Research Article

Clinical Profile, Aetiology and Management of Severe Anemia in a Secondary Care Hospital in North - East India

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Abstract

Background: This study was conducted in a secondary care hospital without a Blood bank in North- East India, which provides healthcare to patients from Assam and Arunachal Pradesh, the majority of whom belong to low socioeconomic strata.

Aims and objectives: The aim of this study was to examine aetiology, clinical profile, morphology, contributing factors and blood transfusions given to patients with haemoglobin below 5.0 grams/decilitre (gm/dl) in a secondary care set up.

Methods: This retrospective observational study included 122 subjects with haemoglobin <5.0 gm/dl who visited the hospital as outdoor patients or were admitted in the hospital. Samples were collected in K-EDTA vacutainers and processed in Sysmex XS -800i Hematology cell counter for complete blood count followed by peripheral blood smear examination. Renal and liver functions were evaluated when clinically indicated. Follow up data of patients where available, was collected for one year- until October 2018. Anemia was categorized under the predominant cause, which made the patient seek treatment.

Results: Of the 122 patients studied, 70 (57.4%) were females. The average duration of hospitalization was 3.43days with a maximum of 30 days' hospitalization. Forty-six (37.7%) patients had only single contact with the hospital. Sixty-one (50%) patients were given two or more units of blood, while 37 (30%) patients were not transfused. Malnutrition and infection were found to be the most common causes contributing to anemia.

Conclusion: The hospital was successful in providing economical and adequate treatment to the patients with hemoglobin <5.0 gm/dl.

Keywords: Severe anemia; North-East India; Blood transfusion; Radial distribution width

Abbreviations

K_2-EDTA: Dipotassium Salt of Ethylene Diamine Tetracetic Acid; gm/dl: grams/decilitre; CBC: Complete Blood Count; RDW-CV: Radialdistribution Width Coefficient of Variation; LFT: Liver Function Tests

Introduction

Anemia is very common in India and its prevalence is 35% to 75%

in various parts of the country [1]. Data from secondary care centers is limited as it is not often not possible to provide complete diagnosis and comprehensive management due to limited resources.

This retrospective study was carried out in a 120 bedded secondary care hospital without a Blood Bank, providing both outdoor and indoor treatment to patients from Assam and other northeastern states of India, especially Arunachal Pradesh. Blood requirements of patients are met from two government blood banks in the city on replacement basis without leukodepletion, irradiation or removal of plasma. Usually voluntary donors are not available, and it is entirely up to the patients' relatives to arrange blood. The nearest component blood bank is 150 kilometers away. As most patients belong to poor socioeconomic strata, it was imperative to diagnose with minimum tests and provide immediate management options, including referral to higher centers.

Severe anemia is nearly always of multifactorial aetiology resulting from malnutrition, chronic infections, hemoglobinopathies, chronic hemorrhage, renal failure and malignancies. A study in 10,137 children aged 1-6 years from North - East India, showed 52.5% children to be

anemic, of which 1.9% had severe anemia [2]. The global statistics of anemia is equally alarming -almost 1/3 of the world's population in developing countries is anemic with iron deficiency accounting for half these cases. Estimated prevalence of anemia is 39% in children under five years age and 48% in those aged between 5-14 years, 42% and 30% in women and men between 15-59 years respectively, and 45% in adults over 60 years [3]. Malnutrition is rampant in India with an average frequency twice as high as the children residing in sub - Saharan Africa [4]. WHO classification for severe anemia varies according to age, gender and in females based on whether pregnant; the lowest cut off is 7.0 gm/dl for pregnant women and children under six months age [5]. The aim of this study was to examine the aetiology, morphology, clinical profile and blood transfusion administered to patients with hemoglobin <5.0 grams /deciliter (gm/dl) in our center. No similar study which included severe anemia of diverse aetiology was found on searching available literature.

Patients and Methods

A retrospective observational study was conducted to examine the aetiology, demography, morphology and management of 122 non-consecutive patients, with severe anemia. Anemia was diagnosed either clinically or following lab investigations in patients who visited the hospital for outdoor or in-patient treatment. Haemoglobin level of <5.0 gm/dl was taken as cut off because it was intended to include the most severe of cases treated in the centre with potentially life threatening anemia. Data of patients with Haemoglobin <5 gm /dl for the period October 2017 to April 2018 was obtained from the IT department. It is imperative to understand that the majority of patients are very poor and hence number of investigations is restricted to minimum because over 90% have to bear the cost of treatment and investigations themselves. Institutional Ethical Committee was obtained for the study.

Samples for complete blood count (CBC) are collected in 3 ml K_2-EDTA vacutainers and processed in Sysmex XS-800i Hematology cell counter and the findings were correlated by peripheral blood smear examination. All samples with Hemoglobin <3.0gm /dl were also tested on Sysmex KX-21, a second 18-parameter, 3-part Differential Haematology cell counter.

Liver Function Tests (LFT) for 90 (73.8%) and serum creatinines for 107 (87.7%) samples were performed on- Vitros 250 dry chemistry fully automated analyzer which is a closed system. LFT included total protein, serum albumin, serum bilirubin, transaminases and serum alkaline phosphatase. Blood culture was done on single sample from 41 patients in BD BACTEC-9050 Blood Culture System. Screening for HIV, Hepatitis B surface antigen and anti-Hepatitis C antibodies was performed by card based tests.

Other relevant investigations carried out on patients included ECG, endoscopy, imaging studies as per requirement, serum electrolytes, blood sugar in diabetics, urine routine examination, and site based cultures for infections when indicated. These are not included in the purview of this study.

Only absolutely mandatory investigations were performed and the duration of treatment was minimized. Patients were divided into seven categories as enumerated below:

1.   Hematological conditions including those where anemia was the predominant finding

2.   Chronic Liver Disease associated with anemia

3.   Chronic Kidney disease associated with anemia

4.   Peptic Ulcer disease

5.   Blood loss as major cause for anemia

6.   Non-Haematological malignancies presenting with anemia

7.   Miscellaneous conditions associated with anemia other than those mentioned above

The duration of hospitalization and number of blood transfusions were also calculated.
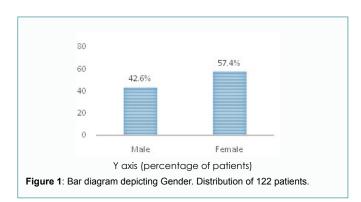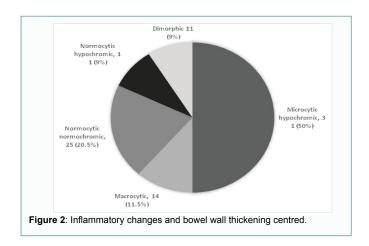
Results

The mean age of patients was 36.5 years with a range of 0.75 to 88 years. Female patients (n=70) accounted for 57.4% of the subjects (Figure 1). Haemoglobin levels ranged from 1.2 to 4.8 gm/dl with a mean of 2.5 gm/dl. Anisocytosis was observed in 120 patients (normal RDW-CV 11.5% to 14.5%). Mean RDW-CV for this cohort was 23.2% (Range 13.4% to 44.8%) with 97 samples (79.5% showing RDW>18%; which is another pointer for a coexisting nutritional aetiology of iron deficiency [7]. Figure 2 shows the classification of anemia as per morphology of the peripheral blood film which was correlated with the haematological indices. Details of etiological classification for the study are shown in Table 1 and broad classification in Figure 3. Figure 4 depicts the results of serum creatinine and LFT. The commonest LFT abnormality was low serum proteins (37/41%), followed by hypoalbuminemia (34/27.9%), elevated enzymes (16/13.1%) and raised serum bilirubin (14 /11.5%). None of the patients in this study tested positive for any of the viral markers. Alcoholic liver disease was documented in 61.1% of patients with liver involvement on the basis of history and LFT results. Leukocyte and platelet counts are shown in Figure 5. Of the 85 patients who were transfused, 61 received two or more units (Figure 6). Bone marrow examination was carried out only for two patients both of which showed megaloblastic marrow. All leukemias were diagnosed on the basis of peripheral blood smear and the patients were referred immediately.
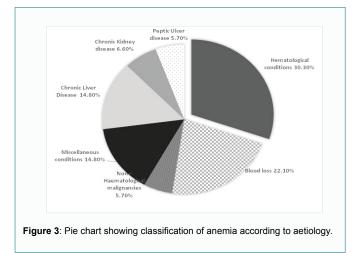
The city did not have a facility for iron profile which has been commenced after actually realizing the enormity of the problem. Vitamin B_{12} levels were tested in two patients due to the high cost and three days' delay in getting results -being an outsourced test.

Blood transfusions, hospitalization and hospital deaths

The number of patients receiving no transfusion, single, two units and three or more units was 37, 24, 26 and 35 respectively (Figure 6). Average number of hospitalization days was 3.47 with 52 patients being admitted for three or more days; while 46 patients (37.7%) had only single contact with treating physicians.

Figure 1: Bar diagram depicting Gender. Distribution of 122 patients.

Figure 2: Inflammatory changes and bowel wall thickening centred.

Figure 3: Pie chart showing classification of anemia according to aetiology.

Figure 4: Serum creatinine and Liver function tests.

Figure 5: Leukocyte and Platelet counts.

Figure 6: Bar diagram showing the number of transfusions given.

Follow up

Five patients were unable to arrange for blood and hence left against medical advice. Twenty-two patients were referred including patients with chronic kidney disease (n=9), end stage liver disease with hepatic encephalopathy sever upper gastrointestinal hemorrhage (n=3), malignancies (n=6), pancytopenia (n=4). Seven patients died while in hospital which included three with severe GI haemorrhage, two due to septic shock and one each with sickle cell crisis and chronic kidney disease. Except for the patient with sickle cell crisis all hospital deaths occurred on the very day the patients were brought to the hospital. Salient features of five interesting cases of this cohort are brought out in discussion.

Discussion

Twenty- eight patients (23%) had clinical or laboratory evidence of infection such as fever, tachycardia, toxemia, neutrophilia, toxic granules/vacuolation or response to treatment. Only eight were corroborated by culture positivity or microscopy which could be due to early antibiotic administration or inadequate sampling. The isolates included *Enterococcus* and *Pseudomonas. aeruginosa* (from Pyothorax), *Escherichia. coli* (n=2) -one in blood and one in urine, coagulase positive Staphylococcus (n=2), *Kleibsella.* aerogenes (n=1), acid fast bacilli on microscopy (n=2) from clinically suspected Tuberculosis. None of the 18 patients with chronic liver disease were positive for any of the Hepatitis markers on testing for Hepatitis B surface antigen and anti-Hepatitis C antibodies by card based testing. On the basis of history and substantiated by liver function tests and ultrasonography alcohol was the cause for liver disease in 14 (11.5%) patients.

Sixteen anemic patients grouped as "Others" under haemtological conditions (Table 1) had anemia as predominant finding with no other contributory factors. Anemia was microcytic hypochromic in 13 (81%) and macrocytic in three patients. Four (25%) had a history of fever but were culture negative. Only six (37.5) of these patients had more than one contact with the physicians so additional incriminating factor other than nutritional inadequacy was not identifiable.

A suspicion of nutritional anemia was made on the basis of clinical evidence of malnutrition, low serum proteins with or without hypoalbuminemia and macrocytic/microcytic hypochromic anemia with RDW >19.0%. The laboratory did not have a test for Iron deficiency which has been commenced after actually realizing the enormity of the problem. Vitamin B_{12} levels were tested in two patients due to the high cost and three days' delay in g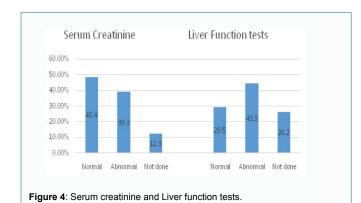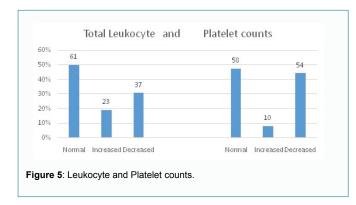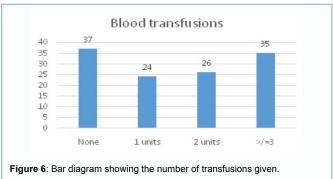etting results – being an outsourced test. A study from India mentions that RDW had sensitivity 82.3% and specificity 97.4% in comparison to MCV, MCH

Table 1: Etiological classification of 122 patients with severe anemia.

Hematological conditions including those with anemia as predominant finding (n=38)	Thalassemia major	3
	Pancytopenia	8
	Hemolytic Anemia	2
	Sickle Cell Disease	4
	ALL	2
	AML	1
	CML	1
	Haemophilia	1
	Others	16
Blood loss as major cause for anemia (n =26)	Obstetrical or complications related	6
	DUB	10
	Intestinal perforation	1
	Bladder rupture	1
	GI Haemorrhage	5
	Septic shock	2
	Fracture radius and femur	1
Non-Haematological malignancies presenting with anemia (n=7)	Carcinoma Gall Bladder	3
	Carcinoma Lung with Thyroid metastasis	1
	Hodgkin's Lymphoma	1
	Metastatic Prostate cancer	1
	Carcinoma Esophagus	1
Miscellaneous conditions associated with anemia (n =18)	PEM	2
	Heart Disease	2
	Tuberculosis? Lymphoma	1
	Infections (culture / microscopy positive)	8
	Rheumatoid arthritis	1
	Down's syndrome	1
	Hypothyroidism, Diabetes Mellitus	1
	Developmental disorder	1
	Systemic Lupus Erythematosus	1
Chronic Liver Disease associated with anemia (n=18)		18
Chronic Kidney disease associated with anemia (n=8)		8
Peptic Ulcer disease (n=7)		7

and MCHC had 29.2%, 68.1% and 15% sensitivity but specificity was 98.7%, 83.1% and 96.1% for detection of iron deficiency [7].

Five patients with unusual and interesting features are briefly mentioned below, although it was not possible to do complete work up in our centre. A seven years old child had history of ten days malena was found to have severe anemia, hypoproteinemia and hypoalbuminemia, with all other investigations within normal limits including prothrombin time and activated thromboplastin time. He was transfused three units of whole blood after hospitalization and while in hospital had three episodes of malena and hematemesis and a single episode of generalized seizure. Additional investigations were not performed due to financial constraints. The second patient was a 46 years old lady with history of small and large joint pain since many years, weakness since one year and five episodes of vomiting in last 24 hrs. On examination the only positive finding was marked pallor; investigations showed severe microcytic hypochromic anemia (Haemoglobin 3.6 gm/dl), iron profile confirmed severe iron deficiency, C reactive protein of 140mg/L and Rheumatoid factor 179 IU/ml; ECG showed left ventricular hypertrophy which was corroborated on Chest radiography. No additional investigations were done. There was one case each of Down's Syndrome and documented Haemophilia that presented with normocytic -normochromic anemia. A 15 years old boy was found to have generalized scabies, multiple abscesses over left chest, left ankle and neck, pyomyositis right thigh and right distal femur Osteomyelitis. The patient was admitted for staphylococcal sepsis (positive blood and pus culture) and was treated aggressively. He was discharged and is under follow up in OPD. The commonest symptoms were easy fatigability and breathlessness or routine activities in patients without localizing symptoms.

Of the 27 (22.1%) patients with documented history of significant blood loss 16 (59.3%) were females with obstetrical or gynecological conditions including twin pregnancy, breech delivery, ruptured tubal pregnancy, puerperal sepsis, Intrauterine death, induced incomplete abortion, vaginal polyp and pubertal menorrhagia non- responsive to hormonal treatment- one each. The remaining had history of menorrhagia (n=4) or DUB (n=4).

As all the patients had severe anemia, whole blood transfusion was the mainstay of treatment, along with essential life saving measures and symptomatic treatment to the extent possible in a secondary care centre without in-house blood bank. Blood transfusion was given to patients who were able to arrange for whole blood from either of the two blood banks in the city. Patients with end stage renal disease, cancers and those requiring urgent treatment were referred after stabilizing the condition. The number of transfusions and hospitalization was kept low for better blood management has been described in a study [8].

The hospital was able to provide optimal medical care to the patients with severe anemia of diverse origin with less than 3.5 days of average hospitalization. Patients were referred when required after providing essential medical care. All but one hospital death took place on the very day of admission which was attributable to the fact that the patients were brought at a very late stage in the disease. The only patient who expired after five days of admission was a case of Sickle cell anemia who had suffered from hemolytic crisis and renal shut down.

The study has several limitations which include inability to provide complete work up due to lack of facilities in the lab, poor patient paying capacity and lack of follow up information for 46 patients who had a single contact with the hospital. This is in spite of the fact that the centre is the best within 250 kilometers, and many such similar or even more inadequate centers have to provide healthcare to a large number of patients. This study was carried out to provide insight into the magnitude of the problem and how within constraints effective healthcare was provided.

Management of the patients with potentially life threatening anemia was a major challenge in view of severe economic constraints

and non- availability of an in-house Blood Bank. It is pr291304 opposed to establish blood bank and dialysis facilities in the next one year so that the hospital can improve further the healthcare provided to its clientele.

Conclusion

The study included 122 severely anemic patients (Haemoglobin <5.0 gm/dl) managed in a secondary care centre with all its constraints including absence of blood bank. In spite of its limitations the hospital was able to provide economical and timely healthcare to this category of severely ill patients.

Acknowledgment

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