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Original Research Article

A hospital-based study of severe anemia in adults in Eastern India

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ABSTRACT

Background: Anemia remains a crucial health problem in developing countries. Cardiac compromise and fatal complications usually occur at Hb of <5g/dL. The aim of the study was to determine possible etiologic and clinical profile in adult patients with very severe anemia (Hb of <5g/dL).
Methods: A prospective observational study was conducted in a teaching hospital of Odisha over a period of 12months. A total of 70 patients of both men and non-pregnant women admitted to the medicine wards were included after exclusion. Detailed history, clinical examination and investigation findings were recorded. Independent 't' test, Wilcoxon rank sum test, Pearson chi-square test and Fisher exact test were used as applicable, to compare the variables.
Results: The mean Hb (g/dL) was 3.73 ±0.85 and the mean age of the study group was 53.34±17.75years. No significant difference was observed in the severity of anemia between the female (mean Hb of 3.56±0.93) and male patients (mean Hb of 3.87±0.77) (p=0.130). The most frequent etiology found was absolute iron deficiency (44.3%, n=31) and mostly (41.9%) found in the age group of ≥65years (p<0.001). Congestive cardiac failure was found in 20% (n=14) of patients and majority of patients (64.2%, n=9) were males (p<0.001).
Conclusions: Iron deficiency is the principal cause of very severe anemia in adults rather than malignancy or anemia of chronic disease and only about one fourth of patients develop heart failure even with very severe anemia.

Keywords: ACD, Heart failure, Iron deficiency, Very severe anemia

INTRODUCTION

Decrease in circulating RBC mass defines anemia and is usually diagnosed by blood hemoglobin (Hb) concentration lower than normal. Anemia is an important health problem all over the world due to its significant morbidity and mortality.

WHO (World Health Organization) has defined anemia as Hb of <13g/dL in men and <12g/dL in non-pregnant women for the age group of 15years and above.[1] A WHO study in 2011, reported the global prevalence of anemia as 42.6% whereas, in South East Asia, the prevalence is 53.8% and 1.5% for severe anaemia.[2] The National Family Health Survey (NFHS-4) estimated the prevalence of anemia in India as 22.7% in men and 53.2% in non-pregnant women aged 15-49years.[3]

Chronic anemia is well tolerated but patients may have fatigue, weakness, breathlessness, malaise, reduced muscle strength, dizziness, depression, all leading to reduced work capacity.[4,5] In severe cases, it may cause angina, heart failure or syncope.[6]

Severity of manifestation increases with severity of anemia. Cardiac compromise and circulatory failure usually occur at Hb level of <5g/dL. Tissue hypoxia and lactic acidosis in severe anemia may eventually lead to pulmonary edema and even death.[7] Often, anemia has an underlying etiology and broadly, it can be due to blood

loss, decreased production or increased destruction of RBCs.[6] Though, iron deficiency is the principal cause, other factors like vitamin B12 and folic acid deficiency, worm infestations, acute and chronic inflammation, renal impairment are also major contributors for anaemia.[8]

This study was done in a tertiary care center to determine the possible etiologic profile and clinical characteristics of very severe anemia (Hb <5g/dL) in men and non-pregnant women of 15years of age and above.

METHODS

A prospective observational study was carried out in a teaching hospital of Odisha from September 2017 to October 2018. Institution's Ethical committee approval and informed consents of patients were taken prior to the study.

Patients with Hb of less than 5g/dL and15years of age and above were included in the study after the hemoglobin estimation done in patients admitted to the medicine wards. Pregnant patients, patients with inherited blood disorders and patients already on treatment were excluded.

Clinical data including demographics, presenting symptoms, comorbidities, blood transfusion, drug intake, worm infestations, obstetrics and gynecology history, dietary habit, addiction, clinical examination findings and relevant laboratory investigation results were all recorded.

Investigations included complete hemogram with reticulocyte count, red cell distribution width (RDW), peripheral smear, erythrocyte sedimentation rate (ESR) and renal function test, serum uric acid, liver function test, blood sugars, routine urine examination, stool examination for parasites and occult blood, serum iron, serum ferritin (SF), total iron binding capacity (TIBC).

Bone marrow study (aspiration+biopsy) along with prussian blue staining for iron store, vitamin B12, folate level, C-reactive protein (CRP), serum protein electrophoresis, Hb electrophoresis, thyroid function test, antinuclear antibody, lactate dehydrogenase (LDH), direct Coomb's test were done as indicated.

CBC with reticulocyte count were analyzed by automated analyzer Sysmex XN-300. Ferritin was estimated by electro-chemiluminescence immunoassay (ECLIA) method by Cobas e 411 analyzer and iron and TIBC were estimated by ferrozine method without deproteination by Cobas integra 400 plus analyzer.

Transferrin saturation (TSAT) was calculated by the formula ((serum iron/TIBC)x100).[9] Imaging studies (chest radiograph, ultrasonography of abdomen and pelvis, computed tomography scan/ magnetic resonance imaging of chest, abdomen and pelvis), ECG, echocardiogram, upper gastrointestinal endoscopy (UGIE), colonoscopy were done in patients, when indicated.

Defining different anemias, many literatures were reviewed and absolute iron deficiency anemia (IDA) was defined in patients with SF of <30µg/L, anemia of chronic disease (ACD) in patients with SF of >100µg/L and features of inflammation (elevated ESR and CRP >1mg/dL), functional IDA (or ACD with IDA) in patients with SF of 30-100µg/L and TSAT of <20%, anemia of chronic renal insufficiency (or renal anemia) in patients with serum creatinine of >1.8mg/dL.[6,9,10-12]

Vitamin B12 level of <150pg/mL and folate level of <2.5ng/mL defined the deficiency state. Creatinine clearance (Ccr) was determined by the Cockcroft formula [Ccr= (((l40-age) x weight)/(72xScr))x 0.85 (if female)).[13] The morphologic type of anemia (microcytic, normocytic, macrocytic/dimorphic) was determined from peripheral smear and values of mean corpuscular volume (MCV).[6]

Rural and urban population was defined according to the census India 2011.[14] Patients were further classified into 6 groups based on age: 15-24years, 25-34years, 35-44years, 45-54, 55-64years and ≥65 years. All the data were analyzed by using statistical package SPSS, version 20.

Mean with standard deviation, median and range were used for continuous variables and numbers and percentages for categorical variables. Independent 't' test, Wilcoxon rank sum test, Pearson chi-squared test and Fisher exact test were used as applicable, to compare the variables. P value of <0.05 was of statistical significance.

RESULTS

Out of total 5026 patients admitted during this period, 70 patients (1.39%) were found to have very severe anemia (Hb <5g/dL). The mean Hb was 3.73±0.85g/dL. The mean age of the study group was 53.34±17.75 and females comprised of 44.3%.

No significant gender difference was observed in the severity of anemia as the mean Hb (g/dl) was 3.56±0.93 in females and 3.87±0.77 in male patients (p=0.130). Other socio-demographic and baseline characteristics are described in Table 1.

Microcytic anemia was the commonest morphologic type (58.6%, n=41) followed by normocytic (31.4%, n=22) and macrocytic/dimorphic anemia (10%, n=7).

Absolute IDA was found in 44.3% (n=31) of patients and all patients had microcytic anemia (p<0.001) except one patient who had dimorphic but predominantly microcytic hypochromic anemia. The SF, TSAT, RDW-cv were described in Table 1. There was no significant difference

between male (41%, n=16) and female (48.3%, n=15) patients having absolute IDA (p=0.790) (Table 2). Most of the patients having IDA were belonged to the age group of ≥65years (41.9%, n=13) followed by age groups of 45-54years (19.3%, n=6) which was statistically significant (p<0.001) (Table 3).

Chronic blood loss (58%, n=18) was the most common cause found in IDA (Figure 1). Among patients with chronic blood loss, 44.4% (n=8) patients had upper gastrointestinal (UGI) bleed, 22.2% (n=4) had menorrhagia, 11.1% (n=2) with hookworm dudenopathy, 16.6% (n=3) had bleeding hemorrhoids and 5.5% (n=1) had both upper and lower GI bleed. Nutritional cause (16.1%, n=5) was found in two patients having tuberculosis, one patient had consecutive 3 delivery, one had non-specific duodenitis and another patient had atrophic gastritis with vitamin B12 deficiency along with iron deficiency.

The malignancies (12.9%, n=4) associated with IDA were all GI malignancies and no cause could be found in two patients. UGI endoscopy findings were suggestive of gastroduodenal erosions (n=4), esophageal erosion (n=1), gastroduodenal ulcers (n=3), hookworm (n=2), infiltrating adenocarcinoma (n=3), atrophic gastritis (n=1), non-specific duodenitis (n=1) and normal endoscopy (n=2).

Table 1: Demographic and baseline characteristics of patients (N=70).

Parameters			Results
Age (years)	Mean±SD		53.34±17.75
	Range		15-87
BMI	Mean±SD		20.36±4.23
	Range		12.91-35.71
Gender	Female % (n)		44.3 (31)
Residence	Rural % (n)		65.7 (46)
Diet	Mixed % (n)		70.0 (49)
Hb (g/dL)	Mean (median)±SD (Range)		3.73 (3.85) ±0.85 (1.9 -4.9)
SF (µg/dL)	Mean ±SD (Range)		214.40±716.13 (2.09-4114.00)
TSAT (%)	Mean ±SD (Range)		15.73±24.73 (0.85-92.56)
IDA(A)	SF (µg/dL)	Mean±SD (Range)	8.27±5.63 (2.09-24.0)
	TSAT (%)	Mean±SD (Range)	4.71±3.12 (0.85-16.01)
	RDW-cv	Mean±SD (Range)	23.06±3.55 (14.10-30.70)
IDA(F)	SF (µg/dL)	Mean±SD (Range)	57.84±20.52 (34.72-92.94)
	TSAT (%)	Mean±SD (Range)	7.12±3.81 (3-13.72)
ACD	SF (µg/dL)	Mean±SD (Range)	491.15±1093.26 (49.20-4114.0)
	CRP (mg/dL)	Mean±SD (Range)	2.5±0.51 (1.42-3.26)
MA	Vit. B12 (pg/mL)	Mean±SD (Range)	77.70±29.49 (50-125.60)
	RDW-cv	Mean±SD (Range)	22.21±7.11 (15.90-37.20)
RA	SF	Mean±SD (Range)	195.90±209.37 (34.72-556.90)
	Cr (mg/dL)	Mean±SD (Range)	12.94±9.10 (2.2-37.55)
	Ccr (mL/min)	Mean±SD (Range)	7.06±5.51 (1.67-22.16)

SF-Serum Ferritin, TSAT-Transferrin Saturation, RDW-cv-Red cell Distribution Width co-efficient vector, Cr-Creatinine, Ccr-Creatinine clearance, IDA (A)-Absolute Iron Deficiency Anemia, IDA(F)-Functional Iron Deficiency Anemia, ACD-Anemia of Chronic Disease, MA-Vitamin B12 deficiency, RA -Renal Anaemia.

Table 2: Etiologies and morphologies of severe anemia across the genders.

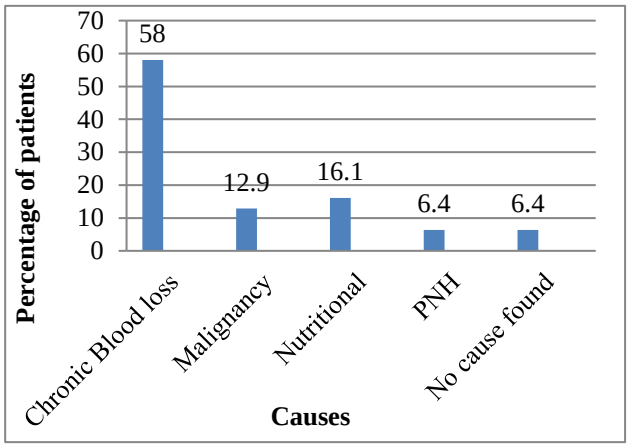
Characteristics	Male (N=39), % (n)	Female (N=31), % (n)	Fisher's Exact test*, p-value
IDA(A)	41.0 (16)	48.3 (15)	P=0.790
IDA(F)	10.2 (4)	6.4 (2)	P=0.687
ACD	20.5 (8)	25.8 (8)	P<0.05
RA	25.6 (10)	16.1 (5)	P=0.520
Vit B12 deficiency	10.2 (4)	16.1 (5)	P=0.560
Microcytic anemia	61.5 (24)	54.8 (17)	P<0.05
Normocytic anemia	30.7 (12)	32.2 (10)	P<0.05
Macrocytic anemia	7.6 (3)	12.9 (4)	P<0.05

*Except in IDA(A) where Chi-square test was applied. IDA(A)-Absolute Iron Deficiency Anemia, IDA(F)-Functional Iron Deficiency Anemia, ACD-Anemia of Chronic Disease, RA-Renal Anaemia.

Table 3: Etiologies of severe anemia across the age groups.

Age groups (Years)	Total (N=70) % (n)	A-IDA(N=31) % (n)	F-IDA(N=6) % (n)	ACD(N=16) % (n)	RA(N=15) % (n)	MA(N=9) % (n)
15-24	8.6 (6)	9.6 (3)	16.6 (1)	0 (0)	0 (0)	22.2 (2)
25-34	11.4 (8)	12.9 (4)	0 (0)	12.5 (2)	6.6 (1)	11.1 (1)
35-44	7.1 (5)	9.6 (3)	0 (0)	6.2 (1)	6.6 (1)	0 (0)
45-54	17.1 (12)	19.3 (6)	0 (0)	12.5 (2)	20.0 (3)	11.1 (1)
55-64	24.3 (17)	6.4 (2)	66.6 (4)	37.5 (6)	40.0 (6)	33.3 (3)
≥65	31.4 (22)	41.9 (13)	16.6 (1)	31.2 (5)	26.6 (4)	22.2 (2)
*p value		P<0.001	P=0.195	P=0.678	P=0.596	P=0.614

*Statistic used was Fisher's Exact test. A-IDA-Absolute Iron Deficiency Anemia, F-IDA- Functional Iron Deficiency Anemia, ACD-Anemia of Chronic Disease, MA-Vitamin B12 deficiency, RA-Renal Anaemia.

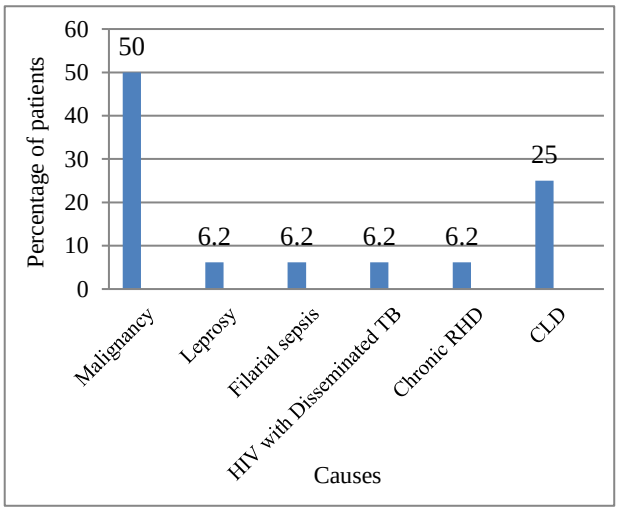


PNH: Paroxysmal nocturnal hemoglobinuria

Figure 1: Causes of absolute iron deficiency anemia (N=31).

Colonoscopy was done (n=4) and suggestive of cecal angiectasis (n=1) and normal (n=3) in patients with IDA. Functional IDA was found in 8.6% (n=6) of patients. Normocytic anemia was present in 50% of patients (n=3) and microcytic in 33.3% (n=2). Four patients of functional IDA had UGI bleed in endoscopy. Stool occult blood test was done in all patients and found to be positive in 18.9% (n=7). Drugs like NSAID (n=6) and acitrom (n=2) were taken by 21.6% of patients. Bone marrow study was done in 54% (n=20) where marrow iron was absent in 14 patients and decreased in 6 patients.

ACD was found in 22.8% (n=16) of patients including two patients with functional IDA. Normocytic anemia was the most common (75%, n=12) followed by microcytic (12.5%, n=2) (p<0.001) and 25.8% (n=8) of females and 20.5% (n=8) of male patients had ACD (p<0.05). Though, the advanced age groups had ACD more frequently (37.5% in age group of 55-64years and 31.2% in age group of ≥65years), it was statistically not significant (p=0.678) (Table 3). The underlying cause was malignancy in 50% of patients (n=8) followed by chronic liver disease (25%, n=4). Other causes were described in Figure 2. Two patients had multifactorial etiology- one had chronic pancreatitis besides malignancy and another had chronic renal insufficiency (CRI), hypothyroid and CLD. Besides, two patients of ACD (chronic rheumatic heart disease, poorly differentiating adenocarcinoma of stomach) had functional iron deficiency. BM study was suggestive of hematologic malignancy in 7 patients. A total of 17.1% (n=12) patients had malignancy as etiology of very severe anemia out of which 41.6% (n=5) were GI malignancies and 58.3% (n=7) were hematologic malignancies.



Chronic RHD: Chronic Rheumatic Heart Disease, CLD: Chronic Liver Disease

Figure 2: Causes of anemia of chronic disease (N=16).

Renal anemia (RA) was found in 21.4% (n=15) of patients and all patients had CRI. The mean serum creatinine level was 12.94±9.10mg/dL and creatinine clearance were 7.06±5.51mL/min. Functional ID was present in 4 patients of RA and one of them had vitamin B12 deficiency along with iron deficiency. Besides, one patient had ACD. UGIE detected gastroduodenal ulcers and erosions in 3 patients of renal anemia.

Vitamin B12 deficiency was found in 12.8% (n=9) of patients and one patient (1.4%) had folate deficiency along with vitamin B12 deficiency. All patients were vegetarian. The mean vitamin B12 level was

77.7±29.49pg/mL. Dimorphic picture was present in 2 patients, one patient had absolute IDA and one had functional IDA. Out of the remaining seven patients, two had ACD (chronic liver disease) as well. Pancytopenia was present in 4 patients and bi-cytopenia in 3 patients of vitamin B12 deficiency. Pancytopenia was present in 15.7% (n=11) and bi-cytopenia in 37.1% (n=26) of all patients. Aplastic anemia was diagnosed in one patient. Myelodysplastic syndrome (MDS) was diagnosed in 3 patients, 2 patients had MDS with dysplastic marrow and one patient with hypoplastic MDS. Of all patients with severe anemia, 15.7% patients (n=11) had multifactorial etiology.

Hypothyroidism was present in 8.5% (n=6) of patients and associated with absolute IDA (n=3), macrocytic (n=2) and normocytic anemia (n=1). The most common symptom was fatigue (68.6%, n=48) followed by breathlessness on exertion (57.1%, n=40), anorexia (32.9%, n=23), light headedness or dizziness (27.1%, n=19), palpitation (25.7%, n=18) and 2.9% (n=2) patients had syncope but most of the patients had presented with multiple symptoms (75%, n=53). Fatigue was the only symptom in 14.2% (n=10) of patients, anorexia in 5.7% (n=4), breathlessness (n=2) and one patient presented with joint pain and backache as only symptom.

Peripheral edema was the most frequent finding (57.1%, n=40) followed by ascites (21.4%, n=15) and pleural effusion (16.9%, n=12). Splenomegaly was found in11.4% (n=8), hepatomegaly in 5.7% (n=4) and hepato-splenomegaly in 2.9% (n=2), glossitis in 7.1% (n=5) and lymphadenopathy in 2.9% (n=2) of patients. Heart failure was found in 20% (n=14) patients and the mean Hb was 3.42±0.79g/dL (p=0.135). Male patients (64.2%, n=9) were more affected than females (35.7%, n=5) (p<0.001).

DISCUSSION

In this study, 1.39% of adult patients found to have very severe anemia. Females comprised of 44.3% and 65.7% (n=46) of patients were from rural area. Alvarez-Uria G et al, studied 69,440 patients in India and observed that males had progressive decline in Hb after age of 40years and a progressive increase from mild to severe anemia with age.[15] In this study, 55.7% (n=39) of patients were ≥55 years of age and may have contributed to the slight male preponderance.

Iron deficiency (ID) is the foremost cause of anemia worldwide and accounts for almost 50% of all anemias.[2,16] This study also, observed ID as the predominant cause in adults with very severe anaemia (44.3%, n=31) and it was most prevalent in the age group of ≥65years (p<0.01). However, there was no difference in prevalence of IDA across the genders (p= 0.790). One of the frequent causes of anemia in elderly is due to iron deficiency and typically results from chronic blood loss through GI tract. Iron deficiency can result from poor dietary intake, increased demand, poor absorption or increased loss. Aslam F et al, studied 243 patients (18-40years of age) with IDA who had undergone UGIE and colonoscopy and observed most of the patients had gastritis (55.5%), varices (16%), gastroduodenal ulcers (11.4%), hemorrhoids (8.7%) and concluded that non-malignant pathologies were the most common findings.[17] In a study by Ioannou GN et al, which included persons of 25-74years of age, none of the premenopausal women (n=93) with IDA were diagnosed with malignancy and among postmenopausal women and men with IDA, 6% had GI malignancy.[18]. Another study on patients with IDA, observed GI malignancy in 11% of patients.[19] In this study, the commonest cause of IDA was chronic blood loss due to non-malignant lesion (58%, n=18) and the next common causes were nutritional (16.1%, n=5) and GI malignancy (12.9%, n=4). Peng G et al, studied 742 patients of paroxysmal nocturnal hemoglobinuria (PNH) and concluded that these patients especially with classical PNH, were prone to iron deficiency.[20] This study observed PNH in 2.9% of patients with IDA. Functional IDA is iron deficiency associated with anemia of chronic disease and observed in 8.6% of patients. ACD which results from infections, malignancy, auto-immune disorders, chronic kidney disorders, is mostly prevalent in hospitalized patients.[21] Hepcidin, cytokines from inflammation dysregulate iron homeostasis, decrease the response to erythropoietin and depress erythropoiesis.[22] Estimation of serum ferritin is the most reliable method to detect IDA. However, co-existence of IDA and ACD makes the diagnosis difficult as ferritin is also an acute phase reactant and elevated by inflammation. The most sensitive and specific method to diagnose absolute iron deficiency is the serum ferritin level of <30µg/L.[23]

Ferritin values of ≥100µg/L generally exclude iron deficiency anaemia.[24] Transferrin saturation was decreased in both IDA and ACD but not the ferritin. So, decreased transferrin saturation of <20% and ferritin level between 30-100µg/L differentiate between ACD and IDA co-existing with ACD.[10,24] Other tests like soluble transferrin receptor, erythrocyte protoporphyrin testing, or the soluble transferrin receptor and log ferritin level ratio (<1 in ACD alone and >2 with both iron deficiency and ACD) are proposed for further confirmation but not commonly used in clinical practice and neither can be affordable by resource limited centers.[23,25] Besides, features of inflammation like elevated CRP level was also present in ACD. Shavelle RM et al, in their study found ACD in 26% of persons (≥50years of age) with anaemia.[26] This study observed ACD in 22.8% (n=16) of patients and renal anemia in 21.4% (n=15) of patients. Eisenga MF et al, studied 975 patients (62±12years of age) of chronic kidney disease and 16.8% (n=164) of patients developed anemia on follow up of median 8years.[27] Anemia is a common complication of CRI and the usual cause is erythropoietin deficiency. Again, these patients are prone to develop functional IDA as CRI is a proinflammatory state.[28] This study observed functional ID in 26.6% (n=4) of patients with CRI. Vitamin B12 deficiency is one of the leading causes of megaloblastic

anemia and commonly found in older persons. Nine patients (12.8%) had vitamin B12 deficiency, of which 55.5% (n=5) were older adults (≥55years of age) in this study. However, estimation of serum vitamin B12 level alone, may not reliably detect the deficiency state where as a combination of tests including estimation of serum homocysteine level, methyl-malonic acid, holo-trans-cobalamin level increases the accuracy of diagnosis.[29]

Myelodysplastic syndrome and aplastic anemia both are part of bone marrow failure syndrome. The marrow is hypocellular or acellular in aplastic anemia whereas marrow is usually hypercellular and dysplastic in MDS. However, a subset of MDS diagnosed as hypoplastic type, is difficult to differentiate from aplastic anemia and needs chromosomal study though both the cases can be treated initially with immuno-suppressive therapy.[30] Bastida JM et al, studied patients with anemia of uncertain etiology and found hematologic disorders in 25 patients of which 14 were diagnosed with MDS.[31]

In this study, MDS was diagnosed in 3 patients and aplastic anemia in one patient. Multifactor etiology is frequently found as causation of anemia and Petrosyan I et al, reported 46.3% of patients having anemia of multifactorial etiology in their study.[32]. However, this study found multifactor etiology in 15.7% (n=11) of patients.

Left ventricular dysfunction begins at Hb level of ~7g/dL and further deteriorates when the Hb drops further.[7] Alvares JF in their study, observed 27% of patients with a mean Hb level of 5g/dL had CHF.[33]. This study observed heart failure in only 20% of patients and the mean Hb was 3.42±0.79g/dL and majority of patients (64.2%, n=9) were males ($p<0.001$). Hypothyroid can cause all three types of anemia. Normocytic anemia by deficient hormone itself, microcytic by menorrhagia and malabsorption of iron, and macrocytic due to malabsorption of vitamin B12. Das C et al in their study, reported 20% of patients (19-67years of age) with hypothyroidism had severe anemia and among them 4.8% had normocytic and 14.4% had microcytic anaemia.[34] However, this study observed hypothyroidism in 8.5% of patients with very severe anemia and 4.2% had absolute IDA and 2.8% had macrocytic and 1.4% had normocytic anemia.

The major limitation of this study was the smaller sample size and comparatively larger study groups including pregnant females may be needed for better analysis to ascertain the etiologies and clinical profile of very severe anemia.

CONCLUSION

Iron deficiency is the most leading factor in very severe anemia in adults rather than malignancy or anemia of chronic disease. Majority of patients having severe anemia are from rural areas. Severe anemia due to iron deficiency is most prevalent in adults with advanced age and has no female preponderance. Even very severe anemia is well tolerated by majority of patients and cardiac compromise occurs in about one fourth of patients though males are more susceptible.

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REFERENCES

1. WHO. Hemoglobin concentrations for the diagnosis of anemia and assessment of severity, 2011. Available at: https://www.who.int/vmnis/indicators/haemoglobin/en/. Accessed 3 Nov 2018.
2. WHO. The global prevalence of anemia in 2011, 2015. Available at: http://www.who.int/iris/handle/10665/177094. Accessed 3 Nov 2018.
3. International Institute for Population Sciences (IIPS). The national family health survey (2015-16), 2018. Available at: http://www.rchiips.org/nfhs. Accessed 6 Nov 2018.
4. Haas JD, Brownlie IV T. Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship. J Nutrition. 2001;131(2):676S-90S.
5. Penninx BW, Pahor M, Cesari M, Corsi AM, Woodman RC, Bandinelli S, et al. Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. J Am Geriatrics Soc. 2004;52(5):719-24.
6. Amy Z, Tom R, Ronald J, Morey B. Hematologic disorders and transfusion therapy. In: Bhat P, Dretler A, Gdowski M, eds. The Washington Manual of Medical Therapeutics. 35th ed. St. Louis, Missouri: Wolters Kluwer; 2016:647-677.
7. Hegde N, Rich MW, Gayomali C. The cardiomyopathy of iron deficiency. Texas Heart Ins J. 2006;33(3):340-44.
8. Tolentino K, Friedman JF. An update on anemia in less developed countries. Am J Trop Med Hyg. 2007;77(1):44-51.
9. John W Adamson. Iron deficiency and other hypoproliferative anemias. In: Kasper DL, Fauci AS,Hauser SL, Longo DL, Jameson JL, Loscalzo j eds. Harrison's Principle of Internal Medicine. 19th ed. New York, NY: Mc Graw Hill; 2016:625-630.
10. Dignass AU, Gasche C, Bettenworth D, Birgegård G, Danese S, Gisbert JP, et al. European consensus on the diagnosis and management of iron deficiency and anaemia in inflammatory bowel diseases. J Crohn's Colitis. 2015;9(3):211-22.
11. Short MW, Domagalski JE. Iron deficiency anemia: evaluation and management. Am Family Physician. 2013;87(2):98-104.

12. Cullis JO. Diagnosis and management of anaemia of chronic disease: current status. Brit J Haematol. 2011;154(3):289-300.
13. Cockcroft DW, Gault H. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16(1):31-41.
14. Office of The Registrar General and Census Commissioner, Census of India, 2011. Available at: www.censusindia.gov.in/2011census. Accessed 3 November 2018.
15. Alvarez-Uria G, Naik PK, Midde M, Yalla PS, Pakam R. Prevalence and severity of anaemia stratified by age and gender in rural India. Anemia. 2014;2014.
16. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014;123(5):615-24.
17. Aslam F, bin Khalid A, Siddiqui F, Jadoon Y. Predictors of serious findings on bi-directional endoscopy in young patients with anemia and GI symptoms. Pak J Med Sci. 2018;34(4):1004-9.
18. Ioannou GN, Rockey DC, Bryson CL, Weiss NS. Iron deficiency and gastrointestinal malignancy: a population-based cohort study. Am J Med. 2002;113(4):276-80.
19. Yates JM, Logan EC, Stewart RM. Iron deficiency anaemia in general practice: clinical outcomes over three years and factors influencing diagnostic investigations. Postgraduate Med J. 2004;80(945):405-10.
20. Peng G, Yang W, Jing L, Zhang L, Li Y, Ye L, et al. Iron deficiency in patients with paroxysmal nocturnal hemoglobinuria: a cross-sectional survey from a single institution in china. Med Sci Monitor: Inter Med J Exp Clin Res. 2018;24:7256-63.
21. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood. 2018:blood-2018.
22. Madu AJ, Ughasoro MD. Anaemia of chronic disease: an in-depth review. Med Principles Practice. 2017;26(1):1-9.
23. Skikne BS, Punnonen K, Caldron PH, Bennett MT, Rehu M, Gasior GH, et al. Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: a prospective multicentre evaluation of soluble transferrin receptor and the sTfR/log ferritin index. Am J Hematol. 2011;86(11):923-7.
24. Douglas L. Smith. Anemia in the elderly. Am Fam Physician. 2000;62(7):1565-1572.
25. Camaschella C. Iron deficiency: new insights into diagnosis and treatment. ASH Education Program Book. 2015;2015(1):8-13.
26. Shavelle RM, MacKenzie R, Paculdo DR. Anemia and mortality in older persons: does the type of anemia affect survival?. Inter J Hematol. 2012;95(3):248-56.
27. Eisenga MF, Nolte IM, van der Meer P, Bakker SJ, Gaillard CA. Association of different iron deficiency cut offs with adverse outcomes in chronic kidney disease. BMC Nephrol. 2018;19(1):225.
28. Minutolo R, Conte G, Cianciaruso B, Bellizzi V, Camocardi A, De Paola L, et al. Hypo-responsiveness to erythropoiesis-stimulating agents and renal survival in non-dialysis CKD patients. Nephrol Dialysis Transplantation. 2012;27:2880-6.
29. Green R. Vitamin B12 deficiency from the perspective of a practicing hematologist. Blood. 2017;129(19):2603-11.
30. Orazi A, Maher A, Heerema NA, Haskins S, Neiman RS. Hypoplastic myelodysplastic syndromes can be distinguished from acquired aplastic anemia by CD34 and PCNA immunostaining of bone marrow biopsy specimens. Am J Clin Pathol. 1997;107(3):268-74.
31. Bastida JM, López-Godino O, Vicente-Sánchez A, Bonanad-Boix S, Xicoy-Cirici B, Hernández-Sánchez JM, et al. Hidden myelodysplastic syndrome (MDS): a prospective study to confirm or exclude MDS in patients with anemia of uncertain etiology. Inter J Lab Hematol. 2018.
32. Petrosyan I, Blaison G, Andrès E, Federici L. Anaemia in the elderly: an aetiologic profile of a prospective cohort of 95 hospitalised patients. Euro J Int Med. 2012;23(6):524-8.
33. Alvares JF, Oak JL, Pathare AV. Evaluation of cardiac function in iron deficiency anemia before and after total dose iron therapy. J Assoc Physicians India. 2000;48(2):204-6.
34. Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. Ind J Endocrinol Metab. 2012;16(2):S361.

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