Original Article

Anemia and Nutritional Status in Tuberculosis Patients

Sandeep Chhabra, Anil Kashyap[1], Monica Bhagat, Rajesh Mahajan, Suman Sethi[2]

Departments of Medicine, [1]Chest, [2]Nephrology, Dayanand Medical College and Hospital, Ludhiana, India

Abstract

Introduction: Anemia is a common complication of pulmonary tuberculosis (TB). Nutritional deficiency and malabsorption syndrome can deepen the severity of anemia. The aim of the present study was to study anemia and nutritional status in patients with TB at a tertiary care center. **Materials and Methods:** All patients diagnosed with TB (pulmonary and extrapulmonary), registered with Revised National TB Control Programme (RNTCP), taking DOTS regimen, attending the outpatient department as well as those admitted in the medicine and chest units of a tertiary care hospital, were enrolled in the present study. **Results:** Anemia was more common between the age groups of 51 and 60 years, with distribution of males (87 [58%]), patients with diabetes (49 [32%]), and hypertensive patients (29 [19.3%]). In our study, 48 (85.7%) out of 56 patients diagnosed with extrapulmonary TB were found to have anemia; similarly, 77 (88.5%) out of 87 patients diagnosed to have pulmonary TB were anemic. Anemia of chronic disease (128 [97.17%]) was higher when compared to that of those with iron-deficiency anemia (3 [2.29%]). According to body mass index (BMI), 135 (90%) patients were underweight; according to mid-arm circumference (MAC), 131 (87.3%) patients had severe malnutrition; and according to waist–hip ratio [WHR], 96 (64%) patients were underweight. **Conclusion:** Anemia was common in males and alcoholics, and there was a high prevalence of anemia of chronic disease. In addition, anemia was associated with high erythrocyte sedimentation rate and C-reactive protein. High proportions of TB patients (pulmonary and extrapulmonary) were classified as underweight and malnourished on the basis of different parameters (BMI, MAC, and WHR); in addition, the degree of malnutrition was higher in patients with anemia than in those without.

Keywords: *Anemia, extrapulmonary, nutrition, pulmonary, tuberculosis*

Introduction

Tuberculosis (TB) has been a leading cause of disease and enemy of humanity for millennia. Mycobacterial infections causing TB and leprosy are bacterial diseases of global importance. According to the World Health Organization (WHO) estimates, one-third of the world population is infected with *Mycobacterium tuberculosis*. It is estimated that approximately 8.8 million new cases of TB occur each year. Genetic studies suggest that *M. tuberculosis* has been present since ancient times. Evidence of TB in humans dates back around 2400 BC.[1]

Many patients with pulmonary TB exhibit decreased levels of hemoglobin, which can directly impact TB-associated morbidity. WHO criteria were used to classify the severity of anemia (hemoglobin [Hb] 13.0 g/dL for men and 12.0 g/dL for women), mild anemia (11.0 ± 12.9 g/dL for men and 11.0 ± 11.9 g/dL for women), moderate anemia (8.0 ± 10.9 g/dL for men and women), or severe anemia (8.0 g/dL for men and women).[2] Anemia of chronic diseases, also known as anemia of inflammation, is a clinical syndrome characterized by the development of anemia in patients with (fungal, bacterial, or viral) infectious diseases, such as inflammatory diseases, TB, neoplastic diseases, and autoimmune diseases. The association between TB and malnutrition consists of two interactions: effect of malnutrition on the clinical manifestations of TB and the effect of TB on nutritional status, as a result of immunological impairment.[3] Many studies have been done which show a high prevalence of anemia among TB patients, and there is some evidence to suggest that at the time of diagnosis, it is associated with an increased risk of mortality.[3] Among the anemias that are characterized by altered iron metabolism, iron-deficiency anemia and anemia of chronic disease are the most common. Malnutrition and TB

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Address for correspondence:
Dr. Suman Sethi, Department of Nephrology, Dayanand Medical College and Hospital, Ludhiana, India.
E-mail: suminitin@gmail.com

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are both problems of considerable magnitude in most of the underdeveloped regions of the world, mainly in South Asian countries. It is important to consider, how these two problems tend to interact with each other.[4] Malnutrition is associated with an increased severity, frequency, and fatality of infections, including TB, while infections in turn lead to malnutrition. At the population level in India, malnutrition is the most widely prevalent risk factor for TB. The prevalence of widespread malnutrition in the population may be expected to pose some problems with regard to the control of TB in developing countries, from the larger point of view of prevention, and therapeutic management of individual cases, from the narrower clinical point of view.[4,5]

Materials and Methods

All patients who have been diagnosed with TB (pulmonary and extrapulmonary), registered with RNTCP and taking DOTS regimen, attending the outpatient department as well as those admitted in the medicine and chest units of a tertiary care center, were enrolled in this study. The inclusion criteria were as follows: patients with age more than 18 years diagnosed to have TB (pulmonary and extrapulmonary), those with positive smear- or culture-compatible pathology result, or those with CBNAAT/line probe/positive TB polymerase chain reaction, or those with lymphocyte-dominant exudate pleural effusion with high ADA. The exclusion criteria were as follows: patients with age <18, those with malignancy, those with chronic renal disease, those with congestive cardiac failure, pregnant women, and patients who did not give consent for the study.

We included 150 patients in our study, on the basis of the following formula: $n = (Z^2\alpha \times P \times [1 - P])/d^2$, assuming confidence level at 95% and precision (d) at ± 7%. Detailed clinical data of the patients were recorded as per pro forma. Baseline hemogram was noted, on the basis of which patients were divided into anemic and nonanemic groups. Those patients who were found to have anemia (131 patients) were studied in detail for the type of anemia. Their mean corpuscular volume (MCV), red cell distribution width (RDW), serum iron, ferritin levels, and total iron-binding capacity (TIBC) were studied, and patients were classified into groups of anemia chronic disorder and iron deficiency of anemia. Other investigations done were as follows: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), liver function tests, and renal function tests. Iron-deficiency anemia was characterized by decreased level of iron and ferritin and increased level of TIBC. Anemia of chronic disorder was characterized by decreased level of iron TIBC and increased levels of ferritin.

In addition, the nutritional status of the patients was studied based on various indices such as weight, height to calculate body mass index (BMI), mid-arm circumference (MAC), waist–hip ratio (WHR), and subjective global assessment (SGA) to identify patients who were underweight, healthy, and overweight.

A written informed consent was taken from the patients. The study protocol was approved by the institutional ethics committee, and it conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Appropriate statistical tests were applied to analyze the data. Descriptive statistics were performed; Student's *t*-test was used to compare means with normal distribution between the groups of patients with and without anemia. Chi-square test was used to identify associations among categorical variables. Values of $P < 0.05$ were considered statistically significant.

Results

Majority of the patients were male (87 [58%]) and 63 (42%) patients were females. Forty-nine (32.7%) patients were diabetic, 29 (19.3%) were hypertensive, and 2 (1.3%) had bronchial asthma [Table 1].

A total of 87 (58%) patients had pulmonary TB, 56 (37.3%) patients had extrapulmonary TB, and 7 (4.7%) had both pulmonary and extrapulmonary TB. All anemic patients (128 [97.7%]) had anemia of chronic disorder and 3 (2.29%) had iron-deficiency anemia.

A total of 114 (87%) patients had low TIBC levels, 3 (2.3%) patients had high TIBC levels, and 14 (10.7%) had normal TIBC levels. A total of 89 (67.9%) patients had normal MCV levels and 42 (32.1%) patients had low MCV levels. A total of 64 (48.69%) patients had low folic acid levels and 61 (46.6%) patients had normal folic acid levels and 6 (4.6%) patients had high folic acid levels. A total of 98 (74.8%) patients had high ferritin levels, 30 (22.9%) patients had normal ferritin levels, and 3 (2.3%) patients had low ferritin levels.

A total of 130 (99.2%) patients had high ESR levels and 1 (0.8%) patient had low ESR levels. A total of 135 (90%) patients were underweight, 15 (10%) patients had normal weight, and none of the patients were overweight. A total of 131 (87.3%) were severely malnourished, 18 (12%)

Table 1: Characteristics of patients

Presenting complaints	Number of cases (n=150), n (%)
Fever	101 (67.3)
Cough	48 (32.0)
Decreased appetite	40 (26.7)
Headache	30 (20.0)
Vomiting	15 (10.0)
Altered sensorium	2 (1.3)
Shortness of breath	2 (1.3)
Irrelevant talk	1 (0.7)
Throat pain	1 (0.7)

were moderately malnourished, and 1 (0.7%) patient had normal nutritional status [Table 2].

A total of 137 (91.3%) patients had low level of serum albumin and 13 (8.7%) patients had normal albumin levels. A total of 96 (64%) patients were underweight, 45 (30%) patients had ideal weight, and 9 (6%) patients were overweight. SGA is summarized in Table 3.

Forty-five (91.84%) out of 49 patients who were diabetic had anemia and 28 (96.5%) out of 29 patients who were hypertensive had anemia. There was no statistical association between anemia and comorbidities as the number of patients without anemia was less.

Fifty-three females (84.13%) out of 63 patients were anemic and 78 males (89.6%) out of 87 patients were anemic. The association between anemia and gender was found to be statistically insignificant (P = 0.315). The two groups were comparable with respect to the number of anemic patients; hence, no statistical significance was seen (P = 0.879) [Table 4].

Majority of the patients were found to have normal to raised ferritin levels with low iron levels, suggesting anemia of chronic disorder. A total of 111 patients had decreased levels of iron, 4 patients had decreased ferritin levels, and 3 patients had increased TIBC levels, suggesting 52 patients with iron-deficiency anemia. There was no significant association found between the components of iron metabolism and red cell morphology. ESR was raised in almost all the patients irrespective of the status of anemia. An association between anemia and inflammatory markers was seen. The patients who were anemic had significantly raised ESR (82.64 ± 46.80) as compared to those who were not anemic (60.47 ± 24.28) (P = 0.045) [Table 5].

Table 2: Mid-arm circumference

MAC (cm)	Number of cases (n=150), n (%)
Severe (<21)	131 (87.3)
Moderate (22-23)	18 (12.0)
Normal (>23)	1 (0.7)

MAC: Mid-arm circumference

Table 3: Subjective global assessment

Subjective global assessment	Number of cases (n=150), n (%)
A (well nourished)	12 (8.0)
B (mild to moderate)	56 (37.3)
C (severely malnourished)	82 (54.7)

Table 4: Association between anemia and type of tuberculosis

Type of tuberculosis	Anemia		Total	χ^2	P
	N (n=19), n (%)	Y (n=131), n (%)			
E	8 (14.29)	48 (85.71)	56	0.257	0.879
P	10 (11.49)	77 (88.51)	87		
P + E	1 (14.29)	6 (85.71)	7		

E: Extrapulmonary, P: Pulmonary, P + E: Both pulmonary and extrapulmonary

Discussion

In this study, the mean age of the anemic patients was 51.28 ± 16.17 years, with the maximum number of patients 42 (28%) being in the age group of 51–60 years: males (87 [58%]) and females (63 [42%]). In this study, it was found that of the total 150 patients, majority of the patients had pulmonary TB (87 [58%]) followed by extrapulmonary TB (56 [37.3%]). In our study, 48 (85.7%) out of the 56 patients diagnosed with extrapulmonary TB were found to have anemia; similarly, 77 (88.5%) out of the 87 patients diagnosed to have pulmonary TB were anemic. The two groups were comparable with respect to the number of anemic patients; hence, no statistical significance was seen. Lee *et al*.[6] in their study found that out of the total 880 patients, 596 (67.7%) had pulmonary TB, 72 (8.2%) had TB pleurisy, 67 (7.6%) had TB lymphadenitis, and 47 (5.3%) had musculoskeletal TB, which were similar to the observation in our study. In this study, 131 (87.3%) out of 150 patients had anemia. The proportion of patients with anemia of chronic disease (128 [97.17%]) was higher than was that of those with iron-deficiency anemia (3 [2.29%]). This finding was similar to that reported in a study conducted by Oliveira *et al*.,[7] who included 166 patients, of which 18 (10.9%) had no anemia and 148 (89.1%) had anemia. The prevalence of anemia of chronic disease and iron-deficiency anemia was, respectively, 75.9% and 2.4%. Anemia was more pronounced in advanced TB as diagnosed by chest radiography. Lower hemoglobin (Hb) concentrations in TB patients were accompanied by lower plasma Fe concentrations, lower iron-binding capacity, and higher plasma ferritin; similar results were found in our study. In this study, we found 111 patients with decreased levels of iron, 4 patients with decreased ferritin levels, and 3 patients with increased TIBC levels, which suggested iron-deficiency anemia. Most of the patients in our study had normal to raised ferritin levels with low iron levels, suggesting anemia of chronic disorder in these patients. The RDW test measures variation in red blood cell (RBC) size or RBC volume as a part of a complete blood count, and it is used along with other RBC indices, especially MCV, to help determine the causes of anemia.[8] It is concluded that RDW values in the chronic inflammatory disorder TB are not significantly different from those occurring in iron-deficiency anemia. MCV is the average volume of red cells in a specimen. MCV is elevated or decreased in accordance with average red cell size, i.e. low MCV indicates microcytic RBCs (small average RBC size), normal MCV indicates normocytic RBCs (normal average RBC size), and high MCV indicates macrocytic RBCs (large average RBC

Table 5: Association between anemia and hematological parameters

Parameter	Anemia		Total	χ^2	*P*
	N (*n*=19), *n* (%)	Y (*n*=131), *n* (%)			
Iron					
Low	15 (78.95)	111 (84.73)	126	0.413	0.509
Normal	4 (21.05)	20 (15.27)	24		
TIBC					
High	0	3 (2.29)	3	0.831	0.660
Low	16 (84.21)	114 (87.02)	130		
Normal	3 (15.79)	14 (10.69)	17		
MCV					
Low	6 (31.58)	42 (32.06)	48	0.002	0.966
Normal	13 (68.42)	89 (67.94)	102		
RDW					
Low	1 (5.26)	1 (0.76)	2	2.713	0.258
Normal	3 (15.79)	27 (20.61)	30		
High	15 (78.95)	103 (78.63)	118		
Folic acid					
Low	9 (47.37)	64 (48.85)	73	0.026	0.987
Normal	9 (47.37)	61 (46.56)	70		
High	1 (5.26)	6 (4.58)	7		
Ferritin					
Normal	9 (47.37)	29 (22.14)	38	5.883	0.053
Low	0	4 (3.05)	4		
High	10 (52.63)	98 (74.81)	108		
ESR					
Low	1 (5.26)	1 (0.76)	2	2.554	0.238
Normal	18 (94.74)	130 (99.24)	148		

TIBC: Total iron-binding capacity, MCV: Mean corpuscular volume, RDW: Red cell distribution width, ESR: Erythrocyte sedimentation rate

size).[8] In this study, by distributing patients into different groups, we found that 89 (67.9%) patients had normal MCV levels and 42 (32.1%) had low MCV levels. This study showed that 122 (93.1%) patients had normal MCH levels, 7 (5.3%) had low MCH levels, and 2 (1.5%) patients had high MCH levels. RBC morphology was estimated by correlating Hb concentration, MCV, mean Hb concentration, and RDW. RBC morphology was considered predominantly normocytic normochromic RBCs, in which MCV was within 80 fl to 100 fl, MCH was 27 pg–32 pg. The ESR and CRP are among the oldest laboratory tests, which are still in use. Both blood tests are used to detect inflammation in the body. Inflammation can present as either acute (i.e. from injury or infection) or chronic. Regarding the inflammatory state, the results showed that ESR was higher in patients with anemia than in those without. ESR increases in response to anemia.[9] When we compared the groups of patients with and without anemia in terms of their nutritional status, we found that malnutrition was more severe in the former, who had low serum concentrations of TIBC and high serum concentrations of ferritin. In this study, we found that 135 (90%) patients were underweight, 15 (10%) had normal nutritional status, and none of the patients were overweight.

On the basis of the MAC and WHR, 131 (87.3%) of the 150 patients and 96 (64%) of the 150 patients were found to be malnourished. Contrary to our results, Lombardo *et al*.[10] found that the weight was measured to the nearest 0.1 kg and height to the nearest 1 mm. Mid upper-arm circumference (MUAC) was measured to the nearest 1 mm and skin fold thickness was measured to the nearest 0.2 mm. The median BMI for TB cases was 18.80 kg/m^2. There was a statistically significant difference in weight (P = 0.002) and MUAC (P = 0.000) between the groups. Similar results were found in a study conducted by Tungdim *et al*.[11] In their study, several anthropometric measurements and the indices of adiposity such as BMI, WHR, waist–height ratio, and grand mean thickness were studied. Wasting of muscle mass and decrease in fat percentage because of chronic disease (TB). SGA appears to be a useful tool for nutritional assessment of patients with TB (pulmonary and extrapulmonary). In this study, on the basis of SGA, 12 patients (8%) were categorized as SGA Class A, 56 patients (37.3%) as Class B, and 82 patients (54.7%) as Class C. Similar results were observed by Miyata *et al*.[12] that the majority of patients were male (64.1%). Twelve patients (30.1%) were categorized as SGA Class A, 14 patients (35.9%) as Class B, and 13 patients (33.3%) as Class C. Our study's significance was in gaining knowledge about TB-associated anemia by clarifying its prevalence, characteristics through involving and to study nutritional status in patients with pulmonary and extrapulmonary 62 TB. This study was also not without its limitations. First, the study was applied to a single tertiary care center and had limited number of patients. Therefore, multicentric studies performed by multiple observers with larger populations of patients are necessary to confirm the present finding. Second, we could not follow-up the patients.

Ethical clearance

Institutional Ethics Committee, Dayanand Medical College and Hospital.

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Conflicts of interest

There are no conflicts of interest.

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