Journal of Hematology and Blood Disorders
Volume 9 | Issue 1
ISSN: 2455-7641

Research Article Open Access

# Clinico - Etiological and Hematological Profile of Severe Anemia in Pediatric Population Aged 1-13 Years at A Tertiary Care Center

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**Citation:** Foram A Patel, Dhruti M Pandya, Kamlesh kumar G Rathod, Bharat Muliya (2023) Clinico - Etiological and Hematological Profile of Severe Anemia in Pediatric Population Aged 1-13 Years at A Tertiary Care Center. J Hematol Blood Disord 9(1): 103

## Abstract

This study is an attempt to emphasize the prevalence of severe anemia in pediatric age group and characterize different clinical and Hematological findings among them. Anemia is a major global health problem, especially in developing countries like India, despite the fact that this problem is largely preventable & easily treatable. It leads to morbidity and mortality in children and establish a public health problem of substantial importance. Anemia in children differs from those of adults as they tend to be more pronounced and develop rapidly. Study conducted at tertiary center with sample size of 100 cases. Children wssssith Hb less than or equal to 7gm/dl were included. Morphological study was carried out manually as well as cell counter includes red cell indices, peripheral Blood Examination, Biochemical studies, Bone Marrow Examination and HPLC were done. Nutritional deficiencies were most common cause found in this study. Among them iron deficiency anemia was predominant. Diamorphic anemia was second most common cause, following Only vitamin B12 deficiency & Folic acid deficiency cases respectively. Female predominance were seen with most affected age group of < 3 years. The major areas for improvement in primary health care is prevention and early diagnosis of as it's associated with delay in psychomotor development especially in preschool age. Preventive measures for control of anemia in children must be accompanied by measures of providing appropriate nutritional requirements.

**Keywords:** Sever anemia pediatric age; Iron deficiency anemia; Vitamin B12 and folic acid; Dimorphic anemia

## Introduction

Anemia is a major global health problem, especially in developing countries like India, despite the fact that this problem is largely preventable & easily treatable. It leads to morbidity and mortality in children and establish a public health problem of substantial import Ammon belief that iron deficiency (ID) is the main cause of anemia worldwide mainly comes from estimates which used Hb as a proxy to estimate the prevalence of IDA [3]. Nevertheless, anemia is multifactorial. Indeed, anemia can result from other nutritional deficiencies such as folate, vitamin B12 or vitamin A [4, 5] or from parasitic diseases such as malaria [6] and helminthiases [7], as a consequence from chronic inflammatory diseases [8] or from genetic disorders such as hemoglobinonce [1]. Anemia in children differs from those of adults as they tend to be more pronounced and develop rapidly [2]. About 30% or nearly one third of world's population is suffering from anemia due to various causes. The copathies [9,10], or glucose-6-phosphate dehydrogenase deficiency [11]. Anemia can be the consequence of a decreased production of RBC, an increased destruction of RBC and/or direct blood loss. These conditions are seen in all types of medical practice ranging from neonatology to geriatrics and public health and are an ongoing concern to all physicians. Constant monitoring is needed while providing public health nutrition programs to eradicate anemia. Different biochemical and hematological tests are done to evaluate Anemia in children. Hence the present study was conducted to find out the clinic hematological & etiological profile of Anemia in pediatric age group.

## Methods

It is an observational study conducted in the department of Pediatrics at tertiary care center in Surendranagar, Gujarat with sample size of 100 cases. Children with severe anemia satisfying eligibility criteria with Hb less than or equal to 7gm/dl in age group 1 year to 13 years [12]. Associated complaints and clinical features were studied, Blood samples (2 ml each) were taken in EDTA vacutainers and plain vials morphological study was carried out manually as well as cell counter (Automated Hematology Analyzer) includes red cell indices (MCV, MCH, MCHC, PCV, RBC, RDW) platelet count (by automated analyzer) and peripheral Blood Examination (by Leishman-stained smears). Biochemical studies (wherever necessary) were done which includes Serum iron, Serum ferritin, Vit B12, TIBC & Folic acid. Bone Marrow Examination (wherever necessary) and HPLC (High performance liquid chromatography)- by D-10 method. An Informed consent was taken from parents of all children who were included in the study. A detailed history was recorded with particular emphasis on symptoms suggestive of severe anemia. A thorough clinical examination of every child was done.

## Results

In subgroup analysis, the prevalence of anemia was higher among children under 3 years of age (46%) than for children 3–5 years of age (23%). This may be because children born from malnourished mothers have poor stores of iron; infants are more susceptible to infections and diseases that result in poor absorption of iron [13], the low concentration of iron in breast milk and the introduction of complementary foods often occurs at this age group results high prevalence of anemia compared with children 3–5 years of age. [Table 1]

| Age in years | Number of cases | Percentage |
|---|---|---|
| 1- 3 | 46 | 46% |
| 3 - 5 | 23 | 23% |
| 5 - 7 | 13 | 13% |
| 7 - 9 | 06 | 06% |
| 9 - 11 | 09 | 09% |
| 11 - 13 | 03 | 03% |

**Table 1:** Age wise distribution of the cases (N=100)

Anaemia is a condition in which the number of red blood cells or the hemoglobin concentration within them is lower than normal. Hemoglobin is needed to carry oxygen and if you have too few or abnormal red blood cells, or not enough hemoglobin, there will be a decreased capacity of the blood to carry oxygen to the body's tissues. This results in symptoms such as Pallor (100%) seen in all patients followed by fever, fatigue and weakness (93%), dizziness and shortness of breath (88%), Innocent heart murmurs are hearth murmurs that occur in patients with a normal heart structure seen in (84%) patients [Table 2]

| Clinical sign & symptoms | No of cases | Percentage |
|---|---|---|
| Pallor | 100 | 100% |
| Fever | 93 | 93% |
| Weakness & Fatigue | 93 | 93% |
| Breathing difficulty | 88 | 88% |
| Hemic murmur | 84 | 84% |
| Cough | 81 | 81% |
| Tachycardia | 76 | 76% |
| History of PICA | 39 | 39% |
| Knuckle pigmentation | 37 | 37% |
| Tremors | 31 | 31% |
| Irritability | 23 | 23% |
| Icterus | 18 | 18% |
| Abdominal distension | 11 | 11% |

**Table 2:** Clinical features associated with cases of severe anemia (N=100)

Sever acute malnutrition and anemia have aninterply association [14] In other words, childhood anemia might occur as a result of macronutrient deficiency (particularly protein), or it precipitates the occurrence of undernutrition owing to the poor synthesis of macronutrients notably protein [14]. Worldwide, about 18.7 million children are severely malnourished and have prominent micronutrient deficiency, of which 18.5 million are from lower- and middle-income countries [15] SAM is characterized by the presence of bilateral pitting edema and severe wasting (weight-for-height/length 70% /<−3 standard deviation) and mid upper arm circumference (MUAC) of below 11.5 cm (children older than 6 months) [16] [Table 3]

| Protein energy malnutrition | No of cases | Percentage |
|---|---|---|
| Normal | 17 | 17% |
| Grade 1 | 12 | 12% |
| Grade 2 | 31 | 31% |
| Grade 3 | 26 | 26% |
| Grade 4 | 14 | 14% |

**Table 3:** Nutritional status of children with severe anemia (N=100)

Anemia can be classified as microcytic (41%), normocytic (11%) or macrocytic (11%), depending on MCV. it can be hypo-regenerative or regenerative, which depends on the number of reticulocytes. Using both, the list of possible diagnoses in the individual patient is reduced considerably. Both parameters can be supplied routinely by most of the automatic hematological cell counters. Prevalence of microcytic hypocromic morphology seen (41%) cases. [Table 4]

| Type of anemia | No of cases | Percentage |
|---|---|---|
| Microcytic Hypocromic | 41 | 41% |
| Normocytic Hypocromic | 11 | 11% |
| Dimorphic | 21 | 21% |
| Normocytic Normocromic | 16 | 16% |
| Macrocytic | 11 | 11% |

**Table 4:** Morphological type of case of severe anemia(N=100)

According to WHO, severity of anemia is defined depending on Hb value. Extreme lower range of hemoglobin 1-2 gm/dl fund in total 18 cases with female (11 cases, 61%) predominance. Most command range of hemoglobin was between 2-4 gm/dl total (39cases) with female (21cases,53.8%) predominance. This extreme presentation was the consequence of a very slow decrease of hemoglobin values occurring over years, due to the simultaneous presence of two different well-known causes of chronic anemization during childhood: iron deficiency anemia and homozygous sickle cell disease [Table 5].

| Range of Hb(gm/dl) | No of cases | Male | Female |
|---|---|---|---|
| 1 - 2 | 18 | 07 | 11 |
| 2 - 4 | 39 | 18 | 21 |
| 4 - 6 | 21 | 09 | 12 |
| 6 - 7 | 22 | 09 | 13 |

**Table 5:** Level of hemoglobin associated with cases of severe anemia (N=100)

Acute illness is associated with severe anemia. The pathogenesis of this anemia does not appear to be associated with disruption of iron metabolism. Anemia is not a specific disease entity but is a condition caused by various underlying pathologic processes. It can be acute illness or chronic illness. Nutritional deficiencies most common founding (26%). Higher incidence of upper respiratory tract infections (14%) seen with patients of severe anemia [Table 6].

| Associated disease condition | No of cases | Percentage |
|---|---|---|
| Nutritional deficiencies | 26 | 26% |
| Upper respiratory tract infections | 14 | 14% |
| Thalassemia | 11 | 11% |
| Liver disease | 09 | 09% |
| Dengue | 09 | 09% |
| Malaria | 07 | 07% |
| Cardiac conditions | 05 | 05% |
| GI infections | 04 | 04% |
| Septicemia | 04 | 04% |
| CNS infections | 03 | 03% |
| ITP | 02 | 02% |
| Renal infections | 02 | 02% |
| Sickle cell anemia | 02 | 02% |
| Hemophilia | 01 | 01% |
| Aplastic Anemia | 01 | 01% |

**Table 6:** Disease associated with cases of severe anemia at the time of admission (N =100)

Subclinical Vitamin B12 deficiency is a very common entity in the Indian subcontinent with devastating clinical and socio-economic consequences. There was a bimodal age distribution with regard to B12 deficiency. Neurological manifestations were predominant in younger children [< 6 year] and hematological abnormalities were more frequent in older children [ ≥ 6 years].

This study reporting Diamorphic anemia caes was 62.5%, Macrocytic anemia 30.5%. Only vitamin B12 deficiency & Folic acid deficiency were present in 46.8% and 34.3% cases respectively. Both Vitamin B12 and folic acid deficiency present in 15.6% cases.

The present study comprised of 100 subjects, out of which 43% were males and 57% were female. Preferential nourishment of the male child over the female child can result in vitamin B12 deficiency in female children and adolescents, who later can transmit this deficiency state to the fetus in the intra uterine period [Table 7].

| Anemia type | Only B12 level decrease | Only folic acid decrease | Both decrease | Total | percentage |
|---|---|---|---|---|---|
| Dimorphic (N=21) | 08 | 10 | 2 | 20 | 62.5% |
| Macrocytic (N=11) | 07 | 01 | 03 | 11 | 30.5% |

**Table 7:** Distribution of anemia according to vit. B12 and folic acid (N=32)

Iron deficiency anemia is typically associated with low iron saturation of available transferrin. Iron is loaded onto diferric transferrin from three sources: the gut (diet), macrophages (recycled iron), and the liver (stored ferritin iron). In general, iron stores are reduced or lost before the host develops anemia. Therefore, dietary and erythrocyte-recycled iron must meet the demands for erythrocyte production. If iron losses continue, the newly produced erythrocytes will have decreased hemoglobin, causing the amount of iron provided by the same number of senescent. Iron deficiency is the most common nutritional deficiency found here (41%) [Table 8].

IDA is associated with impaired neurocognitive function and exercise intolerance and the association exists even after its successful treatment. Therefore, preventing the progression of iron deficiency is especially important during infancy and early childhood when the rapid growth and development rate, especially of the brain [17] increases the vulnerability to IDA-induced impairment [Table 8].

| Anemia type | S. Iron | TIBC | S. Ferritin | Total | Percentage |
|---|---|---|---|---|---|
| IDA | decrease | increase | decrease | 41 | 41% |

**Table 8:** Distribution of anemia according to Iron profile (N=100)

Total 100 cases observed for final diagnosis among them most common cause for severe anemia in pediatric age group found to be nutritional deficiencies, Iron deficiency being most common accounted for 41% [Table 8 & 9]. Dietary iron deficiency anemia It is most prevalent from age 6 months to 3 years. while second being Vita B12 deficiency around 15% and folic acid deficiency11%, Diamorphic picture of anemia found in 5% cases [Table 7 & 9].

| Final diagnosis | No of cases | Percentage |
|---|---|---|
| IDA | 41 | 41% |
| VitaB12 deficiency anemia | 15 | 15% |
| Folic acid deficiency anemia | 11 | 11% |
| Thalassemia | 11 | 11% |
| Malaria | 07 | 07% |
| Dengue fever | 06 | 06% |
| Dimorphic anemia | 05 | 05% |
| Sickle cell anemia | 02 | 02% |
| Aplastic anemia | 01 | 01% |
| Hemophilia | 01 | 01% |
| Total Cases | 100 | 100% |

**Table 9:** Final diagnosis of severe anemia cases in our study

Among hemoglobinopathies as cause of severe anemia in pediatric age group, Thalassemia was major cause for severe anemia around 11% followed by sickle cell anemia 2%, Aplastic Anemia 1% and Hemophilia 1% [Table 9]. Chronic anemia cases should be screened for hemoglobinopathies as these genetic disorders are commonly seen in pediatric age group. As the definitive treatment of hemoglobinopathies is still difficult to avail in this region, genetic counseling should be considered for hemoglobinopathy patients and their families as well, to prevent new cases.

Cause of severe anemia due to untreated chronic disease found 13% [Table 9]. Alterations in the metabolism of iron via the molecule hepcidin and ferritin are largely responsible for the consequent anaemia. Concomitant iron deficiency might be present and could affect the diagnosis and therapeutic protocol. Treatment options involve the use of erythropoiesis-stimulating agents, blood transfusion, and iron supplementation, in addition to treating the underlying disease.

Ferritin is the intracellular storage form of iron found chiefly in the cytoplasm of the cells of the reticuloendothelial system. It can be quantitated in serum using immunoenzymatic assays. Serum ferritin concentrations have been documented to give an accurate indication of the amount of storage iron in healthy individuals and in patients with iron deficiency or iron overload [18]. It is the most specific biochemical test for iron deficiency anemia (IDA) because it correlates with total body iron stores. Low serum

ferritin concentration reflects depleted iron stores IDA was diagnosed when serum iron was decreased, TIBC increased and serum ferritin decreased, which was reported 41%. [Table 8]

Total 32 patients were studied for vitamin B12 and folic acid deficiency anemia, among which Diamorphic anemia was 62.5%, Macrocytic anemia 30.5%. Only vitamin B12 deficiency & Folic acid deficiency were present in 46.8% and 34.3% cases respectively. Both Vitamin B12 and folic acid deficiency present in 15.6% cases [Table 7].

The present study comprised of 100 subjects, out of which 43% were males and 57% were female. [Table 5] This study can be concluded that incidence of severe anemia was more in < 3 years age group (46%) followed by 3–5-year age group (23%). [Table 1] WHO estimates that 42% of children less than 5 years of age and 40% of pregnant women worldwide are anaemic [16].

A higher prevalence of anemia was noted in female in this study. [Table 5] Most common presenting symptom was paleness of body (100%) followed by fever (93%), weakness & fatigue (93%), Breathing difficulties (88%), Tremors (31%), association with hepatosplenomegaly present in (7%) [Table 2].

Anemia in association with malnutrition is widely prevalent in India. IAP grading use to classify PEM, in our study most cases fall in Grade 2 malnutrition (31%). [Table 3] Microcytic Hypochromic is most common finding (41%) in morphological type followed by dimorphic (21%) and normocytic normochromic (16%) [Table 4].

In maximum cases level of hemoglobin falls between 2-4 gm/dl (39 cases) with female predominance (21 cases) followed by 18 cases had hemoglobin level between 1- 2 gm/dl [Table5].

This study concludes that etiology in majority cases of anemia was nutritional deficiency. Pallor, fever, weakness & faigue and breathing difficulties were the commonest presenting symptoms. [Table 2].

## Conclusion

The major areas for improvement in primary health care are prevention and early diagnosis of anemia because it has been associated with delay in psychomotor development especially in preschool age. The results show that the DQ value of total neurobehavioral development and the values of gross motor, fine movement, and adaptability development of children with anemia were significantly lower than those of children without anemia, which was consistent with the research of Yang.

Appropriate screening and diagnostic modalities will allow most cases of anemia to be diagnosed at the earliest. Preventive strategies is recommended in the form of counseling the parents for proper child feeding practices, immunization and sickness recognition.

Preventive measures for control of anemia in children must be accompanied by measures of providing appropriate nutritional requirements.

Spectrum of measures including child feeding, health and environmental measures will provide complete congenial environment for healthy growth of children. Basic blood parameters are must done before treating children with anemia to avoid unwanted side effects.

## Author Contributions

FAP, DMP and KGR substantially contributed to research design; FAP performed the study acquisition; FAP, KGR and DMP analyzed the data and wrote the paper; FAP, DMP, KGR and BM revised it critically, and approved the final manuscript.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

## Ethical Approval Statement

The study was approved by the Institutional Ethics Committee.

## Patients Consent Statement

A written informed consent was taken from the parents or guardian after explaining them about the study.

## Declaration of Competing Interest

The authors have no conflict of interest to declare.

## Acknowledgments

Authors would like to acknowledge the cooperation from all the participants who were enrolled in this study.

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