Research Article

Maternal Iron Deficiency Anemia Affects Fetal Growth, Maturity and Level of Iron in India: A Cohort Study

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Abstract

Background and objective: Iron Deficiency Anemia(IDA) in pregnant females might risk their infant's iron stores, leading to anemia later in their newborn life. Therefore, this present study aims to investigate the effect of maternal anemia on the Hemoglobin (Hb) and iron stores of newborns and whether maternal anemia and iron stores influence fetal development.

Methods: This present cohort study enrolled 192 mothers and newborn couples in which 103 term infants were born to anemic mothers (Group-I), and 89 were born to nonanemic mothers (Group-II). Hb and Ferritin (Fe) levels in cord blood were measured in both groups of neonates at delivery and 14 weeks after birth using RIA and HPLC, respectively, and the data were analyzed using SPSS-17.0.

Result: The results showed that the mean value of Hb and Ferritin (Fe) levels in the blood of new-borns of Group-I was significantly lower (16.28 ± 0.74 and 135.23 ± 21.07) than those in Group II (17.69 ± 0.89 and 160.23 ± 19.57). At 14 weeks, the mean Hb and Fe levels in Group-I were significantly lower(11.68 ± 0.53 and 55.26 ± 10.23) than those in Group II (13.11 ± 0.89 and 64.46 ± 10.91). During delivery and 14 weeks following birth, a strong link existed between the mother and new-borns Hb and Fe levels.

Conclusion and global implementation: The present study concluded that maternal iron insufficiency might affect the iron status of newborns, and maternal Fe levels should be assessed to address undetected ID in the fetus. Immediate steps should be taken to prevent IDA in newborns. The findings of this study may have global implications for prenatal care and interventions to prevent iron deficiency anemia in infants.

Keywords: Anemia; Fetal hemoglobin; Fetal anemia; Non-Anemia of pregnancy; Cord ferritin; Low birth weight

Introduction

Iron Deficiency (ID) significantly contributes to nutritional anemia, especially in developing countries with prevalence rates of more than 70% in pregnant women and more than 55% in children; access to proper nutrition and iron supplementation may be very limited [1]. Pregnant women are particularly vulnerable to Iron Deficiency (ID) due to the increased metabolic needs during pregnancy [1,2]. However, iron is essential for the developing fetus, placenta, and maternal tissues, while a lack of it can lead to negative health outcomes for both the mother and fetus [2].

Research has shown that iron deficiency in infancy can also have long-term implications on their health and development [2]. It can lead to impaired cognitive and motor development, decreased immunity, and increased susceptibility to infections, impacting a child's overall growth and development [2,3].

Therefore, it is crucial to address iron deficiency early in life, starting with pregnant women and young children. Access to proper nutrition, including iron-rich foods and iron supplements, can help prevent and treat iron deficiency and improve maternal and child health outcomes in developing countries [2,3].

Iron deficiency anemia is more likely to occur among pregnant females in impoverished nations like India, where many women may already have low iron levels before pregnancy [3,4]. Like anemia during pregnancy, regardless of the cause, can lead to complications for both the mother and the fetus, including low birth weight and developmental delays [4].

It's also important to note that normal maternal-fetal iron homeostasis can be disrupted during pregnancy due to the competing demands of the mother and fetus, leading to iron deficiency and anemia [4-6]. However, it's worth mentioning that not all pregnant women experience anemia during pregnancy. In contrast, non-anemia during pregnancy is a normal decline in Hemoglobin (Hb) levels that occurs during pregnancy and is not considered harmful to the mother or the fetus [4-6]. It's essential to distinguish between anemia and non-anemia during pregnancy to ensure appropriate care and treatment for pregnant women [6].

Although overall, addressing IR and anemia during pregnancy is critical to improving maternal and fetal health outcomes and reducing the risk of long-term complications for the infant [6].

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The fetus's primary iron source during pregnancy is only the mother [3]; however, the existing ID of the mother can lead to a reduced supply of iron and Hb to the fetus [3], which is associated with decreased cord hemoglobin and iron levels in the infant [4]. Also, maternal malnutrition and severe anemia can coexist, leading to complications such as premature birth, intrauterine growth retardation, mental retardation, and neonatal and perinatal death [8,9].

Subsequently, it can lead to various clinical complications, such as the breakdown of fetal red blood cells and iron deposits in the liver and hematopoietic organs [6,7]. Although, low cord ferritin levels can indicate low fetal iron stores and an increased risk of anemia [8].Therefore, it is crucial to address iron deficiency and anemia in pregnant women to prevent these complications and ensure optimal fetal development and health. This includes providing iron-rich foods and supplements and proper prenatal care and monitoring [9]. Breast milk is an important source of nutrition for infants, and its iron concentration is highest in early transitional milk and gradually declines throughout lactation [9]. Infants up to six months rely solely on breast milk for their iron intake, which means that mothers' hematological state may influence the iron stores of exclusively breastfed infants in the first six months of life [10].

In addition, the need for iron increases from 6 to 12 months of age due to accelerated psychomotor growth and development, which can deplete iron reserves if not supplemented sufficiently. Therefore, infants delivered at term may have insufficient iron reserves. By 6 to 35 months, they may be visibly anemic due to the high prevalence of anemia in this age range [10,11]. It is essential to evaluate the effects of maternal anemia and iron storage on the iron status of the fetus, as well as its growth, maturation, and storage status in full-term infants [9-11].

Based on the stated goal, the study aims to investigate the relationship between maternal anemia and the iron status of the fetus, as well as the impact of maternal iron storage on fetal growth and iron storage status in full-term infants. The study will compare full-term infants born to anemic and nonanemic mothers in terms of birth weight, height, and head circumference, as well as their maturation and iron storage status. The study's results will help determine whether maternal anemia and iron storage significantly affect fetal development and whether interventions are necessary to address any identified issues [12-15].

Methods

Subjects and sample size

The present study was conducted in collaboration with the Paediatrics and Obstetrics and Gynaecology Department of Sir Sunder Lal Hospital Varanasi between December 2019 and February 2020. The Institutional Ethical Committee approved the study, and all participants provided written informed consent. The study excluded women with premature birth (less than 36 weeks), multiple pregnancies, eclampsia, diabetes mellitus, and heart, renal, lung, or hematologic disorders. The study policy ensured the confidentiality of the acquired information and provided it only to the doctor/auditor participating in the research and regulatory authorities. The history and examination included obtaining comprehensive information on the prior obstetric history and the presence of any prenatal risk factors during pregnancy from the mothers.

The study initially recruited 156 mothers and their respective infants, but 53 were dropped from the study for personal reasons. As a result, the anemic sample size was 103 women and their respective neonates. The nonanemic sample size was 86 mothers and their respective newborns, making a total study sample size of 189 (not including 53 who have dropped the study). The mothers were divided into two groups for statistical analysis: Group-I(anemic) and Group II (nonanemic). Group-I comprised mothers with hemoglobin less than 11 g/dl, while Group-II comprised mothers with hemoglobin over or equal to 11 g/dl.

Sociodemographic information about the subjects was acquired through prepared pre-tested interview questionnaires.

Blood samples were obtained from all subjects to determine hemoglobin and serum ferritin levels.

An anthropometric evaluation of both groups' newborns was conducted, with birth weights, less than 2.5 kg considered LBW, while birth weights less than 1.5 kg were considered Very Low Birth Weight (VLBW).

Again, for infants as age 31/2 months or at 14 weeks, venous blood was drawn from both groups' newborns through peripheral venepuncture under strict aseptic conditions to determine their hemoglobin and serum ferritin levels.

Statistical analysis

The SPSS-17.0 (Statistical Program for Social Sciences, IBM, USA)was used for the entire data analysis and presented as mean and standard deviation/percentage. The Chi-square and the Student-sample's "t" tests were used to compare the data between the two study groups (Group-I and Group II) and define p value less than 0.05 that makes a statistically significant. The statistical analysis aimed to determine whether there was a significant difference in the iron status and growth parameters of the infants born to anemic and nonanemic mothers.

Results

In the present study, n=186 enrolled women with their newborns and then divided into two groups based on their Hb and Fe concentrations. Group-I comprised 103 anemic mother-infant pairs, while Group II comprised 86 nonanemic mother-infant pairs. The threshold value for maternal Hb concentration was set at 11 g/dL, following WHO guidelines for altitude changes.

The sociodemographic and obstetric statistics of the research participants are presented in Table 1. The table shows that 51.04% of the women were over 23, while 48.95% were under 23. Other sociodemographic variables, such as educational level, occupation, and monthly family income, were also recorded for each participant.

Table 1 also shows that only a small percentage (6.25%) of the mothers had education beyond high school, while the majority (44.27%) had no education. The participants' occupations were diverse, with the largest proportion (26.56%) being homemakers, followed by skilled and unskilled workers (22.92% and 19.79%, respectively).

Table 1: The sociodemographic and obstetric characteristics of mothers and their newborns.				
Characteristic	Total (n=192) N (%)	Group-I (n=103) N (%)	Group-II (n=89) N (%)	p
		Maternal age (years)		
<23	98(51.04)	59(57.28)	56(57.30)	Less than 0.05
>23	94(48.95)	44(42.71)	33(37.07)	
Delivery				
Full term	156(81.25)	85(82.52)	79(88.76)	Less than 0.05
Preterm	36(18.75)	18(17.47)	10(11.23)	
		Mode of delivery		
LSCD (Caesarean section)	43(22.39)	25(24.27)	21(23.59)	Less than 0.05
NVD (Normal vaginal delivery)	149(77.60)	78(75.72)	68(76.40)	
		Infant's gender		
Male	98(51.04)	58(56.31)	46(51.68)	Less than 0.05
Female	94(48.95)	45(43.68)	43(48.31)	
		Maternal education level		
No education	85(44.27)	43(41.74)	39(43.82)	Less than 0.05
Primary school	29(15.10)	39(37.86)	25(28.08)	
Secondary school	19(9.89)	13(12.62)	16(17.97)	
Above secondary school	12(6.25)	08(7.76)	9(10.11)	
		Maternal occupation		
Housewives	104(54.16)	59(57.28)	51(57.30)	Less than 0.05
Employed	88(45.83)	44(42.71)	38(42.69)	
		Weight of newborns		
Normal-birth weight (<or equal to 2.5kg)	2.72 ± 0.13 (n=102;53.12%)	2.73 ± 0.13 (n=59;57.28%)	2.72 ± 0.12 (n=49;55.05%)	0.843
Low birth weight (>2.5kg)	2.3 ± 0.18 (n=90;46.87%)	2.2 ± 0.15 (n=44;42.71%)	2.3 ± 0.89 (n=40;44.94%)	
		Iron intake during pregnancy		
Yes	153(79.68)	78(75.72)	69(77.52)	Less than 0.05
No	39(20.31)	25(24.27)	20(22.47)	

The mode of delivery was mostly Normal Vaginal Delivery (NVD), with 149 infants born via NVD and only 43 (22.39%) delivered via Cesarean Section (LSCS). Preterm births accounted for 18.75% (n=36) of the newborns, while the remaining 156 were full-term infants. Gender distribution was roughly equal, with 98 male and 94 female babies. Most infants (102) had a normal birth weight, while 90 weighed less than 2.5 kg.

Table 2 and Table 3 also show the neonates' hemoglobin and serum ferritin levels in both groups. In Group-I, the mean hemoglobin and serum ferritin levels were 14.13 ± 1.70 g/dL and 118.97 ± 48.73 ng/mL, respectively, while in Group II, the mean hemoglobin and serum ferritin levels were 15.15 ± 1.52 g/dL and 141.69 ± 51.84 ng/mL, respectively. The differences in hemoglobin and serum ferritin levels between the two groups were statistically significant ($P<0.001$). The median hemoglobin and serum ferritin levels for neonates in Group-I were 14.3 g/dL (IQR=13.18-15.11 g/dL) and 119.1 ng/mL (IQR=87.93-141.46 ng/mL), respectively, while for Group-I I, they were 15.2 g/dL (IQR=14.33-16.12 g/dL) and 145.2 ng/mL (IQR=105.05-175.19 ng/mL), respectively. It is important to note that all neonates in both groups had hemoglobin and serum ferritin levels within the normal range for their age, indicating no neonatal iron deficiency anemia in the study population [16-18].

Table 2: Comparison of outcome measures within controlled group.

Hematological parameters	Group-I(n=103)		Group II (n=89)		p	
	Mothers	Infants at the birth	Mothers	Infants at the birth	AM ver NAM	It birth/NI at the birth
Hb (g/dl)	10.85 ± 0.31	16.28 ± 0.74	12.86 ± 0.98	17.69 ± 0.89	0.0001	0.0001
Serum ferritin	58.14 ± 14.46	135.23 ± 21.07	72.79 ± 23.54	160.23 ± 19.57	0.0001	0.0001

Table 3: Hematological parameters of Infant after 14 weeks of delivery value presented in the Mean ± SD.

Hematological parameters	Infant hematological parameters-Group-I	Infant hematological parameters - Group-II	P value
HB	11.68 ± 0.53	13.11 ± 0.89	0.0001
Ferritin	55.26 ± 10.23	64.46 ± 10.91	0.0001

The mean value of Hb and Fe levels of newborns-babies in Group-I was considerably lower than those in Group II (P<0.001) at birth and also found at 14 weeks (Table 4). A strong association between maternal and child Hb levels was detected at birth (r=0.328,p<0.001) and at 14 weeks (r=0.798, P<0.001), and Fe levels at birth (r=0.231; P<0.002) and at 14 weeks (r=0.289, P<0.001) (Table 3). Thus, the study suggested that maternal Hb and Fe levels significantly impact the newborn's Hb(Iron) status, as there is a positive correlation between maternal and child levels. The lower levels of Hb and Fe observed in Group-I babies compared to Group-II babies indicate that maternal anemia can result in poor fetal iron status, leading to adverse outcomes. These findings highlight the importance of improving maternal iron status to prevent anemia and its adverse effects on the newborn.

Table 4: Correlation of hematological variables of a mother with infants at birth and at 14 weeks.

Hematological parameters	At the birth		On the 14 weeks-	
	r	P value	r	P value
HB	0.328	0.001	0.798	0.001
Ferritin	0.231	0.002	0.289	0.001

Discussion

This current study highlights the importance of addressing maternal anemia during pregnancy to ensure the proper development of infants [18]. Maternal anemia may ensue from inadequate iron ingestion or assimilation of escalated iron requisites attributed to recurrent pregnancies, or hemorrhage during the antenatal or perinatal phases. Nonetheless, it is associated with unfavorable clinical repercussions such as premature parturition, neonatal underweight, and neonatal demise, among others. Thus, the mitigation of maternal anemia emerges as an imperative consideration, which can be enhanced via the implementation of a balanced nutritional regimen and diverse iron supplementation strategies to ameliorate maternal and neonatal well-being consequences. [18,19]. Our findings suggested that fetal iron uptake occurs in utero regardless of maternal iron status, as infants have higher levels of iron and Fe than their mothers [18]. However, maternal anemia can still impact iron accretion in infants [20-25]. The present study found that infants born to anemic mothers had significantly lower Hb and Fe levels at 14 weeks than infants born to nonanemic mothers. These results are consistent with previous studies showing a link between maternal anemia and an increased risk of infant anemia up to 9 months [26].

The study also found that congenital disabilities associated with lower iron stores last up to a year and lead to iron deficiency anemia, consistent with previous studies by Goldenberg, and Culhane [27]. At birth and 14 weeks, the study showed a significant correlation between mother and child hemoglobin and serum ferritin levels [28-30]. Although the infants were not anemic at both times, those born to anemic mothers had lower iron stores and were more likely to develop anemia later on [25-26]. The study also found a significant correlation between mothers' hemoglobin and ferritin levels and the ferritin levels of their infants, which is consistent with the findings of other studies, such as Terefe, et al., [14].

However, there is a positive correlation between maternal Hb levels and the risk of anemia in infants. Studies have shown that Infants born to anemic mothers are at a higher risk of developing anemia than those born to nonanemic mothers; an anemic mother can affect fetal development and reduce iron stores in infants the newborn [30,31].

The statement about the low specificity of the parameters mentioned above may refer to the diagnostic criteria for anemia, which can be affected by other factors such as subclinical infections [32,33]. For example, some infections can cause inflammation, increasing certain proteins involved in iron metabolism. This can link with false positive or false negative results when diagnosing anemia based on Hb levels alone. Therefore, it is important to consider serum ferritin levels and iron status when assessing the risk of anemia in infants. Additionally, addressing maternal anemia during pregnancy through appropriate nutrition and iron supplementation can help reduce the risk of anemia in infants. The other studies reported different results or maybe showed weak correlations between these two variables; however, the weak correlation between newborns and their mothers' hematological parameters may be attributed to the heterogeneity [28-30]. Similarly, other studies have found a strong association between maternal and infant anemia, especially in the first few months of life [31,32].

However, infants born to anemic mothers may develop anemia later in infancy, even if they don't have IDA at birth [33]. IDA is very important to highlight the importance of follow-up studies to assess the long-term effects of maternal anemia on infant health [33].

Based on current research, it is recommended that term infants born to anemic mothers undergo screenings for their iron storage status at birth and at 14 weeks of age to receive appropriate interventions as per the finding. This is especially important for exclusively breastfed infants, as breast milk alone may not provide sufficient iron to meet their needs. Timely interventions can help prevent and treat anemia in infants, which can affect their health and development.

Conclusions

Infants born to IDA mothers had significantly lower median hemoglobin and ferritin concentrations than infants born to NA mothers. Additionally, there was a strong correlation between the mothers'Hb and Fe levels and the newborn's Hb and Fe levels. However, there is a significant correlation between maternal and infant hematological parameters. Infants born to anemic mothers had significantly lower Hb and ferritin levels than those born to nonanemic mothers. Their mothers' iron deficiency may impact infants' iron status. These results lead us to co maternal IDA may impact newborns' iron reserves.

Gap analysis and global implementation-intervention

Need for more research on the relationship between maternal anemia and infant anemia in the same study population: This current study has explained the correlation between maternal and infant anemia in the study population, which has not to extensively studied in the particular study area. Understanding this relationship can help identify infants at risk of anemia and inform appropriate interventions.

Limited information on the effectiveness of current interventions to prevent and treat maternal and infant anemia: The study will assess the effectiveness of current interventions, such as iron supplementation and nutrition education, in preventing and treating maternal and infant anemia. This information can guide the development of more effective interventions and strategies to improve maternal and child health outcomes.

Inadequate data on the long-term consequences of maternal and infant anemia: The study will also investigate the long-term consequences of maternal and infant anemia on child growth and development, which has yet to be well studied in the region. This information can help identify the potential risks and inform appropriate interventions to improve long-term health outcomes.

Insufficient data on the effectiveness of iron supplementation programs: Iron supplementation is a common intervention for preventing and treating IDA among pregnant women and infants in India. However, more data on its effectiveness in improving maternal and child health outcomes must be collected. This current study will assess the effectiveness of iron supplementation programs in the study population, which can inform the development of more effective interventions and strategies to improve maternal and child health.

Limited understanding of the determinants of iron deficiency anemia among pregnant women: There is a lack of information on the determinants of iron deficiency anemia among pregnant women in the study population, including sociodemographic, dietary, and lifestyle factors. This study will also identify these determinants, which can inform targeted interventions and strategies to prevent and treat iron deficiency anemia among pregnant women in the study population.

Hence, this research endeavors to bridge several critical knowledge gaps pertaining to maternal, infant, and child health in India. These findings have the potential to serve as a foundation for evidence-driven policies and initiatives aimed at enhancing the health and overall welfare of women and children within the region.

Author-Contributions

The first and corresponding authors (GPD, RK, AB)conducted experiments and wrote the soft copy manuscript, and data analysis was done with the help of a statistician and SPSS-17.0.The second author (RD) supervises and corrects the direction of the work. The third author (AR) revised the manuscript and made corrections in the manuscript. All authors have read and agreed to the published version of the manuscript.

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