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Analysis of Severe Anemia Management in a Tertiary Care Hospital: A Prospective Observational Study

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ABSTRACT

Background Severe anemia is a serious health concern, especially in tertiary care hospitals, where patients frequently present with multiple complaints . It is essential to understand the various patterns, causes, and treatment approaches for optimising patient care. This study aims to evaluate the etiology, treatment approaches, and clinical outcomes in the management of severe anemia.

Materials and methods: Study included 85 patients diagnosed with severe anemia (hemoglobin <7.7 g/dl). Patients were followed up daily, and their demographic, laboratory, medication, and blood transfusion details were collected and analysed.

Results: The demographic of 85 patients showed mean age of 56.7 ± 15.2 years. Majority were above 60 years (43.52%), and male (58.8%) patients were more. The average hospital stay duration was 1.8 ± 1.2 weeks, whereas 44.7% discharged within one week. The NCNC (64.70%) anemia was the most prevalent morphological form, and ACD (60%) was the etiological form. The major comorbidities were hypertension (52.9%) and diabetes mellitus (48.2%). Most prescribed drug combination therapy was MVI plus thiamine (50%). All the treatment regimens, including PRBC transfusion (8.8%) and erythropoietin (21.1%), significantly increased the hemoglobin concentration. from baseline to final value (95%CI, 6.66 ± 0.77 g/dL vs 8.44 ± 1.21 g/dL, P < 0.001). One case of an adverse reaction following PRBC transfusion was reported.

Conclusion: Treating severe anemia with combination therapy, PRBC transfusion, and erythropoietin was effective because it significantly increased the hemoglobin concentration. The LOS of patients also depends on the comorbidities.

INTRODUCTION

Anemia is a hematologic disorder in which hemoglobin or red blood cells (RBCs) are in decreased quantity in the blood (1). Hemoglobin is essential because it transports oxygen to different parts of the body; an insufficient amount of hemoglobin or abnormal red blood cells will cause tissue hypoxia, leading to symptoms such as fatigue, weakness, tachycardia, pallor or jaundice, dizziness, and shortness of breath (2).

Worldwide, people of all genders and ages are affected by it and it is one of the most common medical conditions (3). A total of 1.76 billion individuals worldwide suffered from anemia (4), among them 40% were pregnant women worldwide, and 42% were children below 5 years of age (5). It is a serious global public health issue that has an impact on social and economic development, human health, and both in developing and developed nations.

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It happens at every phase of the life cycle (6). The World Health Organisation (WHO) has recommended cut-off points of 13.0g/dl for males and 12.0g/dl for females (7). The ICMR has classified anaemia into four categories (mild, moderate, severe and very severe) depending upon the Hb level.1.Mild Hb% 10–10.9 g/dl

2. Moderate Hb% 7.8–10 g/dl

3. Severe Hb% 4–7.7g/dl

4. Very severe:<4g/dl[8]

Anaemia can have many different etiologies, such as nutritional deficiencies (iron or vitamin B12 deficiency), infectious diseases (malaria, hookworm, HIV/AIDS), and genetic disorders like thalassemia or sickle cell disease (9).

Anemia can have many different etiologies, such as nutritional deficiencies (iron or vitamin B12 deficiency), infectious diseases (malaria, hookworm, HIV/AIDS), and genetic disorders like thalassemia or sickle cell disease (9). Among these, iron deficiency anemia (IDA) is the most common, followed by anemia of chronic disease (ACD) (10), which is the second most prevalent type. Worldwide, 40% of elderly patients present with ACD (11) is associated with a variety of conditions like chronic infection (bacterial endocarditis, chronic urinary tract infections), non-infective chronic inflammatory disorder (rheumatoid arthritis, inflammatory bowel disease), malignant diseases, congestive cardiac failure, acute kidney infection, chronic liver disease, and chronic kidney disease (12).

Studies have found that severe anemia is more frequently observed in CKD patients. The incidence is less than 10% in stage I and II; 20%-40% in stage III; 50%-60% in stage IV; and in patients with stage V, it is more than 70%(13).

Undiagnosed or untreated anemia can have serious consequences, including reduced oxygen supply to tissues, irregular heartbeat, organ dysfunction, poor brain development shown as cognitive, behavioural, and developmental abnormalities, and even death(14)

Severe anaemia must be managed effectively to improve patient outcomes and decrease these unfavourable effects. Managing severe anaemia is challenging for patients when the cause is unclear, or there are several co-morbidities, so correct diagnosis is very important to select proper treatment1 (5). The most common parameters used for diagnosis include measurement of blood Hb concentration, hematocrit (packed cell volume), and RBC parameters such as MCV and MCHC (16). Anaemia is commonly managed by vitamin supplements to treat the underlying cause. Intravenous (IV) iron and erythropoietin are non-transfusion-based therapies that are used in severe cases, along with or without transfusion, in managing severe anaemia (17,18).

According to the American Association of Blood Banks' (AABB's) current RBC transfusion recommendations, patients who are hospitalised should follow a restrictive transfusion strategy, with haemoglobin (Hb) requirements of fewer than 7 g/dL for those patients and less than 8 g/dL for those who have concurrent cardiovascular illness and are having cardiac or orthopaedic surgery (19). Those suffering from chronic renal illness frequently have anaemia. The quality of life in these individuals has been significantly improved by erythropoietin therapy(20).

This study aims to evaluate existing treatment options and results in a tertiary care hospital, since better management strategies are required. In order to find treatment gaps and propose evidence-based approaches that might enhance patient outcomes and lower the morbidity and mortality linked to severe anemia, this study used a thorough prospective observational analysis. It is anticipated that the results of this study will direct future investigations into the treatment of anemia and help to enhance current practices.

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MATERIALS AND METHODS

Study Design:

Analysis of severe anemia management in a tertiary care hospital – a prospective observational study.

Study Population:

The study included patients aged 18 years and above who were diagnosed with severe anemia (Hb <7.8 g/dL). Among them, pregnant women, cancer patients, and those who had recently undergone major surgery were excluded

Method of Collection of Data:

A prospective observational study was done in all the departments of Bangalore Baptist Hospital. The patients who met the inclusion criteria were enrolled in the study. The first step was the collection of patient demographic details like age, sex, weight, and date of admission of patients diagnosed with severe anemia. Then, the information on proper diagnostic tests and categorization of anemia type was done. After that, blood sample reports were collected from eligible patients for laboratory testing, including complete blood counts (CBC) and other relevant hematologic parameters assessed. Interpretation of laboratory findings in conjunction with clinical data was done to assess treatment efficacy and guide clinical decision-making. An extensive history interview was taken with the patient and also the caregiver about any previous or present medical conditions. Then, the assessment of the risks and benefits of the drug based on the outcome was done. The patients were followed up throughout their treatment and assessed. Regular follow-up was done in patients to assess treatment response and clinical progress and to capture any adverse events or complications that occurred. Any changes in treatment regimens, clinical outcomes, or patient-reported symptoms were followed up during the visit, and it was documented.

Statistical Analysis:

In this study, data was collected and entered into Microsoft Excel. A software application, Jeffreys's Amazing Statistics Program (JASP) version 0.16.4, was used to perform different statistical analyses. We performed The student's t-test was to compare the mean difference of base and final hemoglobin (Hb), hematological, and other biochemical parameters. To check the association between age and gender, a morphology and gender chi-square test was done. For all the tests, statistical significance was defined at $p<0.05$.

RESULTS

A total of 85 patients were included in the study; among them, 15.29% were young adults with a mean age of 30.4 ± 5.63 years, 41.17% were middle-aged adults with a mean age of 49.9 ± 6.24 years, and 43.52% of the elderly patients hospitalised due to severe anemia, with a mean age of 70 ± 6.85(Table 1). The gender distribution of the study population revealed a higher proportion of male patients (58.8%) than female patients (41.2%). The length of stay (LOS) the patients spent in the hospital, revealed that the majority of them (44.70%) were discharged within 1 week, followed by 27.05% in the second week, 14.11% in the third week, 8.23% in the fourth week, and 5.88% were admitted for more than 4 weeks. The most common morphological type of anemia was NCNC, accounting for 64.70%, followed by MIHY (18.8%), whereas both MANC and MINC were the least common morphological patterns, accounting for 8.23%.

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Table 1: Baseline demographics of the study population (N = 60)

DEMOGRAPHICS(N=85)	N (%)	[Mean ± SD]
Age in years with Mean and SD 18 – 39 40 – 59 >60	 13(15.29) 35(41.17) 37(43.52)	 30.4 ± 5.63 49.9 ± 6.24 70 ± 6.85
Gender	**N(%)**	
Male Female	50(58.8) 35(41.2)	
Length of Stay (in weeks)	**N (%)**	
1 week 2 weeks 3 weeks 4 weeks > 4 weeks	38(44.70) 23(27.05) 12(14.11) 7(8.23) 5(5.88)	

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DIAGNOSIS AND COMORBIDITIES	
Morphological classification	**N(%)**
1 MIHY 2 MANC 3 MINC 4 NCNC	16(18.8) 7(8.23) 7(8.23) 55(64.70)
Etiological classification	**N(%)**
1 Anemia of CD 2 Bleeding 3 Vitamin B12 4 MA 5 IDA 6 AA	51(60) 20(23.52) 2(2.35) 1(1.17) 9(10.58) 2(2.35)
Comorbidities	**N(%)**
1 Hypertension 2 DM 3 Ischemic Heart Failure 4 Acute coronary syndrome 5 Heart failure 6 Seizure 7 Hypothyroidism 8 COPD	45(52.9) 41(48.23) 8(9.41) 2(2.35) 4(4.70) 4(4.70) 6(7.05) 1(1.17)
Therapy	**N(%)**
Number of patients with PRBC infusion	67(78.82)
Number of patients with Erythropoietin	18(21.17)

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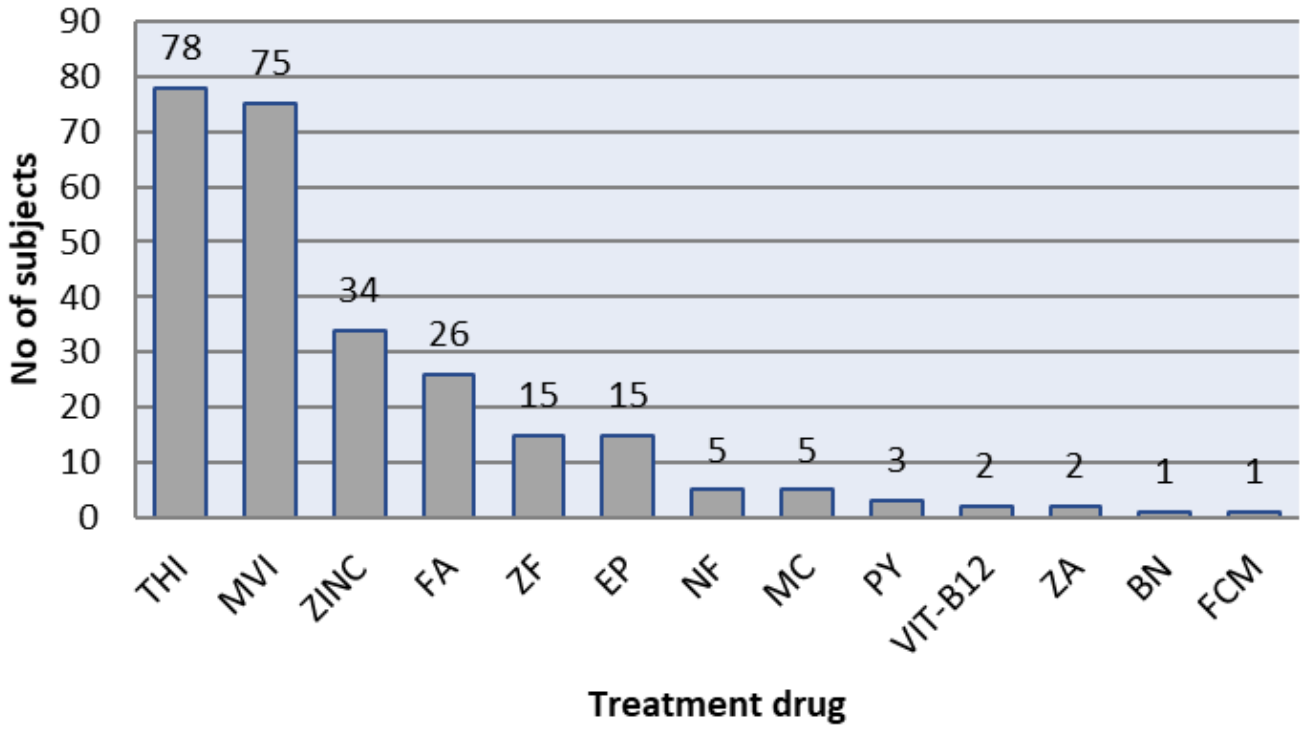
In the etiological classification of anemia, the study found that ACD (60%) was the most common cause, followed by bleeding at 23.52%. The less common causes were Vit-B12 at 2.35%, AA at 2.35%, and MA at 1.17%. In the study population, hypertension accounted for 52.9% of all detected comorbidities, followed by DM at 48.23%, IHD at 9.41%, hypothyroidism at 7.05%, heart failure at 4.70%, seizures at 4.70%, ACS at 2.35%, and COPD at 1.17%. Out of 85 participants, 78.82% had received PRBC transfusion, with a mean of 1.776 ± 1.324, as shown in Table1. Table 2 presents the baseline and final values of different haematological and biochemical markers to assess the effectiveness of the treatment plan. A statistically significant rise was observed in hemoglobin level from baseline value to final value (95%CI, 6.66 ± 0.77g/dl to 8.44 ± 1.21g/dl, p<0.001).

A comparable pattern was noted for PCV, which increased from 21.52 ± 4.67% to 25.85 ± 3.84%, with a mean difference of +4.33(p<0.001). Similar significant mean differences improvement was observed for MCV (+0.32), MCHC (+24.03), RBC (+0.23), and Na (+2.67). The PL count did not rise significantly (+25.07). While the mean difference tend to be decreased in WBC (-1.03), serum K (-0.21mmol/l) and serum Cr (-0.79mg). For the treatment of severe anemia, MVI+THI, MVI+THI+ZINC, and MVI+THI+ZINC+FA were the most prescribed medications among 42 patients. MVI+THI was prescribed to 50% of patients and increased the Hb level from 6.604 ± 0.94g/dl to 8.109 ± 1.26g/dl, with a mean difference of +1.505g/dl.

Figure 1: Prescribing pattern in the management of severe anemia in the study population.



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This was followed by MVI+THI+ZINC prescribed to 35.72%, which increased the Hb level from 6.78 ± 0.55g/dl to 8.54 ± 1.25g/dl with a mean difference of +1.76g/dl, and MVI+THI+ZINC+FA to 14.28%, that increased the Hb level from 6.63 ± 0.72g/dl to 8.9 ± 1.48g/dl with a mean difference of +2.267. The above drug combinations significantly raised the Hb level.

A total of 85 patients were enrolled in the study, which comprised 50 males and 35 females. The highest proportion of male patients (44%) belonged to the 40-59 years age group, whereas among females, 51.42% were aged over 60 years of age group. A chi-square test was performed to see the association between age and gender (Table 4). However, no statistically significant association was observed (p=0.043).

Table 5 presents the association between Morphology and Gender of patients, a chi-square test was performed to see the association. The study revealed 68% of males and 60% of females had NCNC anemia, making it the most prevalent form in both genders. MANC was found in 8% of men and 8.5% of females whereas MINC was found in 10% of males and in 5.8% of females. MIHY was more common in females (25.7%) compared to males (14%). The distribution of anemia types between male and female does not differ statistically significantly according to the results of a chi-square test (P > 0.05). In Figure 1 the most often recommended medications for treating severe anemia were THI and MVI, which were given to 78 patients and 75 patients, respectively. ZINC was given to 34 patients, while FA was given to 26 patients.

Table 2: Descriptive statistics of laboratory parameters in the study population

Descriptive Statistics Of Serum Markers(N=85)	Baseline value	Final value	Mean Difference	P value	Remark
	Mean ± SD	Mean ± SD			
Hb(g/dl)	6.66 ±0.77	8.44 ±1.21	1.78	<0.001	S
PCV(%)	21.52 ±4.67	25.85 ±3.84	4.33	<0.001	S
MCV (FL)	32.66 ±1.98	32.98 ±3.34	0.32	0.049	S
PL (x10^3)	189.329 ±116.308	214.396 ±153.839	25.067	0.066	NS
RBC(10^6/mm^3)	2.79 ±0.71	3.02 ±0.67	0.23	0.004	S
WBC(10^3/mm^3)	10.86±7.89	9.83±5.30	-1.03	0.126	NS
Na(mmol/L)	135±6.86	137.67±6.55	2.67	0.003	S
K+(mmol/L)	4.36±0.88	4.15±0.64	-0.21	0.049	S
S.Cr(mg/dl)	3.69±3.58	2.90±2.63	-0.79	<0.001	S
S: Significant, NS: Not Significant					

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Table 3: Difference between Hemoglobin levels of the most commonly prescribed therapy for the management of severe anemia in the study population.

Type of management	Number of Subjects N=42	The least hemoglobin value	Final hemoglobin value	Mean Difference	P value	Remark
	N(%)	Mean ± SD	Mean ± SD			
MVI + THI	21(50)	6.604±0.94	8.109±1.26	1.505	0.0001	S
MVI + THI+PRBC	18(42.8)	6.604±0.98	8.109±1.26	1.505	0.0001	S
MVI + THI+ZINC+PRBC	12(28.5)	6.678±0.50	8.54±1.25	1.76	0.0001	S
MVI + THI+ZINC+FA+PRBC	4(9.52)	6.63±0.720	8.9±1.48	2.267	0.0073	S

Table 4: Association between Age and Gender of patients admitted with severe anemia in the study population

Age (in years)	Male		Female		Chi-Square test X2 Mean ± SD	P Value	Remark
	No of subjects (N)	percentage	No of subjects (N)	percentage			
18-39	9	18%	4	11.44%	X2 = 1.6693	P = 0.43	NS
40-59	22	44%	13	37.14%			
>60	19	38%	18	51.42%			
Total	50	100	35	100			

NS: Not Significant

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Table 5: Association between Morphology and Gender of patients admitted with severe anaemia in the study population

Morphological classification	Male N (%)		Female N (%)		Chi-Square test X2 Mean ± SD	P Value	Remark
	No of subjects (N)	percentage	No of subjects (N)	percentage			
NCNC	34	68%	21	60%	X2 = 2.172	P = 0.538	NS
MIHY	7	14%	9	25.70%			
MANC	4	8%	3	8.50%			
MINC	5	10%	2	5.80%			
TOTAL	50%	100%	35%	100%			
NS: Not Significant							

DISCUSSION

A total of 85 patients were included in the study, of which 58.8% were male and 41.17% were female, which was consistent with a study carried out by Dr. Waseem Hussain Bhat et al. (21). In this study, among 85 subjects, the highest number of patients with severe anemia were found in the age group of >60 years (43.52%), followed by 40-59 years (41.17%) and 18-39 years (15.29%), which was consistent with the study conducted by Kossinnage Chethana Chathurangani et al (22) and Dr. Waseem Hussain Bhat et al. (21). In this study among 85 subjects, the highest number of patients with severe anemia were found in the age group of >60 years (43.52%), followed by 40-59 years (41.17%) and 18-39 years (15.29%), which was consistent with the study conducted by Kossinnage Chethana Chathurangani et al.[16] and Dr. Waseem Hussain Bhat et al.(21) where the majority of the patients were >60 years. This study was different from the study that was conducted by Dr Faiza Hafiz (23), where 58% of the patients were in the age range of 21 to 40; this might be due to a lack of additional comorbidities. In this study, the prevalence of severe anaemia based on morphological classification, NCNC (64.7%) anaemia, was observed in the majority of the patients, followed by 18.8% of MIHY and 8.23% of both the MINC and MANC, similar to the study conducted by Dr Waseem Hussain Bhat et al. (21) where NCNC (57%) anemia was the most prevalent morphological form of anemia, followed by MINC (24%), MHYC (9%), and MANC (6%) anemia. Anemia was also classified based on etiology, where the majority of the study population had ACD (60%), but 20% of the study population had anemia because of bleeding, followed by 2%

of the patients having anemia associated with Vit-B12 deficiency, and 10.58% of the study population had IDA concomitant to the study conducted by Kossinnage Chethana Chathurangani et al.(22) . In the study population, hypertension accounted for 52.9% of all detected comorbidities, followed by DM at 48.23%, IHD at 9.41%, hypothyroidism at 7.05%, heart failure at 4.70%, seizures at 4.70%, ACS at 2.35%, and COPD at 1.17%, whereas the study conducted by Dr. Waseem Hussain Bhat et al.[21] showed DM as a major comorbidity, which was almost consistent with this study. Regarding the length of hospitalization, the patients were mostly hospitalized for less than 1 week, which accounts for 44.70% of total cases (N=85), followed by 23% of the patients who were hospitalized for less than 2 weeks and 12% of the patients who were discharged within 3 weeks. 7% of the patients were hospitalized for a month, and the remaining 5% were hospitalized for more than 4 weeks, but the result of this study was different from the study conducted by T.S. Dharmarajan et al (24) . The difference might be due to comorbidities because the LOS of anemia patients also depends on the comorbidities.

In Table 2, mean hemoglobin increased from 6.66 ± 0.77 g/dL to 8.44 ± 1.21 g/dL ($p < 0.001$), indicating a positive response to treatment therapy, which was similar to the study conducted by Blanca et al.(19). It was also observed that packed cell volume (PCV) increased from 21.52 ± 4.67% to 25.85 ± 3.84% ($p < 0.001$), and RBC count increased from 2.79 ± 0.71 to 3.02 ± 0.67 × 10^6/mm^3 ($p = 0.004$), which was similar to a study conducted by Thomas et al.[26], where hematologic improvements were seen. The above table revealed sodium levels slightly increased ($p = 0.003$), while potassium levels decreased ($p = 0.049$), which was similar to a study by Frenkel et al. [26].

It was also seen that serum creatinine levels dropped from 3.69 ± 3.58 mg/dL to 2.90 ± 2.63 mg/dL ($p < 0.001$), indicating renal improvement, which was consistent with the findings of Jeon et al.(27). In the above table (3], it was seen hemoglobin rose from 6.60 ± 0.94 g/dL to 8.11 ± 1.26 g/dL (mean difference 1.505 g/dL, $p = 0.0001$) in 50% of patients receiving MVI + THI therapy, which was similar to the study conducted by Blanca et al. [19] Patients treated with MVI + THI + PRBC also showed an increase in mean hemoglobin level of 1.505 g/dL ($p = 0.0001$), similar to the study conducted by Thomas et al.[26]. In patients who received MVI + THI + ZINC and MVI + THI + ZINC + PRBC therapy, hemoglobin increased from 6.78 ± 0.50 g/dL to 8.54 ± 1.25 g/dL (mean difference 1.76 g/dL, $p = 0.0001$). A similar kind of hemoglobin improvement was seen in the study conducted by Jeon et al.[27]. Patients treated with MVI + THI + ZINC + FA and MVI + THI + ZINC + FA + PRBC had the highest mean hemoglobin gain of 2.267 g/dL ($p = 0.0073$); a similar observation was seen in the study conducted by Elamin et al.[20]

To see the association between age and gender, a chi-square test was performed, [Table 4] but no statistically significant difference was found ($\chi^2 = 1.6693$, $p = 0.43$). It was observed that women (51.42%) over 60 years of age were affected slightly more as compared to men (38%); however, this difference was not statistically significant. Anemia was more prevalent in older persons, particularly in women; it could be due to chronic disease or nutritional deficiencies. A study was conducted by Wang et al.[28], the findings of their study are consistent with our study. To examine the association between gender and morphology the chi-square test was performed [Table 5] , but no significant correlation ($\chi^2 = 2.172$, $p = 0.538$) was found. In a study, conducted by Singh et al. [29]

it observed that normocytic normochromic anemia was the predominant type, with no significant gender difference. similar findings were seen in our study, where 68% male and 60% female revealed NCNC anemia, followed by microcytic hypochromic anemia where females (25.7%) were slightly affected higher than male (14%) , this findigs was similar to study conducted by by Abshirini et al.(30)

CONCLUSION

This prospective observational study reflects the different treatment strategies to treat severe anemia, and it also estimates the prevalence and type of anemia based on morphology and etiology. This study revealed that NCNC anemia was more prevalent among the study population, and ACD was found to be the primary cause of severe anemia, followed by bleeding. The major comorbidities involved in the study population were hypertension (52.9%) and DM (48.23%). This study emphasizes the regular monitoring of the hematological parameters and ADR after the PRBC transfusion. According to this study, most of the patients underwent PRBC transfusion, with a majority of 78.82%, and 21.17% were prescribed recombinant erythropoietin. Improvement was found in the patient after the treatment therapy, as an elevation in the hemoglobin level was seen in the study. Out of 85 patients, one ADR was found; the patient had facial edema with difficulty in breathing. The study also revealed that the most common combination prescribed to the patient was MVI+THI, followed by MVI+THI+ZINC and MVI+THI+ZINC+FA.

LIMITATIONS

This study needs to be carried out in a larger population and for a long duration because it was conducted only for six months, so it had a small sample size. All the documents and laboratory values required were not available, so assessment of the reliable documents was only done.

ABBREVIATIONS

NCNC (Normocytic Normochromic), MIHY (Microcytic Hypochromic), MANC (Macrocytic Normochromic), MINC (Microcytic Normochromic), RBC (Red Blood Cells), WBC (White Blood Cells), ACD (Anemia of Chronic Disease), Vit-B12 (Vitamin B12), MA (Megaloblastic Anemia), IDA (Iron Deficiency Anemia), AA (Aplastic Anemia), DM (Diabetes Mellitus), IHD (Ischemic Heart Disease), ACS (Acute Coronary Syndrome), HF (Heart Failure), COPD (Chronic Obstructive Pulmonary Disease), PRBC (Packed Red Blood Cells), ICMR (Indian Council of Medical Research), WHO (World Health Organization), MVI (Multivitamin), THI (Thiamine), ZINC (Zincovit), FA (Folic Acid), EP (Erythropoietin), NF (Neurobion Forte), MC (Methylcobalamin), FCM (Ferric Carboxymaltose), Hb (Hemoglobin), PCV (Packed Cell Volume), MCV (Mean Corpuscular Volume), MCHC (Mean Corpuscular Hemoglobin Concentration), PL (Platelets), Na (Sodium), K^+ (Potassium), Cr (Creatinine), and LOS (Length of Stay).

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Conflicts of Interest

The authors declare that there are no conflicts of interest related to this study. The research was conducted independently, and the findings represent the unbiased results and interpretations of the authors.

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Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data will be made available to qualified researchers for non-commercial purposes only, subject to ethical and privacy considerations. Due to privacy restrictions, participant data cannot be publicly shared, but can be accessed by contacting the corresponding author.

Protection of humans and animals.

The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval

The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence.

The authors declare that no generative artificial intelligence was used in the writing of this manuscript