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Meta-Analysis: The Effect of Anemia, Pre-Eclampsia and Parity on the Prevalence of Low-Birth-Weight Infants in Indonesia

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ABSTRACT

The incidence of LBW in Indonesia varies greatly from one region to another. Nationally based on the Indonesian health demographic survey, the incidence of LBW has increased to 6.2% in 2018. This study aims to determine the magnitude of anemia, pre-eclampsia and parity on the incidence of LBW. LBW in Indonesia. This study is a meta-analysis using PRISMA, obtained 22 journals containing case-control and cross-sectional journals from 1219 from two databases, namely PubMed and scholar, data presentation using forest plots obtained using the Rev.Man 5.3 application. The magnitude of the combined odds ratio (OR) shows that the effect of anemia on LBW is 3.25, anemia tends to have a large effect on the incidence of LBW with a value of 3.65, then the effect of pre-eclampsia on LBW is 2.70, pre-eclampsia tends to have a similar effect. large in the incidence of LBW with a value of 5.50 while the effect of parity on LBW is 1.45 parity tends to have a large effect on the incidence of LBW with a value of 1.30. In the three variables analyzed by meta-analysis, the greatest influence on the incidence of LBW is pre-eclampsia. There is an influence of anemia, pre-eclampsia and parity on the incidence of LBW, early detection of anemia should be carried out early and need to be evaluated after giving Fe. In pre-eclampsia, it is necessary to have an early examination during pregnancy visits, while at parity, it must be socialized and evaluated again for the family planning program. so that the incidence of LBW can be reduced.

Keywords: anemia, pre-eclampsia, parity, LBW, meta-analysis

INTRODUCTION

Low Birth Weight (LBW) is defined as a baby born weighing less than 2500 grams. LBW is the highest predictor of infant mortality, especially in the first month of life (MoH RI, 2015). LBW cases are a global health problem that has long-term and short-term effects. The prevalence of LBW is estimated at 15% of all births globally, with a range of 3.3-38%. Overall it is estimated that 15-20% of the 20 million live births per year in the world are LBW. The incidence of LBW is in Sub-Saharan Africa (13%), South Asia (28%), East Asia and the Pacific (6%), Latin America (9%), and in developed countries (13%) (Indri, 2018) LBW babies have a 20-fold greater risk of death compared to babies born with normal weight. More than 20 million babies worldwide are born with LBW, and 95.6% of LBW babies are born in developing countries (MoH RI, 2015).

There are 20 million cases of low birth weight babies in developing countries, and more than half of them occur in Southeast Asia, including Indonesia. In one year, 89,000 babies died due to low birth weight babies. Statistically, 90% of LBW cases occur in developing countries and the mortality rate is 35 times higher than in

infants with a birth weight of more than 2,500 grams alive (Word Health Statistics, 2015).

The incidence of LBW in Indonesia varies greatly from one area to another, ranging from 9-30% and the results of studies in 7 multicenter areas showed that LBW rates ranged from 2.1-17.2%. Nationally, based on the Indonesian health demographic survey, the incidence of LBW is also constant, at The Indonesia Basic of Health Research in 2013 Indonesia was at 5.7% and in 2018 it increased to 6.2% (The Indonesia Basic of Health Research, 2018).

Anemia in pregnancy is a common problem and 50% of pregnant women in developing countries experience anemia. LBW is a major determinant of death, illness and disability in infants and children and has a long-term impact on life. The biggest contributor to the incidence of LBW in Indonesia is anemia in pregnant women, which is around 50.9% with the most common cause being iron deficiency anemia (Indira, 2019).

Preeclampsia, apart from being one of the biggest causes of maternal mortality and morbidity, also affects the condition of the fetus and newborn (Wibowo & Rachimhadhi, 2006). One of the changes that greatly affect the fetus is changes in the placenta and uterus. In pre-eclampsia, there is spasm of decidual spiral arterioles, resulting in decreased blood flow to the placenta. Decreased blood flow to the placenta results in decreased perfusion and over time will cause a hypoxic state and malnutrition in the fetus (Cunningham, 2012). This situation if it occurs for a long time causes impaired fetal growth, in more severe cases can occur fetal distress to death due to lack of oxygenation. There is an increase in uterine tone and sensitivity to stimulation in the uterus so that it is easy for premature labor to occur (Birawa et al., 2009). Fetal growth disorders and premature parturition resulting from pre-eclampsia can cause low birth weight (LBW) babies.

Parity has a risk of 68.2% for giving birth to LBW. Unsafe parity is parity 1 and >3, Parity 1 still has less knowledge and has no experience about pregnancy to affect their pregnancy. Readiness in dealing with pregnancy, both physically and mentally, tends to be lacking to affect the pattern of maintaining the health of the fetus it contains. This is due to the unprepared function of the organs in maintaining pregnancy and accepting the condition of the fetus. Factors that influence high parity are education, economic conditions, and culture. Efforts to prevent high parity can be done by using family planning, which can be done by women and use family planning (Lestari, 2019).

Based on the search results of a systematic review and analysis of the effect of anemia, pre-eclampsia and parity on the incidence of LBW, several studies that provide information on how big the problem is in Indonesia so that we can see a targeted analysis of the risk of anemia, pre-eclampsia and parity on the incidence of babies with weight no review clearly analyzes the effect of anemia, pre-eclampsia and parity on the incidence of low-birth-weight babies. This analysis will provide the basic data needed to plan a strategy to reduce the number of LBW.

MATERIALS & METHODS

The research design used is a meta-analysis study. References for formulating research questions can use "PICO". The identification in this study are as follows:

a. P (Patient, Population, Problem): Low Birth Weight
b. I (Intervention, Prognostic Factor, or Exposure): Anemia, Pre-eclampsia and Parity
c. C (Comparison or Intervention): the incidence of normal birth weight
d. (Outcome): the effect of anemia in pregnancy, pre-eclampsia and parity on the incidence of low-birth-weight babies.

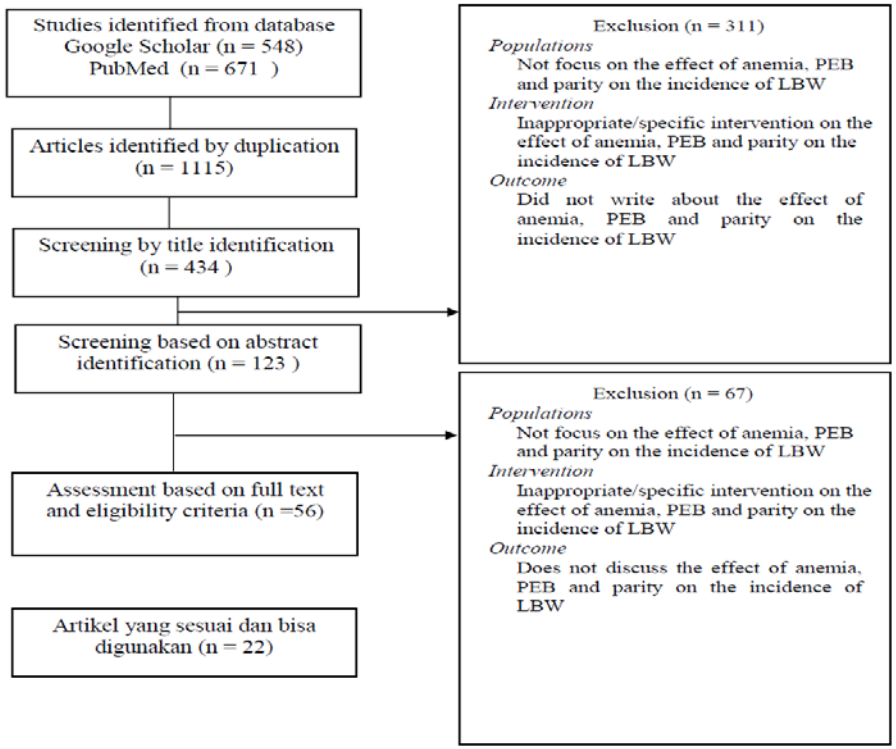

Figure 1: Flow Chart PRISMA

RESULT

Table 1: List and details of articles

No	Researcher	Research purposes	Study Place	Research methods	Number of Samples	JBI Score	Research result	OR value
1	Anna Veronica Pont, Rafika (2017)	This study aimed to determine the effect of anemia during pregnancy on LBW at Anutapura General Hospital Palu.	Anutapura Hospital, Palu.	Cross-Sectional	43	5	There is an effect of anemia in mothers during pregnancy on LBW at Anutapura Hospital Palu	OR Anemia: 17.6
2	Astrisa Faadhillah, Helda (2020)	Relationship of Preeclampsia with LBW Kejadian	Tangerang Regency General Hospital	Cross-Sectional	1036	6	This study found a significant relationship between pre-eclampsia and the incidence of LBW after controlling for confounding variables (gestational age, premature rupture of membranes, oligohydramnios, twin pregnancy, and IUGR).	OR Pre-Eclampsia: 2,003
3	Eka Maya Putri (2017)	Knowing the factors associated with the incidence of Low Birth Weight (LBW) infants in Arifin Achmad Hospital, Riau Province in 2014	Arifin Achmad Hospital, Riau Province	Cross-Sectional	93	6	The results showed that there was a relationship between age, gestational distance, anemia and multiple pregnancies with the incidence of LBW	OR Anemia: 4,426

Table no 1: continued……								
4	Rina Wijayanti, Rina Nanda Pagestu (2020)	Knowing the factors related to LBW in women giving birth in the Maternity Room of the Johar Baru Regional General Hospital in 2017.	Johar Baru Regional General Hospital Maternity Room	Cross-Sectional	184	6	The results obtained that there is a relationship between BMI, Parity and Hb Levels	OR Anemia: 16.64 OR Parity: 4.28
5	Tonasih, Diyanah Kumalasary (2018)	Knowing the factors that influence the incidence of LBW in the Harjamukti Regional Health Center, Cirebon City in 2016	Harjamukti Regional Health Center, Cirebon City	Cross-Sectional	976	6	Factors related to the incidence of LBW include age, parity and multiple pregnancies.	OR Parity: 2.060
6	Siti Jumhati, Dian Novianti (2018)	Knowing the factors associated with the occurrence of Low Birth Weight (LBW) at Permata Cibubur Hospital	Permata Cibubur Hospital	Cross Sectional	97	6	From the results of the study, it was revealed that 90.3% of the occurrence of LBW in infants weighing 1500 grams - 2499 grams caused by factors of gestational age, parity, gestational distance, PEB, and Gemeli	OR Parity: 0.001 OR Pre-eclampsia : 16.80
7	Sarma Nursani Lumbanraja (2017)	Develop a scoring system to predict LBW in disadvantaged areas	Padang Sidempuan General Hospital	Case-Control	62 Cases, 62 Controls	10	Four variables were significant: occupation, antenatal care, history of anemia in pregnancy, and history of placenta previa during pregnancy.	OR Anemia: 11,598 OR Parity : 1000 OR Pre-Eclampsia: 2.476
8	Susanti Suhartati, Nita Hestiyana, Laila Rahmawaty (2017)	Analyzing the relationship between anemia in pregnant women and the incidence of low birth weight babies (LBW) in the work area of the Tanta Health Center in 2016	Tanta Health Center, Tabalong Regency, South Kalimantan	Case-Control	36 Cases, 72 Controls	9	Mothers who are anemic have a 9 times greater risk of giving birth to low birth weight babies	OR Anemia: 9.19
9	Intan Kumalasari, RM. Suryadi Tjekyan, M. Zulkarnain (2018)	Knowing the risk factors and the incidence of LBW in Dr. M. Hoesin Palembang.	RSUP Dr. M. Hoesin Palembang	Cross Sectional	1582	6	The results showed that there was a significant relationship between gestational age, multiple pregnancy, eclampsia, pre-eclampsia, Hb levels and education with the incidence of LBW. Gestational age is the most dominant factor causing low birth weight after controlling for other variables.	OR Parity: 1.33 OR Anemia: 1.663 OR Pre-eclampsia : 1.84
10	Anjas Dwi Purwanto, Chatarina Umbul Wahyuni (2016)	Analyzing the factors associated with the incidence of LBW	Kendangsari Mother and Child Hospital Surabaya	Case-Control	120	9	There are 4 factors associated with the incidence of LBW, namely gestational age, multiple pregnancy, hypertension, and anemia during pregnancy	OR Parity : 1,152 OR Anemia : 4,030
11	Padma Permana, Gede Bagus Rawida Wijaya (2019)	Determining several risk factors related to LBW at UPT Kesmas Gianyar I during the 2016-2017 period	Integrated Service Unit (UPT) for Public Health (Kesmas) Gianyar I	Case-Control	53 Cases, 53 Controls	9	There is no significant relationship between maternal age, parity, anemia status, nutritional status, and distance between pregnancies and the incidence of LBW, however, multiple pregnancies and gestational age show an association with LBW.	OR Parity : 0.5 OR Anemia: 0.6
12	Nursusila.H.Ruslan Majid, La Ode Ali Imran Ahmad (2017)	Knowing the risk factors for the incidence of Low Birth Weight (LBW) at the General Hospital of Southeast Sulawesi Province in 2016	Southeast Sulawesi Provincial General Hospital	Case-Control	47 Cases, 47 Controls	8	The results showed that ANC and anemia were risk factors for the incidence of LBW, while parity was not a risk factor	OR Parity :6.04 OR Anemia: 6.036
13	Fitri Handayani, Wa Ode Ikrawati, Herlin Fitriani (2019)	Knowing the relationship between anemia and hypertension with the incidence of LBW	Wates Public Health Center, Kulon Progo Regency	Case-Control	40 Cases, 40 Controls	9	There is a relationship between anemia and the incidence of LBW, the relationship between hypertension and the incidence of LBW	OR Anemia: 0.356

Table no 1: continued……								
14	Ika Popi Sundani (2020)	Knowing the factors related to the incidence of LBW in shallot farmers in Keanggungan District, Brebes Regency, Central Java Province in 2017	District of Accountability, Brebes Regency, Central Java Province	Case-Control	120	8	Of the 11 factors that have a relationship with the incidence of LBW, there are 5 dominant factors that influence the occurrence of LBW mothers, namely maternal knowledge, parity, maternal nutritional status, frequency of ANC examination and length of work.	OR Parity: 6.769
15	Hanum Sasmita, Husnul Khotimah (2020)	Knowing the relationship between gestational age, parity and pre-eclampsia with the incidence of LBW in the perinatology room of the Regional General Hospital (RSUD) Drajat Prawiranegara	Regional General Hospital (RSUD) Drajat Prawiranegara	Case-Control	26 Cases, 26 Controls	7	There is a relationship between parity, gestational age and pre-eclampsia with LBW and the dominant factor that most influences the incidence of LBW is pre-eclampsia.	OR Parity: 4.5 OR Pre-Eclampsia: 8.6
16	Lydia Febrina, Triana Sri Herdjanti, Siti Nikmah (2019)	Knowing the risk factors for the occurrence of low birth weight babies at the Karang Kobar Health Center, Banjarnegara Regency in 2018	Karang Kobar Health Center, Banjarnegara Regency	Case-Control	32 Cases, 32 Controls	8	Factors associated with LBW incidence are maternal age during pregnancy, gestational age, anemia, and LiLA <23.5 cm.	OR Anemia: 2.806 OR Pre-eclampsia : 1,190 :
17	Iva Inpresari, Wiwik Eko Pertiwi (2020)	Knowing the factors associated with the incidence of Low Birth Weight (LBW)	Jawilan and Lightning Health Center, Serang Regency	Case-Control	71 Cases, 71 Controls	8	The results showed a significant relationship between the frequency of ANC and the size of LILA with LBW. there is no relationship between gestational interval and pre-eclampsia with LBW	OR Pre-Eclampsia: 2.10
18	Ayu Rosida Setiati, Sunarsih Rahayu (2017)	Knowing the factors that influence the incidence of low birth weight in the neonatal intensive care unit DR Moewardi Hospital	DR Moewardi. Hospital	Cross-Sectional	33	6	Of the 11 factors that influence the incidence of LBW, there are 6 factors related to the incidence of LBW, namely age, hypertension, parity, antepartum bleeding, eclampsia/pre-eclampsia and PROM.	OR Anemia: 1.33 OR Pre-eclampsia: 4.67 OR Parity: 0.18
19	Amima Fajriana (2018)	Analyzing the relationship between maternal age during pregnancy, gestational age, Upper Arm Circumference (LILA), hemoglobin (Hb) levels and cigarette smoke exposure status with the incidence of LBW in Semampir District, Surabaya	Semampir District, Surabaya	Case-Control	22 Cases, 22 Controls	8	There is no relationship between maternal age during pregnancy, Hb levels and cigarette smoke exposure status with LBW, but it is known that there is a relationship between gestational age and LILA with the incidence of LBW	OR Anemia: 2,308
20	Endah Luqmanasari, Muliana (2020)	Knowing the maternal factors associated with low birth weight (LBW) infants	Amelia Pare Hospital, Kediri	Case Control	107	9	Based on the analysis results, there is a significant relationship between maternal factors related to the incidence of LBW, including maternal age, nutritional status, and pre-eclampsia.	OR Parity: 2.06 OR Pre-eclampsia: 12.00
21	Lisnawati, Nindy Nadyar Humairah, Arie Maineny (2019)	Knowing the relationship between pre-eclampsia and LBW at Anutapura Hospital Palu	Anutapura Hospital Palu	Case-Control	186	10	There is no significant effect between pre-eclampsia on the incidence of low birth weight babies.	OR Pre-Eclampsia: 1.939
22	Juli Widiyanto, Geni Lismawati (2019)	Analyzing maternal age and anemia are risk factors for low birth weight babies	Arifin Achmad Hospital, Riau Province	Case-Control	32 Cases, 32 Controls	10	Maternal age and anemia have an effect on low birth weight in newborns	OR Anemia: 1.86

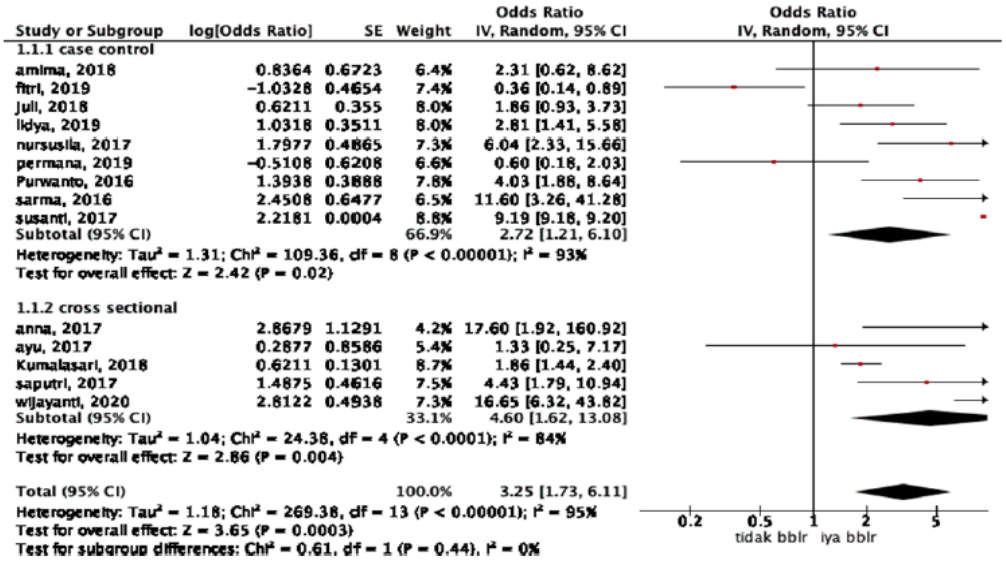

Figure 2: Forest plot of Anemia with LBW

Figure 2 shows that the effect size value of the influence of anemia on LBW is 3.25 with a 95% CI value (1.73-6.11), this means that an anemic mother has a 3 times greater risk of giving birth to a low birth weight baby. low, the quality of the data that builds the combined risk factors (combined OR) can be seen from the chi-squared heterogeneity which shows the results that the combined OR has a heterogeneous distribution (p=0.00033 under p<0.05). In the figure above, it can be seen that the width of the confidence interval (95%CI) of the combined OR does not cut across the entire study confidence interval. I-squared variance (variation in OR attributable to heterogeneity) = 95%, which means greater heterogeneity.

The analysis results in Figure 3 show that the circles contained in the funnel plot graph depicting the articles being analyzed are not symmetrical between the 4 quadrants, namely the left (top and bottom) and right (top and bottom). So it can be concluded that this research is publication bias. This may be due to the unequal number of large and small samples in the analyzed articles, causing bias.

Figure 4 shows that the quality of the data that builds the combined risk factor (OR) value of the effect size of pre-eclampsia on LBW is 2.70 with a 95% CI value (1.83-3.97). This means that an anemic mother have 2 times greater risk of giving birth to low birth weight babies. The quality of the data that builds the combined risk factors (combined OR) can be seen from the chi-squared heterogeneity which shows the results that the combined OR has a heterogeneous distribution (p=0.02 below p< 0.05). The figure above shows the wide confidence interval (95%CI) of the combined OR that does not cut across the entire study confidence interval. I-squared variance (variation in OR attributable to heterogeneity) = 55%.

In Figure 5 the funnel plot shows that the circles contained in the funnel plot graph depicting the articles being analyzed are not symmetrical between the 4 quadrants, namely the left (top and bottom) and right (top and bottom). So it can be concluded that this research is publication bias. This may be due to the unequal number of large and small samples in the analyzed articles, causing bias.

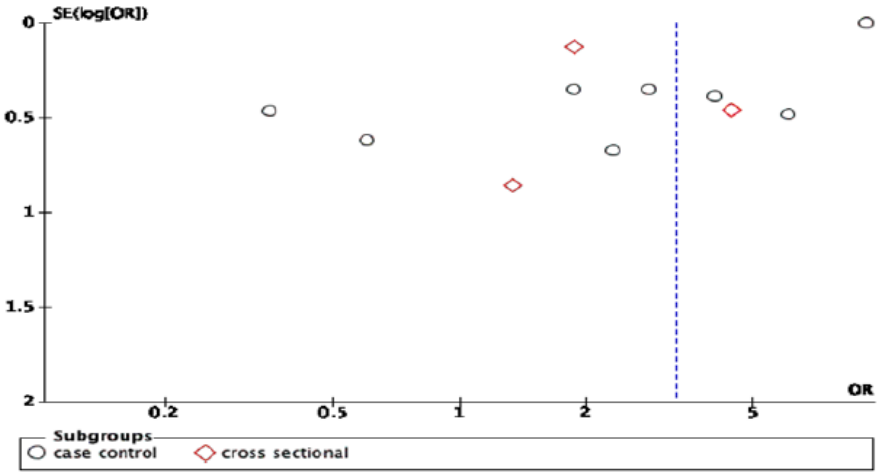

Figure 3: Funnel Plot Graphic of Anemia with LBW

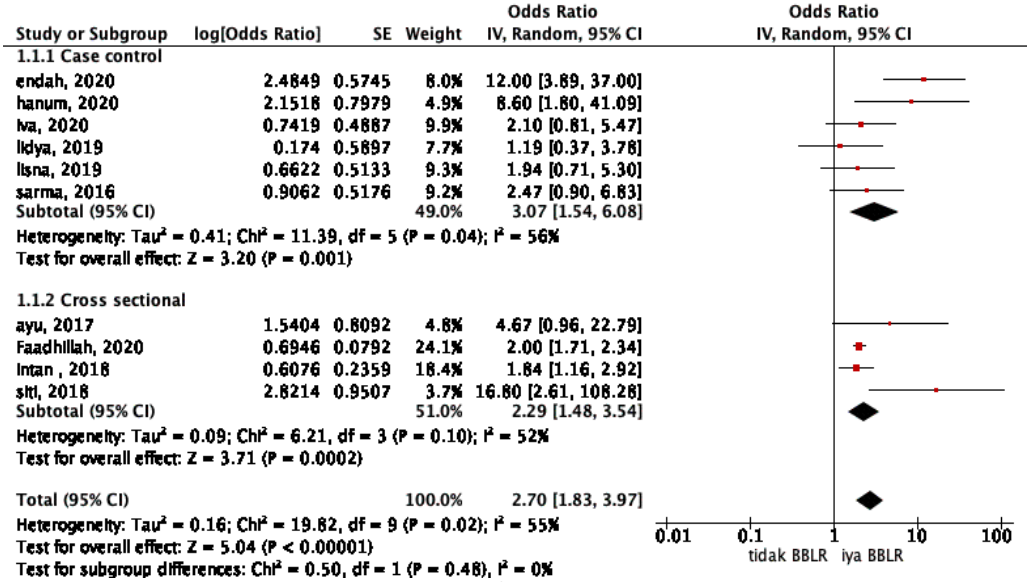

Figure 4: Forest plot of Pre-eclampsia with LBW

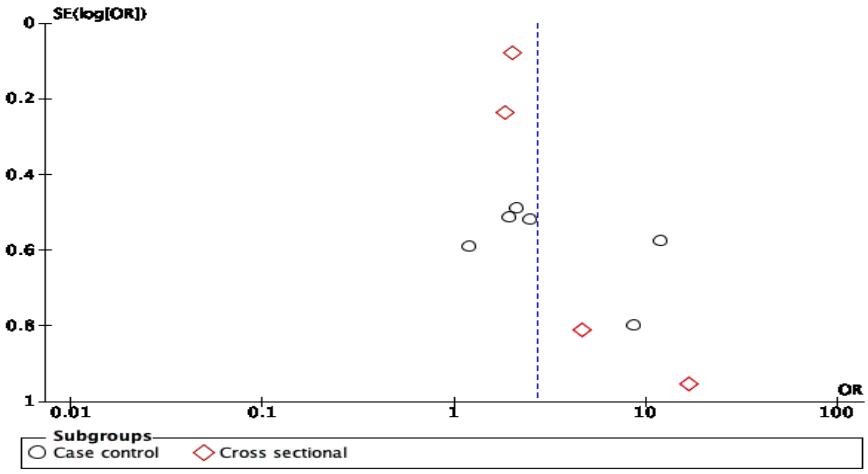

Figure 5: Funnel Plot of Pre-eclampsia with LBW

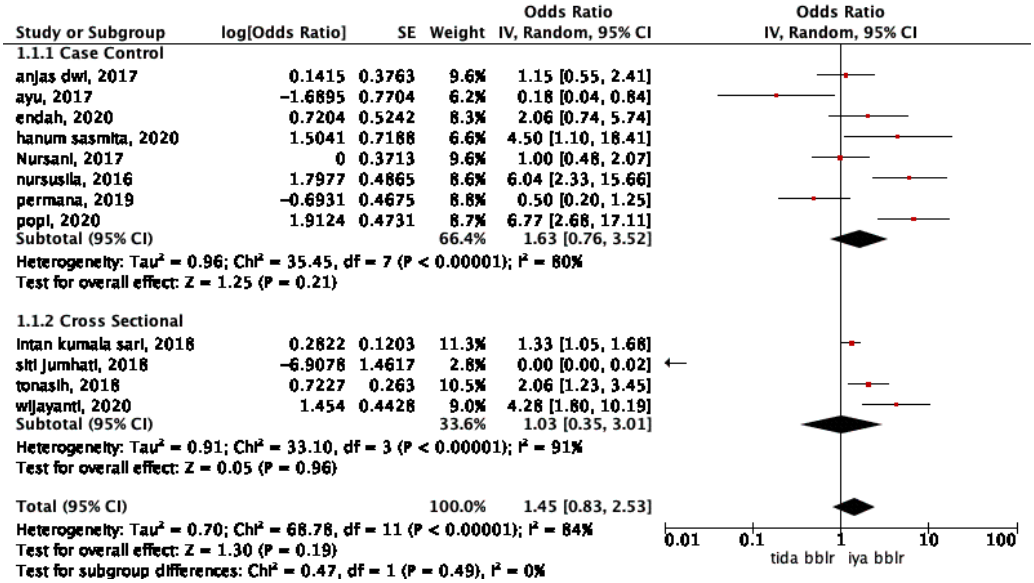

Figure 6: Forest Plot Parity with LBW

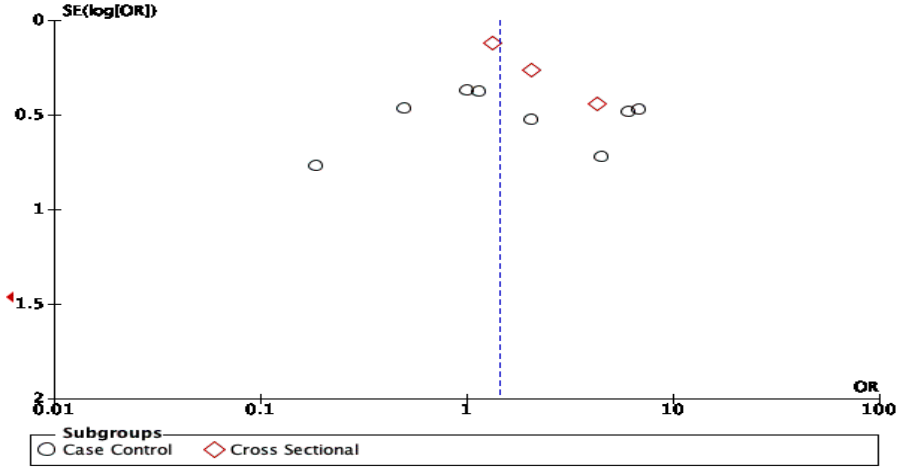

Figure 7: Funnel Plot Parity with LBW

Figure 6 shows that the quality of the data that builds the combined risk factor (OR) effect size value of the effect of anemia on LBW is 1.45 with a 95% CI value (0.83-2.53), this means that an anemic mother has 1 times greater risk for giving birth to low birth weight babies. The quality of the data that builds the combined risk factors (combined OR) can be seen from the chi-squared heterogeneity which shows the results that the combined OR has a heterogeneous distribution (p=0.00001 below p<0 ,05). In the figure above, it can be seen that the width of the confidence interval (95%CI) of the combined OR does not cut across the entire study confidence interval. I-squared variance (variation in OR attributable to heterogeneity) = 84%, which means greater heterogeneity.

In Figure 7 the funnel plot shows that the circles contained in the funnel plot graph depicting the articles being analyzed are not symmetrical between the 4 quadrants, namely the left (top and bottom) and right (top and bottom). So it can be concluded that this research is publication bias. This may be due to the unequal number of large and small samples in the analyzed articles, causing bias.

DISCUSSION

Effect of Anemia with LBW

A meta-analysis study on the relationship between anemic pregnant

women and LBW in children has been carried out by Figueiredo (2018) concluded that anemia in pregnant women is a risk factor for low birth weight in infants (OR: 1.23; 95%CI: 1.06-1.43). While a meta-analysis study conducted by Rahmati (2016) on 30 articles showed that anemia in pregnant women in the first trimester showed a significant relationship with low birth weight (RR: 1.28, 95%CI: 1.10-1.50, p <0.01), then in Aditianti's (2020) meta-analysis study resulted in the magnitude of the risk of pregnant women with anemia affecting the occurrence of LBW in babies born by 1.495 times compared to mothers who were not anemic (95%CI: 1.36-1.66) (Aditianti, 2020).

Analysis of the study in this study found 14 articles which were analyzed by 11 articles, namely Anna (2017), Eka (2017), Wijayanti (2020), Sarma (2017), Suhartati (2017), Anjas (2016), Nursusila (2017) , Handayani (2019), Febrina (2019) and Widyanto (2019) mention that anemia in pregnant women is a risk factor for LBW, while 3 other articles, namely Permana (2019), Rosida (2017) and Fajrina (2018) mention that anemia in pregnant women did not show significant results in the incidence of LBW.

Based on Figure 1 above, it shows that the variation between studies is heterogeneous. The p-value evidence this in the heterogeneity test of less than 0.05, namely P < 0.00001 and the I^2 value of more than 50%, namely I2 = 95%. So in this analysis using a random effect model. In the article analysis using the case-control method, the effect size value was 2.72 (95% CI 1.21-6.10), then in the article using the cross-sectional method, the effect size value was 4.60 (95% CI 1 .62-13.08) while the total odds ratio is 3.25 and the Z value which shows the combined or overall effect on the articles analyzed (test for overall effect) is 3.65 and with a p-value of 0.0003.

Based on the meta-analysis results of this study, anemia in pregnant women has a significant effect on the incidence of low birth weight (LBW). According to a study by Mutthaya (2009) which reviewed articles on the importance of nutrition during pregnancy and low birth weight, most of the incidence of anemia in pregnant women was caused by iron (Fe) deficiency. Meanwhile, a study conducted by Allen (2001) explains that the mechanism of anemia that affects birth weight can be explained by several conditions, namely the lack of Fe intake can disrupt the immune system which can then increase the body's vulnerability to infectious diseases such as genital infection, urinary tract infection, malaria, and hepatitis. In addition, iron deficiency can increase the production of the stress hormones norepinephrine and cortisol. Low blood Hb levels can cause fetal hypoxia which then stimulates the body to produce corticotrophin hormones. These hormones can affect placental development by decreasing blood flow to the fetus. If it occurs continuously, the fetus will experience growth restriction and the mother is at risk for giving birth to low birth weight. A study conducted by Novianti and Aisyah (2018) stated a relationship between anemia in pregnant women and the incidence of LBW. Anemia in pregnancy can be bad for both the mother and the fetus. Anemia in pregnancy will disrupt the flow of oxygen and supply of nutrients from the mother to the fetus. As a result, the fetus will experience weight gain disorders resulting in LBW.

The results of the Forest plot test above show that the pooled odds ratio or the overall Odds Ratio value obtained is 3.25 (95% CI 1.73-6.11). So it can be concluded that the effect size of the effect of anemia on the incidence of LBW is 3.65, which means that anemia is included in the category of large effect on the incidence of LBW. This is in line with a study conducted by Novianti (2018), which states a relationship between anemia in pregnant women and the incidence of LBW. Anemia in pregnancy can be bad for both the mother and the fetus. Anemia in pregnancy will disrupt the flow of oxygen and supply of nutrients from the mother to the fetus. As a result, the fetus

will experience weight gain disorders resulting in LBW.

Iron deficiency anemia can cause stress for the mother and fetus due to the production of corticotropin-releasing hormone (CRH) which controls the body's response to physical and emotional stress, and is responsible for suppressing appetite and triggering anxiety. premature birth, pregnancy-induced hypertension. Besides that, it also has an impact on fetal growth (Suhartati, 2017). Research conducted by Georgieft (2008) states that the incidence of iron deficiency in early fetal life impacts the fetal need for intrauterine growth and development obtained by the fetus from the nutrients in the mother's body. Fetal needs are transferred from the mother's body through the placenta. Fetal needs that are not met can disrupt fetal growth and development and can cause stunted fetal growth and low birth weight.

The supply of nutrients to the growing fetus depends on the volume of maternal blood flowing to the placenta and the nutrients it transports and anemia can also affect the function of the placenta. According to researchers, the incidence of anemia can be prevented by eating iron-containing foods and consuming Fe tablets so that the incidence of LBW is low. can decrease, the class management program for pregnant women can be one of the programs that can be done by providing material about anemia mothers and the incidence of LBW, normal pregnant women need at least 300 mg of iron reserves. This reserve is needed to meet iron needs during pregnancy Bothwell (2000) this is because iron needs during pregnancy increase to 1,240 mg and cannot be met from food intake alone. Pregnant women who experience a lack of iron reserves, especially until they suffer from anemia are very at risk in their pregnancy, the risk will increase according to the severity of anemia and gestational age (Milman, 2012).

The technique used to identify publication bias in this study is to use a funnel plot. Funnel plots are used to see the distribution of articles that are combined in the meta-analysis. If the distribution of articles is not symmetrical, there will be publication bias in the variables studied (Hasanah, 2020).

Based on the results of the analysis in Figure 2, it can be seen that the circles contained in the funnel plot graph depicting the articles analyzed are not symmetrical between the 4 quadrants, namely the left (top and bottom) and right (top and bottom). So it can be concluded that this research is publication bias. This may be due to the unequal number of large and small samples in the analyzed articles, causing bias.

Supplementation of blood-added tablets in pregnant women is associated with the incidence of LBW. Mothers who consume iron for less than 90 days are almost 3 times more likely to have LBW babies than mothers who consume iron for more than 90 days. In line with this, a study conducted by Rizki (2017) showed a significant relationship between Fe supplementation and anemia status of pregnant women in the third trimester. Pregnant women's need for Fe increases, especially during the 2nd and 3rd trimesters due to increased blood volume and plasma volume during the third trimester of pregnancy. This will cause hemodilution, the amount of iron absorbed from food and reserves in the body is usually not sufficient for the mother's needs during pregnancy so that additional iron intake is needed through supplementation of Fe tablets.

Effect of Pre-eclampsia with LBW

Pregnant women with pre-eclampsia experience decreased uteroplacental perfusion, hypovolemia, vasospasm, and damage to endothelial cells of placental blood vessels. Abnormalities of placental blood vessels in pre-eclampsia/eclampsia mothers can cause chronic hypoxia and impaired fetal nutrition so that fetal growth retardation often occurs which can end in low birth weight (LBW) (Proverawati & Ismawati, 2010)

According to Manuaba (2012), LBW can occur due to growth inhibition while in the womb. Intrauterine growth retardation is associated with conditions that impair placental circulation and efficiency with fetal growth and development or with maternal general health and nutrition. This situation results in a chronic lack of oxygen and nutrients for a long time for growth and lack of oxygen resulting in fetal distress. In pre-eclampsia and eclampsia, there is often an increase in uterine muscle tone and sensitivity to stimuli, resulting in premature labor.

Analysis of the studies in this study found 10 which were analyzed by researchers in 5 articles, namely Faadhilah (2020), Jumhati (2018), Kumalasari (2018), Sasmita (2020) and Luqmanasari (2019) which stated that Pre-eclampsia in pregnant women is a risk factor for the occurrence of pregnancy. LBW, while 5 other articles, namely Lisnawati (2019), Rosida (2017), Inpresari (2020), Febrina (2019) and Nursani (2017) stated that Pre-eclampsia did not show significant results in the incidence of LBW.

Based on Figure 3 above, it shows that the variation between studies is heterogeneous. The P-value evidences this in the heterogeneity test of less than 0.05, namely $P < 0.00001$ and the I^2 value of more than 50%, namely I2 = 55%. So in this analysis using a random effect model. In the article analysis using the case-control method, the effect size value was 3.07 (95% CI 1.54-6.08), then in the article using the cross-sectional method, the effect size value was 2.29 (95% CI 1 .48-.3.54) and the Z value which indicates the combined or overall effect on the analyzed articles (test for overall effect) is 5.04 and with a P-value = 0.00001

The results of the Forest plot test in Figure 4 show that the pooled odds ratio or the overall Odds Ratio value obtained is 2.70 (95% CI 1.83-3.97). So it can be concluded that the effect size of pre-eclampsia on the incidence of LBW is 5.04 which means that pre-eclampsia is included in the category of large effects on the incidence. This is in line with research that pregnancy with pre-eclampsia occurs spasm of blood vessels to the tissues, blood pressure will rise in an effort so that oxygenation of tissues including the placenta can be fulfilled and by narrowing of blood vessels causing retroplacental blood circulation disorders so that the blood supply transported to the uterus becomes less. As a result, the placenta becomes small and the transfer of nutrients to the fetus decreases, this condition causes slow fetal growth so that the baby's birth weight becomes low (Manuaba, 2010).

Pregnancy with pre-eclampsia can cause vasoconstriction of blood vessels in the uterus which causes peripheral resistance increasing blood pressure. Reduction of the lumen of blood vessels in the uterus can decrease blood flow so that the supply of oxygen and nutrients to the fetus is reduced. When this happens, it can cause intrauterine growth retardation (IUGR) and give birth to LBW babies. Other factors are premature birth and pregnancy gemelli, the occurrence of excessive uterine distension, exceeding the tolerance limit and frequent premature labor. Mothers with pre-eclampsia are at risk of giving birth to babies with LBW. Decreased blood flow to the uteroplacental can cause placental hypoxia and ischemia, resulting in fetal growth retardation (Prawirohardjo, 2010).

Placenta that is ischemia and hypoxia will produce free radicals in the form of reactive hydroxyl radicals and lipid peroxides, which will circulate in the bloodstream to damage cell membranes, nucleus, and endothelial cell proteins, resulting in endothelial dysfunction (Hartati, 2018).

From the results of his research, Ukah (2017), by examining documentation sheets from the Canadian Institutes of Health Research (CIHR) concluded that 70% of hypertension in pregnancy is a causative factor that affects the growth of the placenta which will lead to the birth of

babies with low birth weight. Preeclampsia will cause trophoblast cell invasion in some spiral arteries in the myometrium area, resulting in impaired uteroplacental function. So that the placenta cannot meet the blood needs for nutrients and oxygen to the fetus. Impaired placental function can cause stunted fetal growth. This will trigger oxidative stress on the placenta, increase uterine tone, and sensitivity to stimuli, ultimately leading to impaired fetal growth or premature parturition with low birth weight (LBW) babies.

According to Manuaba (2012), LBW can occur due to growth inhibition while in the womb. Intrauterine growth retardation is associated with conditions that impair placental circulation and efficiency with fetal growth and development or with maternal general health and nutrition. This situation results in a chronic lack of oxygen and nutrients for a long time for growth and lack of oxygen resulting in fetal distress. In pre-eclampsia and eclampsia, there is often an increase in uterine muscle tone and sensitivity to stimuli, resulting in premature labor.

Pre-eclampsia can be detected early when a pregnant woman routinely checks her pregnancy and conducts regular checks to detect early the risk of pre-eclampsia. It will reduce one of the factors causing LBW, the support of all parties is very important. This means that in addition to public health workers, they must also be educated early on the importance of routine examinations for early detection of pre-eclampsia to reduce the incidence of LBW, it is recommended that health workers make home visits to residents who are pregnant to minimize mothers who do not routinely carry out pregnancy checks.

Effect of Parity with LBW

Mothers who are included in parity 2-4 have had previous experience of pregnancy and childbirth so that they are better able to maintain pregnancy and are better prepared to face the labor that will be experienced The readiness of the mother, in maintaining pregnancy and childbirth, affects the process of pregnancy and childbirth. The function of the mother's reproductive organs with parity 2-4 has also not experienced a decline so that the reproductive organs can function properly so as to ensure better fetal growth and development. This is following the theory which states that the condition of the uterus is very good as a place for the insertion of the placenta, then the function of the placenta which connects and drains the mother's blood to the fetus which contains food, oxygen, and substances can affect the growth and development of the fetus (Depkes RI, 2010).).

Analysis of the studies in this study found 12 articles, 8 of which were Wijayanti (2020), Tonasih (2018), Jumhati (2018), Kumalasari (2018), Anjas (2016), Popi (2020), Sasmita (2020) and Rosida (2017), states that parity in pregnant women is a risk factor for LBW while 4 other articles, namely, Nursani (2017), Permana (2019), Nursusila (2017) and Luqmanasari (2020) state that parity does not show significant results in the incidence of LBW.

Based on Figure 3 above, it shows that the variation between studies is heterogeneous. The p-value evidences this in the heterogeneity test of less than 0.05, namely $P < 0.00001$ and the I^2 value of more than 50%, namely I2 = 84%. So, the effect size value was 1.63 (95% CI 0.76-3.52), then in the article using the cross sectional method, the effect size value was 1.03 (95% CI 0). .35-.3.01) and the Z value which indicates the combined or overall effect on the analyzed articles (test for overall effect) is 1.30 and with p-value = 0.19

The results of the Forest plot test above show that the pooled odds ratio or the overall Odds Ratio value obtained is 1.45 (95% CI 0.83-2.53). that the result of the effect size of the effect of parity on the incidence of LBW is 1.30 which means that parity is included in the category of large effect on the incidence.l. This is in line with this meaning that parity has a large effect

size on the incidence of LBW, high parity will have an impact on the emergence of various health problems for both mothers and babies born, repeated pregnancy and childbirth cause damage to blood vessels in the uterine wall and a decline in the flexural power (elasticity) of tissues that have been repeatedly stretched during pregnancy so that there is a tendency for abnormalities in the location or growth of the placenta and fetal growth to occur, resulting in low birth weight birth. Wiknjosastro (2017) states that a uterus that has given birth to many children tends to be inefficient in all stages of labor. This is because the uterus has changed its elasticity. One of the complications that can arise due to pregnancy of more than four children, namely LBW, is due to disruption of the uterus, especially in terms of blood vessel function which can affect fetal nutrition, causing growth disorders.

Parity causes the risk of mothers giving birth to babies with low body weight. This is due to the condition of the uterus getting weaker due to reduced function of the reproductive organs and muscle cells are starting to decrease in function and other body parts. All of these conditions can cause and increase the possibility of babies experiencing LBW. In addition, mothers who give birth frequently increase the chance of LBW because of the possibility of damage to the cardiovascular system in the uterus which will affect nutritional intake for the fetus during the next pregnancy, and in the end will result in the baby experiencing LBW (Khoiriah, 2017).

Based on Pamungkas' research (2016) which found that the group of mothers with parity 1 time (primipara) was the group that gave birth to the most babies with LBW conditions, namely 56 percent. At parity >4 according to Abubakari et al, it will result in disruption of the uterus in terms of blood vessel function, as well as repeated pregnancies. It can cause damage to the uterine blood vessel walls.Furthermore, it can interfere with or inhibit maternal nutrition to the fetus during pregnancy which will subsequently affect fetal growth disorders, causing poor birth outcomes such as low birth weight, an effort that is very often associated with suppressing the parity factor is the use of contraception, which is because the number of children still living affects a person's participation in the family planning program. Rahayu's research (2015) explains that low economic factors, which are closely related to the ability to buy contraception used and low education, however, the family planning program is still prioritized as an effort to regulate childbirth, distance, ideal age of delivery to regulate pregnancy through promotion and as a form of protection in realizing a quality family (Hasmawati, 2019).

In mothers with parity > 3 times, the risk of the child experiencing preterm labor is higher, this is because repeated pregnancies (high parity) will make the uterus stretch, so that it can cause abnormalities in the position of the fetus and placenta which will ultimately adversely affect the delivery process. and the ability to push during childbirth has begun to decrease in line with the age of the mother herself. Mothers with parity 1 are at risk for giving birth to LBW because the function of the reproductive organs is not ready to maintain and accept pregnancy (Kosim, 2019).

Subekti's research (2014) shows that primiparas (parity 1 have a 4.09 times greater risk of giving birth to LBW. Pramono's research (2015) shows that parity 1 and > 3 have a 1.31 times greater risk of giving birth to LBW. Sulistyorini's research (2013)) indicates that there is a significant relationship between parity and the incidence of LBW.

The technique used to identify the existence of publication bias in this study is to use a funnel plot. Funnel plots are used to see the distribution of articles that are combined in the meta-analysis. If the distribution of articles is not symmetrical, there will be publication bias in the variables studied (Hasanah, 2020).

Based on the results of the analysis in Figure 6, it can be seen that the circles contained in the funnel plot graph depicting the articles being analyzed are not symmetrical between the 4 quadrants, namely the left (top and bottom) and right (top and bottom). So it can be concluded that this research is publication bias. This may be due to the unequal number of large and small samples in the analyzed articles, causing bias.

The results of the analysis show that the high incidence of LBW in multipara and grandemultipara is related to the function of the mother's reproductive organs, also related to the health conditions experienced by the mother. Mothers who experience pregnancy and give birth to children 4 times are more likely to experience health problems, malnutrition and anemia. This high parity can also be caused by socio-cultural factors that are still attached to married couples and their religious understanding of the prohibition of family planning programs, so the risk factors for parity can already be prevented with family planning programs that have been widely used so far. socialized, based on the results of this study, the parity problem can be a common concern so that a smart generation can be printed by minimizing the incidence of LBW through the family planning program by having only two children and a predetermined interval of pregnancy.

The limitation of this meta-analysis study is that the index of the journals analyzed is limited to Scopus and Sinta 1-4, in this study not all studies can be analyzed because of the limited index for the journals analyzed, some studies cannot be analyzed because they are not in the category of sinta 1-4, this categorization is actually needed to sort out the quality of the data, but we can also assess the quality of the article using critical appraisal. Then in this study there is a publication bias due to the unequal number of large and small samples in the articles being analyzed. The published literature may not represent the research that has been done on anemia, pre-eclampsia, partias and LBW, most of the published literature tends to produce or show significant results, only a small number of non-significant studies are published. One way to overcome bias is to compare the effect sizes in formally published articles with the effect sizes of unpublished studies. This method requires access for unpublished articles, and if you have that access, then there is no problem. However, this seems difficult to do. Perhaps using a truly comprehensive literature search approach can reduce bias.

In addition, this analysis does not limit the research design because there are still limited references that describe the OR value, exposure prevalence and research results tables, so that if one of these is not present then articles like this cannot be included in the meta-analysis study of this study.

CONCLUSION

Analysis of articles on the anemia variable on the incidence of LBW obtained 14 articles analyzed by the researchers 11 articles wrote that anemia in pregnant women is a risk factor for LBW. In comparison, 3 articles that anemia in pregnant women did not show significant results in the incidence of LBW Then the analysis of articles on the pre-eclampsia variable found 10 articles analyzed by researchers, 5 articles wrote that pre-eclampsia had an effect on the incidence of LBW. In comparison, 5 other articles wrote that pre-eclampsia did not show significant results. And the analysis of articles on the parity variable found 12 articles analyzed by researchers, 8 articles wrote that parity affected the incidence of LBW, while 4 other articles wrote that parity did not show significant results.

Based on the analysis of 14 journals, it was found that the effect of anemia on the incidence of LBW total odds ratio was 3.25 with an effect size value of 3.65. The results of the analysis of 10 journals showed that the effect of pre-eclampsia on the incidence of LBW total odds ratio was 2 .70 with an

effect size value of 5.50 and the results of the analysis from 12 journals found that the magnitude of the effect of parity on the incidence of LBW total odds ratio of 1.45 with an effect size value of 1.30 on the three variables analyzed by meta-analysis obtained the greatest effect on the pre-variable eclampsia with an effect size value of 5.50.

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