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Research Article

MORTALITY RISK FACTORS AMONG HOSPITALIZED SMEAR POSITIVE PULMONARY TUBERCULOSIS PATIENTS

¹Dr Samreen Javed, ²Dr Shabana Shaheen, ³Dr Manahil Masood¹Fatima Jinnah Medical University, Lahore., ²Fatima Jinnah Medical University, Lahore., ³King Edward Medical University, Lahore.**Article Received:** October 2020**Accepted:** November 2020**Published:** December 2020**Abstract:****Aim:** To assess risk factors that have a significant impact on mortality in patients with positive pulmonary tuberculosis (PTB) test result**Methods:** A descriptive cross-sectional study was conducted at the Chest Medicine Department of Sir Ganga-ram Hospital Lahore for one-year duration from June 2019 to June 2020. One hundred and seventy (170) Acid Fast Bacilli (AFB) confirmed PTB-positive patients, aged 13 to 80 years, were enrolled in the continuous sampling study, while patients with drug-resistant tuberculosis (TB) and extrapulmonary tuberculosis remained excluded from the study. Selected patients were interviewed to collect demographic and risk factor data using a standardized questionnaire.**Results:** Out of 170 patients treated with PTB, mortality was found in 23 (13.5%) patients, including 12 (52.2%) men and 11 (47.8%) women. Mortality was significantly related to age ($p = 0.003$), socioeconomic status ($p = 0.019$), anemia ($p = 0.03$), chronic liver disease (CLD) ($p = 0.005$), diabetes mellitus (DM) ($p = 0.001$), Human Immunodeficiency Virus (HIV) ($p = 0.007$), hypertension (HTN) ($p = 0.006$), recurrent tuberculosis ($p = 0.001$), and smoking ($p = 0.001$).**Conclusions:** Aging, poverty, smoking and the presence of comorbidities such as DM, CLD, HIV, hypertension and anemia are associated with higher mortality in cases of PTB with positive smear results.**Keywords:** mortality, positive smear, pulmonary tuberculosis, risk factors, coexisting diseases.**Corresponding author:****Dr Samreen Javed**

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INTRODUCTION:

Tuberculosis (TB) is one of the oldest infectious epidemic diseases caused by airborne bacteria, or *Mycobacterium tuberculosis*. It is a multi-systemic infectious disease that most commonly affects the lungs, commonly known as pulmonary tuberculosis (PTB). Tuberculosis affects various systems of the body, including the respiratory, gastrointestinal, lymphoid, musculoskeletal, reproductive, and central nervous systems. It is one of the major health problems in the world, affecting 1/3 of the population late in life. The World Health Organization (WHO) reports ten million new cases of tuberculosis in 2017, including 5.8 million men, 3.2 million women, and one million children. Pakistan is one of the top eight countries with 66.6% of new PTB reported cases. The Human Immunodeficiency Virus (HIV) is the major risk factor reported by WHO, accounting for 11% of newly diagnosed PTB. Patients with pulmonary tuberculosis often experience cough with or without sputum, fever, weight loss, night sweats, shortness of breath, and chest pain. Sputum swab is the most commonly used diagnostic method in patients with PTB. Patients with PTB with a positive smear are considered the most infectious as they are able to transmit the infection to 15 people without PTB per year. The smear test is a cornerstone in the early diagnosis of PTB in patients and the initiation of anti-tuberculosis treatment (ATT). Despite this, PTB is diagnosed and treated early, but is still the leading cause of mortality. WHO reports 1.3 million and 0.3 million deaths worldwide in 2017 from HIV-negative tuberculosis and HIV-positive tuberculosis, respectively. The mortality rate of PTB varies in different regions of the world, in developing countries with high mortality, while in developed countries with low mortality. However, PTB is directly related to various risk factors that increase mortality, such as delayed diagnosis of PTB, poor ATT compliance, lack of adequate health facilities and patients' ignorance of health in developing countries, homelessness, aging, HIV infection, anemia, DM, CLD, HTN, recurrent tuberculosis and smoking. These several risk factors increase the chances of developing drug resistance that lead to treatment failure, relapse of PTB, and eventually patient death. The aim of the study was to assess the risk factors associated with mortality in patients with PTB positive smear treated at the Ojha Institute for Chest Diseases.

METHODS:

A descriptive cross-sectional study was conducted at the Chest Medicine Department of Sir Ganga-ram Hospital Lahore for one-year duration from June 2019 to June 2020. One hundred seventy (170) patients hospitalized from PTB positive smear patients receiving Category I ATT were selected in the first four months of the study, and each patient was followed during the intensive treatment phase, ie for two months. Patients with PTB aged 13-80 years were enrolled in the method of taking subsequent samples, and patients with drug-resistant tuberculosis and extrapulmonary tuberculosis were excluded from the study. Study approval was obtained from the Institutional Review Board (IRB). Selected patients were interviewed to gather demographics and related risk factors such as; anemia, CLD, DM, HIV, HTN, and smoking history and PTB using a standardized questionnaire. Patients' socioeconomic status has been divided into different classes based on monthly Pakistani rupee (PKR) income, such as lower class (PKR <20,000), middle class (PKR 20,000-50,000) and upper class (> 50,000 PKR). Various risk factors were confirmed using a standard protocol. The blood pressure of each patient with PTB was measured to confirm hypertension. Special laboratory tests have been performed to confirm related risk factors such as complete blood count (CBC) for anemia, fasting and random blood sugar (RBS) for diabetes, HIV screening, abdominal ultrasound and liver function tests (LFT) in chronic liver disease. All data collected were interpreted by SPSS version 22 using the chi-square test and using <0.05 as the significant p value.

RESULTS:

During the one-year study, 170 patients with PTB were assessed for various risk factors, the majority of whom were 92 men (54.1%) and 78 (45.9%) women. Patients of all age groups suffered from PTB, most of them 58 (34.1%) in 13-30 years, then 43 (25.3%) in 46-60 years, 36 (21.2%) in 31-45 years and 33 (19.4%) in 61-80 years. Most of the patients were in the lower socioeconomic class of 95 (55.9%), then the middle class of 67 (39.4%) and only 8 (4.7%) of the higher. Most of the patients were illiterate 60 (35.3%) and only 14 (8.2%) were graduates. Most of the patients with PTB were married 125 (73.5%), followed by 38 (22.4%) unmarried (Table I).

Table-I: Demographic Data.

Variable	Frequency (n=170)	Percentage
Gender		
Male	92	54.1
Female	78	45.9
Age (Years)		
13-30	58	
31-45	36	
46-60	43	34.1 21.2 25.3
61-80	33	19.4
Socioeconomic Status		
Lower	95	55.9
Middle	67	39.4
Upper	8	4.7
Marital Status		
Single	38	22.4
Married	125	73.5
Divorced	2	1.2
Widowed	5	2.9
Education		
Illiterate	60	
Primary	22	
Middle	17	
Matriculation	25	35.3 12.9 10.0 14.7
Intermediate	32	18.8
Graduate	14	8.2

At study entry, most patients experienced a cough > 2 weeks 109 (64.1%), followed by weight loss 73 (42.9%), dyspnea 31 (18.2%), pyrexia 27 (15.9%), chest pain in 21 (12.4%), and night sweats in 13 (7.6%). Chest X-ray was correct only in 2.9% and abnormal in 97.1%. Infiltration in CXR was most often observed in 55 (32.4%) patients, consolidation in 51 (30.4%), and cavitation in 39 (22.9%) patients. PTB was unilateral in 101 (59.4%) and bilateral in 69 (40.6%) patients (Table II).

Table-II: Clinical Presentation of PTB patients

Variable	Frequency (n=170)	Percentage
Sign and symptoms		
Cough	109	
Fever	27	
Weight Loss	73	64.1 15.9
Night sweats	13	42.9 7.6
Breathlessness	31	18.2
Chest pain	21	12.4
CXR		
Normal	5	
Consolidation	51	
Infiltrates	55	2.9
Cavitation	39	30.0 32.4
Consolidation + Infiltrate	3	22.9
Cavitation + Infiltrate	13	1.8 7.6
Consolidation + Cavitation	4	2.4
Extensive Disease		
Unilateral	101	59.4
Bilateral	69	40.6

The majority of patients hospitalized after PTB, ie 147 (86.5%) were treated and discharged (DC) from the hospital, while 23 (13.5%) patients hospitalized with PTB died during treatment. After treatment of patients with PTB in the hospital, the mortality of 23 patients with PTB was followed and assessed for various risk factors, of which 12 (52.2%) and 11

(47.8%) patients were male and female, respectively. Various risk factors significantly related to mortality were assessed during the study, such as: age ($p = 0.003$), socioeconomic status ($p = 0.019$), anemia ($p = 0.03$), CLD ($p = 0.005$), DM ($p = 0.001$), HIV ($p = 0.007$), HTN ($p = 0.006$), recurrent tuberculosis ($p = 0.001$), and smoking ($p = 0.001$) (Table III).

Table-III: Risk factors of Mortality.

Variables	Outcome		Total (n=170)	P-value
	Treated & DC (n=147)	Expired (n=23)		
Gender				
Male	80 (54.4%)	12 (52.2%)	92 (54.1%)	0.8
Female	67 (45.6%)	11 (47.8%)	78 (45.9%)	
Age				
13-30	55 (37.5%)	3 (13.0%)	58 (34.1%)	0.003
31-45	32 (21.8%)	4 (17.4%)	36 (21.2%)	
46-60	38 (25.8%)	5 (21.7%)	43 (25.3%)	
61-80	22 (14.9%)	11 (47.8%)	33 (19.4%)	
Socioeconomic status				
Lower	76 (51.7%)	19 (82.6%)	95 (55.9%)	0.019
Middle	63 (62.9%)	4 (17.4%)	67 (39.4%)	
Upper	8 (5.4%)	0 (0.0%)	8 (4.7%)	
Educational status				
Illiterate	49 (33.3%)	11 (47.8%)	60 (35.3%)	0.8
Primary	20 (13.6%)	2 (8.7%)	22 (12.9%)	
Middle	15 (10.2%)	2 (8.7%)	17 (10.0%)	
Matriculation	22 (15.0%)	3 (13.0%)	25 (14.7%)	
Intermediate	28 (19.0%)	4 (17.4%)	32 (18.8%)	
Graduate	13 (8.8%)	1 (4.3%)	14 (8.2%)	
Anemia				
Yes	74 (50.3%)	17 (73.9%)	91 (53.5%)	0.03
No	73 (49.7%)	6 (26.1%)	79 (46.5%)	
CLD				
Yes	18 (12.2%)	8 (34.8%)	26 (15.3%)	0.005
No	129 (87.8%)	15 (65.2%)	144 (84.7%)	
DM				
Yes	17 (11.6%)	15 (65.2%)	32 (18.8%)	0.001
No	130 (88.4%)	8 (34.8%)	138 (81.2%)	
HIV				
Yes	1 (0.7%)	2 (8.7%)	3 (1.8%)	0.007
No	146 (99.3%)	21 (91.3%)	167 (98.2%)	
HTN				
Yes	8 (5.4%)	5 (21.7%)	13 (7.6%)	0.006
No	139 (94.6%)	18 (78.3%)	157 (92.4%)	
Recurrent TB				
Yes	53 (36.1%)	1 (4.3%)	54 (31.8%)	0.001
No	94 (63.9%)	22 (95.7%)	116 (68.2%)	
Smoker				
Yes	35 (23.8%)	16 (69.6%)	51 (30.0%)	0.001
No	112 (76.2%)	7 (30.4%)	119 (70.0%)	

DISCUSSION:

Pulmonary tuberculosis (PTB) is one of the major health problems in developing or low-income countries. Despite widespread medical advances and improvements in health facilities, PTB continues to be a life-threatening disease in poor countries. The direct involvement of various risk factors for this dilemma is a clear cause of the increasing susceptibility to infection and the progression of PTB. These factors also play a significant role in predicting mortality in patients with PTB, such as aging, poor health care due to poverty, low income, anemia, CLD, DM, HIV, HTN, recurrent tuberculosis, and smoking. The WHO reports that tuberculosis morbidity and mortality is steadily increasing worldwide, and tuberculosis is the leading cause of infectious disease mortality.^{4,5} The current study has two important findings, the first being increased mortality in patients with PTB and the second being a significant association between risk factors from PTB. The first major finding of the current study was a higher mortality rate in patients with PTB, i.e. 13.5%, while most other studies showed a lower mortality than the current study, such as Asgedom SW et al., 11.3%, Shahrezaei M et al. 1.6% and Rodrigo T et al. 3.5%. In another study by Takarinda KC et al. Reported a higher mortality rate of 22.0% among patients with tuberculosis. In the present study, mortality was high for several reasons, including illiteracy, poverty, and comorbid disease. The second important finding is the direct and significant relationship of various risk factors with mortality in patients with PTB. Mortality is significantly associated with age, poverty, anemia, CLD, DM, HIV, HTN, recurrent tuberculosis, and smoking. As with our score, different studies show the importance of different risk factors and mortality. A study from Pakistan by Khaliq A et al on various social and environmental risk factors in patients with PTB found a significant association of PTB mortality with male gender, poverty, smoking, diabetes, asthma, HIV, and tuberculosis relapse. A study by Shahrezaei M et al. Found a significant relationship between mortality and age, body weight and tuberculosis incidence. Other important factors reported are DM and HIV. In another study, Alavi-Naini R et al. Cited anemia, smoking, DM, HIV, drug abuse, hepatitis, and recurrent tuberculosis as predictors of PTB mortality. In low-income countries, poverty is the most common cause of increasing malnutrition and diseases such as tuberculosis. Malnutrition directly affects cellular immunity, ie the primary defense against tuberculosis leading to the rapid progression of tuberculosis in malnourished patients as well as in immunocompromised patients such as HIV. Aging is

another important factor that increases comorbidities and worsens the situation with appropriate TB treatment, ultimately increasing mortality. PTB patients suffering from DM are at greater risk of developing tuberculosis with increased progression and mortality. Tuberculosis is most commonly known as the disease of poverty because of its direct relationship with other risk factors that increase the onset and progression of tuberculosis. The current study also indicates a higher incidence of illiteracy, lower socioeconomic status, and the presence of comorbidities that are not only directly related to PTB progression, but also increase the likelihood of treatment failure resulting in patients' death. Study limitation: Patients were followed for a short period of time, ie in the intensive phase, and the severity of comorbidities was not assessed. Poor healthcare conditions, diagnosis delays, non-adherence to treatment, and the emergence of resistance can be further investigated as an associated risk factor for mortality in patients with smear positive PTB.

CONCLUSION:

The study shows that the mortality rate was high among patients hospitalized for PTB treatment. Risk factors; such as age, poverty, anemia, CLD, DM, HIV, hypertension, recurrent tuberculosis and smoking are significantly associated with mortality in these patients.

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