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ORIGINAL RESEARCH

Associations between iron deficiency anemia and clinical features among pregnant women: a prospective cohort study

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Background: Iron deficiency anemia (IDA) during pregnancy is a common and preventable disorder. It remains a contributing factor to maternal morbidity and mortality and is associated with high perinatal mortality rate.

Objective: To determine the prevalence of IDA and its associated clinical features among pregnant women.

Methods: This analytical prospective cohort study included 1,579 pregnant women who attended an antenatal clinic, Women's Specialized Hospital, King Fahad Medical City, Riyadh, Saudi Arabia, between January 20[illegible] April 2018. The type of anemia and its associated maternal and fetal outcomes were determined.

Results: About 702 women were confirmed to have IDA, with a prevalence of 44.5 %. Most women (79.2%) were younger than 35 years. A low hemoglobin concentration was reported in 45 % of participants. The major type of anemia was microcytic hypochromic anemia (98.7%). More than half of the participants (57.3%) reported use of iron supplementation during pregnancy. IDA anemia was highest in pregnant women with gravidity >8 in 40 (56.3%) compared to normal pregnant women 31 (43.7%), and lowest in those with gravidity ≤2 in 281 (41.4%) compared to normal pregnant women 397 (58.6%). The difference was statistically significant, P=0.024. Similarly, this type of anemia was highest in those with parity of >3 (53.3%) and lowest in nulliparous women (39.3%) compared to normal pregnant women (46.7%) and (60.7%), respectively. This was statistically significant P=0.002. IDA had significantly (P=0.012) lower spontaneous vaginal delivery rates compared with normal pregnant women (44.5% vs 55.5%, respectively). IDA had significantly (P=0.017) lower antenatal fetal distress rates compared to normal pregnant women (68.5% vs 31.5%, respectively).

Conclusion: Anemia in general and microcytic hypochromic anemia in particular were significantly associated with higher gravidity and parity. The significant outcome associated with IDA during pregnancy was a lower rate of spontaneous vaginal delivery and antenatal fetal distress. Compliance with iron supplementation in order to prevent maternal and fetal adverse outcomes was observed.

Keywords: microcytic hypochromic anemia, pregnancy, iron deficiency anemia

Introduction

Iron deficiency anemia (IDA) is the most common nutritional deficiency problem affecting pregnant women worldwide.[1] The high prevalence of iron and other micronutrient deficiencies among women during pregnancy in developing countries is of concern, and maternal anemia is still a cause of considerable perinatal morbidity and mortality.[2–4] Overall prevalence of iron deficiency in pregnant women in the US is

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about 18%,[5] and in the UK, the prevalence was estimated to be 24% in a recent cross-sectional study.[6]

IDA in pregnancy has been defined by the National Academy of Sciences panel on nutrition and pregnancy as ferritin levels of less than 12 µg/L.[7] Serum ferritin may be a better indicator of iron status, as examination of iron stores in bone marrow is impractical.[8] However, historically, blood hemoglobin (Hb) levels have been used, this test being simple and inexpensive. The WHO defines anemia in pregnancy as Hb levels of less than 11 g/dL.[9]

Most women begin their pregnancy with partially or completely depleted iron reserves.[10] During pregnancy, there is an increase in both red cell mass and plasma volume to accommodate the needs of the growing uterus and fetus.[11] The plasma volume increases more than the red cell mass does, leading to a fall in the concentration of Hb in the blood, despite an increase in the total number of red cells. This drop in Hb concentration decreases blood viscosity and is thought to enhance placental perfusion, providing better maternal-fetal gas and nutrient exchange.[12] Nonetheless, the significance of this physiological hemodilu of pregnancy for women and their babies is controversi as is the level of Hb at which they would derive a benefit from iron treatment.[13] Maternal iron requireme s av age 1,000 mg/d.[14]

Severe anemia during pregnancy results in ma al and fetal adverse outcomes. Maternal adverse utcomes in de preterm labor, preeclampsia, sepsis, post rtu hemorrhage, and an increased need for blood transfusion.[15] e fetal adverse outcome consists of a high tal mortality rate at the third trimester of gestation.[16] In ditio IDA of moderate degree can impact the motor and tal de elopment of children and adolescents.[17,18]

In the present study, we med t determine the prevalence of IDA in pregnant wome nd it associated clinical features by comparing these outcomes w h those of pregnant women with normal Hb levels.

Methods

An analytical prospective cohort study was carried out, which included 1,579 pregnant women who attended Women's Specialized Hospital, King Fahad Medical City, Riyadh, Saudi Arabia, between January 2018 and April 2018. We examined the hematological status and serum ferritin between 16 and 20 weeks of pregnancy. Exclusion criteria included malignancies, chronic renal or liver diseases, diabetic, hypertension disorder, known cases of thalassemia and hemoglobinopathies, vitamin B12 deficiency anemia, folic acid deficiency anemia, chronic inflammatory diseases, and having had a blood transfusion within 6 months before enrolment in the study.

Data were collected from the perinatal database, which consists of information collected uniformly according to predefined criteria immediately after delivery by an obstetrician. Coding is done after assessing the medical prenatal care record and th outine hospital documents. We analyzed the llowing ch acteristics: maternal age, gravidity, parity, abo ions, tw n pregnancy, medical history (diabetes mellitus, hy tension, and preeclampsia), and iron su leme tation. We also examined the following obstetric cha eristics: apparent congenital malformation, in auterine g th (defined as birth weight below the s -sp cific 5th percentile of weights for gestational age), antenata tal distress, and mode of delivery (vaginal: s ontaneous or induced, instrumental: forceps or ventouse, and cesare : elective or emergency). In addition, we investigated ma rnal and perinatal outcomes: preterm labor (de ed s birth before 37 completed weeks of gestation), postpartum hemorrhage, packed cell transfusion, maternal death, Apgar score at 1 minute and 5 minutes, birth weight, admission to the neonatal intensive care unit (NICU), and perinatal mortality.

As study criteria, we used the WHO definition of anemia in pregnancy (Hb levels of less than 11 g/dL)[9] and the definition by the National Academy of Sciences panel on nutrition and pregnancy of IDA (microcytic hypochromic anemia) in pregnancy (ferritin levels of less than 12 µg/L).[7] We recorded Hb, hematocrit (HCT), red cell distribution width (RDW; erythrocyte volume), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH). We then determined the types of anemia on the basis of these variables.

The protocol was reviewed and approved by the Institutional Review Board of King Fahad Medical City in Riyadh, Saudi Arabia. All data were entered into an electronic database without personal identifiers to maintain confidentiality. Patient consent was waived as no patient identifiers were included nor was the patient care affected or influenced in any way. This article does not contain any studies with animals performed by any of the authors.

The data were analyzed by using SPSS version 22.0. Demographic characteristics were expressed as mean (± SD) and range. The outcome variables were expressed as the absolute number (percentage). The *P*-value was based on Fisher's exact test for categorical data and the Mann–Whitney *U* test for quantitative variables. A *P*-value of <0.05 was considered to be statistically significant.

Results

The study included 1,579 pregnant women. About 702 women were confirmed to have IDA, with a prevalence of 44.5%. Patients' demographics are presented in Table 1. Most of the participants (1,260 [79.8%]) were younger than 35 years. The median value of gravidity was 3, ranged between 1 and 15; of parity was 2, ranged between 1 and 13; and of abortion was 1, ranged between 1 and 11. Intrauterine growth restriction was reported in 52 (3.3%) participants and antenatal fetal distress in 73 (4.6%) participants. Cesarean delivery was reported in 630 (39.9%) participants, whereas instrumental or vacuum-assisted delivery was used in 66 (4.2%). Spontaneous vaginal delivery was reported in almost half of the cases (883 [55.9%]), and most of them were spontaneous (753 [47.7%]). Emergency cesarean section was reported in 383 (24.3%) cases. Preterm labor was reported in 191 (12.1%) cases. The Apgar score at 1 minute ranged between 0 and 10 with a mean of 9.2±1.6, whereas that at 5 minutes ranged between 0 and 9 with a mean of 8.2±1.6. Apparent congenital malformation was observed in 51 (3.2%), admission to NICU in 136 (8.6%), postpartum hemorrhage in 59 (3.7%), and intrauterine fetal death in 29 (1.8%) cases.

From Table 1, low level of Hb concentration was reported in 711 (45%) participants, low HCT values in 97 (61.9%), and low RDW values in 52 (3.4%). The MCH concentration was below normal in 10.8% of the cases. The ferritin level was low in 702 (45%) cases. The MCV was below normal in 486 (30.7%) and the mean corpuscular Hb was below normal in 531 (33.6%) cases. The major reported type of anemia was microcytic hypochromic anemia (702 [98.7%]). More than half of the participants (905 [57.3%]) reported the use of iron supplementation during pregnancy. The birth weight of the first baby was 2.99±0.64 kg and of the twin babies was 2.15±0.67 kg.

From (Table 2), it is evident that the studied factors could be associated with IDA. IDA anemia was highest in pregnant women with gravidity >8 at 40 years (56.3%) compared to normal pregnant women at 31 years (43.7%), and lowest in those with gravidity ≤2 (281 [41.4%]) compared to normal pregnant women (397 [58.6%]). The difference was statistically significant (P=0.024). Similarly, this type of anemia was highest in those with parity of >3 (53.3%) and lowest in nulliparous women (39.3%) compared to normal pregnant women (46.7%) and (60.7%), respectively. This was statistically significant (P=0.002). IDA had significantly (P=0.012) lower spontaneous vaginal delivery rates compared with normal pregnant women (44.5% vs 55.5%, respectively). This anemia was reported in more than half of the women (132 [54.3%]) who delivered by elective cesarean section, in 153 (40.2%) of those who delivered by emergency cesarean section, and in 32 (50%) of those who delivered by ventouse. IDA had significantly (P=0.017) lower antenatal fetal distress rates compared with normal pregnant women (68.5% vs 31.5%, respectively). There is some missing data in this study parameter and hence is not included in this analysis. IDA was not significantly associated with other maternal and fetal characteristics as illustrated in Table 2.

Discussion

The prevalence of anemia was reported to be the highest in Indian women (89%, while it was 16% in black Caribbean women and 6%–7% in Irish and Chinese women. In this study the prevalence was 44.5%, which is slightly higher than that reported in these countries, and the prevalence based on low HCT was 61.9%, which is higher than that reported in European countries (at about 50%).[19,20] A higher gravidity and parity was reported in women with anemia in general and IDA in particular. Similar results have been reported previously.[19]

Much of the information regarding IDA in pregnancy and its adverse outcomes is controversial. Two important points should be considered: the gestational age at which the determination of Hb is performed and the degree of anemia identified. Regarding the first point, throughout the first and second trimesters of pregnancy, Hb and HCT levels decline because of the physiological expansion of plasma volume.[21] Late in the second to early third trimester, Hb and HCT levels reaches its lowest level and then rises again nearer to term. Therefore, the best time to detect any risk associated with maternal anemia would be early in pregnancy, a fact that has been demonstrated in many studies.[22,23] Thus, any estimation of Hb concentration after 20 weeks of gestation is reasonably representative of the fall in concentration induced by pregnancy.[24]

The second point that should be considered is IDA during pregnancy, as the association with adverse pregnancy outcomes is also controversial. The association between IDA and birth weight has been documented, as has been the association between IDA and preterm delivery.[25] However, in the present study, anemia was significantly associated with a lower rate of spontaneous vaginal delivery. This finding might be attributed to the fact that anemia in our study was mostly mild and most participants were taking iron supplements. In agreement with others, we assume that iron supplementation during pregnancy may have a protective effect against adverse outcomes. On the other hand, it has been reported in several studies that severe maternal anemia in the first trimester is

Table 1 Characteristics of 1,579 study subjects

Characteristics	Characteristics	n (%)[a]
Mother's age, years	<35	1,260 (79.8)
	≥35	319 (20.2)
Gravida	1–2	685 (43.4)
	3–4	475 (30.1)
	5–6	254 (16.1)
	7–8	92 (5.8)
	>8	73 (4.6)
	Median (min, max)	3 (1, 15)
Parity	Nulliparous	428 (27.1)
	1–3	900 (57.0)
	>3	251 (15.9)
	Median (min, max)	2 (1, 13)
Abortions	No	1,044 (66.1)
	1–3	484 (30.7)
	>3	51 (3.2)
	Median (min, max)	1 (1, 11)
Intrauterine growth restriction		52 (3.3)
Antenatal fetal distress		73 (4.6)
Mode of delivery	Vaginal	883 (55.9)
	Cesarean	630 (39.9)
	Instrumental/vacuum assisted	66 (4.2)
Type of cesarean	Elective	249 (15.8)
	Emergency	383 (24.3)
Type of vaginal delivery	Spontaneous	753 (47.7)
	Induced	128 (8.1)
Type of instrumental delivery	Forceps	2 (0.1)
	Ventouse	64 (4.1)
Preterm labor		191 (12.1)
Maternal death		0 (0.0)
1-minute Apgar score	≥7	1,461 (92.5)
	4–3	51 (3.2)
	4	67 (4.2)
	Mean ± SD (min, max)	9.2±1.6 (0, 10)
5-minute Apgar score	≥7	1,529 (96.8)
	4–3	38 (2.4)
	4–6	12 (.8)
	Mean ± SD (min, max)	8.2±1.6 (0, 9)
Twin pregnancy		66 (4.2)
Apparent congenital malformation		51 (3.2)
Admission to NICU		136 (8.6)
Postpartum hemorrhage		59 (3.7)
Intrauterine fetal death		29 (1.8)
Hb	Normal	867 (54.9)
	Low	711 (45.0)
	High	1 (0.0)
HCT	Normal	601 (38)
	Low	975 (61.9)
	High	3 (.2)
Ferritin level	Normal	868 (54.9)
	Low	702 (45)
	High	9 (0.9)
RDW (erythrocyte volume)	Normal	1,100 (69.6)
	Low	52 (3.4)
	High	427 (27)

(*Continued*)

Table 1 (*Continued*)

	Characteristics	n (%)[a]
MCV	Normal	1,068 (68)
	Low	486 (30.7)
	High	25 (1.3)
MCH	Normal	986 (62.8)
	Low	531 (33.6)
	High	62 (3.6)
Anemia type	Normal (MCV + MCH): Normocytic normochromic	2 (0.3)
	Low (MCV + MCH): Microcytic hypochromic ane a	702 (98.7)
	High (MCV + MCH): Macrocytic hyperchromic mia	7 (1.0)
MCHC (erythrocyte)	Normal	1,379 (87.3)
	Low	170 (10.8)
	High	30 (1.9)
Iron used	No	674 (42.8)
	Yes	905 (57.3)
Birth weight (kg) of first baby	Mean ± SD (min, max)	2.99±0.64 (0.32, 6.32)
Birth weight (kg) of twin baby	Mean ± SD (min, max)	2.15±0.67 (0.41, 3.28)

Notes: [a]Data are presented as n (%) except where otherwise indicated.
Abbreviations: Hb, hemoglobin; HCT, hematocrit; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; NICU, neonatal intensive care unit; RDW, red cell distribution width.

Table 2 Microcytic hypochromic anemia (MHA) in study subjects

Characteristics		Normal (n=867)[a]	MHA (n=702)[a]	*P*-value
Mother's age, years	<35	692 (55.5)	555 (44.5)	0.381
	≥35	164 (52.7)	147 (47.3)	
Gravida	1–2	397 (58.6)	281 (41.4)	0.024
	3–4	259 (55.3)	209 (44.7)	
	5–6	123 (49.4)	126 (50.6)	
	7–8	46 (50.0)	46 (50.0)	
	>8	31 (43.7)	40 (56.3)	
Parity	Nulliparous	256 (60.7)	166 (39.3)	0.002
	–3	485 (54.5)	405 (45.5)	
	>3	115 (46.7)	131 (53.3)	
Abortions	No	579 (56.2)	452 (43.8)	0.374
		252 (52.8)	225 (47.2)	
	>3	25 (50.0)	25 (50.0)	
Gestational age, weeks	≥37	755 (54.5)	631 (45.5)	0.291
	<37	101 (58.7)	71 (41.3)	
Intrauterine growth restriction	No	825 (54.7)	682 (45.3)	0.394
	Yes	31 (60.8)	20 (39.2)	
Antenatal fetal distress	No	806 (54.3)	679 (45.7)	0.017
	Yes	50 (68.5)	23 (31.5)	
Mode of delivery	Vaginal	485 (55.7)	385 (44.3)	0.709
	Cesarean	337 (54.2)	285 (45.8)	
	Instrumental or vacuum assisted	34 (51.5)	32 (48.5)	
Delivery type	Elective CS	111 (45.7)	132 (54.3)	0.012
	Emergency CS	228 (59.8)	153 (40.2)	
	Forceps	2 (100.0)	0 (0)	
	Induced	72 (56.3)	56 (43.8)	
	Spontaneous	411 (55.5)	329 (44.5)	
	Ventouse	32 (50.0)	32 (50.0)	
Preterm labor	No	753 (54.8)	622 (45.2)	0.698
	Yes	103 (56.3)	80 (43.7)	

(*Continued*)

Table 2 (*Continued*)

Characteristics		Normal (n=867)[a]	MHA (n=702)[a]	*P*-value
Admission to NICU	No	854 (55.0)	698 (45.0)	0.286
	Yes	2 (33.3)	4 (66.7)	
Maternal death	No	855 (54.9)	702 (45.1)	
	Yes	0 (.0)	0 (.0)	
1-minute Apgar score	≥7	801 (55.5)	643 (44.5)	0.289
	0–3	24 (51.1)	23 (48.9)	
	4–6	31 (46.3)	36 (53.7)	
5-minute Apgar score	≥7	831 (55.0)	31 (45.0)	0.946
	0–3	18 (52.9)	(47.1)	
	4–6	7 (58.3)	(41.7)	
Birth weight (kg)	≥2.5	721 (54.5)	603 (45.5)	0.359
	<2.5	135 (57.7)	99 (42.3)	
Twin pregnancy	No	818 (55.8)	674 (45.2)	0.66
	Yes	38 (57.6)	28 (42.4)	
Apparent congenital malformation	No	28 (54.9)	679 (45.1)	0.995
	Yes	28 (54.9)	23 (45.1)	
Admission to NICU	No	773 (54.3)	650 (45.7)	0.126
	Yes	82 (61.2)	52 (38.8)	
Postpartum hemorrhage	No	819 (54.6)	681 (45.4)	0.167
	Yes	37 (63.8)	21 (36.2)	
Intrauterine fetal death	No	842 (55.0)	689 (45.0)	0.745
	Yes	14 (51.9)	13 (48.1)	
Iron used	No	381 (57.5)	282 (42.5)	0.14
	Yes	473 (53.0)	420 (47.0)	

Notes: Data are presented as n (%).[a]Statistically significant.
Abbreviation: NICU, neonatal intensive care unit; CS, cesarean section.

associated with adverse outcomes such as preterm birth, intrauterine growth restriction, low birth weight, low Apgar score, and cesarean deliveries.[26–31]

The association between IDA and adverse outcomes has been confirmed in many studies.[26–30] In a study conducted by Patra et al,[31] very high maternal mortality (6.2%) and perinatal mortality (60%) were observed in severely anemic women during the third trimester of pregnancy. Most women in the present study were at a gestational age of >37 weeks and had mild anemia, which might explain the absence of an association of anemia with adverse outcomes, other than the relatively lower rate of antenatal fetal distress.

The limitations of our study were that it was limited to Women's Specialized Hospital, and some data regarding the study parameter were missing. Also, we did not classify IDA into mild or severe. We recommend that information, education, and counseling about this disease be provided to pregnant women. This information might aid physicians in guiding their patients and taking optimal clinical decisions together.

In conclusion, IDA during pregnancy continues to be a major health problem worldwide. Anemia in general and microcytic hypochromic anemia in particular are significantly associated with higher gravidity and parity. The significant outcome associated with IDA during pregnancy was a lower rate of spontaneous vaginal delivery and antenatal fetal distress. Compliance with iron supplementation in order to prevent maternal and fetal adverse outcomes was observed.

In light of these results, we recommend hematological screening for Hb and iron status in early pregnancy. There is no need for further checks of these values if the pregnancy is uncomplicated and there is compliance with iron supplementation to prevent maternal and fetal adverse outcomes.

Disclosure

The authors report no conflicts of interest in this work.

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