

Risk Factors and Clinical Aspects of Anemia in a Tertiary Care Hospital

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ABSTRACT

Background: Anemia is the indicator of any related illness. More than two thirds of people have Anemia, which is frequently a sign of upcoming diseases. Identifying its clinical aspects will aim towards tailored, primary approach to treat and manage anemia. Our study aims to analyse severity of Anemia, risk factors and its impact on length of hospitalization signifying multidimensional loss of function in hospitalized patient due to Anemia. **Materials and Methods:** It is a prospective observational study conducted for 6 months in a tertiary care hospital among 150 patients. The data procured on various required parameters and decisive data was analysed using SPSS (IBM SPSS) version 29.0.2.0. **Results:** In a sample size of 150, 58% were males and 42% were females. Males were more frequent for susceptibility to every degree of anemia. Severe anemia was treated extensively whereas there is no treatment approach for any milder cases. Majority of cases had length of hospitalization for more than 15 days. Risk factors associated with anemia were Male gender (OR: 4.117), Smoking (OR: 12.304 for mild anemia and OR: 10.879 for moderate anemia) were found. **Conclusion:** Prevalence of anemia was found high in patients with alcoholic liver disease. Anemia prolongs hospital stays and exacerbates outcomes in patients with comorbidities. The study underscores the urgency of early intervention to treat milder cases and avert complications, given the elevated incidence of severe Anemia.

Keywords: Anemia, Risk factors, Length of hospitalization, Hemoglobin, Red Blood Cells.

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INTRODUCTION

Anemia is defined as decreased number of RBC being circulated,^{1,2} or oxygen insufficiency due to inadequate RBC circulation.^{2,3} Hemoglobin is the most usual measure used in clinical practice to assess Anemia.^{3,4} Anemia is a condition characterized by hemoglobin levels <12.0 g/dL in women and <13.0 g/dL in men with accordance to WHO. Decreased availability of oxygen, reduced quality of life and impaired exercise tolerance is linked to Anemia. It is allied with exacerbating conditions such as renal failure, cardiac decompensation and myocardial infarction.^{5,6} Fatigue, breathlessness, pallor, palpitations are some of the symptoms due to oxygen deprived tissues caused by decrease in hemoglobin concentration.^{7,8} Pallor is observed to be usual sight in people with Anemia; it is noticeable in the oral mucosa, particularly in the Tongue, soft palate and sublingual tissues, alongside in the nail beds and palpebral conjunctiva.^{8,9} Females are more prone to Anemia when contrasted to male.⁹ The incidence of Anemia shoots up with increasing age.^{10,11}

Anemia has been linked to higher rates of hospitalization and longer stays in hospitals. This suggests that individuals with anemia may experience more severe health issues requiring medical attention. Understanding this association can help healthcare providers better manage and treat anemic patients to potentially reduce hospital admissions and improve outcomes.^{11,12}

Equal nutrient absorption and digestion is necessary for nutritional balance, but a number of circumstances can throw this equilibrium off. Nutrient deficiencies can be either relative or absolute and can result from increased losses, needs, or decreased intake, absorption, or utilisation. Since imbalances may lead to a variety of health problems, maintaining balance is essential for general health and wellbeing.

Anemia diagnosis involves a full blood count, which include hematocrit, Red blood cells and Hemoglobin values. Several red blood cells indices can help identify the factor linked to anemia. If aberrant cells are detected, a peripheral smear of blood may be initiated.^{12,13} The most effective test for determining iron reserves is serum ferritin. Megaloblastic macrocytic anemia is a symptom of vitamin B₁₂ insufficiency, which can be identified by testing for methyl malonic acidemia. Similar symptoms can be identified in cases of folate insufficiency, which is verified by high homocysteine levels.



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Reduced erythropoietin production is the cause of anemia in renal disease, which can happen even with mild declines in renal function, usually shown by creatinine clearance values less than 30 mL/min.^{13,14}

Blood transfusion is opted either in the case of severe or life-threatening Anemia of hemoglobin levels (<8 g/dL and <6.6 g/dL) respectively.^{14,15} A single adult iron injection should take three to 5 min and have 20 mg/mL. Dosage for the first injection should be 50 mg, followed by 100 mg and 200 mg and once per 24 hr if intolerance isn't evident.^{15,16} Vitamin B₁₂ injections, known as cyanocobalamin or hydroxocobalamin, are recommended for severe abnormalities. About 10% of the dose is retained and 1000 µg injections should be given multiple times a week for one to two weeks, then weekly until improvement is evident.¹⁶ Prior to starting an erythropoietic agent treatment, iron deficiency needs to be checked out. Hemoglobin levels should be measured following 4 weeks of therapy and every two to four weeks after that it is deemed to track the response to erythropoietic drugs. Iron supplementation should be taken into consideration and the iron status should be reassessed if the hemoglobin level rises by less than 1 g per decilitre.^{17,18}

Lal *et al.* found that cast iron cookware, used in Indian households for over forty years, provides more dietary iron. This iron is well-absorbed and can be used to fortify supplementary meals for newborns and early children. Iron-fortified cereals can effectively prevent and treat babies with iron insufficiency. Condiment iron fortification is also effective in preventing nutritional anemia and iron deficiency. Indian researchers have successfully tested iron-fortified salt in the field. Iron sprinkles, a small sachet containing iron and other minerals, have been proven effective in treating anemia. Regular consumption of iron-rich foods, folic acid and vitamin C foods is recommended for all age groups. Infants ought to get lactation four months, followed by supplementary foods at four to six months. Leafy green vegetables, vitamin C and lemon juice can also aid in iron absorption.^{19,20}

Conditions like Anemia, particularly Iron deficiency Anemia, adversely impact a child's brain development by hindering these essential processes. It compromises neurotransmitter production and myelination in the hippocampus and frontal cortex, resulting in long-term cognitive deficiencies and behavioural issues.^{20,21}

Previous findings by Zaninetti *C et al.* deduces the significant impact of Anemia on duration of hospital stay where the degree of Anemia severity also have its major role to elevate the hospital stay illustrating increased financial burden.^{21,22} Dharmarajan TS *et al.* research emphasizes exposure to an expanded length of hospital stay is found to be enhanced by Anemia, particularly by severe Anemia during the time of admission, thus early identification and intervention will halt the higher hospital stay and decrease the additional expenses to the patient and

to the outside providers.^{22,23} Cleland JG *et al* study reveals worsening cardiovascular health precipitate both Anemia and iron deficiency which suggest deficiency in iron can play a role in potential higher mortality.^{23,24} Gonzalez-Casas R *et al* analysis says that hematological anomalies are often encountered in liver diseases which result in Anemia of various causes that can be associated with adverse effect of treatment for hepatitis, flaw in coagulation of blood and bleeding. Alcoholic liver disease can act as a catalyst for the occurrence of malabsorption, malnutrition and hence accurate treatment is essential.^{24,25} Goodnough *et al.* delving into anemia concluded intervention such as antagonist to hepcidin, iron chelation therapy is the possible forward strategy in the management of Anemia due to chronic disease. Existing treatments involve blood transfusion, Iron supplements, erythropoietin therapy and therapeutic measures for causative disease condition are useful in current era due to advancement in the understanding of Anemia of Chronic diseases. This also highlights the relevance of conductive controlled trails to know the impact of these treatments in handling the underlying condition.^{25,26} Zilinski J *et al* experimentation identify a connection between Anemia and the diminishment in various functions in older persons. It put forward the need for regular monitoring of blood parameters for early detection in hemoglobin parameters, which may act as valuable tool to screen elderly for any associated deterioration in their health.^{26,27} A study by Tettamanti M *et al.* asserts the prevalence of undiagnosed mild Anemia in elder population is high which contributes to the decreased quality of life by augmenting impairment in day-to-day work, mortality and morbidity. Understanding the Pathophysiological changes will help in gaining insights in cause of decreased hemoglobin concentration and unexplained Anemia. The gained knowledge can be used as a source to control Anemia in healthcare.^{27,28}

Investigation done by Nathavitharana RL *et al.* reveal the significant deficit in the understanding and awareness of Anemia which is encountered as a common challenge in medical inpatient.

This issue can be addressed with periodic assessment and treatment of hemoglobin inadequacy. Anemia anticipates longer duration of hospital stay, increased rate of mortality and frequent hospital visits.^{28,29}

The purpose of the study is to study and propose Anemia as an additional indicator to the multidimensional loss of function in hospitalized patient. This research dwells around the present risk factors, treatment and outcomes of Anemia in Hospitalized Patients.

MATERIALS AND METHODS

This research was conducted for a period of 6 months in a tertiary care hospital. Diagnosed cases of anemia were reviewed from department of General medicine. This was a prospective clinical study conducted after informed consent on a total of 150

consecutive cases meeting the eligibility requirements for the study.

The study recruited inpatients of either gender (aged 15-80) from the general medicine department. Participants were eligible if they exhibited Anemia, defined as a hemoglobin level below 13 g/dL for males or 12 g/dL for females and provided comprehensive blood count reports. Individuals with genetic Anemia, pregnant or breastfeeding females and children under 15 were excluded from the study.

Procedure

Following informed consent, a prospective analysis was conducted on a cohort of patients. Medical and laboratory data were collected and patient outcomes were monitored. Risk

Table 1: Demographic details and clinical features of the study cohort (n=150).

Characteristics	Results
<u>Age</u>	
Young (<20-30)	40 (26.67%)
Middle age (31-50)	90 (60%)
Elderly (51-80)	20 (13.33%)
<u>Sex</u>	
Male	87(58%)
Female	63(42%)
<u>Severity of Anemia</u>	
Mild (Male)	15 (10%)
Moderate (Male)	20 (13.66%)
Severe (Male)	52 (34.66%)
Mild (Female)	4 (2.66%)
Moderate (Female)	16 (13.33%)
Severe (Female)	43 (28.66%)
Duration of hospital stay	19.30±6.26

Table 2: Severity of Anemia and Pharmacological Intervention wise distribution.

Type of treatment	Mild	Moderate	Severe
Blood transfusion	0	0	41
Iron supplements	0	24	93
Vitamin supplements	0	18	35

Table 3: Duration of hospital stay and Gender wise distribution.

Length of hospital stay	Male	Percentage (%)	Female	Percentage (%)	Total (%)
<5	0	0	0	0	0; 0
5 to 10	9	6	3	2	12;8
11 to 15	31	20.66	9	6	40;26.66
>15	47	31.33	51	34	98;65.33

factors and other relevant parameters were then compared and statistically evaluated as potential clinical indicators of anemia.

Statistical Analysis

Statistical analysis was carried out by using the Statistical Package for Social Sciences version 29.0.2.0. The Fisher's exact test or the χ^2 test was used to compare the categorical variables. Multivariate analysis was performed with the logistic regression to identify the Risk factors. Regression analysis is used for understanding and quantifying the relationships between variables. Considering non-normality of the data, Spearman correlation was used for measuring the strength and direction of the relationship between two variables.

RESULTS

Inference

The preceding table shows there isn't any treatment approach towards milder cases of Anemia, while blood transfusion along with both iron and vitamin Supplements was strictly approached for patients with severe Anemia. Moderate Anemia was managed by Iron and vitamin supplements.

Inference

There was no patient who got discharge in less than 5 days (0%), while the stay sustained for 5-10 days, there were 6% males and 3% females. In 11-15 days, category, 20.66% males and 6% females were recorded. For the stay going beyond 15 days, majority of the females (34%) were observed to have increased hospital stay when compared to males (31.33%).

Inference

The above table presenting risk factors associated with Anemia shows that ALD is the most common condition associated with anemia, followed by vitamin B₁₂ deficiency, SPM, CLD, IDA and HF.

Table 4: Regression analysis of length of stay with severity and hemoglobin.

	Regression weight	B	t	p-value
	Severity- LOS	4.569	4.062	<.001
	Hemoglobin-LOS	-1.048	-2.759	0.007
R ²	0.454			<.001
F (3,146)	40.419			

Note: $p < 0.05$, LOS: Length of hospital stay.

Table 5: Survival analysis.

Variable	B	d _r	Sig.	Exp(B)	95% CI for Exp(B)
Hemoglobin	.892	1	<.001	2.439	1.927-3.086

Table 6: Risk factors with one and other combination (Co-morbidities) wise distribution.

Risk factors	Number of patients (n=150)	Percentage (%)
ALD	102	17.49
CLD	75	12.86
HF	59	10.12
SPM	92	15.7
PHT	87	14.9
IDA	75	12.86
VIT B ₁₂ DEFICIENCY	93	15.95
	583	100

Note: **ALD**: Alcoholic liver disease, **CLD**: Chronic liver disease, **HF**: Heart failure, **SPM**: Splenomegaly, **PHT**: Pulmonary hypertension, **IDA**: Iron deficiency Anemia.

Table 7: Multivariate analysis of risk factors.

Risk factors	OR (confidence interval)	p value
Male gender (Mild anemia)	4.117 (1.031-16.443)	0.045
Smoker Mild anemia	12.304 (3.008-50.334)	<0.001
Moderate anemia	10.879 (3.963-29.864)	<0.001
Alcoholic (Mild anemia)	1.926E-8 (4.207E-9 – 8.814E-8)	<0.001

Note: Severe Anemia as reference category. OR for alcoholic is significantly negligible due to its very low OR value.

Inference

Logistic regression analysis indicates that males have 4.114 times higher odds of mild anemia compared to females, with a significant association. Smoking is associated with 12.304- and 10.879-times higher odds of mild and moderate anemia, respectively, while alcohol intake increases the odds of mild anemia by 1.926E times compared to non-drinkers.

Inference

Severity of Anemia shows a significant positive influence on length of hospital stay ($B=4.569$, $T=4.062$, $p < .001$). Hemoglobin shows a significant negative influence on length of hospital stay ($b=-1.048$, $t=-2.759$, $p=0.007$). RBC shows a significant positive influence on length of hospital stay ($B=2.076$, $t=2.637$, $p=0.009$).

Inference

Hemoglobin shows a potential significance with B coefficient of 0.892 ($p < .001$) which shows a significant positive association between the hemoglobin and the possibility of getting discharge. The Exp (B) which is hazard ratio for hemoglobin was 2.439 (95% CI: 1.927-3.086), suggesting for every one unit increase in hemoglobin, the probability of getting discharge increases by 143.9%. Cox regression survival analysis was performed to analyse ($n=150$) the discharge time from the hospital (in days) considering “discharged” as event.

DISCUSSION

In this study with a sample size of 150, males (58%) were found to be more susceptible to Anemia when compared to Females (42%) as shown in Table 1. This study evaluated male gender as a risk factor to develop Anemia ($OR=4.117(1.031-16.443)$, $p=.045$). This finding is analogous to the study done by Zeleke MB *et al.*²⁹ Age was categorised as Young from 15-30; Middle aged from 31-60 and Elderly as 61-80. Middle aged individuals of age 51-60 (30.66%) were observed to be vulnerable to Anemia after which by age group of 21-30 (18%), 41-50 (16%), 31-40 (13.33), 61-70 (10%), <20 (8.66%) and the least vulnerable group was 71-80 (3.33%). Following middle age (60%), young (26.67%) individuals come second in the vulnerable group of Anemia and least by elderly (13.33%) group [See Table 1 for more details]. This observation doesn't go parallel to the study done by Alvarez-uria G *et al.*³⁰ Severe Anemia was dominant among other severity of Anemia with 63.33%, accompanied by Moderate Anemia (24%) and Mild (12.66%). These findings are relevant to the analysis done by Assefa s *et al.*³¹ Males were more prevalent to all the severity of Anemia (Severe (34.66%), Moderate (13.66%) and Mild (10%)) and then Females (Severe (28.66%), Moderate (13.33%) and Mild

(2.66%) as seen in Table 1. The treatment approach to severity of Anemia was also observed and identified that all the severe cases of Anemia have been steadily addressed with all the patient (63.33%) receiving treatment, while there was no treatment given for patient (0%) with Mild Anemia. 16% and 8% of the patient with Moderate Anemia have received and not received treatment respectively mentioned in Table 2. Analysis of length of hospital stay mean duration of (19.30±6.26) revealed that 65.33% of patient has more than 15 days of stay at hospital in which females (34%) weighed against males (31.33%). Meanwhile, there were 20.66% male and 6% female for 11 to 15 days (26.66%), also 6% males and 3% female sustained in hospital for 5 to 10 days (8%) evident in Table 3. A regression analysis ($R^2=0.454$ (Adjusted $R^2=0.442$)) showed that Severity of Anemia shows a significant positive influence on length of hospital stay ($B=4.569$, $T=4.062$, $p<0.001$) whereas, Hemoglobin shows a significant negative influence on length of hospital stay ($b=-1.048$, $t=-2.759$, $p=0.007$) that can be reviewed in Table 4.

Survival analysis was executed for length of hospital stay considering getting discharge as an event. It was found that Hemoglobin factor shows a potential significance with B coefficient of 0.892 with ($p<0.001$) which shows significant positive association between the hemoglobin and the hazard of getting discharge. The Exp (B) which is hazard ratio for hemoglobin was 2.439 (95% CI: 1.927-3.086), [Shown in Table 5] suggesting for each unit raise in hemoglobin, the likelihood of getting discharge increases by 143.9%. The finding which depicts that anemic individuals with lesser hemoglobin level (Higher severity of Anemia) have a longer hospital stay is nearly comparable to the study conducted by Wouters HJ *et al.*³² Among the sample size of 150, Majority of the patients were evaluated with Alcoholic liver disease followed by Cobalamin deficiency, Chronic liver disease, iron deficiency Anemia and heart failure which has been depicted in Table 6. Upon multivariate logistic regression interpretation, it was seen that men were forward in vulnerability to mild Anemia (OR=4.117, $p=0.045$), smoking is found to be a risk factor for mild and moderate Anemia (OR=12.304, $p<0.001$), (OR=10.879, $p<0.001$) respectively in Comparison to severe Anemia as reference category. Alcohol consumption has a significantly negligible effect on mild severity of Anemia due to its extremely low odd's ratio seen in Table 7.

Acknowledgment of severe Anemia for its influence on hospital stay prolongation can contribute in directing subsequent research on Anemia. This study purposes at providing insight for further research in governing most favourable approaches to manage Anemia. Our finding will add up to the knowledge of current research considering severity of Anemia and factors influencing it.

The characterised data in this study that is all the patient got discharged with no censored data limits any establishment of survival probabilities and hazard rate in the study, but this also

show a consistency in the follow up of the subject during the study period. Quantitative data such as quantity of alcohol intake, timeframe of smoking and other hematological components was not considered. Shorter duration of study and single centered study are some of the limitations of the study.

CONCLUSION

Any kind of interventional therapy wasn't given for milder cases which explain the high proportion of severe anemic patients in the study that indicate early interventions to mild Anemia can hinder the progression to further decrease in hemoglobin levels and result in decreased hospital stay. Anemia increases length of hospital stay which impact the economic burden on patients, reduces quality of life and increases morbidity.

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CERTIFICATE OF INSTITUTIONAL ETHICS COMMITTEE

Ethics letter no: CMRCP/IEC/2023-2024/09

PATIENT CONSENT

I conform that the study was conducted in accordance with ethical guidelines and that patient consent was secured to view their data.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

SPSS: Statistical Package for the Social Sciences; **OR:** Odd's ratio; **CI:** Class interval; **RBC:** Red blood cells; **WHO:** World health organization.

SUMMARY

A prospective observational study was done taking 150 sample sizes considering both male and female to determine clinical aspects of Anemia in a tertiary care hospital. Patients were selected considering inclusion and exclusion criteria. The data was documented and analyzed using descriptive statistics and SPSS. The results show male gender being prone to anemia which can be an insult due to increased prevalence of alcoholic liver disease in males. Moreover, increased hospital stay worsens the risk of anemia without proper intervention at early stage.

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