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Original Research Article

Effect of maternal haemoglobin, serum ferritin and gestational age on neonatal iron indices

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ABSTRACT

Background: Iron is the most common micronutrient deficiency in pregnant women and infants throughout the world, mainly in developing countries like India. 30 to 50% of the pregnancies are affected by maternal iron deficiency and in developing countries, more than 80% of the pregnant women are estimated to be anemic. The effects of perinatal iron deficiency are anemia and most importantly neurodevelopmental impairments which are long-lasting and sometimes irreversible. The main goal of this study was to determine the influence of maternal and neonatal factors on the iron stores in neonates and to estimate the appropriate time to supplement iron for neonates in different scenarios.

Methods: This is a prospective observational study. 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 hemoglobin, 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. The correlation between maternal neonatal iron indices and the influence of the gestational age and IUGR on cord serum ferritin levels was analyzed by using paired t-test and chi-square test for multiple groups. A probability of $p<0.05$ (two-sided) was used to consider the difference as significant.

Results: 125 term and 47 preterm neonates were included in the study. There was correlation between maternal and neonatal iron profiles at birth when there was severe depletion of maternal ferritin (<12µg/dl) with p values less than 0.05 for hemoglobin and serum ferritn levels. Serum ferritin levels at birth were less in preterm as compared to term neonates (mean of 128.9µg/l in the preterm vs. 156.9µg/l in the term, $p=0.04$). There was a significant correlation between neonatal iron indices at birth with that at 28 days of life ($p<0.01$).

Conclusions: Neonatal iron stores are not affected unless there was severe depletion of maternal iron stores. 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. As the most significant adverse effects of iron deficiency are irreversible and long-lasting neurodevelopmental impairments. The term and preterm babies should take prophylactic iron from eight weeks and four weeks of age respectively and continued up to the introduction of iron-fortified cereals as recommended by the American academy of paediatrics.

Keywords: Ferritin, Haemoglobin, Iron, Maternal, Neonate

INTRODUCTION

Iron is the most common micronutrient deficiency in pregnant women and infants throughout the world, mainly in developing countries like India.[1] 30 to 50% of the pregnancies are affected by maternal iron deficiency and in developing countries, more than 80% of the pregnant women are estimated to be anemic.[2-4] As the prevalence of maternal anaemia is very high and iron supply in utero is entirely from maternal stores and breast milk contains only 0.03mg/dl of iron which stresses the apparent burden of iron deficiency in infants.[5] Multiple maternal factors influence the iron status in the neonate. Iron is essential for growth of foetus and neonate. Iron is a part of haemoglobin, myoglobin, cytochromes, and various enzymes. It is required for electron transport, adenosine triphosphate (ATP) production, DNA synthesis, mitochondrial function, neurotransmitter synthesis, and myelination and is critical for early brain growth and function during the foetal period and infancy.[6-7] The effects of perinatal iron deficiency are anemia and most importantly neurodevelopmental impairments which are long lasting and sometimes irreversible.[7-9] 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.[8-13] 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. Thus, finally to suggest any need for screening and iron supplementation in infants if so, when?

METHODS

This prospective observational study was done in maharajah's institute of medical sciences from March 2020 to march 2022 after getting approval from the institutional ethics committee. All mother-neonate pairs who were delivered in MIMS, 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 haemorrhage, 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 47 infants were enrolled in both the groups. To enroll 47 preterm's total of 172 neonates which included 47 preterm and 125 term neonates were included in the study. 188 mother-neonate pairs met the eligibility criteria, of them, 16 were excluded because of inadequate or haemolysed samples and very high serum ferritin levels (>370µg/l). 172 mother-neonate pairs were enrolled in the study. All data were expressed as Mean±SD. We performed a statistical comparison by using a paired 't'-test and Chi-square test for multiple groups. A probability of $p<0.05$ (two-sided) was used to consider the difference as significant and to reject the null hypothesis. Baseline variables were described using descriptive statistics. Effects of maternal variables like maternal ferritin, anaemia, pregnancy-induced hypertension (PIH), gestational age, and IUGR on the neonatal iron profile was done by independent samples t-test for normally distributed variables and by Mann-Whitney test for variables with skewed distribution. All analyses were performed with IBM SPSS version 26 (IBM Corporation, Armonk, New York, USA), STATA software (version 13.1, Stata Corp, College Station, TX, USA) MedCalc version 19.1, and GraphPad Prism 8.

RESULTS

The mean gestational age of the neonates enrolled is 37.3±2.3 weeks and the mean birth weight is 2780±419 grams. The mean maternal age of the study population enrolled is 22.6±2.6 years. 41.2% belong to high socioeconomic status and 58.8% 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).

Table 1: Neonatal characteristics of the study sample.

Neonatal characteristics	% (N)
Males	54.7 (94)
Females	45.3 (78)
Preterm	27.3 (47)
Term	72.7 (125)
Appropriate for gestational age (AGA)	73.3 (126)
Small for gestational age (SGA)	26.7 (46)

Table 2: Maternal characteristics of study sample.

Maternal characteristics	% (n=172)
Anemia	49.4
Pregnancy induced hypertension (PIH)	6.4
PIH and anemia	2.3
Gestational diabetes	1.2
Hypothyroidism	1.2
No co morbidity	39.5

To assess whether maternal haemoglobin level at the time of delivery affects the iron indices at birth, iron indices of those neonates born with maternal haemoglobin level <10gm/dl were compared with those born with maternal haemoglobin level >10gm/dl using independent samples t-test. There is a significant effect of maternal haemoglobins levels on neonatal TIBC and tranferrin saturations (p=0.01 and p=0.00) but not on other indices, results are shown in (Table 3).

Table 3: Effect of maternal hemoglobin on neonatal iron indices at birth.

Neonatal iron profile	Maternal Hb < 10 gm/dl	Maternal Hb > 10 gm/dl	P value
Hemoglobin (Hb gm/dl)	15.0±2.3	15.4±1.7	0.23
Iron (µg/dl)	140.1±43	123.7±68.9	0.06
Total iron binding capacity (TIBC in µg/dl)	240.8±60.6	267.1±72.4	0.01
Transferrin (%)	60.8±21.8	39.6±22.1	0.00
Ferritin	151.8±76.4	147±85.2	0.7

Table 4: Effect of maternal ferritin levels on neonatal iron indices at birth.

New born iron profile	Maternal serum ferritin <12µg/dl	Maternal serum ferritin >12µg/dl	P value
Hemoglobin (Hb)	16.3±1.9	17.1±2.1	0.03
Iron (µg/dl)	143.1±57.5	128.6±57.4	0.24
TIBC (µg/dl)	278.9±79.8	248.8±76.9	0.07
Transferrin (%)	48.6±19.5	53.8±24.6	0.37
Ferritin (µg/dl)	115.2±65	155.1±81	0.02

Table 5: Comparison of neonatal iron indices between preterm and term babies at birth and 28 days of life.

Iron profile	Pre-term		Term		P value	
	Cord blood	Day 28	Cord blood	Day 28	Cord blood	Day 28
Hemoglobin (Hb)	14.5±2.1	11.9±1.8	15.0±2.1	12.1±1.7	0.02	0.66
Iron (µg/dl)	136.2±74.4	35.5±33.7	128.6±49.7	75.5±54.7	0.44	0.01
TIBC (µg/dl)	261.8±100	139±49.6	249.9±67.7	160.7±95.9	0.37	0.03
Transferrin (%)	47.4±27.6	179.7±69.2	53.9±23.4	117.6±90.7	0.3	0.09
Ferritin (µg/dl)	128.9±80.7	218.2±212.6	156.9±78.6	226.3±153.5	0.04	0.87

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) were compared with those who had normal maternal ferritin levels (>12µg/dl). The mean difference was analysed using independent samples t-test. Babies with deficient maternal stores had significantly low haemoglobin and ferritin concentrations at birth (p=0.02), The results are shown in (Table 4). Iron indices at birth were compared between preterm and term neonates to evaluate whether gestational age can influence iron stores. The mean difference was analysed using the independent samples t-test. At birth neonatal haemoglobin concentrations (p=0.02) and ferritin levels(p=0.04) 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=0.01). The results are shown in (Table 5).

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.[14-15] The iron utilisation in newborn period is tightly regulated so most of the iron released from senescent RBC is reutilised 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.[16-19]

Neonates had significantly low haemoglobin and ferritin concentrations only if the mother has severely depleted iron stores that are maternal ferritin less than 12µg/dl. This finding is in agreement with Jaime-Perez et al, Ilyes et al, Puolakka et al studies.[4,20,21] In this study, no significant correlation between pregnancy-induced hypertension in mothers and neonatal iron profile which is against Chockalingal et al study which might be due to very few babies of PIH mothers being compared with a very large group of babies of non-PIH mothers.[22] Kilbride et al study on iron indices of preterm and term neonates of anaemic mothers showed iron stores are similar in both groups which are identical to this study but they found that the incidence of iron deficiency anaemia was higher in babies born to anaemic mothers throughout the infantile period when compared to controls.[3] 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.[23] Siddappa et al also concluded that serum ferritin varies with gestational age.[24,25] 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.

Limitations

The limitations of the study are we did not categorise preterms based on gestational age as there are fewer preterm babies and the current study could not prove the effect of PIH and GDM on neonatal iron stores due to very few PIH and GDM mothers. In this study, babies are not followed after four weeks.

CONCLUSION

Neonatal iron stores are not affected unless there was severe depletion of maternal ferritin below 12µg/dl. 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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