients without a history of postpartum hemorrhage. The bleeding results during delivery were related to a history of postpartum hemorrhage in the first and second deliveries. The results of other studies that are in line with this research are conducted by Nyflot LT and coathors. His research found that a history of postpartum hemorrhage was the strongest factor causing postpartum hemorrhage with various causes [*Nyfløt LT et al., 2017a; Nyfløt LT et al., 2017b*].

Limitations in this study include that there are some missing and incomplete data. There is a history of postpartum hemorrhage in the variable before writing the data. It is not known the cause of the hemorrhage history in the research subject, causing difficulties in determining conclusions. Almost all research subjects are referred patients so that cases occur due to multi factors and there is no known history of previous examinations.

CONCLUSION

Based on the research objectives to be achieved and the research results obtained, the following are the conclusions of this study. The distribution of the frequency of the incidence of postpartum hemorrhage due to uterine atony is 32 patients with a large percentage of 33.3% with age at delivery, namely in healthy reproductive age in the age range of 20-35 years, experiencing anemia with Hb <11, uterine overdistension and total parity in the multiparous group. Three risk factors had a significant correlation with postpartum hemorrhage due to uterine atony, namely anemia, uterine overdistention, and previous history of postpartum hemorrhage. Therefore it is recommended for the public to increase awareness of the importance of antenatal care early and regularly to identify risk factors and can provide a deeper understanding of the various risk factors that cause uterine atony in both community and clinical areas to prevent an increase in morbidity and mortality due to postpartum hemorrhage, moderate to severe bleeding.

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