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Original Research Article

STUDY OF IRON PROFILE IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Abstract

Background: Tuberculosis (TB) is a major cause of illness and death worldwide, its incidence and mortality rates have increased in recent years. Iron and iron metabolism is essential for normal physiological function and TB-causing bacteria, but its availability is regulated by the host's immune system. **Aims and Objectives:** 1. To assess the serum iron parameters in patients with pulmonary tuberculosis. 2. To estimate the association between serum iron levels and disease severity. **Material and Methods:** Settings and Design - Cross sectional study, Source of Data – Medical record department. Sampling method – Consecutive sampling method, Sampling period – May 2021 to May 2022. Statistical analysis used - Descriptive statistics and Chi-square test. **Results:** Among the 100 participants,71 patients (71%) were males and 29 patients (29%) females, and the mean age of the participants was 49.23±16.70. Physical examination showed that most participants had pallor. In terms of biochemical profile, the mean haemoglobin level was low(9.39±1.28 g/dl),the mean serum iron level was low(30.80±17.31 µg/dl)which is associated with severity of disease, the mean serum TIBC level was 163.16±66.67 µg/dl, with a median value of 156.5 µg/dl, indicating normal to high levels of TIBC in the blood, the mean transferrin saturation level was low(21.65±14.21%),the mean serum ferritin level was high(652.92±525.22 ng/ml),the mean serum CRP level was high(81.18±82.20 mg/l), indicating a high level of inflammation in the body. **Conclusion:** Most of the patients diagnosed with pulmonary tuberculosis have iron deficiency and which is directly associated with severity of disease.

INTRODUCTION

Tuberculosis (TB) is a communicable disease that is a major cause of ill health and also it is one of the leading causes of death worldwide. TB is caused by the bacillus Mycobacterium tuberculosis, which is spread mainly through aerosols. The disease commonly affects the lungs (pulmonary TB) but can affect other sites as well. Iron is required for many vital functions including transport of oxygen and energy metabolism. Epidemiological evidences indicate that iron stores are associated with disease susceptibility and mortality. Iron is an essential micronutrient for both humans and pathogenic microbe. Mycobacterium tuberculosis bacilli requires iron for survival and competes with the host for the same iron pool. It releases siderophores, namely exochelins, which have a high affinity for iron and can remove it from the host's iron-binding molecules. Mycobacterium tuberculosis (MTB) disrupts phagolysosome maturation, an iron dependent process critical for pathogen survival and utilize several mechanisms to obtain host iron. Evidence links iron with Pulmonary TB pathogenesis both from the perspective of the pathogen and the host. Most strikingly, a pattern of altered host iron status characterized by high ferritin, low transferrin, and low haemoglobin has been identified as a risk factor for progression to Pulmonary tuberculosis. Targeting iron metabolism has the potential to directly inhibit the growth of MTB, by interfering with MTB specific iron pathways and its survival mechanisms. Many studies had documented high prevalence of anaemia in TB patients and its association with severity.[1] Studies have also shown that excess iron may enhance growth of MTB and have an adverse outcome of human tuberculosis.[2] When Fe builds

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up in tissue there is increased risk of diabetes, arthritis, cancer, liver problems, and heart failure. High iron stores are associated with many infectious diseases and inflammatory response, as seen in malaria, viral and neurodegenerative diseases.[3]

Mycobacterium tuberculosis (MTB) has an absolute requirement of Iron (Fe) for growth and multiplication. In MTB, Fe enters via siderophore mediated uptake where it is essential 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]

Our study is done to examine the iron levels in Pulmonary Tuberculosis patients and its association with the disease severity.

MATERIALS AND METHODS

Ours is a hospital based cross sectional study. Data is collected from 100 patients who are diagnosed with pulmonary tuberculosis on outpatient department basis and patients admitted to SDM hospital ward from May 2021 to May 2022, after taking the institutional ethical clearance. A pre-designed and pre-tested questionnaire was used to collect personal and sociodemographic data. General and systemic examination was done. Assessment of disease severity is done by "Bandim TB Score" system. It classifies Pulmonary tuberculosis into different classes of severity. The score consists of five symptoms: cough, haemoptysis, dyspnoea, chest pain, and night sweats followed by six signs: anaemia, tachycardia (pulse >90/min), abnormalities in chest auscultation, fever, body mass index (BMI), and MUAC. Severity of disease is classified as Class I (for score 0-5) is least severe, Class II (for score 6-7) is moderately severe and Class III (for score 8-13) is most severe. Baseline haematological and biochemical parameters will be assessed. Statistical analysis was done using SPSS version 23.0. Descriptive statistics and Chi-square test was used to assess the association between two variables. A $p \leq 0.05$ was considered as statistically significant.

Ethical committee: Ethical clearance was obtained from Institutional Ethical Committee (Ref no – SDMCMS&H/IEC :28 :2021).

RESULTS

Total 100 patients are included in the study. Table 1 represents the general characteristics and biochemical profile of the study population. The study included 100 participants, out of which 71 (71%) males and 29 (29%) females. The mean age of the participants was 49.23±16 years. Regarding general physical examinations, 69 (69%) patients had pallor, while 1 (1%) had icterus, 11 (11%) had pallor and clubbing, 2 (2%) had pallor and cyanosis, 2 (2%) had pallor and icterus, and 12 (12%) had pallor and lymphadenopathy. Additionally, 3 (3%) participants had pallor, clubbing, and lymphadenopathy. The sputum status of the participants revealed that 30 (30%) had AFB, while 70 (70%) had CBNAAT. In terms of biochemical profile, the mean blood sugar level was 97.64±22.34 mg/dL, the mean serum protein level was 6.31±0.59 gm/dL, and 73 (73%) participants had serum albumin levels below 3.5 gm/dL, while 26 (26%) had levels above 3.5 gm/dL. Albumin is a component of plasma antioxidant activity and a negative Acute Phase Protein whose concentration decreases in any inflammatory condition, injury or stress as a result of increased metabolic need for tissue repair and free radical neutralization.[5]

Table 2 represents the mean and standard deviation values of various biochemical parameters measured in the study population. The findings show that the mean haemoglobin level was 9.39±1.28 gm/dl, which is lower than the normal range. The mean serum iron level was 30.80±17.31 µg/dl, indicating a low level of iron in the blood. The mean serum TIBC level was 163.16±66.67 µg/dl, with a median value of 156.5 µg/dl and an interquartile range of 123.25-200 µg/dl, indicating normal to high levels of TIBC in the blood. The mean transferrin saturation level was 21.65±14.21%, which is lower than the normal range. The mean serum ferritin level was 652.92±525.22 ng/ml, which is higher than the normal range. The mean serum CRP level was 81.18±82.20 mg/l, indicating a high level of inflammation in the body.

Table 3 provides information on the mean comparison between different biochemical parameters among the two groups according to the severity of disease. It was found that mean difference of Serum iron levels, serum TIBC and serum ferritin levels between the two groups was significantly different. (P<0.05).

Table 1: General characteristics and Biochemical profile of study population

S. No	General Characteristics	N (%)	Mean ± SD
1.	**Total Participants**	100(100)	
2.	**Mean Age in years**		49.23±16.70
3.	**Sex**		
	Males	71(71)	
	Female	29(29)	
4.	**General Physical Examination**		
	Pallor	69(69)	
	Icterus	1(1)	
	Pallor and Clubbing	11(11)	
	Pallor and Cyanosis	2(2)	
	Pallor and Icterus	2(2)	

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	Pallor and Lymphadenopathy		12(12)	
	Pallor, Clubbing, Lymphadenopathy		3(3)	
6.	**Sputum status**	AFB	30(30)	
		CBNAAT	70(70)	
7.	**Blood Sugar (mg/dl)**			97.64±22.34
8.	**Serum Urea (mg/dl)**			19.69±9.67
9.	**Serum Creatinine (mg/dl)**			0.77±0.25
10.	**Serum Protein (g/dl)**			6.31±.59
11.	**Serum Albumin**	<3.5 g/dl	73(73)	
		>3.5 g/dl	26(26)	

Statistical significance – p value < 0.05

Table 2: Iron profile and CRP level in Pulmonary Tuberculosis patients

S. No.	Biochemical Parameters	Mean± S.D
1.	Hemoglobin (g/dl)	9.39±1.28
2.	Serum Iron (µg/dl)	30.80±17.31
3.	Serum TIBC (µg/dl)	163.16±66.67
4.	Transferrin saturation (%)	21.65±14.21
5.	Serum Ferritin (ng/ml)	652.92±525.22
6.	Serum CRP (mg/l)	81.18±82.20

Statistical significance – p value < 0.05

Table 3: Association between biochemical parameters and disease severity

Biochemical Parameters	Disease severity.		P value
	Severe	Normal	
Hemoglobin (g/dl)	9.1	11.2	0.82
Serum Iron (µg/dl)	24.5	34.6	**0.04**
Serum TIBC (µg/dl)	152.4	174.5	**0.03**
Transferrin saturation (%)	18.2	22.6	0.94
Serum Ferritin (ng/ml)	612.5	666.6	**0.05**
Serum CRP (mg/l)	80.18	89.6	0.76

Statistical significance – p value < 0.05

DISCUSSION

Iron deficiency anaemia and malnutrition is common in developing countries and is a major pre-disposing factor in Pulmonary Tuberculosis (PTB). Iron metabolism which is tightly regulated in normal condition is often found to be disturbed in various pathological conditions. Both deficiency and excess of free iron compromise the cellular and immune functions and also affect disease susceptibility and outcome6. In our study mean age of study participants was 49.23±16.70 years with 71% males and 29% females. In a study by Sharma C et7 al,79 65% were males and 35% were females with mean age of 43.56±15.63 years and these findings were comparable to our study.

In this study, mean haemoglobin level was 9.39±1.28 gm/dl, which is lower than the normal range. The mean serum iron level was 30.80±17.31 µg/dl, indicating a low level of iron in the blood. The mean serum TIBC level was 163.16±66.67 µg/dl, with a median value of 156.5 µg/dl and an interquartile range of 123.25-200 µg/dl, indicating normal to high levels of TIBC in the blood. The mean transferrin saturation level was 21.65±14.21%, which is lower than the normal range. The mean serum ferritin level was 652.92±525.22 ng/ml, which is higher than the normal range, the mean serum CRP level was 81.18±82.20 mg/l, indicating a high level of inflammation in the body. Overall, the findings suggest that the study population may have iron deficiency anaemia, given the low levels of haemoglobin and serum iron. The high levels of serum ferritin may also indicate iron overload or chronic inflammation8. The low transferrin saturation level may be due to iron deficiency or other factors such as chronic disease or inflammation. The high serum CRP level further supports the presence of inflammation in the body9, which could be related to an underlying condition. Further diagnostic tests may be necessary to identify the underlying cause of these findings and provide appropriate treatment. CRP is synthesized by hepatocytes, under the influence of interleukin-I and other types of cytokines at the infection site. CRP suggests a beneficial role in the evaluation of respiratory tract infection in adults and often normalizes with therapy and treatment.[10] Breen et al showed that elevated CRP could detect TB cases also.[11] Malabsorption due to hookworm or other infections, inadequate and iron-deficient diet or blood loss in pulmonary tuberculosis is bound to reduce iron stores in body.[12] Very high ferritin level shows oxidative stress and association of ferritin with lung function and smoking habit has been seen, showing its role in pulmonary infections. As observed by Lee et al, Huang et al,[13,14] and in our study also, levels of CRP and ferritin reflected a possible extent of oxidative stress and inflammation among patients, making them useful markers of PTB and its associated risks Among all markers found to change with treatment, Ferritin was one of them. It indicates its usefulness in monitoring

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treatment response and effective management of chronic illness.[15] In the absence of infection, Ferritin can be used as indicator of Iron stores at a cut off < 30.0ug/L.[16] Ferritin in PTB patients is more of an inflammatory marker and patients with adequate haemoglobin also showed lower ferritin levels. In studies by Misra S et al,[17] ferritin has been found to be having positive correlation to inflammation and severity of disease. Transferrin typically decreases in any infectious conditions. It is both a marker of nutritional status as well as a negative acute phase protein, such that its level is affected by protein diet and malnutrition state. In the patients or cases studied here, it was found that TB is causing low levels of transferrin but not so significant. Where as in a study by Sharma C et al,[7] there was significant low level of transferrin. Research also showed decrease in concentration of Transferrin correlated with severity of PTB or the degree of inflammation.[18] Quiet clearly, this study has shown that iron metabolism is altered during pulmonary tuberculosis. Serum iron levels, serum TIBC and serum ferritin showed strong relation with the severity of disease.

Limitations of the study

1. Convenience sampling technique was used to select the study participants, which may lead to selection bias and limit the generalizability of the study results to the overall population.
2. The study was conducted only in one hospital, which may limit the generalizability of the study results in other settings.
3. The study design was cross-sectional, which limits the ability to establish causal relationships between the variables studied.
4. The study did not collect information on potential confounding variables such as diet, lifestyle factors, and medication use, which may limit the ability to adjust for these factors in the analysis.
5. The study did not provide information on the reliability and validity of the questionnaire used to collect personal and sociodemographic data, which may limit the internal validity of the study.

CONCLUSION

The study concluded that patients with pulmonary tuberculosis have low haemoglobin, low serum iron level, increased TIBC level, low transferrin saturation level, low serum albumin and high CRP, which are directly associated with disease severity and mortality. had significant abnormalities in their haematological and biochemical parameters.

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REFERENCES

1. Isanka S, Mugusi F, Urassa W, Willett W C et al. Iron deficiency and Anemia predict mortality in patients with Tuberculosis. J Nutr. 2012; 142: 350-357.
2. Castellano A D, Muniain A, Rodriguez Bano J et al, Factors associated with time to sputum smear conversion in Active Pulmonary Tuberculosis. The International Journal of Tuberculosis and Lung Diseases. 2003; 7 (5): 432-438.
3. Kim J and Resnick MW. The role of Iron metabolism in Lung Inflammation and Injury. J Aller Ther. 2012; S4: 2155-6121.
4. WHO/UNICEF/UNU. Iron deficiency anaemia: assessment, prevention and control, a guide for programme managers. Geneva, WHO, 2001. Availablehttp://www.who.int/nutrition/publi cations/micronutrients/anaemia.
5. Akiibinu MO, Arinola OG, Ogunlewe JO and Onih EA. Non-enzymatic Antioxidant Sandhya Mishra et al. Study of Iron Metabolism in Pulmonary Tuberculosis Patients International Journal of Health Sciences & Research (www.ijhsr.org) 77 Vol.8; Issue: 3; March 2018 and Nutritional profile in Newly Diagnosed Pulmonary Tuberculosis Patients in Nigeria. African J. of Biomedical Research. 2007; 10: 223-228.
6. Phelan JJ, Basdeo SA, Tazoll SC, McGivern S, Saborido JR, Keane J. Modulating Iron for Metabolic Support of TB Host Defense. Front Immunol. 2018 Oct 15; 9:2296.
7. Sharma C, Badyal A. Role of iron metabolism in pulmonary tuberculosis: a case control study in Katra. Int J Sci Rep 2021;7(6):298-3013.
8. Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: Past, present and future. Biochim Biophys Acta. 2010;1800(8):760-9
9. Mishra S, Taparia P, Yadav D et al. Study of iron metabolism in pulmonary tuberculosis patients. Int J Health Sci Res. 2018; 8(3):70-77.
10. Miranda P, Gil-Santana L, Oliveira MG, Mesquita ED, Silva E, Rauwerdink A, Cobelens F, Oliveira MM, Andrade BB, Kritski A. Sustained elevated levels of C-reactive protein and ferritin in pulmonary tuberculosis patients remaining culture positive upon treatment initiation. PLoS One. 2017;12(4): e0175278.
11. Breen RAM, Leonard O, Perrin FMR, Smith CJ. How good are systemic symptoms and blood inflammatory markers at detecting individuals with tuberculosis? Int J Tuberc Lung Dis. 2008;12(1):44- 9.
12. Gil-Santana L, Cruz LAB, Arriaga MB, Miranda PFC, Fukutani KF, SilveiraMattos PS, et al. Tuberculosis-associated anemia is linked to a distinct inflammatory profile that persists after initiation of antitubercular therapy. Sci Rep. 2019; 9:1381
13. Lee CH, Goag EK, Lee SH, Chung KS, Jung JY, Park MS, et al. Association of serum ferritin levels with smoking and lung function in the Korean adult population: analysis of the fourth and fifth Korean national health and nutrition examination survey. Int Int J Chron Obstruct Pulmon Dis. 2016; 11:3001-6.
14. Huang HH, Yan HC, Han CL, Yu FC, Kao W, Chen W, et al. Association of in vitro oxidative stress, serum ferritin concentration and C-reactive protein in febrile emergency room patients. Clin Invest Med. 2005;28(2):48-54
15. Josephine O, Evelyn EA, Euphoria AC. Prognostic value of some Acute Phase Reactant in the management of Pulmonary Tuberculosis Disease. International Journal of Virology and AIDS. 2014; 1:1-3.
16. Kotru M, Rusia U, Sikka M, Chaturvedi S, Jain A. K. Evaluation of serum Ferritin in screening for iron deficiency in tuberculosis. Ann Haematol.2004; 83: 95-100.
17. Mishra S, Taparia P, Yadav D, Koolwal F. Study of iron metabolism in pulmonary tuberculosis patients. Int J Health Sci Res. 2018;8(3):70-7.
18. Bapat PR, Satav AR, Hussain AA, Shekhawat SD et al. Differential level of alpha-2 macroglobulin, Haptoglobin and Sero transferring as adjunct marker for TB diagnosis, Disease progression in malnourished Tribal population of Mlghat, India. PLOS ONE, 2015; e0133928.

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