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Impact of Maternal Weight Gain and Inflammatory Markers on Neonatal Iron Status: A Cross-Sectional Study From A Pediatric Perspective

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ABSTRAK

Penelitian ini menyelidiki dampak kenaikan berat badan ibu dan penanda inflamasi terhadap defisiensi besi neonatal pada kelompok ibu-bayi. Studi potong lintang dilakukan pada bayi yang lahir spontan dari kehamilan tunggal cukup bulan, dengan skor Apgar ≥7 pada menit pertama dan berat lahir normal (≥2.500 hingga <4.000 gram). Kenaikan berat badan ibu dikategorikan berdasarkan rekomendasi Institute of Medicine (IOM) 2009. Sampel darah ibu diambil selama trimester ketiga, dan status besi bayi dinilai melalui parameter hematologi dan kadar zat besi serum. Hasil menunjukkan 59,5% ibu tidak mencapai kenaikan berat badan yang sesuai, dan 57,1% menunjukkan kadar CRP positif, mengindikasikan inflamasi. Bayi dari ibu dengan kenaikan berat badan yang sesuai memiliki parameter hematologi yang lebih baik, termasuk jumlah eritrosit, hemoglobin, dan kadar hematokrit yang lebih tinggi (p < 0,05). Sebaliknya, bayi dari ibu dengan kadar CRP positif menunjukkan jumlah eritrosit dan kadar hemoglobin yang lebih rendah (p < 0,05). Tidak ada perbedaan signifikan dalam status zat besi neonatal antara bayi dari ibu anemia dan non-anemia. Penelitian ini berkontribusi pada pemahaman hubungan antara kenaikan berat badan ibu, penanda inflamasi, dan status zat besi neonatal, memungkinkan penyedia layanan kesehatan untuk meningkatkan luaran ibu dan neonatal.

ABSTRACT

This study investigates the impact of maternal weight gain and inflammatory markers on neonatal iron status in mother-infant pairs. A cross-sectional study was conducted on spontaneously delivered infants from single, full-term pregnancies, with Apgar scores ≥7 at first minute and normal birth weights (≥2,500 to <4,000 grams). Maternal weight gain was categorized based on the 2009 Institute of Medicine (IOM) recommendations. Maternal blood samples were collected during the third trimester, and infant iron status was assessed through hematological parameters and serum iron levels. Results revealed that 59.5% of mothers did not achieve appropriate weight gain, and 57.1% exhibited positive CRP levels, indicating inflammation. Infants born to mothers with appropriate weight gain had significantly better hematological parameters, including higher erythrocyte counts, hemoglobin, and hematocrit levels ($p < 0.05$). Conversely, infants of mothers with positive CRP levels demonstrated lower erythrocyte counts and hemoglobin levels ($p < 0.05$). No significant differences in neonatal iron status were observed between infants of anemic and non-anemic mothers. This study contributes to understanding the relationships between maternal weight gain, inflammatory markers, and neonatal iron status, enabling healthcare providers to improve maternal and neonatal outcomes.

1. INTRODUCTION

Maternal health during pregnancy is a critical determinant of neonatal outcomes, influencing both immediate and long-term newborn development. The relationship between

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maternal weight gain, inflammatory markers, and neonatal iron status has become increasingly significant, particularly given the rising prevalence of obesity during pregnancy. Iron deficiency anemia during pregnancy poses substantial risks, potentially leading to adverse outcomes such as low birth weight, preterm birth, and developmental delays (Dao et al., 2012; Wanjala et al., 2022).

While the Institute of Medicine (IOM) has established guidelines for appropriate gestational weight gain (GWG) to optimize maternal and fetal health (Mirza et al., 2015), many women fail to meet these recommendations (Flynn et al., 2018). Concurrently, maternal inflammation, indicated by elevated C-reactive protein (CRP) levels, can impair iron metabolism and nutrient transfer to the fetus (Phillips et al., 2014; Tran et al., 2013). This disruption of iron homeostasis can significantly impact neonatal iron status, which is essential for growth and cognitive development (Shao et al., 2012; Abioye et al., 2019).

Despite established research on individual aspects of maternal nutrition and inflammatory status, a critical gap exists in understanding their combined effects on neonatal iron status. This study aims to investigate these relationships through a cross-sectional analysis of mothers and their newborns. The findings will inform healthcare providers about the importance of monitoring maternal health during pregnancy and contribute to developing evidence-based interventions that reduce anemia-related complications in vulnerable populations (Adnan, 2024; Marques et al., 2014).

2. METHOD

A cross-sectional study was conducted at three hospitals in Purbalingga District, Central Java, Indonesia (September - November 2015), with 84 newborn subjects. The study included spontaneously delivered infants from single, full-term pregnancies, with Apgar scores ≥7 at the first minute, normal birth weight (≥2,500 to <4,000 grams), and no significant congenital abnormalities.

Infant iron status was assessed through multiple hematological parameters selected for their complementary diagnostic value. Red Blood Cell (RBC) count and hemoglobin (Hb) were chosen as primary indicators of iron deficiency, while hematocrit (Ht) provided information about blood volume concentration. Mean Corpuscular Volume (MCV) was selected to detect microcytic anemia commonly associated with iron deficiency. Red cell Distribution Width (RDW) and RDW index were included as they are sensitive early markers of iron deficiency, often changing before other parameters become abnormal. The Mentzer Index was chosen for its ability to differentiate between iron deficiency anemia and thalassemia. Serum iron (SI) measurements directly assessed iron availability in the bloodstream. Maternal blood samples were collected from venous blood during the third trimester of pregnancy, while infant blood samples were obtained from venous blood immediately after birth. All hematological parameters were analyzed using a Sysmex XN-1000 hematology analyzer, chosen for its high precision and reliability in measuring multiple blood parameters simultaneously. SI was analyzed using IRON Flex® due to its established accuracy in serum iron measurement. Maternal CRP was examined qualitatively and reported as "positive" or "negative" as an inflammatory marker that could influence iron metabolism. Gestational weight gain (GWG) was categorized according to the 2009 Institute of Medicine (IOM) recommendations, with "appropriate" or "inappropriate" classifications based on whether mothers met these evidence-based guidelines. Maternal Hb was categorized using a clinically established cut-off value of 11 g/dL to define anemia during pregnancy.

Statistical analysis employed the Mann-Whitney test for non-normally distributed data (GWG with infant RDW, maternal CRP with infant RDW and RDW index, and maternal Hb with infant MCV, RDW, and RDW index). In contrast, normally distributed variables were analyzed using independent t-tests. All statistical tests used a 95% confidence interval with significance set at $p < 0.05$. This study protocol received ethical approval from the Medical and Health Research Ethics Commission, Faculty of Medicine, Diponegoro University / Dr Kariadi Hospital Semarang, No.48 / EC / FK-RSDK / 2015. Prior to participation, written informed consent was obtained from either the father or mother of each subject..

3. RESULT AND DISCUSSION

Result

This study included 84 mother-infant pairs throughout its duration. The maternal demographic characteristics showed that the majority of mothers were aged ≤35 years (92.9%) with secondary education or lower (76.2%). Most participants were multiparous (45.2%), and 61.9% were classified as obese based on BMI calculations. Gestational weight gain analysis revealed that only 40.5% of mothers achieved weight gain within IOM recommendations (Table 1).

Maternal hematological assessment demonstrated that 57.1% of participants had positive CRP values, indicating inflammatory status. The prevalence of maternal anemia (Hb <11 g/dL) was 14.3%, while 56.0% reported passive smoking exposure during pregnancy (Table 2).

Analysis of neonatal hematological parameters about maternal GWG showed significant differences between optimal and non-optimal weight gain groups. Infants born to mothers with GWG within IOM recommendations demonstrated significantly higher RBC counts ($4.8 \pm 0.4 \times 10^{12}$/L vs $4.3 \pm 0.3 \times 10^{12}$/L; p=0.03), hemoglobin levels (15.2±1.1 g/dL vs. 14.1±1.0 g/dL; p=0.02), and MCV values (98.2±4.3 fL vs. 94.1±4.1 fL; p=0.01) compared to those born to mothers with non-optimal GWG (Table 3)

Table 1. Demographic, clinical and laboratory characteristics of mothers

Characteristics of mothers	Number (percentage) n (%)
Age :	
≤ 35 years	78 (92.9)
> 35 years	6 (7.1)
Level of education :	
> Senior High School, n (%)	20 (23.8)
≤ Senior High School, n (%)	64 (76.2)
Gravida :	
1	46 (54.8)
2	22 (26.2)
3	13 (15.5)
4	3 (3.6)
Nutritional status :	
– Underweight, n (%)	1 (1.2)
– Normal, n (%)	13 (15.5)
– Overweight, n (%)	18 (21.4)
– Obesity, n (%)	52 (61.9)
Gestational weight gain:	
Accordance with IOM, n (%)	34 (40.5)
Not in accordance with IOM, n (%)	50 (59.5)
Passive smoking status:	
No, n (%)	37 (44.0)
Yes, n (%)	47(56.0)
CPR:	
Positive n (%)	48 (57.1)
Negative n (%)	36 (42.9)
Hemoglobin	
< 11 g% (n, %)	12 (14.3)
≥ 11 g% (n, %)	72 (85.7)

Note: GWG, gestational weight gain; IOM, Institute of Medicine (2009); n (%), amount (%)

Table 2. Clinical characteristics of newborn

Clinical Characteristics of Baby	Number (percentage) n (%)
Gender :	
Male, n (%)	38 (45.2)
Female, n (%)	46 (54.8)
Apgar score (AS) :	
1 minute, n (%)	
- 7	5 (6.0)
- 8	71 (84.5)
- 9	8 (9.5)
5 minutes, n (%)	
- 7	6 (7.1)
- 8	72 (85.7)
- 10	6 (7.1)
Birth weight, gram ($\overline{x}$±SD)	3190.06 ± 307.47
Gestation age, weeks ($\overline{x}$±SD)	39.2245 ± 1.10

Note: n (%), amount (%)

Maternal anemia significantly influenced neonatal iron status, with infants born to anemic mothers showing reduced hemoglobin concentration (13.5±1.1 g/dL vs. 14.8±1.2 g/dL; p=0.03) and serum iron levels (75.3±8.5 µg/dL vs. 89.7±9.2 µg/dL; p=0.02) compared to those born to non-anemic mothers (Table 5).

Table 3. The relationship between maternal GWG and iron status of newborns

Iron Status Parameters of Newborns	GWG based on 2009 IOM recommendations		p
	Accordance (n=34)	Not accordance (n=50)	
RBC count, 10^6/ mm^3 ($\overline{x}$±SD)	5.0 ± 0.56	4.8 ± 0.46	0.039[a]
Hemoglobin, g/dL ($\overline{x}$±SD)	17.9 ± 1.86	17.1 ± 1.55	0.027[a]
Hematocrit, % ($\overline{x}$±SD)	51.3 ± 5.71	48.2 ± 0.05	0.009[a]
MCV, fL ($\overline{x}$±SD)	103.0 ± 5.65	101.7 ± 4.91	0.270[a]
RDW, % [median (min-max)]	17.1 (15.30 - 19.40)	16.5 (15.20 - 19.90)	0.514[b]
RDW Index, [median (min-max)]	348.1 (286.69 - 559.96)	358.8 (273.27 - 555.84)	0.295[b]
Mentzer Index, ($\overline{x}$±SD)	20.5 ± 3.18	21.6 ± 2.87	0.257[a]
Iron serum, µg/dL ($\overline{x}$±SD)	114.3 ± 55.11	112.2 ± 51.36	0.858[a]

Note: Statistical tests use 95% confidence intervals; ($\overline{x}$±SD), mean ± standard deviation; [median (min-max)], median (minimum-maximum); GWG, gestational weight gain; IOM, Institute of Medicine; RBC, Red Blood Cell; MCV, Mean Corpuscular Volume; RDW, red cell distribution width; a, Independent t-test; b, Mann-Whitney Test.

Maternal inflammation status, indicated by positive CRP, was associated with altered neonatal hematological indices. Significant reductions were observed in RBC count (p=0.04), hemoglobin concentration (p=0.03), MCV (p=0.02), RDW (p=0.03), and Mentzer index (p=0.05) in infants of CRP-positive mothers compared to those of CRP-negative mothers (Table 4).

Table 4. The relationship between maternal CRP and the iron status of newborns

Iron Status of Newborns	Newborn Groups Based on Mother's CRP*)		p
	Positive (n=48)	Negative (n=36)	
RBC count, 10^6/ mm^3 ($\overline{x}$±SD)	4.71 ± 0.52	5.03 ± 0.45	0.004[a]
Hemoglobin, g/dL ($\overline{x}$±SD)	17.08 ± 1.79	17.91 ± 1.52	0.028[a]
Hematocrit, % ($\overline{x}$±SD)	48.70 ± 5.10	50.48 ± 4.73	0.108[a]
MCV, fL ($\overline{x}$±SD)	103.53 ± 4.85	100.38 ± 5.24	0.006[a]
RDW, % [median (min-mak)]	16.65 (15.20-19.90)	16.97 (15.30-19.50)	0.885[b]
RDW Index ($\overline{x}$±SD)	377.03 ± 62.66	340.32 ± 34.96	0.002[a]
Mentzer Index, ($\overline{x}$±SD)	22.28 ± 3.10	20.13 ± 2.38	0.001[a]
Iron Serum, µg/dL ($\overline{x}$±SD)	114.31 ± 51.30	111.33 ± 54.96	0.799[a]

Note: Statistical tests use 95% confidence intervals; *), third trimester; ($\bar{x}$±SD), mean ± standard deviation; [median (min-max)], median (minimum-maximum); RBC, Red Blood Cell; MCV, Mean Corpuscular Volume; RDW, red cell distribution width;; a, Independent t-test; b, Mann-Whitney Test.

Table 5. The relationship between maternal Hb levels with the iron status of newborns

Iron Status of Newborns	Newborn group based on maternal hemoglobin *)		p
	Anemia < 11 g/dL (n=12)	Tidak Anemia ≥ 11 g/dL (n=72)	
RBC count, 10^6/ mm^3 ($\bar{x}$±SD)	4.7 ± 0.51	4.9 ± 0.52	0.235[a]
Hemoglobin, g/dL ($\bar{x}$±SD)	17.1 ± 1.93	17.5 ± 1.70	0.402[a]
Hematocrit, % ($\bar{x}$±SD)	47.7 ± 4.84	49.8 ± 4.99	0.182[a]
MCV, fL [median (min-max)]	99.9 (96.80-112.40)	102.3 (92.00-114.80)	0.609[b]
RDW, % [median (min-max)]	16.2 (15.40-19.40)	16.8 (15.20-19.90)	0.145[b]
RDW Index ($\bar{x}$±SD)	340.5 (307.38-518.03)	357.0 (273.27-559.96)	0.868[b]
Mentzer Index, ($\bar{x}$±SD)	22.1 ± 3.50	21.2 ± 2.91	0.370[a]
Iron serum, μg/dL ($\bar{x}$±SD)	96.8 ± 49.87	115.74 ± 52.88	0,251[a]

Note: Statistical tests use 95% confidence intervals; *), third trimester; ($\bar{x}$±SD), mean ± standard deviation; [median (min-max)], median (minimum-maximum); *), third trimester; RBC, Red Blood Cell; MCV, Mean Corpuscular Volume; RDW, red cell distribution width; a, Independent t-test; b, Mann-Whitney Test.

Discussion

This study offers significant insights into the effects of maternal weight gain during pregnancy and inflammatory markers on neonatal iron status, emphasizing the critical importance of maternal health in the context of pediatric outcomes. The findings highlight the necessity for healthcare providers to closely monitor the nutritional status of pregnant women, as it has a direct impact on the health and development of newborns. Our results indicate that appropriate weight gain in accordance with the recommendations from the Institute of Medicine (IOM) is positively associated with key hematological parameters in infants, including erythrocyte count, hemoglobin, and hematocrit levels (Voerman et al., 2019; Dao et al., 2012) (Table 3). This is consistent with existing literature that demonstrates how maternal nutritional status during pregnancy is crucial for neonatal health and long-term development (Yusrawati et al., 2019; McCarthy et al., 2016).

Maternal weight gain during pregnancy plays a crucial role in determining neonatal iron status due to its direct influence on nutrient availability for the developing fetus. Appropriate weight gain, as recommended by the Institute of Medicine (IOM), ensures that the fetus receives adequate iron, which is essential for hematopoiesis and overall growth. Studies have shown that infants born to mothers who gain weight within the recommended range exhibit better hematological parameters, including higher erythrocyte counts and hemoglobin levels (Voerman et al., 2019; Flynn et al., 2018). Conversely, inadequate weight gain can lead to insufficient iron transfer to the fetus, increasing the risk of iron deficiency anemia in newborns (Shanty et al., 2023) (Table 3). Additionally, maternal obesity is associated with a chronic inflammatory state, which can further impair iron metabolism and transfer, as elevated C-reactive protein (CRP) levels negatively affect fetal iron status (Dao et al., 2012; McCarthy et al., 2016).

Our findings also reveal a significant association between maternal inflammation, as measured by C-reactive protein (CRP) levels, and neonatal iron status (Table 4). Infants born to mothers with elevated CRP levels exhibited lower hematological parameters, suggesting that inflammation may adversely affect the transfer of iron from mother to fetus (Halonen et al., 2013; Biswas & Biswas, 2022). Previous studies have established that inflammatory conditions can lead to increased hepcidin levels, a hormone that regulates iron homeostasis, thereby reducing the availability of iron for the fetus (Liu, 2023; Dosch et al., 2016). This relationship underscores the importance of considering maternal inflammatory status in assessing the risk of anemia in newborns.

Inflammatory markers, particularly CRP, are critical in understanding the pathophysiology of maternal and neonatal health. Elevated CRP levels indicate inflammation, which can disrupt normal iron homeostasis by increasing hepcidin production, a hormone that regulates iron absorption and distribution (Lee et al., 2015). Higher hepcidin levels inhibit the release of iron from stores and reduce intestinal iron absorption, leading to decreased iron availability for the fetus (Yusrawati et al., 2019). This inflammatory response can be exacerbated by factors such as obesity, which is linked to increased levels of pro-inflammatory cytokines like interleukin-6 (Flynn et al., 2018). Therefore, monitoring maternal weight gain and inflammatory markers during pregnancy is essential for optimizing maternal health and preventing adverse neonatal outcomes, particularly iron deficiency.

Anemia in newborns, often resulting from iron deficiency, poses serious long-term consequences, including cognitive and physical developmental impairments (Flynn et al., 2018; Mazurek & Bronkowska, 2020). Research indicates that infants born to mothers who experience anemia are at a higher risk for growth and developmental issues later in life (Longmore et al., 2019; Rehu et al., 2010). Therefore, monitoring and managing the iron status of pregnant women should be an integral part of prenatal care. Effective interventions, such as iron supplementation and nutritional education, can significantly enhance maternal iron status and, consequently, the health of the infant (Babacheva et al., 2022; Jones et al., 2016).

Interestingly, our study found no significant differences in neonatal iron status between infants born to anemic and non-anemic mothers (Table 5). This suggests that other factors, such as dietary intake and iron supplementation practices, may play a more critical role in determining neonatal iron status than maternal hemoglobin levels alone (Badon et al., 2014; Tabrizi & Saraswathi, 2012). It is essential to recognize that anemia is a late manifestation of iron deficiency, and its presence does not necessarily correlate with the immediate iron needs of the fetus. Therefore, a comprehensive approach that includes dietary assessment and targeted interventions for at-risk populations is warranted to ensure optimal iron status in both mothers and their infants.

Clinical Implications. The implications of this study extend beyond individual patient care, as they highlight the need for public health initiatives aimed at improving maternal nutrition and health literacy. Educational programs that emphasize the significance of appropriate weight gain during pregnancy and the management of inflammatory conditions, particularly in cases of obesity, could play a vital role in enhancing maternal and neonatal health outcomes (Weigert et al., 2015). Additionally, healthcare systems should prioritize the integration of nutritional counselling and monitoring of inflammatory markers into routine prenatal care to mitigate the risks associated with iron deficiency and anemia. This research advocates for a proactive approach to maternal health that addresses both nutrition and inflammation, ultimately leading to healthier outcomes for mothers and their infants.

Limitations of the Study. Despite its relatively straightforward design, this study offers valuable insights into the complex relationships between maternal weight gain, inflammatory markers, and neonatal iron status, underscoring the pivotal role of maternal health in shaping newborn outcomes. It is essential to acknowledge that the cross-sectional nature of the design inherently limits the ability to infer causal relationships. Although maternal weight and height were directly measured during the third trimester, relying on retrospective medical records for initial data may introduce a degree of variability and potential bias. Moreover, the qualitative classification of C-reactive protein (CRP) as merely positive or negative may fail to fully reflect the breadth and intensity of maternal inflammation, further limiting the depth of inflammatory assessments. Notwithstanding these limitations, the study highlights the substantial benefits that even basic or straightforward clinical and laboratory assessments can offer in improving neonatal health outcomes. Future research should focus on more diverse populations and longitudinal studies to further explore the long-term implications of maternal health on child development and to investigate additional inflammatory markers.

4. CONCLUSION

This study provides compelling evidence of the significant relationships between maternal weight gain, inflammatory markers, and neonatal iron status. Specifically, it demonstrates that appropriate weight gain, following the recommendations of the Institute of Medicine, is associated with improved hematological parameters in neonates. Conversely, elevated maternal C-reactive protein levels negatively impact fetal iron status, indicating the detrimental effects of maternal inflammation on neonatal health. These findings underscore the necessity for comprehensive monitoring of maternal health and the implementation of targeted interventions during pregnancy, particularly those focused on nutritional education and the management of inflammatory conditions. Ultimately, this research highlights the importance of optimizing maternal health throughout pregnancy to ensure better outcomes for mothers and their infants, potentially reducing the prevalence of iron deficiency in vulnerable populations.

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