

Radiological difference between new sputum-positive and sputum-negative pulmonary tuberculosis

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ABSTRACT

Introduction: The current guidelines for the diagnosis of pulmonary tuberculosis (PTB) are based primarily on the demonstration of acid-fast bacilli (AFB) on sputum microscopy and chest radiograph. Knowing various radiological manifestations and their association with sputum microscopy findings can allow for early diagnosis and early initiation of treatment. **Aims:** This study was performed to compare the chest radiograph features seen in sputum-positive and sputum-negative tuberculosis patients, respectively. **Materials and Methods:** It was a prospective observational study, which included 147 consecutive patients newly diagnosed and treated as PTB between Jan 2018 and July 2018. Chest X-ray was reviewed by 2 independent radiologists and the findings were compared between sputum-positive and sputum-negative PTB cases. The obtained data were analyzed by statistics using SPSS version 15 for Windows (SPSS Inc., Chicago, IL) and χ^2 test and Student *t* test were used for statistical analysis. *P* values < 0.05 were considered statistically significant. **Results:** Out of a total of 147 patients, 38 (25 males and 13 females, mean age 35.23 ± 18.40) were sputum positive and 109 (77 males and 32 females, mean age 36.07 ± 18.15) were sputum negative. The frequency of patchy consolidation (78.94% vs 49.54%) and cavitation (36.84% vs 15.59%) was significantly higher in sputum-positive PTB (*P* < 0.05). Radiological lesions like nodular shadow (10.09% vs 2.63%), cystic lesion (13.76% vs 5.26%), fibrosis (12.84% vs 7.89%), miliary shadows (2.75% vs 2.63%), and pleural effusion (1.83% vs 0%) were seen more commonly with sputum-negative PTB but the difference was not statistically significant for any of these features. Sputum-positive PTB tends to occur more commonly on the left side (47.36%) compared with sputum-negative PTB (27.52%) (*P* < 0.05). 34.21% and 35.77% of the chest X-ray lesions were bilateral in sputum-positive and sputum-negative PTB, respectively. **Conclusion:** Patchy infiltration and cavitation on chest X-ray are seen more frequently in sputum-positive cases of PTB compared with sputum-negative cases.

Keywords: Acid-fast bacilli, cavity, chest X-ray, pulmonary tuberculosis

Introduction

Tuberculosis (TB) is one of the major public health problems globally. More than 1.7 billion people, that is, about 25% of the world population, are estimated to be infected with *Mycobacterium tuberculosis*.^[1] According to the World Health Organization (WHO), in 2017, 10 million individuals became ill with TB and 1.6 million died of the disease.^[2]

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Received: 14-08-2019 **Revised:** 14-08-2019 **Accepted:** 03-09-2019

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_652_19

Prompt diagnosis of active TB facilitates timely therapeutic interventions and minimizes community transmission.^[3] The diagnosis of pulmonary TB (PTB) should be suspected in any patient presenting with cough for >2 weeks, fever, night sweats, weight loss, or hemoptysis. All presumptive TB should undergo 2 sputum smear examinations and a chest X-ray (CXR) routinely. One sputum-negative PTB can contaminate 2 people in a year and so rapid diagnosis of this category is as important as that of smear-positive patients. In both smear-negative and smear-positive cases, radiographic changes are helpful in diagnosis.

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How to cite this article: Rai DK, Kirti R, Kumar S, Karmakar S, Thakur S. Radiological difference between new sputum-positive and sputum-negative pulmonary tuberculosis. J Family Med Prim Care 2019;8:2810-3.

Reactivation PTB classically presents with focal infiltration of the upper lobe or the lower lobe. The disease may be unilateral or bilateral. Cavitation may be present, and inflammation and tissue destruction may result in fibrosis with traction and/or enlargement of hilar and mediastinal lymph nodes.

Active PTB often cannot be distinguished from the inactive disease on the basis of radiography alone, and readings of “fibrosis” or “scarring” must be interpreted in the context of the clinical and epidemiologic presentation. Knowing the various radiological manifestations and their associations with sputum microscopy findings allow for early diagnosis and rapid initiation of treatment.

This study was performed to compare the CXR changes seen in sputum-positive and sputum-negative TB patients.

Materials and Methods

It was a prospective observational study, which included all patients who presented to the pulmonary OPD of a tertiary hospital between Jan 2018 and July 2018 and were diagnosed and treated as new cases of PTB.

Exclusion criteria

Patients previously treated for TB.

All presumptive cases of TB underwent 2 sputum smear examinations (spot–early morning or spot–spot) and CXR routinely. All the sputum samples also underwent GeneXpert (CB-NAAT) test.

Following definitions were used for sputum-positive and sputum-negative PTB, respectively.

Sputum-positive PTB

A case was defined as sputum-positive PTB when at least 2 sputum smears were positive for acid-fast bacilli (AFB) or when there was 1 positive sputum smear associated with either 1 positive sputum culture or chest radiographic findings compatible with PTB.

Sputum-negative PTB

A case was defined as sputum negative when the 2 initial sputum samples were negative for AFB but positive for GeneXpert or when there were positive radiographic changes compatible with PTB in the absence of sputum-positive samples.

All CXRs were reviewed independently by 2 radiologists who were unaware of the sputum status. CXR findings like patchy infiltrate, cavity, miliary pattern, cystic lesions, fibrosis, mediastinal adenopathy, and pleural effusion were compared between sputum-positive and sputum-negative cases. The CXRs were classified using the criteria used by the National Tuberculosis Association of USA.^[4,5]

Lesions with slight to moderate density but not containing any demonstrable cavitation were defined as *minimal lesions*. They could involve a small part of 1 or both the lungs, but the total extent, regardless of distribution, should not have exceeded the volume of the lung on 1 side occupying the space above the second chondrosternal junction and the spine of the fourth or body of the fifth vertebra.

Moderately advanced lesions were defined as lesions present in 1 or both lungs, but the total extent not exceeding the following limits: disseminated lesions of slight to moderate density that could extend throughout the total volume of 1 lung or the equivalent in both lungs; dense and confluent lesions limited in extent to one-third the volume of 1 lung; total diameter of cavitation, if present, <4 cm.

Lesions more extensive than moderately advanced were defined as *far advanced lesions*.

Statistical analysis

Categorical data were expressed as proportion and continuous data were expressed as mean ± SD. The obtained data were analyzed by means of frequency distribution table and descriptive statistics using SPSS version 15 for Windows (SPSS Inc., Chicago, IL) and χ^2 test and Student *t* test were used for statistical analysis. *P* values <0.05 were considered statistically significant.

Results

Total 147 patients comply with inclusion criteria; among 38 cases were sputum positive, whereas 109 cases were sputum negative. Baseline characteristics of study patients are given in Table 1.

The most common chest radiograph finding in sputum-positive patients was patchy infiltrate and cavitation, whereas cystic, fibrosis, nodule, and mediastinal adenopathy were found more commonly with sputum-negative PTB [Table 2 and Figure 1].

Sputum-positive PTB was found more commonly on the left side (47.36%) compared with sputum-negative PTB (27.52%) (*P* < 0.05). 34.21% and 35.77% of radiological lesions were bilateral in sputum-positive and sputum-negative PTB, respectively. The frequency of patchy infiltration and cavitation was significantly higher in sputum-positive PTB in compare with sputum-negative PTB (*P* < 0.05). The radiological lesions like

Table 1: Baseline characteristics of the study patients

Characteristics	Sputum-positive PTB (n=38) (25.85%)	Sputum-negative PTB (n=109) (74.14%)	Z score	P
Age (mean±SD)	35.23±18.40	36.07±18.15	N/A	0.807
Male	25 (65.78)	77 (70.64)	0.312	0.722
Female	13 (34.21)	32 (29.35)	0.312	0.722
Diabetic	4 (10.52)	10 (9.17)	0.059	0.939

Numbers in brackets show percentage, PTB: pulmonary tuberculosis

Table 2: Radiological changes in sputum-positive and sputum-negative PTB

Chest X-ray finding	Sputum-positive PTB (n-38)	Sputum-negative PTB (109)	Z score	P
Upper zone predominance	32 (84.21)	84 (77.06)	0.864	0.484
Lower zone predominance	6 (15.78)	25 (22.29)	0.864	0.352
Right	7 (18.42)	40 (36.69)	4.327	0.037
Left	18 (47.36)	30 (27.52)	5.046	0.024
Bilateral	13 (34.21)	39 (35.77)	0.030	0.861
Patchy infiltrate	30 (78.94)	54 (49.54)	9.949	0.003
Cavity	14 (36.84)	17 (15.59)	7.642	0.011
Mediastinal lymphadenopathy	0 (0.00)	4 (3.66)	N/A	N/A
Cystic	2 (5.26)	15 (13.76)	1.989	0.158
Nodular	1 (2.63)	12 (10.09)	1.079	0.472
Miliary	1 (2.63)	3 (2.75)	0.001	0.968
Fibrosis	3 (7.89)	14 (12.84)	0.674	0.59
Pleural effusion	0 (0.00)	2 (1.83)	N/A	N/A
Radiological classification				
Minimal	17 (44.73)	47 (43.11)	0.03	0.986
Moderate	13 (34.21)	48 (44.03)	1.120	0.289
Advanced	6 (15.78)	14 (12.84)	0.208	0.648

P value in bold number showing significant ($P < 0.05$). Numbers in brackets show percentage, N/A: not applicable; PTB: pulmonary tuberculosis

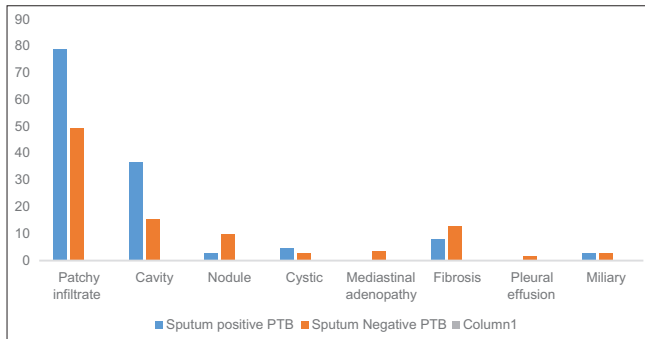


Figure 1: Comparison of chest X-ray lesions between sputum-positive and sputum-negative PTB. Numbers on Y axis represent percentage. (This figure highlighting difference in chest radiograph presentation between sputum-positive and sputum-negative PTB. It is clear that patchy infiltrate and cavity are more common in sputum-positive PTB, whereas nodule and fibrosis are more common in sputum-negative PTB)

nodular shadow, cystic lesion, fibrosis, miliary shadow, and pleural effusion were found more commonly with sputum-negative PTB although statistically not significant ($P = NS$).

Discussion

Out of a total of 147 patients included in the study, 38 (25.85%) cases were sputum positive, whereas 109 (74.14%) were sputum negative. Chest radiography is generally initial approach to diagnostic evaluation of a patient with suspected TB.^[6] Chest radiograph has a high sensitivity for PTB and thus is a valuable modality to identify TB as a differential diagnosis for patients, especially when the X-ray is read to identify any abnormality that is consistent with TB. However, CXR has poor specificity; although some chest radiograph abnormalities are rather specific for PTB (for example, cavities), many chest radiograph abnormalities that are consistent with PTB are seen also in several other lung pathologies and, therefore, are indicative not only of TB but also of other pathologies. Along with there is

also significant intraobserver and interobserver variation in the interpretation of chest radiograph.^[7] So this study was performed to characterized radiological difference between sputum-positive and sputum-negative PTB that help in early identification of TB. PTB classically presents with focal infiltration of the upper lobe that may cavitate and generally associated with sputum positive for AFB. The frequency of cavitation was significantly higher in sputum-positive PTB in comparison with sputum-negative PTB (36.84% vs 15.59%, $P = 0.001$). In the study conducted by Rathman *et al.*,^[8] of the 1389 cases suspected for TB, 34% were smear positive and 66% were smear negative. Cavitation was found more frequently in sputum-positive cases (40% vs. 25%) that is in line with our study. Similarly, patchy infiltration on CXR was found in a significantly higher proportion of sputum-positive cases ($P = 0.003$). Similar findings were noted by another study conducted at the University of Pennsylvania.^[9]

Three-fourth of the lesions were found in the upper zone in both sputum-positive and sputum-negative PTB. The presence of cavities and consolidations in the upper lung fields have been considered to be suggestive of active TB in several prediction models.^[10,11] Radiological lesions like nodular shadow, cystic lesions, fibrosis, miliary shadow, and pleural effusion were seen more frequently with sputum-negative PTB although not to the extent of statistical significance. In the study conducted by the Gatner and Burkhardt, pulmonary lesions compatible with smear-negative PTB were mediastinal adenopathy and pleural effusion.^[12] However, another study found reticulonodular infiltration (98%), cavity (60%), pleural thickening (45%), adenopathy (36%), and fibrosis (30%) were the most common radiological findings in smear-positive PTB.^[13] These unexpectedly high figures maybe because of the inclusion of chronic cases of TB. Thus, the current study, in line with the findings of previous studies, suggests that some CXR lesions like patchy infiltration and cavitation are seen more frequently

in sputum-positive PTB. These findings may be useful to the clinician in reaching a diagnosis.

It is worth noting that in the study by Jones and Schaffner noted that 20% of the patients in a prison with smear-negative PTB might have been missed as the radiographic changes were ignored.^[14] Interestingly, the current study also noted that left-sided lesions were found more frequently in sputum-positive PTB compared with sputum-negative PTB (47.26% vs 27.52%) ($P = 0.024$). In contrast, right-sided lesions were more frequent in sputum-negative PTB (36.69% vs 18.42%) ($P = 0.037$).

This is the first study comparing the CXR findings between new sputum-positive and sputum-negative PTB. Previously treated cases were excluded to avoid post-tuberculosis radiological sequelae that may have lead to misleading results.

A major limitation of the study was confirmation of sputum-negative PTB. Most of the sputum-negative PTB cases were confirmed by the clinical and radiological features and GenXpert positivity but none of the patients had sputum culture, which is the confirmatory test. Another limitation was the small sample size, especially the small number of sputum-positive PTB cases.

Conclusion

The presence of patchy infiltration or cavitation on CXR of suspected cases of PTB favors sputum positivity for AFB. Further research is needed to establish whether cystic and nodular lesions, mediastinal lymphadenopathy, and pleural effusion are more common in sputum-negative PTB.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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