Etenesh Tewolde, Asfaw Atnafu, Tesfaye Kebede, Yared Tedla, Getachew Assefa, Alemayehu Bedane, Fikre Enquselassie. *Ethiop Med J, 2015, Vol. 53, No. 2*

ORIGINAL ARTICLE

EVALUATING THE VALIDITY AND RELIABILITY OF CHEST RADIOGRAPHY IN THE DIAGNOSIS OF TUBERCULOSIS AMONG SMEAR NEGATIVE PULMONARY TUBERCULOSIS PATIENTS

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ABSTRACT

Background: *Tuberculosis (TB) is a mycobacterial infection mainly affecting the lungs. Early and correct diagnosis of sputum smear negative patients by chest radiography (CXR) is challenging since it depends on reader's ability to detect abnormal findings and to interpret it correctly.*

Objectives: *To evaluate the validity and reliability of CXR the diagnosis of TB among smear negative pulmonary tuberculosis (PTB)*

Methods: *An institutional based cross-sectional study was conducted at seven selected health facilities from October 2011 to September 2012 on 159 adults aged 18 years and above who were newly diagnosed smear negative for PTB patients diagnosed using Chest X-ray (CXR). Morning sputum was collected and cultured from each patient using Lowenstein Jensen media. All the CXRs were revised by senior radiologists in conjunction with the principal investigator. A structured questionnaire was used to collect socio-demographic, clinical and radiological data. Sensitivity and specificity measures of the CXR findings were calculated in comparison to the gold standard sputum culture results.*

Results: *The mean (SD) age of patients involved in the study was 37.1(16.7), ranging from 18 to 87 years. Of the total 159 smear negative PTB patients, the most common CXR finding was consolidation (40.3%) followed by cavitations (23.9%) and nodular lesions (17.0%). Sputum culture results showed that, 47(29.6%) were culture positive, 103(64.7%) were culture negative and 9(5.6%) were contaminated. About 14% (22/159) of the study subjects were HIV positive. The sensitivity and specificity of CXR findings were 77.1% (37/48) and 36.9% (41/111), respectively. The positive and negative predictive values were 34.6% (37/107) and 78.8% (41/52), respectively.*

Conclusion: *CXR can be used as supportive investigative modality to diagnose smear negative Pulmonary TB in conditions where TB culture is no more feasible.*

INTRODUCTION

Pulmonary Tuberculosis is a bacterial infection mainly affecting the lungs. It is a global health problem, though the morbidity and mortality is very high in sub-Saharan Africa and Asia.(1) Ethiopia ranks 8th among the 22 high burden countries in the world and the third in Africa. WHO estimated epidemiological burden of (all forms of TB) prevalence, incidence and mortality to be at 572, 359 and 64 /100,000 populations respectively (2).

Globally, the proportion of P.TB cases is expected to be 85% of all TB cases and the proportion of smear positive pulmonary cases to be 75-80%, but in contrast to this figure, our country's data showed that the proportion of P.TB among all forms of TB cases is only 60-65%. And among those cases, the number of smear negative cases are more than the smear positives (2).

Ethiopia follows the 2007 WHO guidelines to diagnose TB (3). Sputum smear examination for Acid Fast Bacilli is the most important and practical confirmatory test, but sensitivity of a single sputum test is low and about 5000bacilli/ml must be present to be positive (4). Chest radiography is the next most important investigative modality in Ethiopia to diagnose P.TB when the sputum is negative for AFB (3). Conventional Radiography is limited in its sensitivity

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and specificity, where the sensitivity in Ethiopia is 53% done at Alert Hospital (5).

In 2005, a study was done in Nairobi, Kenya to assess the role and performance of chest x-ray for the diagnosis of tuberculosis, Sensitivity and specificity of the CXR score "TB" among smear negative suspects were 80% and 67%, respectively (6).

P.TB especially post primary disease, nearly always cause abnormalities on chest radiographs, upper lobe involvement with cavitations and the absence of lymphadenopathy are helpful in distinguishing post primary TB from primary TB. In addition to the usually involved pulmonary segments namely, the apical or posterior segments of the upper lobe, the superior segments of a lower lobe, anterior or basal segments may be involved as many as 75% of cases (7). As many as 15% of patients with P.TB have normal chest radiographic findings, clinical suspicion must remain high for prompt diagnosis (8).

There was a research done in Tokyo to see the influence of experience on chest radiography reading results. The average rate of under-reading was 21.8% and that of over-reading was 19.5%. The rate of under-reading among readers who had more than 10 years experience or who had been reading more than 20,000 films a year were lower about 6-8% than those among the other readers. However, there was not a single reader who did not make at least two misreading (8).

The usefulness of chest radiography is determined by the reader's ability to detect abnormal opacities and interpret them correctly(9). In our country, the number of radiologists are few and worse is the number of experienced radiologists, who are very few in number, they could have played a key role in correctly diagnosing P.TB and narrowed the discrepancy of under-reading or over-reading with their respective consequences. Although, the gold-standard diagnostic modality in detecting P.TB is culture but it is expensive, and takes 6-8 weeks until the result are revealed. Thus this study attempts to evaluate the validity and reliability of CXR findings in comparison with the gold standard test, sputum culture and assess agreement between readers.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted at seven selected health facilities in Addis Ababa which give TB treatments between October 2011 and September 2012.

Study participants were new smear negative P.TB patients, diagnosed by CXR, aged 18 years and above. Morning sputum for culture examination, and their CXRs was taken for re-reading on 159 patients. Health care providers working at TB clinic were data collectors using a structured questionnaire which includes the socio-demographic and clinical data. Eligible patients were given a standard test tube to bring the appropriate amount of morning sputum after washing their mouth three times, and their CXRs were also taken.

The sputum samples were transported to St. Peter's Hospital in triple package and cultured using Lowenstein Jensen media. Colonies detected in the artificial media checked using Ziehl-Neelsen staining and species of mycobacterium tuberculosis complex confirmed with MPT64 antigen immunochromatographic kit.

CXRs of eligible patients were collected and radiological data were entered by two senior radiologists in conjunction with the principal investigator, and when there is a disagreement about the conclusion two other senior radiologists revise the CXRs and the final result is taken. CDC guidelines for evaluating CXR was used to interpret the film CXR findings that can suggest active TB:

1. Infiltrate or consolidation–on ant. Seg. of up per lobes & sup. seg of lower lobes.
2. Any active cavitary lesion having thick walls.
3. Nodule with poorly defined margins
4. Pleural effusion
5. Hilar or mediastinal lymphadenopathy
6. Reticulonodular infiltrates, and others like milliary TB (10)

In conclusion the findings on the CXR were:-

1. No pathology
2. Pathology not suggestive of active TB
3. Pathology not suggestive of TB
4. TB is possible
5. Pathology suggestive of TB
6. Pathology highly suggestive of TB
7. Sub-optimal film, results from 1-3 are scored as no TB,

A four point scoring system is used as
1-No TB, 2-TB is possible, 3-Suggestive of TB 4-Highly suggestive of TB, In our study results from 2-4 are taken as TB cases.(6)

The research proposal was approved by the institutional research board (IRB), of College of Health

Sciences, Addis Ababa University and verbal consent was sought from the study participants.

Frequency distribution and percentage calculation were made to describe socio-demographic and clinical characteristics of the study participants. Sensitivity, specificity and predictive values of CXR were calculated using culture as gold standard. The following equations were used to calculate the sensitivity, specificity and predictive values of the CXR.(11)
Sensitivity = TP/CP
Specificity = TN/CN
Positive predictive value=TP/TP +TN=True positive/ Total positive
Negative predictive value=TN/TN + FP=True negative/Total negative

RESULTS

A total of 159 patients were included in the study of whom 93(58.4%) were males and 66 (41.5%) were females. The mean (SD) age of patients was 37.1 (16.7), with higher proportion (45.5%) in the age group of 18-29 followed by 17.5% aged 60 and above years. The mean (SD) of family size was 3.97 (1.946). One hundred and fifty five (97.4%) of the patients presented with cough, followed by night sweating on 140(88.1%) patients. Twenty two (13.8%) of the study participants were HIV co-infected patients. Sputum culture examination was done for all the 159 smear negative cases, of which 47(29.6%) were culture positive, while 103(64.7%) were culture negative and 9(5.6%) were contaminated (Table 1).

Table 1. Socio-demographic and clinical characteristics of study participants (n=159)

Characteristics	Number	Percent
Age		
18-29	68	45.5
30-39	21	13.6
40-49	20	13.0
50-59	16	10.4
60+	27	17.5
Mean (SD)	37.1(17.6)	
Sex		
Male	93	58.5
Female	66	41.5
Symptoms on presentation		
Chest pain	110	69.2
Cough	155	97.4
Night sweating	140	88.1
LFG	128	80.5
Loss of appetite	124	78.0
Weight loss	113	71.1
Others	33	20.8
HIV Status		
Positive	22	13.8
Negative	137	85.2
Sputum culture result		
Positive	47	64.8
Negative	103	29.6
Contaminated	9	5.7

Patterns of appearance on the CXR results in relation to culture results are presented on Table 2 for all culture positive and negative patients. The commonest CXR findings for both culture positive and culture negative patients were consolidation which is an air space opacity (40.3%) followed by cavitations and nodules 23.9 and 17.0%, respectively.

Three patients are found to have culture positive while their CXR findings were normal so clinical suspicion must remain high for those patients even if CXR is normal. Although, not shown in the table our finding also revealed that consolidation followed by cavitations and nodules were the commonest findings for both HIV positive patients.

Table 2. Patterns of appearance on CXR results in relation to culture results (n=176)

Appearance	**Culture Results**		**Total* n(%)**
	Positive	**Negative**	
Consolidation	25	39	64 (40.3)
Cavitations	15	23	38 (23.9)
Nodules	13	14	27 (17.0)
Pleural effusion	3	20	23 (14.5)
Fibrosis	2	9	11 (6.9)
Normal	3	9	12 (7.5)
Reticulo-nodule	3	5	8 (5.0)
Bronchiectasis	4	5	9 (5.7)
Collapse-consolidation	3	5	8 (5.0)
Others	4	26	30 (18.9)

*Multiple appearances are possible

Fig. 1. A case of culture positive P.TB patient with CXR finding of consolidation with air bronchogram involving the left upper lobe.

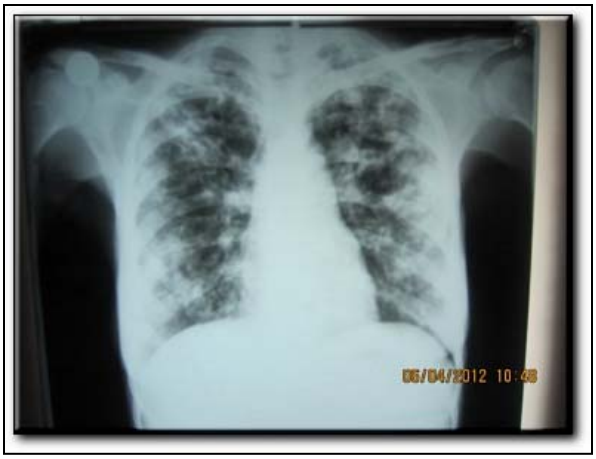

Fig. 2. A case of ill defined nodules seen on both lung fields.

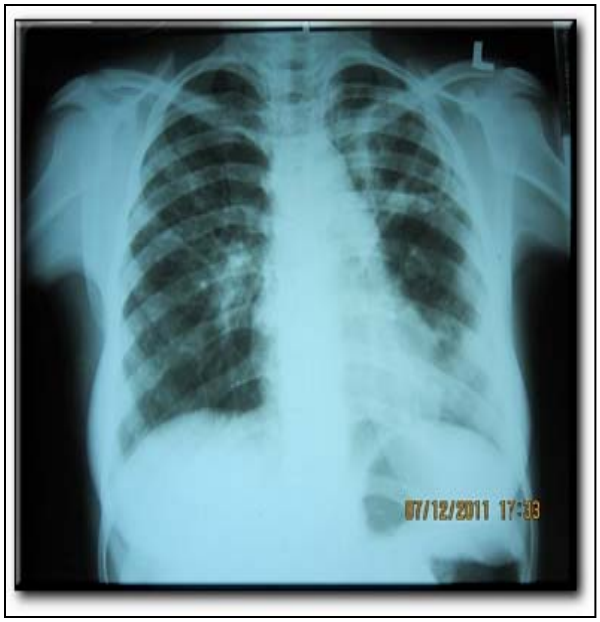

Fig. 3. A thick walled cavitation is seen on left upper lung field.

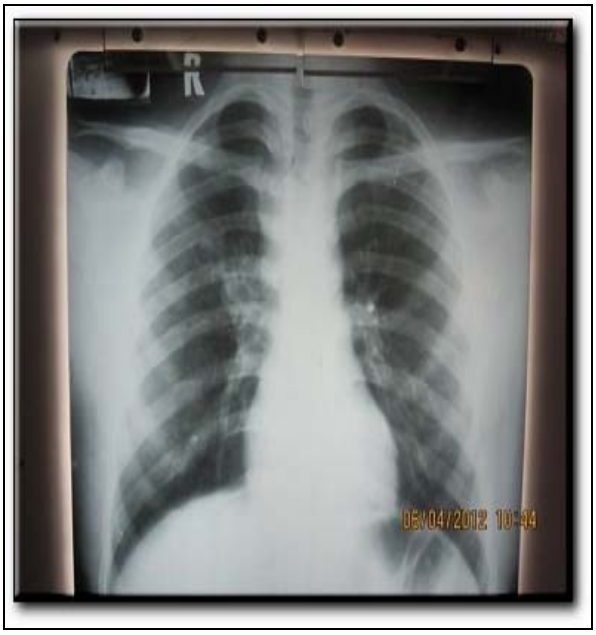

Fig 4. A normal CXR is found as seen on this case where sputum culture is positive, so clinical suspicion must remain high for those cases.

Concerning radiologic site, the commonest radiologic site of pathologic involvement for both culture positive and culture negative patients was the right upper lung field (36.5%) followed by left upper lung field (30.2%) (Table 3).

Table 3. Radiologic site of pathologic involvement distribution of study participants

	Culture Results		**Total**
	Positive	**Negative**	
Right upper lung field	22	36	58
Right middle lung field	8	13	21
Right lower lung field	4	26	30
Left upper lung field	17	31	48
Left lingular seg.	4	4	8
Left lower lung field	6	23	29

Validity and reliability of the CXR findings were calculated on the total 159; smear negative PTB patients. Accordingly sensitivity and specificity results were 77.1% (37/48) and 36.9% (41/111), respectively.

The positive and negative predictive values were 34.6% (37/107) and 78.8% (41/52), respectively (Table 4).

Table 4. Evaluation of CXR against Culture results (n=159)

CXR results	Sputum Culture Results Positive	Negative	Total	Validity/Reliability Values
Positive	37	70	107	Sensitivity=77.1%
Negative	11	41	52	Specificity= 36.9%
Total	48	111	159	PPV =34.6%
				NPV = 78.8%

DISCUSSION

Many studies including previous studies done in Ethiopia indicate that CXR has limited reliability for the diagnosis of TB with limited sensitivity and specificity (5,12), in contrast to other studies, we found that CXR to have a better sensitivity reaching to 77%, suggesting that it can be used as an important alternative investigative modality for diagnosing PTB next to sputum smear examination, provided that experienced radiologists are involved in interpreting the film, but the specificity is low, which is about 36.9%, and it remains the subject of concern.

As seen from the results, 45%of cases are 18-29 years, followed by 13.6% with age range of 30-39 years, this showed that peoples at their productive ages are affected by PTB, which emphasizes the need for correct diagnosis and early treatment.

The commonest radiologic site of involvements are the right upper lung field followed by left upper lung field which is consistent with many studies (7). Consolidation followed by cavitations and nodular changes are the commonest radiologic findings; 14% of the study subjects are HIV positive with similar radiologic findings of consolidation, followed by nodules and cavitary changes, but they also present with primary TB findings like lymphadenopathies which is consistent with other studies(8).

Cases with upper lung consolidative changes which overlap with the diagnosis of pneumonia should be seen cautiously, the presence of clinical data, treatment history and previous films for comparison are of paramount importance to the radiologist for better diagnosis of PTB.

Normal CXRs are seen in our studies, with culture positive result in 12% of cases as seen in, similar to other studies done in Canada (12). There are many possible reasons for this increasing occurrence although the incidence of HIV/AIDS has also increased during this period, this association was present in two patients in our study, A likely explanation may be improved detection of early disease by using good laboratory tests before the radiological manifestations seen. The presentation of TB, and consequently the performance of the CXR reading, is also influenced by delay in accessing diagnosis with longer delays associated with high number of cavities.

The low specificity of CXR which is 39.6% in our study of smear negative PTB patients is a subject of concern. The challenge is to increase the specificity of CXR and diminish the proportion of overdiagnosis of smear negative cases. The scoring system used in interpreting the film as No TB, TB is possible, suggestive of TB and highly suggestive TB cases and if Anti-TB started only for highly suggestive of TB cases, and for the others (TB is possible and suggestive of TB cases) if broad spectrum antibiotic started first, this will greatly improve the specificity, in line with studies done in Kenya(6). With the current introduction of modern digitalized X-ray machines, in almost all government and most private hospitals and the commencement of fellowship training programs for radiologists will also maximize the quality of the diagnosis, with significant improvement of the sensitivity and specificity of CXR in diagnosing PTB.

CXRs are also used in HIV infected patients as screening tool to rule out active TB before starting Ionized preventive therapy, CXRs with no pathologies are found in 88% cases with culture negative result, more or less consistent with study done in Botswana with certainty of 90% to rule out active TB (14).

In conclusion, CXR can be used as supportive investigative modality with better sensitivity to diagnose smears negative Pulmonary TB in conditions where

TB culture is no more feasible. The four point scoring systems used in interpreting CXR film helps to improve the specificity of CXR in diagnosing smear negative P.TB. Most of the CXR findings of Pulmonary TB patients overlap with other pulmonary pathologies, so detailed **CLINICAL DATA** with treatment history and previous films should be available to professionals who are interpreting the CXRs.

There should be a system to consult senior radiologists in difficult cases. Lateral films should be taken where necessary. Optimal films are mandatory so well trained technicians/technologists should take the films. Further studies are recommended with large sample size.

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