

Research Article

A Study of Platelet Parameters and Their Correlation with Different Clinical Manifestations of Tuberculosis: A Pre- and Post-Treatment Analysis

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A B S T R A C T

Introduction: Recent studies show that platelets play a pivotal role in the pathogenesis of chronic diseases. However, the exact variation of platelet parameters in different manifestations of tuberculosis has not yet been studied effectively.

Objectives: To explore the variation of platelet count, Mean Platelet Volume (MPV), and Platelet Distribution Width (PDW) in tuberculosis and the changes in indices after 2 months of initiation of antitubercular treatment

Materials and Methods: This was a cross sectional study where the haematological reports of 150 patients attending the Department of Pulmonary Medicine were studied. The platelet indices of these patients were followed up 2 months after initiation of treatment and compared with the initial data.

Results: Out of the 150 treatment naïve patients, 97 were of pulmonary tuberculosis with no drug resistance. Their initial mean platelet count was 1,07,000/mm³, which increased to 2,52,000 after 2 months. The initial mean PDW was 21.2 reduced to 17.7 after two months of treatment. The initial MPV was 12 fL, which became 11.2 fL after two months. In the remaining 53 patients including those with drug resistance, tubercular pleural effusion, and military tuberculosis, the initial mean platelet count, PDW, and MPV were 95000/mm³, 25.2 and 7.1 fL that transformed to a mean of 1,18,000/mm³, 19.7 and 7.7 fL respectively, 2 months after initiating treatment.

Conclusion: This study indicates a tendency towards thrombocytopenia in tuberculosis patients and an increase in PDW. However following the initiation of treatment, the platelet count increased rapidly with a decrease in other indices.

Keywords: Tuberculosis, Platelet, Platelet Distribution Width, Mean Platelet Volume, Thrombocytopenia, Antitubercular Treatment

Introduction

The tubercle bacilli has been a major cause of global public health problem since times immemorial, with widespread menace in middle- and low-income group countries of South-East Asia. According to the India TB Report 2023, issued by the Ministry of Health and Family Welfare, 2022 was a milestone year, with a record-high TB notification rate of 24.2 lakh cases, translating to an increase of 13% as compared to 2021. The total number of MDR TB cases was recorded to be 63,801.¹ World Health Organization data mentions the WHO regions of South East Asia and the Western Pacific to be recording the maximum reduction in TB notification rate in 2021 as compared to the rest of the world.²

A plethora of virulence pathways have been elucidated in many previous studies to decode the pathogenesis of tuberculosis. The major pathogenic events of the bacteria involve the interaction of the cell wall constituents including lipoarabinomannan, trehalose dimycolate, and phthiocerol dimycocerate with host macrophage receptors like CR1 and CR3 complement receptors, thereby preventing phagolysosome fusion involving TACO protein.³ However, the role of other cellular elements also needs to be pondered upon in order to obtain a panoramic overview of the behaviour of the bacteria in the human body.

Shah et al. inferred in their cross-sectional study in 2013 that conditions like ischaemic heart disease and hypertension are associated with a rise in Mean Platelet Volume (MPV) whereas diabetes is associated with a reduced MPV.⁴ Apart from the usual contents of the alpha, dense, and lysosomal granules, platelets also express important mediators of innate immunity including receptors like pattern recognition receptors (TLR 1–9), complement, and immunoglobulin receptors.⁵ However, only a very limited number of studies (as retrievable from previous data) have analysed the correlation of platelet parameters to different clinical manifestations of tuberculosis.

Thus, the present study was conducted with the following objectives: (1) to examine the demographic distribution of age and gender in relation to the different clinical manifestations of tuberculosis; (2) to compare the Total Platelet Count (TPC) and platelet indices in treatment-naïve tuberculosis patients with those of a control group; and (3) compare the pretreatment TPC and platelet indices of tuberculosis patients with those measured two months after the completion of treatment.

Materials and Methods

The present study was a cross sectional comparative observational study, which was carried out at the outpatient suite of the Department of Tuberculosis and Respiratory

Diseases (TBRD) of JNMCH, AMU over a period of 4 months between May 2023 and August 2023. Initially, a total of 161 patients positive for tuberculosis infection, as diagnosed by the Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) were included in the study. All these patients had no prior exposure to antitubercular treatment.

Informed consent for the study was obtained from all the patients and they were explained about the utility of the study. Antitubercular treatment was initiated as per standard protocol following CBNAAT proven diagnosis.

The patients were divided into two groups:

Group A (103 patients): Patients diagnosed with pulmonary tuberculosis by CBNAAT and had no drug resistance:

- Clinical features of pulmonary tuberculosis
- Sputum positive for Acid-fast tubercle bacilli using Ziehl–Neelson staining
- Radiological evidence of apical lung consolidation

Group B (58 patients): This group included the following patients:

- Patients with pulmonary tuberculosis having resistance to one or more of the 1st antitubercular drugs as determined by line probe assay- 23 patients
- Patients having tubercular pleural effusion as confirmed by radiology- 17 patients
- Patients having extrapulmonary tuberculosis- 10 patients.
- Patients having disseminated military tuberculosis as confirmed by radiology- 8 patients

Along with the above, 80 randomly selected patients with clinically diagnosed viral or bacterial pneumonia with negative CBNAAT results were chosen as a control to compare their platelet parameters with that of the patient group. The haematological reports of the patients' and the control group, as available from Central Lab, JNMCH were carefully studied and a statistical comparison was drawn between the two groups using the student's t test to find out the level of significance in the difference of results.

The patients were initiated on antitubercular therapy and were followed up after a period of two months following the start of treatment. Out of the total 161 patients, 11 patients (6 patients of Group A and 5 patients of Group B) were lost to follow-up and were eventually excluded from the ongoing study. Hence for the remaining 150 patients, the haematological reports were studied after 2 months of initiation of therapy. A comparison was drawn between the value of the platelet indices before and 2 months after the initiation of treatment. The paired t test was used to determine the level of significance between the values before and after the initiation of treatment.

Results

Demographic Variables

Out of the total 150 patients included in the study, 87 (58%) were males and 63 (42%) were females. This included 69 males and 28 females in Group A and 28 males and 35 females in Group B as shown in Table 1. The control group included 40 males and 40 females. The mean age of patients in Group A was 29.2 ± 7.1 years, while that of Group B patients was 31.4 ± 8.5 years. The mean age of patients in the control group was 26.3 ± 7.4 years.

The treatment-naïve tuberculosis patients, both in Group A and Group B, showed a significantly low platelet count as compared to the control group. The mean platelet count in Group A patients was 107.0 ± 56.5 ($\times 10^3/\text{mm}^3$) while that in Group B patients was 95.0 ± 37.6 ($\times 10^3/\text{mm}^3$). The corresponding mean platelet count in the control group was significantly higher than that of both the patient groups [286 ± 73.2 ($\times 10^3/\text{mm}^3$)] (Table 2). The mean Platelet Distribution Width (PDW) in Group A patients was $21.2 \pm$

5.6 % and in Group B patients, it was 19.7 ± 5.1 %. These values were higher than that in the control group with a mean PDW of 10.2 ± 4.8 %. The mean of the MPV in Group A patients was 12 ± 3.4 fL, while it was 7.1 ± 2.4 fL in Group B patients. These values were slightly higher than that in the control group, with a mean MPV of 6.2 ± 1.9 fL.

Platelet Indices after Two Months

The total platelet count and platelet indices of the 150 patients were reanalysed 2 months following the initiation of antitubercular treatment. The mean total platelet count in Group A patients increased from 107 ± 56.5 to 252 ± 68.7 ($\times 10^3/\text{mm}^3$) (Table 3). The increase in Group B patients was from 95 ± 37.6 to 118 ± 28.3 ($\times 10^3/\text{mm}^3$) (Table 4). The mean PDW in Group A patients reduced from 21.2 ± 5.6 % to 17.7 ± 3.4 %. In Group B patients, it decreased from 25.2 ± 5.1 to 19.7 ± 4.1 %. As for MPV, the mean value decreased from 12 ± 3.4 fL to 11.2 ± 1.9 fL in 2 months in Group A patients, while in Group B patients, it slightly increased from 7.1 ± 2.4 fL to 7.7 ± 1.9 fL.

Table 1. Distribution of Patients and Controls as per their Gender

Sex	Group A n (%)	Group B n (%)	Control n (%)	Total (Group A + Group B) n (%)
Male	69 (75.8)	28 (52.8)	40 (50.0)	87 (58.0)
Female	28 (24.2)	35 (47.2)	40 (50.0)	63 (42.0)
Total	97 (100.0)	53 (100.0)	80 (100.0)	150 (100.0)

Table 2. Initial Platelet Indices

Parameters	Group A (N = 97)	Group B (N = 53)	Control Group (N = 80)	p Value
Total platelet count ($10^3/\text{mm}^3$)	107.0 ± 56.5	95.0 ± 37.6	286.0 ± 73.2	< 0.002
Platelet Distribution Width (PDW) (%)	21.2 ± 5.6	25.2 ± 5.1	10.2 ± 4.8	< 0.004
Mean Platelet Volume (MPV) (fL)	12.0 ± 3.4	7.1 ± 2.4	6.2 ± 1.9	< 0.006

Table 3. Change in Platelet Parameters in Group A Patients after 2 Months of Treatment

Parameters	Before Treatment	After Treatment	Change (%)
Total platelet count ($10^3/\text{mm}^3$)	107.0 ± 56.5	252.0 ± 68.7	135.5
Platelet Distribution Width (PDW) (%)	21.2 ± 5.6	17.7 ± 3.4	6.5
Mean Platelet Volume (MPV) (fL)	12.0 ± 3.4	11.2 ± 1.9	6.6

Table 4. Change in Platelet Parameters in Group B Patients after 2 Months of Treatment

Parameters	Before Treatment	After Treatment	Change (%)
Total platelet count ($10^3/\text{mm}^3$)	95.0 ± 37.6	118.0 ± 28.3	24.2
Platelet Distribution Width (PDW) (%)	25.2 ± 5.1	19.7 ± 4.1	21.8
Mean Platelet Volume (MPV) (fL)	7.1 ± 2.4	7.7 ± 1.9	8.4

Discussion

This study demonstrates that active tuberculosis is associated with a tendency towards thrombocytopenia, although the platelets tend to be larger in volume with a greater variation in size. The initiation of antitubercular therapy was associated with an increase in platelet count while the PDW and MPV decreased. The results of this study partially match the ones of the study conducted by Tozkoparan et al. and Sahin et al. However, unlike our study, these studies computed an increase in platelet count in newly diagnosed patients of tuberculosis that decreased after the initiation of antitubercular treatment.^{6,7} However similar to our study, Rohini et al. also demonstrated thrombocytopenia in cases of active pulmonary tuberculosis.⁸ The increased MPV and PDW have been elucidated by all the studies conducted so far on the correlation of platelet parameters with tuberculosis. The exaggerated platelet response in tuberculosis has been correlated with acute phase reactants and the severity of the disease.⁷ Increased production of cytokines such as IL-6 has been linked with granuloma formation and increased platelet activation and aggregation.⁹ However, most of the patients initially diagnosed with tuberculosis, especially in India are severely immunocompromised. This results in a reduced synthetic drive to the bone marrow thereby resulting in a tendency of platelet count to remain towards the lower side of normal. Platelet count has also been seen to vary with the duration of the disease. The newly diagnosed disease is associated with a strong proinflammatory drive by chemokines including IFN gamma and TNF alpha, thereby resulting in increased expression of acute phase reactants including platelets. However, with the progression of the disease, anti-inflammatory mediators including TGF beta and IL10 tend to be manufactured in greater amounts thereby cooling down inflammatory activity.¹⁰ Although the increase in platelet count in our study is primarily attributed to improvement in immunity and a shift of chemokinesis from pro-inflammatory to anti-inflammatory, the possible effect of the antitubercular drugs on platelet parameters also needs to be considered. Nagu et al. and Von Drygalski et al. concluded that antitubercular therapy results in the

immune destruction of platelets due to binding of the drug to epitopes on G_p IIb/ IIIa and G_p I β X receptors.^{11,12}

Conclusion

Sophisticated diagnostic modalities have a limited scope of application in resource-limited settings as they are associated with a higher learning curve and financial constraints. Hence the utility of ancillary and subsidiary routinely available haematological parameters including platelet count and indices needs to be explored in conjunction with radiological investigations. The behaviour of platelets in the pathophysiology of tuberculosis, requires higher magnification, scrutiny, and research in order to come up with improved management facilities for this staggering public health menace.

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