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Clinical Factors Predictive of High Bacillary Load in Pulmonary Tuberculosis

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Abstract

Introduction: Tuberculosis (TB) remains the leading cause of preventable death from an infectious agent. Sputum smear-positive pulmonary tuberculosis (SSB) is the primary vehicle of transmission. TB contagiousness and patient prognosis are influenced by the bacterial load of the index case. This study aimed to identify clinical signs predictive of a High Bacterial Load (HBL) defined as a sputum smear microscopy result at 3+ that could guide treatment decisions or shorten the time to treatment initiation. **Materials and Methods**: This was a cross-sectional, analytical study conducted in the Pneumology Department of the Point G University Hospital between January 2022 and November 2025. The study population consisted of new cases of smear positive and culture-confirmed pulmonary tuberculosis (PTB+). Sociodemographic, clinical, and bacteriological data were collected in an Excel file and then analyzed using SPSS 25. Descriptive analyses, association analyses, and logistic regression were performed. The significance level was set at a 5% to 95% confidence interval. **Results**: A total of 464 culture-confirmed PTB+ patients were analyzed, of whom 72.0% were male, and 28.0% were female. The mean age was 33.7 ± 12.7 years, and 63.6% were ≤35 years old. HIV co-infection was present in 9.7% of cases, smoking was reported in 36.0%, and 9.9% consumed alcohol. Tuberculosis contact was reported in 23.5%, hemoptysis in 9.9%, and fever in 13.1%. Patients with High Bacterial Load (HBL) represented 74.1% of the study sample. Univariate analysis showed an association between HBL and male sex with an OR of 2.08, p = 0.001; smoking with an OR of 1.96, p = 0.004. Fever (OR = 2.24, p = 0.023) and hemoptysis (OR = 3.62, p = 0.003) were predictors of HBL. Conversely, the presence of chronic conditions and HIV infection was associated with a low risk of HBL, with ORs of 0.38 (p = 0.001)

and 0.31 (p = 0.0003), respectively. Logistic regression identified smoking (OR = 1.74, p = 0.036), fever (OR = 2.19, p = 0.047), and hemoptysis (OR = 2.95, p = 0.032) as predictors of HBL. HIV was a predictor of paucibacillary sputum (OR = 0.30, p = 0.046). **Conclusion**: The study identified clinical predictors of a high bacillary load as determined by Sputum Smear Microscopy (SSM). These predictors could assist clinicians in triage and isolate highly contagious TB cases, as well as provide rapid care to improve patient outcomes.

Keywords

Tuberculosis, High Bacterial Load, Clinical, Predictors, Mali

1. Introduction

Tuberculosis (TB) is one of the contagious infectious diseases whose causative agent is genetically well characterized. However, no long-term protective vaccine is available that can be administered at any age [1]. The incidence of TB has been declining over the years according to World Health Organization (WHO) indicators, but it remains the leading cause of death from an infectious agent despite the availability of diagnostic tools and effective treatment [2] [3]. The introduction of Xpert MTB/RIF® as a first-line test for TB diagnosis has significantly improved the case detection rate [4] [5]. Despite improvements in diagnostic capabilities, the time to diagnosis of TB remains long. This diagnostic delay is associated with several factors, including medical, social, and personal reasons. A systematic review and meta-analysis reported that the diagnostic delay for TB varies between high-income and low-income countries [6] In Mali, a study conducted in 2022 found a median diagnostic delay of 114 days (~4 months) between the onset of cough and the date of TB diagnosis, including a medical delay median of 57 days between the date of the first consultation and the date of diagnosis. Among the reasons identified were delayed consultation, traditional treatment, and failure to request sputum testing during consultations [7]. A study conducted in Bangui, Central African Republic, reported that failure to request sputum smear microscopy increases the risk of delayed TB diagnosis six-fold [aOR = 6.09 (3.70 - 17.69)] [8]. Delayed diagnosis and prolonged contact with contagious TB cases are sources of transmission and contribute to the increased mortality rate of the disease. The spread of TB infection is partly linked to delayed diagnosis, leading to high bacterial loads in patients that can be complicated by sepsis and/or hemoptysis. Pulmonary cavitation resulting from destruction of the lung parenchyma by the bacillus and necrosis is associated with TB transmission, according to several studies [9] [10]. In low-income countries, and particularly in community health centers, the use of Xpert MTB/RIF® is hampered by frequent cartridge shortages or low power supply. Therefore, microscopy remains the most consistent and universal diagnostic method for TB.

Very few studies have been conducted to determine the predictors of High Bac-

terial Load (HBL) in patients with pulmonary TB. Most studies on bacillary load have focused on monitoring sputum smears during TB treatment. However, the lack of knowledge regarding the contagiousness level of a patient suspected of having TB increases the risk of transmission to family contacts, on public transportation, and in the workplace. To contribute to reducing TB transmission and mortality, this study was initiated to determine the predictors of a high bacillary load. Identifying these predictors will guide rapid triage, isolation, testing, and initiation of TB treatment for highly contagious cases, thus reducing TB transmission.

2. Materials and Methods

A descriptive and analytical cross-sectional study was conducted on TB patients at the Pneumology department of the Centre Hospitalier Universitaire of Point G (CHU-PG) between January 1, 2022, and January 30, 2025. The CHU-PG is a tertiary referral hospital located in the district of Bamako, the capital of Mali. The department is the highest referral center for respiratory diseases in Mali. It offers specialized technical facilities for diagnosis and exploratory examinations, as well as a platform for Pneumology training and disease research. The study population included smear-positive pulmonary TB patients diagnosed with microscopy and/or Xpert MTB/RIF® who were initiated on TB treatment at the CHU-PG during the study period. We analyzed data from TB-confirmed patients by Xpert MTB/RIF® detecting *Mycobacterium tuberculosis* (MTB) genome. We excluded unconfirmed TB cases who had sputum AFB-positive and positive Xpert MTB/RIF® suspected of Non-tuberculosis Mycobacteria (NTM). Data were collected from patient records using a questionnaire designed and tested specifically for this study. This included sociodemographic information (age, sex, occupation, usual residence, education level, marital status), lifestyle (smoking, alcohol consumption), chronic diseases such as diabetes, HIV, and sickle cell disease, and clinical information including fever, chest pain, hemoptysis, temperature, and Body Mass Index (BMI). The results of acquired immunodeficiency virus (HIV) test, microscopy, and Xpert MTB/RIF® were performed either at the biosafety level 3 laboratory at the University Clinical Research Center (UCRC) of the University of Sciences, Techniques, and Technologies of Bamako (USTTB) or TB laboratory of the National Institute of Public Health of Mali. Data was entered into an Excel 13.0 spreadsheet and then analyzed using SPSS version 25.0. Patients were divided into two categories: those with a 3+ bacillary load (3 crosses) were designated High Bacillary Load (HBL), and those with a 2+ (2 crosses), 1+ (1 cross), or +F (weakly positive) bacillary load. Patients were grouped based on the existence of comorbidities, such as HIV, diabetes, or sickle cell disease (called chronic diseases) due to their detrimental effect on immunity. Occupations were classified as formal for subjects working in a public or private structure with a monthly salary, and informal for those engaged in self-employment. Sociodemographic data were described, univariate association tests (chi-square) were performed to determine Odds Ratios (OR), and binary logistic regression was conducted to calculate ad-

justed Odds Ratios (aOR) to identify clinical predictors of HBL. Differences observed between the two groups were considered statistically significant if the p-value was < 5% (0.05). Ethical procedures were followed in the collection and processing of information gathered from patient records. Each record was assigned a number in addition to the patient's initials for identification. The study was approved by the Director of the CHU-PG and Ethics Committee of the University of Sciences, Techniques and Technologies of Bamako (USTTB) before data collection.

3. Results

Data from 464 patients with bacteriologically confirmed pulmonary TB were analyzed. Sociodemographic and clinical characteristics are described in Table 1. Males were predominant, with 334 cases (72.0%), while females comprised 28.0%. The 26 - 35 year and ≤ 25 years age groups were the most frequent, with 149 cases (32.1%) and 146 cases (31.5%), respectively. The mean age was 33.7 ± 12.7 years, with a range of 14 to 78 years. Illiterate individuals were the most represented, with 191 cases (41.2%). Married individuals accounted for more than half of the cases (58.4%), and the primary residence was Bamako-Urbain in 56.0% of cases. Informal occupation was the most frequent at 78.4%, and HIV and diabetes were the most common chronic conditions, with 45 cases (9.7%) and 14 cases (3.0%), respectively. Smoking was found in 164 cases (36.0%), and alcohol consumption in 46 cases (9.9%). Prior contact with a TB patient was reported in 109 patients (23.5%), and hemoptysis in 46 cases (9.9%). Fever (temperature > 38.0˚C) was found in 61 cases (13.1%), underweight (BMI ≤ 18.5 kg/m^2) in 293 cases (63.1%), and high bacterial load (BAR = 3+) in 344 cases (74.1%). Univariate analysis showed an association between High Bacterial Load (HBL) and male sex: OR = 2.08 (1.35 - 3.20), p = 0.001; smoking: OR = 1.96 (1.25 - 3.06), p = 0.004; fever: OR = 2.24 (1.10 - 4.56), p = 0.023; hemoptysis: OR = 3.62 (1.40 - 9.37), p = 0.003. In contrast, the presence of chronic immunosuppressive disease (HIV, diabetes, and sickle cell disease) and HIV were associated with a low risk of HBL, respectively aOR = 0.38 (0.22 - 0.65), p = 0.001 and aOR = 0.31 (0.17 - 0.58), p = 0.0003 (Table 2). Binary logistic regression analysis identified smoking (aOR = 1.74 [1.04 - 2.92], p = 0.036), fever (temperature ≥ 38˚C) (aOR = 2.19 [1.01 - 4.74], p = 0.047), and hemoptysis (aOR = 2.95 [1.10 - 7.94], p = 0.032) as predictors of HBL. Conversely, HIV infection was a predictor of lower bacillary load in sputum (aOR = 0.30 [0.09 - 0.98], p = 0.046) (Table 3).

Table 1. Socio-demographic and clinical characteristics of the study patients.

Parameters		Effective	Percentage
Age ranges (years)	14 - 25	146	31.5
	26 - 35	149	32.1
	36 - 45	87	18.8
	46 and over	82	17.7

Continued

Sex	Male	334	72.0
	Female	130	28.0
Education Level	Unliterate	191	41.2
	Primary	113	24.4
	Secondary	114	24.6
	University	46	9.9
Marital status	Single	193	41.6
	Married	271	58.4
Residence	*BKO/Neighborhood	260	56.0
	*Regions/Foreigners	204	44.0
Professional sector	Formal	100	21.6
	Informal	364	78.4
Medical History	Diabetes	14	3.0
	HIV	45	9.7
	Sickle cell disease	4	0.9
	Hypertension	2	0.4
	None	401	86.4
Smoking	No	297	64.0
	Yes	164	36.0
Alcohol consumption	No	418	90.1
	Yes	46	9.9
Tuberculous Contact	No	355	76.5
	Yes	109	23.5
Hemoptysis	No	418	90.1
	Yes	46	9.9
Fever (≥38˚C)	No	403	86.9
	Yes	61	13.1
*BMI (Kg/m^2)	Malnutrition ≤ 18.5	293	63.1
	Normal or overweight	171	36.9
Bacterial Load in sputum	Scanty+	8	1.7
	1+	32	6.9
	2+	80	17.2
	3+	344	74.1

*BKO: Bamako city; BMI: Body Mass Index; BKO/Neighborhood: Patients living in Bamako, the capital city of Mali or surrounding areas; Regions/Foreigners: Patients living in other administrative regions of Mali and those who travelled from a neighboring country.

Table 2. Parameters associated with High Bacterial Load in the sputum at microscopy.

Parameters		LBL (<3+)	HBL (3+)	95% CI	P-value
Age (years)	≤35	76	219	0.75 (0.49 - 1.13)	0.167
	>35	54	115		
Sex	Female	52	78	2.08 (1.35 - 3.20)	0.001*
	Male	81	253		
Education	<Secondary	85	219	0.91 (0.60 - 1.38)	0.666
	≥Secondary	48	112		
Marital status	Single	49	144	0.76 (0.50 - 1.15)	0.212
	Married	84	187		
Residence	*BKO/Neighborhood	68	192	0.76 (0.51 - 1.13)	0.181
	Regions/Foreigners	65	139		
Occupation	Not Structured	104	260	0.98 (0.60 - 1.60)	1.0
	Structured	29	71		
TB Contact	No	107	248	1.38 (0.84 - 2.26)	0.227
	Yes	26	83		
Chronic Disease	No	103	299	0.38 (0.22 - 0.65)	0.001*
	Yes	30	33		
Smoking	No	99	198	1.96 (1.25 - 3.06)	0.004*
	Yes	34	133		
Alcohol	No	119	299	0.91 (0.47 - 1.77)	0.864
	Yes	14	32		
Fever (≥38˚C)	No	123	280	2.24 (1.10 - 4.56)	0.023*
	Yes	10	51		
Weight Loss	No	56	153	0.85 (0.56 - 1.27)	0.470
	Yes	77	178		
HIV	Negative	109	310	0.31 (0.17 - 0.58)	0.0003*
	Positive	24	21		
Hemoptysis	No	128	290	3.62 (1.40 - 9.37)	0.003*
	Yes	5	41		

An association was observed between high bacterial load and male sex, smoking, fever, and hemoptysis. Conversely, HIV and the presence of chronic disease were associated with low bacterial load in sputum.

Table 3. Predictors of High Bacterial Load at Sputum Microscopy.

Parameters		Low BAC	BAAR 3+	Gold, 95% CI	P-value	aOR, 95% CI	P-Value
Age (years)	≤ 35	76	219	0.75 (0.49 - 1.13)	0.167	1.36 (0.86 - 2.13)	0.189
	> 35	54	115				
Sex	Female	52	78	2.08 (1.35 - 3.20)	0.001	1.46 (0.89 - 2.41)	1.135
	Male	81	253				
Chronic Disease	No	103	298	0.38 (0.22 - 0.65)	0.001	1.01 (0.35 - 2.92)	0.979
	Yes	30	33				
Smoking	No	99	198	1.96 (1.25 - 3.06	0.004	1.74(1.04 - 2.92)	0.036*
	Yes	34	133				
Fever (≥38˚C)	No	123	280	2.24 (1.10 - 4.56)	0.023	2.19 (1.01 - 4.74)	0.047*
	Yes	10	51				
HIV	Negative	109	310	0.31 (0.17 - 0.58)	0.0003	0.30 (0.09 - 0.98)	0.046*
	Positive	24	21				
Hemoptysis	No	128	290	3.62 (1.40 - 9.37)	0.003	2.95 (1.10 - 7.94)	0.032*
	Yes	5	41				

Logistic regression results show that smoking, fever, and hemoptysis are predictors of a high bacterial load. Conversely, HIV infection is associated with low bacterial load in sputum.

4. Discussion

Tuberculosis is a disease of younger and older people due to their weakened immune systems. The predominance of TB in males compared to females is almost constantly reported in several studies as well as in WHO annual TB reports [11]-[14]. In many countries around the world, particularly in Africa, tests used for TB diagnosis have turnaround times ranging from 24 hours for Xpert MTB/RIF®, 48-72 hours for microscopy, to several weeks for culture. The Xpert MTB/RIF® is the fastest test widely used worldwide, with a turnaround time of 2 hours [15]. In community settings, TB diagnosis is generally based on microscopy staining by observation of Acid-Fast Bacilli (AFB) in samples requiring 2 - 3 sputum samples [16]. Death is more often linked to complications related to comorbidities, anemia due to frequent hemoptysis, septic shock, and fever that is responsible for dehydration [17]. While early diagnosis of TB is crucial for the patient's prognosis, isolation of the TB patient is also crucial to stop TB transmission. According to a chapter on TB transmission, the probability of TB contagion to their contacts depends on the bacterial load of the source case [18]. Our study observed that the following clinical factors are associated with a high bacterial load: tobacco use (aOR = 1.74, p = 0.036); fever (temperature ≥ 38˚C) (aOR = 2.19, p = 0.047); and the presence of hemoptysis (aOR = 2.95, p = 0.032). HIV co-infection is a predictor of paucibacillary TB (aOR = 0.30, p = 0.046). A study in China reported that hemoptysis is a predictor of TB infectivity [19]. In Vietnam, hemoptysis was twice as frequent in patients with AFB-positive TB compared to those with AFB-nega-

tive TB [20]. A study in Thailand reported that TB patients with Sputum Smear Cytology (SSC) had a two-fold increased risk of TB transmission to their contacts (aOR = 2.95%) [21]. One study reported that coughing is not necessarily required for TB transmission; bacilli can be disseminated through respiration and sneezing. These findings support the argument that every minute counts in saving people in contact with a smear-positive pulmonary TB patient [22]. HIV impairs immune function through a progressive decline in lymphocyte T-cells. During HIV infection, the inflammatory response against TB is weak, which promotes bacterial dissemination and fewer cavitary lesions, resulting in extrapulmonary localizations and low bacterial load. Diagnosing TB in HIV-positive individuals requires meticulous detection of lesions on imaging and careful selection of the appropriate tests for confirmation. The Xpert MTB/RIF Ultra is one of the diagnostic tools for TB in immune-compromised individuals, the elderly, and children. A patient with a strong suspicion of TB but a negative microscopy should alert the clinician to further appropriate testing [23]-[25]. Conversely, some studies have used monitoring of bacillary load as an indicator of treatment success. In a multicenter study collecting data from four sites in three countries, including Tanzania, Mozambique, and Malawi, patients with sputum smear microscopy before treatment initiation (> 5.5 log10 CFU/ml) were less likely to test negative at 2 months of treatment than those with a low load (<5.5 log10eCFU/ml), HR 3.1, 95% CI (1.6 to 5.6), p = 0.0005, regardless of the treatment regimen [26]. A study in Ethiopia reported that highly positive sputum smear in drug-resistant TB patients was significantly associated with ≥2 prior TB treatments [27]. In resource-limited countries, a large proportion of TB cases are diagnosed in the community through microscopy. Therefore, the identified clinical predictors can assist practitioners in peripheral health centers in triaging patients suspected of having TB, isolating them, and prioritizing their bacteriological testing. The identified positive predictors of HBL in PTB (fever, smoking, hemoptysis) could be integrated into a simple clinical checklist or triage tool for use in peripheral health centers with limited diagnostic capacity. A low bacterial load should be a warning on the patient's immunological profile, thus propose a screening for HIV status.

5. Conclusion

This study identified predictors of TB patients with High Bacterial Load. These indicators could help clinicians in triage and isolation of highly contagious TB cases to prevent community-level TB transmission. They also serve for faster management of smear-positive TB cases, ultimately improving survival rates and limiting long-term TB consequences.

Limitations of the Study

This study revealed predictors of high tuberculosis bacterial load that could be used in our clinical practice to reduce TB transmission in the community. However, it had some limitations. Imaging was not included in the data analysis, which

would have provided additional predictors. Furthermore, the study did not include patient follow-up to monitor sputum smear grades during the treatment and predict patient outcomes. Nevertheless, in a setting without imaging capabilities, these predictors can be useful for preventing transmission through prompt testing, isolation, and early initiation of treatment.

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Conflicts of Interest

The authors have no conflict of interest.

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