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Iron Deficiency and Iron Storage Markers in Different Pregnancy Stages in Sudanese Women of Different Age

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Abstract

Background: The aim of this study was to evaluate the ID and iron storage markers in pregnant women suffering from anemia during various trimesters attending Omdurman Maternity Hospital in Sudan.

Methods and Results: This cross-sectional study included 205 pregnant women aged 15 to 45 in various trimesters who attended Omdurman Maternity Hospital (Sudan) between May 2022 and January 2023. All pregnant women were divided into two groups: the case group included 159 pregnant women with anemia, and the control group included 46 apparently healthy pregnant women. The blood test parameters were measured using a Sysmex XT-1800i Automated Hematology Analyzer (Japan). The levels of serum iron (SI) and total iron-binding capacity (TIBC) were measured using a Vitrous-350 Chemistry Analyzer (USA). The serum ferritin (SF) levels were measured by electrochemiluminescence immunoassay on the Cobas e411 analyzer (Roche).

Among anemic pregnant women, 33(20.8%) were in the first trimester of pregnancy, 68(42.8%) in the second trimester, and 58(36.5%) in the third. In the case group, more than six deliveries were found in 50.3% of cases, compared to 23.9% in the control group (P=0.0015). The blood levels of Hb and SF were significantly lower in all trimesters in the case group than in the control group. The SI level showed a significantly low level only in the third trimester in the case group, compared to the control group (P<0.05). In the case group, TIBC levels increased from trimester to trimester, reaching maximum values in the third trimester, indicating a low iron level in the blood. In the case group, in the first trimester, the levels of Hb and ferritin did not differ between the age groups of 15-25 years and >26 years. However, in the second trimester, the SF level was statistically lower in the age group of >26 years than in the age group of 15-25 years (45.83±5.0 vs. 49.02±3.71 ng/mL, P=0.0038), but in the third trimester, there was the opposite (37.50±4.9 vs. 26.9±4.5 ng/mL, P=0.000), which indicated a presence of IDA in the age subgroup of 15-25 years.

Conclusion: Pregnant women are at high risk of developing or worsening ID. Every pregnant Sudanese woman should be screened for IDA. (**International Journal of Biomedicine. 2023;13(2):296-300.**)

Keywords: iron deficiency anemia • serum ferritin • serum iron • total iron-binding capacity

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Abbreviations

CBC, complete blood count; **Hb**, hemoglobin; **ID**, iron deficiency**; IDA**, iron deficiency anemia; **RBC**, red blood cell; **SF**, serum ferritin; **SI**, serum iron; **TIBC**, total iron-binding capacity.

Introduction

Iron deficiency (ID) is the most common micronutrient deficiency in children and pregnant women worldwide.[1] ID can be caused by several factors. These causes are classified as follows: increased demand for iron that the diet cannot meet, increased iron loss (usually through blood loss), and nutritional deficiency. During pregnancy, physiologic iron demands increase substantially, and about 1g of iron must be acquired to preserve the maternal iron balance and support fetoplacental development.[2]

In pregnancy, there is a physiological expansion of plasma volume beginning in the first trimester and plateauing by the third,[3] which exceeds the increased production of RBCs and hemoglobin. The resulting hemodilution contributes to the fall in Hb during pregnancy. Anemia in pregnancy can be caused by numerous other factors, including vitamin B12 and folate deficiency, the presence of thalassemia, inflammatory disorders, and, most commonly, ID. As the pregnancy advances, maternal RBC mass increases and placental and fetal growth accelerates, which result in the rise in physiologic iron requirements to 3.0–7.5mg/d in the third trimester.[4]

The World Health Organization (WHO) defines anemia of pregnancy as Hb<11g/dL, or hematocrit <33%, at any time during the pregnancy.[5] The Centers for Disease Control and Prevention (CDC) define anemia of pregnancy as Hb<11g/dL, or hematocrit <33% during the first and third trimesters, and <10.5g/dL or a hematocrit <32% in the second trimester.[6] The WHO defines severe anemia in all persons as a Hb of <7 g/dL and very severe anemia as a Hb of <4 g/dL.[7]

The reticuloendothelial system stores and recycles iron in the body by hemolyzing aged RBCs. Different from iron absorption and recycling, iron excretion lacks a physiologic regulatory system. Iron is stored in the bone marrow, liver, and spleen as ferritin. The ferritin stores in the liver are the body's primary physiologic origin of stockpile iron.

Serum ferritin (SF) concentration is a marker of reticuloendothelial iron stores, and SF concentration below the normal range is the most specific biochemical indicator of ID.[8] Thresholds of SF concentration for identifying ID in pregnancy range from 10µg/L to 30µg/L.[9] The systematic review findings by Daru et al.[10] show that the most frequently used thresholds for defining ID in pregnancy (<12 and <15µg/L) are based on international guidelines informed by consensus meetings undertaken more than 15 years ago,[1,2] not on published evidence. According to UK guidelines on the management of IF in pregnancy, an SF level of <30µg/L in pregnancy is indicative of ID.[11] Low maternal serum ferritin concentrations are associated with ID in neonates.[12,13]

The aim of this study was to evaluate the ID and iron storage markers in pregnant women suffering from anemia during various trimesters attending Omdurman Maternity Hospital in Sudan.

Materials and Methods

This cross-sectional study included 205 pregnant women aged 15 to 45 in various trimesters who attended Omdurman Maternity Hospital (Sudan) between May 2022 and January 2023. All pregnant women were divided into two groups: the case group included 159 pregnant women with anemia, and the control group included 46 apparently healthy pregnant women.

Blood sample collection and IDA diagnosis

About 6mL venous blood was drawn from each pregnant woman: 2mL were placed in an EDTA container to measure CBC using a Sysmex XT-1800i Automated Hematology Analyzer (Japan), and 4 mL were placed in gel tube to measure SI, TIBC using a Vitrous-350 Chemistry Analyzer (USA). SF levels were measured by electrochemiluminescence immunoassay on the Cobas e411 analyzer (Roche).

The normal SI level for women is 60 mcg/dL to 140 mcg/dL, and normal TIBC is 250 mcg/dL to 450 mcg/dL. A TIBC value >450 mcg/dL usually means a low blood iron level.[14]

Statistical analysis was performed using statistical software package SPSS version 21.0 (SPSS Inc, Armonk, NY: IBM Corp). For descriptive analysis, results are presented as mean (M) ± standard deviation (SD). Inter-group comparisons were performed using Student's t-test. Categorical variables were analyzed using the chisquare test with the Yates' correction. A probability value of $P<0.05$ was considered statistically significant.

Results

Among anemic pregnant women, 33(20.8%) were in the first trimester of pregnancy, 68(42.8%) in the second trimester, and 58(36.5%) in the third. In the case group, more than six deliveries were found in 50.3% of cases, compared to 23.9% in the control group ($P=0.0015$). Four to six deliveries were found in 39.6% and 69.6% of subjects in the case and control groups, respectively ($P=0.0003$). In the case group, the interval of <2 years between pregnancies was found in 29.6% of cases versus 4.3% of cases in the control group ($P=0.0004$) (Table 1).

Table 1

The general characteristics of the study groups.

Number of deliveries	Case group n=159	Control group n=46
1-3 times	16 (10.1%)	3 (6.5%)
4-6 times	63 (39.6%)	32 (69.6%)
> 6 times	80 (50.3%)	11 (23.9%)
Interval between pregnancies		
> 2 years	112(70.4%)	44 (95.7%)
< 2 years	47(29.6%)	2 (4.3%)

The blood levels of Hb and SF were significantly lower in all trimesters in the case group than in the control group. The SI level showed a significantly low level only in the third trimester in the case group, compared to the control group ($P<0.05$). In the

case group, TIBC levels increased from trimester to trimester, reaching maximum values in the third trimester, indicating a low iron level in the blood (Table 2).

Table 2.

The levels of Hb, SF, TIBC, and SI in different pregnancy stages.

Pregnancy stage	Parameter	Case group	Control group	*P*-value
First trimester	Hb, g/dL	10.6±0.8	12.4±0.3	0.000
	SF, ng/mL	45.5±6.1	55.2±23.4	0.04
	TIBC, mcg/dL	443.7±108.7	331.5±29.9	0.000
	SI, µg/ dL	46.5±33.4	50.0±9.1	0.652
Second trimester	Hb, g/dl	10.4+±1.0	12.6±0.4	0.000
	SF, ng/mL	55.2±33.6	64.9±34.1	0.008
	TIBC, mcg/dL	488.6±105.1	423.2±86.6	0.026
	SI, µg/ dL	72.5±45.1	59.8±22.7	0.179
Third trimester	Hb, g/dl	10.3±0.9	12.7±0.7	0.000
	SF, ng/mL	58.3±34.5	80.2±53.2	0.001
	TIBC, mcg/dL	522.7±141.1	485.0±70.9	0.09
	SI, µg/ dL	42.9±27.8	74.6 ± 3.01	0.000

We did not find significant differences in the size of the age subgroups (15-25 years and >26 years) between the case and control groups in each trimester (Table 3). In the case group, in the first trimester, the levels of Hb and ferritin did not differ between the age groups of 15-25 years and >26 years. However, in the second trimester, the SF level was statistically lower in the age group of >26 years than in the age group of 15-25 years (45.83±5.0 vs. 49.02±3.71 ng/mL, P=0.0038), but in the third trimester, there was the opposite (37.50±4.9 vs. 26.9±4.5 ng/mL, P<0.0001), which indicated a presence of IDA in the age subgroup of 15-25 years (Table 4).

Table 3.

The size of the age subgroups in different pregnancy stages.

Pregnancy stage	Age subgroup	Case group n (%)	Control group n (%)	*P*-value
First trimester	15-25 yrs.	18 (54.5)	3 (60)	0.956*
	>26 yrs.	15 (45.4)	2 (40)	
Second trimester	15-25 yrs.	35 (51.5)	3 (23.1)	0.060
	>26 yrs.	33 (48.5)	10 (76.9)	
Third trimester	15-25 yrs.	26 (44.8)	7 (25.0)	0.076
	>26 yrs.	32 (55.2)	21 (75.0)	

**Yates' P-value*

Table 4.

The levels of Hb and SF in anemic women of different age subgroups in different pregnancy stages.

Pregnancy stage	Parameter	Age group (years)	mean ± SD	*P*-value
First trimester	Hb, g/dL	15-25 (n=18)	10.5±0.7	0.2417
		>26 (n=15)	10.9±1.2	
	SF, ng/mL	15-25 (n=18)	50.1±3.88	0.9302
		>26 (n=15)	50.0±3.33	
Second trimester	Hb, g/dL	15-25 (n=35)	10.4±1.0	0.7224
		>26 (n=33)	10.3±1.3	
	SF, ng/mL	15-25 (n=35)	49.02 ±3.71	0.0038
		>26 (n=33)	45.83±5.0	
Third trimester	Hb, g/dL	15-25 (n-26)	10.2±0.9	0.6561
		>26 (n=32)	10.3±0.8	
	SF, ng/mL	15-25 (n-26)	26.9±4.5	<0.0001
		>26 (n=32)	37.50±4.9	

Discussion

IDA is still a pervasive public health issue in most developing countries. Pregnant women require iron to compensate for basic losses that cannot be compensated by food alone. The important variable of IDA is the number of pregnancies (gravidity). The present study showed that the risk of developing anemia during pregnancy is significantly associated with more than six deliveries in the patient's history. This conclusion is consistent with data from studies conducted in Saudi Arabia and India, which revealed that many pregnancies and deliveries are linked to a higher likelihood of developing IDA.[15] This could be attributable to iron and other nutrient loss during multiple pregnancies and resource sharing with the fetus. Nevertheless, other studies in Ethiopia and Nepal revealed no link between pregnancy and anemia.[16]

Shorter time intervals between deliveries are another cause of anemia. Our results for the association of anemia of pregnancy with the interval of <2 years between pregnancies are consistent with previous reports.[17-19] This is likely because mothers may not yet replenish essential nutrients, especially iron and folic acid, which were depleted by the previous pregnancy. A study by Mremi et al.[20] showed that post-partum women with less than two-year intervals between the last two pregnancies were about 18 times more likely to have anemia than women with more than two-year intervals (COR=18; 95% CI 8.617–38.617).

The prevalence of anemia in pregnancy is quite high. In a study by Kumar et al.,[21] among 1000 mothers admitted for delivery, more than 50% were anemic at some point of time during their pregnancy, and 39% were anemic throughout.

Physiological changes occur in the second trimester, increasing plasma volume alongside a smaller increase in red cell mass, resulting in hemodilution – recognized as "physiological anemia." In our study, perhaps due to the small size of the control group, we did not observe such dynamics, and in the case group, the Hb level in all semesters was <11g/dL. The incidence of anemia was highest in the second trimester (42.8%) than in the third (36.5%) and first trimesters (20.8%) due to the mother's blood volume expanding and the fetus growing and developing.

Hemoglobin concentration alone lacks sufficient sensitivity and specificity to diagnose ID in pregnancy. Iron-specific biomarkers, such as SF and TIBC, can be utilized to distinguish IDA from other causes of anemia. In our study, the values of SI and TIBC were found to show significant variations between the various trimesters of pregnancy. TIBC levels significantly increased during pregnancy among our subjects, indicating a low iron level in the blood in the third trimester.

The best parameter of maternal iron status currently available is SF concentration. An SF<30 ng/mL is diagnostic for absolute ID, independently of any other parameter.[22] Clinically, the finding of low SF concentration is highly diagnostic for ID. Because ferritin is an acute phase reactant, a normal SF concentration may mask an iron-deficient state if inflammation is present. Measuring C-reactive protein is important if you have to interpret the SF level in conditions of possible inflammation.[23]

Our study found absolute ID in 16.4% of cases among pregnant women with anemia, indicating IDA in the age group of 15-25 years in the third trimester of pregnancy. Many factors may contribute to an increased risk of anemia in people aged 15 to 25, such as rapid growth, blood loss during their monthly periods, and a low-iron diet. Young reproductive-age women differ in many ways from older reproductive-age women, including nutritional requirements, duration of menses, and contraceptive use.[24]

Iron utilization is increased during pregnancy, as iron is required for fetal growth and development,[25] as well as for increased maternal erythropoiesis.[4,11] Until now, the recommended dose of elemental iron for the treatment of ID has been 100–200mg daily.[26,27]) In most studies, supplementing anemic women with iron during pregnancy reduces the rate of iron deficiency anemia and nonanemic ID at term. In some studies, it reduces the risk of adverse outcomes, suggesting that supplementation in this population is beneficial.[28,29] At the same time, the World Health Organization currently recommends universal daily supplementation with 30 to 60mg elemental iron during pregnancy in regions where the prevalence of anemia is 20% or higher; this recommendation also notes the need to take into account a stipulation in malaria-endemic areas where supplementation should be given in conjunction with "adequate measures to prevent, diagnose and treat malaria,"[30] which is especially important for Sudan. According to WHO's latest World Malaria report, Sudan carried the heaviest burden of malaria in the Eastern Mediterranean Region in 2020, accounting for more than half of all cases (56%) and deaths (61%).[31]

In conclusion, pregnant women are at high risk of developing or worsening ID. Every pregnant woman should be screened for IDA. Moreover, the American College of Gynecology and Obstetrics[32] recommends low-dose iron supplementation in the first trimester for all women, regardless of their iron status.

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Competing Interests

The authors declare that they have no competing interests.

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