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EXPOSURE OF LEAD IN BONE OF PREGNANT WOMEN AND THE INCIDENCE OF LOW BIRTH WEIGHT IN INFANTS

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ABSTRACT

The number of Low Birth Weight Babies (LBW) in Indonesia is still quite high. WHO data records that Indonesia is ranked ninth in the world with a percentage of LBW more than 15.5% of baby births each year. Brebes Regency is an agricultural area which in daily operations always uses pesticides. Where in previous research stated that in pesticides there are levels of lead. This study aims to analyze lead in bone exposure in pregnant women and its effect on the incidence of Low Birth Weight (LBW) based on a case control study in the Agricultural Area of Brebes Regency, Central Java.This study used a case control study which was conducted from December 2019 to March 2020 with the total population of the study being mothers who gave birth to live babies and at the time of the study the babies were ≤ 6 months old, and met the research requirements. The sample in this study was obtained using purposive sampling technique while to get the respondent used accidental sampling until the number of samples is met.The results of multivariate analysis using logistic regression showed that the bone lead level was not high as a protective factor for the occurrence of LBW (OR: 0.038; 95% CI: 0.245-0.959). In other words, low or not high levels of lead in bone reduced the risk of LBW, while 51.5% of the risk of LBW incidence was found in respondents with high bone lead levels.The results of this study showed a significant relationship between lead levels in the bone in mothers with the incidence of LBW. Lead metal that has accumulated in bones can replace the presence of calcium ions, this can be anticipated by adding calcium supplements during pregnancy to reduce the negative effects of lead poisoning, one of which is giving birth to a baby with LBW.

Keywords: Lead, Bone, Low Birth Weight (LBW), Pregnant Women, Infants.

I. BACKGROUND

The World Health Organization (WHO) defines Low Birth Weight (LBW) as babies born weighing less than 2500 grams.[1] The effects of LBW for health both in the short and long term are still being a problem in public health.[2] In 2011, 15% of babies worldwide (more than 20 million people) were born with LBW.[3] Based on WHO data, babies with low birth weight contribute 60% to 80% of all neonatal deaths[4] and have a risk of death 20 times greater than babies with normal weight up to one year of age, so babies with low birth weight have the higher possibility of morbidity and mortality.[5]According to WHO, most of the babies with LBW were born in developing countries including Indonesia, especially in areas with vulnerable populations.[6,7] LBW is not the only leading cause of prenatal morbidity and mortality. Another study found that LBW in the future can increase the risk for non-communicable diseases such as diabetes and cardiovascular disease.[8] This condition does not yet describe the true incidence of LBW, because the recorded LBW figures are obtained from documents/records owned by household members[9] (Maternal and Child Health Book and Kartu Menuju Sehat). In fact, the number of babies who do not have a birth weight record is much higher.[10] This makes it very possible for the lack of data so that babies born with LBW are not recorded and the number is much higher.[4]

In Indonesia, The incidence of LBW (<2,500 grams) reach up to 6.2%[11] (Riskesdas 2018) and it needs attention, because the long-term impact caused by LBW is very serious and complex.[12] LBW especially in preterm births occur due to immaturity of the organ systems in infants.[13,14] LBW conditions have a tendency to increase infectious diseases and susceptible to complications.[15] In infants with LBW, problems that often occur include

disorders of the respiratory system, central nervous system, cardiovascular, hematology, gastro-intestinal, kidney, and thermoregulation.[16,17]

In New York, examination of lead exposure in the blood of pregnant women showed a significant relationship between the results of measuring lead in the blood ranging from 5 - 10 μg / dL to reduce birth weight by an average of 61 - 87 grams[18]. In addition, other studies also stated that maternal age, race and education level were significantly associated with blood lead exposure ($p < 0.05$), and mothers aged 40 - 44 years with OR 7.69 (95% CI = 3, 49 - 16.93), meaning that mothers aged 40-44 years have a 7.69 times risk of being exposed to lead in their blood.[19] Another study in Mexico City found that women exposed to lead were more likely to give birth to babies with low birth weight than women not exposed to lead (OR = 1.1, 95% CI = 0.98 - 1.29). And also found that maternal bone lead load was inversely related to birth weight,[20] birth length and head circumference at birth.[21]

Indonesia is an agricultural country with the largest population as farmers. Based on the results of the 2013 agricultural census, the average area of agricultural land controlled by agricultural business households was 0.86 hectares, which increases compared to 2003 that was recorded at 0.35 hectares.[22] Agricultural activities carried out in Indonesia in almost all regions use pesticides as a toxic chemical that is used to control disturbing bodies that harm humans. Pesticides have been used in agriculture for a long time.[23] The types of pesticides that are most widely used in Indonesia are the types of organophosphates and carbamates.[24]

The negative impact of using pesticides is poisoning farmers and pesticide users. In 1996/1997, from 27 provinces in Indonesia, the results of examination of 11,419 blood preparations showed that 61.82% were normal (not exposed to pesticides), 1.3% were in the category of severe poisoning and 26.89% were mildly poisoned.[25] The results of other studies showed that 67% of respondents experienced signs of poisoning.[26] Another study conducted on members of the Combined Farmer Group of Campang Village, Tanggamus District, Lampung in 2009 by measuring the activity level of the cholinesterase enzyme in the blood of farmers showed that all respondents were poisoned with a proportion of 71.4% mild poisoning and 28.6% moderate poisoning.[27] Meanwhile, the results of research conducted in Tejosari Village, Ngablak District, Magelang Regency in August-October 2008, by examining the levels of cholinesterase enzymes and blood hemoglobin, it was found that farmers suffering from poisoning were 96.2% and suffering from anemia as much as 80.8%.[28]

Lead that has been identified in Indonesia is related to pesticides, so that the pesticides used in agriculture contain lead.[29] Based on the results of the examination by the Semarang Industrial Research and Development Center, it is known that some pesticides contain the heavy metal lead, namely Antracol 70 WP, Dithane M 45 80 WP, Furadon 3G, Goal 240 EC, Buldog 25 EC, Hostathion 200 EC, and Profile 430 EC. The indication of the possibility of lead in pesticides, is suspected that the pesticide itself may contain the heavy metal lead, because the pesticide raw material comes from oil drilling. The results of research regarding the levels of Lead in shallot bulbs in Kersana District. Brebes Regency prove that the shallot bulbs in that location contain lead with an average of 0.18 mg/kg.[30]

Lead excretion is generally very slow. When lead enters the body, the half-life in the blood is approximately 25 days, in soft tissue 40 days, while in bone is 25 years. This slow excretion causes lead to easily accumulate in the body. Both in occupational and non-occupational exposures.[31] In adults, about 95% of the lead in the body is deposited in the bones, while in children about 70%. Lead concentration in bone may increase with age and this increase is more pronounced in men where the tibia is denser.[32] The concentration of lead present in adult bone can work to maintain blood lead (BLL) levels after exposure has ended.[33–37]. The impact of lead heavy metal pollution needs special attention because it is very influential on human health and can even cause death.[38] In tissues or organs, lead metal will accumulate in bones, because this metal in the form of ions (Pb^{2+}) can replace the presence of Ca^{2+} ions present in bone tissue.[39] In addition, in pregnant women, lead can cross the placenta and then enter the fetal circulatory system and then after the baby is born, lead will be excreted with milk.[40]

The number of Low Birth Weight Babies (LBW) in Indonesia is still quite high. WHO data records that Indonesia is ranked ninth in the world with a percentage of LBW of more than 15.5% of baby births each year.[41] Brebes Regency is an agricultural area which in daily operations always uses pesticides. Where in previous research stated that in pesticides there are levels of lead. Lead is a source of contaminants that can interfere with health, such as causing anemia, lowering IQ in children and so on. Based on this, the risk of lead for pregnant women in Brebes Regency is very likely to be exposed to lead and it is feared that it will interfere with their reproductive

health during pregnancy, especially the health condition of the fetus that is conceived which can be seen from the side of the baby's birth weight.

The incidence of LBW in Central Java is not much different from the national percentage, which is in the range of 10% based on Riskesdas 2013 data. Meanwhile, the BBLR rate in Central Java is 6.1% where the proportion of LBW nationally is 6.2%, meaning that it is not much different from the national percentage, this is based on data from Riskesdas in 2018.[11] Brebes Regency in 2012 was ranked the second highest in Central Java after Banyumas Regency, where Brebes Regency is one of the districts in Central Java with the number of cases of babies with low birth weight so it needs attention special.[42]

The data obtained from the Health Office of Brebes Regency shows that Brebes Regency is in a coastal area and from this data it was found that the number of LBW in 2016 was 1,470 babies born with Low Birth Weight conditions out of 33,086 babies born (4.44%).[43] The coastal areas / areas tend to experience contamination by heavy metals (Lead), which comes from several industries. From research conducted in industrial areas on the North Coast of Java Island, it was found that 40% of the tuna (Euthynnus sp.) Samples studied had lead heavy metal levels above the maximum allowable standard (<0.3 mg / kg).[44]

The amount of lead in bone depends on the individual's lead exposure history. Smith, et al. Determined that the contribution of lead in the bones of 40 - 70% comes from lead in the blood.[45] Bone lead measurement requires specialized equipment and a trained operator. Therefore, it is unlikely that this method will have such a broad clinical application. However, these biomarkers are useful tools in research efforts to understand and detect the cumulative health impacts of lead exposure.[46] This study aims to analyze lead in bone exposure in pregnant women and its effect on the incidence of Low Birth Weight Infants (LBW) based on a case control study in the Agricultural Area of Brebes Regency, Central Java.

II. MATERIALS AND METHODS

Research Area

Brebes Regency is an area located along the north coast of the Java Sea with an area of 1,769.62 km^2. Brebes Regency has the following boundaries, in the north it is bordered by the Java Sea, in the east it is bordered by the city of Tegal and Tegal regency, in the south it is bordered by Banyumas and Cilacap districts, and in the west it is bordered by West Java Province. Brebes Regency consists of 17 sub-districts with the widest sub-district being Bantarkawung district with an area of 208.18 km^2 and the smallest sub-district is Kersana District with an area of 26.97 km^2. The research location consisted of three areas, namely Bulakamba Primary Health Care, Wanasari Primary Health Care and Tanjung Primary Health Care. The research location was chosen purposively based on information about the case of LBW from the Brebes District Health Office.

Research Design and Population

This study used a case control study which was conducted from December 2019 to March 2020 with the total population of the study being mothers who gave birth to live babies and at the time of the study the babies were ≤ 6 months old, and met the research requirements. The sample in this study was obtained using purposive sampling technique (determination of the sample using certain considerations and determined by the researcher in order to get a sample that suits the research needs), while to get the respondent used Accidental Sampling until the number of samples is met. The case inclusion criteria in this study were babies in the work area of Bulakamba Primary Health Care, Wanasari Primary Health Care and Tanjung Primary Health Care who at the time of the study were ≤ 6 months old with birth weight <2,500 grams with mothers who did not have a history of serious illness during pregnancy and length of stay in place. now at least 1 year. While the control inclusion criteria in this study were babies in the work area of Bulakamba Primary Health Care, Wanasari Primary Health Care and Tanjung Primary Health Care who at the time of the study were ≤ 6 months old with normal birth weight ≥ 2500 grams with mothers who did not have a history of serious illness during pregnancy and length of stay in the place is now at least 1 year.

Research Participants

The research subjects were selected in two stages, namely the first stage of screening, collecting data from the Brebes District Health Office to see the number of LBW cases in Brebes Regency. After obtaining the LBW data, 3 Primary Health Care with the most LBW cases were selected, the Bulakamba Primary Health Care, Wanasari Primary Health Care and Tanjung Primary Health Care were selected. The second stage, namely determining the

sample with the criteria of mothers who have babies aged 0-6 months with a gestational age at birth above 36 weeks, obtained 155 people. The flow chart or stages of selecting the subject is presented in Figure 1. below.

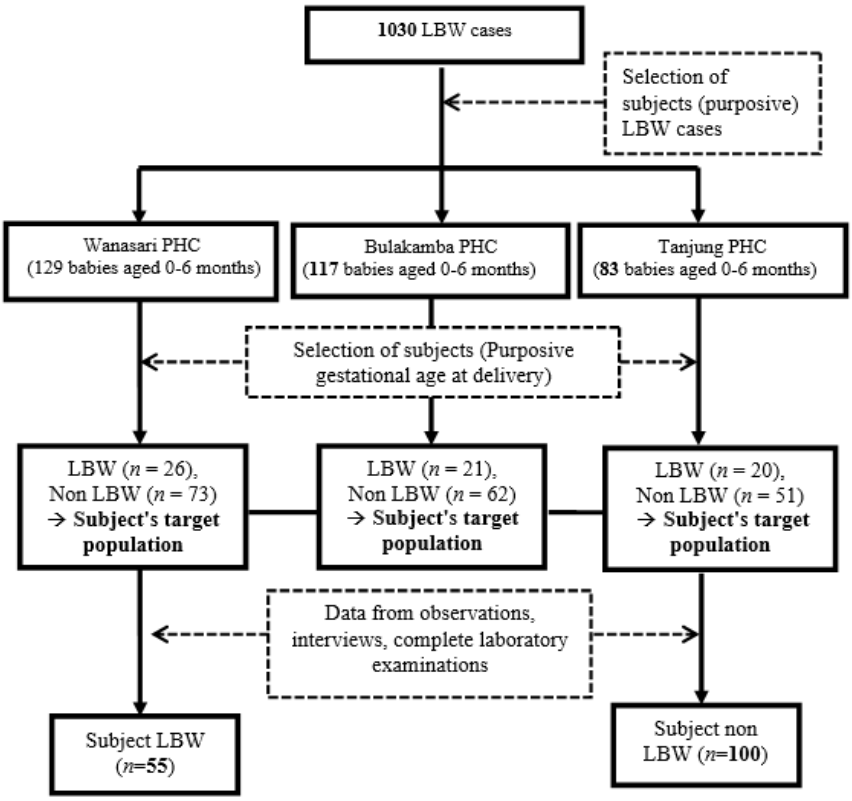

Figure 1. Flow of Research Subject Selection

Data and Variables

The method of data collection was carried out by using the Mix-Method, namely measuring quantitatively and also conducting in-depth interviews (qualitative) to obtain more detailed information about lead exposure to cause LBW. The type of mix-method used in this research is the qualitative measurement results supporting the quantitative research results. The variables studied in this study were the dependent variable, namely Birth Weight (LBW) and the independent variable, namely the history of lead in bone exposure (determination of the cut off point for lead levels in bone was carried out using the Receiver Operating Characteristic(ROC) method (Figure 2.) and obtained cut off point value> 1652.75), mother's age, history of disease during pregnancy, and quality of Antenatal Care (ANC).

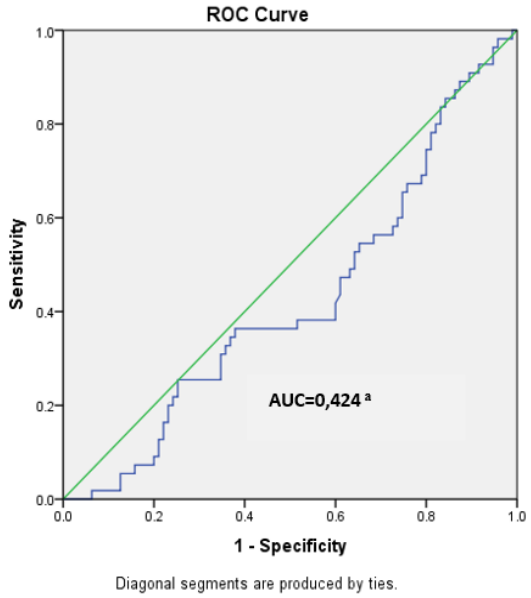

Figure 2.ROC for Determination of the Cut off Point of Lead in Bone

Description: [a]Area Under the Curve

Ethical Considerations

This research was approved by the Ethics Commission for Health Research, Faculty of Public Health, Diponegoro University, (No:530/EA/KEPK-FKM/2019). To ensure the confidentiality of the information, the database is kept under the supervision of the Ethics Commission for Health Research, Faculty of Public Health, Diponegoro University.

III. RESULTS

The results of the study on 155 mothers showed that the characteristics of subjects including age, weight, height, gravida, labor, abortion, parity, education, occupation in the case and control groups were not significantly different (all p> 0.05) (Table 1.).

Table 1. Differences in maternal characteristics between case and control groups

Characteristics	LBW *n*=55	Non LBW *n*=100	*p*
Age (years), (Median; min-max)	26,0;16,0-46,0	28,0;16,0-44,0	0,649 [a]
Weight (Kg), (mean ± SD)	53,9±11,5	55,9±10,2	0,288 [b]
Height (cm), (mean ± SD)	150,0±4,26	149,1±6,4	0,356 [b]
Gravida, *n* (%)[d]			
Primigravida (first pregnancy)	23 (41,8)	26(27,4)	0,101[c]
Multigravida > 1 pregnancy)	32 (58,2)	69 (72,6)	
Labor,*n* (%)[d]			
≤ 2 times	42(76,4)	70 (73,7)	0,866 [c]
> 2 times	13(23,6)	25 (26,3)	
Abortion,*n* (%)[d]			
< 1 time	49 (89,1)	84 (88,4)	1,000 [c]
≥ 1 time	6 (10,9)	11 (11,6)	
Parity, *n* (%)[d]			
Primipara	22 (40,0)	26 (27,4)	0, 157 [c]
Multiparous	33 (60,0)	69 (72,6)	
Education, *n* (%)			
Not completed in primary school	4 (7,3)	11(11,0)	
Primary School	26 (47,3)	41 (41,0)	0,383 [c]
Junior high school	16 (29,1)	32 (32,0)	
High school	5 (9,1)	14 (14,0)	
College	4 (7,3)	2 (2,0)	
Employment, *n* (%)			
Housewife	42 (76,4)	89 (89,0)	0,146 [c]
Farm workers	3 (5,5)	5 (5,0)	
Farmers	2 (3,6)	0 (0,0)	
Traders/Enterpreneurs	4 (7,3)	4 (4,0)	
Private employees	3 (5,5)	2 (2,0)	
Civil servants	1 (1,8)	0 (0,0)	

Notes: [a]Mann-Whitney test, [b]Independent t-test, [c]Chi-square; [d]LBW = 55, non LBW = 95

The results of the study on 155 infants showed that the characteristics of the subjects including age, sex, age at birth, in the case and control groups, were not significantly different (p> 0.05). For the variables of birth weight, birth length, gestational age at delivery, there was a significant difference in the case and control groups (p <0.05). Babies in the LBW group were 50.9% male and 49.1% female, while in the non-LBW group there were 48.0% male and 52.0% female. Gestational age at delivery in the LBW group was mostly premature (50.9%), while the non-LBW group was mostly Aterm (80.0%). Most types of delivery in the LBW and non-LBW group were caesarean section, namely 76.4% and 80.0%. (Table 2.)

Table 2. Differences in infants characteristics between case and control groups

Characteristics	LBW *n*=55	Non LBW *n*=100	*p*
Age (Month), (Median; min-max)	4,2;1,0-6,0	3,8;1,0-6,0	0,099 [a]

Weight (Kg), (Median; min-max)	2079,8;1220,0-2450,0	3148,5;2500,0-4800,0	0,001[a]
Length (cm), (Median; min-max)	45,2;38,0-50,0	48,3;33,0-54,0	0,001[a]
Gender, *n* (%)			
Male	28 (50,9)	48(48,0)	0,858[b]
Female	27 (49,1)	52 (52,0)	
Gestational age at delivery, *n* (%)			
Premature (< 38 minggu)	28 (50,9)	18 (18,0)	
Aterm (38-42 minggu)	27 (49,1)	80 (80,0)	0,001[b]
Postterm (>42 minggu)	0 (0,0)	2 (2,0)	
Type of delivery, *n* (%)[c]			
Sectio caesaria	42 (76,4)	76 (80,0)	0,751[b]
Normal	13 (23,6)	19 (20,0)	

Notes: [a]Mann-Whitney test, [b]Chi-square test; [c]LBW = 55, Non LBW = 95

The results of the analysis using the chi square test based on the results of bone examinations on 150 mothers showed that there was a significant relationship between lead levels in the bones and the incidence of LBW (p <0.05). The level of lead in bone is not high (<1652.75) is a protective factor for the occurrence of LBW. This is indicated by OR = 0.629; 95% CI = 0.409-0.966, meaning that mothers with low bone lead levels were 0.629 times less likely to have children with LBW. The results of the analysis using the chi square test showed that the variables of maternal age, medical history during pregnancy and ANC quality did not have a significant relationship with the incidence of LBW (p> 0.05). Most of the mothers in the LBW and not LBW group were 20 to 35 years old with the respective percentages of 65.5% and 80.0%. 10.9% of mothers with LBW children still had a history of disease during pregnancy and in the non-LBW group, 10.5% still had a history of illness during pregnancy. The ANC quality of the mothers in the non-LBW and non-LBW group was mostly good with the respective percentages of 85.5% and 94.7% (Table 3.)

Table 3. Relationship between lead levels in bone, maternal age, history of disease during pregnancy, and quality of ANC with LBW incidence

Variable	LBW *n*= 55	Non LBW *n*= 100	P	OR (95%CI)
Pb bone [a]				
High (≥1652,75)	23 (41,8)	57 (60,0)	0,048	0,629
Not High (<1652,75)	32 (58,3)	38 (40,0)		(0,409-0,966)
Mother's age				
< 20 years	7 (12,7)	6 (6,0)	0,122 [a]	1,046 [b]
20-35 years	36 (65,5)	80 (80,0)		(0,538-2,033)
> 35 years	12 (21,8)	14 (14,0)		
History of illness during pregnancy[c]				
Yes	6 (10,9)	10 (10,5)	1,000 [a]	1,206
No	49 (89,1)	85 (89,5)		(0,524-2,006)
ANC quality[c]				
Bad (<4 times)	8 (14,5)	5 (5,3)	0,070 [a]	0,326
Good (≥ 4 times)	47 (85,5)	90 (94,7)		(0,101-1,053)

Notes: [a]*Chi square test*, [b]*Logistic regression*,[c]LBW= 55, Non LBW= 95

Multivariate analysis was carried out to see which variables were risk factors for the incidence of LBW. Variables that can be continued into multivariate analysis are lead levels in bone, age of mother, quality of ANC. The results of multivariate analysis using logistic regression showed that the bone lead level was not high as a protective factor for the occurrence of LBW (OR: 0.038; 95% CI: 0.245-0.959). In other words, low or not high levels of lead in bone reduced the risk of LBW, while 51.5% of the risk of LBW incidence was found in respondents with high bone lead levels (Table 4.).

Table 4. Multivariate Analysis Result

Variable	B	P value	OR (95%CI)
Not high levels of lead in bone	-0,724	0,038	0,485 (0,245-0,959)

Constanta: 0,-279

IV. DISCUSSION

In a case control study of 55 babies with LBW and 100 not LBW, it was found that there was no significant relationship between maternal age, history of disease during pregnancy, and ANC quality with the incidence of LBW (p value> 0.05). The mean maternal age of LBW infants was 26 years with a minimum age of 16 years and a maximum of 46 years. This shows that there is an extreme pregnancy in young adolescents and older women (> 40 years) where according to some research results there is a high risk of giving birth to a baby with LBW.[47,48]

Research on pregnancies in adolescents who are at risk of giving birth to LBW babies has been widely conducted, however, research on risky pregnancies in older women has been conducted less frequently despite the fact that it is still common.[48] In adolescent pregnancy, the high incidence of low birth weight indicates a lack of ANC examination status and poor sociodemographic effects, while in late pregnancy, it reflects the aging of the mother's biological tissue and there is a cumulative effect of the mother's disease.[49]

The results also showed that there was no significant relationship between medical history during pregnancy and the incidence of LBW. This is not in accordance with the research conducted by Sharma and Mishra (2013) which states that maternal health and general medical conditions can affect the fetus in many ways. As well as the supply of several nutrients and oxygen as key factors for fetal growth. Any change in this can lead to changes in fetal growth. Maternal infections that are transmitted through the placenta can also affect fetal growth.[50] Some history of disease, both infectious and non-communicable, may have occurred before pregnancy, during pregnancy or be exacerbated by pregnancy. For example, heart disease, anemia, essential hypertension, diabetes mellitus, gestational diabetes, hemoglobinopathy, poisoning, general peritonitis, pneumonia, abdominal typhus, malaria, TORCH, chikungunya can reduce the general condition of the mother. In addition, toxins, bacteria, viruses, plasmodium can pass through the placenta and then enter the fetus which then interferes with fetal growth and development.[51]

In the ANC quality variable, there was also no significant relationship with the incidence of LBW. This is not in line with the research conducted by Oulay, et al. (2018) which states that mothers who during their pregnancy made ANC visits less than 4 times, at risk of giving birth to babies with LBW 2.8 times compared to mothers who during pregnancy made ANC visits. more than 4 times.[52] ANC visits from pregnant women are very important for them in providing opportunities to monitor fetal well-being and allow timely intervention for maternal protection.[3]The results of bivariate and multivariate analysis on the variable lead levels in bone showed a significant relationship with the incidence of LBW. The variable lead levels in bone was not high (<1652.75) as a protective factor against the incidence of LBW. This is in line with research conducted by Zhang, et al. (2015) who conducted a study of 522 boys and 477 girls in Mexico City and reported that maternal bone Pb tested after delivery had a significant correlation with body weight lower than time to time among girls but not boys up to 5 years[53].

Lead excretion is generally very slow. When lead enters the body, the half-life in the blood is approximately 25 days, in soft tissue 40 days, while in bone it is 25 years. This slow excretion causes lead to easily accumulate in the body. Both in occupational and non-occupational exposures.[31] In adults, about 95% of the lead in the body is deposited in the bones, while in children about 70%. Lead concentration in bone may increase with age and this increase is more pronounced in men where the tibia is denser.[32]In tissues or organs, lead metal will accumulate in bones, because this metal in the form of ions (Pb2 +) can replace the presence of Ca2 + ions present in bone tissue[39]. In addition, in pregnant women, lead can cross the placenta and then enter the fetal circulatory system and then after the baby is born, lead will be excreted with milk.[40]

The concentration of lead present in adult bone can work to maintain blood lead (BLL) levels after exposure has ended.[33–37] Chuang et al. (2001) suggest that lead exposure has far-reaching consequences. Long exposure, at some point in time, will indeed decrease, but this has not been proven, but past exposure to lead will clearly affect the health of the mother and fetus in the future and lead "deposits" in bones will be toxic in the body for a long time. long enough.[54]

V. CONCLUSION

The results of this study showed a significant relationship between lead levels in the bone in mothers with the incidence of LBW, but on the other hand, there was no significant relationship between maternal age, history of illness during pregnancy, and quality of ANC with the incidence of LBW. Lead metal that has accumulated in

bones can replace the presence of calcium ions, this can be anticipated by adding calcium supplements during pregnancy to reduce the negative effects of lead poisoning, one of which is giving birth to a baby with LBW.

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