Original Article

Clinical Pattern Of Non Nutritional Anemia In Children With Severe Anemia In The Age Group Of 6 Months To 5 Years In Western Maharashtra

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Abstract

Back ground Anemia is known to be a 'silent killer'. Worldwide the prevalence of anemia among the pre-school age group of 6 months to 5 years is 293 million out of these, 89 millionchildren are from India. The NFHS-4 survey revealed that at least 59 % of children between 6months to 5 years were anemic. The prevalence rates of mild, moderate and severe anemia were 28%, 29% and 2% respectively. The present study was undertaken with an aim to perform a clinico-etiological assessment in children presenting with severe anemia to a tertiary care center. **Methods** An observational study was conducted at a tertiary health care center. Children with severe anemia satisfying the eligibility criteria with Hb less than 7 g/dl in the age group of 6 months to 60 months as per WHO recommendation were included.

Physical examination including anthropometric and systemic examination were performed. An etiological assessment was performed and patients were grouped according to the cause of anemia. **Results** Out of 1000 patients, 57 patients had severe anemia (5.7%) with 32% of children with heamoglobin levels of <5g/dl. The male to female ratio was 1.5:1. The medianage of the children was 22 months. Lower socio-economic status, incomplete immunisation, maternal anemia and malnutrition were observed in patients with severe anemia. The mean hemoglobin was 5.5 g/dl and lowest recorded Hb was 2.6 g/dl. Specific investigations were performed to evaluate for the cause of severe anemia.Nutritional deficiency anemia was the most common cause (82.5%). The other causes of severe anemia were thalassemia (5.35%), infections (5.35%), leukemia (3.5%), other malignancies (1.8%) and aplastic anemia (1.8%).**Conclusion** The prevalence of severe anemia was 5.7%. Anemia is

frequently missed for early diagnosis and they present with symptoms only when there is significantly less hemoglobin levels. Apart from most common cause as nutritional deficiency other serious etiologies also contribute to occurrence of severe anaemia. Early detection and managementmay result in better outcome.

INTRODUCTION

Aneamia is a serious global health problem that particularly affects young children and pregnant women.WHO estimates that 42% of children and pregnant women world wide are anemic. Anemia is generally defined as a reduction in red cell volume or hemoglobin concentration below the range of values occurring in healthy children of the same age .

The common causes of non nutritional anemia are hemoglobinopathies , chronic diseases, malignancy, aplastic anemia, leukemia .

Red flag signs of severe anemia are Abnormal vital signs (tachycardia, hypo or hypertension), Neutropenia and/or thrombocytopenia, High MCV with Normal RDW, Blastson PBS, Firm Adenopathy, Bruising and bleeding, Weight loss, Shortness of breath, Fever, Hypoxia, Organomegaly, Edema, Oliguria-anuria, Bloody diarrhea, Hemoglobinuria, Familyhistory if anemia.

The classification of anemia is based on 3 aspects. These include the following: Physiologic Classification, Morphologic Classification, Classification based on MCV& RDW.

The most common cause of severe anemia is nutritional anemia, other causes of severe anemia are haemolytic anemia's, hemoglobinopathies, anemia of chronic diseases, anemia inleukaemia, aplastic anemia.

Haemolytic anemia : Hemolysis is defined as premature destruction of red blood cells,anemiaresults when rate of destruction exceeds the capacity of marrow to produce RBC's.

Classification of haemolytic anemia **1)cellular defects** a)membrane defects (hereditary sperocytosis, hereditary elliptocytosis, paroxysmal nocturnal hemoglobinuria b) enzymedeficiencies (G6PD deficiency, pyruvate kinase deficiency) c) Hemoglobinopathies.

2) Extra cellular defects a) autoimmune haemolytic anemia(warm and cold antibody), b)iso immune haemolytic anemia, fragmentation Hemolysis, hypersplenism, plasma factors

The clinical features of hemolytic anemia[26] include positive family history and commonly manifest in second and six months of life, anemia, jaundice, spleenomegaly, hemoglobinuria and signs of cholelithiasis. In severe chronic hemolytic anemia, there may be undue accumulation of iron containing pigments in body tissues (hemosiderosis) which may be augmented by massive transfusion therapy which may lead to hepatic enlargement and distinctive greenish brown discolouration of the skin. Cardiac arrhythmias and cardiac failureare terminal events. Diagnosis can be made by recognition of Hemolysis which show evidence of increased erythrocytes destruction features like increased unconjugated hyperbilirubinemia, increased Urobilinogen excretion in urine, decreased plasma haptoglobin and hemopixin, evidences of increased erythrocytes production with features like increased reticulocyte count, microcytosis, erythrocytes hyperplasia, evidences of intravascular

Hemolysis like hemoglobinuria, methemoglobinemia, hemosiderin. Peripheral blood smear shows microcytosis, hypochromia, bizzare fragmented rbc's, electrophoresis shows raised HbF levels. Hereditary sperocytosis shows spherocytes on blood film, negative Coomb's test,increased MCHC, increased osmotic fragility and acidified glycerol lysis test. Hypersplenism shows thrombocytopenia, neutropenia. HUS shows RBC fragments, spherocytes, helmet cellson pbs.

Hemoglobinopathies like thalassemia major shows peculiar mongoloid appearance caused byenlargement of cranial and facial bones, combined with skin discolouration, anemia, splenomegaly and hepatomegaly— the first description of thalassemia by Cooley and lee.

Now this disease is known to be a single gene disorder inherited in a mendelian recessive manner. This is clinical significant problem that depends on blood transfusion which resultsin either decreased or absent synthesis of one or more globin chains as a compensatory response increased amounts of HbF are produced in rbc's. An excess of alpha chains is produced which aggregate into unstable units, resembling Heinz bodies that

damage RBC membrane.

Anemia in malaria : Malaria is the one of the leading causes of morbidity and mortality in tropics. Anemia is one of the complications in children living in endemic areas especially those with infections due to plasmodium falciparum. Three mechanisms have been suggested Hemolysis of parasitised red cells, Hemolysis of non parasitised cells, dyserythropoeisis. PBSshows normocytic normocbromic anemia.

Anemia due to infections : bacterial sepsis due to H influenza, staphylococci, streptococcimay be complicated by direct Hemolysis of rbc's.

Anemia in chronic infections

Anemia in renal insufficiency : chronic renal failure is usually associated with moderate to severe hypoproliferative anemia. Mechanisms being decreased erythropoietin, impaired response to erythropoietin, Hemolysis due to uremic plasma resulting in deformed rbc's.
Bone marrow is normal, RBC life span is reduced.

Anemia in leukaemia : Leukemia is due to bone marrow infiltration of leukaemia cells,leading to bleeding or erythropoietin failure or in part due to decreased survival of
erythrocytes. Factors predisposing would be genetic conditions like Down's syndrome, fanconi'sanemia, Bloom syndrome etc., environmental conditions like ionising radiation,drugs, alkylation agents, benzene exposure.

Materials and methods

The research includes 1000 children aged 6months to 60 months.

Inclusion criteria

After institutional ethical committe approval and informed consent from parents,children aged 6months to 60 months with anemia were included in the study.

Diagnosis and clinical evaluation

Each patient's socio demographic and medical history was meticulously documented and a thorough examination was performed.

In present study, 1000 patients in the age group of 6-60months were screened for thepresence of anemia < 11g/dl. All the patients of severe anemia with Hb < 7 g/dl were evaluated.

Routine investigations like he organ, RBC indices and PBS were performed. The patientswith hemoglobin of less than 7g/dl were evaluated further. A detailed history was taken regarding presenting illness, family history, past medical history, birth history and socio economic history. General and systemic evaluation was done to see whether the other systems are involved. The required laboratory investigations were sent for definitive diagnosis. Investigations sent were reticulocyte count, LDH and ESR, serum iron studies, Hemoglobin electrophoresis, VIT B12 levels, Sickling test, Bone marrow aspiration and biopsy, Stool and iron routine microscopy.

OBSERVATION AND RESULTS :

In this present study, 1000 patients in the age group of 6-60months were screened for presence of severe anemia(Hb < 7g/dl) were evaluated for assessing the clinicoetiologicalpattern of severe anemia.

Table 1 Gender and age wise distribution based on severe anemia.(n=630)

SEX	mild anemia %	mod anemia %	severe anemia %	total	Age	mild anemia%	mod anemia%	sev anemia %	total

Fch	137/ 42.4%	164/ 50.8%	22/ 6.8%	323/ 51.2 %	**6-24m**	139/ 49.4%	110/ 39.1%	32/ 11.5%	281/ 44.6 %
Mch	143/ 46.6%	129/ 42%	35/ 11.4%	307/ 48.8 %	**25-60m**	141/ 40.4%	183/ 52.4%	25/ 7.2%	349/ 55.4 %
Total	280/ 44.4%	293/ 46.5%	57/ 9.1%	630/ 100 %	**total**	280/ 44.4%	293/ 46.5%	57/ 9.1%	630/ 100%

Table 1 shows severe anemia is more common in the male children, Chi square test was applied, p value is < 0.05. Therefore it is significant and it can be stated that male gender is more affected by severe anemia compared to female gender. Age wisedistribution showed severe anemia is more common in the age group of 6-24months compared to 25-60 months.

Table 2 clinical findings in severe anemia patients (n= 57)

Sr. No.	Clinical Findings	Number of severe anemia patients(%)
1	Pallor	57 (100)
2	Lymphadenopathy	17 (30)
3	Hepatosplenomegaly	10 (17.5)
4	Hepatomegaly	9 (15.7)
5	Edema	5 (10)
6	Icterus	4 (7)
7	Signs of cardiac failure	4 (7)
8	Splenomegaly	3 (5.3)
9	Hyperpigmentation of knuckles	2 (3.5)
10	Frontal bossing	1(1.8)
11	Tender Joint swelling	1 (1.8)
12	Clubbing	1 (1.8)
13	Koilonychia/Platynychia	1 (1.8)
14	Cyanosis	0

Severe pallor is present in all the patients. Icterus was seen in 7% of severe anemiapatients. 30% pats showed lymphadenopathy, 7% presented with cardiac failure, 3.5% patients presented with hyperpigmented knuckles.

On examination hepatospleenomeagly was seen in 10 pots including one Pt each ofthalassemia, IDA secondary to malignancy and ALL.

Table 3 : hemoglobin concentration in severe anemia (n=57)

Severity of anemia	Hemoglobin concentration (g/dl)	Number of severe anemia patients (%)
Very Severe Anemia	<5	18 (31.6)
Severe Anemia	5-7	39 (68.4)
Total		57 (100)

Table 3 shows that 32% of the severe anemia patients had hemoglobinuria less than 5g/dl as per WHO guidelines.

Table 4 Distribution of MCV/MCHC in severe anemia (n=57)

MCV (fL)	Number of cases (%)	MCH pgms	number of cases (%)	MCHC g/dl	number of cases(%)
<40	1 (1.8)	<27	40(70.2)	<20	1(1.8)
40-60	23 (40.3)	27-32	7(12.3)	20-25	8(14)
60-80	21 (36.8)	>32	10(17.5)	25-30	18(31.6)
80-100	6 (10.5)			30-35	18(31.6)
100-120	5 (8.8)			35-40	8(14)
>120	1 (1.8)			40-45	4(7)
Total	57 (100)		57(100)		57(100)

MCV was between 40-60 fL in 40 % and between 60-80 fL in 37% of the severe anemia patients. Majority of the severe anemia cases (70.2%) had an MCH of less than 27 leading to hypochromia. Remaining patients had an MCH of 27-32 (12.3%) and more than 32(17.5%) respectively.31.6 % cases had a MCHC between 30-35 g/dl which indicates normochromia. MCHC between 20-25 g/dl and between 25-30 g/dl together form 45.6% cases which indicates hypochromia. MCHC >35 g/dl and <20 g/dl together form 22.8% casesof severe anemia.

Table 5 Distribution of Reticulocyte count in Severe Anemia patients (n=57)

Reticulocyte count (%)	Number of cases (%)
<2	36 (63.2)
2.1-10	21 (36.8)
Total	57 (100)

A reticulocyte count of less than or equal to 2% was seen in 63% of the patients. This is dueto iron deficiency anemia in the above patients. In few patients with iron deficiency anemia,the reticulocyte count was higher as these patients were possibly on iron treatment.

Table 6 Classification of Severe Anemia based on the Etiology (n=57)

Sr. No.	Type of anemia	Number of patients (%)
1	Anemia due to nutritional deficiencies	**47 (82.5)**
	a. IDA	36 (63.2)
	b. Megaloblastic	1 (1.8)
	c. Dimorphic	10 (17.5)
2	Anemia due to Hemolysis	**3 (5.35)**
	a. Thalassemia	3 (5.35)
3	Aplastic anemia	**1 (1.8)**
4	Leukemia	**2 (3.5)**
5	Others	**4 (7.15%)**
	a. Acute and chronic infections	3 (5.35)
	b. Malignancy (other than leukemia)	1 (1.8)
	Total	**57 (100)**

As per table 6, 47 cases (82.5%) had nutritional deficiency anemia. The other causes of severe anemia include thalassemia(5.35%), infections(5.35%), leukemia(3.5%), other malignancies(1.8%) and aplastic anemia (1.8%). One patient of ALL presented with blood instools and tender joint swelling and the other with fever and severe thrombocytopenia.

DISCUSSION

In the present study, 1000 children between age group of 6-60 months were screenedfor the presence of anemia.

1. Prevalence of Anemia the present study, the prevalence of anemia was found to be 63%. As per NFHS-

4 data[3], prevalence of anemia in children between 6-59 months of age in India was 59%. As per the Comprehensive National Nutrition Survey (CNNS) in children 1 -4 years of age, the prevalence of anemia is 40.6%. The prevalence of anemia was lower compared to study conducted by Kanchana et al[66] (78%), Firdos et al[60] (73%), R.K. Singh et al[61] (71%), Shally et al[53] (70%), Sinha et al[55] (80%) and Thome et al[59] in West Africa (80%) with their sample sizes being 500,882, 16000,1200,772 and 872 respectively. The prevalencein the present study was higher than CNNS[74], Sharma et al[65] in Nepal (47%), Bajracharya et al[54] in Nepal (46%), Wenfang Yang et al[56] in China (35.1%), Gebremedhin et al[58] in Addis Ababa (37.3%), Melku et al[70] in Ethiopia (28.5%) and Umasanker et al[73] (56%) with their sample size being 17,000, 250, 100, 336, 568,775 and 198 respectively.

The plausible reason for the variability in the anemia prevalence in the present studyand the above mentioned studies could be because of geographical variation of risk factors, differences in the socio-economic status and feeding practices in these areas.

2. Severity of Anemia In this study, the prevalence of mild, moderate and severe anemiain the age of 6 months to 5 years is 44%, 47% and 9% respectively. It was similar to NFHS-4data[3]. However, the prevalence of severe anemia in our study (9%) is higher than NFHS-4 data[3] (3.1%).Similarly, the prevalence of severe anemia in this study was higher than the other studies, namely by Kanchana et al[66] (3.6%), Sharma et al[65] (5.7%), Shally et al[53] (6.7%), Sinha et al[55] (1.3%), Thorne et al[59] (3%) and Melku et al (2.5%). It was similar to study earned out by Firdos et al[60] (8.4%).In the present study, moderate anemia was the mostcommon (47%) type of anemia. The possible explanation for higher prevalence of moderate anemia in this study is the associated infections and ongoing disease pathology leading to hemolysis and loss of appetite when the patients reached in the hospital for treatment. As anemia is an otherwise silent disease, cases of mild anemia did not reach the hospital as they were probably asymptomatic at the time. A similar observation was seen in the studies carried out by Kanchana et al[66], Sinha et al" and Thome et al[59].However, mild anemia was the most prevalent type of anemia in studies earned out by Bajracharya et al[54] in Nepal, Wenfang Yang et aP[6] in China, Gebremedhin et al[58] in Addis Ababa and Melku et al[70] in Ethiopia. The first possible reason being the children studied had one or more micronutrient deficiencies due to variable food practices leading to improper breast feeding and inadequatecomplementary feeding. The second reason being that these studies were mostly community-based outreach studies which included more disease-free children.

3. Distribution of Anemia in the present study, the age group studied was between 6-60 months. The age group of 25-60 months was more commonly involved than 6-24 months of age.This was not consistent with findings of Sinha et al[55] and Melku et al[70] wherein, the age groups studied were between 6-35 months and 6-59 months respectively; and the most affected groups were 6-11 months and 6-24 months of age respectively.The reason for this isstudies were community-based studies, wherein improper nourishment of the growing children with respect to their demands was the major problem. However, this study being hospital-based had anemia cases presenting with other morbidities like acute and chronic infections, moderate to severe malnutrition and chronic diseases of the respiratory or cardio-vascular system

4. Sexwise Distribution of Anemia In the present study, male to female ratio was 0.96:1which was consistent with NFHS-4 data[3]. It was 1:1 as per the CNNS data[74].It was similar tostudy carried out by Sinha et al[55] in Wardha i.e. 1:1. On the other hand, the study carried out by Bajracharya et aP[4] and Melku et al[70] had a ratio of 2.6:1 and 1.2:1 respectively.In the present study, male patients had higher preponderance for anemia and this was statistically significant (p value <0.05). Also, male patients were more affected by mild and severe anemia compared to females and this was statistically significant (p value <0.05).

5. Characteristics of Severe Anemia Prevalence of severe anemia was 9% (57 cases) in the present study. The male to female ratioJ and the age group of 6-24 months was more commonly affected compared than the age group of 25-60 months. It was compared with the NFHS-4 data[3] where the most affected age group was6- 24 months and male to female ratio was 1.07:1. Melku et al[70] also reported a similar male to female ratio of 1.5:1. Similarly, Janjale et al reported 59 cases of severe anemia with a male to female ratio of 1 45: J and most common age group affected was in children less than 3.tBfcars of age. Madoori et al reported 316 cases with severe pallor between 2 months-14 years of age and a male to femaleratio of 1.2:1. Sixty three percent of the patients presented with fever and 53% with cough and cold. This indicates the low immunity in patients of severe anemia leading to increased susceptibility to infections in them. Pallor was the most consistent finding in this study. This was

comparable to the report by Janjale et al[7]L 7% of our patients presented with features of CCF. It was 3.4% and 3.5% in the study carried out by Janjale and Madoori et al respectively.This is probably due to the chronicity of anemia in these patients. In the present study, 31.6%of the patients had very severe anemia (Hb less than 5 g/dl). Similarly, Janjale et al reported 24% w[r]ith very severe anemia. 38.5% of the severe anemia patients had co-existing malnutrition in the present study. On the other hand, Janjale et al[71] reported malnutrition in 80% of the cases. Low serum iron levels (<60 mcg/dl) were seen in 42 patients. Serum ferritin was low (<12 ng/ml) and it is confirmatory of iron deficiency anemia.

6. Etiological assessment of Severe Anemia : In this study, the most common cause of severe anemia was nutritional deficiency anemia (82.5%) wherein iron deficiency was the most common nutrition deficiency. The other causes of severe anemia include thalassemia (5.35%), infections (5.35%), leukemia (3.5%), other malignancies (1.8%) and aplastic anemia(1.8%). Janjale et al[71] reported nutritional anemia as the most common cause of severe anemia (56%). Madoori et al[64] reported the most common cause was IDA (58%) followed by sickle cell anemia (27%), thalassemia (9%), megaloblastic anemia (5%) and aplastic anemia (2%).

CONCLUSION :

Anemia is a common observation in children between age group of 6monthsto 5years. Anemia was present in more than 60% of the enrolled patients. Severe anemia was present in 9% of the anemia patients. Rest were mildly anemic(44%). Anemia is most often asymptomatic in the mild stage and is therefore frequently missed from early diagnosis. Such patients are infrequently picked up at the time of routine immunisation andfollow up. Thus, they may present with symptoms only when the hemoglobin levels have significantly fallen leading to moderate to severe anemia. It is therefore important to diagnose anemia during an early stage by mode of screening, and to prevent further worsening of the disease process with its extension into adolescence in the form of growth and cognitive delay. The most common cause is nutritional anemia but non nutritionalcauses of anemia are also to be evaluated.

Conflict of interest : NIL Source of support : NONE

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