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Original Research Article

CLINICAL AND AETIOLOGICAL PROFILE OF SEVERE ANEMIA IN 6 MONTHS TO 12 YEARS CHILDREN: A CROSS-SECTIONAL STUDY

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Abstract

Background: Anemia is a global health burden affecting 42% of children below 5 years of age globally. In India, 67% of children between 6 months to 5 years are affected by anemia. Anemia is an important cause of impaired cognition, growth delay, and psychomotor development. This study aimed to determine the clinical and aetiological profiles of severe anemia in children between 6 months to 12 years of age. **Materials and Methods:** This is a prospective cross-sectional study conducted in the department of Pediatrics of a tertiary care hospital from central India between December 2019 to May 2021. The study included children between 6 months-2 year of age admitted with severe anemia. Chi-square test was used for analysing qualitative data and Student T test for quantitative data by using SPSS 20 software. **Result:** Total 165 children were studied, of these 50.3% were males and 49.7% were females. 52.12% children between 6 months to 2 years age, 20% children 2-5 years age and 27.88% children 5-12 years age had severe anemia. Nutritional anemia was the most common cause with 43.78% iron deficiency, 21.84% megaloblastic and 34.48% dimorphic anemia. Among hemolytic anemia, sickle cell disease was seen in 53.97% children and thalassemia major in 30.16% children. Various degree of malnutrition (74.54%), wasting (55.94%), and stunting (49.7%) were seen in children. **Conclusion:** Children especially those younger than 2 years are at higher risk of developing severe anemia. Nutritional awareness with emphasis on complementary feeding, and screening for hemoglobinopathies are essential components for successful prevention of anemia.

INTRODUCTION

Anemia is a global public health problem causing significant morbidity in children. The World Health Organisation estimates that 42% of children below 5 years are affected by anemia.[1] As per the fifth National Family health Survey of India (NFHS-5), 67% of children between 6 months to 5 years are anaemic.[2] Anemia is defined as a hemoglobin level or haematocrit values below the 5th percentile for age and sex. Severe anemia is defined as hemoglobin levels below 7 gm/dL.

Anemia can be caused by various underlying pathologic processes. The Comprehensive National Nutrition Survey conducted in 2016-2018, revealed that nutritional anemia was seen in 68.9% children aged 1-4 years, 50.9% children aged 5-9 years, and 65.1% children between 10-19 years. The survey also reported that 41% preschool children were anaemic compared to 24% school age children and 28% adolescents.[3] The majority of nutritional anemias are due to deficiency of iron, vitamin B12 and folic acid. Recently, the role of vitamin D, vitamin A, vitamin C and pyridoxine is being recognised in the process of erythropoiesis.[4]

Chronic anemia has long lasting effects on linear growth of the child during all stages of growth. Iron deficiency anemia affect brain growth and metabolism right from in utero and early life. Children with anemia have impaired psychomotor development which may be irreversible.[5] Children with chronic hemolytic anemias have delayed pubertal growth due to iron deposition in endocrine organs. They are predisposed to hypothyroidism, hypogonadotropic hypogonadism, and diabetes mallitus. Iron overload leads to liver failure and cardiac arrhythmias. Short stature is a common problem even in children with adequate blood transfusion and iron chelation therapy. Megaloblastic anemia due to deficiency of vitamin B12 and folic acid is a common clinical entity among children. In addition to the hematological manifestations, it can affect gastrointestinal and nervous system. Failure to treat vitamin B12 deficiency may lead to permanent neurologic damage.

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Anaemia not only adversely affect the health of an individual but also has long lasting impact on economic and social development. Therefore, the importance of knowledge about clinical profile and causes of anemia in children cannot be undermined. This knowledge can help in better planning and implementation of anemia eradication programs. The present study was conducted to study the clinical profile and various aetiologies for severe anemia in children at a tertiary care centre from central India.

Objectives-

The primary objective was to determine the clinical profile and aetiology of severe anemia in children aged 6 months to 12 years admitted in a tertiary care hospital from central India. The secondary objective was to study the short-term outcomes of children with severe anemia.

MATERIALS AND METHODS

This prospective observational study was conducted in the department of Pediatrics of a tertiary care center from central India. The study duration was December 2019 to May 2021. The study included all the children between 6 months to 12 years of age admitted in Paediatric ward and Paediatric Intensive care unit with hemoglobin level < 7 gm/dl. The exclusion criteria were children with anemia occurring secondary to an acute episode of blood loss due to trauma, injury or surgery and whose parents did not consent for participation in the study. Consecutive sampling method was used for enrolling children satisfying the inclusion criteria and exclusion criteria. Detailed history was taken and thorough clinical examination were done at the time of admission and recorded in a case record form. The venous blood samples were taken for complete blood count, peripheral smear, reticulocyte count, serum iron, serum vitamin B12 levels, serum ferritin and high-performance liquid chromatography. Bone marrow biopsy and aspiration was done in selected cases who were undiagnosed or to rule out bone marrow infiltration. All the study participants were categorised according to their weight into normal, Grade I, Grade II, Grade III, and Grade IV as per the Indian Academy of Paediatric Classification. Based on their height, all the children were classified as normal, I-degree stunting, II-degree stunting, and III-degree stunting as per Waterlow classification. Similarly, Waterlow classification for wasting was used to classify children as per their weight for height.

The ethical clearance was obtained from Institutional Ethics Committee (Letter no- IEC/PED/116/2019).

All the demographic details, history, clinical examination findings, and all laboratory investigations were entered in the predesigned standard case record form. The data was analyzed using SPSS 20 (IBM Corporation, Armonk, NY, USA). The continuous data was expressed as Mean ± Standard Deviation and the categorical data as percentages. The qualitative data will be analysed using Chi-square test and Fisher's exact test while the quantitative data will be analysed using Student t test.

RESULTS

Of the 165 children with severe anemia admitted in the paediatric ward and intensive care unit during the study period, 86 (52.12%) children were in the age group 6 months-2 year, 33 (20%) children in the age group 2-5 year, and 46 (27.88%) children in the age group 5-12 year. There were 83 (50.30%) males and 82 (49.70%) females in the study. In the study, severe anemia was seen more commonly among males between 6 months- 2 years (55.8%) and 2-5 years (51.51%) while females were commonly affected in 5-12 years age group (60.8%). The patient characteristics [Table 1].

In the study, mean hemoglobin value was 5.33 ± 1.36 gm/dl, mean haematocrit was 16.69 ±5.83, mean platelet count was 211.65±147.46. Among 165 children, 74.54% children had low red cell counts, 92.72% had high red cell distribution width. Among study participants, 29.09% had low reticulocyte counts, 29.70% had normal counts and 41.21% had high reticulocyte counts. On peripheral smear, anisopoikilocytosis was seen in 69.09% children, pencil cells in 44.24%, tear drop cells in 33.94%, macrocytes in 27.27%, sickle cells in 24.24%, fragmented cells in 4.24%, and blast cells in 1.82% children.

The nutritional details of the children [Table 2]. Of 165 children, 27.28% had grade I PEM, 30.30% had grade II PEM, 15.75% had grade III, 1.22% had grade IV, and 25.45% were not underweight. Protein energy malnutrition was common among children in 6 months to 2 years age group. Similarly, 27.27% children had grade I stunting, 17.58% had grade II stunting, 4.85% had grade III stunting, and 50.30% had no stunting. Grade I and grade III stunting were more common among children of age group 6 months-2 year while grade II stunting was seen more commonly among children of age group 5-12 year. Among 165 children, 24.86% were mildly wasted, 20.60% were moderately and 8.48% children were severely wasted. 46.06% children had no wasting.

Fever was the commonest presenting symptom in the study seen in 60.61% children. Other symptoms were cough (24.24%), cold (23.64%), limb pain (21.82%), jaundice (12.7%), breathlessness (11.50%), pedal oedema (7.85%), and convulsions (6.67%). Splenomegaly was the commonest examination finding seen in 18.78% of children. Other examination findings were hepatosplenomegaly (16.97%), hepatomegaly (9.09%), crackles (3.64%), rhonchi (3.64%), and ascites (1.21%). Out of 165 children, nutritional anemia was present in 87 (52.73%) children, hemolytic anemia in 63 (38.18%), mixed causes in 8 children (4.85%), and bone marrow disease in 7 children (4.24%).

In the study, 74.54% children had low and 25.46% children had normal red blood cell counts. Red cell

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distribution width was increased in 92.72% children, normal in 6.67%, and lower in 0.61% children. According to morphological classification, microcytic hypochromic anemia was the most common type seen in 76.36% children, followed by normocytic normochromic (18.79%), macrocytic normochromic (3.64%) and normocytic hypochromic (1.21%). The nutritional anemia was the commonest cause of severe anemia among children 6 months-2 years age group. Among nutritional anemia, 43.78% had iron deficiency, 21.84% had megaloblastic anemia, and 34.48% had dimorphic anemia. Among hemolytic anemia, Sickle cell disease (53.97%) was the commonest cause of hemolytic anemia among children, followed by thalassemia major (30.16%), sickle cell trait (7.93%), thalassemia intermedia (6.35%), and G6 PD deficiency (1.59%). Acute Myeloid Leukemia (57.13%) constituted majority of bone marrow disease while aplastic anemia, congenital dyserythropoietic anemia and pure red cell aplasia constituted to 14.29% of cases each. Aplastic anemia with sickle cell trait, Iron deficiency anemia with sickle cell trait and sickle cell disease constituted 25% of cases in mixed disorders while dimorphic anemia with sickle cell disease and thalassemia minor with sickle cell trait were seen in 12.5% cases each [Table 4].

In the present study, nutritional anemia was commonest cause of anemia in children between 6 months-2 year, while hemolytic anemia was more common cause of anemia among children 5-12 year age group. The various causes of anemia are shown in Table III. In the study, 95.75% children with anemia were discharged, 1.82% were referred to higher center for further management and 0.61% were discharged against medical advice. 1.82% i.e., 3 children died during the study period due to their illness.

The study found statistically significant association between type of anemia and age of the child (p=<0.00001), while there was no significant association between gender of the child and type of anemia (p=0.52) [Table 5].

Table 1: Characteristics of Children with Severe Anemia.

Characteristics		Frequency (n)	Proportion (%)
Gender	Male	83	50.3
	Female	82	49.7
Age	6 months- 2 years	86	52.12
	2-5 year	33	20
	5-12 year	46	27.88
Duration of Hospitalisation	<5 days	101	61.21
	5-10 days	50	30.30
	>10 days	14	8.49
Immediate Outcomes	Discharge	158	95.75
	Referral	3	1.82
	Death	3	1.82
	DAMA	1	0.61

Table 2: Anthropometric status of children with severe anemia

Characteristics		Frequency (n)	Proportion (%)
Underweight	No underweight	42	25.46
	Grade I	45	27.27
	Grade II	50	30.37
	Grade III	26	15.76
	Grade IV	2	1.21
Wasting	No	76	46.06
	Mild	41	24.85
	Moderate	34	20.61
	Severe	14	8.48
Stunting	No	83	50.3
	I Degree	45	27.27
	II Degree	29	17.58
	III Degree	8	4.85

Table 3: Clinical Presentation and Examination findings among study subjects

Parameter	Frequency (%)
Pallor	165 (100%)
Fever	115 (69.7%)
Icterus	21 (12.73%)
Lymphadenopathy	20 (12.12%)
Hyperpigmented Knuckles	16 (9.7%)
Pedal Oedema	11 (6.67%)
Koilonychia	5 (3.03%)
Hemolytic facies	3 (1.82%)
Systemic Examination	
Splenomegaly	31 (18.78%)
Hepatomegaly	15 (9.09%)

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Hepatosplenomegaly	28 (16.97%)
Bilateral Crepitations	6 (3.64%)
Rhonchi	6 (3.64%)
Systolic Murmur	5 (3.03%)
Ascites	2 (1.21%)

Table 4: Type of anemia and Age-wise Distribution

Type of Anemia		6 months-2 years	2-5 years	5-12 years
Nutritional anemia	Iron Deficiency Anemia	28 (32.56)	5 (15.15%)	5 (10.87%)
	Dimorphic Anemia	27 (31.40%)	1 (3.03%)	2 (4.35%)
	Megaloblastic anemia	15 (17.44%)	2 (6.06%)	2 (4.35%)
Hemolytic anemia	Sickle cell Trait	2 (2.33%)	2 (6.06%)	1 (2.17%)
	Sickle cell Disease	5 (5.81%)	12 (36.36%)	17 (36.96%)
	Thalassemia Major	4 (4.65%)	7 (21.21%)	8 (17.39%)
	Thalassemia Intermedia	1 (1.16%)	1 (3.03%)	2 (4.35%)
	G6PD deficiency	0	0	1 (2.17%)
Bone Marrow Disorders	Acute Myeloid Leukemia	0	0	4 (8.69%)
	Aplastic anemia	0	0	1 (2.17%)
	Congenital Dyserythropoietic anemia	1(1.16%)	0	0
	Pure red cell aplasia	0	1(3.03%)	0
Mixed Disorders	Aplastic with Sickle cell trait	0	0	2 (4.35%)
	Dimorphic with Sickle cell disease	1 (1.16%)	0	0
	Iron Deficiency with Sickle cell Disease	1 (1.16%)	1 (3.03%)	0
	Iron Deficiency with Sickle cell trait	1 (1.16%)	0	1 (2.17%)
	Sickle cell trait with Thalassemia minor	0	1 (3.03%)	0

Table 5: Comparison of various types of anemia with gender and age of children

Variables	Gender			P-value
	Male	Female		
Type of anemia				
Nutritional	42	45		0.52
Hemolytic	32	31		
Bone marrow disorder	3	4		
Mixed	6	2		
Gender	6 months-2 years	2-5 years	5-12 years	
Male	48	17	28	0.72
Female	38	16	18	
Type of anemia				
Nutritional anemia	70	8	9	<0.00001
Hemolytic anemia	12	22	29	
Bone marrow disorder	1	1	5	
Mixed anemia	3	2	3	

DISCUSSION

We studied the clinical profile and various aetiological factors in 165 children between 6 months to 12 years of age admitted in a tertiary care center with severe anemia. In this study, children between 6 months-2 years were affected more commonly by severe anemia (52.12%) compared to children in 2-5 years and 5-12 years age group. Similar results were reported by Kokku P K et al [6] (39.6%) and Janjale A et al,[7] (50.58%). Shankar P et al study also reported a high prevalence of anemia among children younger than 2 years of age (60%).[8] This study reported a high prevalence of severe anemia among male children. Male predominance was also seen in studies by Marken P et al (58%),[9] Jaiswal N,[10] (68%) and Janjale A (59.32%).[7]

The present study reported that varying degree of PEM was seen in 74.54% of children, of which 30.37% had Grade II PEM. Similarly, 24.85% children had mild wasting and 20.61% had moderate wasting. Stunting was seen in 49.7% of children, of which maximum 27.27% had I degree stunting. Janjale A et al,[7] study also reported large number of children with severe anemia had Grade II and III PEM (22.03% each). However, lower prevalence of malnutrition (29.70%) was present in children with severe anemia in Kokku P K et al,[6] study. A study from Ethiopia shows that 28.5% children had severe undernutrition, 20.5% had severe wasting and 33.4% children had severe stunting.[11] Ramawat P study reported that severe anemia was seen in 31.4% moderate acute malnourished and 28.5% severe acute malnourished children.[12] In the study, 25.46% children with severe anemia were well nourished. This highlights the problem of hidden hunger in India. Ramawat P,[12] study also reported severe anemia among 40% of well-nourished children.

The most common clinical sign was pallor which was seen in all patients while the next common sign was fever which was seen in 69.7% of children. Splenomegaly was the most common examination finding seen in 18.87% children followed by hepatosplenomegaly (16.96%). Similar findings were observed by Janjale A et al,[7] study, where all children had pallor and 66% children had fever. Hepatosplenomegaly was seen in 16.95% children.

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The present study reported nutritional anemia as the most common cause of severe anemia in children i.e., 52.73%. There was no significant association between the type of anemia and gender of the child (p=0.52). It is in accordance with the results of Kokku P K et al,[6] study which also reported a high prevalence of nutritional anemia among children with severe anemia (85%). The younger age group children were at more risk of developing anemia compared to older children (p=<0.00001). Iron deficiency was the commonest cause of nutritional anemia followed by dimorphic and megaloblastic anemia. These findings are in accordance with study by Kubavat K who reported 88% of iron deficiency, 9% of dimorphic anemia and 3% of megaloblastic anemia among children with nutritional anemia.[13] Similarly, Jaiswal N,[10] also in their study reported iron deficiency in 92% cases and megaloblastic anemia in 8% cases. 31.18% children had hemoglobinopathies and 53.9% had sickle cell disease followed by 30% thalassemia major. This is not in accordance with Shankar P,[8] study who reported 17% thalassemia major and 5% sickle cell disease among children with anemia.

CONCLUSION

This study reveals that the severe anemia is more prevalent in children between 6 months to 2 years of age. The nutritional anemia followed by hemolytic anemia were the most common causes of severe anemia among children. Therefore, more awareness is needed about the nutrition, complementary feeding, and family screening for hemoglobinopathies for prevention of severe anemia in children. There is urgent need for better implementation of diagnostic and preventive strategies by the government and health policy makers.

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