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Original Research Article

Influence of Maternal Hemoglobin Levels, Serum Ferritin, and Gestational Age on Neonatal Iron Indices

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Abstract

Background and Aim: One of the commonest causes of anemia in pregnancy is iron deficiency. This study aims at understanding and exploring the association between fetal and maternal iron status. This study evaluated various maternal and neonatal factors that influence iron status at birth and at four weeks.

Material and Methods: Mother-infant pairs were enrolled in the study by following specific inclusion and exclusion criteria. Maternal demographic details, complications during pregnancy, intrapartum details, and neonatal details were recorded. The maternal and cord blood samples were collected for measurement of haemoglobin, serum ferritin, serum iron, total iron-binding capacity, and transferrin saturation. If failed to collect the cord blood sample, the first 24hour sample of the baby was taken into consideration in place of it.

Results: There is a significant effect of maternal hemoglobin levels on neonatal TIBC and tranferrin saturations ($p \leq 0.05$) but not on other indices. Babies with deficient maternal stores had significantly low hemoglobin and ferritin concentrations at birth ($p \leq 0.05$), At birth neonatal hemoglobin concentrations ($p \leq 0.05$) and ferritin levels ($p \leq 0.05$) were significantly low in the preterm group as compared to the term group and in follow-up at four weeks preterms have significantly lower serum iron concentrations when compared to term babies ($p \leq 0.05$).

Conclusion: The neonates with low cord blood iron stores are likely to have low iron stores at four weeks of gestational age. As the most significant adverse effects of iron deficiency are neurodevelopmental impairments every mother should be counselled about the importance of iron supplementation during pregnancy.

Keywords: Hemoglobin, Gestational Age, Neonatal Iron Indices, Serum Ferritin.

Introduction

Iron (Fe) is essential for physiological functions, including hemoglobin (Hb) synthesis, and cell growth and development. [1] Iron deficiency results from depletion of stored iron. Increased iron demand during pregnancy can worsen this, resulting in iron deficient erythropoiesis and, eventually, iron deficiency anemia. [2] If the body iron store is deficient at conception, it is unlikely that dietary iron would be able to match the pregnancy-induced increase in demand. [3] Therefore, assessment of body iron status during pregnancy is crucial. While ferritin is the most commonly used indicator, providers often rely on Hb levels to assess iron deficiency at the population level. This use of Hb levels is problematic for two reasons. First, decreased Hb levels can result from causes other than iron deficiency. [4-6] Pregnancy is commonly complicated by iron deficiency anemia (IDA). IDA is also prevalent in early childhood especially in developing countries. The physiological changes and metabolic demands of pregnancy cause an increased requirement of iron, which is not met by the normal daily diet. In the absence of adequate supplementation of iron or presence of maternal malnutrition, the risk of developing IDA increases. [7] World Health Organization defines maternal anemia as a hemoglobin (Hb) level of less than 11 g/dl. For newborns, Hb less than 2 standard deviations is taken as anemia which is around 13.5g/dle14.5 g/dl, subsequently in infants 6-24 months Hb < 11 g/dl is anemia. Serum ferritin (SF) is a measure of iron stores of an individual. In IDA, SF is low, except in the presence of inflammation or infection. Siddappa et al [8] studied SF in cord blood of preterm and term neonates. He found that cord levels of SF rise with gestational age. The transfer of iron from the mother to the fetus is regulated by the placenta. The rate of iron uptake in the fetus is 1.35 mg/kg/d during the third trimester. Expanding maternal blood volume and fetal red cell mass leads to an increased requirement of iron in the second and third trimesters. [9] Maternal and neonatal iron demand determines the placental transferrin receptor (TfR) expression. It may be increased in healthy pregnant women as a response to iron deficiency. When the mother is iron deficient, transfer of iron to the fetus by the placental system may be inadequate. [10,11]

The effects of perinatal iron deficiency are anemia and most importantly neurodevelopmental impairments which are long lasting and sometimes irreversible. [12-14] So it is very essential to maintain adequate iron stores in the perinatal and infantile period. Conversely excess iron has a risk of generating toxic free radicals in preterm neonates with low levels of iron-binding proteins and immature antioxidant systems. There is the paucity of data on neonatal iron stores and the factors influencing them and there is no standard protocol in developing countries on the optimal time for iron supplementation in neonates in different scenarios. Hence this study evaluated various maternal and neonatal factors that influence iron status at birth and at four weeks.

Material and Methods

This prospective observational study was done in Tertiary Care Teaching Institute of India for the duration of 1 year. After getting approval from the institutional ethics committee. All mother-neonate pairs who were delivered in Institute, and who satisfy the eligibility criteria, were enrolled in the study after taking informed consent from one of the parents. Only inborn mother-neonate pair with a birth weight of more than 1.5 kg was included in the study. Mothers with antepartum hemorrhage, chronic systemic disorders, acute infections, and blood transfusions during the antenatal period were excluded. Neonates with congenital heart diseases, malformations, sepsis, shock, Rh incompatibility, Cord serum ferritin more than 370µg/l, multiple pregnancies, blood transfusion during the neonatal period, and who did not give consent were excluded from the study.

The sample size was calculated based on a previous review to detect a 25% difference in levels of serum ferritin between preterm and term babies, with an alpha error of 5% and a power of 80%. To account for an attrition rate of 10% for sampling errors 50 infants were enrolled in both the groups. To enroll 50 preterm's total of 175 neonates which included 50 preterm and 125 term neonates were included in the study. Quantitative variables were described as means and standard deviations or median and interquartile range based on their distribution. Qualitative variables were presented as count and percentages. The associations of qualitative variables between the treatments were analyzed using Chi square test or Fisher Exact test as appropriate. Normally distributed quantitative variables were analysed using independent samples student t-test between the groups and repeated measures ANOVA for within group analysis of time course data. Non normally distributed quantitative data and ordinal data were analysed using Mann-whitney U test for between group comparison and Friedman's test for within group analysis of time course data.

Results

The mean gestational age of the neonates enrolled is 37.5±2.5 weeks and the mean birth weight is 2775±420 grams. The mean maternal age of the study population enrolled is 22.5±2.5 years. 41.5% belong to high socioeconomic status and 58.5% belong to low socioeconomic status. The demographic profile and baseline characteristics of neonates of the study population are summarized in (Table 1) and of the mothers are summarized in (Table 2).

To assess whether maternal hemoglobin level at the time of delivery affects the iron indices at birth, iron indices of those neonates born with maternal hemoglobin level hemoglobin level >10gm/dl using independent samples t test. There is a significant effect of maternal haemoglobins levels on neonatal TIBC and tranferrin saturations ($p \leq 0.05$) but not on other indices.

In order to know the effect of maternal iron stores on the accumulation of iron stores in neonates, iron indices of neonates with deficient maternal ferritin levels (12µg/dl). The mean difference was analyzed using independent samples t-test. Babies with deficient maternal stores had significantly low hemoglobin and ferritin concentrations at birth ($p \leq 0.05$), Iron indices at birth were compared between preterm and term neonates to evaluate whether gestational age can influence iron stores. The mean difference was analyzed using the independent samples t-test. At birth neonatal hemoglobin concentrations ($p \leq 0.05$) and ferritin levels ($p \leq 0.05$) were significantly low in the preterm group as compared to the term group and in follow-up at four weeks preterms have significantly lower serum iron concentrations when compared to term babies ($p \leq 0.05$).

Table 1: Neonatal characteristics of the study sample

Neonatal characteristics	Number	percentage
Males	95	54.28
Females	80	45.71
Pretem	50	28.57
Term	125	71.42

Appropriate for gestational age (AGA)	130	74.28
Small for gestational age (SGA)	45	25.71

Table 2: Maternal characteristics of study sample

Maternal characteristics	Percentage (%) (n=175)
Anemia	49.55
Pregnancy induced hypertension (PIH)	6.5
PIH and anemia	2.5
Gestational diabetes	1.4
Hypothyroidism	1.4
No co morbidity	39.2

Discussion

Iron metabolism undergoes major changes during the last trimester and early postnatal period, at a time when the baby is sensitive to both iron deficiency and iron overload. [15,16] The iron utilization in newborn period is tightly regulated so most of the iron released from senescent RBC is reutilized and the bioavailability of very less iron available in breast milk is high. Various maternal and neonatal conditions can affect iron load at birth.

In the current study, there is no significant correlation between maternal and neonatal iron indices. This finding is similar to previous studies done by Lao et al, Hussain et al, Messer et al, Siimes et al [17-20] Kilbride et al study on iron indices of preterm and term neonates of anemic mothers showed iron stores are similar in both groups which are identical to this study but they found that the incidence of iron deficiency anemia was higher in babies born to anemic mothers throughout the infantile period when compared to controls. [20]

Our findings are consistent with previous studies reporting the associations between high maternal ferritin, measured between GW26 and GW36, and preterm birth, fetal growth restriction, or birth weight. [21-23] On the other hand, Vazirinejad and colleagues reported a positive correlation between maternal ferritin and both birth weight and length. [24] Of note, in Vazirinejad's study, blood samples for ferritin were collected just before delivery, a period at which fetal growth would have been completed. In a study of pregnant adolescents from America, Lee et al. [25] found that 21% of the neonates were anemic (Hb < 13.0 g/dl) and 25% had low iron stores (ferritin<76 ug/l). They did not find any significant association between cord SF concentrations and gestational age at birth.

However, they reported that a low maternal SF <12 mg/l in midpregnancy was associated with significantly lower SF in neonates, but this association was not seen at delivery. They inferred that inflammation due to labour may cause altered ferritin concentrations leading to this difference. In our study, we could not follow up with babies further than four weeks. Jansson et al showed that serum ferritin concentrations measured in the preterm infants were significantly lower. [26] Siddappa et al also concluded that serum ferritin varies with gestational age. [27] In the current study, neonatal ferritin levels were significantly low in preterm group as compared to term group. This is in agreement with the aforementioned studies. In the current study, there was significant positive correlation between haemoglobin, serum iron, and ferritin concentrations at birth and those at four weeks. Hence those neonates born with low iron stores at birth are likely to have low iron stores at four weeks.

The limitation of the study is babies are not followed after four weeks in the present study.

Conclusion

Preterm neonates have low iron stores compared to term neonates. Gestational age is the major determinant for iron stores at birth as compared to other maternal and neonatal factors. The neonates with low cord blood iron stores are likely to have low iron stores at four weeks of gestational age. As the most significant adverse effects of iron deficiency are neurodevelopmental impairments every mother should be counselled about the importance of iron supplementation during pregnancy.

The term and preterm babies should take prophylactic iron from eight weeks and four weeks of age and continued up to the introduction of iron-fortified cereals as recommended by the American academy of paediatrics.

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