ORIGINAL RESEARCH ARTICLE

Fecal Myeloperoxidase Levels in Pregnant Women and Risk Factors to Low Birth Weight in A Makassar Slum Settlement: A Sub-Study of The Indonesian Birth Cohort Study

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ABSTRACT

Purpose: Intestinal inflammation can affect the absorption of micronutrients from the bowel, which can lead to maternal malnutrition and adverse pregnancy outcomes. This study aimed to measure fecal myeloperoxidase (MPO) levels as a biomarker of inflammation in pregnant women and explore risk factors for low birth weight in the slum area of the Tallo District, Makassar City.

Method: This study used a retrospective cohort study design with a purposive sample of 172 pregnant women. Stool specimens were collected and tested using a human myeloperoxidase enzyme-linked immunosorbent assay kit. Data were collected through interviews using the Kobo Toolbox.

Result: The median fecal myeloperoxidase level in pregnant women was 24.2 ng/ml. The correlation with low birth weight was insignificant (r = -0.0037, p = 0.96). Based on bivariate analysis, the risk factors significantly associated with low birth weight were first parity (RR = 2.8 (95% CI: 1.3-6.4), and preterm birth (RR = 3.9 (95% CI: 1.9-8.3), while the multivariate analysis showed that the most significant risk variable for low birth weight was preterm birth (ARR = 4.9 (95% CI: 2.6-9.1).

Conclusion: This study found that gestational age at birth was significantly associated with low birth weight in infants. There was no significant association with fecal myeloperoxidase level in the pregnant mother.

Keywords: myeloperoxidase, inflammation, pregnant women, infants

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INTRODUCTION

Low birth weight (LBW) is an important predictor of newborn survival.[1-2] Babies born with low weight have an increased risk of death during the neonatal period.[3] The World Health Organization has reported that mortality in infants with low birth weight globally contributes to 60-80% of all neonatal deaths in developed and developing countries.[1,4] The risk of neonatal death in babies with LBW is three times higher than in babies with normal birth weight.[5] This is in line with research in Burkina Faso reporting a 21% increase in the risk of neonatal death in babies with a birth weight of less than 2,500 grams.[6]

Studies on pregnant women remain essential to support recommendations that ensure the health of mothers and babies during the first 1,000 days of the child's life. During pregnancy, especially in the second and third trimesters, the fetus's growth and development require adequate nutritional intake.[6] If nutritional intake is disturbed during this phase, this will have an impact on the baby to be born, namely inhibition of fetal growth or LBW. A factor that may inhibit the absorption of nutrients in pregnant women is intestinal inflammation.

Intestinal inflammation is associated with impaired absorption of macro- and micronutrients. Inadequate regulation of food intake and eating patterns accompanied by exposure to an unhealthy environment will weaken the body's immune system, which may trigger inflammation.[7] A study in Bangladesh revealed a significant difference in the microbiota of groups of children and adults living in slums with a high prevalence of intestinal inflammation compared to the microbiota of US children with a more affluent and healthier lifestyle.[8] Understanding the interaction between the microbiota and the immune system will assist in tackling inflammation and developing new approaches to disease prevention and management.[9]

Intestinal inflammation may be caused by an imbalance of the microbiota in the gut (dysbiosis). Dysbiosis is an increase in the number of pathogenic bacteria in the intestine, which can lead to increased intestinal permeability, immunological dysfunction, intestinal epithelial destruction, and metabolic failure.[10] This will affect the digestive system's function, particularly food absorption, potentially leading to malnutrition.[7] In pregnant women, this may affect the development and growth of the embryo or fetus in the womb[11-12] and may result in low birth weight.

One of the biomarkers that can identify inflammation in the intestine is myeloperoxidase (MPO)[13], an enzyme that is active during inflammation, killing foreign microorganisms. The MPO concentration formed is 30% of the total released protein content[14] and is always present in the body irrespective of age.[15] It has become an appropriate non-invasive fecal biomarker for inflammatory activation in the bowel.

Inflammation of the intestine is generally associated with high exposure to environmental enteropathogens due to poor environmental quality. Poor environmental quality is synonymous with slum settlements, whose function as a place of residence has deteriorated and where people with low economic status congregate. More than one billion people in low-income and middle-income countries live in rapidly growing informal settlements with poor water, sanitation, and hygiene conditions. This study aimed to measure fecal myeloperoxidase levels as a biomarker of bowel inflammation in pregnant women and explore factors associated with low birth weight in the slum area of the Tallo District, Makassar City.

METHODOLOGY

Study Design: This study is a sub study of the Indonesian Birth Cohort Study (INABCS). INABCS is ongoing, dynamic, and large-scale study rich in field and laboratory data that assesses environmental exposure to maternal and child health in the slum area of the Tallo subdistrict, one of the heavily slum areas in Makassar City, Indonesia. This study examines a section of the study. We used a retrospective cohort design to assess the relationship between MPO and birth weight and to identify other factors potentially related to low birth weight.

Participant and Procedure: The population in this study consisted of pregnant women in the second and third trimesters of pregnancy. The population was identified in 2022 from secondary data in three Public Health Center areas: Kaluku Bodoa; Jumpandang Baru; and Rappokalling. There were records for 215 pregnant women. Purposive sampling following criteria defined by the researcher resulted in 172 respondents. The exclusion criteria are multiple pregnancy, unable to cooperate in study, and planned to moved domicile. Data were collected through interviews using the KoboToolbox.

Pregnancy data were collected from women who had signed an informed consent after receiving an explanation regarding the implementation of the research. The interviews, conducted during home visits, used a structured questionnaire to assess socioeconomic characteristics and obstetric factors potentially related to LBW. Furthermore, pregnant women were asked to collect fecal samples after receiving instructions from the researcher. Fecal samples were collected from respondents in the first and second trimesters, while birth weight (outcomes) were collected based on the time of birth of each respondent at least 48 hours after birth. Besides that, the means of smoke exposure in this research is active and passive exposure experienced by pregnant women.

Ethical approval was obtained from the Hasanuddin University Health Research Ethics Committee with ethical approval recommendation number 15005/UN4.14.1/TP.01.02/2022. Then, informed consent was obtained from all participants.

Specimen examination was carried out by the Microbiology Laboratory Unit at Hasanuddin University Hospital using the ELISA method (Human Myeloperoxidase ELISA Kit Cat No. MBS016509, MyBioSource, Southern California San Diego, USA). Specimen concentration readings were calculated directly from the standard curve using the SkanIt function of the Curve Expert software 3.1.

Statistical Analysis: The research data were analyzed using Stata Version 14 (Stata Corp LLC, 4905 Lakeway Drive, college station Texas), serial number 301406358211. The relationship between MPO level and infant birth weight was evaluated using Spearman's correlation, assuming that MPO concentration in human feces is not normally distributed. The relative risk test (RR) was used to evaluate risk factors associated with low birth weight. The confidence level was established at 95% and significance was set at $p < 0.05$.

RESULTS

Socioeconomic characteristics: The average age of the 172 respondents was 27 years, with an average gestational age of 38 weeks. The most frequent age group was 20-35 years (75.5%), the most common education level was high school graduate (69.8%), most respondents were housewives (85.47%), and, based on total family income, most lived in low-income families (58.14%). Most babies were boys (58.1%) (table 1).

Obstetric characteristics: Preterm births occurred in 9.8% of pregnancies. Most respondents were parity 2-3 (54.1%), had had more than one pregnancy (72.1%), and did not suffer from chronic energy deficiency (CED) according to the mid-upper arm circumference (MUAC) test (82.6%). Approximately half of the pregnant women had a pregnancy interval of < 24 months (53.5%), and 13.4% of babies had a low birth weight (table 2).

Bivariate and Multivariate analysis: This study found that the mean fecal MPO level of pregnant women was 24.2 ng/ml. The correlation coefficient between the MPO level in pregnant women and the infant's birth weight was -0.0037. The negative value means that, at higher MOP concentrations in the stools of pregnant women, the birth weight of the baby will be lower. However, this relationship is weak and non-significant (p = 0.96) (table 3).

The scatter graph in figure 1 indicates no significant linearity between MPO concertation with birth weight. Therefore, there is no relationship between MPO values and infant weight In the LBW group and normal weight group as demonstrated in figure 2 and 3. Furthermore, the scatter graph shows that the MPO value in most pregnant women was below 100 ng/ml and no linear relationship was observed.

Table 1: Distribution of socioeconomic characteristics of pregnant women in the slum settlements of the Tallo District, Makassar City

Socioeconomic Characteristics	Frequency (%)
Age (y)	
< 20	23 (13.4)
20-35	130 (75.5)
> 35	19 (11.1)
Education	
Elementary	35 (20.4)
Secondary	120 (69.8)
College graduated	17 (9.8)
Occupation	
Housewife	147 (85.5)
Self-employed	12 (6.9)
Laborer/farmer	13 (7.6)
Family Income	
Low income (< Rp. 3.294.467)	100 (58.1)
Moderate (≥ Rp. 3.294.467)	72 (41.9)
Infant Sex	
Male	100 (58.1)
Female	72 (41.9)

Table 2: Distribution of characteristics related to maternal obstetrics in the slum settlements of the Tallo District, Makassar City

Obstetric Characteristic	Frequency (%)
Gestational age at birth	
Term	155 (90.2)
Preterm	17 (9.8)
Parity	
1	53 (30.8)
3-Feb	93 (54.1)
>3	26 (15.1)
MUAC*	
CED** (< 23,5 cm)	30 (17.4)
Normal (≥ 23,5 cm)	142 (82.6)
Pregnancy interval	
<24 months	92 (53.5)
≥24 months	80 (46.5)
Birth weight	
Low	23 (13.4)
Normal	149 (86.6)

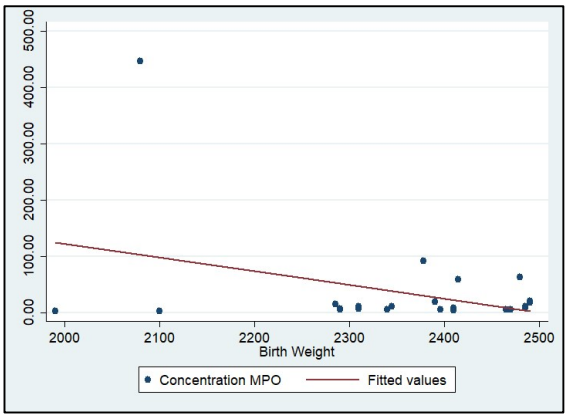
*Mid-upper arm circumference; **Chronic energy deficiency

The risk factors associated with low birth weight are presented in Table 5. The relationship between MPO concentration and the incidence of LBW was not significant (p = 0.67) and fecal MPO was not a risk factor (RR=0,8). In the bivariate test, the risk for LBW was 2.8 (95% CI: 1.3-6.4) times higher in mothers who gave birth for the first time (24.5%) compared to women who had given birth more than once. Preterm births had a 3.9 times higher risk of LBW than term births (95% CI: 1.9-8.3). In the multivariate analysis, the variables with the most significant risk of low birth weight were preterm birth, with an adjusted RR value of 4.9 (95% CI: 2.6-9.1) and parity with an adjusted RR of 3.4 (95% CI: 1.1-11.02) for primigravid women.

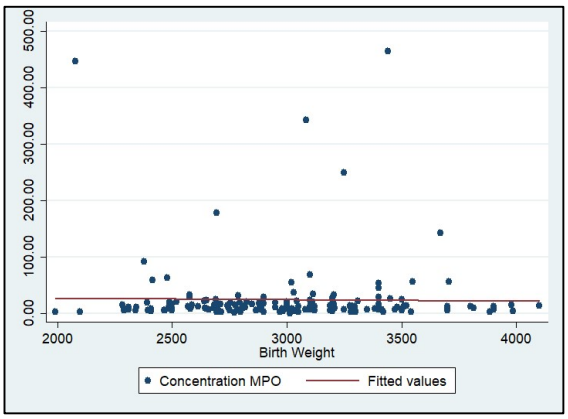
Table 3: The association between fecal myeloperoxidase (MPO) concentration during pregnancy and birth weight

Variable	Mean ± SD
MPO level	24.2 ng/ml ± 59.6
Birth Weight	2991.3 gr ± 424.7
Correlation coefficient (r)	-0.0037
p-value	0.96

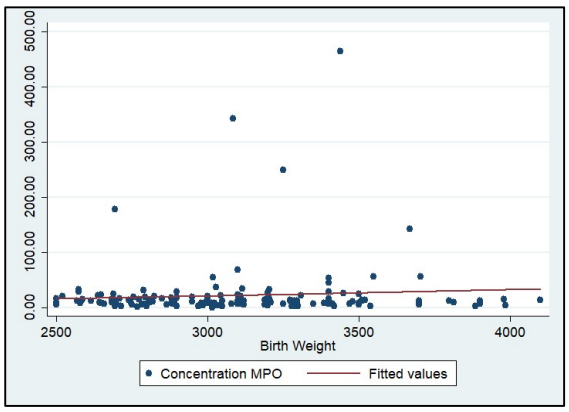
Figure 1: Scatter graph for relationship between MPO and A) birth weight, B) Low birth weight, and C) Normal birth weight



B)



A)



C)

Table 5: Factors associated with low birth weight

Variable	Low Birth Weight		Crude Risk Ratio (CI 95%)	p-value
	Yes (%)	No (%)		
MPO levels				
≤ 24,2 ng/ml	19 (82,6)	128 (85,9)	1	
>24,2 ng/ml	4 (17,4)	21 (14,1)	1,2(0,4- 3,3)	0,67
Household income				
Low income	12 (12)	88 (88)	0.8 (0.4-1.7)	0.53
Moderate income	11 (15.3)	61 (84.7)	1	
Educational level				
Elementary	4 (11.4)	31 (88.6)	0.6 (0.2-2.6)	0.53
Secondary School	16 (13.3)	104 (86.7)	0.7 (0.2-2.3)	0.62
College graduated	3 (17.7)	14 (82.3)	1	
Age (y)				
<20	4 (17.4)	19 (82.6)	1.3 (0.5-3.5)	0.57
20-35	17 (13.1)	113 (86.9)	1	
>35	2 (10.5)	89 (89.5)	0.8 (0.2-3.2)	0.75
MUAC				
<23,5 cm	6 (20)	24 (80)	1.7 (0.7-3.8)	0.23
≥23,5 cm	17 (11.9)	125 (88.1)	1	
Parity				
1	13 (24.5)	40 (75.5)	2.8 (1.3-6.4)	0.012*
2 - 3	8 (8.6)	85 (91.4)	1	
>3	2 (7.7)	24 (92.3)	0.8 (0.2-3.9)	0.88
Abortus				
Yes	5 (15.6)	27 (84.4)	1.2 (0.4-3.01)	0.67
No	18 (12.8)	122 (87.2)	1	
Smoke exposure				
Exposed	20 (14.5)	118 (85.5)	1.6 (0.5-5.2)	0.39
Not exposed	3 (8.8)	31 (91.2)	1	
Pregnancy interval (months)				
< 24	16 (17.4)	76 (82.6)	1.9 (0.8-4.5)	0.107
≥ 24	7 (8.8)	73 (91.2)	1	
Gestational age				
Preterm	7 (41.2)	10 (58.8)	3.9 (1.9-8.3)	0.000*
Term	16 (10.3)	139 (89.7)	1	

Table 6: Multivariate analysis for factors associated with low birth weight in

Variable	Crude RR (CI 95%)	P-value	Adjusted RR (CI 95%)	P-value
MPO levels				
≤ 24,2 ng/ml	1		1	
>24,2 ng/ml	1,2(0,4- 3,3)	0.67	0.8(0.37-1.9)	0.72
Household income				
Low income	0.8 (0.4-1.7)	0.53	1,04(0,5-2,1)	0.9
Moderate income	1		1	
Educational level				
Elementary	0.6 (0.2-2.6)	0.53	0.9 (0.3-3.4)	0.94
Secondary School	0.7 (0.2-2.3)	0.62	0.9(0.4-2.2)	0.88
College graduated	1		1	
Age (y)				
<20	1.3 (0.5-3.5)	0.57	0.6 (0.3-1.4)	0.21
20-35	1		1	
>35	0.8 (0.2-3.2)	0.75	1.5(0.3-8.8)	0.59
MUAC				
<23,5 cm	1.7 (0.7-3.8)	0.23	1.6(0.6-3.9)	0.27
≥23,5 cm	1		1	
Parity				
1	2.8 (1.3-6.4)	0.012*	3.4(1.1-11.02)	0.04*
2-3	1		1	
>3	0.8 (0.2-3.9)	0.88	0.6 (0.09-3.3)	0.53
Abortus				
Yes	1.2 (0.4-3.01)	0.67	1,09 (1.09-1.09)	0.000
No	1		1	
Smoke exposure				
Exposed	1.6 (0.5-5.2)	0.39	2.4 (0.6-8.1)	0.17
Not exposed	1		1	
Pregnancy interval (months)				
< 24	1.9 (0.8-4.5)	0.107	0.7 (0.2-3)	0.74
≥ 24	1		1	
Gestational age				
Preterm (20-37 Week)	3.9 (1.9-8.3)	0.000*	4.9 (2.6-9.1)	0.000*
Term (>37 Week)	1		1	

DISCUSSION

MPO levels and low birth weight

This study revealed an LBW rate of 13% in the slums of the Tallo subdistrict, Makassar City, which is higher than the general incidence of LBW in Indonesia in 2021 (2.5%), and the rate of LBW in South Sulawesi Province (4.24%). Still, this number is below the global prevalence of 15.5% to 20%.[13]

Our study did not find a significant relationship between the fecal concentration of MPO in pregnant women and the birth weight of the baby. Although the relationship was not significant, its direction was negative, and it can be assumed that, at a higher concentration of myeloperoxidase in the stools of the mother, the birth weight of the baby will be lower, but the strength of the relationship in this study was weak.

Several previous studies that also used fecal myeloperoxidase as a biomarker to assess the presence of intestinal inflammation showed significant results in children. Brazilian research showed a significant relationship between myeloperoxidase concentrations and the occurrence of malnutrition in children aged 6-26 months.[14-15] A study conducted in Timor-Leste to evaluate the effect of interventions regarding sanitation, water, and environmental hygiene on subclinical inflammation and permeability of the small intestine showed that myeloperoxidase concentrations were significantly higher in younger children (coefficient: -0.29, p = 0.002)(3). However, another study did not find a significant relationship between myeloperoxidase and child growth; neither did it find a significant relationship with family socioeconomic variables.[17]

MPO is a fecal biomarker that can be used to measure neutrophil activity and inflammation in the gut because this lysosomal protein is overproduced during inflammation to destroy the foreign microorganisms that are the cause.[18] Based on previous research, intestinal inflammation can be a significant factor in malnutrition, growth disorders, and stunting in children. In this study, we used fecal specimens from pregnant women to see if there was a relationship between bowel inflammation in pregnant women and the birth weight of their children.

Myeloperoxidase is the main component of primary (azurophilic) granules of neutrophils; its activity has been observed in the intestinal mucosa and intestinal lavage of inflammatory bowel disease patients. Subclinical disturbances and intestinal mucosa permeability will affect intestinal function, leading to malabsorption, which affects the absorption of micronutrients from the bowel[7]. If this occurs in pregnant

women, the baby's growth and birth weight may be affected. However, our study did not find this relationship.

This study found a mean value of 24.2 ng/ml for fecal MPO concentrations in pregnant women. No previous studies have evaluated MPO biomarkers in pregnant women. Previous research has measured fecal MPO concentrations in children under five years of age to assess the effects of malnutrition on child growth.[14-17,19-20] This study evaluated fecal MPO concentrations in adults, specifically pregnant women, and then correlated the concentration with the birth weight of their children.

Risk factors for low birth weight

The variables tested in this study show that obstetric and socioeconomic factors are related to LBW, including parity, and gestational age at birth. This finding is in line with a study in central Ethiopia, which showed a significant relationship of parity and gestational age with LBW.[13] Another Ethiopian study in the city of Dire Dawa found that nutritional counseling, gestational age, maternal height, and exposure to cigarette smoke were associated with LBW.[21]

In the multivariate analysis, the most important risk factors for LBW were gestational age at birth and parity of the mother. This was also found in studies in Nepal[22] and Africa[23]. The gestational age of concern is less than 37 weeks. These babies are considered preterm. At this gestational age, most of the fetus's bones have not properly matured, which can result in stunted growth and low birth weight.[24] In addition, inflammation experienced by the mother during pregnancy can result in nutritional deficiencies that can cause preterm birth.[12,25]

Similar to our study, a study in Western Australia found an increased risk for LBW in women with a first-time pregnancy.[26] This may be related to the experience of first-time motherhood, where their reproductive organs may not be fully prepared medically. They may also lack experience in healthcare and preventing high risk conditions during pregnancy, which can increase the like hood of pregnancy or childbirth complications associated with low birth weight in infants.[27,28] In addition, it is related to changes in the physiological condition of the mother during the process of fetal growth in the first pregnancy.[29,30]

Conclusion

Despite the absence of a statistically significant relationship between fecal myeloperoxidase levels and birth weight, a negative correlation was observed. This suggests that higher levels of MPO are associated with lower birth weight. Additionally, gestational age at birth and parity were identified as the primary risk factors for low birth weight. The outcomes of this study have implications for the improvement of services offered to pregnant women, particularly with regard to education aimed at ensuring healthy pregnancies. Such education could be provided through a family-oriented approach to prevent adverse pregnancy outcomes. One noteworthy feature of this study is that no previous research has examined MPO levels among healthy pregnant women, resulting in the absence of reference values for MPO in fecal samples among healthy populations. As a recommendation for future studies, we propose that multiple inflammatory biomarkers be evaluated to strengthen the evidence of intestinal inflammation and that the results of several biomarkers be compared. Furthermore, this research is expected to be a reference for development of the same research but with a large sample size.

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