Pak. J. Chest Med. 2022;28(02)

Original Article

journal homepage: https:/www.pjcm.net/

Pakistan Journal of Chest Medicine

Official journal of Pakistan Chest Society

Assessment of Hematological Parameters in Tuberculosis Patients: An Analytical Study

Sahar Farzand[1], Syed Tabish Rehman[2], Muhammad Khan[3], Amanullah Khokhar[4], Fahad Sarfraz[5]✉, Ghazal Irfan[3]

[1]Department of General Medicine, Combined Military Hospital (CMH), Quetta - Pakistan [2]Department of Chest Medicine, Liaquat National Hospital, Karachi - Pakistan [3]Department of Pathology, Baqai Medical College, Karachi - Pakistan
[4]Department of Medicine. Al Tibri Medical College and Hospital Malir Karachi, Isra University Campus, Hyderabad - Pakistan
[5]Department of Medical Education, Sahara Medical College, Narowal - Pakistan

Corresponding author:
Fahad Sarfraz
Department of Medical Education,
Sahara Medical College,
Narowal - Pakistan
Email: dfsarfraz@gmail.com

Article History:

Received:	Nov 11, 2021
Revised:	Mar 10, 2022
Accepted:	May 20, 2022
Available Online:	June 02, 2022

Author Contributions:
SF conceived idea, STR MK drafted the study, SF collected data, AK did statistical analysis and interpretation of data, FS GI critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests:
The authors declare that there is no conflict of interest.

How to cite this article:
Farzand S, Rehman ST, Khan M, Khokhar A, Sarfraz F, Irfan G. Assessment of Hematological Parameters in Tuberculosis Patients: An Analytical Study. Pak J Chest Med. 2022; 28(02):229-235

A B S T R A C T

Background: Despite that hematological abnormalities are commonly seen in patients with tuberculosis, little is known about their importance as prognostic markers in drug resistant tuberculosis (DR-TB) cases.

Objective: To find out relationship between tuberculosis and hematological parameters among these patients.

Methodology: This was a prospective case-control study was conducted at CMH and Fatimah Jinnah General and Chest Hospital, Quetta from January 2019 to July 2021. A total of in this study, 278 consenting adults were particular, comprising 50 healthy individuals and 114 patients with drug-resistant tuberculosis (DR-TB) and 114 with drug-susceptible tuberculosis (DS-TB). A systematic questionnaire was used to collect demographic data. Five milliliters (5 mL) of blood were drawn and placed in EDTA containers. The Mindary-BG5380 5-part automated system and the impedance approach were used to analyze hematological parameters. Data was analyzed using IBM Statistics SPSS version 27.

Result: The mean hemoglobin levels were significantly lower in DR-TB patients (11.33±2.14 g/dL) than in DS-TB patients (12.47±2.99 g/dL) and healthy group (13.97±2.99 g/dL) with a mean difference of -15.11±8.12 g/dL. The mean MCH and MCHC levels were also slightly lower in DR-TB patients 27.1±2.91pg and 29.89±2.11 g/dL respectively), The WBC count in three groups are statistically strong significant association at P-value < 0.001.

Conclusion: The increased inflammation commonly associated with drug-resistant tuberculosis (DR-TB) may be the cause of the decreased mean haemoglobin levels seen in these individuals when compared to drug-susceptible tuberculosis (DS-TB) patients. Comparable white blood cell counts between the two groups suggest that both DR-TB and DS-TB patients' immune systems responded similarly to the infection.

Keyword: Haematological Parameters; Drug-Resistant Tuberculosis; Pakistan

Introduction

Tuberculosis (TB) is an airborne bacterial infection that affects any part of the body and often affects the lungs. TB infection can travel to the lungs, larynx, lymph nodes, spinal cord, bones or kidneys, and TB bacilli are transferred directly to any part of the body through blood flow or lymphatic ducts.[1] TB kills millions of people each year and the emergence of drug-resistant tuberculosis (DR-TB) presents a serious obstacle to international public health strategies aimed to treat and managing tuberculosis.[2] Patients' lack of compliance to anti-TB drugs contributes to genetically mutated strains of M. tuberculosis resistance.[3]

The World Health Organization (WHO) estimates that every year, almost half a million people get drug-resistance and about 214,000 of them pass away from the illness. One of the key components of the WHO's End TB Strategy is expediting the detection and treatment of drug-resistant TB (DR-TB).[4] Patients who have previously undergone antitubercular treatment (ATT) are at a higher risk of developing DR-TB. So, it is of most important that DR-TB treated timely as it is very difficult to treat DR-TB. There are different types of DR-TB of which Multidrug-Resistant Tuberculosis (MDR-TB) is the most prevalent one and is defined as Mycobacterium tuberculosis (MTB) strains that are simultaneously resistant to isoniazid (H) and rifampicin (R).[5]

TB is a serious infectious disease that can affect blood's cellular components is tuberculosis.[6] For example, it can harm the bone marrow, which produces red blood cells, which can result in anaemia. Moreover, white blood cells—which are essential for fight infections—can be reduced by tuberculosis. Moreover, it can increase platelet counts, which are vital for blood coagulation.[7-8] TB infection can have a significant effect on myeloid and lymphoid cell lines, as well as plasma components, within the hematopoietic system. Several haematological disorders linked to tuberculosis have been reported by different researchers. These variations in blood parameters can be useful indicators for TB diagnosis, prognosis prediction, and therapeutic response evaluation. Nonetheless, there is still much to learn about the frequency and consequences of haematological abnormalities, as well as the adverse consequences of antituberculous treatment on a range of haematological parameters.[6]

For this reason, TB patients are advised for complete blood count (CBC) during their treatment in order to provide thorough insights into blood cell-related disorders. This contains important information about hematocrit, haemoglobin levels, RBC indices, differentials between white blood cells and red blood cells, erythrocyte sedimentation rate, and red cell distribution width. These indicators provide vital information that is necessary for early treatment decision-making.[9-10]

So, this topic is of much interest and for this reason the present study was planned to better understand the hematological alterations associated with tuberculosis, particularly in the context of drug-resistant cases. While it is well established that tuberculosis can cause significant disruptions in hematological parameters, there is limited knowledge about how these changes differ between drug-susceptible and drug-resistant tuberculosis (DR-TB) patients. Given the global rise of DR-TB, which poses a serious challenge to TB management and eradication efforts, identifying reliable prognostic markers is crucial. This study aims to fill the gap by analyzing hematological parameters, such as hemoglobin levels, MCH, MCHC, and WBC counts, among DR-TB and DS-TB patients, thereby contributing valuable insights into the potential use of these parameters as indicators of disease severity and treatment response in DR-TB cases.

Objective

To investigate hematological markers in patients treated for tuberculosis.

Methodology

This was a prospective case-control study was conducted at CMH and Fatimah Jinnah General and Chest Hospital, Quetta from January 2019 to July 2021. For study purposes, three distinct groups were created: drug-resistant tuberculosis patients (DR-TB Group), drug-susceptible tuberculosis patients (DS-TB Group), and a control group of healthy individuals (HI Group). The study covered sample collection, processing, and analysis over the course of study.

Prior to study enrollment, informed consent was obtained from all participants. Eligibility for the trial was limited to individuals diagnosed with tuberculosis who agreed to sign the informed consent form. It also included people confirmed not to have tuberculosis by GeneXpert testing. The study did not include those who declined to participate. After enrollment in the study, a standardised questionnaire was given to each participant in order to collect information about their sociodemographic status, their medical related history, and TB treatment history.

A total of 278 cases were included in the study, following the rule that the number of patients with tuberculosis should be twice that of healthy individuals. Based on this guideline, the trial included 114 cases in the DR-TB group, 114 cases in the DS-TB group, and 50 healthy control individuals.

At start of all patient were advised for sputum samples for testing purpose with the goal of evaluating the efficacy of the Xpert® RIF/MTB test utilizing sputum samples. To identify resistance to RIF and INH. Furthermore, 5ml of venous blood was drawn into EDTA vials for every patient classified as having Drug-Resistant Tuberculosis (DR-

Table 1. Sociological and demographic characteristics

Variable	DR-TB n=114 (%)	DS-TB n=114 (%)	Control n=50 (%)	Total n=278
Gender				
Male	32(11.51%)	67(24.10%)	25(8.99%)	124(44.60%)
Female	46(16.54%)	83(29.85%)	25(8.99%)	154(55.39%)
Age (years)				
≤ 20	25(8.99%)	38(13.66%)	19(6.83%)	82(29.49%)
21-40	34(12.23%)	58(20.86%)	16(5.75%)	108(38.84%)
41-60	33(11.87%)	20(7.19%)	6(2.15%)	59(21.22%)
>60	9(3.23%)	19(6.83%)	1(0.35%)	29(10.43%)
Marital Status				
Unmarried	68(24.46%)	53(19.06%)	31(11.15%)	152(54.67%)
Married	61(21.94%)	46(16.54%)	19(6.83%)	126(45.32%)
Education				
Educated	55(19.78%)	90(32.37%)	27(9.71%)	172(61.87%)
Uneducated	32(11.51%)	51(18.34%)	23(8.27%)	106(38.12%)
Occupation				
Employed	63(22.66%)	41(14.74%)	19(6.83%)	123(44.24%)
Unemployed	31(11.15%)	72(25.89%)	31(11.15%)	155(55.75%)

TB), Drug-Susceptible Tuberculosis (DST), and healthy patients. The erythrocyte sedimentation rate (ESR) and other haematological parameters were examined using this blood. The Mindray BC5380 (5-part) haematological analyzer was used to analyze the blood samples in order to ascertain the haematological parameters. The samples were diluted, aspirated, and mixed in accordance with the manufacturer's instructions prior to analysis. The manufacturer's instructions were strictly followed in determining each parameter.

The Statistical Package for Social Sciences (SPSS) was used to analyze the data, and descriptive statistics were used in the preliminary analysis. Calculations involving statistical comparisons were performed using unpaired t-tests. When correlating the haematological data at the designated p-value, the Pearson correlation coefficient, analysis of variance (ANOVA), and regression analysis were used to determine the significance of variations in haematological parameters among the DR-TB, DS-TB, and control groups.

Result

A total 278 cases were included in this study which were divided into three groups DR-TB (n=114), DS-TB (n=114) and Control group (n=50). Females 154 (55.39%) percentage are high than males 124 (44.60%). Majority of the patients 108 (38.84%) were from age group 21 - 40 years.

Table 2. Comparison of Hematological parameters between different group (one way ANOVA)

Parameter	DR-TB Mean ± SD	DS-TB Mean ± SD	Healthy control Mean ± SD	F-Value	P-Value
RBC Counts (10^{12}/L)	3.49 ± 0.33	4.81 ± 1.12	6.01 ± 0.65	1.76	0.35
PCV (%)	37.41 ± 7.99	41.01 ± 9.19	43.01 ± 11.19	1.54	0.31
HB(g/dL)	11.33 ± 2.14	12.47 ± 2.99	13.97 ± 2.99	5.01	<0.01
MCV(FL)	87.01 ± 9.23	85.1 ± 13.8	89.98 ± 14.01	2.98	<0.05
MCH (pg)	27.1 ± 2.91	24.98 ± 1.99	28.91 ± 4.98	10.01	<0.05
MCHC(g/dL)	29.89 ± 2.11	31.19 ± 2.21	33.98 ± 2.97	27.03	<0.05

The number of married cases were 126 (45.32%), while 152 (54.67%) were unmarried. On the basis of their education status, number of educated cases were 172 (61.87%) while 106 (38.12%) were uneducated. Among study cases, 123 (44.24%) were employed at the time of study while rest 155 (55.75%) were unemployed (Table 1).
Among study cases, the mean RBC counts was significantly lower (3.49 g/dL) in DR-TB compared to healthy patients (6.01g/dL) and DS-TB (4.81g/dL). Also, in case of PCV and HB the means are lower in case of DR-TB than DS-TB and healthy patients. The one-way ANOVA analysis demonstrated a statistically significant association of MCV, MCH, and MCHC when comparing all three groups (DR-TB, DS-TB, and Healthy control) which are <0.05 is typically considered to be statistically significant.
Using one-way Anova, there was a statistically significant association of WBC when comparing the three groups (DR-TB, DS-TB and Healthy control as shown on the (Table 3). When comparing the WBC counts among the three groups it shows statistically strong significant association at P-value < 0.001.

Discussion

Prevalence of TB is higher in Khyber Pakhtunkhwa due to different factors like internally displaced TB patients (IDPs) which will possibly lead to TB transmission among healthy individuals. Avoiding the identification and treatment of tuberculosis (TB) increases the risk of severe sickness for those who already have it as well as the spread of the disease to healthy people. It is believed that one active TB patient can infect between 10 and 15 uninfected individuals on average.[11] In low- and middle-income countries (LMICs), it is therefore crucial to make significant efforts to address the problem of undiagnosed

Table 3. Comparison of White Blood Cells between the three groups (one – way ANOVA)

Parameter	DR-TB Mean ± SD	DS-TB Mean ± SD	Healthy control Mean ± SD	P-Value
WBC Counts (10^9 /L)	8.11± 2.99	8.24 ± 3.11	56.01 ± 15.99	<0.001
Neutrophil (%)	57.51 ± 16.33	62.21 ± 17.11	57.01 ± 14.53	0.39
Basophil (%)	0.64 ± 0.39	0.61 ± 0.24	Three 0.62 ± 0.63	0.71
Eosinophil (%)	2.99 ± 3.99	3.01 ± 4.02	3.49 ± 2.98	0.59
Monocyte (%)	5.11 ± 2.99	4.76 ± 2.65	5.01 ± 2.97	0.68
Lymphocytes (%)	31.69 ± 36.56	29.67 ± 13.54	31.01 ± 15.78	0.51

TB cases at both the national and subnational levels, with a special emphasis on the most susceptible TB populations.[12]

Numerous investigations show that haematological abnormalities, such as anaemia, folate insufficiency, and sideroblastic illness, are frequently observed in patients diagnosed with tuberculosis (TB). The health of TB patients may be greatly impacted by these disorders. Significant relationships have been observed between non-iron-deficient anaemia and death, TB recurrence, and HIV disease progression, indicating that anaemia is associated with unfavourable clinical outcomes for reasons other than iron deficiency. TB causes a systemic inflammatory response, which in turn causes hepatocytes and macrophages to produce hepcidin.[13]

In our study we have three distinct groups: drug-resistant tuberculosis patients (DR-TB Group), drug-susceptible tuberculosis patients (DS-TB Group), and a control group of healthy individuals (HI Group). According to our investigation, there were 154 cases (55.39%) of the illness in females compared to 124 cases (44.60%) in males. These results line up with earlier research by Ayaz et al., Baloch et al., and Ullah et al.,[14-15] which similarly found that females had a higher prevalence of the condition. The variation could be caused by a number of things, such as women's restricted access to hospitals and medical services, a lack of diagnostic centres in local communities, communal living arrangements in rural areas that encourage the spread of disease among women, and the higher rates of illiteracy among women in our society.

The disease was equally prevalent in all age categories in our analysis, with the highest incidence 108 (38.84%) occurring in those among the ages of 21 to 40. This result is in line with earlier study by Ullah et al.,[16] which found that tuberculosis primarily affects the adult productive age group, which is usually between the ages of 20 and 50. This age group may be more susceptible to tuberculosis infection because of things like more frequent social interactions and contacts, which raise the risk of transmission. Furthermore, immunity begins to decline with age, making older people more vulnerable to tuberculosis infection.

Haematological studies have been conducted by different authors in the past with different results. In our study we comparing DR-TB patients to DS-TB patients, no appreciable differences were found in the packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), or red blood cell count (RBC). This result is in line with earlier studies carried out by Minardi and Ursavas et al., who similarly noted noticeably reduced in patients with DR-TB had significantly lower hemoglobin levels than patients with DS-TB.[17,18]

Comparing patients with DR-TB to those with DS-TB, there were no appreciable changes in RBC, PCV or MCV. This indicates that the anaemia in MDR-TB patients is not caused by alterations in the size or form of red blood cells, but rather by a reduction in the overall quantity of red blood cells.[18]

In earlier research by Lombard and Mansvelt and Charles et al., tuberculosis patients were frequently found to have low haemoglobin levels (g/dL).[19] This behaviour can be explained by the cytokines that activated macrophages release in response to tubercle bacilli. These cytokines prevent the reticuloendothelial system from transferring iron to growing red blood cells and decrease erythropoietic development. Additionally, the effects of antituberculosis medications given during the course of treatment may have an impact on the drop in haemoglobin levels.

Haemoglobin and packed cell volume (PCV) examinations, however, frequently gradually improve towards normal ranges while patients get chemotherapy, demonstrating a favourable response to treatment. Haemoglobin and hematocrit levels rising can act as indicators of how well the treatment plan is working.[20]

White blood cell (WBC) counts in our investigation showed a variety of irregular patterns, with neutrophilia and lymphocytosis being the most common abnormalities. This result is consistent with a prior study from Ibadan, Nigeria[21] which found that individuals with tuberculosis (TB) had higher levels of neutrophils and lymphocytes.

The heightened production of neutrophils and lymphocytes in tuberculosis patients could be explained by the body's cellular immunity resulting from bacterial encounters. A component of the body's defence against tuberculosis infection is this immunological response.[22]

Furthermore, when compared to healthy controls, the only technically significant change observed in drug-resistant tuberculosis (DR-TB) patients was an increase in white blood cell (WBC) counts; neutrophil, lymphocyte, monocyte, basophil, and eosinophil counts did not significantly alter. This result is consistent with a study,[12] which found that WBC levels were predictive of impending leucocytosis in patients with multidrug-resistant tuberculosis (MDR-TB). The persistent inflammatory response that these patients frequently experience may be the cause of the increased WBC count.

Another study also,[13] also demonstrating that individuals with drug-resistant tuberculosis (DR-TB) had considerably greater neutrophil counts and lower lymphocyte counts than those with drug-susceptible tuberculosis (DS-TB).

Conclusion

This study highlights a significant difference in haemoglobin levels between patients with DR-TB and those with DS-TB, with the former group having lower haemoglobin levels. Different degrees of neutropenia and lymphopenia were seen in the WBC.Patients with pulmonary tubercu-

losis frequently exhibit certain haematological abnormalities, thus medical professionals need to keep watch out for these abnormalities when diagnosing pulmonary tuberculosis in these patients.

Limitation of the study

Hematological changes observed in MDR-TB patients are often nonspecific and can be indicative of various other conditions or infections. For example, anemia, leukocytosis, or thrombocytosis can occur in response to inflammation or secondary infections.
Hematological parameters can vary widely among individuals, making it challenging to establish universal baseline values for comparison. Factors such as age, sex, genetics, and underlying health conditions can influence baseline hematological parameters, complicating the interpretation of changes.

References

1. Dye C, Lonnroth K, Jaramillo E, Williams BG, Raviglione M. Trends in tuberculosis incidence and their determinants in 134 countries. Bull World Health Organ. 2009;87(9):683-91.
2. Atomsa D, Abebe G, Sewunet T. Immunological markers and hematological parameters among newly diagnosed tuberculosis patients at Jimma University Specialized Hospital. Ethiop J Health Sci. 2014;24(4): 311-8.
3. Kassa E, Enawgaw B, Gelaw A, Gelaw B. Effect of anti-tuberculosis drugs on hematological profiles of tuberculosis patients attending at University of Gondar Hospital, Northwest Ethiopia. BMC Hem. 2016;16:1-1.
4. World Health Organization. Global tuberculosis report 2013. World Health Organization; 2013.
5. Mulenga CM, Kayembe JM, Kabengele BO, Bakebe A. Anemia and hematologic characteristics in newly diagnosed pulmonary tuberculosis patients at diagnosis in Kinshasa. J Tuberc Res. 2017;5(4):243-57.
6. Balepur SS, Schlossberg D. Hematologic complications of tuberculosis. Tub Nontuberculous Myc Infec. 2017:529-39.
7. Yaranal PJ, Umashankar T, Harish SG. Hematological profile in pulmonary tuberculosis. Int J Health Rehabil Sci. 2013;2(1):50.
8. Morris CD, Bird AR, Nell H. The haematological and biochemical changes in severe pulmonary tuberculosis. Int J Med. 1989;73(3):1151-9.
9. Abay F, Yalew A, Shibabaw A, Enawgaw B. Hematological Abnormalities of Pulmonary Tuberculosis Patients with and without HIV at the University of Gondar Hospital, Northwest Ethiopia: A Comparative Cross-Sectional Study. Tuberc Res Treat. 2018(1): 5740951.
10. Bolarinwa OA. Sample size estimation for health and social science researchers: the principles and considerations for different study designs. Niger Postgrad Med J. 2020;27(2):67.
11. Datiko DG, Jerene D, Suarez P. Stigma matters in ending tuberculosis: Nationwide survey of stigma in Ethiopia. BMC Public Health. 2020;20(1):190.
12. Fuge TG, Bawore SG, Solomon DW, Hegana TY. Patient delay in seeking tuberculosis diagnosis and associated factors in Hadiya Zone, Southern Ethiopia. BMC Res Notes. 2018; 11:1-6.
13. Gebreegziabher SB, Bjune GA, Yimer SA. Total delay is associated with unfavorable treatment outcome among pulmonary tuberculosis patients in west Gojjam zone, Northwest Ethiopia: a prospective cohort study. PloS One. 2016;11(7):e0159579.
14. Ayaz S, Nosheen T, Khan S, Khan SN, Rubab L, Akhtar M. Pulmonary tuberculosis: still prevalent in human in Peshawar, Khyber Pakhtunkhwa, Pakistan. Tuberculosis (TB). 2012;10:39-41.
15. Ullah S, Shah SH, Rehman A, Kamal A, Begum N, Khan G. Extrapulmonary tuberculosis in Lady Reading Hospital Peshawar, NWFP, Pakistan: survey of biopsy results. J Ayub Med Coll Abbottabad. 2008;20(2):43-6.
16. Ullah H, Iqbal Z, Ullah Z, Mahboob A, ur Rehman M. Frequency of pulmonary tuberculosis in patients presenting with diabetes. Pak J Chest Med. 2009; 15(4).
17. Minardi ML, Fato I, Di Gennaro F, Mosti S, Mastrobattista A, Cerva C, Libertone R, Saracino A, Goletti D, Girardi E, Andreoni M. Common and rare hematological manifestations and adverse drug events during treatment of active TB: a state of art. Microorganisms. 2021;9(7):1477.
18. Ursavas A, Ediger D, Ali R, Köprücüoglu D, Bahçetepe D, Kocamaz G, et al. Immune thrombocytopenia associated with pulmonary tuberculosis. 2010.
19. Lombard EH, Mansvelt EP. Haematological changes associated with miliary tuberculosis of the bone marrow. Tubercle and Lung Dis. 1993;74(2):131-5.
20. Al-Omar IA, Al-Ashban R, Shah A. Hematological abnormalities in Saudis suffering from pulmonary tuberculosis and their response to the treatment. Res J Pharma. 2009;3(4):78-85.

21. Olaniyi JA, Aken'Ova YA. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. Afr J Med Med Sci. 2003;32(3):239-42.

22. Hungund BR, Sangolli SS, Bannur HB, Malur PR, Pilli GS, Chavan RY, Dafale SR, Joshi AV. Blood and bone marrow findings in tuberculosis in adults-A cross sectional study. Al Ameen J Med Sci. 2012;5(4):362-6.