Original article

Maternal iron stores and its association with newborn iron dynamics and outcomes

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Abstract

Objectives: In pregnant women in developing nations iron deficiency anemia is common. The mother-fetus homeostasis may be adversely affected by the demands in pregnancy. This can lead to adverse feto-maternal outcomes like intrauterine growth retardation ,premature delivery, and neonatal and perinatal death. Therefore it is important to understand the relation between maternal and fetal iron handling as this may help in further implementation of measures to prevent iron deficiency in pregnancy and infancy and improve outcomes. Thus, this study was conducted to explore the effect of maternal iron deficiency anemia on newborn iron stores. ***Methods:*** The study was conducted in the Department of Obstetrics and Gynecology, Smt. Sucheta Kriplani Hospital, New Delhi, India between November 2014 to March 2016. It was an observational cross sectional study with sample size of 100 antenatal women diagnosed with iron deficiency anemia.We divided the mothers into groups with mild, moderate and severe anemia respectively. The maternal serum ferritin levels were compared with the newborn hemoglobin and serum ferritin levels. ***Results:*** Between the three groups the baseline characteristics were comparable. The newborns of mothers with severe anemia had lower Apgar scores and a greater risk of admission. The birth weight did not differ among the groups. The severity of anemia increased with the parity.The cord blood hemoglobin between the groups was comparable, however the cord blood ferritin levels were directly related to maternal hemoglobin values . In those with severe anemia, a positive association was found between maternal ferritin and cord blood hemoglobin and maternal hemoglobin and cord blood serum ferritin. A positive association was also found between maternal hemoglobin and cord blood hemoglobin. ***Conclusion:*** The study supports the fact that fetal needs dictate the placental iron demand. With increasing severity of anemia the fetus starts showing decreased serum ferritin and this finally results in iron deficiency at birth. Although the fetal weight and haemoglobin are not compromised with increasing severity of anemia in our study, increased fetal risk manifested by worsening Apgar scores and increased newborn admissions occurred as anemia worsened. This study supports the fact that maternal deficiency of iron affects the newborn iron profile and this reiterates the imperative role of iron supplementation during pregnancy.

Keywords: Iron deficiency anemia; pregnancy;newborn serum ferritin; cord blood haemoglobin**.**

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Introduction

Anemia occurs when the circulating levels of haemoglobin (Hb) are quantitatively lower than normal.[1] Iron deficiency anemia (IDA) is the commonest anemia type in the developing nations.[2]

The World Health Organization (WHO) cut-off point for diagnosis of anemia in pregnancy is Hb less than 11g/dl.[3]Anemia is further classifiedas mild anemia with Hb between 10-10.9gm/dl, moderate anemia in the range of 7-9.9gm/dl, severe anemia with Hb less than 7gm/dl and very severe anemia when the Hb is below 4gm/dl.[4] The increased plasma volume and red cell mass during pregnancy consequent to augmented erythropoiesis, which is associated with increased demand of erythropoietic factors,

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iron being the most important poses a risk of iron store depletion. This results in increased demand of iron which is mobilized from the stores which are mainly in the form of ferritin in our body[5] During pregnancy, because of the increasing demands of the growing fetus there is a high risk of IDA. In developing countries baseline low stores of iron due to socioeconomic and dietary factors poses a greater risk for IDA.[6,7]

Maternal iron deficiency affects fetal iron stores. The fetal iron supply is from the maternal circulation via a unidirectional transplacental process. Maternal transferrin is the molecule through which the maternal iron reaches the placenta. Fetal transferrin then relays the iron across the placenta and the fetal circulation to the fetal tissue.[9] Serum ferritin is a better indicatorof iron status than Hb.[10]During pregnancy there is a manifold increase in maternal iron absorption which complements the increased fetal demands. A pregnant woman requires around 1000mg/day of iron to meet the needs of pregnancy.[11]Fetal iron accumulation occurs at about 1.35mg/kg/day of fetal weight in third trimester and this helps in fetal brain development.[12]Poor maternal iron status upregulatesplacental transferrin receptors (TfR)to increase placental iron uptake.[9]When this mechanism fails,the fetalserum ferritin falls and the fetal iron status is compromised.[13]

During pregnancy the maternal system may compete with the fetus for her iron needs and disrupt the feto-maternal iron homeostasis.This can have adversely affectfeto-maternal outcomes.[14]The relation between maternal iron and fetal iron status is imperative to understand, to help prevention of maternal-fetal IDA. Thus, this study was planned to evaluate the effect of maternal IDA on new born iron stores.

Material and methods

The study was done with the aim to determine association between maternal and newborn serum ferritin levels. Approval from the Institutional Ethics Committee was taken to carry out this study. The study was conducted in the Department Of Obstetrics and Gynaecology, Smt. Sucheta Kriplani Hospital,New Delhi, India between November 2014 to March 2016. It was an observational cross sectionalstudy with sample size of 100 antenatal women.Pregnant women more than 20 years of age,with period of gestation greater than 37 weeks, diagnosed with IDA were included in the study. Those with maternal chronic illness like diabetes, hypertension, haemoglobinopathies, history of antepartum hemorrhage, high risk pregnancy like history of recurrent abortions, trauma, infection, hyperemesis gravidarum, pre-eclampsia and multiple pregnancies were excluded from the study.

Methodology:Antenatal women fulfilling the inclusion criteria were evaluated. Baseline maternal data in relation to age, parity, socio-economic status and previous obstetric history were recorded in all cases. Details of clinical examination wererecorded including obstetric findings. Ultrasonographic examination was done to assess fetal well-being. Standard hospital protocols were followed in the management of labour in all the patients. Strict aseptic precautions were observed during vaginal examination and conduct of delivery. Blood sampling for serum ferritin estimation was done. After delivery of the fetus and cord clamping, blood samples were taken from placental side of the cord for Hb and ferritin estimation. The mothers were carefully monitored for any complications.Patients and their neonates were followed till discharge.

The maternal serum ferritin levels were compared with the newborn Hb and serum ferritin levels. The maternal serum ferritin, below which iron stores are considered to be depleted is less that 15microgram/land ferritin levels less than 12microgram/l are associated with IDA. The cut-off for maternal serum ferritin in this study was considered <15microgram/l.

The variables in this study are presented as percentage and mean with standard deviation. The categorical variables were compared using chi-square testand Mann-Whitney U test for non-parametric data. Statistical package SPSS (SPSS version 16, for Windows) was used to carry out statistical analysis. A p-value of less than 0.05 was considered statistically significant. Correlations were done using the Pearson's rank correlation coefficient.

Results

Among the 100 antenatal women recruited in the study, 50 had mild anemia, 35 had moderate anemia and 15 were severely anemic.In participants with mild anemia the mean Hblevels were 10.29±0.20g/dl. For those with moderate anemia the mean Hb levels were 9.06± 0.57g/dl, while for those with severe anemia the Hbhad a mean value of 5.99± 0.91 g/dl (Table1).

The baseline characteristics amongst the three groups viz age, parity, gestational age, birth weight of the newborns were comparable amongst the three groups

(Table1).Amongst the neonates born to mothers with mild anemia, 4% had Apgar score of <7 at 5 minutes, with moderate anemia 20% had Apgar score <7 at 5minutes and those born to mothers with severe anemia 40% had Apgar score < 7 at 5 minutes.(p value =0.03) [Table 1]

Most of the neonates with poor Apgar score at 5 minutes were admitted to the neonatal intensive care unit for observation with an admission rate of 4% in the mild anemia group, 17.14% in moderate anemia group and 26.67% severe anemia group which was significant (p value = 0.03). [Table 1]

Parity had a significance for severity of anemia with the severity increasing with the parity(p-value=0.002).

The birth weight of neonates did not differ between the groups. The mean birth weight of all neonates born was 2.56±0.31kg. The mean birth weight of the neonatesborn to mothers with mild anemia was 2.64± 0.34 kg, with moderate anemia was 2.49 ±0.34 kg and with severe anemia was 2.42 ±0.25 kg.(p value=NS) [Table 1]

The maternal serum ferritin levels in participants with mild anemia had a mean value 12.64± 1.87 micrograms/l. Those with moderate anemia the mean ferritin value was 7.87±1.04 microgram/l. In the participants with severe anemia, serum ferritin had a mean value of 4.67 ±1.56 microgram/l. No correlation was found between the maternal Hb and maternal serum ferritin levels in women with mild and moderate anemia with a p value of 0.926 and 0.115 respectively. But in cases of severe anemia a positive correlation was found with a p-value of <0.001. [Table 1]

Table 1: Baseline characteristics of the three groups (mothers with Mild/Moderate /Severe anemia)

Characteristics	Mild anemia (n=50)	Moderate anemia (n=35)	Severe anemia (n=15)	p value (chi-square)
Maternal Hb (g/dl)	10.29±0.20	9.06±0.57	5.99±0.91	<0.001
Age (years)	25.12 ± 2.71	25.17 ± 2.61	26.27± 4.74	NS
Parity (N/P/M) in %	32/52/16	25.7/65.7/5.7	20/46.7/33.3	0.002
Gestational age (weeks)*	38.44 ± 0.80	38.27±0.83	38.23 ±0.87	NS
Birth weight (kg)	2.64±0.34	2.49 ± 0.34	2.42 ±0.25	NS
Maternal serum ferritin (microgram/l)	12.64± 1.87	7.87 ±1.04	4.67 ±1.56	0.926 0.115 0.000
Cord blood Hb (g/dl)	15.10 ±.88	14.79 ± 0.91	13.41±1.15	0.552
Cord blood ferritin (microgram/l)	69.47±12.8	55.36±8.73	21.66±5.18	0.0234
Poor Apgar <7 at 5 minutes (%)*	4.0	17.1	26.7	0.03

*: Expressed as % ; other variables have been expressed as mean±standard deviation. NS: Non significant ; N/P/M: nulliparous/primiparous/multiparous; Hb :hemoglobin

Cord blood Hb from neonates of anemic mothers was estimated. The mean cord blood Hb in our study was 14.75±1.08 g/dl.In mothers with mild anemia, the neonatal cord blood Hb had a mean value of 15.10±0.88g/dl. Those with moderate anemia, mean value was 14.79 ±0.91 g/dl.In severely anemic mothers, the mean cord blood Hb value was 13.41±1.15g/dl. The cord blood Hb was comparable between the groups. [Table 1]

Cord blood serum ferritin from neonates of anemic mothers was also estimated. The mean of cord blood serum ferritin in our study was 57.36±19.48 micrograms/l.In mothers with mild anemia, the cord blood serum ferritin had a mean value of 69.47±12.8 micrograms/l. Those with moderate anemia, mean value was 55.36±8.73 micrograms/l.While in those with severe anemia, the mean cord blood serum ferritin value was 21.66±5.18 micrograms/l.There was a significant difference between the cord blood serum ferritin values between the groups.(p=0.023) [Table 1]

After comparing the demographic characteristics in the participants with mild, moderate and severe anemia association between various parameters were established. [Table 2]

Table 2: Correlation between maternal and neonatal iron stores

Groups	Characteristics	Maternal serum ferritin	Cord blood Hb	Cord blood ferritin
Mild Anemia	Maternal Hb	0.013(0.926)	-0.169(0.234)	0.086(0.552)
	Maternal serum ferritin		0.062(0.668)	-0.006(0.966)
	Cord blood Hb			0.155(0.277)
Moderate Anemia	Maternal Hb	0.262(0.115)	0.625(0.000)	0.697(0.000)
	Maternal serum ferritin		0.295(0.073)	0.181(0.292)
	Cord blood Hb			0.468(0.002)
Severe Anemia	Maternal Hb	0.763(0.000)	0.369(0.007)	0.633(0.002)
	Maternal serum ferritin		0.491(0.036)	0.574(0.009)
	Cord blood Hb			0.502(0.031)

[All the values have been expressed as Pearson's rank correlation coefficient (p -value)]

In the group with mild anemia, no association was found between maternal Hb and cord blood serum ferritin.There wasno association between maternal serum ferritin and cord blood Hb with and between maternal serum ferritin and cord blood serum ferritin. There was no association between maternal Hb and cord blood Hb.

In the participants group with moderate anemia the positive correlations found were between maternal Hb and cord blood Hb and between maternal Hb and cord blood serum ferritin (both p values <0.001).

In those with severe anemia, a positive association was found between maternal serum ferritin and cord blood Hb and maternal Hb and cord blood serum ferritin. A positive association was also found between maternal Hb and cord blood Hb (all p values were <0.05).

Blood transfusion was given according to severity of anemia. 93.33% participants in the group with severe anemia received blood transfusion,which was significant. (p-value< 0.001).

Discussion

Anemia has been associated with poor pregnancy outcomes in developing countries. IDA is the commonest cause of anemia in pregnancy and it can result in direct as well as indirect incidences of maternal mortality. InIndia20% of the maternal deaths can be directly attributable to anemia.[15] The same authors in another study, conducted in a rural setting found in 200 women with moderate and severe anemia that , microcytic hypochromic anemia was the commonest type of anemia, and illiteracy, poverty, crowding , malnutrition and inappropriate antenatal care were risk factors for the anemia.[16]

In this study we found that more pregnant women had mild anemia. Only 15% women had severe anemia. The incidence of anemia increased with parity of the mother. Successive pregnancies can add to maternal stress and render her at risk of severe IDA. The birth weight of newborn was comparable between the groups, implying that the fetal homeostasis is robust enough to not let a compromise in its growth happen even at the expense of maternal nutritional depletion. Similar findings of increasing severity of anemia with parity have been found in other studies.[17]

Although the cord blood hemoglobin values did not differ among the groups, the risk of a fetal compromise happening, reflected by progressively worsening Apgar scores and also an increase in the neonatal admission rates, increased with anemia severity. This may imply that iron may be involved in other aspects of fetal homeostasis apart from hemoglobin levels and oxygen transport. Alterations in these, which may not be picked up by Hb and ferritin levels may result in fetal compromise.Iron requirements are high during pregnancy because it is an important nutrient required for the development of the brain, red blood cells and muscle mass in the fetus.[18]We also found that the cord blood serum ferritin levels declined with worsening maternal anemia although the cord blood Hb levels remained comparable. Thus the priority of the fetus to maintain the Hb level is utmost, even at the cost of extraction from the stores, reflected by serum ferritin levels. This may however imply that the iron may be less available for its other purposes in the fetal body.

In our study we found that low maternal Hb correlated with cord blood Hb and cord blood serum ferritin for the patients with moderate anemia. In

severely anemic women the correlation of maternal Hb and ferritin with cord blood Hb and ferritin was stronger. This supports the fact that, when subjected to progressively declining iron availability, the fetal hemoglobin is the last to get compromised. Maternal iron deficiency if uncorrected,leads to depletion of maternal stores, followed by the fetal stores and lastly the fetal Hb.

Betelihem Terefe[19] et al in Ethiopia, did a similar study to compare iron status of newborns born to anemic mothers. Like our study they too found that maternal IDA affected the newborn stores. Hadipour[20]did a study to analyse the Hb and ferritin levels of newborns of anemic mothers. They did not find any correlation between maternal and serum ferritin, but anemic mothers had newborns with lower Hb.

A case–control study was done by Adiwumi[21] et al (n=142)in pregnant women and their newborns. Maternal anemia correlated with low cord blood ferritin in this study.Jie Shao[22] et al similarly found in a study done in rural China, with a sample size of 3702 term pregnancies. Low maternal ferritin correlated with low cord blood ferritin. As seen in our cohort in this study too, fetal compromise of Hb and cord blood ferritin occurred only in severely anemic mothers..

Conclusion

The study supports the fact that fetal needs are the driver of placental iron absorption. Maternal iron can be drained due to the placental response of increased binding receptors, in case of fetal iron need. This can be sustainable to a limit but if the compensatory mechanisms fail , as in severely anemic mothers the maternal side is deficient of iron and enough iron cannot be transferred to the fetus. The fetus progressively shows decreased serum ferritin, then low Hb followed by other signs.Although the fetal weight and Hb were not compromised with increasing severity of anemia in our study, increased fetal risk manifested by worsening Apgar scores and increased newborn admissions occurred as anemia worsened. Thus, our findings prove that maternal IDA if severe can adversely affect fetal and neonatal iron status. Iron supplementation is therefore essential during pregnancy.

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Ethical clearance: The prior approval to conduct the study was taken from the Institutional Ethics Committee, Lady Hardinge Medical College, New Delhi, India.

Authors's contribution: Concept and design of study: RY and NJ; Data curation and analysis: NG; Writing the manuscript: NG, RY and NJ; All authors contributed equally to the editing and approval of the final version of the manuscript.

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