ECRONICON OPEN ACCESS

EC GYNAECOLOGY
Research Article

Maternal Iron Deficiency Anaemia and its Association with Intrauterine Growth Restriction (IUGR) and Small Fetal Growth in DAHC

Mervat Moreis*

Department of Primary Health, Women Health Unit, DHA Dubai, United Arab Emirates

***Corresponding Author:** Mervat Moreis, Department of Primary Health, Women Health Unit, DHA Dubai, United Arab Emirates.

Received: November 18, 2024; **Published:** November 28, 2024

Abstract

Introduction: Maternal iron deficiency anemia (IDA) is a prevalent condition during pregnancy associated with negative perinatal outcomes, such as intrauterine growth restriction (IUGR) and low birth weight (LBW). This study investigates the correlation between maternal iron deficiency anemia and these outcomes in a tertiary care environment within Dubai Health Centers.

Methodology: This retrospective observational study examined the electronic medical records of pregnant women who received antenatal care and delivered at a tertiary hospital within Dubai Health facilities from June 1, 2020, to December 30, 2022. Women exhibiting hemoglobin levels below 11 g/dL during the third trimester (28 - 40 weeks) were categorized as having iron deficiency anemia (IDA). The study evaluated birth outcomes, including intrauterine growth restriction (IUGR) and low birth weight (LBW), to determine its correlation with maternal iron deficiency anemia (IDA).

Results: The study encompassed records of women with mild anemia (hemoglobin < 11 g/dL) and moderate anemia (hemoglobin < 9 g/dL). A notable correlation was identified between maternal iron deficiency anemia (IDA) and birth weight (P = 0.041), indicating that infants born to mothers with mild anemia were more likely to achieve normal birth weight than those born to mothers with intermediate anemia. Nonetheless, no substantial changes were observed in the prevalence of IUGR, gestational age at birth (P = 0.149), or fetal scan outcomes (P = 0.233).

Conclusion: Maternal iron deficiency anemia, especially its severity, affects birth weight but does not impact gestational age or intrauterine growth restriction outcomes in well-managed healthcare environments. Thorough prenatal care, encompassing the early detection and therapy of iron deficiency anemia, is essential for enhancing pregnancy outcomes. Additional research is required to investigate the long-term impacts of maternal iron deficiency anemia on neonatal health.

Keywords: *Maternal Iron Deficiency Anemia; Intrauterine Growth Restriction; Low Birth Weight; Third Trimester; Pregnancy Outcomes; Anemia Severity; Antenatal Care; Dubai Health Facilities; Retrospective Study; Fetal Growth*

Introduction

Maternal iron deficiency anemia (IDA) is a significant risk factor for adverse pregnancy outcomes, including intrauterine growth restriction (IUGR) and small fetal growth. Severe maternal IDA leads to lower ferritin and hemoglobin levels in infants at birth, increasing the risk of iron deficiency in the first year of life, which further impacts infant growth and development. Maternal anemia reduces the iron supply to the fetus, leading to lower levels of hemoglobin, serum iron, transferrin saturation, and ferritin in newborns, all of which are critical for normal growth [1].

IDA during pregnancy is closely associated with small fetal growth and IUGR, emphasizing the importance of early iron supplementation to mitigate these risks. Additionally, maternal iron levels have been shown to correlate positively with neonatal weight and Apgar scores, with lower maternal iron-binding capacity leading to poorer fetal outcomes. This condition not only affects neonatal birth weight but also places newborns at risk of developmental delays and long-term health consequences [2].

The body's compensatory mechanisms, such as the upregulation of placental iron transporters like DMT1, FPN1, and GDF15, work to ensure fetal iron transfer even under maternal iron insufficiency, but these mechanisms may not fully prevent adverse outcomes. This underscores the need for iron supplementation during pregnancy to improve both maternal and fetal health [3].

Maternal serum ferritin levels during pregnancy have been explored as a potential biomarker for predicting intrauterine growth restriction (IUGR). Several studies have highlighted that low maternal serum ferritin levels may be indicative of fetal growth restrictions, particularly asymmetric IUGR. For instance, a cutoff value of 48 µg/L for ferritin levels at 34 - 36 weeks' gestation has been shown to effectively distinguish IUGR cases from appropriate for gestational age (AGA) pregnancies. Similarly, another study found that maternal ferritin levels above 13.6 µg/L at 30 - 32 weeks were associated with a significantly higher probability of delivering a low birth weight newborn [4].

Furthermore, low serum ferritin levels have been linked to symmetric IUGR, whereas elevated levels are more commonly associated with asymmetric fetal growth restrictions. Monitoring maternal ferritin levels during pregnancy can provide a useful clinical tool for identifying high-risk pregnancies and guiding timely interventions [5].

The biological mechanisms underlying iron's effects on fetal growth and preterm birth involve several complex pathways, all linked to iron's essential roles in oxygen transport, cellular metabolism, and gene regulation during pregnancy. Some of the primary mechanisms include:

- Iron deficiency in pregnancy can induce hypoxia, as iron is critical for oxygen transport via hemoglobin. This hypoxia triggers maternal and fetal stress responses, including increased levels of serum norepinephrine and corticotropin-releasing hormone (CRH), which are known to influence labor timing and fetal development, contributing to preterm birth and intrauterine growth restriction (IUGR) [6].
- Iron imbalance can lead to the generation of reactive oxygen species (ROS), which cause oxidative stress. Elevated oxidative stress during pregnancy can activate cell death pathways such as ferroptosis, damaging placental and fetal tissues, potentially leading to preterm labor and impaired fetal growth [7].
- Iron deficiency impacts placental growth and gene expression. Changes in placental function, including altered trophoblast differentiation and nutrient transfer, may contribute to fetal growth restriction and increase the risk of fetal distress. Placental iron transport also plays a critical role in ensuring sufficient iron reaches the fetus, with maternal iron deficiency impairing this process [8].
- Maternal iron deficiency has been shown to negatively affect the iron stores of newborns, leading to an increased risk of infant anemia, particularly in the first year of life. Infants born to mothers with IDA often have lower levels of ferritin and hemoglobin at birth, putting them at risk for developmental delays and long-term health consequences. A global review highlighted that up to 52% of pregnant women are affected by iron deficiency, which may cause low birth weight and developmental issues in children [9].
- Maternal serum ferritin levels have been identified as a predictor of fetal growth. Higher ferritin levels are associated with better neonatal outcomes, such as higher birth weight and improved Apgar scores, while low ferritin levels correlate with increased risks of intrauterine growth restriction (IUGR). Moreover, maternal iron deficiency has been linked to reduced fetal iron supply, with iron transporter proteins in the placenta playing a crucial role in ensuring iron delivery to the fetus despite maternal deficiency [3].

- Iron deficiency without anemia can also result in adverse fetal outcomes, including poor fetal growth and preterm delivery. If left untreated, maternal IDA can result in long-lasting effects on the child's neurodevelopment, potentially leading to cognitive impairments later in life. Preventative iron therapy during pregnancy can significantly mitigate these risks and improve neonatal iron status [2].

Aim of the Study

- The primary aim of this study is to determine whether iron deficiency anaemia during the third trimester is associated with an increased risk of intrauterine growth restriction (IUGR), small-for-gestational-age (SGA), and low birth weight at delivery.
- The secondary aim is to explore the relationship between the severity of iron deficiency anaemia and the extent of fetal growth restriction. This includes categorizing anaemia into mild, moderate, and severe forms, and analyzing how these severity levels impact fetal development, with a focus on IUGR and SGA incidence.

Methodology

Study design

This retrospective observational study will utilize the electronic medical records of pregnant women who were seen and delivered at a tertiary hospital within the Dubai Health facilities between June 1, 2020, and December 30, 2022. The primary objective of the study is to investigate the association between maternal iron deficiency anaemia (IDA) and intrauterine growth restriction (IUGR) or low birth weight (LBW) in the third trimester (28 - 40 weeks of gestation).

Study population

The study population will consist of pregnant women who were diagnosed with IUGR or low birth weight during their third trimester. Only cases associated with iron deficiency anaemia will be included in the analysis. Iron deficiency anaemia will be diagnosed using complete blood count (CBC) results, with anaemia defined as a haemoglobin level of less than 11 mg/dL and a serum ferritin level of less than 15 mcg/L. To categorize the severity of iron deficiency anaemia, we will group patients into 3 categories based on their haemoglobin levels: those with normal haemoglobin (11 mg/dL or higher), mild anaemia (less than 11 mg/dL), moderate anaemia (less than 9 mg/dL). This categorization will allow for a detailed analysis of the correlation between the severity of anaemia and the occurrence of adverse fetal outcomes.

Inclusion criteria

The study will include pregnant women diagnosed with iron deficiency anaemia (IDA) during their third trimester of pregnancy, specifically between 28 and 40 weeks of gestation.

Eligibility will be determined by haemoglobin (HB) levels of less than 11 gm/dL and serum ferritin levels below 15 mcg/L, which align with the standard diagnostic criteria for IDA. Participants must have received antenatal care through the Primary Health Care Services System (PHCSS) and be registered within the Dubai Health facilities. These women must have been diagnosed with intrauterine growth restriction (IUGR) or low birth weight during this gestational period to explore the association between IDA and adverse fetal outcomes.

Exclusion criteria

The study will exclude pregnant women with anaemia resulting from causes other than iron deficiency. Specific exclusion criteria include women diagnosed with hereditary anaemias such as beta-thalassemia, beta-thalassemia trait, and sickle cell anaemia. Additionally, women with megaloblastic anaemia, sideroblastic anaemia, or other forms of anaemia unrelated to iron deficiency will be excluded.

Data collection

Clinical data will be extracted from the electronic medical record system used by the Dubai Health facilities, known as Slama. The following maternal and fetal characteristics will be collected: maternal age, parity, gestational age at the time of IUGR or low birth weight diagnosis, nationality, and delivery method (vaginal or caesarean section). Additional data related to fetal outcomes will include foetal delivery weight, foetal growth measurements, and serum ferritin levels in the mother. The fetal weight at the time of diagnosis will also be recorded to provide a comprehensive overview of how maternal iron levels might influence fetal development during pregnancy.

Ethical considerations: Ethical considerations are of utmost importance in this study. Ethical approval will be obtained from the relevant committee to ensure compliance with all guidelines for research involving human participants. To maintain patient confidentiality, no personal identifiers, such as medical record numbers (MRNs) or patient names, will be used in the analysis. Data will be securely stored on the Dubai Health server, with each researcher assigned a unique username and password to access the information. All records will be anonymized, and appropriate safeguards will be implemented to prevent unauthorized access to sensitive data.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Kolmogorov-Smirnov was used to verify the normality of distribution of variables, Paired t-test was used to compare two periods for normally distributed quantitative variables while ANOVA with repeated measures was used for comparing the different studied periods for normally distributed quantitative variables and followed by Post Hoc test (Bonferroni adjusted) for pairwise comparison. Pearson coefficient to correlate between two normally distributed quantitative variables. Significance of the obtained results was judged at the 5% level.

Results

Demographic Data n = (131)	
Parity	
Primigravida	38 (29%)
Multigravidas	93 (71%)
Nationality	
Emirates	99 (75.6%)
Non Emirates	32 (24.4%)
Birth weight	
Normal	110 (84%)
Low birth weight	21 (16%)
Delivery Gestational age	
Term	118 (90.1%)
Preterm	13 (9.9%)
Fetal scan	
Normal	114 (87%)
IUGR	9 (6.9%)
SGA	8 (6.1%)
Anaemia	
Mild HB < 11	114 (87%)
Moderate HB <9	17 (13%)

Delivery method	
Normal	105 (80.2%)
lscs	26 (19.8%)
Delivery weight	
Normal	117 (89.3%)
Abnormal	14 (10.7%)
Fetal incubation	
Yes	43 (32.8%)
No	88 (67.2%)

Table 1: *Demographic data in study population.*

The study's demographic data reveals key insights into the maternal and fetal health of 131 participants. Most women were multiparous (71%) and Emirati (75.6%), with a smaller percentage being primigravida (29%) and non-Emirati (24.4%). Regarding pregnancy outcomes, 84% of the infants had normal birth weights, while 16% had low birth weight, with 9.9% being preterm deliveries. Notably, 87% of the mothers had mild anemia, with 13% experiencing moderate anemia, which could be a risk factor for fetal growth complications.

Fetal health assessments showed that 87% of pregnancies had normal fetal scans, while 6.9% exhibited intrauterine growth restriction (IUGR) and 6.1% were classified as small for gestational age (SGA). These findings suggest a moderate prevalence of growth issues potentially linked to maternal anemia. Furthermore, 32.8% of the infants required incubation, which could be indicative of respiratory or growth-related concerns at birth. The majority of deliveries were vaginal (80.2%), and most infants had normal delivery weights (89.3%).

	Mild HB < 11	**Moderate HB <9**	**P value**	**Statistically significant**
	N = 114	**N = 17**		
Birth weight				
Normal	93 (82.3%)	17 (15.04%)	0.041	Sig.
Low birth weight	21 (18.58%)	0 (0%)		
Delivery Gestational age				
Term	101 (89.38%)	17 (15.04%)	0.149	N. S
Preterm	13 (11.5%)	0 (0%)		
Fetal scan				
Normal	97 (85.84%)	17 (15.04%)	0.233	N. S
IUGR	9 (7.96%)	0 (0%)		
SGA	8 (7.08%)	0 (0%)		
Delivery method				
Normal	100 (88.5%)	17 (15.04%)	0.552	N. S
lscs	14 (12.39%)	0 (0%)		
Fetal incubation				
Yes	38 (33.63%)	5 (4.42%)	0.492	N. S
No	76 (67.26%)	12 (10.62%)		

Table 2: *Comparison of pregnancy outcomes between women with mild and moderate anemia.*

Statistical test used: Chi-square test.

p-value ≤ 0.05 considered statistically significant (95% confidence interval).

Table 2 compares pregnancy outcomes in women with mild (hemoglobin < 11 g/dL) and moderate anemia (hemoglobin < 9 g/dL). A significant difference was observed in birth weight (P = 0.041), with 82.3% of women with mild anemia having infants with normal birth weight, while only 15.04% in the moderate anemia group did. Interestingly, no infants born to women with moderate anemia had low birth weight, suggesting that the severity of anemia may be more closely linked to birth weight outcomes in women with mild anemia.

There were no significant differences in gestational age at delivery (P = 0.149), with both groups showing mostly term pregnancies (89.38% in mild anemia and 100% in moderate anemia) and low rates of preterm births (11.5% and 0%, respectively). Similarly, fetal scan results showed no significant association (P = 0.233), as both groups had high rates of normal fetal scans, and no moderate anemia cases exhibited intrauterine growth restriction (IUGR) or small for gestational age (SGA).

Regarding delivery method (P = 0.552), both groups had similar proportions of normal vaginal deliveries (88.5% for mild anemia, 100% for moderate anemia). Fetal incubation was slightly higher in the mild anemia group (33.63%) compared to moderate anemia (4.42%), but this difference was not statistically significant (P = 0.492).

Discussion

Our research demonstrates a substantial correlation between maternal anemia, particularly varying hemoglobin levels, and newborn birth weight. Multiple studies demonstrate a correlation between maternal anemia and adverse pregnancy outcomes, particularly in relation to birth weight. Kashyap., *et al*. [10] and Chaudhary., *et al*. [11] corroborate our findings, demonstrating that decreased hemoglobin levels lead to lower birth weights.

Conversely, study by Sekhavat., *et al*. [12] found that a hemoglobin concentration below 10 g/dL significantly increased the risk of low birth weight, highlighting the need of addressing anemia as a crucial factor in prenatal development. Dhar., *et al*. [13] also noted a heightened incidence of low birth weight in mothers with hemoglobin levels under 9 g/dL.

The studies conducted by Garshasbi and Nader [2006] and Nahum and Stanislaw [14] confirm that anemia during pregnancy, particularly in severe instances, correlates with adverse delivery outcomes, such as low birth weight and preterm births.

Our study found that maternal iron deficiency anemia did not significantly affect gestational age at delivery, fetal growth, or incidence of intrauterine growth restriction (IUGR) or small for gestational age (SGA) in the study population. Both groups had predominantly term pregnancies and low preterm birth rates. Fetal scan results showed no significant association between maternal anemia and fetal outcomes, suggesting that optimal maternal care, supplementation, or socioeconomic factors may prevent adverse outcomes.

Numerous research have underscored the possible effects of maternal iron deficiency anemia on pregnancy outcomes. Davidson., *et al*. [9] indicated that severe maternal anemia correlates with diminished ferritin and hemoglobin levels in neonates, thereby heightening the risk of intrauterine growth restriction (IUGR) and small for gestational age (SGA). Their findings underscore the imperative of preventive iron supplementation to mitigate these hazards. Schwartz and Thurnau [15] examined the prevalence of iron deficiency anemia in pregnancy and its possible negative impact on pregnancy outcomes, especially when it arises in the first trimester. The authors acknowledged the uncertainties regarding its precise effects on IUGR and SGA, yet they recommended thorough nutritional evaluations and prompt supplementation.

Sharma., *et al*. [16] emphasized the critical need of managing iron deficiency anemia to enhance mother and child health, due to its potential association with problems such as intrauterine growth restriction (IUGR) and small for gestational age (SGA). Chandru, Kabadi, and Lalla [17] emphasized the significance of maternal serum ferritin as a biomarker for forecasting unfavorable outcomes, such as low birth weight and developmental delays, hence underscoring the necessity for early monitoring and intervention. Abu-Ouf and Jan [18]

similarly underscored that maternal anemia is significantly correlated with low birth weight, intrauterine growth restriction (IUGR), and small for gestational age (SGA), and recommended early diagnosis and good management measures [19].

Conclusion

This study highlights that anemia severity impacts birth weight, with mild anemia showing a stronger association with normal birth weight compared to moderate anemia. Gestational age, delivery methods, and fetal outcomes were unaffected by anemia severity. Comprehensive antenatal care appears critical in mitigating adverse outcomes across varying anemia levels during pregnancy.

Bibliography

1. Davidson EM., *et al*. "The interplay between maternal-infant anemia and iron deficiency". *Nutrition Reviews* 81.4 (2023): 480-491.
2. Labib H., *et al*. "Effect of moderate iron deficiency anemia during pregnancy on maternal and fetal outcome". *Al-Azhar International Medical Journal* 51.2 (2021): 1075-1086.
3. Santhakumar S., *et al*. "Impact of maternal iron deficiency anemia on fetal iron status and placental iron transporters in human pregnancy". *Blood Cells, Molecules, and Diseases* 99 (2023): 102727.
4. Akkurt MO., *et al*. "Maternal serum ferritin as a clinical tool at 34-36 weeks' gestation for distinguishing subgroups of fetal growth restriction". *The Journal of Maternal-Fetal and Neonatal Medicine* 30.4 (2017): 452-456.
5. Milašinović L., *et al*. "Significance of serum ferritin level in the prediction of delivery of low birth weight newborns for gestational age". *Srpski Arhiv za Celokupno Lekarstvo* 141.5-6 (2013): 337-343.
6. Allen LH. "Biological mechanisms that might underlie iron's effects on fetal growth and preterm birth". *The Journal of Nutrition* 131.2 (2001): 581S-589S.
7. Zhang Y., *et al*. "Iron metabolism and ferroptosis in physiological and pathological pregnancy". *International Journal of Molecular Sciences* 23.16 (2022): 9395.
8. Roberts H., *et al*. "Maternal iron deficiency alters trophoblast differentiation and placental development in rat pregnancy". *Endocrinology* 162.12 (2021): bqab215.
9. Davidson EM., *et al*. "The interplay between maternal-infant anemia and iron deficiency". *Nutrition Reviews* 81.4 (2023): 480-491.
10. Kashyap A., *et al*. "Association of new-born birth weight with maternal parameters". *International Journal of Reproduction, Contraception, Obstetrics and Gynecology* 8.9 (2019): 3453-3459.
11. Chaudhary MK., *et al*. "P446 Association of maternal hemoglobin level with gestational age and birth weight of babies" (2019).
12. Sekhavat L., *et al*. "Relationship between maternal hemoglobin concentration and neonatal birth weight". *Hematology* 16.6 (2011): 373-376.
13. Dhar B., *et al*. "Newborn anthropometry and its relationship with maternal factors". *Bangladesh Medical Research Council Bulletin* 29.2 (2003): 48-58.
14. Nahum GG and Stanislaw H. "Hemoglobin, altitude and birth weight: does maternal anemia during pregnancy influence fetal growth?". *The Journal of Reproductive Medicine* 49.4 (2004): 297-305.

15. Schwartz William J III and Thurnau Gary R. "Iron deficiency anemia in pregnancy". *Clinical Obstetrics and Gynecology* 38.3 (1995): 443-454.

16. Sharma S., *et al*. "Iron deficiency anemia in pregnancy". *ECS Transactions* 107.1 (2022): 15777.

17. Chandru MC., *et al*. "Serum ferritin level in primigravida and multigravida women". *International Journal of Clinical Biochemistry and Research* 10.2 (2023): 114-117.

18. Abu-Ouf NM and Jan MM. "The impact of maternal iron deficiency and iron deficiency anemia on child's health". *Saudi Medical Journal* 36.2 (2015): 146-149.

19. Lawoyin TO. "The relationship between maternal weight gain in pregnancy, hemoglobin level, stature, antenatal attendance and low birth weight". *The Southeast Asian Journal of Tropical Medicine and Public Health* 28.4 (1997): 873-876.

Volume 13 Issue 12 December 2024