

Descriptive Study of the Spectrum of Disorders Presenting as Normocytic Normochromic Anaemia from a Tertiary Care Setting at Ernakulam, Kerala, India

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ABSTRACT

Introduction: Anaemia is a common problem discovered on routine laboratory tests. Based on red cell morphology, anaemia can be classified as microcytic hypochromic, macrocytic and Normocytic Normochromic Anaemia (NNA). Anaemia is not a diagnosis in itself, but merely an objective sign of underlying disease. The correct treatment requires an understanding of the pathogenesis of the condition. Varied number of clinical disorders manifests as NNA and pose a great challenge to the clinician.

Aim: To identify the spectrum of disorders presenting as NNA and to grade anaemia across age and sex of individual using World Health Organisation (WHO) criteria.

Materials and Methods: This prospective descriptive study was conducted in a tertiary care teaching hospital, Ernakulam, Kerala, India during one year period of February 2017-January 2018. Total of 514 patients meeting the inclusion criteria were recruited for the study. After taking detailed history and clinical examination, investigations were done including Complete Blood Count (CBC), peripheral smear preparation, reticulocyte count, Renal Function Tests (RFT), Liver Function Tests (LFT) and if necessary, bone marrow study and radiological studies

were done. The data obtained was statistically analysed using Microsoft Excel 365. Descriptive statistics viz., number of cases, percentage, concomitant involvement with other disorders, differential involvement with various age groups, male:female ratio, and grade of anaemia were utilised to describe the spectrum of disorders presenting as NNA.

Results: Of the 514 patients, 433 were adults and 81 were in paediatric age group. The average age in adult males were 58 years and in females 57 years with Haemoglobin (Hb) being 9.04 g/dL and 8.99 g/dL, respectively. Paediatric population had an average Hb of 10.18 g/dL. A total of 106 conditions were seen among the 514 patients. The disease conditions were further categorised into 10 subtypes. Type 2 Diabetes Mellitus (T2DM) constituted single most common associated disorder (112 cases) seen along NNA followed by Coronary Artery Disease (CAD) (74 cases). Idiopathic cases constituted 79 cases.

Conclusion: The NNA constituted 25% of the cases presented to the laboratory during the study period. T2DM was associated with NNA along with CAD. An understanding of the categories of anaemia along with a diagnostic protocol will go a long way in better management of the patient.

Keywords: Cardiovascular disease, Diabetes, Grading, Haemoglobin, Inflammation

INTRODUCTION

Anaemia is a condition in which the number of red blood cells or the haemoglobin concentration is lower than normal. The optimal haemoglobin concentration needed to meet physiological needs varies by age, sex and pregnancy status. Globally, anaemia affects 1.62 billion people (95% CI: 1.50-1.74 billion), which corresponds to 24.8% of the population (95% CI: 22.9-26.7%) [1]. Anaemia is a serious global public health problem that particularly affects young children and pregnant women. Morphologically, it can be classified as microcytic hypochromic, macrocytic and NNA [2]. Unlike the other two morphological subtypes, varied number of clinical disorders manifests as NNA and pose a great challenge to the clinician diagnostically. The pathophysiology of NNA varies widely according to disease and by itself can cause further complications. Hastka J and Metzgeroth G, in their study observed that anaemia of chronic disorders which manifests as NNA is the commonest cause of anaemia in hospitalised patients [3]. A comprehensive study to observe the clinical spectrum presenting as normocytic anaemia was not available. Present study aimed at understanding the clinical and diagnostic challenges presented by NNA taking into consideration the clinical spectrum, grading, variation in prevalence among different age groups, gender as well as paediatric population, thereby to provide clinician a detailed insight into the aetiology of NNA.

MATERIALS AND METHODS

The present study was a prospective descriptive study conducted for the period of one year (February 2017-January 2018) in the Clinical Pathology Laboratory, Department of Pathology, Government Medical College Ernakulam, Kerala, India. Approval from Institutional Ethical Committee (IEC) was obtained (approval number IEC/08/17). Informed consent was taken from the study population.

Inclusion criteria: Patients of all age groups including newborn, presenting with NNA willing to participate in the research were included.

Exclusion criteria: Patients already receiving treatment for anaemia were excluded.

Sample size calculation: The sample size of 470 was obtained, calculated based on the database of Worldwide prevalence of anaemia by WHO and the equation $n=4pq/d^2$. Prevalence of anaemia (p) according to the database was 24.8%. ($p=24.8$, $q=100-24.8=75.2$, $d=16\%$ of $p=4$) [1].

Study Procedure

A total of 514 (433 adults and 81 being of paediatric population) patients who presented with NNA in the Clinical Laboratory, Department of Pathology, Government Medical College, Ernakulam, Kerala, India were studied. A detailed history was taken regarding any chronic infectious conditions like tuberculosis, Human Immunodeficiency

Virus (HIV), chronic inflammatory conditions like rheumatoid arthritis, collagen vascular disorders, metabolic disorders including diabetes mellitus, Chronic Kidney Disease (CKD), liver disorders, malignancies, physiological conditions like pregnancy, anaemias associated with newborn, malnutrition in paediatric population etc., to name few. Clinical examination was done with detailed systemic examination to look for any disorders. Laboratory investigations were done including CBC (with Haematology analyser 5 part Model: BC6800/Shenzhen Mindray Biomedical Electronics), peripheral smear preparation, Erythrocyte Sedimentation Rate (ESR), reticulocyte count, routine urine examination, biochemical tests to rule out diabetes mellitus, RFT, LFT and if necessary, bone marrow and radiological studies.

Normocytic anaemia is defined as anaemia in which the values for Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC) are within the normal range, corresponding to normal size and haemoglobinisation of red cells in the blood film [2].

The normal MCV and haemoglobin values vary according to age of the individual as shown in [Table/Fig-1]. The table shows normal MCV values of RBCs in childhood as well as adults to define an RBC as 'Normocytic' and the lowest normal Hb for the age group. Reference levels for Haemoglobin were adopted from Wintrobe's Clinical Hematology, 14th edition [4].

Age	Lowest normal Hb (g/dL)	Blood cell size (fL)
Birth	14.0	100-130
1 month	12.0	90-110
2 months	10.5	80-100
3-6 month	10.5	75-90
6 month-1 year	11.0	70-85
1 year-4 year	11.0	70-85
4 year-puberty	11.5	75-00
Adult female	12.0	80-100
Adult male	13.0	80-100

[Table/Fig-1]: Red blood cell characteristics in Childhood and Adult based on 'Wintrobe's Clinical Hematology', 14th Edition [4].

The conditions associated with anaemia of inflammation were broadly categorised into the following, based on the approach by 'Wintrobe's Clinical Haematology', 14th Edition [5].

1. Chronic Infections- e.g., tuberculosis, HIV.
2. Chronic Non Infectious Inflammation- e.g., rheumatoid arthritis, severe trauma.
3. Malignancy.
4. Anaemia associated with pregnancy and associated diseases.
5. Anaemia of newborn, infants and paediatric population- prematurity, neonatal sepsis, malnutrition.
6. Anaemia associated with various systemic diseases including chronic diseases- Cardiovascular System Disorders (CVD), Chronic Kidney Disease (CKD).
7. Anaemia associated with acute infection and inflammation.
8. Anaemia associated with metabolic disorders and hormonal disorders- diabetes Mellitus, hypothyroidism.
9. Anaemia associated with electrolyte disorders.
10. Idiopathic.

The grading of anaemia into mild, moderate and severe in children, non pregnant women, pregnant women and men was done based on the WHO criteria, given in [Table/Fig-2] [6].

STATISTICAL ANALYSIS

The data obtained was statistically analysed using Microsoft Excel 365. Descriptive statistics viz., number of cases, percentage, concomitant involvement with other disorders, differential involvement

Anaemia				
Population	Non anaemia	Mild	Moderate	Severe
Children 6-59 months	110 or higher	100-109	70-99	Lower than 70
Children 5-11 years of age	115 or higher	110-114	80-109	Lower than 80
Children 12-14 years	120 or higher	110-119	80-109	Lower than 80
Non pregnant women	120 or higher	110-119	80-109	Lower than 80
Pregnant women	110 or higher	100-109	70-99	Lower than 70
Men	130 or higher	110-129	80-109	Lower than 80

[Table/Fig-2]: Haemoglobin levels to diagnose anaemia at sea level (g/L), WHO criteria [6].

with various age groups, male:female ratio, and grade of anaemia were utilised to describe the spectrum of disorders presenting as NNA.

RESULTS

A total of 514 cases of NNA were studied during the period of 2017-2018, of 2,081 patients presented to the clinical pathology laboratory during the same period which means 25% of the patients presenting to the laboratory were having normocytic anaemia. Of the study population 433 were adults and 81 were of paediatric population. Among the adults, 180 were males and 253 were females. Of the paediatric population 40 were boys and 41 girls. All the patients (514) were associated with 845 (756 in adults and 89 in paediatric population) disorders and another 96 (79 in adult and 17 in paediatric population) were idiopathic conditions (unknown aetiology). The distribution of cases in adults and paediatric population is given in [Table/Fig-3].

S. No.	Disease condition	Number of cases in adults	Number of cases in paediatric population
1	Chronic infections	70	3
2	Chronic non infectious inflammation	58	3
3	Malignancy	33	1
4	Anaemia associated with pregnancy and associated diseases	24	-
5	Anaemia unique to newborn, infants and paediatric population	-	24
6	Anaemia associated with various systemic diseases including chronic diseases	315	14
7	Anaemia associated with acute infection and inflammation	97	40
8	Anaemia associated with metabolic disorders and hormonal disorders	143	3
9	Anaemia associated with electrolyte disorders	16	1
10	Idiopathic	79	17

[Table/Fig-3]: Distribution of cases of Normocytic Normochromic Anaemia (NNA) in adults and paediatric population.

The haemoglobin values of males and females across various age groups is given [Table/Fig-4]. Maximum haemoglobin in males was found in 18-30 years age group, in females 18-30 and 31-40 age group. The distribution of various disease categories across different age groups in adults is given in [Table/Fig-5]. Chronic non infectious inflammation was more prevalent in 61-80 years (total 39 patients), 315 patients were categorised under miscellaneous including systemic disorders, 47 patients having hormonal and metabolic disorders idiopathic falls under 61-70 years age group.

Haemoglobin in g/dL across various disease categories and age groups in adults is given in [Table/Fig-6]. Grading of anaemia in adult population (mild, moderate and severe) across various disease categories according to WHO criteria of grading is given in [Table/Fig-7].

A total of 70 cases were associated with chronic infections of which 21 were having tuberculosis and another 21 had recovered from tuberculosis. The remaining 28 cases were distributed among UTI,

Age group (years)	Male Hb (g/dL)	Female Hb (g/dL)	Average Hb (g/dL)
18-30	10.16	9.67	9.86
31-40	8.75	9.67	9.44
41-50	8.92	9.36	9.16
51-60	9.06	9.29	9.18
61-70	8.84	8.46	8.62
71-80	8.95	8.62	8.79
81-90	8.98	8.47	8.61
91-100	NIL	7.77	7.77
Total	9.04	8.99	9.01

[Table/Fig-4]: Haemoglobin values (g/dL) in adult males and females across various age groups.

*NIL: No patient reported in the particular age group

A total of 58 cases had chronic non infectious inflammation, 22 had COPD and 29 had fractures. The remaining seven cases were distributed among bronchial asthma, rheumatoid arthritis, interstitial lung disease and inflammatory disease. An 18/22 COPD cases had moderate degrees of anaemia. Of the 29 cases of fracture, 18 were of severe anaemia and 11 were having moderate anaemia. The average age was 78 years for severe cases and 76 years in cases of moderate anaemia. Females outnumbered males approximately 4:1.

A total of 33 cases of neoplastic conditions were there of which 17 were males and 16 females. The average Hb was 8.46 g/dL. A 10/33 cases had severe anaemia whereas 21/33 cases had moderate anaemia. The mean age of neoplastic cases was 63 years. Of these 11 cases were of carcinoma lung and six cases were gastrointestinal malignancy. Of the remaining 16 cases, carcinoma breast constituted

Age group (Years)	Chronic infections	Chronic non infectious inflammation	Malignancy	Miscellaneous including systemic disorders	Pregnancy and related disorders	Hormonal and metabolic disorders	Electrolyte disorders	Acute infections	Idiopathic	Total cases	Total patients
18-30	4	0	2	9	13	5	0	22	7	62	45
31-40	6	2	1	16	9	8	3	12	11	68	40
41-50	15	1	2	34	2	28	2	8	12	104	56
51-60	17	7	12	56	0	22	2	19	10	145	77
61-70	15	20	10	110	0	47	1	21	21	245	112
71-80	11	19	4	60	0	26	5	13	13	151	70
81-90	2	8	1	27	0	7	3	2	4	54	30
91-100	0	1	1	3	0	0	0	0	1	6	3
Total	70	58	33	315	24	143	16	97	79	835	433

[Table/Fig-5]: The distribution of various disease categories across different age groups (Adults). Each column represents various disease groups. The last column represents the number of patients in each age group. The penultimate column represents the number of cases in each age group. Number of cases is usually more than number of patients as each patient may have more than one disease.

Age group (Years)	Chronic infections	Chronic non infectious inflammation	Malignancy	Miscellaneous including systemic disorders	Pregnancy and related disorders	Hormonal and metabolic disorders	Electrolyte disorders	Acute infections	Idiopathic
18-30	9.23	Nil	8.39	9.90	10.08	9.99	0	9.99	9.80
30-40	9.91	9.65	9.63	9.43	10.10	9.92	9.91	8.85	9.53
40-50	9.60	6.41	10.60	8.88	10.20	9.05	11.05	9.09	9.30
50-60	8.48	9.44	8.88	9.37	Nil	9.51	7.38	9.38	8.96
60-70	9.14	8.30	7.82	8.84	Nil	8.70	9.6	8.92	8.37
70-80	8.69	8.42	7.79	9.26	Nil	9.13	9.78	9.6	8.47
80-90	8.05	Nil	10.1	9.05	Nil	9.08	8.79	9.31	8.6
90-100	Nil	Nil	6.10	7.13	Nil	Nil	Nil	Nil	9.06
Total	8.60	8.42	8.46	9.10	10.09	9.11	9.44	9.36	8.91

[Table/Fig-6]: Haemoglobin in g/dL across various disease categories and age groups (Adults).

*NIL: No cases reported in the particular disease category and age group

S. No.	Disease condition	Male			Female			M	F
		Mild	Moderate	Severe	Mild	Moderate	Severe		
1	C/C Infections	2	22	11	1	29	5	35	35
2	C/C Non infectious inflammation	2	15	6	1	18	16	23	35
3	Malignancy	2	11	4	0	10	6	17	16
4	Anaemia associated with pregnancy and associated diseases	-	-	-	16	8	0	-	24
5	Anaemia associated with various systemic diseases including chronic diseases	15	110	31	9	112	38	156	159
6	Anaemia associated with acute infection and inflammation	12	24	10	7	39	5	46	51
7	Anaemia associated with metabolic disorders and hormonal disorders	7	34	11	4	72	15	52	91
8	Anaemia associated with electrolyte disorders	2	3	0	0	9	2	5	11
9	Idiopathic	1	22	3	2	37	14	26	53
Total		43	241	76	40	334	101	360	475

[Table/Fig-7]: Grading of anaemia in adult population (mild, moderate and severe) across various disease categories according to WHO criteria of grading.

typhoid, abscess, HIV, necrotising fasciitis, tonsillitis. A 63% in males and 83% in females had moderate degrees of anaemia. The average Hb was 9.05 the average age was 56 years.

three cases and the remaining 13 neoplastic conditions were divided among non hodgkin lymphoma, acute myeloid leukaemia, acute lymphoblastic leukaemia, thyroid, larynx, bladder, uterus and skin.

Anaemia associated with pregnancy and associated diseases of the 24 cases, 16 were having mild anaemia and 8 had moderate anaemia. None of them had severe anaemia. Minimum age was 19 and maximum age 50 with an average of 28 years. Anaemia associated with various systemic diseases including chronic diseases- included predominantly cardiovascular disorders, CKD, and liver diseases.

Cardiovascular disorders: Included hypertension, Coronary Artery Disease (CAD), Congestive Cardiac Failure (CCF) and Cerebrovascular Accident (CVA). Cerebrovascular accident and CAD were included under CVD. There were 81 cases of hypertension, 74 cases of CAD, 29 cases of CVA and eight cases of CCF. Total number of Cardiovascular disorders were 192 (81+74+29+8). Of the 81 cases of hypertension, 43/81 cases (53%) had associated CAD, 21/81 cases (26%) had associated CKD and 14/81 (17%) had associated CVA. A 61 cases (25 males, 36 females) had moderate anaemia and 15 (5 males, 10 females) had severe anaemia. Age group affected was 68 years for moderate anaemia and 65 years for severe anaemia. Of the 74 cases of CAD, 33 were males and 41 females. Fifty five cases (23 males and 32 females) had moderate anaemia and 14 (6 males and 8 females) had severe anaemia. A 43/74 cases were associated with hypertension, 35 with diabetes mellitus and 5 had CCF. There were 6 cases with a combination of diabetes, CAD, Hypertension and CKD. Minimum Hb was 5.82 g/dL and maximum of 11.6 g/dL. Of the 29 cases of CVA, 22 cases (11 males and 11 females) had moderate anaemia and 6 (all males) had severe anaemia. Males had average Hb of 9.38 g/dL and females had only 8.40 g/dL. Hypertension and diabetes mellitus are independent risk factors. Among the liver diseases, cirrhosis, chronic liver disease, alcoholic liver disease, and hepatitis constituted 37 cases with an average Hb of 9.32 g/dL. Thirty seven cases presented with CKD. Diabetes mellitus complicates CKD and here 22 of them had CKD. A 20% of diabetes mellitus cases with NNA were having CKD.

A total of 97 cases associated with acute infection and inflammation 46 in males and 51 in females. Lower Respiratory Tract Infection (LRTI) constituted 39 cases, viral fever-17, dengue-12 constituted the major infectious conditions along with acute bronchitis -10 cases. The remaining 19 were distributed among malaria, osteomyelitis, leptospirosis, hidradenitis, sepsis, pyoderma and acute appendicitis. A 24/46 in males had moderate and 10/46 had

severe anaemia in males whereas in females 39/51 were moderate and 5/51 were severe.

A total of 143 cases had anaemia associated with metabolic disorders and hormonal disorders of which 112 (46 males and 66 females) were of T2DM. Fourteen cases of hypothyroidism were noted. The remaining 17 were distributed among dyslipoproteinemia, hypoalbuminemia, gestational diabetes and hyperthyroidism. A 30/46 had moderate anaemia in males and 10/46 had severe anaemia. A 51/66 females had moderate anaemia and 14/66 had severe anaemia. Fourteen cases had hypothyroidism with 2 in males and 12 in females. The average age was 62 years.

Sixteen cases of electrolyte disorders were associated with Normocytic anaemia. Thirteen (5 males and 8 females) were having hyponatremia. Of the remaining three, two cases of hypokalemia and one case of hyperkalemia were there. A 9/13 had moderate anaemia and 2 had severe anaemia.

A total of 79 (26 males and 53 females) cases were idiopathic with no known aetiologic factors. Twenty two males and 37 females had moderate degrees of anaemia. Three males and 14 females had severe anaemia.

Paediatric population: Distribution of number of cases in each age group in paediatric population is given in [Table/Fig-8]. Maximum patients (40) had acute infections in paediatric population. Age group 6-59 months had maximum patients (50) suffering with any of the disease. Acute infections constituted 40/106 cases (38%), with respiratory infections being 25 (24%). Idiopathic cases included 17/106 cases (16%). Twelve new born patients presented with 15 cases, 5/12 were having prematurity and another 5 had idiopathic. The rest were divided amongst neonatal sepsis, neonatal hyperbilirubinaemia, ABO incompatibility and LRTI. Grading of anaemia in paediatric population across various disease categories according to WHO criteria is given in [Table/Fig-9].

DISCUSSION

Present study was a descriptive study which included 514 patients with 105 disorders and pregnancy. Total cases constituted 941 as individual patients had more than one disorders. WHO has devised criteria for grading of anaemia based on age and sex. Individual cases are

Age group (Years)	Chronic infections	Chronic noninfectious inflammation	Malignancy	Miscellaneous including systemic disorders	Unique to newborn and paediatric	Hormonal and metabolic disorders	Electrolyte disorders	Acute infections	Idiopathic	Total
Newborn	0	0	0	0	8	0	0	2	5	15
1-6 months	0	0	0	5	2	1	0	5	0	13
6-59 months	1	3	1	5	11	1	1	22	5	50
5-18 years	2	0	0	4	3	1	0	11	7	28
Total	3	3	1	14	24	3	1	40	17	106

[Table/Fig-8]: Distribution of number of cases in each age group in paediatric population. Last column represents total number of cases and the last row represents total number of cases with each disease category.

S. No.	Disease condition	6 months-59 months			5 years-18 years		
		Mild	Moderate	Severe	Mild	Moderate	Severe
1	C/C Infections	1	0	0	1	1	0
2	C/C Non infectious inflammation	0	1	0	2	0	0
3	Malignancy	0	0	1	0	0	0
4	Anaemia associated with various systemic diseases including chronic diseases	4	0	1	3	1	0
5	Anaemia associated with acute infection and inflammation	9	10	1	11	2	0
6	Anaemia unique to paediatric population	4	6	1	3	0	0
7	Anaemia associated with metabolic disorders and hormonal disorders	1	0	0	1	0	0
8	Anaemia associated with electrolyte disorders	0	0	1	0	0	0
9	Idiopathic	4	0	0	6	2	0
Total		23	17	5	27	6	0

[Table/Fig-9]: Grading of anaemia in paediatric population across various disease categories according to WHO criteria of grading. Grading could be done only in 6 month to 59 month category and 5 years to 18 years category.

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, it's nearly impossible to describe the characters associated with all the 105 disorders in one study, it was categorised into 10 different entities. Authors confine the discussion to the most common disorders observed during the study covering adults, pregnant ladies, paediatric population, and neonates.

The disease conditions seems to rise from the age of 50, continues to peak into the 60s and falls slightly into the 70s and 80s. All disease groups including idiopathic cases follow the same pattern with the exception of physiological condition of pregnancy.

Chronic infections constituted a total of 70 cases of which 42 were Tuberculosis (21 active cases and 21 cases of recovery). Of the total cases 72.8% had moderate degrees of anaemia whereas severe cases constituted 23%. Mukherjee A et al., in their study observed that mild anaemia (61.8%) and NNA is the most common type of anaemia in new patients of pulmonary tuberculosis [7]. In the present study, moderate and severe anaemia were more common.

Chronic non infectious inflammation- of the 58 cases, 22 had COPD and 29 had fractures. Among the COPD patients studied, the mean age was 67.13 years with 66.56 in males and 68.67 in females. An 82% had moderate anaemia and 14% had severe anaemia. A 73% were males and 27% were females. Parveen S et al., in their study observed that 18% of patients with COPD had anaemia and of that 88.89% had NNA. In contrast with present study, in the cited study, 59.5% of patients were males whereas females constituted 40.5% of subjects [8].

Anaemia seems complicating or even contributing to fracture in elderly people. In present study, there 29 patients had fracture, 23 females (8 moderate and 15 severe anaemia) and six males (3 moderate and 3 severe anaemia). Ryan G et al., came to the conclusion that anaemia at presentation is associated with greater 30-day postoperative morbidity and mortality in geriatric hip fracture patients [9]. Valderrábano RJ et al., observed that community-dwelling older men with anaemia had a 57-72% increase in non spine fracture risk independent of BMD and bone loss [10]. The average age was 78 years for severe cases and 76 years in cases of moderate anaemia. Females outnumbered males approximately 4:1.

Among 33 patients with neoplasia, the average Hb was 8.46. A 33% cases were of carcinoma lung and 18% cases were of gastrointestinal malignancy. The mean age of neoplastic cases was 63 years. Kifle E et al., in their study observed that 83.5% patients had mild to moderate anaemia whereas in the present study 64% had moderate anaemia and 30% had severe anaemia. The predominant cases in the cited study were gynaecologic malignancies [11]. Barca-Hernando M et al., in their study came to the conclusion that quality of life was better in cancer patients without anaemia than those with anaemia [12]. In the case of multiple myeloma, Rajkumar SV has included anaemia as one of the myeloma defining events [13].

Of the 24 cases with pregnancy and associated diseases, 16 were having mild anaemia and 8 had moderate anaemia. None of them had severe anaemia. Minimum age was 19 years and maximum age 50 years with an average of 28 years. Of the 24 cases with pregnancy and associated diseases, 16 were having mild anaemia and 8 had moderate anaemia. None of them had severe anaemia. Minimum age was 19 years and maximum age 50 years with an average of 28 years. Six individuals were having Pregnancy Induced Hypertension (PIH) and Gestational Diabetes Mellitus. Three cases had both Pregnancy Induced Hypertension and Gestational Diabetes Mellitus.

Though the sample size was quite small, it does point to the importance of searching for underlying PIH and GDM. Ottanelli S et al., observed that insulin resistance in the third trimester of gestation was a significant independent predictor of preeclampsia after adjustment for these common risk factors, suggesting an independent effect [14]. The prevalence of anaemia in pregnancy in India according to WHO is 50.1% [15]. Sarojamma C and Atchutha

S, observed that anaemia of pregnancy may be due to physiologic anaemia of pregnancy, deficiency of nutrients, haemolysis, or even unrelated aetiologies as observed by. The study also came to conclusion that of 60 cases studied 20% belonged to NNA [16].

Anaemia associated with various systemic diseases including chronic diseases included predominantly cardiovascular disorders, CKD and liver disorders. Cardiovascular disorders included 81 cases of hypertension, 74 cases of CAD, 29 cases of CVA and 8 cases of CCF. 81 patients with NNA were having hypertension (10%). This may indicate a higher cardiovascular risk in uncontrolled hypertension. 61 cases (25 males, 36 females) had moderate anaemia and 15 (5 males, 10 females) had severe anaemia. Age group affected was 68 years for moderate anaemia and 65 years for severe anaemia. Paul B et al., in their study concluded that 16% of hypertensive patients had anaemia and haemoglobin levels were lower in patients with essential hypertension [17].

Of the 74 cases of CAD, 55 cases (23 males and 32 females) had moderate anaemia and 14 (6 males and 8 females) had severe anaemia. A total of 43/74 cases were associated with hypertension, 35 with diabetes mellitus and 5 had CCF. There were 6 cases with a combination of diabetes, CAD, hypertension and CKD. Wester A et al., concluded that baseline anaemia in Acute Coronary Syndrome (ACS) patients undergoing percutaneous coronary intervention, treated according to current practice including routine radial artery access, constitutes a high-risk feature for both ischaemic events, bleeding events, and mortality [18].

Hypertension and diabetes mellitus are independent risk factors. Heo J et al., in their study concluded that there is an increased risk in patients with anaemia for developing stroke as well as there is increased risk of mortality compared to the patients without anaemia [19]. Cirrhosis, chronic liver disease, alcoholic liver disease, and hepatitis constituted 37 cases of liver disease with an average Hb of 9.32 g/dL. Singh S et al., in their study observed that 51.4% of the patients with cirrhosis had NNA, 30.9% had macrocytic anaemia, 16.0% had microcytic anaemia and 1.7% had dimorphic anaemia [20]. Stauffer ME and Fan T, in their study concluded that anaemia was twice as prevalent in patients with CKD compared to general population and the prevalence increases from 8.4% at stage 1 to 53.4% at stage 5 of CKD [21].

Anaemia associated with acute infection and inflammation was present in 97 patients. A total of 63 had moderate and 15 had severe anaemia. Ballin A et al., in their study concluded that acute illness was associated with anaemia in children [22]. Still a detailed study is essential in this direction to identify the cause of anaemia associated with acute infection and inflammation. Among the anaemia associated with metabolic disorders and hormonal disorders, diabetes mellitus contributed to the greatest number of individual cases (112 cases). Eighty one cases had moderate anaemia and 24 had severe anaemia. Of these 22 cases were associated with CKD, 35 with CAD, 39 with Hypertension, and 11 with CVA. In the present study, 27% males had moderate anaemia and 9% had severe anaemia, whereas in females 46% had moderate and 13% had severe anaemia associated with diabetes mellitus. Al Dallal SM and Jena N in their study observed that the prevalence of anaemia was significantly greater in diabetic females and in poorly controlled diabetes as in this present study [23]. Anaemia is an independent predictor of mortality in proatherosclerotic conditions with impaired endothelial function, such as diabetes and CKD.

Of the 16 cases of electrolyte disorders, 13 (5 males and 8 females) were having hyponatremia. A 9/13 cases had moderate anaemia and 2 had severe anaemia. Mansoor F et al., in their study observed that sodium levels were significantly lower in patients with anaemia [24]. Further studies are recommended to conclude whether hyponatremia is secondary to anaemia or it's the other way round.

A total of 79 (26 males and 53 females) cases were idiopathic with no known aetiologic factors (15% of total cases). Twenty two males and

37 females had moderate degrees of anaemia. Three males and 14 females had severe anaemia. Alvarez-Payares JC et al., concluded that 30% of anaemias in elderly were anaemia of unexplained origin and associated with worse cognitive and functional outcomes and increased mortality [25]. A comprehensive study is essential for the workout and management of anaemia of unexplained origin.

New-born and rest of paediatric population were categorised as two groups in the present study. Janus J and Moerschel SK, in their study defined anaemia in children and details the approach to anaemias including NNA in children [26]. The average Hb of new-born was 9.39 g/dL with a minimum of 6.23 g/dL and maximum of 12 g/dL. Neonatal anaemia may be due to haemolysis, haemorrhage, congenital infection, and prematurity to name a few. Irwin JJ and Kirchner JT, commented that diagnosis of NNA is difficult as it has many causes. The present study also proves how varied the presentation of normocytic anaemia can be in paediatric population as in adults [27].

Acute infections, particularly respiratory infections constituted the most important associated disorder. Anaemia is contributing to the respiratory infection and other way around. Idiopathic constituted 12 cases which demanded strict scrutiny. Average haemoglobin was least in the age group of 1-6 months. Hence, this study also recommends paediatricians to look carefully at the Hb of this age group.

Limitation(s)

Present study being a hospital-based study, may not truly reflect the frequency of anaemic patients in community at large.

CONCLUSION(S)

Anaemia is a common problem discovered on routine laboratory tests. Constituted 25% of the cases presented to the laboratory. In the present study patients with normochromic anaemia were analysed taking into consideration the clinical spectrum, grading, variation in prevalence among different age groups, males, females, pregnant ladies as well as paediatric population. Type 2 Diabetes Mellitus was constantly associated with NNA. The other common disorders included hypertension, coronary artery disease and tuberculosis. The cases with unknown etiology present a serious challenge, since we are kept in dark regarding etiology. A comprehensive study of NNA is essential considering its magnitude and varying presentation.

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