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Reactive Thrombocytosis in Tuberculosis-

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Abstract

Background: Tuberculosis is a major public health problem in India and it remains an epidemic. hematological changes are commonly associated with TB, data regarding this are lacking in the study area. As hematological changes associated with TB determine its treatment and prognosis, identifying these is crucial for its prompt management. The present study is carried out to know the importance of varied heamotological parameters like thrombocytosis in tuberculosis and its relevance as a marker in diagnosing and treatment of tuberculosis. **Materials And Methods:** It is a prospective case control study conducted in GIMS in patents attending chest and TB ward and OPD during period of July 2022 to June 2023, a total of 12 months. Sample size is 54 pts. Investigations like CBC with platelet count, ESR, LFT, RFT, sputum for AFB, sputum gram staining, CXR, CT chest, ultrasound of the chest / abdomen and body fluid examination done. **Results:** There are 68(97.14%) patients in control group with Platelet count less than 450 and only 2 (2.8%) with platelet count more than 450X103 /ml. Whereas in TB patients group, there are 22 (40.74%) patients with platelet count less than 450X103/ml and 32(59.25%) patients with platelet count of more than 450X103 /ml. **Conclusion:** As thrombocytosis is more seen in tuberculosis cases compared to age and sex matched controls, Just like ESR,a simple test like thrombocytosis can be used as heamotological marker for identifying a TB suspect which can be confirmed later by various relevant tests.

Keywords: Health problem; Haematological changes; Marker; Thrombocytosis; Tuberculosis.

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Introduction

As per the Global TB Report 2022, An estimated global total of 10.6 million people (95% uncertainty interval [UI]: 9.9–11 million) fell ill with TB in 2021, equivalent to 134 cases (95% UI: 125–143) per 100 000 population. the TB incidence rate (new cases per 100 000 population per year) is estimated to have increased by 3.6% between 2020 and 2021, following declines of about 2% per year for most of the past two decades(1).

The differential diagnosis of tuberculosis should be entertained in patients with some abnormal hematological findings (2). Moreover, hematological parameters are useful indicators of severity in TB infection. (3) Hematological changes associated with pulmonary TB infection have been the first documented study in Red Sea State (4).

Thrombocytosis occurs in many chronic inflammatory diseases, including tuberculosis. The precise stimulus for increased platelet production is not clear, but it is associated with

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increased numbers of small megakaryocytes in the marrow, which shows reduced nuclear ploidy.(5) The platelets are also small, but it has recently been suggested, that this may simply reflect the thrombocytosis, as there is normally an inverse correlation between the number and volume of platelets.(6) Reactive thrombocytosis is associated with an increase in erythrocyte sedimentation rate (ESR) and acute phase reactants (fibrinogen, VIII.C, VWF: Ag, C-reactive protein, and interleukin-6 (IL-6)). IL-6 is known to promote megakaryocytopoiesis in vitro and raise platelet counts in vivo.

Platelets are present at the site of TB disease either as a result of extravasation of platelets that localize to the lesion, or secondary to platelet biogenesis within the lung itself. Megakaryocytes have been identified within the lungs and may have the capacity to scale up platelet generation in response to specific stimuli (7). This would support a role of platelets as first responders in M. tb infection, placing them at close proximity to any mycobacterial intruders. Lung tissue from M. tb-infected Balb/C mice has demonstrated the presence of the platelet marker CD41, CD42b which are not detected in uninfected lung. Microthrombi occur around TB cavities and have been proposed to prevent dissemination (8). Platelet aggregations and platelet-neutrophil adhesions have been observed within pulmonary lesions and mycobacteria have been visualized within platelets, located mainly alongside the mitochondria (9)

The protective and pathologic response to M. tuberculosis is complex and multifaceted, involving many components of the immune system. A clear picture of the network of immune responses to this pathogen, as well as an understanding of the effector functions of these components is essential to the design and implementation of effective treatments for TB (7). It is essential to determine immunological and haematological parameters at the baseline of anti-TB treatment for further consideration of supportive care and other treatment options that might be required for some patients to enhance the anti-TB treatment outcome.

Methods

This is a prospective case control study conducted in Gulbarga institute of medical sciences (GIMS) in patients attending CHEST and TB ward and OPD during period of July 2022 to June 2023, a total of 12 months. Sample size- 54 pts. All newly discovered pulmonary and extra pulmonary tuberculosis patients during this period constituted the sample of this study. Each patient will be subjected to routine hematological (complete blood counts and ESR) biochemical (Liver and Renal function tests), bacteriological investigations (sputum acid fast bacilli smears, sputum gram staining and cultures) and X-ray of the chest. Special investigations like Computed Tomography chest, ultrasound of the chest / abdomen and body fluid examination will also be performed in the patients when indicated. Ethical clearance of this study was approved from the hospital Institutional Ethical Committee (IEC). Subjects were admitted to the study only after it had been explained to them and informed consent obtained. **Inclusion criteria:**

Both males and females above 16 years.

Exclusion criteria:

1) Pediatric patients.

2) Pts with thombocytosis due to other reason such as drugs.

3)Any chronic disease affecting body systems including bone marrow and peripheral blood.

Also, patients admitted in medical wards for other reasons with no clinical signs for TB were stratified according to age and sex to match them with the cases and then 70 were selected randomly to be the control group. Data regarding the age and sex and laboratory reports were collected from the medical records. At CSMH about 2.5 ml blood is collected in dipotassium

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ethylene diamine tetra acetic acid (EDTA) tube for measuring the platelets count. Platelet count was done using a coulter method and manual counting method.

Statistical Analysis

Statistical analysis was done using MS Excel 2007. Summary statistics, Correlation R, Chi squared tests and z test were used for analysis. Differences with $p < 0.05$ was considered significant.

Results

Table 1: The Age and Sex distribution of the controls and cases.

S. No	Age	Controls			Cases		
		males	Females	Total	males	Females	Total
1	17-25	8	6	14	8	5	13
2	26-35	16	8	24	13	5	18
3	36-45	8	4	12	6	2	8
4	46-55	7	3	10	5	1	6
5	56-65	5	3	8	6	1	7
6	Above 65	2	0	2	2	0	2
	total	46	24	70	40	14	54

Table 2: Range Of Thombocytosis in cases and controls

S. No	Range	Cases	Controls
1	<200	4	14
2	250-350	8	18
3	350-450	10	36
4	450-700	22	2
5	700-900	9	0
6	>900	1	0

Table 3: Type of Tuberculosis in study population

S. No	Type	No	frequency
1	Pulmonary tb	31	57.40
2	Pleural tuberculosis	8	14.8
3	Abdominal tb	6	11.11
4	Lymphnode	4	7.40
5	Potts spine	1	1.85
6	tuberculous meningitis	2	3.70
7	Both pulmonary and pleural	2	3.70
	Total	54	

Out of 54 cases 40 (74%) were males and 14(25.9%) were females. Out of 70 controls 46(65.7%) were males and 24(34.2%) were females. Cases comprised of 54 TB patients (mean age 37.81 years, SD 15.5 years). The control group of 70 patients, age and sex matched individual (chi square=0.092 and z=2.032 respectively), (mean age 40.8years, SD 15.2 years) was chosen. Among the female Tb patients, mean age was (28.73) years (SD 16.15 years) and among males, the mean age was (40.35) years (SD 16.28years). This gender-wise difference in mean age among cases and control is statistically not significant ($z= 0.668$, $p> 0.05$).

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Thrombocytosis is defined as platelet count more than 450 X103 /ml. There are 68 (97.14%) patients in control group with Platelet count less than 450 and only 2 (2.8%) with platelet count more than 450X103 /ml. Whereas in TB patients group, there are 22 (40.74%) patients with platelet count less than 450X103/ml and 32(59.25%) patients with platelet count of more than 450X103 /ml. This mean difference is highly significant (t-test=12.841, p< 0.001).

In our study, we found that pulmonary TB was commonest, (57.40%), followed by pleural tuberculosis 14.8%, followed by abdominal tuberculosis with 11.11 %, lymph node TB with 7.40%, CNS TB 3.70%, both pulmonary and pleural 3.70% and potts spine of 1.85%. Of the 8 patients with Pleural TB, 7 are pleural effusion, one is hydropneumothorax, of 6 abdominal tb patients 5 have ascites, 1 ileocecal Koch's on ultrasonography,1mesentric lymph adenopathy suggestive of tuberculosis.4 lymph node cases with FNAC showing granulomatos lymphadenopathy with caseous necrosis. Potts spine with MRI suggesting T2 hyperintensity in C4-C5 disc with perivertebral and epidural component causing indentation over ventral surface of cord with secondary myelopathic changes in the cord at C3, C4 and C5. mild marrow edema seen involving body of C3,C4,C5 vertebrae with enhancement of perivertebral phlegmonous soft tissue/collections. Bilateral neural foramina narrowing noted at C3-C4,C4-C5 and C5-C6.

Discussion

World Health Organization has declared tuberculosis is a global emergency in 1993. Tuberculosis continues to be an important communicable disease in the world and is a major public health problem in India. Various hematological manifestations have been described in association with tuberculosis. There is a paucity of literature about the hematologic abnormalities in patients from the Indian population.

In our study, 59.25% of the patients with tuberculosis had thrombocytosis compared to 2.8% of control group. This study correlates with Baynes RD et al(6), Rathod S et al(10) study and Ammaiyappan Palanisawamy(11). which shows thrombocytosis in tuberculosis pts compared to non tb individuals.

In our study pulmonary tuberculosis is the commonest constituting 57.4% compared to all forms of tuberculosis. This study correlates with Rathod S et al(10) study where thrombocytosis is seen in 71.4% of pulmonary tuberculosis.

In our study Thrombocytosis is not only seen in pulmonary form of tuberculosis but also in extra pulmonary form. This study correlates with Andrew Renshaw study (12) which shows granulomas have high platelet counts. Similarly in TMS Tengku Muzaffar et al (13) study where thrombocytosis is associated with Tuberculosis spondylitis patients.

It has been suggested that platelet activation occurs in TB patients and there is a good correlation between platelet activation and the extent of the disease (14). Increased platelet activity may be a response to inherent differences in platelet reactivity among the population, organ infarction, vascular changes, hormonal and autocrine factors such as plasma catecholamines (15-17)

Reactive thrombocytosis is found in a number of clinical situations including infectious diseases. The regulation of thrombopoiesis is under the control of an array of haemopoietic growth factor. Significant elevation of thrombopoietin during the acute phase of infection precedes the development of thrombocytosis, suggesting an important role of thrombopoietin in reactive thrombocytosis. Elevated values of thrombopoietin were found in majority of patients with acute infection and were observed more frequently during the acute phase with fever than after the fever disappeared. The exact mechanism of elevated thrombopoietin levels in reactive thrombocytosis is still unknown; however, it has been observed to be correlated with inflammatory processes. Serum IL- 6 concentration is significantly correlated

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with thrombocyte count and albumin concentration. IL-6 may play a contributory role on reactive thrombocytosis and the acute phase response in pulmonary tuberculosis. The possibility that the increased numbers of small young platelets might be a feature of pulmonary tuberculosis was also considered. The pulmonary vasculature is thought to contribute to the production of platelets by fragmenting proplatelets(18) and the questions arose as to whether a diseased microvasculature in pulmonary tuberculosis might lead to excessive fragmentation and hence smaller platelets.

Conclusion

In our present study thrombocytosis is more seen in tuberculosis cases compared to age and sex matched controls. In view of the varied hematological abnormalities observed in patients with tuberculosis in this part of the world, we suggest the differential diagnosis of tuberculosis should be entertained in patients with varied hematological disorders. Our study highlights the importance of awareness of Hematological changes like thrombocytosis in tuberculosis.Just like ESR,a simple test like thrombocytosis can be used as heamotological marker for identifying a TB suspect which can be confirmed later by various relevant tests. They also can be used to indicate the response to the ATT and thus considerable reduction in the morbidity and mortality. However, a detailed research on this subject with larger number of cases needed to be carried out keeping in mind the present scenario of tuberculosis worldwide.

Conflict of interest: The authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this article.

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