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Study of iron deficiency anemia in infants of 3 to 6 months age group and its risk factors: a cross sectional study

Varun Ganjigunta, Varsha Suresh Ahirrao*, Premalatha R., Ravichander B.

Department of Pediatrics, MVJ Medical College and Research Hospital, Hoskote, Karnataka, India

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*Correspondence:

Dr. Varsha Suresh Ahirrao,

E-mail: drvarsha2006@yahoo.co.in

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ABSTRACT

Background: Iron deficiency anemia in 3-6 months-old infants is often neglected. Its presence in healthy infant of less than 6 months of age is largely debated. Neglecting IDA in this critical phase of growth can lead to serious consequences. The aim and objective of the study was to estimate the frequency of IDA in 3-6 months old infants, admitted in rural tertiary care hospital and to study its risk factors.

Methods: The cross-sectional study was conducted in the pediatric department of rural tertiary care hospital. 100 infants in the age group 3-6 months were included in the study. Relevant maternal and infant factors were noted. CBC with blood indices, peripheral blood smear and reticulocyte count were studied. Anemia in them was defined as hemoglobin <9.5 g/dl. IDA was diagnosed based in history, examination, indices, and peripheral smear.

Results: 22% of infants of 3-6 months had IDA. 40.9% of infants with IDA were low birth weight compared to 11.5% without IDA (p value<0.05). All pre-terms included in the study had IDA. 16% of term, normal birth weight, exclusively breast-fed infants had IDA. Underweight and stunting were seen in 31.8 % and 30.8% of IDA infants compared to 9% and 5.4% of infants without IDA.

Conclusions: IDA was quite common in infants less than 6 months and also seen in healthy, term and exclusively breast-fed babies, so universal iron supplementation before 6 months need to be considered in National Iron plus Initiative in India. Preterm, LBW babies and babies with NICU stay are at higher risk of IDA.

Keywords: Iron deficiency anemia, 3-6 months

INTRODUCTION

Anemia is defined as a reduction in the hemoglobin concentration, hematocrit, or the number of RBCs per cubic millimetre. Anemia is one of the most common and widespread nutritional disorder in developing countries. According to National Family Health Survey (NFHS3), 79% of Indian children have anemia, including 71% of urban children and 81% of those in rural areas.

Iron deficiency anemia is the commonest cause of anemia in infancy and childhood. Infants are at particular risk due to their rapid growth and limited dietary sources of iron.³ Iron is involved in many central nervous system processes that could affect infant behaviour and development.

Iron deficiency anemia has been associated with adverse effects on cognitive and physical development, and on the immune function of children. Midarm circumference and head circumference of children with iron deficiency anemia was significantly lower compared to the control group. Studies have shown that correction of anemia is associated with a reduction in the increased morbidity seen in children with iron deficiency anemia.

There is standard cut-offs for hemoglobin and hematocrit proposed by WHO to define anemia in children more than 6 months of age.⁵ However, there is no standard cut-off of hemoglobin for infants less than 6 months. Conventionally, anemia is also defined as hemoglobin

concentration less than two standard deviation below the mean for that age and sex.¹

It is assumed that young infants up to 6 months of age are protected from ID if the mother had adequate iron stores during pregnancy, the baby is full-term, with normal birth weight, exclusively breast fed, and delayed umbilical cord clamping has been done. Iron provided from exclusive breastfeeding is sufficient till 6 months of age.⁴ Unfortunately, it is rare for all of these conditions to be met and, therefore, most infants in developing countries are at risk of ID during their first 6 months of life.^{6,7} Even in high income settings, where all the aforementioned criteria are more frequently met, few studies have found that the accumulated iron during pregnancy and the amount of iron available in breast milk during 1st 6 months of life is not enough to meet the needs of the infants.

Mild to moderate anemia in 3-6 months of age is often neglected. American academy of Pediatricians recommend iron supplementation to all the infants from 4 months of age. However, in India, as per National Iron Plus Initiative for Anemia control, universal iron supplementation for infants is recommended from 6 months of age. There are few studies on anemia in 3 to 6-months age group of infants. And there is a controversy regarding presence and magnitude of iron deficiency anemia in 3-6 months old healthy infants.

The aim of the study was to evaluate the magnitude and risk factors of iron deficiency anemia in 3-6 months old infants. The objective of the study was to estimate the frequency of Iron deficiency anemia in 3-6 months old infants, admitted in rural tertiary care hospital and to study its risk factors.

METHODS

This observational study was performed in the pediatric ward and pediatric ICU of MVJ Medical College and Research Hospital, Hoskote, Bengaluru from November 2018 to November 2020. All infants in the age group of 3-6 months, admitted in the pediatric wards or pediatric intensive care unit were included. Infants who had cyanotic congenital heart disease or who received blood transfusions within the last 1 month were excluded.

Their demographic profile, socioeconomic status and other relevant maternal and infant related factors were noted. The nutritional status of the mothers was assessed using anthropometric measurements. History such as antenatal iron and folic acid supplementation, maternal weight, her documented hemoglobin were noted down.

Mode of delivery, gestational age, birth weight, and significant postnatal events like NICU admission, repeated blood sampling were noted from history and confirmed by their previous health records. Detailed feeding history was recorded. Morbidity experience of infant was recorded. Relevant family history was taken. Data regarding delayed

cord clamping was not available for most of the infants, so not analyzed.

Study infants were examined for pallor, icterus, dysmorphic facies/hemolytic facies, organomegaly, or any other significant abnormalities. Nutritional status of infant is determined by measuring weight, length, and head circumference.

Complete blood count with indices, peripheral smear and reticulocyte count were done. Infants were diagnosed to be anemic if their hemoglobin levels were less than 9.5 g/dl which was two standard deviation below the mean for infants 3-6 month of age. 8.9 Infant was diagnosed as having iron deficient anemia if indices showed low MCV, low MCH, low MCHC and high RDW, confirmed by peripheral smear and no clinical evidence suggestive of conditions other than iron deficiency anemia.

Frequency of iron deficiency anemia in the study group (3-6 months infants) was calculated. Anemia in 3-6 months old infants was correlated with various maternal and infant factors

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Descriptive statistics (means, percentages, standard deviations, and range) were computed for demographic and socioeconomic data. Analyses were stratified by age, sex and other characteristics.

The Chi-square test and correlation were used to test the strength of association between factors influencing anemia such as nutritional status, birth weight, growth pattern, morbidity status and maternal nutritional status at a significance level of 0.05. Continuous data was represented as mean and standard deviation.

Independent T test was used as test of significance to identify the mean difference between two quantitative variables. P value (probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. The study was approved by the Institutional Ethical Committee.

RESULTS

A total 121 infants of 3-6 months of age fulfilling the criteria were enrolled in our study. Out of them, 21 were excluded. Remaining 100 were included in the study and were studied for presence of iron deficiency anemia and its risk factors.

Majority of infants in study group were term (96%), with normal birth weight (78%), appropriate for gestational age (84%) and exclusively breast fed (96%). Maternal anemia was quite prevalent, seen in 78% of mothers. All mothers except one had taken adequate antenatal supplements. Only one mother had inadequate birth spacing. Out of 100 infants included in study, 22 had iron deficiency anemia.

We correlated various maternal and infant factors with occurrence of iron deficiency anemia. The baseline characteristics of infant factors are cited in Table 1, while the baseline characteristics of maternal and socioeconomic factors are given in Table 2. The factors associated with IDA are given in Table 3. Age, sex, socioeconomic status, maternal weight, height, mode of delivery did not have any significant association with occurrence of iron deficiency anemia in infants. Maternal anemia was more commonly

observed in infants with iron deficiency anemia than without it (90.9% vs 74.4%). However, the difference was not significant. Association of iron deficiency anemia in 3-6 months infants with maternal supplements, inadequate birth spacing, and type of feeding cannot be assessed as almost 99% of them had history of adequate intake of maternal supplements, had adequate birth spacing and exclusively breast fed.

Table 1: Baseline characteristics: infant factors.

Parameters		Number (N)	Percentage (%)
Age (months)	3	33	33
	4	18	18
	5	18	18
	6	31	31
Sex	Male	53	53
	Female	47	47
	<2.5	22	22
Birth weight (kg)	2.5-4	78	78
	>4	0	0
Gestational age (weeks)	<37	4	4
	37-42	96	96
	>42	0	0
Weight for gestational age	SGA	14	14
	AGA	84	84
	LGA	2	2
NICU admission and multiple pricks	Yes	10	10
	No	90	90
Type of feeds	Exclusive breast milk	96	96
	Top feeds	1	1
	Mixed feeds	3	3
Weight for age	Normal	86	86
	<-2SD	14	14
Length for age	Normal	88	88
	<-2SD	12	12

Table 2: Baseline characteristics- maternal and socioeconomic factors.

Parameters		Number (N)	Percentage (%)
Socioeconomical status	4 (Upper lower class)	10	10
	3 (Lower middle class)	46	46
	2 (Upper middle class)	35	35
	1 (Upper class)	9	9
Maternal anemia	Yes	78	78
	No	22	22
Maternal stunting	Yes	13	13
	No	87	87
Maternal BMI	Underweight	4	4
	Normal	69	69
	Overweight	26	26
	Obese	1	1
Antenatal supplements	Yes	99	99
	No	1	1
Birth spacing	Yes	34	34
	No	1	1
	Primigravida	65	65

Table 3: Factors associated with iron deficiency anemia.

		Iron deficiency anemia				
		Present				
Factors		Count	Percentage (%)	Count	Percentage (%)	P value
Age	3	8	36.4	25	32.1	0.940
	4	4	18.2	14	17.9	
	5	3	13.6	15	19.2	
	6	7	31.8	24	30.8	
Gender	Female	10	45.5	37	47.4	0.060
	Male	12	54.5	41	52.6	0.869
	4	1	4.5	9	11.5	
GT	3	11	50.0	35	44.9	0.672
SE status	2	9	40.9	27	34.6	0.672
	1	1	4.5	7	9.0	
Matamal arrest	<11 g/dl	20	90.9	58	74.4	0.000
Maternal anemia	>11g/dl	2	9.1	20	25.6	0.098
	No	17	77.3	70	89.7	0.125
Maternal stunting	Yes	5	22.7	8	10.3	0.125
	Normal	12	54.5	57	73.1	
D1571	Obese	1	4.5	0	0.0	0.134
BMI interpretation	Overweight	8	36.4	18	23.1	
	Underweight	1	4.5	3	3.8	
Antenatal supplements	No	1	4.5	0	0.0	0.058
	Yes	21	95.5	78	100.0	
	LSCS	11	50.0	32	41.0	0.453
Mode of delivery	Vaginal	11	50.0	46	59.0	
	LBW	9	40.9	9	11.5	0.002*
LBW	Normal BW	13	59.1	69	88.5	
	Preterm	4	18.2	0	0	<0.001*
Gestational age	Term	96	81.8	78	100	
	AGA	19	86.4	65	83.3	0.746
Weight for GA	LGA	0	0.0	2	2.6	
Weight for Oil	SGA	3	13.6	11	14.1	
Inadequate birth	Yes	1	4.5	0	0	
spacing	No	21	95.5	78	100	0.135
Twins	No	22	100.0	78	100.0	-
NICU stay and	No	17	77.3	73	93.6	
multiple blood sampling	Yes	5	22.7	5	6.4	0.024*
H/O bleeding	No	22	100.0	78	100.0	-
	Combined/ Formula	2	9	2	2.6	0.146
Feeds	Exclusive breast feeding	20	90.9	76	97.4	
	Underweight	7.	31.8	7	9	0.006*
Weight	Normal	15	68.2	71	91	0.000
	Stunted	8	30.8	4	5.4	<0.001*
Length	Normal	18	69.2	70	94.6	
D_0 05	Horman	10	07.2	70	77.0	

*P=0.05

All pre-terms had iron deficiency anemia. 40.9% of infants with iron deficiency anemia had low birth weight compared to 11.5% of infants without iron deficiency anemia. 22.7% of infants with iron deficiency anemia had h/o NICU stay, and multiple blood sampling compared to 6.4% of infants without iron deficiency anemia (p

value=0.024). 31.8% of infants with iron deficiency anemia were underweight compared to 5.4% of infants without iron deficiency anemia (p value=0.006). 30.8% of infants with iron deficiency anemia were stunted compared to 9% of infants without iron deficiency anemia (p value<0.001).

Total number of terms, normal birth weight, exclusively breast-fed infants were 75. And out of them, 12 had iron deficiency anemia. 16% of term, normal birth weight, exclusively breast-fed infants had iron deficiency anemia with Hb<9.5 g/dl and 48% of them has Hb<10.5 g/dl.

Anemia is one of the most common and widespread nutritional disorder in developing countries. According to National Family Health Survey (NFHS3), 79% of Indian children have anemia, including 71% of urban children and 81% of those in rural areas.¹

Frequency of iron deficiency anemia (Hb cut off- 9.5 g/dl) in infants of 3-6 months of age was 22%. 16% of term, normal birth weight, exclusively breast-fed infants had iron deficiency anemia (Hb<9.5 g/dl) and 48% of them had Hb<10.5 g/dl.

Similarly, study done by Pee et al in rural part of Indonesia observed the prevalence of hemoglobin less than 9 g/dl in 13.4% and less than 10 g/dl in 37% of infants aged 3-5 months. Marques et al in their study observed 3.4% and 23.5% of the infants at 4 and 6 months of age, respectively had iron deficiency anemia. Indian study, done by Krishnaswamy et al at PGI, Chandigarh found higher prevalence of iron deficiency anemia (21.4% and 36.4% respectively) at 4 and 5 months of age in predominantly breast fed, term infants (Hb cut off- 10.5g/dl). Similarly, Hemachitra et al in their study done in South India, found 67.8% of 3-6 month old infants had iron deficiency anemia (Hb cut off- 11 g/dl). Higher prevalence in above Indian studies could be because of higher Hb cut off. 13

Occurrence of iron deficiency anemia in our study was significantly associated with low birth weight, preterm delivery, and NICU stay with multiple blood sampling. All infants born preterm had iron deficiency anemia. Muleviciene et al in their study found a greater number of low-birth-weight and premature infants in the group with iron deficiency anemia than the control group. ¹⁴ Pee et al showed that a lower hemoglobin and serum ferritin levels were related to low birth weight and prematurity in the infants. ¹⁰ Berglund et al in their study have seen a lower prevalence of iron deficiency anemia at 6 months of age in normal birth weight babies, when compared to babies born with marginally low birth weight. ¹⁵ Teixeira et al observed significant association of low birth weight and low hemoglobin at 6 months of age (p value=0.02). ¹⁶

Pre-term infants are prone to develop IDA in the first 4 months of life due to lower iron stores at birth compared with term infants as majority of placental iron transfer occurs in third trimester, rapid growth and iron losses. Most fetal iron is transferred from the mother during the third trimester of gestation. ¹⁷⁻¹⁹ Low birth weight infants have higher iron requirements due to rapid postnatal growth compared to that of term infants and are, therefore, susceptible to a higher risk of developing iron deficiency or iron deficiency anemia.

Even though statistically not significant, history of maternal anemia was more commonly seen in infants with iron deficiency anemia (90.9%) than in infants without iron deficiency anemia (74.4%). Zhang et al have shown that lower hemoglobin(<10.9 g/dl) during 24-28 weeks of gestation was significantly associated with anemia in infants at 5-7 month of age.²⁰ Similarly, hemachitra et al observed the risk of anemia in 3-6 months old infants, born to anemic mothers is 5.9 times greater than those born to non-anemic mother.

The fetus of iron deficient mothers accumulates less iron reserves and has smaller hemoglobin mass than their counterparts. After about 3-4 months of age, a gradual shift occurs from an abundance of iron to limited reserves. This is a period of rapid growth with increased requirements of iron, which in turns leads to iron deficiency anemia.

In our study, we observed that infants with iron deficiency anemia were significantly more likely to be underweight and stunted than infants without iron deficiency anemia (underweight and stunting in 31.8% and 30.8% of iron deficiency anemia infants compared to 9% and 5.4% of infants without iron deficiency anemia). Similar observation was found in study by Pee et al. Rahman et al found higher prevalence of anemia in stunted children (56%) compared to their healthy counterparts (48%).²¹

This important effects of iron on growth can be explained by its essential role in multiple metabolic processes, including oxygen transport, DNA synthesis and electron transport. ²² Iron-sulfur clusters are crucial cofactors of numerous proteins involved in enzyme catalysis, electron transport and regulation of gene expression. ^{23,24} In addition, iron deficiency may affect growth through IGF-I dependent mechanism.

Limitations of the study were that iron studies were not done for diagnosis of iron deficiency anemia. It was diagnosed based on clinical examination, CBC with red blood cells indices, reticulocyte count and peripheral smear. And this was institutional based rather than community-based study.

CONCLUSION

This study shows IDA is quite common in 3-6 months old infants and also seen in healthy, term and exclusively breast-fed babies. So, universal supplementation of iron before 6 months of age like AAP guidelines should be considered in National Iron plus Initiative in India. Preterm, LBW babies and babies with NICU stay are at higher risk of IDA. Iron deficiency in infants significantly affects growth.

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Institutional Ethics Committee

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