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EFFECT OF MODERATE IRON DEFICIENCY ANEMIA DURING PREGNANCY ON MATERNAL AND FETAL OUTCOME

By

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ABSTRACT

Background: Iron deficiency is the most common nutritional deficiency worldwide, particularly among pregnant women. Because of the increased iron requirements during pregnancy, pregnant women are recognized as the group most vulnerable to iron deficiency anemia.

Objective: To evaluate the effect of moderate maternal iron deficiency anemia on maternal outcome (Atonic postpartum hemorrhage or postpartum infections after delivery), and fetal outcome (neonatal weight and Apgar score).

Patients and methods: This was a prospective cohort study carried out at Om El-Masryeen General Hospital on 100 pregnant females, during the period from June 2020 to December 2020 who were admitted to the labor ward for delivery, Before delivery blood samples were collected. They were classified into two equal groups according to hemoglobin level. Group 1 (non-anemic group) included pregnant women with hemoglobin level 11 g/dl or more and group 2 (anemic-Group) which included pregnant women with moderate iron deficiency anemia who had hemoglobin level ranging from 7 to <10 g/dl. The patients were delivered either vaginally or by cesarean section according to obstetric indication. After delivery, maternal outcome was assessed for atonic postpartum hemorrhage or postpartum infections after delivery and all newborns were assessed for neonatal weight and Apgar score.

Results: There was a significant difference of the demographic residence between both study groups ($P<0.05$) with higher number of candidates with moderate anemia residing in rural areas. After delivery, the rate of atonic postpartum hemorrhage among anemic group (10%) was higher than that among the non-anemic group (2%). The rate of postpartum endometritis among anemic group (6%) was found to be also higher than that among non-anemic group (2%). The rate of post-cesarean wound infection among anemic group (6.3%) was found to be also higher than that among non-anemic group (0%). The rate of episiotomy wound infection among anemic group (4%) was found to be also higher than that among non-anemic group (0%). There were positive correlations between the maternal parameters (maternal serum hemoglobin, mean corpuscular volume, means corpuscular hemoglobin, serum iron and serum ferritin) and the fetal outcomes (neonatal weight, Apgar score at 1st and 5th minute). There were negative correlations between maternal total iron binding capacity (TIBC) and the fetal outcomes (neonatal weight, Apgar score at 1st minute and 5th minute).

Conclusion: Maternal iron deficiency anemia affected both maternal outcome (atonic postpartum hemorrhage and postpartum infections after delivery), and also fetal outcome (neonatal weight, Apgar score at 1st and 5th minutes).

Keywords: Iron deficiency anemia; Pregnancy; Maternal outcome & fetal outcome.

INTRODUCTION

Anemia is a common problem in obstetrics and perinatal care. Any hemoglobin (Hb) below 11 g/dl can be regarded as true anemia regardless of gestational age. Main cause of anemia in obstetrics is iron deficiency, which has a worldwide prevalence between estimated 20 and 80% of especially female population. Stages of iron deficiency are depletion of iron stores, iron-deficient erythropoiesis without anemia and iron-deficiency anemia, the most pronounced form of iron deficiency. Pregnancy anemia can be aggravated by various conditions such as uterine or placental bleedings, gastrointestinal bleedings and peripartum blood loss *(Breymann, 2015)*.

Each year more than 500 000 women die from pregnancy-related causes, 99% of these being in developing countries. The incidence of maternal mortality resulting from anemia is 34/100 000 live births. Anemia is probably a chronic rather than an acute condition in many cases. There is a resulting compensatory shift of the oxygen dissociation curve to the right. Thus, women with very low hemoglobin concentrations may be seen during the antenatal period without the expected overt symptoms of cardiac failure. They will, however, easily become tired with any form of physical activity and may decompensate (e.g. as a result of labor) *(Helmy et al., 2018)*.

During pregnancy the fetal demand for iron increases maternal daily iron requirements around 10-fold, increasing from 6 mg/day to 22 mg/day in first and third trimesters of pregnancy, respectively. This increased demand for iron is covered mostly from maternal iron stores, which makes pregnant women at higher risk of developing iron deficiency and IDA. Anemia is a widespread public health problem associated with an increased risk of morbidity and mortality, especially in pregnant. IDA is considered to be one of the top ten contributors to the global burden of disease *(Cordero et al., 2015)*.

Anemic mothers were more likely to be diagnosed with hypertension, diabetes, placental abruption, chorioamnionitis, require a blood transfusion or admission to the intensive care unit. Infants born to anemic mothers were more likely to be born preterm (8.9% versus 6.5%), but not more likely to suffer morbidities associated with prematurity. In a population-based study, the diagnosis of anemia in pregnancy carries a higher risk of peri-partum, intra-partum, and post-partum complications for the mother, and a higher risk of preterm birth for the infant *(Beckert et al., 2019)*.

A recent study indicated that early third trimester severe and moderate iron deficiency anemia is associated with SGA (small for gestational age). When compared with the control group, SGA was found to be increased by 3.8 fold in the severe anemia group and 2.4 fold in the moderate anemia group. Iron deficiency anemia in pregnant women may lead to low birth weight *(Şahin and Madendağ, 2019)*.

The consequences of IDA during pregnancy are often serious and long lasting for both the mother and fetus. Mothers with anemia often experience increased fatigue levels, reduced exercise performance, and reduced mental performance *(Breymann et al., 2011)*.

In our study, we evaluated the effect of moderate maternal iron deficiency anemia on maternal outcome (atonic postpartum hemorrhage or postpartum infections after delivery) and fetal outcome (neonatal weight and Apgar score).

PATIENTS AND METHODS

The current study was carried out at Om El-Masryeen General Hospital from June 2020 to December 2020. This was a prospective cohort study that was conducted among 100 pregnant females who were admitted to the labor ward for delivery, and directly before delivery blood samples were collected. The candidates were selected according to specific inclusion and exclusion criteria.

The ethics committee of the University confirmed the study methodology, and an informed consent was taken from all candidates participating in the study after full explanation of the study purpose.

Inclusion criteria: Age from 21 to 35 years, pregnancy duration was more than 37 weeks (Patient should be sure of her date) and singleton pregnancy.

Exclusion criteria: History of medical disorders (chronic hypertension or diabetes mellitus), history of any type of anemia other than iron deficiency anemia, prolonged rupture of membranes (>18 hours), fever or foul smelling liquor, antepartum hemorrhage, pregnancy-induced hypertension or gestational diabetes mellitus, and women with risk factors for uterine atony as over distended uterus, high parity, history of previous PPH or bleeding tendency.

The included mothers and their newborns were classified into two equal groups according to hemoglobin level:

Group 1 (non-anemic group): Pregnant women with hemoglobin level 11 g/dl or more .

Group 2 (anemic-Group): Pregnant women with moderate iron deficiency anemia who had hemoglobin level ranging from 7 to <10 g/dl.

Maternal hemoglobin was categorized according to the WHO definitions of anemia for pregnant women: severe (<7 g/dl), moderate (7 to <10 g/dl), mild (≥10–<11 g/dl), or normal (≥11 g/dl) (Parks et al., 2019.(

All mothers were subjected to a complete full history taking which included demographic features (age, residence), gravidity, mode of delivery; detailed medical history, and were subjected to clinical examination and laboratory investigations including complete blood count, serum iron, total iron binding capacity, and serum ferritin.

The patients were delivered either vaginally or by cesarean section according to obstetric indication.

All patients with an indication for cesarean section received antibiotic prophylaxis in the form of 1 to 2 grams of third-generation cephalosporin as ceftriaxone. Cesarean section was performed under spinal anesthesia with Pfannenstiel skin incision and lower uterine segment transverse incision. All patients after delivery received oxytocin infusion (20 units in 500 ml normal saline solution infused over 30 min). Uterine repair was done by suturing the uterine incision in two layers using No. 0-1 vicryl

suture material. Abdominal wall was closed in layers; muscle approximation, rectus sheath, subcutaneous fat using vicryl suture material and finally skin sutured with subcuticular prolene suture material.

For patients who delivered vaginally, mediolateral episiotomy was performed only when indicated, and a local anesthetic (e.g. lidocaine) was injected at the site of episiotomy. After delivery of the fetus, oxytocin was infused (20 units in 500 ml normal saline solution infused over 30 min). Vaginal mucosa and submucosa were closed by vicryl 2/0 starting 1 cm beyond the visible apex till the hymeneal ring. Interrupted vicryl 2/0 sutures were used to approximate the muscles, closure of the superficial fascia by continuous vicryl suture, and finally closure of the skin by subcuticular continuous stitches.

Maternal outcome was assessed for atonic postpartum hemorrhage or postpartum infections after delivery. We estimated the blood loss by quantifying the amount of blood loss by collecting blood in graduated volumetric containers. Also, the surgical swabs were weighed and the difference in weight between soaked and dry [1 g =1 ml] was added.

Postpartum endometritis was diagnosed by fever (38.3 °C or higher) on 2 measurements more than 6 hours apart, lower abdominal pain and tenderness, tachycardia, uterine tenderness and purulent lochia.

Wound infection manifested itself with erythema and induration of the incision that usually developed 4 to 7 days after the cesarean section.

Episiotomy site infection was diagnosed by presence of perineal pain, wound dehiscence, or purulent wound discharge.

All newborns were assessed for neonatal weight and Apgar score.

Statistical Analysis:

Pre-coded data were transferred and entered into the Statistical Package for the Social Sciences Software program, version 26 (SPSS) to be statistically analyzed:

- For quantitative variables, data were summarized using mean and standard deviation. Using Kolmogorov-Smirnov Z test, variables that were normally distributed and compared using independent t test, while the not normally distributed data were compared using Mann Whitney U test.
- For qualitative variables, data were described as frequency and percentage and compared using Chi-square test and Fisher exact test.
- Spearman correlation was done for quantitative variables.
- P value < 0.05 was considered Significant.

RESULTS

A significant difference of the demographic residence between both study groups (P<0.05) was found with higher number of candidates with moderate anemia residing in rural areas. No significant difference (P>0.05) was present as regards the frequency of gravidity (primigravida vs. multigravida), and mode of delivery (vaginal vs. cesarean section) between both study groups **(Table 1)**.

Table (1): Distribution of Residence, Gravidity and Delivery in both study groups

Distribution \ Study Groups		Group 1 n.	Group 1 %	Group 2 n.	Group 2 %	P-value
Residence	Urban	29	58	20	40	<0.05
	Rural	21	42	30	60	
Gravidity	Primigravida	19	38	15	30	>0.05
	Multigravida	31	62	35	70	
Delivery	Vaginal Delivery	33	66	34	68	>0.05
	Cesarean Section	17	34	16	32	

Group 1: Non-anemic study group, and Group 2: Moderate anemic study group.

The maternal laboratory parameters (serum hemoglobin level, mean corpuscular volume, mean corpuscular hemoglobin, serum Iron, and serum ferritin level) were higher in the non-anemic than anemic groups, except maternal total iron binding capacity (TIBC) which showed higher means in the anemic group **(Table 2)**.

Table (2): Maternal hematological laboratory parameters in both study groups

Maternal Parameters \ Study Groups	Group 1 N=50 Mean±S.D.	Group 2 N=50 Mean±S.D.	P-value
Maternal Hemoglobin	11.70±0.45	8.53±0.49	<0.05
Maternal Corpuscular Volume (MCV)	88.21±0.96	76.05±4.19	<0.05
Maternal Corpuscular Hemoglobin (MCH)	29.15±0.69	25.46±1.46	<0.05
Maternal Serum Iron	86.58±11.93	33.91±7.33	<0.05
Maternal Total Iron Binding Capacity (TIBC)	338.266±55.762	535.224±46.629	<0.05
Maternal Serum Ferritin	49.36±15.13	20.37±6.45	<0.05

Group 1: Non-anemic study group, and Group 2: Moderate anemic study group.

The rate of atonic postpartum hemorrhage among anemic group was 10%, while that among the non-anemic group was 2%, and the difference was statistically insignificant (P>0.05).

The rate of postpartum endometritis among anemic group was 6%, while that among the non-anemic group was 2 %, and the difference was statistically insignificant (P>0.05).

The rate of postcesarean wound infection among anemic group was 6.3%, while that among the non-anemic group was 0%, and the difference was statistically insignificant (P>0.05).

The rate of episiotomy wound infection among anemic group was 4%, while that among the non-anemic group was 0%, and the difference was statistically insignificant (P>0.05) **(Table 3)**.

Table (3): The maternal outcome differences between both study groups

Study Groups / Maternal outcome		Group1 n. %	Group 2 n. %	P-value
Atonic postpartum hemorrhage	**yes**	1 **2%**	**5 10%**	**>0.05**
	no	**49 98%**	**45 90%**	
Postpartum endometritis	**yes**	**1 2.0%**	**3 6.0%**	**>0.05**
	no	**49 98%**	**47 94.0%**	
Postcesarean wound infection	**yes**	**0 0.0%**	**1 6.3%**	**>0.05**
	no	**17 100.0%**	**15 93.7%**	
Episiotomy wound infection	**yes**	**0 0.0%**	**1 4.0%**	**>0.05**
	no	**27 100.0%**	**24 96.0%**	

Group 1: Non-anemic study group, and Group 2: Moderate anemic study group.

There were significant differences (P-value <0.01) of the fetal outcomes (neonatal weight, Apgar score at 1st and 5th minutes) between both study groups with higher means of all these parameters in the non-anemic group than anemic group. Maternal iron deficiency anemia has a significant correlation with birth weight, and Apgar score at 1st and 5th minutes **(Table 4)**.

Table (4): The fetal outcome differences between both study groups

Study Groups / Neonatal outcome	Group 1 N=50 Mean±S.D.	Group 2 N=50 Mean±S.D.	P-value
Neonatal Weight(Grams)	3375±187	2676±239	**<0.001**
Apgar Score at 1st min.	8±1	6±1	**<0.001**
Apgar Score at 5th min	9±1	8±1	**<0.001**

Group 1: Non-anemic study group, and Group 2: Moderate anemic study group.

Significant (P<0.01) positive correlations between the maternal parameters (maternal serum hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, serum iron and serum ferritin) and the fetal outcomes (neonatal weight, Apgar score at 1st and 5th minute) respectively and separately were found. Significant (P<0.01) negative correlations between maternal total iron binding capacity and the fetal outcomes (neonatal weight, Apgar score at 1st and 5th minute) were also found **(Table 5)**.

Table (5): Spearman's Correlations between maternal laboratory parameters and the fetal outcome criteria

Neonatal parameters \ Maternal parameters		Hb	MCV	MCH	Serum Iron	Serum Ferritin	TIBC
Weight	R	0.768	0.815	0.767	0.78	0.741	-0.724
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
APGAR 1st min.	R	0.64	0.56	0.562	0.636	0.619	-0.516
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
APGAR 5th min.	R	0.535	0.431	0.441	0.452	0.454	-0.409
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Group 1: Non-anemic study group, and Group 2: Moderate anemic study group.

DISCUSSION

In the present study, we evaluated the effect of moderate maternal iron deficiency anemia on maternal outcome (atonic postpartum hemorrhage and postpartum infections after delivery), and fetal outcome (neonatal weight and Apgar score).

We found that pregnant ladies from rural areas have higher incidence of anemia than pregnant ladies from urban areas, and this may be due to different health, behavioral, and socioeconomic factors.

The study showed higher means of maternal laboratory parameters (serum hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, serum iron and serum ferritin) in the non-anemic than the anemic groups, while maternal total iron binding capacity was higher in anemic than non-anemic groups. After delivery, the rate of atonic postpartum hemorrhage among anemic group was higher than that among non-anemic group, and the rate of postpartum endometritis among anemic group was found to be also higher than that among non-anemic group. The rate of post-cesarean wound infection among anemic group was found to be also higher than that among non-anemic group, and the rate of episiotomy wound infection among anemic group was found to be also higher than that among non-anemic group.

Few old studies have linked the risk of PPH by the level of anemia, and indicated a weak association. Little studies demonstrated causal relationship between severe anemia and uterine atony which is the main cause of PPH. A cross-sectional study was carried out, where postpartum hemorrhage developed. 39.6% of cases had severe uterine atony and required

emergency hysterectomy, and 60.37% of cases responded to the conservative measures. Most of the hysterectomized women (80.75%) had Hb levels ≤ 7 versus 12.5% of the nonhysterectomized patients. There was a strong correlation between low Hb levels and blood loss. So, this study supports the association between anemia (Hb< 10) and the risk of PPH, and also provides an evidence of the association between severe anemia and emergency hysterectomy *(Frass, 2015).*

Another study showed significant relation between PPH occurrence and past medical history, anemia and previous PPH *(Ahmed et al., 2020).*

A study showed that, women who had wound dehiscence after cesarean section had high frequency of anemia, and those women were more prone to infection due to the underlying anemia (low Hb) *(Javeria et al., 2017).*

A case-control study evaluated associated factors to surgical site infection after cesarean section, and found that only 2.4% developed surgical site infection. The associated factors to surgical site infection were mild anemia, moderate anemia, number of vaginal examinations higher than five, and onset of labor *(Yerba et al., 2020).*

Our study also showed significant positive correlations between the maternal parameters (maternal serum hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, serum iron and serum ferritin), and the neonatal outcomes (neonatal weight, Apgar score at 1st and 5th minute). Also, it showed significant negative correlations between maternal total iron binding capacity, and the neonatal outcomes (neonatal weight, Apgar score at 1st minute and 5th minute). So, that the severity of maternal iron deficiency anemia have significant correlation with neonatal outcome.

A retrospective cohort study showed that moderate-to-severe anemia (hemoglobin <100 g/l) before pregnancy was associated with preterm birth when compared with prepregnancy hemoglobin of 120–149 g/l. The risk of preterm birth, LBW and SGA across 11 prepregnancy hemoglobin groups depended on the severity of anemia, and a high hemoglobin concentration (⩾150 g/l), however, was not associated with adverse birth outcomes *(Yi et al., 2013).*

There are several reports that correlate anemia during pregnancy with prematurity and low-birth weight infants, indicating a direct relationship between low birth weight and low maternal Hb level. In a large epidemiologic study, it was shown that the risk of a preterm delivery increased by 20% in pregnancies with Hb levels between 10 and 11 g/dl, and by 60% in pregnancies with Hb levels between 9 and 10 g/dl. Studies of cord blood serum iron levels have shown a direct relationship between maternal and fetal iron levels. Additionally, when serum ferritin is used as an indicator of iron status, it was found that babies born to mothers who did not take iron supplements during pregnancy had reduced iron stores at birth. Most authors agree that only severe anemia may have direct adverse effects on the fetus and neonate and that a mild to moderate maternal iron deficiency does not appear to cause a significant effect on fetal hemoglobin concentration *(Geng et al., 2015).*

In another study, the mean hemoglobin level for the cohort was 9.9 g/dl with a standard deviation of 1.0 g/dl. The overall prevalence of anemia (<11 g/dl) in their cohort was 87.8%. They noted a higher rate of stillbirth in women with severe anemia. Although there was an overall increase in the rate of stillbirths amongst women with severe anemia compared to all other women, we were unable to establish any difference in the distribution between fresh stillbirths (generally a marker of intrapartum events) and macerated stillbirths (a marker of antepartum events), and the degree of anemia. Neonatal outcomes were strongly associated with hemoglobin levels. The risk of neonatal mortality at <28 days (primary outcome) was substantially increased in the cohort with severe anemia. There was also a strong association of an increased risk of low birth weight (<2500 g), very low birth weight (<1500 g), preterm birth, and neonatal mortality at <7 days) with severe anemia *(Parks et al., 2019)*.

CONCLUSION

Maternal iron deficiency anemia affected both maternal outcome (atonic postpartum hemorrhage and postpartum infections after delivery), and fetal outcome (neonatal weight, Apgar score at 1st and 5th minutes). So, early diagnosis and treatment of maternal iron deficiency anemia during antenatal follow up was critical to minimize maternal and fetal complications.

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تأثير فقر الدم الناجم عن نقص الحديد المعتدل أثناء الحمل علي صحة الأم والجنين بعد الولادة

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خلفيـــة البحـــث: نقــص الحديــد هــو أكثــر حــالات نقــص التغذيــة شــيوعا فــي العــالم، وخاصة بين الحوامل.

وبســبب زيــادة احتياجــات الحديــد أثنــاء الحمــل أصــبح مــن المعتــرف بــه أن النساء الحوامل هن الفئة الأكثر عرضة للإصابة بفقر الدم الناجم عن نقص الحديد.

الهـدف مـن البحـث: تقيـيم تـأثير فقـر الـدم النـاجم عـن نقـص الحديـد لـدي الأمهـات علـي صـحة الأم فـي صـورة حـدوث نزيـف مـا بعـد الـولادة أو حـدوث تلـوث الجـرح مـا بعـد الولادة وأيضا علي صحة الجنين.

المريضـــات وطـــرق البحـــث: شــملت هــذه الدراســة الســيدات الحوامــل اللاتــي تواجــدن بجنــاح الــولادة بمستشــفي أم المصــريين العــام للــولادة فــي الفتــرة الزمنيــة مــن يونيــو 2020 إلــى ديســمبر 2020 و تــم إختيــار 100 ســيدة حامــل للمشــاركة فــي هــذه الدراســة وتم جمع عينات الدم مباشرة منهم قبل الولادة لعمل تحليل صورة دم كاملة.

نتـــائج البحـــث: إرتفــاع عــدد المصــابين بفقــر الــدم المقيمــين فــي المنــاطق الريفيــة مقارنــة بغيــرهم المقيمــين بالحضــر. و كــان معــدل نزيــف مــا بعــد الــولادة فــي المجموعــة المصــابة بفقــر الــدم (10٪) أعلــى مــن المجموعــة غيرالمصــابة بفقــر الــدم (2٪) و معــدل الإصــابة بالتهــاب بطانــة الــرحم بعــد الــولادة (6٪) كــان أعلــى أيضًــا مــن تلــك الموجــود فــي المجموعــة غيــر مصــابة بفقــر الــدم (2٪)، وكــان معــدل الإصــابة بعــدوى الجــرح بعــد الــولادة القيصــرية فــي المجموعــة المصــابة بفقــر الــدم (6.3٪) و فــي المجموعــة غيــر المصــابة بفقــر الــدم كــان (0٪)، و كــان أيضــا معــدل الإصــابة بعــدوى جــرح شــق العجــان بعــد الــولادة الطبيعيــة أعلــي فــي المجموعــة المصــابة بفقــر الــدم (4٪) عن تلك الموجودة في المجموعة غير مصابة بفقر الدم.

و قد كان مستوى الحديد لدى الأمهات أقل بشكل ملحوظ في المجموعة المصابة بفقر الدم مقارنة بالمجموعة غير المصابة بفقر الدم، ومع ذلك كانت القدرة الكلية على ارتباط الحديد أعلى بشكل ملحوظ في المجموعة المصابة بفقر الدم مقارنة بالمجموعة غير المصابة بفقر الدم.

وعند مقارنة وزن حديثي الولادة للأمهات اللاتي تعانين من فقر الدم والأمهات غير مصابة بفقر الدم، وجد أن فقر الدم لدي الأم له تأثير سلبي على وزن حديثي الولادة.

الإستنتاج: فقر الدم الناجم عن نقص الحديد يؤثر على كل من الأم بصورة سلبية و التي قد تظهر في صورة نزيف ما بعد الولادة و حدوث تلوث الجرح ما بعد الولادة القيصرية، وأيضا له تأثير سلبي علي وزن حديثي الولادة و درجة Apgar في الدقيقة الأولى والخامسة. لذلك، يجب عمل زيارات متابعة حمل منتظمة قبل الولادة مع عمل التحاليل المطلوبة و ذلك من أجل التشخيص المبكر وإعطاء العلاج المناسب لأنيميا نقص الحديد أثناء الحمل.

الكلمات الدالة: أنيميا نقص الحديد، الحمل، صحة الأم و الجنين.