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Prevalence of iron deficiency anaemia in tuberculosis

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***Abstract*---**Introduction: In India, Tuberculosis is endemic disease with more than 90% of population are in latent infection. In this study we measure the prevalence of iron deficiency anaemia in newly diagnosed TB cases. Methodology: An Observational cross-sectional study was conducted at Respiratory Medicine, MIMS, Nellimarla, Vizianagaram District, and Andhra Pradesh State from July 2020 to June 2021. Inclusion criteria were newly diagnosed TB patients of age >18 years. Exclusion criteria were Immunocompromised, Pregnancy, Patients with malignancy, Patients with past history of TB and who are receiving ATT Unwilling to participate. Results: During the one year study period, a total of 50 patients were included. 32 were male and 18 were female. The study showed decrease in Iron, Hemoglobin, Transferrin and Transferrin saturation and increase in TIBC and Ferritin levels. They are many available methods for assessing anaemia at primary care level and to treat or iron prophylactic supplementation. Conclusion: In the present study, it was concluded that iron metabolism was altered in pulmonary tuberculosis. A low serum iron, transferrin and transferrin saturation with increase in ferritin and TIBC. Ferritin plays essential role in iron homeostasis by binding and sequestering intracellular iron. Increase in ferritin in response to infection was attributed to prevent iron availability to MTB

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so as to inhibit its growth and multiplication. Treating or Prophylactic iron supplementation should be implemented for all newly diagnosed Tuberculosis cases.

***Keywords*---**tuberculosis, iron profile, anemia.

Introduction

Tuberculosis (TB), an infectious disease caused by Mycobacterium tuberculosis (MTB), is characterised by tubercle bacilli displaying intracellular survival strategies and chronic pulmonary inflammation.[1] Preventing TB infection is thus a crucial global health issue and assessment of modifiable risk factors helps to formulate TB control policies.[2,3] Some risk factors like DM[4], CKD[5], tobacco smoking[6], alcohol use[7], body mass index[8], HIV infection[9] are known for decades.

In host, excess Fe leads to cellular toxicity by Fe catalyzed generation of harmful Reactive oxygen intermediates and hydroxyl radicals that damage lipids, DNA and Proteins. Build up of Fe in tissue and organs increases risk of arthritis, cancer, liver problems, diabetes and heart failure. High iron stores are related to many infectious diseases and inflammatory response, as exemplified by malaria, viral and neurodegenerative diseases.[10] TB is caused by Mycobacterium tuberculosis (MTB) which has an absolute requirement of Iron (Fe) for growth and multiplication. In MTB, Fe enters via siderophore mediated uptake where it is required for bacterial growth and multiplication, but any excess if occurs in MTB is toxic due to its catalytic role in generation of free radicals.[4]

However, Fe metabolism in MTB is regulated at the level of uptake. In host, Iron hemostasis is maintained by various mechanisms at the level of uptake, transport and storage in healthy conditions this hemostatic mechanism is disturbed in diseased state mediated by acute phase response and effect of infection.[5] The study here will discuss the effect of mycobacterial load and clinical severity of PTB on Fe acquisition by the host in the form of Transferrin and Ferritin. However, only few studies are there to assess link between nutritional iron deficiency and high TB prevalence.

Methodology

Study Design: Observational cross-sectional study
Study Duration**:** July 2020 to June 2021

Inclusion criteria
Newly diagnosed TB patients of age >18 years

Exclusion criteria
Immunocompromised
Pregnancy
Patients with malignancy
Patients with past history of TB and who are receiving ATT
Unwilling to participate

Results

During the study period of 12months, a total of 50 patients were included. Among them, 32 were males (64%) and 18 were females (36%). Average age group is 42years in males and 54 in females. Present study showed decrease in Iron, Hb, Transferrin and Transferrin saturation and increase in TIBC and Ferritin levels.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. A t-test is a statistical test that is used to compare the means of two groups. It is often used in hypothesis testing to determine whether a process or treatment actually has an effect on the population of interest, or whether two groups are different from one another with the null hypothesis (H0) is that the true difference between these group means is zero and the alternate hypothesis (Ha) is that the true difference is different from zero. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Statistical software: The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Table 1: Gender Frequency Distribution of patients studied

Gender	No. of Patients	%
Male	32	64.0
Female	18	36.0
Total	50	100.0

Table 2: Age in yrs- Frequency Distribution of patients studied

Age in Years	Gender		Total
	Male	Female	
<20	1(3.1%)	1(5.6%)	2(4%)
20-30	5(15.6%)	5(27.8%)	10(20%)

31-40	5(15.6%)	4(22.2%)	9(18%)
41-50	13(40.6%)	1(5.6%)	14(28%)
>50	8(25%)	7(38.9%)	15(30%)
Total	32(100%)	18(100%)	50(100%)

P=0.072+, Significant, Fisher Exact Test

Table 3: clinical variables - Frequency Distribution of patients studied

Variables	**Gender**		**Total**	**P Value**
	Male	**Female**		
HAEMOGLOBIN				
<12	28(87.5%)	18(100%)	46(92%)	0.282
12-16	4(12.5%)	0(0%)	4(8%)	
>16	0(0%)	0(0%)	0(0%)	
S.IRON				
<40	15(46.9%)	15(83.3%)	30(60%)	0.026*
40-100	12(37.5%)	3(16.7%)	15(30%)	
>100	5(15.6%)	0(0%)	5(10%)	
FERRITIN				
<10	4(12.5%)	0(0%)	4(8%)	0.069
10-154	18(56.3%)	7(38.9%)	25(50%)	
>154	10(31.3%)	11(61.1%)	21(42%)	
TIBC				
<250	4(12.5%)	0(0%)	4(8%)	0.022*
250-450	14(43.8%)	3(16.7%)	17(34%)	
>450	14(43.8%)	15(83.3%)	29(58%)	
TRANSFERRIN				
<188	17(53.1%)	16(88.9%)	33(66%)	0.031*
188-341	12(37.5%)	2(11.1%)	14(28%)	
>341	3(9.4%)	0(0%)	3(6%)	
TRANSFERRIN SATURATION				

<11	16(50%)	13(72.2%)	29(58%)	0.219
11-50	16(50%)	5(27.8%)	21(42%)	
>50	0(0%)	0(0%)	0(0%)	
Total	32(100%)	18(100%)	50(100%)	

Chi-Square Test/Fisher Exact Test

Table 4: Comparison of Clinical Variables According To Gender

Variables	Gender		Total	P Value
	Male	Female		
AGE IN YEARS	42.34±11.67	41.83±15.09	42.16±12.85	0.894
HAEMOGLOBIN	10.65±1.52	9.14±1.04	10.11±1.54	<0.001**
S.IRON	57.5±33.25	34.33±11.14	49.16±29.47	0.006**
FERRITIN	91.38±60.86	141.56±46.77	109.44±60.78	0.004**
TIBC	425.31±121.84	522.22±77.93	460.2±117.08	0.004**
TRANSFERRIN	173.22±81.19	111.61±40.84	151.04±75.11	0.004**
TRANSFERRIN SATURATION	12.72±5.29	10.5±4.09	11.92±4.96	0.131

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P £ 0.05)
** Strongly significant (P value: P£0.01)

Discussion

TB is one of the most common infectious diseases in developing countries like India due to its relation to poverty. Various risk factors predispose to developing TB. Anemia in TB increases the risk of death.[11] Iron deficiency anemia is one among the risk factors.IDA, itself, is the most common micronutrient deficiency in general population as well as in TB patients. Normally, iron metabolism is tightly regulated. Iron homeostasis is deregulated in several lung diseases like lung cancer. CF, IPF, asthma.[12] Due to high oxygen exchange and large blood supply, lungs are more prone to metal induced oxidative stress. Either deficiency or excess of iron can compromise immune and cellular functions. Low iron status may impair motor activity and enhance disease susceptibility. Hence, we studied the prevalence of anemia in TB cases (16. Cancado R D, Chiattone CS. Anemir da doenca cronica. Res Bras Hematol Hemoter. 2002; 24 (2): 127-36.3).

Out of 50 TB patients, 64% were males and 36% were females. Average age of males was 42.34+ 11.67 years and a females was 41.83+ 15.09. No significant

difference was seen between males and females with regard to age. The present study showed decrease in iron, hemoglobin Transferrin and Transferrin saturation. Whereas increase levels 0f TIBC, Ferritin (Table -3). Mean serum iron in males was 57.50+33.25 and female was 34.33+11.40. Iron levels are low in both males and females which could be due to dietary deficiency, malabsorption due to hook worm infestation or any secondary infection or increased blood loss like hemoptysis. When compared to males, females have very low iron levels.

Iron acts as catalyst for DNA replication and multiplication of TB bacilli. To inhibit the growth of MTB, host innate immunity causes pathogenic iron deficiency by shifting available Fe^{+2}(Ferrous) to stored form Fe^{+3}(Ferric).Thus inhibiting the growth of MTB.[14] This is the major inflammatory response causing anemia in TB. Mean serum Ferritin was 91.38+60. In males and was 141.56+46.70 in females. Ferritin is an acute phase protein that elevates in various infectious and non- infectious conditions. In acute infections and oxidative stress, very high Ferritin levels are noted as seen in a study, where high Ferritin levels are noted as seen in MTB patients accounting for 42% of all cases.[10]

In a study done by Morris et al, High Ferritin levels are seen in 81% of TB patients which gradually becomes normal with the ant tubercular treatment.[15] Ferritin levels was found to be higher in smokers than non smokers, High Ferritin levels indicate the extent of oxidative stress and inflammation, hence can be used as a marker to assess disease activity and mortality risk.[16] Mean Transferrin levels was 173.22+81.19 in males and 111.61+ 40.84 in females with a P valve of 0.004. Transferrin decreases in malnutrition state and in any infectious process. During stress conditions, liver increases the synthesis of inflammatory mediators like cytokines and decreases the synthesis of proteins that are not required for inflammatory response like albumin and Transferrin. Hence Transferrin levels are reduced which is in correlation to our study population.

As the severity of inflammatory response increases, Transferrin levels decreases indicating strong correlation between Transferrin and severity of disease.[17] As the Transferrin decreases< Transferrin saturation also decreases and TIBC increases. A study showed that newly diagnosed TB patients have low Transferrin when compared to TB patients who are already receiving ATT, suggesting that as the inflammation decreases, synthesis of Transferrin by liver also increases.[18]

Conclusion

In the present study, it was concluded that iron metabolism was altered in pulmonary tuberculosis. A low serum iron, transferrin and transferrin saturation with increase in ferritin and TIBC. Ferritin plays essential role in iron homeostasis by binding and sequestering intracellular iron. Increase in ferritin in response to infection was attributed to prevent iron availability to MTB so as to inhibit its growth and multiplication. Treating or Prophylactic iron supplementation should be implemented for all newly diagnosed Tuberculosis cases.

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