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# ARTICLE OPEN Screening for iron deficiency among pregnant women

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Iron deficiency (ID) and iron deficiency anemia (IDA) are extremely common in females in Saudi Arabia and are highly prevalent in pregnancy. The Saudi MOH Mother Health Passport recommends that pregnant women undergo testing for complete blood count and ferritin in every trimester. The purpose of this study was to describe practices of screening pregnant women for ID or IDA during pregnancy and to identify the prevalence of anemia and IDA. The inclusion criteria were all patients who had at least 2 antenatal visits in the same center and 336 women were included. It was noted that 591 (51.5%) hemoglobin tests were performed during pregnancy, a 50% gap in comparison with MOH recommendations of measuring Hb in every trimester. The overall prevalence of anemia was 28.6%, 12.2% in the first trimester, 37.2% in the second trimester, and 36.3% in the third trimester. Ferritin was measured in less than 5% of patients, and most women had ferritin levels below 15 ng/ml. Screening practices for IDA and ID among pregnant women are suboptimal, and the prevalence of both entities is substantial. The development of detailed national guidelines for screening and managing ID and IDA in pregnancy is recommended.

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# INTRODUCTION

The World Health Organization estimates that 37% of pregnant women (32 million) have anemia<sup>1</sup>. Anemia is extremely common in Saudi Arabia among non-pregnant women in the childbearing age. Prevalence of anemia in this age group was found to be 38–40%<sup>2</sup>. In a study of all hospital attendees, anemia was identified in 47.1% of women, with those in childbearing age being the age group most affected<sup>3</sup>. The rate of Iron deficiency anemia (IDA) among pregnant women in Riyadh is identified to be 30% according to the Riyadh Mother and Baby Cohort Study (RAHMA) which included more than 10,000 pregnant women<sup>4</sup>.

Iron deficiency anemia (IDA) is the most common cause of anemia worldwide. In addition to fatigue and lethargy, ID (iron deficiency) and IDA are associated with a multitude of adverse birth complications, and increased risk of adverse neurocognitive events in children, including increased risk of autism and schizophrenia<sup>5,6</sup>.

There is a clear need for the prevention and management of ID and IDA among pregnant women. Improved health outcomes can be clearly illustrated by utilizing evidence-based approaches for the optimization of patients' own blood. This is part of patient blood management (PBM), a term coined in 2005 and is increasingly recognized as a better model for patient care compared to the tolerance of anemia and acceptability of avoidable blood transfusions<sup>7</sup>. The WHO policy brief, released in 2021, urges all countries to implement PBM programs<sup>8</sup>.

A review of clinical effectiveness, cost-effectiveness, and guidelines regarding screening and treatment of obstetric anemia was published by the Canadian Agency for Drugs and Technologies in Health in 2019<sup>9</sup>. Ten guidelines from the WHO and 7 different countries met the inclusion criteria Figs. 1 and 2. Five guidelines recommended hemoglobin measurement at each trimester of pregnancy. Four guidelines recommended routine screening of serum ferritin in the first trimester, and 3 recommended ferritin testing for selected pregnant women, including those with hemoglobinopathies or at risk of iron deficiency. British Society for Haematology (BSH), National Institute for Health and Care Excellence (NICE), South Australia Maternal & Neonatal Community of Practice (SAMNCP), Swiss Society of Gynecology and Obstetrics (SSGO), Danish Society of Obstetrics and Gynecology (DSOG) guidelines suggested use of oral iron as first line of management for IDA, with IV iron being reserved for women who are intolerant or do not respond to oral iron, especially after the first trimester. BSH, SAMNCP, SSGO, and DSOG guidelines recommended treatment for ID even without IDA.

The goal of this study is to understand the patterns of practice of obstetricians in an academic center in Saudi Arabia regarding screening and management of ID and IDA in pregnancy. A secondary goal was to describe the results of such screening, to identify the percentage of pregnant women with ID or IDA and assess for potential associations between anemia with patient characteristics.

# METHODS

### Study design and participants

The study was performed at a tertiary care academic center in Jeddah, Saudi Arabia, and followed a retrospective observational design. Pregnancy records of all women who delivered in our center from the first of January to the end of March 2022 were reviewed. Existing patient and laboratory records were reviewed to collect the following data: laboratory testing dates and results (for anemia and iron deficiency), medication orders, and physician notes for iron supplements or intravenous iron use. Inclusion criteria: booked pregnant women (defined as those who visited the antenatal care clinics at least twice during the current pregnancy) and delivered in our center.

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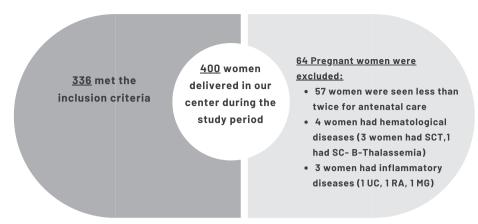


Fig. 1 Flowchart of participants screened for eligibility in the final study. SCT sickle cell Trait, SC-B-Thalassemia sickle cell beta thalassemia, UC ulcerative colitis, RA rheumatoid arthritis, MG myasthenia gravis.

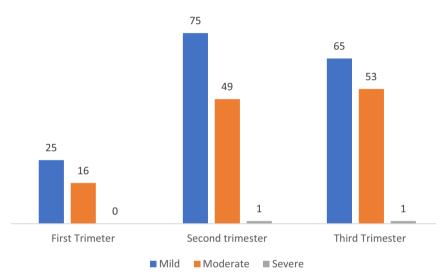


Fig. 2 Prevalence of anemia among pregnant women according to the pregnancy trimester (%) (n = 336).

# **Exclusion criteria**

Pregnant women with thalassemia or sickle cell disease, and those who were critically ill or who had a diagnosis of an inflammatory condition, such as inflammatory bowel diseases or connective tissue diseases.

# Outcomes

The primary outcome of interest was to describe the patterns of anemia screening and management in pregnant women according to the trimester. The secondary outcomes of the study were the prevalence of anemia, the average level of hemoglobin and ferritin, and whether any associations could be identified between anemia and patient characteristics.

Anemia in pregnant women was defined as hemoglobin less than  $11 \text{ g/dL}^{10}$ . Anemia severity was classified into three categories: mild (10-10.9 g/100 ml), moderate (7.0-9.9 g/100 ml), and severe (less than 7.0 g/100 ml). Iron deficiency was defined as ferritin less than or equal 30 ng/mL or transferrin saturation less than  $20\%^{11}$ . The study used one way analysis of variance to compare between group in relation to the study outcomes.

# Data gathering methods

Pregnant women who delivered at our center were identified and screened electronically. Data were collected from electronic medical records using a data collection sheet (Microsoft Excel). Statistical analysis: analyses of the data were done using SPSS Version 26. Multiple regression tests and T-tests were conducted to aid in analyzing the data. A *p*-value less than 0.05 was considered significant.

## RESULTS

A total of 591 (51.5%) hemoglobin tests were conducted during pregnancy for the study sample, where a total of (1008) hemoglobin tests were expected if hemoglobin was evaluated in every trimester<sup>12</sup>. A total of 288 tests were diagnostic of anemia; of whom 41 were identified in the first trimester, 125 in the second, and 122 in the third. The overall prevalence of anemia was 28.6% (288/336), 12.2% (41/336) in the first trimester, 37.2% (125/336) in the second trimester and 36.3% (122/336) in the third trimester. The mean hemoglobin ranged between 10.81 in the second and third trimesters to 11.5 in the first trimester. Table 1 shows the frequencies and prevalence of anemia by trimesters.

<b>Table 1.</b> Prevalence of anemia among pregnant women according to the pregnancy trimester ( $n = 336$ ).					
Hemoglobin level	First trimester (n, %)	Second trimester (n, %)	Third trimester (n, %)	Overall (n, %)	
<11 g/dl	41 (12.2)	125 (37.2)	122 (36.3)	288 (28.6)	
≥ 11 g/dl	88 (26.2)	102 (30.4)	113 (33.6)	303 (30.1)	
No Hb available	207 (61.6)	109 (32.5)	101 (30.1)	417 (41.3)	
Mean (SD) of Hemoglobin	11.50 (1.13)	10.81 (1.16)	10.81 (1.26)	11.04 (1.03)	

<b>Table 2.</b> Level of anemia among anemic pregnant women accordingto the pregnancy trimester.						
Anemia level	First trimester (n, %)	Second trimester (n, %)	Third trimester (n, %)			
Mild	25 (60.9)	75 (60)	68 (55.7)			
Moderate	16 (39.02)	49 (39.2)	53 (43.4)			
Severe	0	1 (2.4)	1 (0.82)			
Anemia Level: Mild Anemia (10–10.9 g/100 ml), Moderate Anemia (7.0–9.9 g/100 ml), and Severe Anemia (less than 7.0 g/100 ml).						

Results shown in Table 2 reveal that most anemic pregnant women were classified as mild and moderate, with only two women having severe anemia detected in the second and third trimesters (Table 3).

In regard to screening for iron deficiency through measurement of ferritin among the 129 women seen in the first trimester, ferritin was tested in 4 (4.5%) women who had no anemia, in 6 (24%) with mild anemia, and in 2 (12.5%) with moderate anemia. Iron was measured in 3 (3.4%) women with no anemia and in 3 (12%) women with mild anemia and 1 (6.3%) with moderate anemia. Total iron binding capacity was not measured for any patient. Among 227 women seen in the second trimester, ferritin was tested in 3 (2.9%) of women who had no anemia, 1 (1.33%) for mild, 7 (14.3%) for moderate, and 1 (100%) for severe. Serum iron was measured in 1 (9.98%) for women who had no anemia, 1 (1.33%) with mild anemia, 5 (10.2%) with moderate anemia, and 1 (100%) with severe anemia. Among 235 women seen in the third trimester, ferritin was tested in 5 (4.4%) women who had no anemia, 4 (5.9%) with mild anemia, 6 (11.3%) with moderate anemia, and 1 (100%) with severe anemia. Serum iron was measured in 1 (0.8%) woman who had no anemia, 2 (2.9%) with mild anemia, 5 (9.4%) with moderate anemia, and 1 (100%) with severe anemia (Table 4).

Ferritin was rarely measured in our cohort, with less than 5% of women having ferritin measured in any trimester (Table 5). When Ferritin was measured, most women had levels below 15 ng/ml.

The pattern of physicians not screening for iron deficiency did not improve as pregnancies progressed. Screening practices and screening results are summarized in Table 6 and Supplementary Materials.

When charts were reviewed for management of pregnant women with anemia, it was noted that almost all patients were prescribed oral iron: 41/41 (100%) in the first trimester, 124/125 (99.2%) in the second trimester, and 121/122 (99.2%) in the third trimester. IV iron was also prescribed in 6/41 (14.6%) in the first trimester, 12/125 (9.6%) in the second trimester, and 16/122 (13.1%) in the third trimester. Blood transfusion was given to 2 patients with severe anemia in the third trimester.

## DISCUSSION

Anemia during pregnancy has significant implications, including altered materno-fetal circulation, deviations from standard uterine artery pulsatility index<sup>13</sup>, umbilical artery<sup>14</sup>, and fetal growth<sup>15</sup>, with potential long-term consequences for newborns in the presence of significant maternal anemia during pregnancy<sup>16</sup>.

Our study shows that the overall prevalence of anemia among pregnant women in our center is 28.6%. The prevalence is high later in pregnancy, reaching 36.3% in the third trimester. This result is consistent with the findings in RAHMA and consistent with the high prevalence of anemia among women in Saudi Arabia<sup>4</sup>. Most patients in our study had mild or moderate anemia, but the 2 patients with severe anemia received blood transfusions which were likely avoidable with earlier anemia identification, iron replacement, and follow-up.

The Saudi MOH recommendations in the Mother Health Passport suggest that a CBC and ferritin level must be tested in every trimester<sup>17</sup>. Following this practice would allow improved identification and follow-up of anemia in this high-risk patient population. According to our data, there is a gap of 50% in orders of CBC (complete blood count) in pregnant women compared to ordering a CBC in every trimester. If the inconvenience of a laboratory visit may be a deterrent for some patients, obstetrics clinics may be equipped with point-of-care testing devices that could provide a hemoglobin and/or hematocrit value within minutes<sup>18</sup>. Point-of-care testing technologies are widely available as handheld devices or compact benchtop devices. Operating these devices requires staff training and competency evaluation.

In a high-resource setting in Canada, Teichman and colleagues demonstrated that more than 50% of pregnancies were complicated by ID, but only 40% of women were screened for it<sup>19</sup>. In our study, less than 5% of pregnant women underwent ferritin evaluation. Among those tested, the majority had ferritin levels below 15 ng/ml. These results should urge physicians to screen more women for ID, with or without anemia. Although not in wide use yet, point of care testing devices have been developed for ferritin measurement<sup>20,21</sup>. Despite limitations of sensitivity and specificity for point-of-care testing in general, their use may be helpful for screening for ID and IDA, reducing the number of patients being sent for central laboratory testing. The study results are consistent with those reported by Drukker, Staines-Urias, Villar, Barros, Carvalho, Munim, McGready, Nosten, Berkley and Norris<sup>1</sup> who found there were no neonatal deaths and satisfactory growth, health and motor 115 development of the infants at 1 and 2 years of age were documented. The only a very small 116 proportion (2.8-6.5%) of the variance of Doppler indices was due to between site differences; 117 in addition standardized site difference estimates were marginally outside this threshold in 118 only one of xx comparisons, and this supported the decision to pool data from the three study 119 sites.

We were reassured to find that almost all patients with anemia received oral iron supplementation, with up to 15% receiving intravenous iron. Although oral iron is usually the first line of

	No anemia (Hb: ≥11) ( <i>N</i> = 88; 26.19%)	Mild anemia (Hb:10–10.9) ( <i>N</i> = 25, 7.44)	Moderate anemia (Hb:9.9–7) (N = 17; 5.06%)	Severe Anemia (HB < 7) (N = 2; 0.05%)	β	Ρ	OR(CI)
Age (mean ± SD)	32.7 ± 5.3	29.5 ± 6.3	32.5 ± 5.6	31.47 ± 4.68	0.028	0.581	1.02 (0.931–1.135)
<30	27 (30.68)	10 (40%)	5 (29.4)	1 (0.2.9%)			1.35 (0.219–8.33)
30–34	28 (31.82)	10 (40)	7 (41.1)	-			1 (0.173–5.79)
35–39	25 (28.41)	3 (12)	2 (11.8)	1 (0.2.9%)			3.12 (0.377-25.91)
40+	8 (9.09)	2 (8)	3 (17.6)	-			1
Gravidity (mean ± SD)	3.35 ± 1.9	3 ± 1.7	4±1.9	3.2 ± 1.29	-0.169	0.271	0.844 (0.645–1.104)
Parity (mean ± SD)	1.86 ± 1.5	1.56 ± 1.2	2.38 ± 1.7	$2.41 \pm 0.64$	-0.219	0.215	0.804 (0.569–1.14)
Abortion (mean ± SD)	$0.47\pm0.86$	$0.44 \pm 0.96$	$0.63 \pm 0.95$	$0.74\pm0.88$	-0.195	0.500	0.823 (0.469–1.45)

Table summarizes the difference in sociodemographic characteristics between anemic and non-anemic women. The mean age was similar in the three groups; however, women ages (35-39) were more likely to be associated with anemia when compared to women in other age groups (odds ratio [OR] = 3.12, Cl 0.337–25.91). The mean gravidity was similar in the three groups; however, the value of beta indicates that there is an inverse relationship between gravidity and hemoglobin. The same was noted for parity and number of abortions.

Table 4.Average hemoglobin and serum ferritin levels of participants by trimesters.					
	Hemoglobin: mean (SD) ( <i>n</i> , %)	Serum ferritin: median (lower quartile-upper quartile			
First trimester	11.50 (1.14)	9.90 (4.07–23.05)			
Second trimester	10.81 (1.16)	10.07 (3.78–20.82)			
Third trimester	10.81 (1.2)	10.40 (4.9–16.1)			
Overall	11.04 (1.03)	10.14 (5.42–18.24)			
P value	0.084	0.645			

The results of one-way analysis of variance showed there are no differences in hemoglobin and ferritin levels of participants by trimesters, where P-value > 0.05.

<b>Table 5.</b> Ferritin levels among pregnant women according to the trimester $(n = 336)$ .						
Level of ferritin	<15	15-30	>30	Not measured		
First trimester (n, %)	9 (2.67)	2 (0.59)	1 (0.3)	324 (96.4)		
Second trimester (n, %)	8 (2.83)	2 (0.59)	2 (0.59)	324 (96.4)		
Third trimester (n, %)	10 (2.97)	3 (0.89)	2 (0.59)	321 (95.5)		
Overall (n, %)	27 (2.67)	7 (0.69)	5 (0.50)	969 (96.13)		

management in patients with ID or IDA, more pregnant women achieve target hemoglobin with intravenous iron, and more patients have a hemoglobin increase in 4 weeks<sup>22</sup>. Among anemic patients in the third trimester, the use of intravenous iron is preferred to rapidly treat anemia before delivery. Intravenous iron is also indicated in patients with intolerance of oral iron or inadequate response to it.

Available research does not clearly identify the hemoglobin level that must trigger a blood transfusion during pregnancy. The Network for the Advancement of Patient Blood Management,

Haemostasis and Thrombosis (NATA) consensus statement about PBM in obstetrics recommends that obstetric units have quidelines for transfusion in non-bleeding patients who are anemic during pregnancy or postpartum<sup>23</sup>. A single unit transfusion is recommended followed by reevaluation for the need of additional units. In general, transfusion in patients with IDA may be avoided with access to early screening and effective management in all patient populations at risk of IDA. Transfusion is associated with a myriad of adverse effects and complications, including alloimmunization which may put future pregnancies at risk of hemolytic disease of the fetus and newborn. Additionally, these results are supported by Kassebaum, Arora, Barber, Bhutta, Brown, Carter, Casey, Charlson, Coates and Coggeshall<sup>2</sup> Who documented that anemia, developmental intellectual disability, hearing loss, epilepsy, and vision loss are important contributors to childhood disability that can arise from multiple causes. Maternal and reproductive health remains a key cause of disease burden in adolescent females, especially in lower-SDI countries. In low-SDI countries, mortality is the primary driver of health loss for children and adolescents, whereas disability predominates in higher-SDI locations; the specific pattern of epidemiological transition varies across diseases and injuries.

We believe that pregnant women and health care professionals in Saudi Arabia would benefit from development of detailed national guidelines to guide screening and management of ID and IDA in pregnancy. Although the Mother Health Passport developed by the MOH suggests measurement of hemoglobin and ferritin in each trimester, it neither recommends a specific ferritin level, nor does it provide guidance of indications of different treatment options. The Anemia Clinical Pathway endorsed by the Saudi Commission for Health Specialties is a helpful document to educate about approaches to anemia investigation and management in general, pregnancy-specific information are limited<sup>24</sup>. Once guidelines are developed, lessons learned through implementation science should be used to improve compliance<sup>25</sup>.

The main limitation of the study is that it was performed in a single tertiary care academic center. Results may be reflective of practices in other academic centers but practice in primary health care centers may be different. The factors that affected ordering practices of intravenous iron could not be identified in this study. **Table 6.** Comparing ferritin testing among women with and without anemia according to trimester (N = 335).

	First trimester		Second trimester		Third trimester	
	Women with	Women without	Women with	Women without	Women with	Women without
	anemia	anemia	anemia	anemia	anemia	anemia
Ferritin testing	8 ferritin test	4 ferritin test	9 ferritin test	3 ferritin test	10 ferritin test	5 ferritin test
performed, %	(19.5%)	(4.5%)	(7.2%)	(2.9%)	(8.2%)	(4.4%)
Median ferritin level (µg/l)	5.50 μg/l	19.90 μg/l	6.80 µg/l	13.20 μg/l	8.46 μg/l	12 µg/l

# DATA AVAILABILITY

The study authors declare that data are available upon request.

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## AUTHOR CONTRIBUTIONS

W.S.A.Q.: Methodology, Data curation, Writing- Original draft preparation, Software, Validation. R.A.A.: Conceptualization, Investigation. R.A.Q.: Writing- Reviewing and Editing. M.A.B.: Conceptualization, Writing- Reviewing and Editing, Supervision. All authors read and approved the final manuscript.

#### **COMPETING INTERESTS**

The authors declare no competing interests.

# **ETHICS APPROVAL**

This research with IRB name: Screening for Iron Deficiency among Pregnant Women has been approved by the KAUH Research ethics committee with reference No. 129-22, Date: March 7, 2022.

#### ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s44294-024-00006-2.

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