

ORIGINAL ARTICLE

Frequency of Anemia in Patients with Newly Diagnosed Pulmonary Tuberculosis Presenting at Dr Ruth K M Pfau Civil Hospital Karachi

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ABSTRACT

OBJECTIVE: To determine the frequency of anemia in patients with newly diagnosed pulmonary Tuberculosis (PTB) presenting at Dr Ruth K M Pfau Civil Hospital Karachi (CHK).

METHODOLOGY: This cross-sectional study was conducted at Dr Ruth KM Pfau CHK from July to August 2023. Newly diagnosed pulmonary tuberculosis cases of either gender, between 14-40 years, were included, while patients with a history of PTB, malnutrition, blood loss, HIV, pregnant females, autoimmune disorders, anemia before the diagnosis of PTB, chronic illness and malignancies were excluded. PTB patients were labeled anemic if the hemoglobin level was <13g/dl in males and <12g/dl in females. Quantitative and qualitative variables were presented as descriptive statistics, giving mean, standard deviation, and frequency and percentages. Correlation and regression analysis of hemoglobin with age, gender and employment status was done. A *P*-value of ≤ 0.05 as significant.

RESULTS: Out of 150 patients, 91(60.7%) were male and 59(39.3%) were female. The frequency of anemia in males and females was 55.4% and 44.6%, respectively, which was not statistically significant ($p = .865$). A strong positive correlation of anemia with increasing age, with the highest frequency of anemia at 66.8% in age groups of >38 years compared to 6.8% in the 18-30 age group ($p < .001$) was present. Regression analysis showed age, gender and employment status were responsible for a 29.4% change in hemoglobin levels.

CONCLUSION: Anemia is common in patients with PTB and more common in patients with advancing age. Females had lower hemoglobin levels than males in PTB patients.

KEYWORDS: Pulmonary Tuberculosis, Anemia, Hemoglobin, iron deficiency anemia, Normocytic normochromic anemia, macrocytic anemia

INTRODUCTION

Tuberculosis is a rampant global health issue and the second most common infectious cause of death globally.¹ Estimated 10 million incident cases of Tuberculosis and around 1.4 million TB-associated deaths were reported in 2020¹. Pakistan stands fifth among countries with the highest burden of Tuberculosis alongside the fourth highest burden of Drug-Resistant Tuberculosis patients globally, with an estimated 510,000 incident cases reported each year². Anemia, affecting around 1.62 billion people globally, is a significant health problem that profoundly affects people's health and social and economic growth worldwide.

Anemia among various haematological and laboratory derangements is most frequently reported in PTB patients³. Several studies show variable frequencies of anemia in PTB patients; reports from Pakistan & India have their prevalence at 82.1% & 72.7%, respectively^{4,5}.

The presence of anemia in patients with PTB raises a four-fold risk of recurrence of PTB and is associated with a more lethal form of the disease and grave outcomes, including death⁶. Moreover, Anemic patients are found to have persistent positive smears by the end of two months of therapy. PTB patients should be periodically assessed for anemia, and if found to be an anemic underlying cause must be treated as there is a difference in response depending upon the underlying cause. Anemia is one of the markers for PTB diagnosis and helps in predicting prognosis and response to therapy⁶.

Anemia causes a delayed rate of sputum conversion and is a significant predictor of mortality in patients with PTB. It also increases the risk of recurrence and results in the worst clinical outcome in patients with PTB.⁷ Pakistan is the country where Tuberculosis is rampant, and because of the lack of local data on the presence of anemia in PTB. Our study will provide much-needed local data on the frequency of anemia in PTB; this will lead to better management and correction of anemia resulting in early sputum clearance and a positive impact on the progression of the disease.

METHODOLOGY

This cross-sectional study was done on patients attending OPD and admitted to Dr. Ruth KM Pfau CHK's medical wards from July to August 2023. The sample size was calculated using the reported prevalence of anemia in PTB of 89.2%⁸, the margin of error was kept at 5% and the confidence level at 95% as 150 patients. The sample size was calculated through Open Epi, Version 3. The sampling technique used was consecutive non-probability sampling.

Patients of PTB of either gender of age 18-45 years, who had one or more sputum smear specimens positive either by ZN Staining or Gene-Xpert at the start of treatment, were inducted into the study after informed written consent. Patients who had a history of pulmonary Tuberculosis in the past, patients on medications which can cause anemia, patients with a history of reduced meat and vegetable intake, patients with a history of Acid Peptic Disease, melena or upper gastrointestinal bleeding, diabetic patients diagnosed with HIC patients, Pregnant females, patients with a history of autoimmune disorders, history of anemia before the diagnosis of Tuberculosis, history of stroke, renal impairment, chronic liver disease and congestive cardiac failure and malignancies were excluded.

Brief information about the demographic characteristics, history of duration of illness, symptoms of Tuberculosis and anemia and compliance to anti-tuberculous drugs, family monthly income status, and occupational status was assessed by a trained interviewer and re-confirmed by the attendant. Demographic data, including age, gender, and duration of PTB, was collected. Blood was withdrawn by a phlebotomist, collected in a purple top EDTA tube, and analyzed by a Sysmex Automated Hematology Analyzer. Anemia was labeled if the hemoglobin level was less than 13.0 g/dl in males and less than 12.0 g/dl in females.

Data was analyzed on SPSS version 26. Mean \pm SD was calculated for quantitative variables like age, hemoglobin level and duration of symptoms of PTB. Frequencies and percentages were calculated for qualitative variables like gender, presence or absence of anemia & occupational status. Hemoglobin values were recorded as anemia present or absent in a new variable using criteria of <13 g/dl in males and <12 g/dl in females. The Student's t-test was used to compare means of hemoglobin and age by gender. The frequency of anemia was compared by gender and employment status by χ^2 -test. Age was stratified in a new variable into two groups of 18-30 years, 31-38 years & >39 years. The frequency of anemia was compared with these age groups by χ^2 -test. The correlation of variables age, gender, hemoglobin, and employment status was checked using the Pearson Correlation Test. Regression analysis was done by keeping the hemoglobin dependent variable while using age, gender, and employment status as independent variables. Significance was set at ≤ 0.05 .

RESULTS

One hundred fifty patients presenting with pulmonary Tuberculosis at the Department of Medicine, Dr Ruth KM Pfau CHK, who met the inclusion and exclusion criteria, were included in this study. The mean age & hemoglobin level in our study was 34.83±7.03 years & 12.10±1.55 mg/dl, respectively. A gender comparison of age was done using the Student's t-test. The mean age in males was 34.91±7.05 years, and in females was 34.71±7.05 years; there was no significant difference in age according to gender ($t(148) = -170, p = .865$). Of 150 patients, 91 (60.7%) were male and 59 (39.3%) were female. Anemia was present in 74 (49.3%) of patients, which included 41 (55.4%) males and 33 (44.6%) females. No statistically significant difference was observed in the frequency of anemia according to gender ($\chi^2(1) = 1.694, p = .193$) and employment status ($\chi^2(1) = .050, p = .823$), but significant differences in frequency of anemia was observed according to age groups showing the increasing frequency with increasing age ($\chi^2(2) = 42.224, p < .001$), details are given in **Table I**. Frequency distribution of occupational status showed that out of 150 patients, 25 (33.8%) were employed and 49 (66.2%) were unemployed.

Table I: Frequency and comparison of Anemia with Age Group, Gender and Employment Status by χ^2 test

		Anemia				Sig.
		Present		Absent		
		N	%	N	%	
Age Group	18-30 years	5	6.8%	29	38.2%	<.001**
	31-38 years	27	36.5%	39	51.3%	
	> 38 years	42	56.8%	8	10.5%	
Gender	Female	33	44.6%	26	34.2%	.193
	Male	41	55.4%	50	65.8%	
Employment Status	Employed	25	33.8%	27	35.5%	.852
	Unemployed	49	66.2%	49	64.5%	

** . Significance at <.01

Correlation between Age, Gender, Hemoglobin & Employment Status was done using Pearson's Correlation Test, and it was found that hemoglobin & age correlated negatively ($p < .001$) and hemoglobin & gender correlated positively ($p < .001$) also employment status & gender positively correlated ($p = .009$), details are given in **Table II**.

Table II: Correlation Matrix of Age, Gender, Hemoglobin & Employment Status by Pearson's Correlation Test

		Age	Gender	Hemoglobin
Gender	Pearson Correlation	.014		--
	Sig. (2-tailed)	.865		--
Hemoglobin	Pearson Correlation	-.388**	.369**	--
	Sig. (2-tailed)	<.001	<.001	--
Employment Status	Pearson Correlation	.047	-.214**	.152
	Sig. (2-tailed)	.571	.009	.064

** . Correlation is significant at <.01

Regression analysis showed the influence of independent variables of age, gender and employment status on hemoglobin levels with an R-square value of .294, showing that these variables were responsible for a 29.4% change in hemoglobin levels. (Table III)

Table III: Regression analysis of hemoglobin with age, gender and employment status

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Durbin-Watson
1	.542 ^a	.294	.280	1.3161	2.229

a. Predictors: (Constant), Employment Status, Age, Gender

b. Dependent Variable: Hemoglobin

DISCUSSION

PTB is a chronic illness caused by *Mycobacterium tuberculosis*. Globally, around 10 million people were affected by this devastating infectious disease in 2020, and it is responsible for the death of around 1.4 million people^{9,10}. Pakistan is among the six countries which hold around two-thirds of the global burden of Tuberculosis, along with the Philippines, Bangladesh, Indonesia, India and China¹⁰. The risk of having TB is 2.01 times greater in anemic than non-anemic patients¹¹.

Our study showed 49.3% of patients with PTB were anemic at the time of diagnosis on baseline investigations. In a multi-centre study, this frequency was quoted as 56%⁶. In our study, a significant increase in the frequency of anemia was observed with age, while no significant difference in frequencies was found between gender and employment status.

Tuberculosis can affect any system of the body, including the hematological system. Many abnormalities in the peripheral blood are reported in patients with pulmonary Tuberculosis that are caused by modulation of normal hematopoiesis^{12,13}. Hematological abnormalities act as a diagnosis marker and help in prognosis and response to treatment¹⁴.

Anemia can occur in any chronic disease, including TB, and many mechanisms have been postulated for this¹⁵. The most widely accepted mechanism is bone marrow suppression, but concomitant nutritional deficiencies and malabsorption abnormalities can enhance the severity of anemia¹⁶⁻¹⁸. It has been observed that there is an absence of iron in TB-associated anemia, and similar red cell distribution width was found in iron deficiency anemia, which is also one of the reported causes of anemia in tuberculous patients^{19,20}.

Our study did not report any significant difference in the frequency of anemia between genders in PTB patients; this is reported to be higher at 72.7% in neighbouring India⁵. Anemia of chronic disease was observed in 58.5%, while iron deficiency and megaloblastic anemia were found in 26.7% and 12.5%, respectively⁵. Forty-four percent pulmonary tuberculosis patients were found to be anemic in a study conducted in Sudan; 34% had anemia of chronic disease, iron deficient anemia was seen in 27%, severe iron deficiency anemia was present in 16%, macrocytic anemia in 5% and normochromic anemia in 18% cases. Anemia was associated with increase mortality and recurrence risk of Pulmonary Tuberculosis^{21,22}. It has also been shown to be an independent risk factor for mortality in PTB and muscle wasting, disease severity and progression^{6,23}.

A Korean study found 31.9% of patients with PTB were anemic. Anemia was more common in females and elderly individuals. Normocytic normochromic anemia was present in 71.9% of individuals in this study. Anemia was resolved in 64.6% of patients during or after anti-tuberculous treatment. Our analysis also showed a strong positive correlation of anemia with increasing age, with the highest frequency of anemia at 66.8% in age groups of >38 years compared to 6.8% in the 18-30 age group.

Another study performed in Brazil found 89.2% of PTB patients with anemia, of which 75.9% had anemia of chronic disease and 2.4% had iron deficiency anemia. Anemia was associated with male gender, low weight, low mean corpuscular volume, high ferritin, and erythrocyte sedimentation rate in this study.²⁴ High frequency of anemia demands screening all PTB patients for anemia and prompt treatment.¹⁵ This study was conducted in a tertiary care hospital. Hence, results need to be validated by performing multi-centric studies, and a workup for nutritional and other causes of anemia should be done.

For better treatment response, support from family and community is required; a survey by **Saqib SE et al.**²⁵ from Pakistan reported that items together for relaxation and help get your mind off things got the poorest support while the best support was noted in items to give you the advice and to prepare your meals, this highlights that these patients need better support in family get-together.

CONCLUSION

Pakistan is among the countries with a high Tuberculosis patient burden. The high frequency of anemia in newly diagnosed cases of PTB is of concern, and a search for its cause should be initiated.

Limitations: This study was conducted in a single centre tertiary care hospital, so results cannot be globalized to the general population; it needs to be validated by performing multicentric studies. We also did not investigate for nutritional and other causes of anemia.

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AUTHOR CONTRIBUTION

Hussain SM: Substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, Final approval of the version to be published

Abbasi A: Substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, Final approval of the version to be published

Zuberi BF: Drafting the article or revising it critically for important intellectual content, Statistical Analysis

Anoshia: Drafting the article or revising it critically for important intellectual content, Statistical Analysis

All authors agree to be accountable for all aspects of the work to ensure that questions related to the accuracy or integrity of any part are appropriately investigated and resolved.

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