

Anemia in early life (up to the age of 6 months) – Is it really a disease burden? A cross-sectional study from Sub-Himalayan region

Charu Maggo¹, Shivani Gahalot², Seema Sharma³

From ¹Intern, Department of Paediatrics, Dr. Rajendra Prasad Government Medical College, Sadarpur, Himachal Pradesh, India, ²Junior Resident, ³Associate Professor, Department of Paediatrics, Dr. Rajendra Prasad Government Medical College, Sadarpur, Himachal Pradesh, India

ABSTRACT

Objectives: To determine whether or not, all breastfed newborns should get preventive iron (up to age of 6 months). It will determine the disease burden and clinicopathological profile of anemia in infants up to 6 months and its correlation with maternal Hb levels. **Materials and Methods:** A 4-month hospital-based cross-sectional study was conducted in all infants under the age of 6 months and their mothers admitted to the pediatric ward of a tertiary health care center in the Sub-Himalayan region. **Results:** About 42% of infants (up to 6 months of age) and 64% of mothers were found to be anemic. It was found that mothers of 74% of total anemic infants were also anemic. Furthermore, in 79% cases mothers with good ferritin stores (≥ 12 ng/ml) also have infants with good ferritin levels (≥ 10 ng/ml). It was found that mothers who have not consumed adequate amount of iron in their pregnancy, 44% of them have anemic infants. Despite the fact that the association between newborn and maternal characteristics is not statistically significant, the results are noteworthy, indicating the need for a more comprehensive investigation to determine the relationship. **Conclusion:** High rates of anemia in early life point to the need of multicentric as well as population-based study so that we can collect evidence to start iron prophylaxis in this highly vulnerable developing age group of 0–6 months. Further higher rates of anemia in mothers warrant the strengthening in the implementation plan of iron and folic acid supplementation to all females of reproductive age group.


Key words: Anemia, Ferritin, Iron and folic acid supplementation, Iron deficiency

Iron deficiency anemia is linked to a long-term developmental disadvantage in children when compared to their peers who have a better iron status [1]. Hence, nutrition interventions are important at many points in life course and attention to practice in the early period will bring benefits throughout [2]. Because newborns are exclusively breastfed for the first 6 months of their lives, the iron and lactoferrin concentrations in breast milk are crucial for maintaining their body iron levels. Maternal anemia may have an impact on these concentrations in breast milk [3]. Mothers' and their children's health and nutrition are inextricably linked [1]. Anemia identified in women early in pregnancy has been linked to an increased risk of autism spectrum disorder and attention deficit hyperactivity disorder and particularly intellectual disability development in offspring [4].

There is an evidence that even children with normal birth weight, but born of anemic mothers will have insufficient iron reserves at birth and are more likely to develop anemia [5]. According to the WHO estimates, anemia affects 24.8% of people

worldwide, with the highest incidence reported in pre-school children (67.6%) and pregnant women (57.1%) in Sub-Saharan Africa [6]. As a result, understanding risk factors, which may be present as early as childhood, is critical for supporting control and preventative initiatives. Iron supplementation for infants is now recommended based on the assumption that iron present at birth and in breast milk is sufficient for the first 6 months of life [7]. This assumption, however, is based on a number of factors that are not always present in low-income countries, including adequate maternal iron and nutritional status, appropriate birth practices that promote the transfer of a portion of the birth iron through placental blood, and exclusively breast feeding, which prevents pathological iron loss due to damage to the intestinal wall [8].

Some exclusively breastfed newborns may develop iron deficiency, according to a WHO committee [9]. Exclusive breastfeeding protects children from iron deficiency anemia in the first 4 months of life, according to Marques *et al.* [10], Glader and Calvo *et al.* in their work have recommended that infants who are solely breastfed should start getting iron supplements at the age of 4 months [11,12]. Dewey *et al.* have also suggested iron drops

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Correspondence to: Charu Maggo, Intern, Department of Paediatrics, Dr. Rajendra Prasad Government Medical College, Sadarpur, Himachal Pradesh, India. E-mail: charumaaggo@gmail.com

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for breastfed newborns weighing between 2500 g and 3000 g at delivery [13]. McMillan *et al.* and Owen *et al.*, on the other hand, found that term breastfed infants did not require supplemental iron until they were 12 months old [14] and 6 months old [15], respectively. Furthermore, Raj *et al.* found that solely breastfed infants of non-anemic and anemic mothers did not develop iron deficit or iron deficiency anemia by the age of 6 months [16].

According to Zavaleta *et al.*, maternal anemia had no effect on the iron or lactoferrin concentration in breast milk at birth or during lactation [17]. Sudaryati *et al.* inferred that anemia in breastfeeding mother was unrelated to infant anemia or stunting [18]. Kemunto concluded that infants who are solely breastfed have a higher risk of getting iron deficiency anemia than those who are given supplemental feeds before the age of 6 months or infant formula in addition to breast milk [19]. As a result, there is a debate concerning whether breast milk is adequate for sustaining optimal iron status in exclusively breastfed infants. Despite the fact that iron deficiency is the most frequent dietary deficit in the world, the literature on the disease burden caused by anemia in early life (up to 6 months) is scarce. Thus, the question of whether all breastfed newborns should be given preventive iron remains unanswered. We have planned to do this study to find the status of disease burden due to anemia in infants up to the age of 6 months so that appropriate measures can be taken for early identification and treatment of anemia in these infants.

MATERIALS AND METHODS

This was a 4-month hospital-based and cross-sectional study done in our tertiary care institute's Department of Pediatrics after receiving Institutional Ethics Committee permission. All the infants up to 6 months of age admitted in pediatric wards and mother-baby pairs were taken into the study group after taking informed consent. Exclusion criteria for infants were: Infants getting discharged after stay in NICU/SNCU during neonatal period, the infants with recurrent admissions and/or suffering from chronic illness, for example, hemolytic diseases, parvovirus infection, chronic kidney disease, etc., infants on iron therapy in the past 1 month, infants who received blood transfusion in the past 2 months or infants who have undergone double volume exchange/partial exchange in the past 2 months, infants with any bleeding disorder or coagulation defect, and infants with any acute blood loss, for example, trauma. Exclusion criteria for enrollment of mothers were: Any chronic illness in the mother, mother who had suffered from any excessive bleeding during antenatal and postpartum period in the past 2 months, mother suffering from any bleeding disorder, mothers who have received blood transfusion in the past 2 months, and mothers who were on therapeutic doses of iron therapy.

After history taking and detailed examination, following investigations were sent for infant-mother pairs – hemogram, peripheral blood film, reticulocyte count, iron studies, Vitamin B12 levels, folate levels, and electrophoresis if there is an evidence of hemolysis. Blood sample was collected using the peripheral venepuncture method, with 5 mL of blood from the mother and

Table 1: Relation of presence of anemia in infant mother pairs

Groups	Mother anemic	Mother non-anemic	Total	p-value
Infant anemic	31	11	42	0.095
Infant non-anemic	33	25	58	
Total	64	36	100	

Table 2: Relationship of ferritin stores in infant-mother pairs

Groups	Mother ferritin in ng/ml		Total	p-value
	<12	≥12		
Infant ferritin in ng/ml				
<10	1	7	8	0.899
≥10	13	79	92	
Total	14	86	100	

Table 3: Relationship of maternal iron intake with anemia in infants

Iron intake	Anemic infants	Non-anemic infants	Total	p-value
<180 days	7	9	16	0.877
≥180 days	35	49	84	
Total	42	58	100	

3 mL from the newborn withdrawn under strict aseptic conditions in EDTA vials and plain vials for further processing. The data were collected using a pre-designed performa, which comprised sociodemographic and socioeconomic information about the households and the caregiver such as name, age, sex, marital status, infant information included type of feeding, feeding practices, complementary feeding practices, health information and anthropometric measurements, and morbidity experience of the infant. Maternal information included maternal nutritional status and iron supplementation status throughout pregnancy (Fig. 1).

Definitions utilized for the present study were – Anemia in infants: Hb levels <10 g/dl for infants up to 5 months (Brault-Dubuc *et al.*) and <11 g/dl for infants of 6 months of age (WHO). Iron deficiency in infants: Plasma ferritin concentration <10 ng/ml. Anemia in mothers: Hb <12 g/dl. (WHO). Iron deficiency in mothers: Plasma ferritin <12 ng/ml. (WHO). The information gathered was then uploaded to a Microsoft Excel spreadsheet for additional analysis. It was analyzed as mean, percentage, and frequency; other statistical tests were applied as per requirement. Chi-square test was used for categorical variables. The value of $p < 0.05$ was considered statistically significant.

RESULTS

During our study period of 4 months, 1750 patients were admitted in the pediatric ward. Out of these, 547 patients were infants. In the infants, 398 were of age ≤6 months. Out of these 398 patients, 298 patients were excluded on the basis of exclusion criteria given in the methodology section. Our study group, hence, comprised of 100 infants. The majority of infants in our study group belong to age group of 0–2 months (38%) followed by 31% of infants each in 2.1–4 and 4.1–6 months. About 68% of total study group

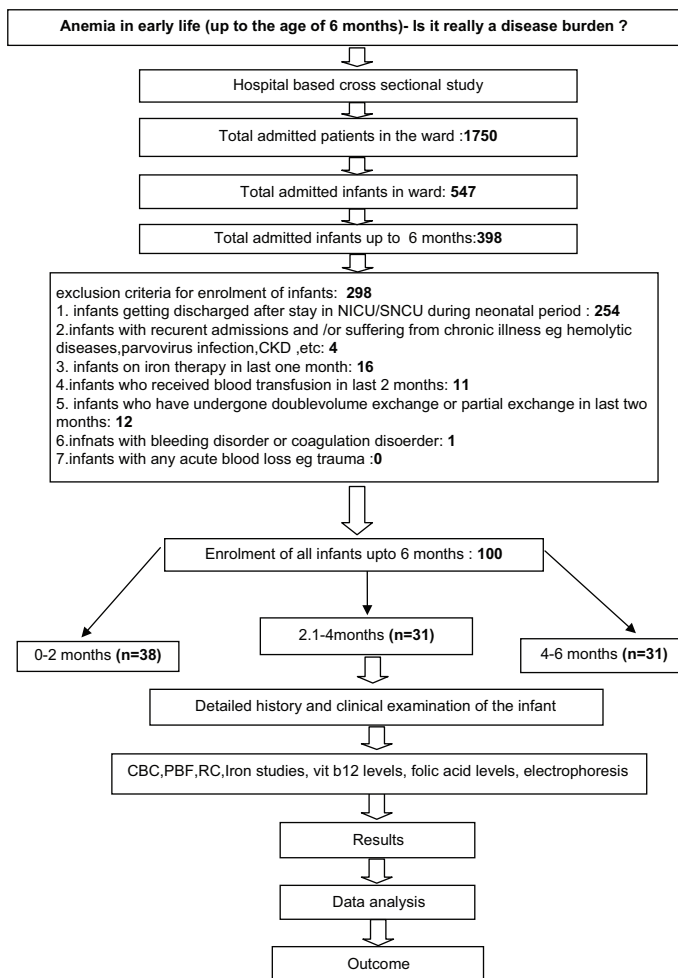


Figure 1: Study design

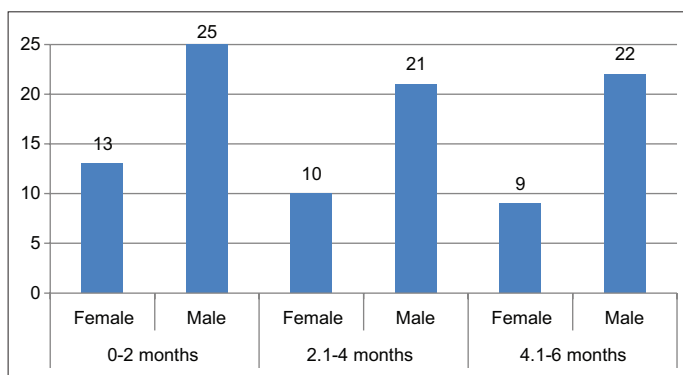


Figure 2: Distribution of infants on basis of age and gender frequency (n=100)

were males, making ratio of male to female of about 2:1 (Fig. 2). The majority of infants presented with chief complaints of cough (54%) followed by fever (51%) (Fig. 3). About 16% of infants have history of the previous hospitalization due to variable complaints. Exclusive breastfeeding was found to be the most common mode of feeding (72%).

A declining trend was observed with increasing age in practice of exclusive breastfeeding as only 51% of total infants of age 4.1–6 months were exclusively breastfed compared to 79% of infants of 0–2 months. The majority of infants (63%) weighed ≥ 2.5 kg at birth. The majority of infant mother pairs

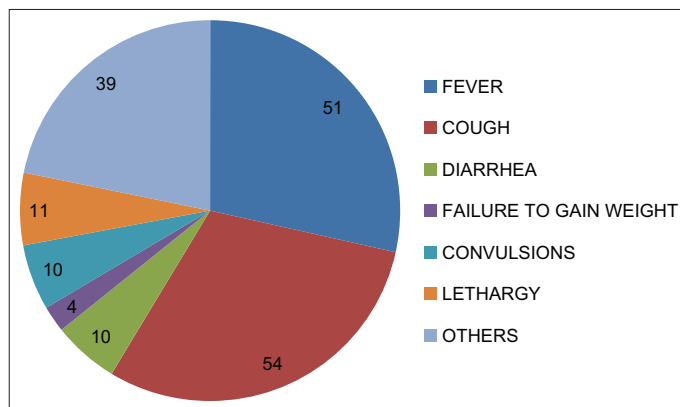


Figure 3: Distribution of infants as per chief complaints at the time of presentation

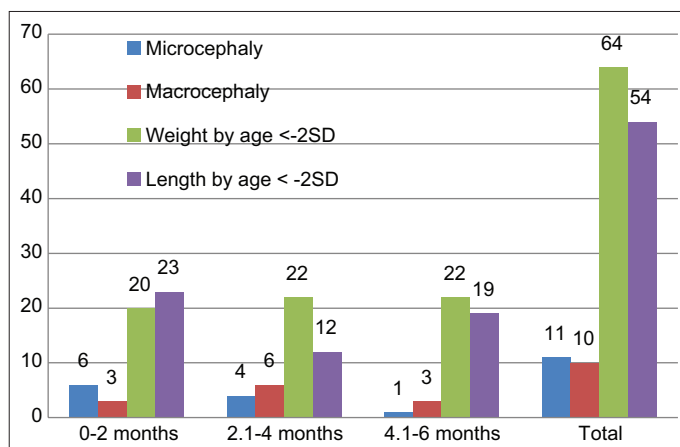


Figure 4: Distribution of infants on basis of anthropometry

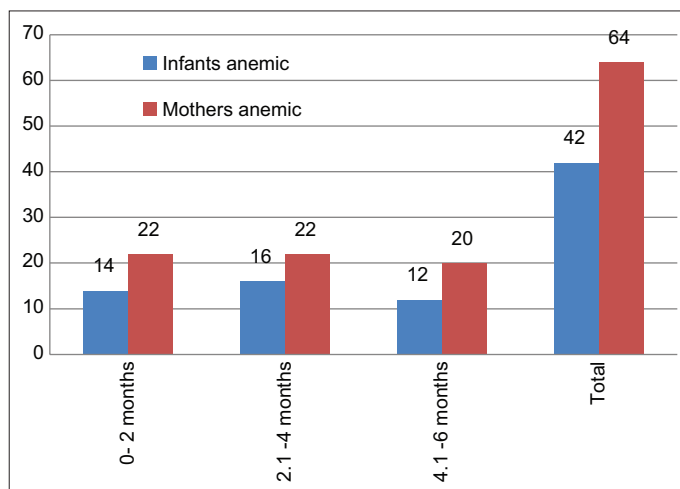


Figure 5: Distribution of infants and mothers on basis of anemia

(64%) belong to the upper middle class according to the modified Kuppuswamy scale. About 21% of infants were found to have abnormal OFC. About 54% of infants were found to have length < -2 SD. About 64% of infants were having weight below -2 SD with maximum cases above 2 months of age (44%) (Fig. 4). About 42% of infants were found to be anemic with maximum cases at 2.1–4 months of age (Fig. 5). About 97% of mothers in our study group were found to be literate. About 61% of them have completed their high school and 24% are graduated.

Total 84% of mothers have taken iron and folic acid supplementation (IFAS) for adequate period. However, 16% have consumed incompletely, out of which 2% have never consumed the prophylaxis. About 64% of mothers were found to be anemic. About 24% of them have mild anemia (11–11.9 g/dl), 35% moderate anemia (8–10.9 g/dl), and 5% severe anemia (Hb <8 g/dl). About 31% of mothers were found to have serum iron <41 µg/dl. About 12% of mothers were found to have poor ferritin stores (<10 ng/ml). It was found that mothers of 74% of total anemic infants were also anemic (Table 1). Furthermore, in 79% cases mothers with good ferritin stores (≥ 12 ng/ml) also have infants with good ferritin stores (≥ 10 ng/ml) (Table 2). It was found that mothers have not consumed adequate amount of iron in their pregnancy, 44% of them have anemic infants (Table 3).

DISCUSSION

During the 4-month study period, 1750 patients were admitted in the pediatric ward. Out of these, 547 patients were infants. In the infants, 398 were of age ≤ 6 months. Hence, the infants up to age of 6 months were 22.7% of total admissions and 72.7% of total infants' admission in pediatric ward during our study period. Out of these 398 patients, 298 patients were excluded on the basis of exclusion criteria given in the methodology section.

Infants Characteristics

Our study group comprised of total 100 infants which were further divided into three age groups. Maximum number of infants were from 0 to 2 months (38%) followed by 31% each of 2.1–4 and 4.1–6 months. About 68% of total study group were males, making ratio of male to female of about 2:1. These findings on age distribution are comparable to those reported by Sudaryati E, in which, 50% of study group was from 0 to 2 months, 31% from 2.1 to 4, and 19% from 4.1 to 6 months [18].

The majority of infants in our study group were admitted with chief complaints of cough (54%) and fever (51%). Other illnesses reported were lethargy, diarrhea, convulsion, failure to thrive, and excessive crying. Almost similar trend was witnessed by Nyamasege who found common cold to be the most common illness in his study group [19]. In our study group, 16% infants also have history of the previous hospitalization due to variable symptoms, with maximum infants admitted due to respiratory illness (38%). This could be due to the fact that infant's immunity is not well developed which make them more prone to infections such as common cold and pneumonia.

Data were collected regarding feeding practices. Exclusive breastfeeding was found to be the most common mode of feeding (72%). A declining trend was observed with increasing age in practice of exclusive breastfeeding as only 51% of total infants of age 4.1–6 months were exclusively breastfed compared to 79% of infants of 0–2 months. Overall, the rate of exclusive breastfeeding is higher when compared to study at Nairobi which reported 57% of exclusive breastfeeding [19]. This could

be attributed to better awareness programs regarding exclusive breast feeding being implemented in India. However, this rate is lower when compared to recommendation of 90% given by the WHO (2009) for exclusive breastfeeding among infants up to age of 6 months.

The majority of infants (63%) weighed ≥ 2.5 kg at birth. The majority of our study population belong to the upper middle class according to the modified Kuppuswamy scale. Anthropometric measurements of infants were done at the time of admission and it was found that 21% of infants were of abnormal head circumference (11% microcephaly and 10% macrocephaly). The mean weight in the study sample was 4.5 ± 1.3 kg with the lightest child weighing 2 kg and heaviest child 11 kg. About 64% of infants have weight for age $< -2SD$, with a drastic increase in number as the age group shifts from 0–2 months (53%) to 2.1–4 months (71%). The mean length was found to be 57.4 ± 6 cm with shortest child of length 37 cm and longest child of 71 cm. About 54% of population have length for age < -2 SD with maximum number in 0–2 months of age (23%). The rates were found to be higher when compared to findings at Nairobi where only 9.2% of infants were found to be suffering from failure to thrive and only 11.2% were stunted [19]. The rates depict the poor nutritional status of infant-mother pairs in India. Reasons could range from poverty (making mothers unable to buy required amount of food) to consumption of highly adulterated foods.

Hematological profile of infants was analyzed and it was observed that 42% of study group were anemic with maximum cases in age group 2.1–4 months (38%). Hemoglobin levels were found to be 9.9 ± 2.7 g/dl on average. Results are comparable to findings of Chandyo *et al.* in Nepal where 49% infants were found to be anemic [20]. These findings were in contrast to assumption that breast fed infants do not develop anemia as they get whatever they need from their mother's milk. Furthermore, 8% of infants in our study groups were found to have low ferritin stores.

Maternal Characteristics

The majority of women in our study group are literate (97%). About 61% of them have completed their high school and 24% are graduated. The values are high when compared to national women literacy rate of 65.46% as per census 2011. Greater educational levels are most likely the cause of our region's higher exclusive breastfeeding rates.

Most mothers (84%) in our study group have consumed IFAS for the required period of 180 days. About 16% mothers have consumed it for lesser duration, out of which 2% have never consumed the prophylaxis. The results are comparable to findings at Nairobi where 73% mothers have consumed IFAS tablets for the required period of time [19]. The number is very high when compared to findings of national family health survey (2015–16) where an average of only 30.3% of mothers consumed IFAS for 100 or more days, this ranged from the lowest in Nagaland (4.4%) to the highest in Lakshadweep (82.1%). The better rates in our region could be attributed to better implementation of government schemes and better educational status of women.

Hematological profile of mothers was analyzed. About 64% of mothers were found to be anemic. About 24% of them have mild anemia (11–11.9 g/dl), 35% moderate anemia (8–10.9 g/dl), and 5% severe anemia (hb <8 g/dl). The figures were less when compared to results of Panyang's cross-sectional study in Assam which found 100% population to be anemic with 91.6% suffering from moderate anemia and 8.4% from severe anemia [21]. The high rates of mild, moderate, and severe anemia demand a due emphasis on implementation of INIPI program and health education regarding consumption of iron rich foods to bring down the prevalence of anemia among the women of reproductive age group in India. About 31% of mothers were found to have low serum iron <41 µg/dl. About 12% of total mothers had low ferritin stores (<10 ng/ml).

It was found that mothers of 74% of total anemic infants were also anemic. Furthermore, in 79% cases, mothers with good ferritin stores (≥ 12 ng/ml) also have infants with good ferritin stores (≥ 10 ng/ml). It was found that mothers have not consumed adequate amount of iron in their pregnancy, 44% of them have anemic infants.

CONCLUSION

In our study, total 42% of infants and 64% of mothers were anemic. Mothers of 74% of total anemic infants were also anemic. About 79% cases mothers with good ferritin stores (≥ 12 ng/ml) also have infants with good ferritin stores (≥ 10 ng/ml). Furthermore, mothers have not consumed adequate amount of iron in their pregnancy, 44% of them have anemic infants. Although the relationship between the two was not statistically significant, the figures are big indicating the need for a further comprehensive study to determine the relationship between infant and maternal parameters.

AUTHORS CONTRIBUTION STATEMENTS

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by Charu Maggo and Shivani Gahalot. The first draft of manuscript was written by Charu Maggo and Shivani Gahalot under supervision of Seema Sharma. The findings were considered by all authors and they all contributed to the final manuscript.

ETHICS APPROVAL

The study received ethical approval from IEC of Dr RPGMC (No: IEC/126/2019)

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