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ORIGINAL RESEARCH OPEN ACCESS

Study of etiological patterns and various clinical presentations of anemia in children aged 6 months to 5 years admitted in a tertiary care hospital

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Abstract

Background: Nutritional anemia (NA) is the commonest cause of anemia in children. Iron deficiency is the most important contributing factor to nutritional anemia. Severe iron deficiency is associated with impaired brain development along with cognitive, behavioural, and psychomotor manifestations, particularly during the first two years. This study aimed to evaluate the clinical and etiological profile of anemia in children aged 6 months to 5 years.

Material and methods: Hospital-based observational study conducted on children between 6 months to 5 years of age, admitted to Government General Hospital, Srikakulam and having anemia according to WHO classification.

Results: Of the 157 children diagnosed with anemia over 18 months period, iron deficiency anemia is the commonest cause of anemia, seen in 107 children followed by sickle cell anemia seen in 21 children. Out of the sampled children, 154 children recovered, and 3 children succumbed to death.

Conclusion: Nutritional anemia, particularly iron deficiency anemia is the most common type of anemia in 6 months to 5 years-old children. Co-morbidities like malnutrition, parasitic infestations, diarrheal diseases, and recurrent respiratory tract infections form a vicious cycle and result in nutritional anemia. Identifying the factors that are leading to iron deficiency anemia and implementing the control measures like early iron supplementation results in reducing morbidity and mortality.

***Keywords**:* iron deficiency anemia; sickle cell anemia; nutritional anemia

Introduction

Anemia is an extensive health problem associated with an increased risk of morbidity and mortality, particularly in young children. According to the estimation by WHO, prevalence of anemia worldwide in 2019 was 39.8% out of which 43% was among children aged 6 to 59 months, and the prevalence in India in this age group was 53.4% [1].

Anemia is the most contributing factor to morbidity and child mortality. Hence it is a critical health issue for children in India. Causative etiologies of anemia are Nutritional deficiencies like iron deficiency, folate, vitamins B12, B6 and E, copper and protein, diseases related to bone marrow and kidney, chronic infections and haemolytic anemias. Vitamin A and D deficiencies are also implied in anemia in recent studies [2, 3]. Approximately half of the cases of nutritional anemia are due to iron deficiency anemia [4].

The main aim of the study was to find various causes of anemia among 6 months to 5 years-old children

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admitted to the Department of Paediatrics and also studied the various clinical presentations of anemia among 6 months to 5 years age group.

Materials and methods

An observational study was done on children admitted to the Department of Paediatrics, Government General Hospital (GGH), Srikakulam, Andhra Pradesh, India from October 2019 to March 2021. Children admitted to GGH and who meet the inclusion criteria were selected and included in the study. Ethical clearance was obtained for this study from the institutional ethics committee. All children within the age group of 6 months to 5-years-old admitted to Department of Paediatrics who had anemia, graded according to World Health Organization (WHO) classification were included in the study.

We excluded the children whose parents did not give informed consent. We excluded the children with already diagnosed anemia and repeated admissions for blood transfusions children admitted with acute blood loss/ active bleeding or children with chronic systemic disorders.

History and examination were documented on a pre-designed proforma. A detailed general and physical examination was done to look for pallor, icterus, oedema, lymphadenopathy, and signs of vitamin deficiency. A thorough systemic examination was also done. All the children were screened initially for the presence of anemia with the investigations, which are complete blood count, red cell indices, peripheral smear study, reticulocyte count, and stool microscopy. A complete hemogram was done using an automated cell analyser for measuring the values such as haemoglobin, red cell count, white cell count, PCV, MCV, MCH, MCHC and platelet count. A peripheral blood smear was prepared, stained using Leishman stain and examined under the microscope. Children who had anemia according to the WHO classification [5] were classified as having microcytic, macrocytic or normocytic anemias according to the peripheral smear and MCV values. The children were subjected to further investigations depending upon the type of peripheral smear which included.

For the identification of iron level, we did serum iron, total iron binding capacity, and serum ferritin. For the identification of hemoglobinopathies, we have done a sickling test, haemoglobin electrophoresis. For identification of suspected cases of immune hemolytic anemias, we did a direct coombs test, lactate dehydrogenase levels, serum bilirubin, urine routine and microscopy, urobilinogen levels. For identification of Leukemias, aplastic anemia we did a bone marrow biopsy and aspiration. For identification of macrocytosis/ dimorphic anemia we have done serum vitamin B12 levels, and folic acid levels.

Other ancillary tests like ultrasound abdomen kidney, urinary bladder, and chest x-ray. To identify infectious causes we did smears for malarial parasites, scrub typhus IgM/IgG, dengue NS1, IgM, urine. Blood cultures and stool cultures were done whenever required.

A total of 157 children with anemia were studied and classified according to age, gender, geographical distribution, clinical presentation, etiological diagnosis, the severity of anemia and degree of malnutrition based on IAP classification of weight for age.

Results

The sample consisted of 157 children who diagnosed with anemia over 18 month's period. Among the total children, the highest number of children with anemia were in the 1 to 2 years age group followed by the 6 months to one year age group (Table 1). Figure 1 showed the incidence of anemia by age and gender in percentages.

Table 1: Age & gender-wise distribution of cases presented with anemia.

Age group	*Number*	*Percentage*	*Boys*	*Girls*
6 months to 1 year	40/157	25%	24	16
13 months to 24 months	61/157	39%	25	36
25 months to 36 months	25/157	16.5%	13	12
37 months to 48 months	16/157	10%	9	7
49 months to 60 months	15/157	9.5%	9	6

Among the 157 children studied the most common aetiology observed was iron deficiency anemia followed by sickle cell anemia, megaloblastic anemia, beta thalassemia major, malaria, autoimmune hemolytic anemia, leukemias and aplastic anemia.

Most of the children in the study population were from rural areas (70) followed by tribal (57) and urban (30) populations (Table 2). Conditions like beta thalassemia major, sickle cell anemia and malaria had a higher incidence in tribal populations when compared to other areas.

In this study out of 157 children, 32 children presented with mild anemia, 73 presented with moderate anemia, and 52 children presented with severe anemia (Table 3) according to WHO classification [5].

Table 2: Etiological diagnosis and geographic distribution of the anemia.

Diagnosis	*No: of cases*	*Percentage*	*Urban-30 (19%)*	*Rural-70 (45%)*	*Tribal-57 (36%)*
Iron-deficiency anemia	107	68%	26	57	24
Sickle cell anemia	21	13.5%	1	5	15
Megaloblastic anemia	7	4.5%	-	3	4
Beta thalassemia	11	7 %	-	2	9
Malaria	5	3.5%	-	1	4
Autoimmune hemolytic anemia	3	2%	3	-	-
Leukemias	2	1%	-	2	-
Aplastic anemia	1	0.5%	-	-	1

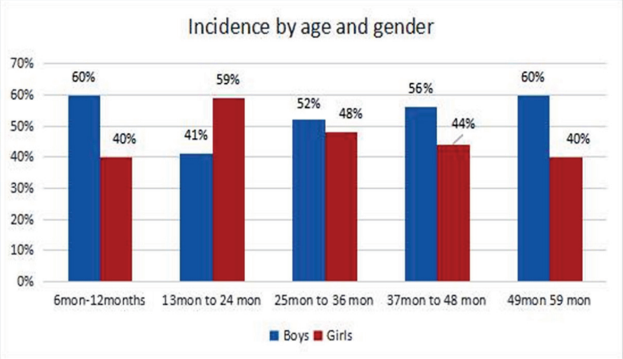

Figure 1: Incidence of anemia by age and gender in percentage.

Table 3: Severity of anemia.

Severity of anemia	*No. of children*
MILD (10-10.9gm/dl)	32(20%)
MODERATE (7-9.9gm/dl)	73(47%)
SEVERE (<7gm/dl)	52(33%)

According to IAP classification [6] based on weight for age, children were classified into mild, moderate, severe, and very severe malnutrition. Children with mild pallor mostly had normal nutritional status or mild malnutrition. Most of the children with moderate pallor had moderate to severe malnutrition.

The majority of the children with severe pallor had severe to very severe malnutrition. An exception to this 3 cases of autoimmune hemolytic anemia which presented with sudden onset of severe pallor but had normal nutritional status (Table 4).

Most of the children had anemia as an incidental finding. Fever is the common presenting complaint followed by cough, difficulty in breathing, and seizures. 14 children presented with febrile seizures and all of them were diagnosed to have iron deficiency anemia. Presenting complaint of sudden onset or progressive pallor was seen in beta-thalassemia, autoimmune hemolytic anemias, and leukaemias (Table 5).

Table 4: Grading of malnutrition about the severity of pallor.

Severity of anemia	*Grade-0 16(10%)*	*Grade-1 23(15%) (mild)*	*Grade-2 (moderate) 60(39%)*	*Grade-3 (severe) 38(24%)*	*Grade-4 (very severe) 19(12%)*
Mild	12	15	5	-	-
Moderate	1	8	48	15	1
Severe	3	-	7	23	18

Apart from pallor on clinical examination, other main clinical findings include jaundice, generalized lymphadenopathy, respiratory distress (tachypnoea, chest retractions), wheeze/ crepitations, s/o congestive cardiac failure (tachycardia, hyperdynamic precordium, bounding pulses), hepatomegaly, splenomegaly. On physical examination, 15 children had mild pallor, 73 children had moderate pallor and 52 children had severe pallor (Figure 2).

Table 5: Presenting complaints in children with anemia.

Presenting complaint	*No. of children*
Fever	141
Cough	70
Difficulty in breathing	67
Seizures	23
Pallor	14
Diarrhoea	8
Decreased urine output	6
Bleeding manifestations	6
High coloured urine	6
Accidental ingestion	3
Unknown snakebite	1

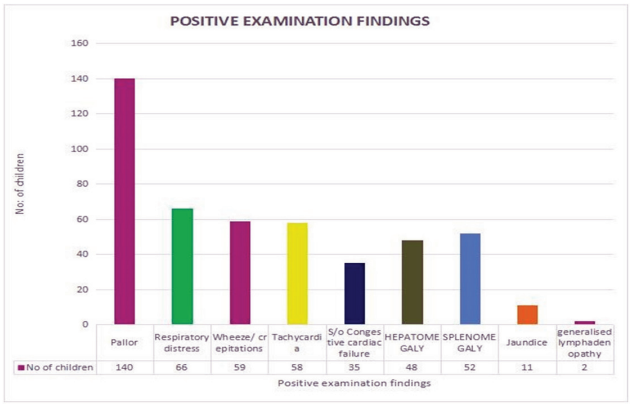

Figure 2: Representation of positive examination findings.

The most common presenting complaint associated with anemia was lower respiratory tract infections which include acute bronchiolitis, WALRI, and pneumonia. This is followed by seizures, acute diarrheal diseases, UTI, scrub typhus, viral pyrexia, post COVID MISC. All the children with simple febrile seizures and breath-holding spells were diagnosed to have iron deficiency anemia. Of the children who presented with anemia, 25 children were found to have positive stool microscopic examinations (Table 6).

Table 6: Clinical diagnoses associated with anemia.

System	*No. of children (%)*
Respiratory	57(36%)
Central nervous system	18(11%)
Gastrointestinal system	12(7%)
Renal (urinary tract infections)	10(6%)
Infectious diseases	55(35%)

The majority of children had microcytic hypochromic anemia. 7 cases had dimorphic anemia which includes combined iron deficiency and megaloblastic anemia. Normocytic anemia was seen in 3 cases i.e., immune hemolytic anemia and 2 cases of malaria (Table 7). In our study 157 children, 154 were recovered and discharged and 3 succumbed to death.

Table 7: Peripheral smear findings.

Peripheral smear findings	*Number of children*
Microcytic hypochromic anemia	148
Pencil shaped RBCs	120
Leukocytosis	55
Target cells	52
Sickle cells	21
Thrombocytopenia	13
Dimorphic anemia	7
Hemoparasites	6
Basophilic stippling	5
Normocytic normochromic anemia	3
RBC clumps	3
Blasts forms	2

Discussion

The present study is comparable with the data published in the National Family Health Survey 4 [7]. According to National Family Health Survey (NFHS-4), nutritional anemia is common in India among 6 months to 5 years age group (53.4%) with the highest incidence in 6 months– 35 months age group. In the present study highest incidence was present in 6 months- 24 months (infants and toddlers) age group i.e., 64%.

Similar results were seen in Narayan et al [8], and Jennifer et al [9] studies. However, Vaswani et al [10] and Kanchana et al [11] who did similar studies in 6 months to 5 years age group reported a higher incidence of anemia in the 25 to 60 months age group i.e., in preschool children. Nilofer et al [12] studies in 6 months to 14 years age children found the highest incidence of anemia in preschool-age children which included 1 to 5 years (48%) followed by 5-14 years (27%) and infants (25%). A study was done by Reddy et al [13], in a tertiary care hospital, Kadapa in less than 5 years age group children reported that the highest incidence of anemia was among the 12 to 23 months age group. In a similar study done by Jose et al [14] in Kerala in a tertiary care hospital setting in 6 months to 5 years children had a higher prevalence of anemia in the 6 to 12 months age group which is contrary to the present study. This difference may be attributed to the limited sample size taken in the study. Ocan et al [15] who conducted a cross-sectional study in 6 months to

5 years age group had the highest prevalence of 30.3% among 12 to 23 months. The higher incidence of anemia under the age of 24 months in the present study may be due to multiple factors like rapid growth in this age, delayed weaning, complementary foods with low iron bioavailability and dietary monotony.

The current study had a higher incidence among boys (51%) compared to girls (49%). Similar results were seen in Jennifer et al [12] and Kanchana et al [11] which showed higher incidence in boys. In other similar studies, Narayan et al [8] and Reddy et al [13] had a higher incidence among girls when compared to boys. However, a study was done by Jose et al [14] in Kerala reported a higher incidence among boys when compared to girls i.e., 56.8%, but the sample size of the study is very limited.

This study reported that nutritional anemia, mostly iron deficiency anemia (68%), is the single most common cause with the highest incidence among 6 months – 24 months age group. The second most common cause of anemia in the present study was sickle cell anemia (13.5 %). Jennifer et al [9] studies reported that 81 per cent of children presented with iron deficiency anemia and the rest of the children had combined B12 and folic Acid deficiency.

In Vaswani et al [10] studies, 51% of cases were diagnosed with iron deficiency anemia followed by megaloblastic anemia. Similar studies like Nilofer et al [12] done in 6 months to 12 years of children reported that 56% of the children had iron deficiency anemia. A similar study was done by Madoori et al [16], in 2 months to 12 years found that 58% of the children had iron deficiency anemia followed by sickle cell anemia (27%).

In the present study, the incidence of moderate anemia (47%) is the highest followed by severe anemia (33%) and mild anemia (20%). Similar results were seen in Narayan et al [8] Jennifer et al [9] and Kanchana et al [11] studies who reported 48%, 46% and 46.8% of moderate anemia respectively. In a study done by Jose et al [14] majorities of children had mild anemia 58.8% followed by moderate (25.4%) and severe anemia (15.8%).

According to NFHS-4 [7], 55.9% of the urban population was anaemic and 59.4% of the rural population was anaemic. In the present study, the majority of the children were from rural populations (45%) followed by tribal (36%) and urban populations (19%). This higher incidence of anemia in rural populations may be because of poor socio-economic background, poor maternal nutrition and low education status of the mothers, which make children more vulnerable to respiratory and intestinal infections compromising gastrointestinal absorption of iron.

The present study also found that major hemoglobinopathies like sickle cell anemia and thalassemia were mostly reported particularly from tribal populations. Similar results were seen in Madoori et al [16] study which was a hospital-based retrospective study done in children of age 2 months to 14 years. This study found that the highest incidence of sickle cell anemia was from the tribal population.

In the present study, common clinical examination findings include pallor, jaundice, hepatomegaly, splenomegaly, generalized lymphadenopathy, and features of congestive cardiac failure (tachycardia, bounding pulses, hyperdynamic precordium). Other studies like ND Vaswani et al study [10] stated that all children had pallor, 10 children had icterus, 4 children had hepatosplenomegaly and 3 children had lymphadenopathy. Similar findings were also seen in Madoori et al [16] studies.

The present study had children mostly with moderate malnutrition (39%) followed by severe (24%), mild (15%) and very severe (12%). 10% of the children had normal nutritional status. In Jennifer et al [9] studies, the majority of the children had Grade 1 malnutrition which is different from the present study where a majority of children had Grade 2 malnutrition.

Vishwani et al [10] showed results similar to the present study with a higher number of children having moderate malnutrition (55%). The most common clinical diagnosis with which children were hospitalized in the present study is lower respiratory tract infections. Simple febrile seizures, viral pyrexias, UTI, and acute diarrheal diseases follow this. Less common associated conditions include scrub typhus, dengue, post COVID MISC. In other studies, like Nilofer et al [12] most common diagnoses associated with anemia were gastrointestinal disorders (Acute diarrheal diseases) followed by respiratory tract infections, CNS disorders, and nutritional and infectious diseases. Jennifer et al [9] reported that the most common system involved was respiratory. In a cross-sectional study done by Reddy et al [13] most common 16% of the children had diarrheal illness followed by respiratory illness (14.7%). This study stated that respiratory illness requires greater utilization of haemoglobin due to increased respiratory effort and due to the underlying disease process. In a hospital-based study done by Anna et al [17] acute respiratory tract infection was the most common clinical

diagnosis associated with anemia followed by enteric fever. This study stated that lower haemoglobin levels may contribute as a risk factor for acute respiratory illness. Studies done by Hussain et al [18] and Mourad et al [19] in children to evaluate low haemoglobin levels as a risk factor for lower respiratory tract infections stated that children with anemia were more susceptible to lower respiratory tract infections compared to normal haemoglobin levels. This association of anemia with acute lower respiratory tract infections is due to an altered immune response seen with low levels of haemoglobin. Particularly iron deficiency anemia is mainly associated with altered humoral and cell-mediated immunity [20].

The present study showed that 94% of children had microcytic and hypochromic anemia, 4% had dimorphic anemia, and 2% had normocytic hypochromic anemia. This is similar to various studies like Jennifer et al [9], Viswani et al [10] and Kanchana et al [11] in which the majority of children had microcytic hypochromic anemia.

In the present study 14 children out of 157 children presented with febrile seizures. All of them were found to have iron deficiency anemia. A similar finding was seen in a prospective case-control study done by Jang et al [21] in South Korea found a significant association between iron deficiency and febrile seizures. Similar results were found by Sathiyasuresh et al [22] in a case-control study done in 6 months to 60 months age group. Dawn et al [23] in a retrospective case-control study done in the age group 6 to 36 months found that children with febrile seizures were almost twice as likely to be iron deficient as those with febrile illnesses alone. As said earlier this higher association of febrile seizures with iron deficiency anemia is due to demyelination and impaired neurotransmitter function.

Conclusion

Nutritional anemia, particularly iron deficiency anemia is the most common type of anemia in 6 months to 5 years age group mainly because of rapid growth during this period and a discrepancy between the energy requirement and energy intake. Rural and tribal children were more commonly affected by nutritional anemia when compared to the urban population, which may be because of lower socio-economic status, making children vulnerable to various infections. Simple febrile seizures were found in high association with iron deficiency anemia identifying the factors that are contributing to iron deficiency anemia and implementing the control measures like early iron supplementation results in reducing morbidity and mortality. Co-morbidities like malnutrition, parasitic infestations, acute diarrheal diseases, and recurrent respiratory tract infections form a vicious cycle and result in nutritional anemia.

Conflict of interest

Authors declare no conflicts of interest.

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