

Clinicohematological Profile Of Anemia In Newborn To Eighteen Years Age Group

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ABSTRACT

Anemia is a major public health concern all over the world. It's been around for a long time, and it's the most widespread complex illness in human history. Complications from anaemia can be avoided, especially throughout adolescence, if it is diagnosed and treated early".¹

Anemia is more in pediatric age group because of^{2,3}

- I) Because of "the quick growth in infancy when the demand of nourishment are significantly larger,"
- II) Lack of immunity and malnutrition have a negative impact on hemopoiesis, making the patient more susceptible to infection.
- III) This is known as "poor storage of hemopietic components," and it leads to "the absence of compensatory adjustment of hemopoiesis as per demand."
- IV) A considerable portion of the population suffers from genetically inherited anaemias, and they often show up in infancy and early childhood.

Thalassemia and sickle cell anaemia are the two most frequent types of hemoglobinopathy seen in India. Approximately 100,000 infants are born each year with a homozygous condition for Thalassemia. At a rate of 22.80 per 1000 live births, it is predicted that in India annually between 8,000 and 10,000 babies are born with Thalassemia. People of Indian, Saudi Arabian, Sub-Saharan African, or Mediterranean ancestry are at increased risk for developing sickle cell anaemia. The prevalence rate varies considerably across India, from 0% in the north-east to 18% in the central region, 22-24% in the west, 0-33.3% in the south, and 0% in the southwest.¹⁰

With all these above in mind, the present study was undertaken in our institute to study pattern of anemia in pediatric age group with its clinicohematological correlation and classify these morphologically and to study cause and risk factors associated with anemia.

Objectives

- "To investigate and morphologically categorise anaemias in children" (from birth to age 18).
- The goal of this study is to investigate the causes of childhood anaemia by combining a clinical and haematological approach.
- The purpose of this research is to identify and analyse potential risk factors for the development of anaemia in children and young adults (aged 0-18).

Review of Literature

The concept of anemia was first introduced by Lieutaud in 1750 to describe a lack of blood and not a specific deficiency of red cells for a disease known as Chlorosis or green sickness, its watery blood regarded as a result of illness.¹¹

Anemia pseudo leukaemia infantum (Von Jaksch's anaemia) was first reported in 1889, marking the beginning of the field of paediatric haematology.^{12,13}

Anemia originates from prehistoric Greek “αναμία”, which means “without blood”.¹⁴ The clinical manifestation of iron deficiency anemia appear to have been recognized in earlier times. In the papyrus Ebers, an Egyptian medical reference book written around 150 B.C., the symptoms of an illness called "pallor, dyspnoea, and edoema" are detailed. Ancylostomal anaemia, a sort of iron deficiency anaemia, is what historians of medicine have concluded caused this sickness thousands of years ago. The most common kind of anaemia in infants, iron deficiency anaemia, was first recognised by Blackfan and Diamond (1994).¹¹

Anemia resulting from isolated erythroid hypoplasia or aplasia in young infants was first described by Josephs. In 1938, Diamond and Blackfan anemia described four cases of congenital hypoplastic anemia in childhood, a syndrome now called as Diamond Blackfan Anemia.²⁰

Erythropoiesis²¹

Development of red cells can be study from careful observation of RBC precursors in bone marrow. Committed erythroid progenitor cells divide and differentiate under the influence of erythropoietin. These cells first differentiate into larger cells named as proerythroblasts in which hemoglobin synthesis is first detected.

The cells can be morphologically recognized as belonging to the erythroid pathway of development at this stage. Proerythroblasts proliferates to generate sequentially basophilic, polychromatic and orthochromatic erythroblast; these cells are named after staining characteristics of cytoplasm. With each stage of development, cell size and nuclear size become smaller, chromatin clump increases and nucleus become pyknotic.

Red cell usually emerges into peripheral blood at this stage. After 1-2 days in the circulation, the reticulocyte loses its polyribosomes and turns into a mature red cell.

Pathophysiology:²⁶

Since the main function of the red cell is to carry hemoglobin which carries oxygen;

Anemia is also defined as a decrease in the oxygen carrying capacity of the blood. The release of oxygen from hemoglobin in the tissue capillaries depends upon,

- (a) pH
- (b) The nature of the globin chain
- (c) Concentration of 2,3-diphosphoglycerate

Normal adult hemoglobin (Hb A) which has two alpha and two gamma globin chains and thus releases a greater proportion of bound oxygen. A fall in pH increases oxygen dissociation by reducing the affinity of

oxyhemoglobin for oxygen and this phenomenon, i.e. Bohr effect, enhances the release of oxygen from erythrocytes.

Table: Who Criteria Of Anemia As Per Degree Of Severity In Context To Age Group:²⁴

Population	Anemia (gm/dl)		
	Mild	Moderate	Severe
Child 6 to 59 months of age	10.0 to 10.9	7.0 to 9.9	<7.0
Child 5 to 11 years of age	11.0 to 11.4	8.0 to 10.9	<8.0
Child 12 to 14 years of age	11.0 to 11.9	8.0 to 10.9	<8.0
Female (14years and above)	11.0 to 11.9	8.0 to 10.9	<8.0
Male (14 years and above)	11.0 to 12.9	8.0 to 10.9	<8.0

Iron Deficiency Anemia:

Definition:¹¹

Iron deficiency anemia is defined as anemia occurring due to lack of sufficient iron stores for hemoglobin synthesis. Deficiency of iron is the most common nutritional disorder in the world. Infants, Preschool children, adolescents and women of child bearing age are at highest risk of development of anemia.

Iron deficiency anemia is characterized by decreased or absent iron stores, low transferrin saturation and low hemoglobin concentration, low serum iron concentration and increased red cell distribution width.

Incidence And Prevalance:^{31,32}

Iron deficiency anaemia is the biggest cause of years spent disabled among women, according to the 2016 Global Burden of Disease research. Iron deficiency anaemia affects an estimated 1.24 billion people worldwide, while prevalence varies widely from low- to high-income regions.”

Etiology Of Iron Deficiency Anemia:³³

I) Genetic forms of iron deficiency anemia:

- a) DMT1 deficiency
- b) Tmprss6 gene mutations. (Divalent metal transporter 1)
- c) Atransferrinemia.
- d) Aceruloplasminemia

II) Dietary deficiency:

- (a) Iron deficiency
- (b) Vitamin A deficiency.

Impaired Hb synthesis:

Microcytosis and then hypochromia of red cells develop as blood iron levels drop and transferrin saturation reaches a crucial value of 15%, respectively.

Dietary Inadequacy:³⁴

Breastfeeding alone does not meet the demands of infant after 6 months of age, because it fails to meet the increased demands of growth. Also presence of high concentration of phytates in the Indian diet

impairs the further absorption of iron further affecting the iron balance. Poor availability iron due to tannates, phosphates and antacids is also known.

Pathogenesis Of Megaloblastic Anemia:³⁷

Decreased Intake:

Deficits in vitamin B12 are common in people who follow vegetarian or malnourished diets, or who are breastfed by mothers with low blood B12 levels. Goats milk has a negligible amount of folate. Folate loss also occurs with prolonged cooking of vegetables at high temperatures.

Impaired Absorption:

Inhibitors of cytochrome P450, such as phenytoin and pyrimethamine, prevent the body from properly metabolising folic acid.

Defective Utilization:

Vitamin B12 malabsorption occurs due to a lack of intrinsic factor secretion, intestinal illness (such as celiac disease, regional ileitis, and intestinal resection), or intestinal trauma.

Increased Demands:

Needs for Folate and Vitamin B12 are increased during infancy, especially in premature babies due to rapid growth. The requirements also increase during recovery from PEM and chronic hemolytic Anemia.

Dimorphic Anemia:³⁶

It is defined as anemia in which iron deficiency is associated with folic acid and/or Vitamin B12 deficiency leading to dimorphic blood picture.

Aplastic Anemia:

Definition:³⁸

Aplastic anemia is characterized by marrow hypoplasia with failure to form blood cells of all three lineages i.e. myeloid, erythroid and megakaryocytic resulting in peripheral cytopenias.

Incidence:^{40,41}

The frequency varies from 1.5 to around 7 cases per million people per year, and the median age at diagnosis is between 25 and 60 years old. 39 Males outnumber females by a ratio of around 1. Aplastic anaemia affects people of all ages, while it is somewhat more common in children. The age group between twenty and twenty-five shows a second spike.

Etiology:⁴²

I) Inherited (80%-85% of cases)

- a) Fanconi's anemia.(Defect in DNA damage repair mechanisms.)
- b) Dyskeratosis congenital.(Telomerase dysfunction)
- c) Reticular dysgenesis.
- d) Schwachman –Diamond syndrome.(Defect in Ribosomal function)
- e) Miscellaneous-e.g. Familial Aplastic Anemia, Monosomy 7, Down syndrome etc.

II) Acquired (15%-20% of cases)

- a) Idiopathic
- b) Secondary

Anemia of Chronic Inflammation/Infection:

The most prevalent kind of anaemia in hospitalised patients is that which results from chronic inflammation or infection. Following iron deficiency anaemia, it is the most common cause of anaemia in children. Because it is frequently misdiagnosed as IDA and is typically a diagnosis of exclusion, tracking down its prevalence rate is challenging. There is a known age-related rise in the prevalence of Anemia of Chronic Disease, which now affects 77% of the elderly in whom no one etiological factor has been identified as the root cause of their anaemia.”⁴⁴

Hemolytic Anemias:

Although 7% of the global population carries the gene for a haemoglobin problem, the prevalence and pattern of inheritance of this condition differs widely between racial and ethnic groups.⁴⁵

Definition:⁴⁶

“Hemolytic Anemias are anemias that result from an increased rate of red cell destruction which exceeds the synthetic capacity of the bone marrow.”

Classification Of Hemolytic Anemias:⁴⁷

- Abnormalities seen deep inside the cortex (intracorpuscular) - sHereditary
- "Abnormalities of the membrane."
- Proteins of the membrane skeleton: spherocytosis and ectocytosis.
- Abetalipoproteinemia, a disorder of membrane lipids
- lack of enzymes
- Glycolytic enzymes: pyruvate kinase and hexokinase.
- Hexose monophosphate enzymes.
- Glutathione synthase:glucose-6-phosphate dehydrogenase shunt.
- Deficiencies in the production of haemoglobin.
- Thalassemia syndromes are characterised by impaired globin production.
- Hemoglobinopathies characterised by structural abnormalities in globin production include sickle cell anaemia.
- membrane defect: paroxysmal nocturnal hemoglobinuria (PNH)

Clinical Features Of Thalassemia:^{85,86}

“These children often begin showing symptoms around the second six months of life, typically including significant weakness and cardiac decompensation as a result of progressive hemolytic anaemia if not treated. Extreme anaemia in infants and children is often diagnosed after the onset of late-onset symptoms such as exhaustion, poor appetite, and lethargy. Chipmunk faces (a severe form of Thalassemic facies), pathologic fractures, significant hepatosplenomegaly, and cachexia are still prevalent in some low-income regions. It's possible that secondary hypersplenism and mechanical pain from a swollen spleen are both possible outcomes of unchecked spleen growth. Ineffective erythropoiesis, enlarged medullary spaces, extramedullary hematopoiesis, and a massive energy expenditure are all symptoms of this condition.”

“Pallor due to anaemia and jaundice from hyperbilirubinemia caused by intravascular hemolysis are two skin symptoms that may present themselves. Anemia's most common early sign is weariness, which patients often complain about. Multiple transfusions can cause chronic iron deposition, which can manifest as bronze skin and ulcers in the extremities. Pain similar to that caused by cholelithiasis, known

as colic, might be the result of bilirubin crystallisation and gallstone formation brought on by chronic hyperbilirubinemia. When hematopoiesis is not properly controlled, persistent hemolysis occurs, which can lead to splenic infarcts or autophagy.

Deposition of Iron in Pancreas lead to Diabetes Mellitus; In the Thyroid presents as Hypothyroidism and in Parathyroid glands causes Hypoparathyroidism, hypocalcemia and osteoporosis. In pituitary, testis and ovary presents as growth retardation and hypogonadotropic hypogonadism. In the heart iron overload manifest as arrhythmias, myocarditis and intractable cardiac failure.

“Hemoglobin (Hb); Hematocrit (HCT); Hemoglobin Level (g/dL); Capillary Zone Electrophoresis Mean cell haemoglobin, mean cell haemoglobin concentration, mean cell volume, and multiplex ligation-dependent probe amplification stand for iron deficiency anaemia, mean cell volume, and mean cell volume, respectively. modified; moderate; Cellular retinol content; We refer to these cells as red blood cells (RBCs) and nucleated red blood cells (NRBCs) respectively. low, slight; A disorder of red blood cell production; thal, thalassemia.”

Prenatal Diagnosis:^{12,52}

Measurement of globin chain synthesis: Obtain fetal blood at 18-20 weeks of gestation and measure α , β and γ chain synthesis by the fetal reticulocytes. A ratio of β to γ and α chains of less than 0.025 suggests Thalassemia major. Ratio between 0.04-0.10 is indicative of Thalassemia Minor. Fetal Mortality Associated with procedure was 5.4% and diagnosis was established late in gestation.

Malnutrition and Development of Anemia

“Anemia and malnutrition are one of the most common health problems affecting children. Anemia affects populations in both rich and poor countries. It is an indicator of both poor nutrition and poor health”¹²⁴. “It has been found that anaemia is a major factor in stunting, the most common form of malnutrition in young children. One in six children is underweight and one in four is stunted due to poor nutrition, which accounts for roughly 45 percent of mortality among children under the age of 5. According to recent reports, India has the highest rate of childhood underweight in the world”¹²⁵

“It is widely recognised that malnutrition has a detrimental effect on human functioning, growth, and development, especially in young children, and so represents a major public health issue. It's a major contributor to infant and young child mortality in low-income nations.”¹²⁶

“Anemia and malnutrition in rural areas are the result of a complex interaction of social, economic, epidemiological, and, maybe, parasitic variables. Anemia and dietary deficiencies have been linked to poor personal cleanliness (low BMI). Low school enrollment, excessive absenteeism, early dropout, and poor classroom performance are all strongly correlated with poor nutritional condition in children of primary school age. Life expectancy is shortened and cognitive development is slowed by chronic undernutrition in childhood. Children's health and nutritional condition must always be evaluated through the use of anthropometric examination since nutritional status is a key indicator of this quality. Weight loss, growth failure, and severe malnutrition are the three forms of poor nutrition in children”¹²⁷

Material and Methods

Present study was a 18 months cross sectional study which was carried out in the hematology section of Pathology Department of a tertiary care hospital from January 2020 to June 2021. Blood samples from

Department of Pediatrics were received, screened and cases having low hemoglobin concentration were included in our study.

Method Of Collection Of Data

Criteria for inclusion:

Patients with anaemia from the paediatric ward who were admitted to the intensive care unit (ICU) between January 2020 and June 2021 were included in the research.

Conditions for exclusion:

Everyone from infants to teenagers who isn't anaemic.

Those with a history of hematolymphoid malignancy were ruled out.

Processing

The cases were divided into 5 groups as per age:0-1 years; 1-5 years; 5-8 years; 8-13 years and 13-18 years.

- Hematological investigations viz.: Complete hemogram and Peripheral blood smear (PBS) with reticulocyte count were done in all cases.
- Criteria for anemia as per age and according to degree of severity in context to age was taken as per Table No 2 & Table No 4.

Clinical Profile:

A detailed history of patient was taken which includes patient’s age, sex, complaints, clinical presentation, dietary and nutritional status in all cases.

While history of prematurity, low birth weight, family history, history of consanguinity in parents, developmental milestones and menstrual history were noted wherever necessary. For nutritional status of patients, weight was taken for all the patients to classify them according to recent IAP guidelines for malnutrition according to age.

Low Birth Weight

Low Birth Weight was defined as first weight recorded within hours of birth weight <2500 gms. Cases fulfilling above criteria were taken in consideration as low birth weight.

Observation and Results

Total number of 176 cases of anemia in newborn to eighteen years of age group were studied in a period of 18 months from January 2020-May 2021.

Maximum no of cases were from the age group (1-5 years) (30.68%) followed by 0-1 years (22.73%). There was slight male preponderance noted. M:F being 1.6:1

Table: Distribution of Cases according to Severity of Anemia in 176 Cases

Age Group (Years)	Mild	Moderate	Severe	Chi Square test	P value	Result
Between 0 to 1 Years	12	19	9	14.078	0.079	Not significant
Between 1 to 5 Years	7	28	19			

Between 5 to 8 Years	5	9	8			at 5%
Between 8 to 13 Years	9	13	10			
Between 13 to 18 Years	5	9	14			
Total	38	78	60			
Percentage (%)	21.59 %	44.32 %	34.09 %			

Moderate degree of anemia was the most common (44.32%) in the present study.

The commonest etiology for anemia in present study was nutritional deficiency (53.4%) in which iron deficiency (35.79%) was the commonest. The commonest morphological type of anemia in present study was microcytic hypochromic anemia (47.73%) followed by normocytic normochromic (21.59%). The commonest grade of severity of anemia was moderate degree among Iron deficiency anemia, Anemia of chronic inflammation/infection, β Thalassemia major, Megaloblastic anemia and Sickle cell anemia. However, Dimorphic anemia and Aplastic anemia had severe degree of anemia as the commonest.

Table: Bone Marrow Aspiration Findings:

Sr.No.	Findings of Bone Marrow	Total No of cases
1.	Megaloblastic Anemia	05
2.	Dimorphic Anemia	02
3.	Aplastic Anemia (Fanconi Anemia)	02
	Total	09

Bone marrow aspiration was done in 09 cases. Findings of the bone marrow aspiration study are shown in above table. Diagnosis of Aplastic anemia (Fanconi's anemia) was give in accordance with genetic work up.

Summary and Conclusion

The present study was a 18 months Cross sectional study which was carried out in the Hematology section of Pathology Department of a tertiary care hospital from January 2020 to June 2021.

- Most cases of anaemia were discovered in children aged 1 to 5 (30.68%), with a small male preponderance (M:F ratio of 1.6:1).
- "Mild anaemia accounted for 21.59 percent of the patients," followed by "moderate anaemia" (44.32) and "severe anaemia" (34.09%)
- "Weakness, easily fatiguability, and irritability" (82.39%) were reported as the most prevalent first symptoms, followed by "loss of appetite, loss of weight, and refusals of feeds" (75.57%).
- "Pale complexion was the most common presenting feature (100%) followed by tachycardia (84.09%) and indicators of malnutrition (80.68%) (delayed developmental milestones, failure to thrive, and low weight for age)."
- Morphological typing of anemia with etiological correlation helps in deciding further work up and treatment modalities.

- Maternal history of anemia, low birth weight, prematurity, malnutrition, improper breastfeeding practices and delayed starting of complementary feeding are important risk factors for development of anemia in infants.
- Family history and history of consanguineous marriage are important risk factors for hemolytic anemia due to hemoglobinopathies.
- Genetic counseling and prevention of consanguineous marriage is a key for prevention of hemoglobinopathies viz. Thalassemia and Sickle cell anemia
- Malnutrition, dietary factors and menstrual irregularities play significant role as risk factors for development of anemia in adolescent girls.
- According to the authors, "the current study emphasises the necessity of routine screening and individual evaluation of etiological and risk factors of anaemia in paediatric age group, allowing prompt commencement of optimum and suitable medication which can avoid additional consequences of anaemia."

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