RESEARCH ARTICLE

CLINICO-LABORATORY PROFILE OF PATIENTS AFFECTED WITH PULMONARY TUBERCULOSIS: RETROSPECTIVE OBSERVATIONS FROM A TERTIARY CARE HOSPITAL

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ABSTRACT: **Background**: Globally, tuberculosis (TB) is one of the top 10 causes of death and India, is one among the leading contributors. This study was undertaken to assess the clinic-laboratory profile of the patients diagnosed with Pulmonary TB (PTB) and evaluate differences between dead and alive PTB patients. **Material and methods**: : This is a retrospective study, conducted in the patients diagnosed with PTB from January 2016 to December 2018. The clinical, hematological and biochemical parameters of the patients diagnosed with Pulmonary TB at the time of presentation to the tertiary care hospital was noted and compared among the age matched healthy individuals. We further looked for prognostic factors among the tuberculosis patients who died and survived. **Results**: A total of 209 patients were diagnosed with PTB during the study period. The prevalence of TB was higher in males. Most of the TB patients belonged to the age group 31-60 years. Among the PTB patients, cough with expectoration was the most common symptoms followed by fever and breathlessness. Nearly 50% patients had symptoms for less than 2 weeks. The right upper zone was the most common zone involved radiologically. When compared to healthy individuals, TB patients had significantly low haemoglobin, while there was raise in total leukocyte count, platelet count ESR, Blood urea, and LFT. The mortality in TB patients was associated with low haemoglobin, lower differential macrophage count and lower globulin. **Conclusion**: In our study population, PTB was common in males, and in age group of 31-60 years. Patients with Cough with expectoration with 2 weeks duration, anaemic, leucocytosis and raised ESR must be investigated extensively for Pulmonary TB. Patients (PTB) with were severe anaemia and lower differential macrophage count had higher mortality rate.

KEYWORDS: Tuberculosis, haematological, biochemical, TB Mortality

INTRODUCTION:

According to World Health Organisation (WHO), Tuberculosis (TB) is one of the leading cause of death, globally[1]. In 2017, 10 million people were diagnosed with TB, among which 5.8 million were men, 3.2 million woman and around 1 million children. Among the 10 million people who developed TB in 2017, India had the highest burden accounting to 27% i.e., around 2.74 million,

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including patients with HIV[1]. With the advent of rise in Multi- drug resistance TB (MDR TB) patients ,i.e., tubercle bacilli resistant to antitubercular drugs - isoniazid and rifampicin, there is great threat to public health and health security. The infection rate is reported to be as high as 204 per 100,000 individuals. India accounts for 24% of the global MDR/RR TB cases. Overall estimated 54 million lives were saved by early diagnosis and treatment in 17 years (2000-2017) [1].Various countries have committed to End the tuberculosis epidemic by 2035 i.e., 95% reduction in TB deaths and 90% reduction in TB incidence, compared to levels in 2015 [2].

Reports indicate that among the pulmonary tuberculosis patients, 25% of them tend to remain asymptomatic. The symptoms related to pulmonary tuberculosis are mainly cough with expectoration, blood tinged sputum, chest pain. In case of cavitary lesion, massive hemoptysis can also occur [3-5]. In the pre-antibiotic era, spontaneous massive hemoptysis was the most dreaded complication leading to death [6]. Bronchiectasis is another complication following primary tuberculosis or after reactivation of TB, it can be associated with hemoptysis [7].The most common change in blood parameters seen in PTB are mild anaemia, leucocytosis, thrombocytosis with elevated ESR., which are non specific [4]. In this study, we have studied the clinical features of the patients who were diagnosed with pulmonary tuberculosis. We have also compared the haematological and biochemical blood parameters among healthy individuals and PTB patients, and among patients who succumbed to PTB. In addition to this, a sub analysis was also done to understand which parameters can have indicator role in patients who succumbed to PTB.

MATERIALS AND METHODS:

This was a retrospective study, conducted at department of Clinical Microbiology at a tertiary care teaching hospital in costal Karnataka, India, after clearance from Institutional ethical committee

(FMIEC/CCM/429/2019). All the adult patients (above 18 years), who were diagnosed as pulmonary tuberculosis as per RNTCP i.e., sputum positive for acid fast bacilli, from January 2016 to December 2018 were included in the study were included in the study. All demographic details, clinical features, haematological and biochemical parameters of all the patients included in the study were collected from the hospital medical record department. For controls, the investigators considered the laboratory details of health individuals who came for a regular health check-up and were devoid of any acute or chronic illness. Care was taken to see that the age and gender matched with that of the test group. The data from individual patients satisfying the inclusion criteria were noted down from individual files and entered into the Microsoft Excel. The demographic details were categorised into frequency, while the haematological and biochemical data were calculated to obtain mean ± standard deviation (SD). All these details are represented in each of the tables. For overall comparison, results were compared with PTB vs healthy adult individuals who had come for health check up and subjected to the Student t-test using the SPSS statistical program 32 ((IBM version 22, Chicago Inc, USA) . A P value of 0.05 was considered significant.

RESULTS:

A total of 209 adult patients were diagnosed with pulmonary tuberculosis as per RNTCP guidelines during the study period. Majority (76%) of the patients were males (**Table 1**).

Table 1. The gender wise distribution and common symptoms in the patients with PTB.

Gender	No of patients	%
Male	160	76.56
Female	49	23.44
Symptoms		
Cough	153	73.21
Fever	124	59.33
Expectoration	80	38.28
Breathlessness	40	19.14
Hemoptysis	21	10.05
Loss of appetite	18	8.61
Weight loss	12	5.74
Vomiting	11	5.26
Abdominal pain	10	4.78

The age group of 46-60yrs accounted for 40% of the diagnosed patients. Geriatric patients (>61 years) accounted for 17% (**Figure 1**).
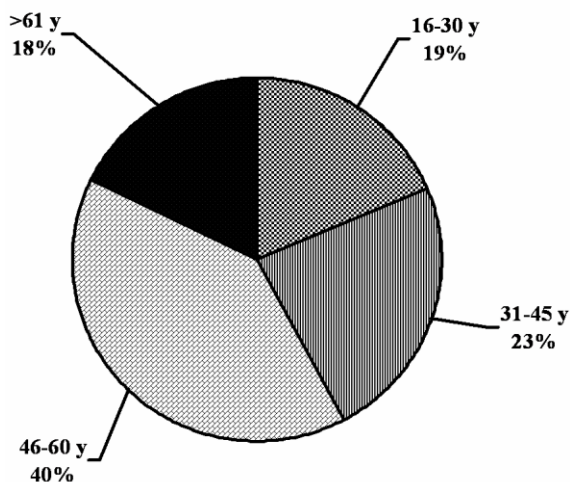

Fig 1.The Distribution of the age group of the patients.

Nearly half of the patients included had symptoms for less than 2 weeks and were diagnosed with pulmonary tuberculosis and nearly 2% patients had symptoms for more than 6 months (**Figure 2**).
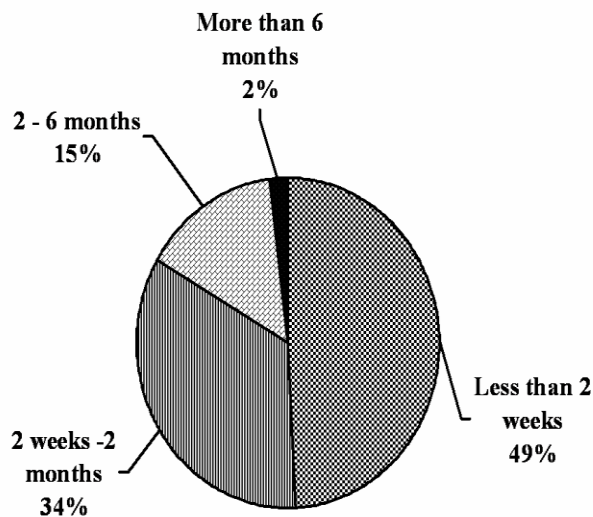

Fig 2. The distribution of the duration of the symptoms patient presented to hospital.

Cough was the most common symptom in PTB, and nearly 75% of the patients presented with cough and Expectoration was observed in 38% of the cases, fever (60%) was the second commonest symptoms. Other associated symptoms like weight loss, loss of appetite and hemoptysis were the presenting symptoms seen in 5-10% of the patients(**Table 2**).The radiological diagnosis showed that the upper zone was the commonest zone for the PTB lesions accounting for 46%, followed by upper and middle zone combined (24%)The right pulmonary parenchymal involvement accounted for 50% of the patients (**Table 2**).

Table 2. Distribution of the Radiological lung zone affected with tuberculosis.

	Left	Right	Bilateral	Total	%
Upper Zone	19	55	23	97	46.41
Upper And Middle Zone	15	23	13	51	24.40
Middle Zone	8	9	5	22	10.53
Middle And Lower Zone	6	11	2	19	9.09
Lower Zone	8	7	5	20	9.57
	56	105	48	209	

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When compared to healthy individuals, it was observed that the PTB patients were more anemic (**Table 3**).

Table 3. Comparison of Laboratory parameters between controls and the PTB patients.

	Control	TB	P value
Haemoglobin (g%)	12.52±1.44	11.07±2.54	<.0001
Total Leucocyte Count (/ mm$^{3)}$)	8448.17±5479.23	10583.43±4165.07	0.001
Differential Neutrophil count	63.06±14.66	75.3±9.35	<.0001
Lymphocyte	30.87±13.99	14.21±7.38	<.0001
Eosinophil	4.3±4.93	2.1±3.15	0.0001
Monocyte	2.54±1.72	8.37±3.27	<.0001
Platelet	221139.8±83235.07	343070.9±153767.2	0.001
ESR (/ 1st hour)	10.76±9.09	62.73±34.72	<.0001
Blood Urea (mg%)	20.74±8.29	21.64±15.69	<.0001
Serum Creatinine(mg%)	0.75±0.25	1.23±1.55	0.002
Total Bilirubin(mg%)	0.57±0.31	0.63±0.72	<.0001
Conjugated Bilirubin(mg%)	0.22±0.12	0.38±0.65	0.003
Unconjugated Bilirubin(mg%)	0.36±0.24	0.26±0.17	0.02
Total Protein (g%)	6.86±0.27	7.06±0.86	0.0145
S.Albumin(g%)	3.84±0.29	3.22±0.65	<.0001
S.Globulin(g%)	2.61±0.12	3.84±0.7	<.0001
A/G RATIO	1.23±0.13	0.87±0.27	<.0001
Aspartate aminotransferase	28.37±11.98	62.1±263.48	0.03
Alanine Aminotransferase	25.13±20.08	41.56±177.97	0.18
Alkaline phosphatase	52.89±9.34	134.35±76.33	<.0001
Sodium (mEq/ml)	137.78±1.25	129.51±11.69	0.23
Potassium (mEq/ml)	4.01±0.21	4.05±0.62	0.48
Chloride (mEq/ml)	99.9±1.37	90.11±6.98	<.0001

The total leucocyte counts, differential count of neutrophils, lymphocytes, platelet count and ESR was high in people affected with PTB. The biochemical values of renal functions like blood urea, serum creatinine were increased significantly. The liver function parameters like total bilirubin, liver enzymes (AST, ALT, ALP) and Serum globulin were increased in PTB patients. Serum albumin and A/G

ratio were also reduced, indicating the chronicity of the disease (**Table 3**).

When the co-morbid conditions were studied among the 23 dead patients, Sepsis was seen in 8 patients, system wise co-morbid conditions revealed 7 individuals had respiratory, CVS 6, hepatic and renal 4 each and CNS 1 (**Figure 3**). The central nervous system (8/11) was the commonest one for the spread of TB from lungs, followed by military (3/11) and military (1/11) (**Figure 4**).
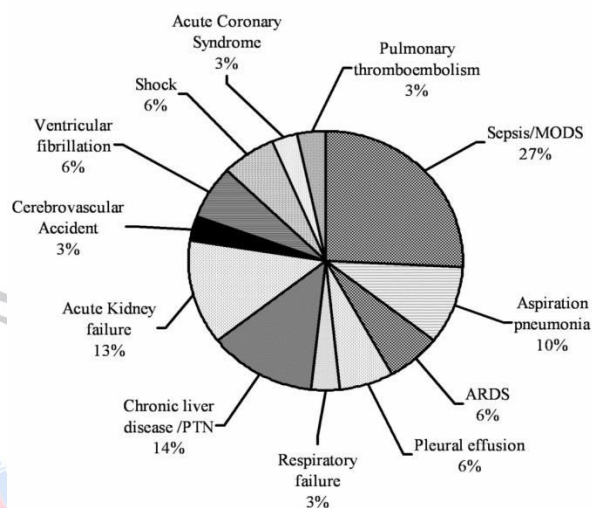
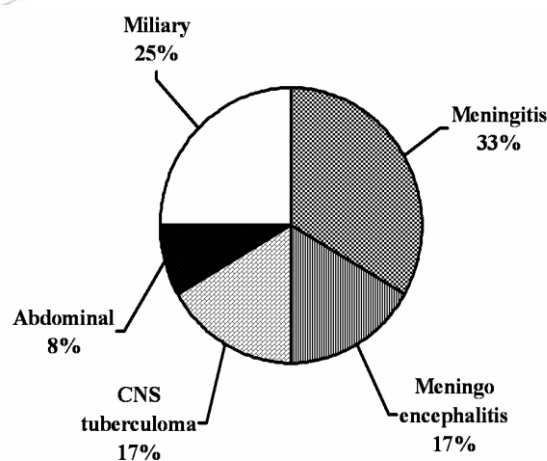**Fig 3: Distribution of the co-morbidities in the dead patients**

Fig 4: Dissemination of the pulmonary Tuberculosis.

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The patient who succumbed to military Tb had co-infection with HIV/ AIDS. The comparison of the laboratory parameters among the alive and dead PTB patients, showed significant reduction observed in haematological parameters like monocyte count, platelet count, ESR among dead PTB (**Table 4**). The PTB individuals who succumbed to the illness had increased blood urea, total bilirubin and reduced total protein, serum globulin, A/G ratio compared to alive patients (**Table 4**).

Table 4. Comparison of Laboratory parameters between alive and dead PTB patients

	TB alive	TB Dead	P value
Haemoglobin (g%)	11.07±2.54	11.57±2.42	0.42
Total Leucocyte Count (/ mm3)	10583.43±4165.07	11456.52±6653.85	0.55
Differential Neutrophil count	75.3±9.35	76.09±9.58	0.71
Lymphocyte	14.21±7.38	24±43.17	0.55
Eosinophil	2.1±3.15	2.3±3.2	0.78
Monocyte	8.37±3.27	6.22±3.45	0.009
Platelet	343070.9±153767.2	231416.7±102834.5	0.0001
ESR (/ 1st hour)	62.73±34.72	28±22.68	<.0001
Blood Urea (mg%)	21.64±15.69	42.39±41.88	0.03
Serum Creatinine	1.23±1.55	1.65±2.02	0.08
Total Bilirubin	0.63±0.72	1.69±2.25	0.04
Conjugated Bilirubin	0.38±0.65	1.19±1.91	0.07
Unconjugated Bilirubin	0.26±0.17	0.81±1.28	0.06
Total Protein	7.06±0.86	6.43±0.96	0.008
S.Albumin	3.22±0.65	3.12±0.86	0.61
S.Globulin	3.84±0.7	3.29±0.73	0.003
A/G ratio	0.87±0.27	1.02±0.37	0.09
Aspartate aminotransferase	62.1±263.48	96.59±120.96	0.30
Alanine Aminotransferase	41.56±177.97	52.55±63.81	0.57
Alkaline phosphatase	134.35±76.33	177.36±171.67	0.27
Sodium (mEq/ml)	129.51±11.69	129.82±7.86	0.87
Potassium	4.05±0.62	4.3±1.19	0.36
Chloride	90.11±6.98	90.38±7.9	0.88

DISCUSSION:

In our study, prevalence of the pulmonary tuberculosis is three times higher in males than females, and is in agreement to the earlier reports from India [8,9] and South East Asian studies [10].

Globally the M: F ratio may ranges from 1.3 in WHO Eastern Mediterranean Region to 2.1 in WHO Western Pacific Region [1]. Majority of the men work in a place, which are overcrowded, with improper ventilation and lack of safety equipments, make them more exposed to TB, and being the main bread earner of the family loss of working days causes a great impact on the socio-economic and educational status. Nearly 60% of the patients belonged to the age group of 31-60years, which again the economically productive age group. This age group very much reported being infected by TB globally.

Systemic symptoms like loss of appetite (8.6%) and significant weight loss (5.74%) were also seen in our patients, which are seen in most of the TB patients. It is in contrary to the other Indian studies, were weight loss in 30%-84% of the PTB cases [8,11]. Most of our cases (around 50%) were diagnosed within 2 weeks of symptoms, this may explains the low percentage of patients having loss of appetite. Around 2% of the patients were having symptoms for more than 6 months, the reason for the delayed intervention is not known, which is significant as delay in treatment exposes more people to TB , whenever patients cough them out through droplet.

Among the lungs , most commonly the right lung is involved in the disease as right bronchus is in line with trachea. Among the various radiological lung zone, upper zone is commonly involved, with typical infiltrate or cavitary lesion as described in scientific literatures[12].

Among the haematological parameters, haemoglobin was significantly low. Anaemia is common in patients with TB and is associated with higher mortality [13,14]. The total leucocyte count, differential lymphocyte and macrophage count was observed to be increased, along with ESR, this is attributed to chronic granulomatous inflammation seen in TB.. In a study conducted in South Indian population, leucocytosis and increased ESR was observed with mild anaemia and thrombocytopenia [13]. Anaemia

and thrombocytopenia with raised ESR is seen in most of the PTB patients [15], whereas varied

haematological abnormalities have also been observed in Indian population. The serum total bilirubin, S. Globulin, A: G ratio, and liver enzymes were increased and serum albumin decreased, this explains that the effect of inflammation in the liver parenchyma and thus deranging the liver parameters, when compared to healthy individuals. Malnutrition and extensive (cavitary) Pulmonary Tuberculosis are associated with deranged liver enzymes [16,17]. When these parameters were compared dead versus alive TB patients, the patient with anaemia, lower differential macrophage count, platelet count, reduced ESR had succumbed to TB. The higher total bilirubin, lower globulin was significantly associated with mortality in TB patients, which are associated with severely compromised liver function test.

CONCLUSION:

In our study population, occurrence of Pulmonary Tb was common in males, and in age group of 31-60 years. Among the PTB patients, Cough with expectoration was the commonest symptoms followed with fever and breathlessness. The TB patients had significant anemia, leucocytosis, thrombocytosis, hypoalbuminemia, uremia, raised ESR and elevated liver enzymes compared to healthy individuals. The mortality in TB patients was associated with severe anaemia, lower differential macrophage count, and lower globulin.

The limitation of the study was that, this was conducted at a tertiary care centre in a city with good medical facility. Attempts are being focused at accruing information from rural and medically underserved areas where the socioeconomic and ignorance to the ailments is different from that in the study area. The other important lacuna was that this was a retrospective study and the parameters considered were at the time of clinical presentation at our center. Prospective studies are being planned to

understand the changes in the clinical and laboratory details, drug adherence, and virulence pattern of the

organism with treatment outcome to the various anti-tubercular therapy. The outcome of this proposed study will have an important bearing from both subject and clinical perspective.

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