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Original Article

Paediatrics Section

Clinico-aetiological Analysis of Anaemia along with Haematological Parameters in Children and Adolescents: A Retrospective Study from a Tertiary Care Hospital, Chhattisgarh, India

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ABSTRACT

Introduction: Anaemia is defined as a decreased concentration of blood haemoglobin. World Health Organisation (WHO) estimates that 42% of children less than five years of age worldwide are anaemic and prevalence of anaemia in India in children 6-59 months for year 2019 was 53.4%. Childhood anaemia not only affects physical health but cognitive and social development as well.

Aim: To determine various causes of anaemia in children in age groups 1-5 years, 6-12 years and 13 to 18 years and to determine clinical features and haematological investigations in moderate to severe anaemia.

Materials and Methods: This retrospective, observational study was conducted in Department of Paediatrics, Shri Shankaracharya Institute of Medical Sciences, Bhilai, Charttisgarh, India, from September 2021 to December 2021. The data collection was done retrospectively over a period of two years, from September 2019 to September 2021 from patients case records which were available from Medical Record Department. A total of 300 patients from age one year to 18 years who were admitted in the paediatric ward with anaemia were included for study. Anaemia was defined and severity categorised based on WHO definition. The aetiology of anaemia was analysed based on Complete Blood Count (CBC) and investigations including serum ferritin, vitamin B12 level, bone marrow examination, High Performance Liquid Chromatography (HPLC) and other relevant investigations. Data was entered in a excel sheet and analysed using software Statistical Package for the Social Sciences (SPSS) version 21.0. Statistical test used was student's t-test for paired and unpaired data for continuous variables. The p-value <0.05 was considered significant.

Results: Out of total 300 patients, 148 (49.3%) were males and 152 (50.7%) were females. Most of the patients were in 1-5 years of age (45.6%), followed by 13-18 years age (29.4%) and 6-12 years (25%). Total 95 (31.6%) patients had mild, 112 (37.3%) had moderate and 93 (31%) had severe anaemia. The three most common causes of anaemia were iron deficiency in 77 patients (37.5%), haemolytic anaemia in 54 patients (26.3%) and vitamin B12 deficiency in 34 patients (16.5%). Mean Red Cell Distribution Width (RDW)(31.1±10.1%) values and mean of Mean Corpuscular Volume (MCV) (98.2±15.2 fL) were higher in vitamin B12 deficiency patients as compared to iron deficiency patients mean RDW (17.2±3.5%) and mean of MCV (58.14±7.3 fL), this difference was found to be significant with p-value <0.001.

Conclusion: Most of the patients had moderate anaemia. Iron deficiency was most common cause of anaemia overall in children and especially below 13 years followed by haemolytic anaemia mainly sickle cell anaemia and Vitamin B12 deficiency anaemia. The MCV and RDW values from CBC can be used to identify two most common causes of nutritional anaemia.

Keywords: Haemoglobin, Iron deficiency, Mean corpuscular volume, Prevalence, Red cell distribution width, Sickle cell disease

INTRODUCTION

Anaemia is defined as a decreased concentration of blood haemoglobin. It is a condition in which the number of red blood cells or their oxygen carrying capacity is insufficient to meet the body's physiological requirements, which vary by age, sex, altitude, smoking habits, and during pregnancy [1-3]. The clinical features of anaemia include pallor, sleepiness, irritability, decreased exercise tolerance and if it remains untreated it may lead to tachypnoea, tachycardia, shortness of breath on exertion, weakness, cardiac dilatation and cardiac failure [3].

As per Comprehensive National Nutrition Survey (CNNS) 2016-2018 data, the prevalence of anaemia in children age 1-4 years was 40.6%, 5-9 years it was 23.5% and 10-19 years it was 28.4% [4]. World Health Organisation (WHO) estimates that 42% of children less than five years of age worldwide are anaemic and prevalence of anaemia in India in children 6-59 months for year 2019 was 53.4% [5]. However, as per National Family Health Survey 5 (NFHS-5) which was done on 2019-2021, children age 6-59 months who were anaemic are 67.1% in India [6]. It has increased from 58.6% which was as per NFHS-4 in 2015-2016 for India [7]. In Chhattisgarh state, it was 67.2% as per NFHS-5, which is even higher than national figure [6]. The increase in the prevalence of anaemia is unfortunate in spite of national nutritional anaemia control program and overall growing economy of India [8]. The most common causes of anaemia include nutritional deficiencies; mainly iron deficiency, folic acid, and vitamin B12 and vitamin A deficiencies. Others include haemoglobinopathies and infectious diseases, such as malaria, tuberculosis, Human Immunodeficiency Virus (HIV) and parasitic infections [7,9].

Iron deficiency is the most common nutritional disorder in the world [10]. There are enough of studies available on anaemia in children under five years of age [11,12]. But very few studies about adolescents are available, who are in their most crucial period of life and are future citizens [13,14]. Childhood anaemia not only affects physical health but cognitive and social development as well [15]. Anaemia causes lethargy, lack of concentration, vulnerable to illness and delayed puberty [16,17]. There are few community based studies which analysed prevalence of anaemia in children from few

districts of Chhattisgarh, but, none of the studies analysed clinical features, aetiology or haematological parameters [18-20].

Thus, the present study being hospital based was conducted to highlight the burden of anaemia among children in Bhilai and nearby areas and also to add to the existing knowledge about clinical features and aetiology of anaemia so that preventive measures and interventions can be taken to build a healthier future. The aim of the present study was to determine various causes of anaemia in children in age groups 1-5 years, 6-12 years and 13 to 18 years; in moderate to severe anaemia cases to determine clinical features and haematological parameters which can help in easy identification of its aetiology.

MATERIALS AND METHODS

This retrospective, observational study was conducted in Department of Paediatrics, Shri Shankaracharya Institute of Medical Sciences, Bhilai, Charttisgarh, India, from September 2021 to December 2021. Institutional Ethical Committee approval was obtained (certificate number SSIMS/IEC/2021/37). Data collection was done for a period of two years, from September 2019 to September 2021 from patient's case records which were available from Medical Record Department.

Inclusion criteria: Paediatric patients from age one year to 18 years who were admitted in the paediatric ward with anaemia were included in the study.

Exclusion criteria: Patients presented in Outpatient Department (OPD), patients admitted in Paediatric Intensive Care Unit (PICU) due to serious illness, shock, sepsis, congestive cardiac failure, COVID-19 positive, immunodeficiency or those that died within 48 hours of admission, patients with insufficient case records or investigations and paediatric surgery patients were excluded from the study.

Sample size calculation: Sample size was calculated by using Cochran's formula [21] $n_0=z^2pq/e^2$.

As the data for prevalence of anaemia is not known for this region hence 'p' is used as 50% in above formula, q is 1-p (50%), z=1.96 for 95% confidence limit and estimated precision(e) was considered as 5%, n=384.

As it was hospital based sample, which has limited number of children, we used Cochran's formula for limited sample size [21] which is:

$n=n_0/1+(n_0-1)/N$

n_0 is sample from population which was 384 and N is sample size which is total paediatric admissions in two years, which were 1106. Hence, final N=284. Out of 1106 admissions, in the study time period between age group one year to 18 years, 300 met the inclusion criteria and is higher than required sample size.

Data Collection

Data collection included detailed clinical presentation like weakness, fever, yellowish discolouration of eyes, progressive pallor, cough, cold, vomiting, abdominal pain, joint pain and any others. Developmental, immunisation and past history related to blood transfusion were noted. Examination findings included detailed general examination and presence of organomegaly (hepatosplenomegaly). Findings for the following Investigations were included; complete blood picture with peripheral smear and reticulocyte count, High Performance Liquid Chromatography (HPLC), serum ferritin, iron profile, vitamin B12 level, Coomb's test and bone marrow examination findings. Anaemia was defined and severity categorised based on WHO definition as shown in [Table/Fig-1] [22].

Iron Deficiency Anaemia (IDA) was diagnosed based on serum ferritin levels.

- In Children aged 1-4 years serum ferritin <12 µg/L.
- In Children aged >5 years serum ferritin <15 µg/L was considered iron deficiency [23].
- Vitamin B12 deficiency was defined as serum vitamin B12 <200 pg/mL [24].

Population	No anaemia (gm/dL)	Anaemia (gm/dL)		
		Mild	Moderate	Severe
Children 6-59 months of age	≥11	10-10.9	7-9.9	<7
Children 5-11 years of age	≥11.5	11-11.4	8-10.9	<8
Children 12-14 years of age	≥12	11-11.9	8-10.9	<8
Non pregnant women (15 years of age and above)	≥12	11-11.9	8-10.9	<8
Pregnant women	≥11	10-10.9	7-9.9	<7
Male, 15 years of age and above	≥13	11-12.9	8-10.9	<8

[Table/Fig-1]: Haemoglobin levels to diagnose anaemia (gm/dL) [22].

HPLC was used for diagnosis of haemoglobinopathies [25]. After data collection patients were classified based on severity of anaemia as mild, moderate and severe based on haemoglobin report [22]. Clinical features and aetiology was analysed for moderate and severe anaemia cases only. The aetiology of anaemia was analysed based on Complete Blood Count (CBC) and peripheral smear report and other investigations as mentioned above.

STATISTICAL ANALYSIS

Data was entered in a excel sheet and analysed using software Statistical Package for the Social Sciences (SPSS) version 21.0. Variables were expressed as mean, standard deviation, and percentage as appropriate. Statistical test used was student's t-test for paired and unpaired data for continuous variables. The p-value <0.05 was considered significant.

RESULTS

Total of 300 patients between one year to 18 years of age were studied, out of which 148 (49.3%) were males and 152 (50.7%) were females. The patients were divided into three age groups. A 45.6% were 1-5 years of age, 29.4% were 13-18 years of age and 25% were 6-12 years of age, as shown in [Table/Fig-2]. There were more number of female patients in 13-18 years age group and more male patients in 1-5 years age group.

Age group	Number of patients (n)	Percentage (%)	Gender distribution	
			Male	Female
1-5 years	137	45.6%	81 (59.1%)	56 (40.8%)
6-12 years	75	25%	33 (44%)	42 (56%)
13-18 years	88	29.4%	34 (38.6%)	54 (61.4%)

[Table/Fig-2]: Age and gender distribution (n=300).

Anaemia patients were divided into three groups based on severity. Overall 95 (31.7%) patients had mild anaemia, 112 (37.3%) had moderate and 93 patients (31%) had severe anaemia.

As shown in [Table/Fig-3] and for age group 1-5 years most patients had moderate anaemia (53.3%), for 6-12 years age most cases had mild anaemia (36%), however, severe anaemia cases was more in 13-18 years age group (55.7%).

Anaemia severity	1-5 years	6-12 years	13-18 years	Total (N)
Mild	43 (31.4%)	27 (36%)	25 (28.4%)	95
Moderate	73 (53.3%)	25 (33.3%)	14 (15.9%)	112
Severe	21 (15.3%)	23 (30.7%)	49 (55.7%)	93
Total	137	75	88	300

[Table/Fig-3]: Age-wise distribution of severity of anaemia.

Aetiology of anaemia was analysed in moderate and severe anaemia cases only which were 205 out of 300. The most common cause of anaemia was found to be IDA in total 77 patients (37.5%), followed by haemolytic anaemia in 54 patients (26.3%), Vitamin B12 deficiency anaemia in 34 patients (16.5%) and other causes as shown in [Table/Fig-4]. Dimorphic anaemia had both iron and Vitamin B12 deficiency. Out of total 54 haemolytic anaemia cases, 10 were sickle cell

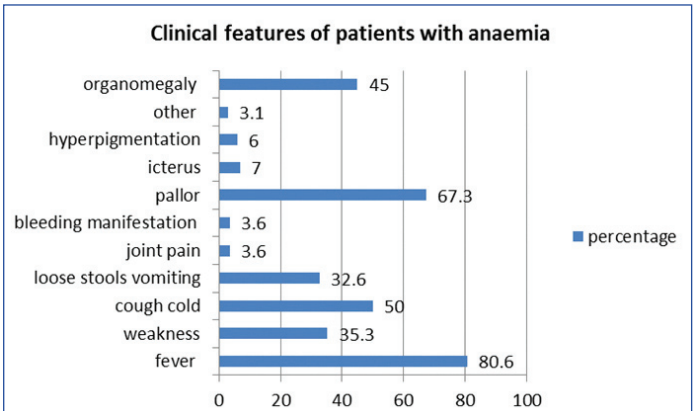
anaemia heterozygous, 29 were sickle cell anaemia homozygous, five were thalassaemia major, four were sickle thalassaemia, one was thalassaemia intermedia, two were sickle cell with iron deficiency and three were sickle cell with vitamin B12 deficiency patients.

Aetiology	1-5 years	6-12 years	13-18 years	Total
Iron deficiency	53	17	7	77 (37.6%)
Vitamin B12 deficiency	5	4	25	34 (16.6%)
Sickle cell anaemia heterozygous	6	3	1	10 (4.9%)
Sickle cell anaemia homozygous	9	11	9	29 (14.1%)
Thalassaemia major	5	0	0	5 (2.4%)
Sickle thalassaemia	0	2	2	4 (1.9%)
Thalassaemia intermedia	0	0	1	1 (0.5%)
Leukaemia	0	0	1	1 (0.5%)
Aplastic anaemia	0	0	1	1 (0.5%)
Fanconi anaemia	0	1	0	1 (0.5%)
Anaemia of chronic illness	0	1	2	3 (1.5%)
Sickle cell homozygous with iron deficiency	2	0	0	2 (1%)
Sickle cell heterozygous with B12 deficiency	0	0	3	3 (1.5%)
Dimorphic anaemia	1	2	10	13 (6.3%)
Not evaluated	13	7	1	21 (10.2%)
Total	94	48	63	205 (100%)

[Table/Fig-4]: Aetiology of anaemia.

Anaemia aetiology could not be evaluated in total 21 patients, as complete investigations were not available to conclude the aetiology, could be due to financial reason or early discharge. Iron deficiency was most common and haemolytic anaemia were second most common aetiology of anaemia in children 1-5 years and 6-12 years age group, however vitamin B12 deficiency anaemia was most common cause in adolescent age group 13-18 years.

The most common clinical feature was fever in 242 (80.6%), followed by cough and cold or breathing difficulty in 150 (50%), loose stools and vomiting in 98 (32.6%), generalised weakness and loss of appetite in 106 (35.3%), bleeding manifestation in 11 (3.6%) joint pains in 11 (3.6%) other causes in 10 (3.1%) which include pain in abdomen in eight and seizures in two patients. Examination findings were pallor (67.3%), icterus (7%), hyperpigmentation (6%) and organomegaly (hepatomegaly or splenomegaly or both in 45%) [Table/Fig-5].



[Table/Fig-5]: Clinical features of patients admitted with anaemia.

Mean haemoglobin was analysed in 205 moderate to severe anaemia cases and it was found to be 7.06±1.2 gm/dL and minimum value was 1.9 gm/dL [Table/Fig-6].

MCV and RDW values were compared for two most common types of nutritional deficiency anaemia. Mean Corpuscular Volume (MCV) was 58.14±7.3 fL for iron deficiency and 98.2±15.2 fL for vitamin b12 deficiency anaemia patients as shown in [Table/Fig-7]. Using student's t-test for independent means for MCV values, there was significant difference in MCV values for IDA and vitamin B12 deficiency anaemia with p-value <0.001.

Age group	Hb (gm/dL) Mean±SD	Minimum Hb (gm/dL)
1-5 year	8±1.64	3
6-12 year	7.47±2.15	1.9
13-18 year	5.7±2.1	2.3

[Table/Fig-6]: Mean haemoglobin (Hb) age-wise distribution.

The difference in Red cell Distribution Width (RDW) between iron deficiency and vitamin B12 deficiency anaemia was also significant with p-value <0.001. The mean RDW value for Vitamin B12 deficiency anaemia was 31.1±10.1% which is significantly high as compared to IDA patients which was 17.2±3.5% [Table/Fig-7].

Aetiology	Number	Hb mean	MCV (Mean ±SD) fL	Range (Minimum -max (fL))	RDW % Mean±SD	RDW % Range
Iron Deficiency Anaemia (IDA)	77	7.6±1.7 Min 2.3	58.14±7.3	38.4-75.3	17.2±3.5	11-33.9
Vitamin B12 deficiency anaemia	34	5.3±1.7 Min-1.9	98.2±15.2	66.2-122.6	31.1±10.1	15.1-54.5
Student's t-test	There was significant difference in MCV values for IDA and vitamin B12 deficiency anaemia with p-value <0.001			The difference in RDW between iron deficiency and vitamin B12 deficiency anaemia was significant with p-value <0.001		

[Table/Fig-7]: MCV and RDW values for Iron deficiency and vitamin B12 deficiency anaemia.
p-value <0.05 was considered significant

DISCUSSION

In the present study, 300 patients of anaemia were analysed out of which 148 (49.3%) were males and 152 (50.7%) were females. Most of the patients (45.6%) were 1-5 years of age, followed by 29.4% were 13-18 years of age and 25% were 6-12 years of age.

A similar study done by Prakash A et al., also found that most of the children were below five years with overall predominance of moderate anaemia cases. They included total of 150 hospitalised children with anaemia and divided them based on age groups, children below five years were 61 (40.7%), 46 (30.7%) were 5-11 years age group, 13 (8.7%) were in 12-14 years and 30 (20%) were 15 years and above. Out of total 150 patients, 30 (20%) children were graded as having mild, 98 (65.3%) moderate and remaining 22 (14.7%) were graded as having severe anaemia [26].

Similar to the present study, Saba F et al., also found that moderate anaemia cases were dominant in their study. They found mild in 12.7%, moderate in 75.82% and severe grades of anaemia in 11.43% patients [27]. However, another study done among children of age group five months to 12 years found that eight out of 100 children had mild, 44 had moderate and 48 had severe anaemia [28].

Balcı YI et al., in their study of total of 1120 patients (672 girls and 448 boys) aged 12-16 years admitted to paediatric outpatient found that 63 of 1120 (5.6%) children were anaemic. When the gender was considered, 8.3% of the girls and 1.6% of the boys had anaemia [29]. This was similar to the present study as we also found more number of female (61.4%) patients in adolescent age group 13-18 years age group as compared to male (38.6%) with anaemia. However, few studies showed male predominance, but most of them were conducted below 14 years age group [30,31]. In the present study, among 205 cases of moderate and severe anaemia most common aetiology of anaemia was found to be iron deficiency in total 37.6%, followed by haemolytic anaemia in 26.3% and vitamin B12 deficiency in 16.6%. In children below 13 years the most common cause of anaemia was iron deficiency, but in

13-18 years vitamin B12 deficiency was most common. Among haemolytic anaemia's sickle cell homozygous was more common (14.1%) than heterozygous (4.8%), this could be due to inclusion of moderate and severe cases only in aetiology analysis [3]. The increasing trend of fast food in India might be adding to the nutritional deficiencies [32-34]. This emphasises the need for early screening and genetic counselling for haemoglobinopathies. Also nutrition counselling not only for small children but also for adolescent age group, which are usually neglected, should become part of daily practice for health care provider.

Marken P et al., in their study also found that IDA was the most common aetiology with 104 (41.6%) patients. Out of 104 IDA patients, 71 (68.2%) were found in age group 1-6 years. Vitamin deficiencies ((vitamin B12, folic acid or both) were found in 34 patients. Most of the (26.4%) vitamin B12 deficiency anaemia patients were from 13-18 age group whereas most of the (17.6%). Folic acid deficiency was found in 7-12 years [13].

Similar findings were seen in the study done by Madoori S et al., in Telangana. The common causes of anaemia in their study were iron deficiency (58%), sickle cell disorders (27%), thalassaemia (9%), 5% cases had megaloblastic anaemia and 2% aplastic anaemia [31]. Another study done among children aged 5-12 years, observed that, iron deficiency was predominant 80/110 (72.7%) followed by megaloblastic anaemia 20/110 (18.1%). Least were aplastic and haemolytic anaemia, 5 cases each (4.5 %). The incidence of IDA was greater in females i.e., 60 (75%) in comparison to males 20 (25%) , whereas, for megaloblastic anaemia the, the incidence was found to be greater in males i.e., 15 (75%) when compared to females, which was 5 (25%) [35].

Prakash A et al., analysed clinical features of patients between six months to 18 years with anaemia and found major presenting complaint as pallor (64%), koilonychias (35.2%), palpitation (35.3%), dysphagia (32.7%), dyspnoea (28.7%) and lack of concentration (27.3%) [26]. Another similar study found that the chief presenting symptoms of anaemia as easy fatigability (34%), loss of appetite (36%), pallor (26), and irritability (24%). The chief clinical signs were pallor of mucosa (76%), pallor of skin, palms, and soles (64%), tachycardia (23%), cheilitis (13%), and hemic murmur (9%) [35]. Clinical features in the present study were similar to above studies. In the present study, higher values of both MCV and RDW were seen in vitamin B12 deficiency and lower MCV and lower RDW values were seen in IDA. This could be helpful if facility is not available everywhere for investigations like serum ferritin, iron profile, vitamin B12 and folic acid Levels, which are costly.

Aulakh R et al., did a study among 151 children with microcytic anaemia (MCV<75 fl) and found that the mean RDW value was 18.37±2.22% in IDA group (97 children) compared to 16.55±1.51% in the non IDA group (54 children) (p-value <0.001, unpaired t-test) [36]. The results were comparable to the present study.

One more study found the sensitivity of RDW at cut-off of 18% to detect IDA was 76.5% and specificity 73.1%. At a cut-off of RDW 16.4%, the sensitivity was found to be 94%, however at a cut-off of 21%, the specificity was 95%. Using combination of haemoglobin ≤10 g/dL and RDW >15%, maximum sensitivity (99%) and specificity (90%) was obtained. Thus, simple coulter analysis for estimating haemoglobin and RDW can be employed for identification of children with IDA who might need iron therapy [37].

A study done by Patel S et al., concluded the sensitivity and specificity of MCV to screen out B12 deficiency were 10.14% and 92.82%, respectively. Accuracy of MCV as an indicator for B12 deficiency was estimated to be 45.05%. The mean MCV value for vitamin B12 deficiency patients was found to be 86.94±10.41 fL [38]. In the present study, mean MCV for vitamin b12 deficiency was 98.2±15.2 fL.

Clinicians can discern definitive diagnoses for the type of anaemia based on the MCV value. Microcytic anaemia is where MCV is less than 80 fL while normal MCV is between 80 to 100 fL. It is commonly seen in chronic iron-deficient anaemia of chronic disease, sideroblastic anaemia, and thalassaemias. Macrocytic anaemia has MCV over 100 fL. Megaloblastic anaemia is commonly secondary to folate (also known as folic acid or vitamin B9) deficiency, cobalamin/ vitamin B12 deficiency, and oroticaciduria. Normocytic anaemia is anaemia with a low haemoglobin and haematocrit range but MCV in the normal range of 80 to 100 fL. This type of anaemia is found in haemolytic causes [39].

Limitation(s)

Limitations of the present study were that being a single medical college hospital based study from Bhilai, though it has wide flow of patients from the state, the results cannot be generalised to entire Chhattisgarh state or country. Authors also could not analyse other causes of anaemia like folic acid deficiency, vitamin A deficiency due lack of facility at our centre.

CONCLUSION(S)

Moderate anaemia was most common; however, severe anaemia was common in adolescent children. Anaemia is more in adolescent females than males. Iron deficiency was most common cause of anaemia overall in children and especially below 13 years, but in adolescent age group B12 deficiency was more common than iron deficiency. Sickle cell anaemia was most common haemolytic anaemia in this region. The use of basic CBC parameters, MCV and RDW can be used to identify two most common causes of nutritional anaemia's if facility is not available for all investigations. Further research can be done which includes the socio-economic background and dietary pattern also as contributing factor for anaemia.

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