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Original Article

Pathology Section

Disorders Presenting as Anaemia among Paediatric Population at a Tertiary Care Centre, Kerala, India: A Cross-sectional Study

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ABSTRACT

Introduction: Anaemia is a condition marked by low Haemoglobin (Hb) concentration and is an important risk factor for the poor health and development of children and adolescents. Anaemia is not a diagnosis, but merely an objective sign of disease. The correct treatment requires an understanding of the pathogenesis of the condition.

Aim: To identify disorders presenting as anaemia in paediatric population. Also to analyse the data by grading of anaemia and to calculate the proportion of anaemia in various paediatric age groups.

Materials and Methods: This cross-sectional study was conducted at Government Medical College, Ernakulum, Kerala, India, from September 2017 to February 2018, on 211 paediatric patients of age groups from newborn upto 18 years. After a detailed clinical history and examination, Complete Blood Count (CBC), peripheral smear preparation, reticulocyte count, renal function tests, liver function tests, and if necessary, radiological and bone marrow examination were done. The mean haemoglobin in the categories were compared with Comprehensive National Nutritional Survey Data. The data obtained were entered in Microsoft excel 365 and further analysed. Categorical variables were analyzed by Fisher's-exact test and continuous variables by Analysis of Variance (ANOVA) and Kruskal-Wallis test and the significance level was set at p-value ≤ 0.05.

Results: Of the 211 patients, 120 (56.87%) were males and 91 (43.13%) were females. The average haemoglobin level varies across age groups and sex. In the case of newborns, average Hb was 9.31 g/dL in males and 10.4 g/dL in females. A total of 211 patients presented with 339 disease conditions, with respiratory disorders in 98, followed by 83 nutritional diseases, 49 infections and 35 systemic diseases. Total of 132 patients in age group of 6 months to 4 years, presented with maximum disorders (206). A total of 186 (54.8%) cases presented with Microcytic Hypochromic Anaemia (MHA), 149 (43.95%) with Normocytic Normochromic Anaemia (NNA) and only 4 (1.18%) with Haemolytic Anaemia (HA). No cases of macrocytic anaemia were noted.

Conclusion: Total of 76.8% cases of MHA (42.1% of total anaemia cases) are associated with Nutritional, Respiratory and Infectious conditions which can be managed by public health measures. The haemoglobin levels in neonates and less than 6 months age group were significantly less than population mean which needs to be addressed. In similar manner, girls in school going age group had significantly lower Hb than boys.

Keywords: Haemoglobin, Microcytic hypochromic anaemia, Neonates, Nutritional disorder, Respiratory disorder

INTRODUCTION

Anaemia is a condition in which the number of red blood cells or the Haemoglobin (Hb) concentration within them is lower than normal [1]. The optimal Hb concentration needed to meet physiologic needs varies by age and sex of individual [1]. The indicator anaemia has a wide variety of causes. Iron deficiency is the most common cause of anaemia; other causes include acute and chronic infections that result in inflammation and blood loss; deficiencies of other vitamins and minerals, especially folate, vitamin B12 and vitamin A; and genetically inherited traits, such as thalassaemia [1,2]. Other conditions (e.g., malaria and other infections, genetic disorders, and cancer) can also play a role in anaemia [2]. Anaemia in India is a severe public health problem among young children, adolescent girls and women. In addition to increased morbidity and negative effects on physical well-being (weakness and/or fatigue) [1,2]. Anaemia is associated with delayed mental and psychomotor development. By the estimate of World Health Organisation (WHO), 42% of children less than 5 years of age and 40% of pregnant women worldwide are found to be anaemic [1]. The global age-standardised prevalence of anaemia was 27% in 2013, down from 33.3% in 1990, a decrease of approximately 21% [2].

Iron deficiency is an important cause of anaemia and of concern at certain points in the life cycle (infancy and adolescence). Micronutrient deficiencies are an important cause of morbidity and mortality, especially in infants and preschool children [3,4]. Even mild to moderate micronutrient deficiencies can lead to impaired cognitive development, poor physical growth, increased morbidity and decreased work productivity in adulthood [4].

Poor nutrition, leading to iron deficiency, is the principal underlying factor in more than 60% of all anaemia cases [3]. Malnutrition has been identified as one of the principal causes limiting India's global economic potential as depicted in Nutrition - Copenhagen Consensus Center [3]. To provide robust data on the shifting conditions of both undernutrition and overweight and obesity, the Ministry of Health conducted the Comprehensive National Nutrition Survey (CNNS) to collect a comprehensive set of data on nutritional status of Indian children from 0-19 years of age. This survey was the largest micronutrient survey ever implemented globally [4].

Anaemia prevalence among pregnant and non pregnant women are included as primary outcome indicators in the core set of indicators for the Global Nutrition Monitoring Framework [5]. These indicators are used to monitor progress towards achieving Global Nutrition Target 2, which is a 50% reduction in anaemia among women of reproductive age by 2025 [5,6]. In 2019, global anaemia prevalence was 39.8% (95% Uncertainty Interval 36.0%, 43.8%) in children aged 6-59 months, equivalent to 269 million children with anaemia [7,8].

To assess the prevalence as well as severity of anaemia in India, three different datasets were utilized, viz, WHO dataset, National Family Health Survey (NFHS) -5 data and CNNS data. According to NFHS

-5 survey, there is a rise in 8.5 % of anaemic cases in the age group of 6 months- 5 years (from 58.6% to 67.5%), whereas in the 15-19 age group there is a 5 % rise in girls (54.1% to 59.1%), and in boys it was 1.9 % rise (29.2% to 31.1%). Data was not available for other age groups in NFHS-5 survey. In India 41% of preschoolers aged 1-4 years, 24% of school-age children aged 5-9 years and 28% of adolescents aged 10-19 years had some degree of anaemia [9].

The global burden of malnutrition is unacceptably high, with nearly half of all deaths in children under five years linked to poor nutrition [9]. Stunting in early life can have long-term effects on health, physical and cognitive development, learning and earning potential, thereby placing an immense human and economic toll at the individual, household, community, and national level. Despite substantial economic growth in India over most recent decades, chronic malnutrition (stunting) in children under five years of age reduced by only one-third between 1992 and 2016 and remains alarmingly high, with 38.4% of children stunted in the country [10,11]. Hence, the present study included children of age groups newborns to 18 years with the aim to understand clinical and diagnostic challenges presented by anaemia in paediatric population with special emphasis on its clinical spectrum, grading, variation in prevalence among different age groups, and sex (males, females) thereby providing a clinician with a detailed insight into the aetiology of anaemia.

MATERIALS AND METHODS

The study was a cross-sectional study conducted in the Clinical Pathology Laboratory, Department of Pathology, Government Medical College, Ernakulam, Kerala, India, from September 2017 to January 2018. Approval from Institutional Ethical Committee was obtained (approval number IEC/33/17). Informed consent was taken from the parents of study population.

Inclusion criteria: All the patients of paediatric age groups from newborns to 18 years of age, who presented with anaemia and were willing to participate were included in the study.

Exclusion criteria: Patients who had already received treatment for anaemia were excluded.

Sample size calculation: Based on the prevalence of anaemia reported by CNNS (prevalence= 41%) [4].

$N= 3.84xpq/d^2$,

Where

q=59%

Precision (d= 20% of 41%= 8).

The optimal sample size calculated was 138. Sampling technique was by consecutive sampling. A total of 211 patients who attended the Outpatient Department (OPD) during the study time period were included.

Procedure

A detailed history was taken regarding any associated disease or conditions, including respiratory disorders, any infections, nutritious disorders including protein energy malnutrition, stunting. If no obvious disorders were noted, they were classified as Idiopathic [5]. Laboratory investigations including Complete Blood Count (CBC) (with haematology analyser 5 part Model: BC6800/ Shenzhen Mindray Biomedical Electronics), peripheral smear preparation, Erythrocyte Sedimentation Rate (ESR), reticulocyte count, routine urine examination, routine biochemical tests including renal function tests, liver function tests and if necessary, bone marrow and radiological examination were performed.

Anaemias were classified as Microcytic Hypochromic, Normocytic normochromic or Macrocytic based on the MCV and haemoglobin values for the age and sex of the patient in comparison with normal values [11]. If haemolysis was noted on peripheral smear study, the cases were classified under haemolytic anaemias. The grading of anaemia into Mild, Moderate and Severe was also done according to World Health Organization (WHO) criteria [12].

STATISTICAL ANALYSIS

The data obtained was statistically analysed using Microsoft Excel 365. Descriptive statistics like, number of cases, percentage, concomitant involvement with other disorders, differential involvement with various age groups, male: female ratio, and grades of anaemia were utilised to describe the spectrum of disorders presenting as anaemia. Inferential statistics were performed and CNNS data [4] was used for comparison as it provided a baseline for proportions of severity in all age groups and Z test of proportions was done. Analysis of Variance (ANOVA) / Kruskal-Wallis test. Student's t-test used to analyse the p-value of mean Hb and age group of newborns and upto 6 months. The grading of anaemia was done as grades 1, 2 and 3 [13]. The significance level being fixed at p value < 0.05. The population mean was obtained from Wintrobe's Clincal Hematology, 12th edition [14].

RESULTS

Of the total study population, 120 (56.87%) were males and 91 (43.13%) were females. The distribution of cases in paediatric population is given in [Table/Fig-1].

Age group	Male	Female	n, %
Newborn/Neonates	9 (4.26%)	8 (3.79%)	17 (8.05%)
Upto 6 months of age	6 (2.84%)	4 (1.89%)	10 (4.74%)
6 months-4 years	82 (38.86%)	50 (23.69%)	132 (62.56%)
5 years-11 years	20 (9.48%)	23 (10.90%)	43 (20.38%)
12 years-18 years	3 (1.42%)	6 (2.84%)	9 (4.26%)
Total	120 (56.87%)	91 (43.13%)	211 (100%)

[Table/Fig-1]: Distribution of cases among various age groups.

Chi-square test was performed (age group vs sex), no significant difference between sex across various age groups (p-value=0.236). The 211 patients were associated with total 339 disorders including 25 idiopathic cases (unknown aetiology). The distribution according to disease conditions, categorised into 12 categories as given in [Table/Fig-2].

Disease condition	Males (n, %)	Females (n, %)	Total (n, %)
Nutritional	40 (11.79%)	43 (12.69%)	83 (24.5%)
Neonatal	6 (1.77%)	4 (1.18%)	10 (2.95%)
Congenital	5 (1.47%)	3 (0.9%)	8 (2.36%)
Respiratory disorders	64 (18.88%)	34 (10.03%)	98 (28.91%)
Congenital heart defects	4 (1.18%)	6 (1.77%)	10 (2.95%)
Infection	24 (7.08%)	25 (7.37%)	49 (14.45%)
Haematologic	2 (0.59%)	3 (0.88%)	5 (1.47%)
Systemic	22 (6.49%)	13 (3.83%)	35 (10.32%)
Metabolic	2 (0.59%)	5 (1.47%)	7 (2.06%)
Poisoning	4 (1.18%)	3 (0.88%)	7 (2.06%)
Trauma	1 (0.29%)	1 (0.29%)	2 (0.59%)
Idiopathic	16 (4.72%)	9 (2.65%)	25 (7.37%)
Total	190 (56.05%)	149 (43.95%)	339 (100%)

[Table/Fig-2]: Distribution of various diseases or conditions in males and females.

[Table/Fig-3] shows the distribution of types of anaemias amongst various disorders of all study subjects. Respiratory disorders (n=98) contributed to most number of cases followed by nutritional diseases (n=83), infections(n=49), and systemic diseases (n=35). The distribution of various disorders with age group criterias are shown in [Table/Fig-4]. Amongst all the study participants, the distribution of various types of anaemias with age groups and gender are shown in [Table/Fig-5]. In the school going population (5-11 years), least studied among the paediatric population, the average Hb levels were significantly less in females (9.35 g/dL) compared to males (10.7 g/dL) (p-value=0.005). The same age group had significant difference

in Hb levels in respiratory disorders in males (11.1 g/dL) compared to females (9.67 g/dL) (p-value=0.01; Welch's t test). Those having Microcytic Hypochromic Anaemia (MHA) had significantly lower Hb (9.23 g/dL) compared to Normocytic Normochromic Anaemia (NNA) with mean Hb level of 10.2 g/dL (p-value=0.02).

Disoder	Anaemia Type			Total
	MHA	NNA	HA	
Nutritional	58 (17.11%)	25 (7.37%)	0	83 (24.48%)
Neonatal	3 (0.88%)	7 (2.06%)	0	10 (2.95%)
Congenital	4 (1.18%)	4 (1.18%)	0	8 (2.36%)
Respiratory	54 (15.93%)	43 (12.68%)	1 (0.29%)	98 (28.91%)
Congenital heart defects	5 (1.47%)	5 (1.47%)	0	10 (2.95%)
Infection	31 (9.14%)	18 (5.31%)	0	49 (14.45%)
Hematologic	1 (0.29%)	1 (0.29%)	3 (0.88%)	5 (1.47%)
Systemic	19 (5.60%)	16 (4.72%)	0	35 (10.32%)
Metabolic	5 (1.47%)	2 (0.59%)	0	7 (2.06%)
Poisoning	5 (1.47%)	2 (0.59%)	0	7 (2.06%)
Trauma	1 (0.29%)	1 (0.29%)	0	2 (0.59%)
Idiopathic	0	2 5(7.37%)	0	25 (7.37%)
Total	186 (54.87%)	149 (43.95%)	4 (1.18%)	339 (100%)

[Table/Fig-3]: Distribution of anaemias in various disorders.
(MHA: Microcytic hypochromic anaemia; NNA: Normocytic normochromic anaemia; HA: Haemolytic anaemia)

Majority of cases included low birth weight patients (nine cases), prematurity (nine cases) and respiratory disorders (nine cases), with one patient presenting with many disorders or conditions [Table/Fig-6].

Age group	Haemoglobin in male (g/dL) (Mean±SD)	Haemoglobin in female (g/dL) (Mean±SD)	Total haemoglobin (g/dL) (Mean±SD)
Newborn	9.31±4.6	10.4±3.12	9.81±4
Newborn- 6 months	9.32±2.42	8.41± 3.32	8.95±2.78
6 month-4 years	9.68±3.12	9.75±2.2	9.7±2.8
5-11 years	10.7±2.56	9.35±3.3	9.97±3.24
12-18 years	10.8±2.66	9.29± 3.52	9.79±3.41

[Table/Fig-6]: Mean haemoglobin levels in various age groups of the study participants.

In patients with respiratory disorders, those having MHA had significantly lower Hb (9.23±1.32 g/dL) level than those with NNA (10.2±1.56 g/dlL (p-value=0.002; Student's test). In the case of infections other than respiratory infections, the difference in Hb levels between MHA (9.48±1.4 g/dL) and NNA (9.79±1.35 g/dL) was not significant (p-value=0.483) as well as in systemic diseases, the difference in Hb between MHA (9.41 g/dL) and NNA (10.1 g/dL) (p-value=0.255). In patients with nutritional disorders those having MHA had significantly lower Hb (9.21±1.96 g/dL) level than those with NNA (10.2±1.7 g/dL) with a p value of 0.044. In case of 10 patients with stunting, seven had mild degrees of anaemia and three had moderate degrees of anaemia. No patient with stunting had severe anaemia. As in the case of Protein Energy Malnutrition (PEM), as the grade of stunting increases, severity also seems to rise, though a statistically insignificant. There were seven cases with metabolic disorders, 5 (71%) with MHA and two cases (29%) had NNA. The metabolic disorders as diagnosed included hypothyroidism (n=3 cases), rickets (n=2 cases), Tay Sachs disease (n=1 case) and alpha ketonuria (n=1 case). There were seven cases of poisoning, five cases of chemical poisoning (kerosene and copper sulphate) and one case each of snake bite and insect bite. All five cases of chemical poisoning were having MHA, whereas snake bite and insect bite had NNA. The average age in case of chemical poisoning is 1.4 years, snake bite -11 years and insect bite -3 years. The average Hb was 9.38±1.02 g/dL in chemical poisoning while it was 10.7 g/dL and 11.1 g/dL in snake bite and insect bite. [Table/Fig-7] Only 2 cases of trauma were noted with mean Hb of 7.63±0.6 g/dL. One was a male with MHA and the second a female with NNA. One case was a fracture and second one was of epistaxis. In 23 cases of anaemia of unknown aetiology, all presented with NNA with a mean Hb of 11±1.03 g/dL.

Moderate degree of anaemias (n=151) were seen predominantly in all classes of disorders except idiopathic cases, where mild grade

Age Group	Total patients (n,%)	Nutritional (n,%)	Neonatal (n,%)	Congenital (n,%)	Respiratory (n,%)	Congenital heart defects (n,%)	Infection (n,%)	Haematologic (n,%)	Systemic (n,%)	Metabolic (n,%)	Poisoning (n,%)	Trauma (n,%)	Idiopathic (n,%)	Total Disorders (n,%)
Newborn	17 (8.05%)	11 (3.24%)	9 (2.65%)	3 (0.88%)	9 (2.65%)	3 (0.88%)	4 (1.18%)	0	0	0	0	0	2 (0.59%)	41 (12.09%)
Upto 6 months	10 (4.74%)	2 (0.59%)	0	0	11 (3.24%)	2 (0.59%)	3 (0.88%)	0	3 (0.88%)	1 (0.29%)	0	0	0	22 (6.49%)
6 months-4 years	132 (62.56%)	54 (15.93%)	1 (0.29%)	3 (0.88%)	64 (18.88%)	4 (1.18%)	27 (7.96%)	3 (0.88%)	22 (6.49%)	6 (1.77%)	6	1 (0.29%)	15 (4.42%)	206 (60.76%)
5-11 years	43 (20.38%)	14 (4.13%)	0	2 (0.59%)	13 (3.83%)	1 (0.29%)	11 (3.24%)	2 (0.59%)	9 (2.65%)	0	1 (0.29%)	1 (0.29%)	1 (0.29%)	59 (17.40%)
12-18 years	9 (4.26%)	2 (0.59%)	0	0	1 (0.29%)	0	4 (1.18%)	0	1 (0.29%)	0	0	0	3 (0.88%)	11 (3.24%)
Total	211 (100%)	83 (24.48%)	10 (2.95%)	8 (2.36%)	98 (28.91%)	10 (2.95%)	49 (14.45%)	5 (1.47%)	35 (10.32%)	7 (2.06%)	7 (2.06%)	2 (0.59%)	25 (7.37%)	339 (100%)

[Table/Fig-4]: Distribution of disorders among various age groups vs disease categories.
Total patients=211; Total disorders=339

Gender	Anaemia	Age group					
		New born	<6 month	6 month-4 year	5-11 year	12-18 year	Total
Male	MHA	22%	50%	66%	30%	33%	55%
	NNA	78%	50%	33%	70%	67%	44%
	HA	-	-	1%	-	-	1%
	Total male	100%	100%	100%	100%	100%	100%
Female	MHA	25%	-	72%	69%	67%	64%
	NNA	75%	100%	28%	22%	33%	34%
	HA	-	-	-	9%	-	2%
	Total male	100%	100%	100%	100%	100%	100%

[Table/Fig-5]: Distribution of various types of Anaemia with age group criterias and gender.

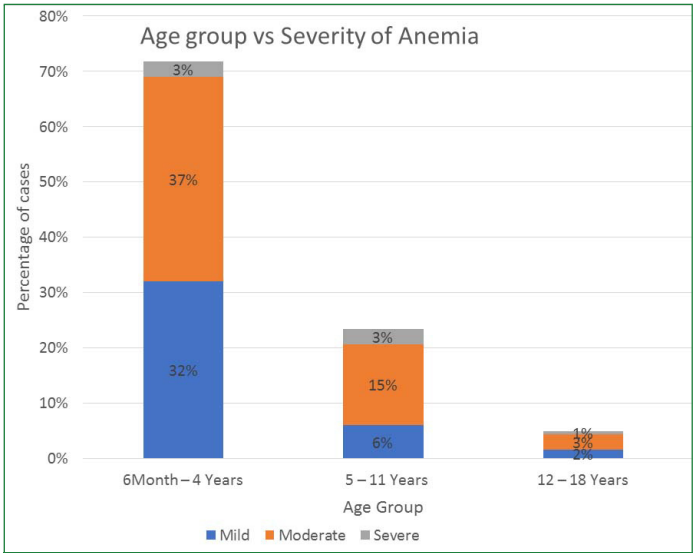
Mean haemoglobin levels of all study participants are shown in [Table/Fig-6]. The mean haemoglobin in male was 9.31 g/dl (95% CI: 7.81-10.8 g/dL and in female was 10.4 g/dL (95% CI: 9.28-11.4 g/dL) difference was insignificant (p-value=0.3; Independent samples t-test). Of the 17 newborns, four were having MHA (mean Hb was 8.39 g/dL) and 13 had NNA (mean Hb was 10.2 g/dL).

Anaemia severity	Nutritional	Neonatal	Con-genital	Respira-tory	Chd	Infection	Haemato-logic	Sys-temic	Meta-bolic	Poisoning	Trau-ma	Idiopathic	Total
Mild	32	0	2	29	1	12	-	12	3	2	-	19	112
Moderate	30	1	3	47	4	30	5	18	3	5	2	3	151
Severe	8	-	-	2	-	-	-	2	-	-	-	1	13
Total	70	1	5	78	5	42	5	32	6	7	2	23	276

[Table/Fig-7]: Distribution of anaemia among various diseases according to WHO criteria (6 Months-18 years).
WHO: World Health Organisation

predominated. [Table/Fig-7] shows distribution of anaemic cases on basis of severity amongst various age groups from 6 months to 18 years. For newborn, the analysis by one sample t-test denoted the p-value for the difference between means of sample and population was highly significant (p-value<0.001). The mean value 9.81±4 g/dL and the difference from population mean (μ=16.5 g/dL) was highly significant. One sample t-test highly significant for less than 6 months (p-value<0.001) category and the mean value was significantly different from population mean (μ=11.5 g/dL). One sample t-test highly significant for 2 months old (p-value=0.001) and 2- 6 months (p-value=0.009) categories and the mean values were significantly different from population means (μ=11.5 g/dL). Grading of the severity of anaemia was done for nutritional disorders. Of the total 83 cases of nutritional disorders, 70 cases of belonged to age group 6 months and above and were graded by World Health Organization criteria. A 32 cases had mild anaemia (males -22, females-10), 30 cases had moderate anaemia (males-18 and females-12) and eight cases had severe anaemia (males-3 and females -5). A Chi-square test of independence showed that there was no significant association between gender and severity of anaemia with p-value = 0.26.

Other than Iron deficiency, Protein Energy Malnutrition (PEM), stunting, low birth weight and acute diarrhoeal diseases were included under nutritional disorders. As the grade of PEM increases from 1 to 4, the severity of anemia seems increasing , though there was no statistically significant relation on doing Fisher's-exact test (p-value=0.119). As in the case of PEM, as the grade of stunting increases, severity also seems to rise, though a statistically significant relation could not be proved on doing Fisher-exact test (p-value=0.183). The haemoglobin levels in neonates and less than 6 months age group were significantly less than population mean which needs to be addressed. [Table/Fig-8] shows distribution of anaemias in various age groups.



[Table/Fig-8]: Distribution of anaemias in various age groups cases from 6 months to 18 years.

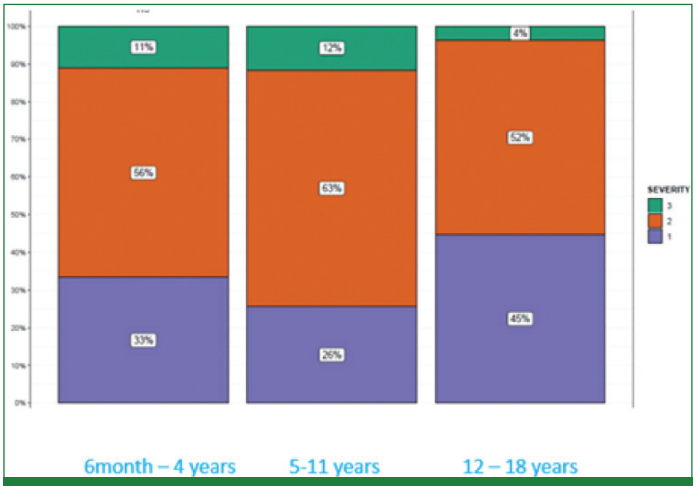
In the present study, among preschoolers (6 months-4 years of age), 32% had mild anaemia, 37% had moderate anaemia and 3% had severe anaemia. Among school-age children (5 years-11 years), 6% had mild anaemia, 15% had moderate anaemia, and 3% had severe anaemia. Among adolescents (12 years-18 years), 2% had mild anaemia, 3% had moderate anaemia and 1% had severe anaemia.

The results of Z-test and p-values of study subjects of 6 months-18 years of age, as compared with the CNNS data are summarised in [Table/Fig-8]. In the preschool age group (6 months- 4 years), on doing Z-test for proportions to compare with CNNS data, difference was highly significant in patients with mild and moderate anaemia, whereas the difference was not significant in those with severe anaemia. In the 5-11 years age group, the difference in proportions was not significant in mild (p-value=0.059) and moderate anaemia (p-value=0.395), whereas it was highly significant in severe anaemia (p-value=0.001). In adolescent category (12 years-18 years), the difference in proportion was significantly lower in the study group in mild and moderate anaemias [Table/Fig-9].

Age group distribution	Severity of Anaemia					
	Mild		Moderate		Severe	
	Z score	p-value	Z score	p-value	Z score	p-value
6 months-4years	3.48	<0.0005	6.82	<0.00001	1.89	0.059
5-11 years	-1.89	0.059	0.85	0.395	3.27	**0.001**
12-18Years	-5.64	<0.00001	-3.32	0.0009	-0.51	0.61

[Table/Fig-9]: Comparison of various grades of anaemia with the CNNS data; Bold p-values are significant.

According to Kruskal-Wallis test, a significant relation was observed between age group and anaemia grade with (p-value=0.035) [Table/Fig-10]. Bonferroni correction for multiple comparisons analysis of the differences between age groups was performed and the significant difference was found between age groups of 6 months-4 years and 5-11 years (p-value=0.034).



[Table/Fig-10]: Bar chart depicting Age group with counts plotted against severity; Grade 1: mild anaemia; Grade 2: moderate anaemia; Grade 3: severe anaemia; By Kruskal Wallis test, age group and anaemia grade p value = 0.035.
X axis represents Age groups, with three stacked bars, 6 month-4 years, 5-11 years, 12 – 18 years; Y axis represents severity of anemia according to WHO, with the legend 1- mild (blue color), 2- moderate (red color) and 3- severe (green color)

The proportion of moderate and severe cases are more in the age group of 5-11 years (75%) compared to other age groups, 67% in preschool category (6 months-4 years) and 56% in adolescents (12-18 years) [Table/Fig-9]. Indeed, the values are from present study. inadvertently omitted from results. Request you to kindly add the Contingency table given below as [Table/Fig-11].

	Age group					
Anaemia	New born	<6 month	6 month-4 year	5-11 year	12-18 year	Total
MHA	4 (24%)	3 (30%)	90 (68.18%)	22 (51%)	5 (56%)	124
NNA	13 (76%)	7 (70%)	41 (31.06%)	19 (44%)	4 (44%)	84
HA	-	-	1 (0.76%)	2 (5%)	-	3
Total	17	10	132 (100%)	43	9	211

[Table/Fig-11]: Distribution of various subtypes of Anemias across the age groups.
MHA: Microcytic hypochromic anemia; NNA: Normocytic normochromic anemia;
HA: Hemolytic anemia

DISCUSSION

Present study was conducted on 211 patients presenting with 339 disorders, single patient presenting with multiple disorders. The WHO has devised criteria for grading of anaemia based on age and sex [1]. Individual cases are analysed based on the variables including age, sex, grade along with category of disease, several patterns emerge which aids the clinician in management and prognostication. Since, its nearly impossible to describe the characters associated with all the 72 disorders in one study, it was categorised into 12 different entities including idiopathic category, observations specified in paediatric population and neonates. Maximum number of cases were seen in the age group of 6 months to 4 years (132 patients with 206 disorders). Most common disorders, associated with anaemia in the present study included respiratory disorders, nutritional diseases, infections and systemic diseases. Onyeneho NG et al., in their study observed that common causative factors of anaemia in India were nutritional causes [15].

In the present study, amongst patients with respiratory and nutritional disorders, those having MHA had significantly lower Hb level than those with NNA. Hussain SQ et al., in their study observed that iron deficiency anaemia was commonly associated with acute lower respiratory tract infection as in the present study [16]. According to CNNS data, among preschoolers (6 months-4 years) mild anaemia was found to be more common. Among school-age children (5 years-11 years), moderate anaemia while among adolescents (12-18 years) mild anaemia was more common as compared to other types [4]. In the case of infections other than respiratory infections, the difference in Hb levels between MHA (9.48±1.4 g/dL) and NNA (9.79±1.35 g/dL) was not significant when compared in the present study, just as other study observing similar findings [17]. There had been past studies depicting, the percentage of severity of anaemia increases with increase in the grade of Protein Energy Malnutrition (PEM). Arya AK et al., in their study observed that 95% of children with severe acute malnutrition had anaemia of which 52% had severe anaemia and 28% had moderate anaemia [18]. As in the case of PEM, as the grade of stunting increases, severity also seems to rise, though a statistically insignificant relation. No case of severe anaemia were observed in this study. In case of grade 1 stunting, 86% cases were having mild anaemia whereas in grade 2 stunting, 33% cases had mild anaemia whereas 67% had severe anaemia as per study by Gosdin L et al., observed that there is a positive association between anaemia and stunting [19]. All cases of prematurity had moderate grade of anaemia, just as in study by Cibulskis CC et al., observed that anaemia of prematurity is normocytic normochromic type [20].

Out of total cases with metabolic disorders, 71 % had MHA and 29% cases had NNA. The metabolic disorders included hypothyroidism, rickets, Tay Sachs disease and alpha ketonuria. A total of 42.85% had mild anaemia while 42.86% had moderate anaemia when grading of severity was performed. Similarly, in previous study by Tavil B et al., reported that 54.3% had anaemia of chronic disease associated with metabolic disorders and only 19.6%, rest contributed by macrocytic anaemia and haemolytic anaemia and the mean age of the children with metabolic diseases was 55.2±64.8 months [21]. The nature of anaemia in cases of insect and snake bites was observed as NNA in the present study, in contrast with previous experiences in which hemolytic anaemia was seen. Also, the average age group affected was lower in chemical poisoning (1.4 years) compared to the average paediatric age group (3.2 years) which highlights need to be careful with toddlers [22-24]. Only two cases of trauma were noted with mean Hb of 7.63±0.6 g/dL, male with fracture presented with MHA and the second, a female with epistaxis, with NNA. In 23 cases of anaemia of unknown aetiology, all presented with NNA with a mean Hb of 11±1.03 g/dL. Neonatal anaemia is defined by a haemoglobin or haematocrit concentration of greater than 2 standard deviations below the mean for postnatal age [4]. The mean value of Hb of neonates in the present study (9.81 g/dL). The mean Hb amongst males and females showed statistically insignificant p-value on independent samples t-test (p value = 0.3) of the 17 neonates, majority presented with conditions of low birth weight, prematurity and respiratory disorders and were diagnosed with NNA (n=13 cases). Li N et al., and Aher S et al., in their study concluded that premature infants had increased risk of anaemia, as in the present study [22,23]. No cases of macrocytic anaemia were encountered during present study.

Among the preschool population (6 months - 4 years), iron deficiency anaemia constituted 68.18%, anaemia of chronic inflammation in 31.06% and haemolytic anaemia in 0.76%. The proportion of iron deficiency anaemia is higher compared to study by Sarna A et al., in which it was 36.5% [24]. The proportion of anaemia of inflammation was 31.06%,14.4% and 66.7% among, preschool, school going category and adolescents respectively compared to 6.5%, 5.4% and 3.4% in the study [25].

In the school going population,the average Hb levels were significantly less in females (9.35 g/dL) compared to males (10.7 g/dL), with significant difference in Hb levels in respiratory disorders cases in males compared to females with a p-value of 0.01 on doing Welch's t test. The present study analysis observed the importance of controlling MHA in the 5-11 year category with main cause as nutritional disorders specifically iron deficiency. Anaemia was associated with lower respiratory tract infection as in the study by Hussain SQ et al., [25]. In the 12-18 years category, there was no significant difference in mean haemoglobin levels between males and females. In the present study, only 3% of total males and 7% of females of paediatric population were there in contrast to males 31.1% and females 59.1% in the adolescent age group in contrast to National Family Health Survey (NFHS-5) data [9]. This highlights need to take screening to the public to bring more anaemic patients from adolescent age group as it is highly likely that the health system is missing a lot of patients from the age group.

Limitation(s)

Present study being a hospital-based study, may not truly reflect the frequency of anaemic patients in community at large. The sample size of adolescents age group (12 years-18 years) was small.

CONCLUSION(S)

The present study observed 54.8% of disorders associated with MHA, 43.9% with NNA and 1.18% cases with haemolytic anaemia. Most common diseases associated with anaemia were respiratory infections, nutritious disorders, infections and systemic diseases. Hence, a control of these diseases can help in reducing the incidence of most cases of anaemia. The mean Hb level in neonates as well as those under 6 months were significantly less than the population mean. This age group needs a closer attention by the clinicians. The mean Hb in females in school going category was significantly less than males which need to be addressed carefully. For adolescent category, future studies with greater sample size need to be conducted.

REFERENCES

[1] World Health Organisation; Anaemia; https://www.who.int/health-topics/anaemia#tab=tab_1.
[2] Kassebaum NJ, Fleming TD, Flaxman A, Phillips DE, Steiner C, Barber RM, et al. The global burden of anemia. Hematol Oncol Clin North Am. 2016;30(2):247-308.
[3] Copenhagen Consensus III | Copenhagen Consensus Center; https://www.copenhagenconsensus.com/post-2015-consensus/nutrition.
[4] National Health Mission: Comprehensive National Nutrition Survey. 2016; http://nhm.gov.in/index1.php?lang=1&level=2&sublinkid=1332&lid=713.
[5] Global Nutrition Monitoring Framework; Operational guidance for tracking progress in meeting targets for 2025 . https://apps.who.int/iris/rest/bitstreams/1093537/retrieve.
[6] Branca F, Luz M, De-Regil K, Engesveen M, Nieves Garcia-Casal S, Kennedy L, et al. Comprehensive implementation plan on maternal, infant and young child nutrition [Internet]. 2012. Available from:http://apps.who.int/iris/bitstream/10665/113048/1/WHO_NMH_NHD_14.1_eng.pdf.
[7] Anaemia in women and children [Internet]. [cited 2022 May 22]. Available from: https://www.who.int/data/gho/data/themes/topics/anaemia_in_women_and_children.
[8] Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis M, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet. 2013;382(9890):427-51. Available from: http://www.thelancet.com/article/S0140673613609037X/fulltext.
[9] National Family Health Survey NFHS-5 http://rchiips.org/nfhs/factsheet_NFHS-5.shtml.
[10] National Family Health Survey [Internet]. [cited 2022 Apr 14]. Available from: http://rchiips.org/nfhs/factsheet_nfhs-4.shtml.
[11] Means RT Jr, Glader B. Anaemia: general considerations. In: Greer J, Arber DA, Glader BE, List AF, Means R, Rodgers GM, editors. Wintrobe's clinical hematology: Fourteenth edition. Philadelphia: Wolters Kluwer; 2018.
[12] World Health Organisation. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. https://apps.who.int/iris/handle/10665/85839.
[13] Defining and recognizing different types of anemia common to the oncology practice; Haematology/Oncology; https://www.healio.com/news/hematology-oncology/20120331/defining-and-recognizing-different-types-of-anemia-common-to-the-oncology-practice#:~:text=Grade%201%2C%20considered%20mild%20anemia,5%20is%20death%20(Table).
[14] Greer J, Foerster A, Glader BE, Paraskevas F, Means R, Rodgers GM. Wintrobe's clinical hematology. 12th edition. Philadelphia: Wolters Kluwer; 2009. Table B.2, Reference Hematologic Intervals In Children And Adults; p.2584.
[15] Onyeneho NG, Ozumba BC, Subramanian SV. Determinants of Childhood Anemia in India. Sci Rep. 2019;9(1):16540. Available from: https://www.nature.com/articles/s41598-019-52793-3.
[16] Hussain SQ, Ashraf M, Wani JG, Ahmed J. Low hemoglobin level a risk factor for acute lower respiratory tract infections (ALRTI) in children. J Clin Diagn Res. 2014;8(4):PC01. Available from: /pmc/articles/PMC4064840/.
[17] Viana MB. Scientific Comments Anemia and infection: A complex relationship. Rev Bras Hematol Hemoter. 2011;33(2):90-95. Available from: www.rbhh.orgorwww.scielo.br/rbhh.
[18] Arya AK, Kumar P, Midha T, Singh M. Hematological profile of children with severe acute malnutrition: A tertiary care centre experience. Int J Contemp Pediatr. 2017;4(5):1577-80.
[19] Gosdin L, Martorell R, Bartolini RM, Mehta R, Srikantiah S, Young MF. The co-occurrence of anaemia and stunting in young children. Matern Child Nutr. 2018;14(3):e12597. Available from: /pmc/articles/PMC6866136/.
[20] Cibulskis CC, Maheshwari A, Rao R, Mathur AM. Anemia of prematurity: How low is too low? J Perinatol. 2021;41(6):1244-57.
[21] Tavil B, Sivri HSK, Coskun T, Gurgey A, Ozyurek E, Dursun A, et al. Haematological findings in children with inborn errors of metabolism. J Inherit Metab Dis. 2006;29(5):607-11. Available from: https://pubmed.ncbi.nlm.nih.gov/16906472/.
[22] Li N, An H, Jin M, Li Z, Zhang Y, Zhang L, et al. Association of infants small for gestational age with anemia under five years old in two large association of infants small for gestational age with anemia under five Years old in two large longitudinal Chinese birth cohorts. Nutrients. 2022;14(5):1006. Available from: https://doi.org/10.3390/nu14051006.
[23] Aher S, Malwatkar K, Kadam S. Neonatal anemia. Seminars in Fetal and Neonatal Medicine. 2008;13(4):239-47.
[24] Sarna A, Porwal A, Ramesh S, Agrawal PK, Acharya R, Johnston R, et al. Characterisation of the types of anaemia prevalent among children and adolescents aged 1–19 years in India: A population-based study. Lancet Child Adolesc Health. 2020;4(7):515-25. Available from: http://www.thelancet.com/article/S2352464220300948/fulltext.
[25] Hussain SQ, Ashraf M, Wani JG, Ahmed J. Low hemoglobin level a risk factor for acute lower respiratory tract infections (ALRTI) in children. J Clin Diagn Res. 2014;8(4);PC01-PC03.

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