



**Reliability of chest X-ray in diagnosing active Pulmonary Tuberculosis in
reference to chest CT at Radiology department of St Paul's Hospital
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II. Abbreviations and Acronyms

A.A – Addis Ababa

CNS – central nervous system

COPD – chronic obstructive pulmonary disease

CT – computed tomography

CXR – chest X-ray

FMOH – Federal Ministry of Health

GUT – Genitourinary tract

HIV – Human Immunodeficiency Virus

HRCT – High resolution computed tomography

PACS – Picture Archiving and Communication System.

PTB – Pulmonary Tuberculosis

RIS – Radiologic Information System

SPHMMC- St Paul's Hospital Millennium Medical College

SPSS – Statistical Package for the Social Sciences

WHO – World Health Organization

Abstract :

Background - Tuberculosis (TB) is a significant public health problem in Ethiopia . Imaging plays a pivotal role in the diagnosis and management of tuberculosis. The introduction of HRCT in radiology field has improved the diagnosis of TB. But the overall utilization of CT is in its infancy in our country due to expensive cost of the machines and inadequate amount of trained radiologists. Chest X ray has been the mainstay of imaging diagnosis for TB and thereby most previous documents in our country compared CXR diagnosis with sputum microscopy and culture.

Objective: To assess the reliability of CXR in the diagnosis of “active” pulmonary TB compared to chest CT in patients with clinical presumptive TB at Saint Paul’s Hospital Millennium Medical College (SPHMMC) radiology department and subsequently characterize the commonly misdiagnosed cases on chest radiographs.

Methods: A retrospective hospital based review was conducted on the chest X rays of outpatients imaged at the SPHMMC radiology department in the 12 months from April 2018 – March 2019 with chest CT suggestive findings of active pulmonary TB. The data was analyzed by percentage agreement and Cohen’s statistics using SPSS version 20.

Result : 40 CXRs were studied and 32 (80 %) were classified as “abnormal TB suggestive” and 8 (20 %) as “normal” or “abnormal but not TB suggestive”. The inter reader agreement calculated showed 77.5 % percentage agreement and a Cohen’s statistic value of 0.477.

Conclusion – This study found a moderate agreement between the two image interpreters on the final diagnosis of active TB with a cohen’s statistic value of 0.477. The specific disease pattern with the highest degree of agreement between the readers was pleural effusion with a Cohen’ value of 0.826 and the lowest for fibrocystic changes of TB.

1. Introduction

1.1 Background

Tuberculosis (TB) is a public health problem worldwide, being one of the top 10 causes of death, and the leading cause from a single infectious agent (above HIV/AIDS); millions of people continue to fall sick with the disease each year. In 2017, TB caused an estimated 1.3 million deaths (range, 1.2–1.4 million) among HIV-negative people, and there were an additional 300 000 deaths from TB (range, 266 000–335 000) among HIV-positive people. There were an estimated 10.0 million new cases of TB (range, 9.0–11.1 million), equivalent to 133 cases (range, 120–148) per 100 000 population. TB affects both sexes and all age groups, but overall the best estimates for 2017 were that 90% of cases were adults (aged ≥ 15 years). It is a public health problem in our country Ethiopia. According to the 2018 WHO global TB report Ethiopia is one of the top 20 TB high burden countries in the world with an annual incidence of 172000 new cases in the year 2017. This figure equated to an incidence per capita of 164 infected people per 100,000 population. TB was responsible for mortality of 29,000 people in Ethiopia in the year 2017 alone and from this number only about 3,600 had HIV co-infection. [1]

Tuberculosis is caused by mycobacterial species in the *Mycobacterium tuberculosis* complex but other species can cause similar disease, including *Mycobacterium bovis*, *Mycobacterium africanum*, *Mycobacterium microti*, and *Mycobacterium canettii*. [2] *Mycobacterium tuberculosis* usually affects the lungs but it can also affect extrapulmonary sites such as lymph nodes, pleura, abdomen, bone & joints, CNS and GUT. Not all individuals exposed to tuberculosis get infected.

Airborne mycobacteria are transmitted by droplets and the probability of transmission to another individual depends on the infectiousness of the tuberculosis source, the environment and duration of exposure, and the immune status of the exposed individual. In approximately 5% of infected individuals, the immune system is inadequate at controlling the initial infection, and active tuberculosis develops within the first 1–2 years;[3] this category is referred to as primary tuberculosis. In another 5% of infected individuals, the immune system is effective at controlling the initial infection, but viable mycobacteria remain dormant and reactivate at a later time; this category is referred to as post primary or reactivation tuberculosis.[3] The remaining 90% of individuals will never develop symptomatic disease and will harbor the infection only at a subclinical level, which is referred to as latent tuberculosis infection.

The gold standard for diagnosis of Tb is demonstration of mycobacteria from various body fluids.[4] The principal means of testing for active pulmonary tuberculosis is sputum analysis, including smear microscopy, culture, and molecular methods (NAA testing). [4,9] Conventional light microscopy of Ziehl Nielsen stained smears from at least two samples is the most widely available test in resource limited settings. These may identify a vast majority of smear positive cases but its sensitivity is variable ranging from 20-80%. [5] The Xpert MTB is a quick and reliable way to increase specificity of diagnosis. Despite its efficacy in diagnosis, the machines are expensive and its cartridge based functionality account for costly individual testing. [5]

But still imaging plays a pivotal role in the diagnosis and management of tuberculosis. The WHO recommends the utilization of CXR as primarily a screening and further more diagnostic tool for TB. Triaging using CXR can help reduce the number of persons who undergo bacteriological TB testing without decreasing the detection of true TB cases.[4] The introduction of HRCT has improved the diagnosis of TB and recent studies indicate that computed tomography is more sensitive than plain chest film in the detection of lung parenchymal lesions and that it plays an important role in evaluating the activity of pulmonary TB. Radiology also provides essential information for management and follow up of the patients and is also extremely valuable to monitor complications.[5]

1.2 Statement of the problem

Sputum smear microscopy despite its availability and being cost effective fails to diagnose most cases of smear negative pulmonary TB. Mycobacterial culture is a more sensitive technique but growth of bacilli on the traditional media require 4-8 weeks [5] which delays treatment in the absence of confirmed diagnosis. In 10% of adult cases, confirmation is never established with culture findings. The rate of culture confirmation is even lower in children, at approximately 28% [6]. The more sensitive gold standard molecular testing methods like Gene Xpert are costly and limited in our country being stationed in selected facilities. Nucleic acid amplification tests in general also have a drawback of amplifying the DNA of dead bacilli making them less efficient for the follow up of patients on treatment.[5]

People with respiratory symptoms who are seeking care need to be evaluated not only for TB but for all relevant respiratory diseases, which may include, for example, non-TB infections, diseases of airflow obstruction (such as COPD or asthma), neoplasms (such as lung cancer or pulmonary metastasis), occupational lung diseases or bronchiectasis. [4] Sputum analysis for Mycobacterium tuberculosis suffers in its inability to diagnose any of the above conditions in the absence of active TB. And although CXR is a useful diagnostic aid for several of these conditions; chest CT, despite its recent introduction in our setup, revolutionizes the diagnostic capability for most respiratory pathologies.

Chest X-ray is useful but is not specific for diagnosing pulmonary TB, and can be normal even when the disease is present. [5] Though stability of radiographic findings for 6 months distinguishes inactive from active disease, post-primary disease activity also cannot be accurately assessed by chest radiography. Therefore, it cannot provide a conclusive independent diagnosis and needs to be followed by sputum testing. Chest CT is an effective diagnostic method when plain films are normal or inconclusive. Chest CT can add valuable information for detecting bacterial activity. [7] Branching opacities, cavitation, or consolidation are clear signs of active TB, but still must be confirmed by analyzing sputum for the presence of bacilli.[5]

1.3 Significance of the study

CT is quite a recent introduction to our medical system resulting in a lack of documents comparing the two mainstays of imaging diagnosis in our setup. Most studies regarding imaging diagnosis of active TB have focused on comparison of the two imaging modalities, chest radiography and chest CT, in regards to a gold standard method of diagnosis involving sputum analysis or culture. The rationale for the study focuses on comparison of the two imaging modalities in setups devoid of the accepted gold standard diagnostic modalities (sputum culture and molecular methods) or when diagnosis by a gold standard causes a delay in initiation of treatment or even unnecessary initiation of empiric therapy as in the case of sputum culture.

The diagnosis of active pulmonary disease primarily by CXR or even less considerably by chest CT requires strong rapport between treating clinicians and the diagnostic radiology team either through direct interaction, which at times could be lacking in the busy era of modern medicine, or a well-developed telecommunication system which is inadequate in our setup all creating gaps causing a diagnostic dilemma for the radiologist and a diagnostic delay for the patient. This study thereby attempts to retrospectively assess which X-ray findings should prompt the radiologist to warrant further chest CT in the absence of necessary clinical/ laboratory data or in cases of unavailable previous chest radiograph of the patient.

The study generally is meant to assess the reliability of CXR for diagnosis of active pulmonary TB cases in regards to chest CT. The study can offer an insight into the commonly missed X-ray appearances of active TB, providing input to radiology residents interpreting X-rays. Following the findings, the study aims to give suggestions to the hospitals imaging protocol for patients with presumed active tuberculosis and also motivate researchers to undertake future prospective studies on the topic.

2. Literature review

Clinical suspicion for tuberculosis may be heightened in patients with various risk factors. Risk factors for tuberculosis can be grouped into two categories: those that cause increased risk of exposure to tuberculosis, and those that increase the risk of developing active disease, once a person is infected. Risk factors associated with a higher risk of progression to active tuberculosis include (a) age younger than 4 years, (b) intravenous drug use, (c) recent tuberculosis infection or test conversion within the past 2 years, and (d) immunodeficiencies, such as those resulting from human immunodeficiency virus (HIV)/AIDS infection, organ transplantation, and treatment with immunosuppressive drugs. HIV infection is the strongest known risk factor for developing active tuberculosis. Other conditions that can increase the risk of active disease include diabetes mellitus, chronic renal failure, low body weight, prior surgery, alcohol or tobacco abuse, and certain malignancies.[1]

The immune response to mycobacteria has important implications for the clinical and imaging appearance of tuberculosis, particularly in immunocompromised patients. Primary tuberculosis occurs most commonly in children and immunocompromised patients, who present with lymphadenopathy, pulmonary consolidation, and pleural effusion. [2,8] Mediastinal and hilar lymphadenopathy is the most common radiologic manifestation of primary tuberculosis. [9] Lymphadenopathy in tuberculosis typically demonstrates a low-attenuation center with peripheral rim enhancement on contrast material - enhanced CT images, findings that are due to central caseous necrosis with peripheral granulomatous inflammatory tissue. Pleural effusion is seen in approximately 25% of primary tuberculosis cases in adults, with the vast majority of such effusions being unilateral [10] whereas Tuberculous empyemas are typically loculated and associated with pleural thickening. [10,11] Bronchial wall involvement may be seen in primary

and postprimary tuberculosis, although it is more common in the former. [12,13]The main radiographic features of proximal airway involvement are indirect, including segmental or lobar atelectasis, lobar hyperinflation, mucoid impaction, and postobstructive pneumonia.[12]

Post primary tuberculosis may manifest with cavities, consolidations, and centrilobular nodules. Patchy, poorly margined consolidation is an early and consistent feature of postprimary tuberculosis. Consolidation and cavitation have a strong predilection for the apical and posterior segments of the upper lobes as well as the superior segments of the lower lobes in postprimary tuberculosis.[12] In postprimary tuberculosis, cavitation is a common finding. Cavities can be several centimeters in largest dimension and can develop thick and irregular walls. Cavitory lesions are often seen within areas of consolidation and may be multifocal. [12]The presence of an air-fluid level within a cavity may be related to the tuberculosis itself or to bacterial/fungal superinfection.[12,14] Miliary tuberculosis refers to hematogenously disseminated disease that is more commonly seen in immunocompromised patients, who present with miliary lung nodules and multiorgan involvement.[15]

CXR may have higher specificity for pulmonary TB than assessing symptoms alone, depending on how the X-ray is read. [4]Regarding diagnosis of smear-negative TB, the clinician often only relies on the CXR result. The radiologist in turn usually has little or no information about the patient and in case of doubt may tend to give a positive result.[16] Beyond identifying active TB disease, CXR also identifies one of the populations at highest risk of developing TB disease: those who have inactive TB or fibrotic lesions.[4] Sequelae of previous tuberculosis that is now inactive manifest characteristically as fibro nodular opacities in the apical and upper lung zones. Once active TB has been excluded, patients with fibrotic lesions should be followed-up, given their high risk for developing active disease.[4]

Important CT findings of active pulmonary tuberculosis are centrilobular nodules and branching linear structures (tree- in-bud appearance), lobular consolidation, and cavitation.[9,17] Active tuberculosis often communicates with the bronchial tree, which results in endobronchial spread. Histologically, caseous necrosis and granulomatous inflammation fill respiratory bronchioles and

alveolar ducts. This histologic finding manifests radiologically as centrilobular nodules and the tree-in-bud sign. Tree-in-bud opacities are also seen in other infections, but when visualized in combination with cavitation or nodular opacities in the upper and posterior lung segments, and in the appropriate clinical setting, a specific diagnosis of pulmonary TB can be established. [17,18] At CT, centrilobular nodules are seen in approximately 95% of cases of active tuberculosis [18]. Unlike cavitory lesions and consolidation, centrilobular nodules may be seen in the lower lobes, distant from the cavitory lesions. [12] Airway involvement is frequently observed in active TB, is often associated with bronchogenic dissemination, and is characterized by increased thickness and dilation of the bronchial walls. [19]

Previous published research shows patients with presumptive PTB are categorized into four groups on chest CT, by radiographic activity, from the highest to lowest grade:

- Definitely active, with lesions including a cavity;
- probably active, showing a tree-in-bud appearance or multiple non-calcified poorly circumscribed nodules without a cavity;
- indeterminate activity, with lesions appearing mainly as non-calcified well-circumscribed nodules; and
- Probably inactive, with lesions appearing mainly as calcified nodules or fibrotic band.[17,18,20]

Further CT findings of inactive pulmonary tuberculosis include calcified nodules or consolidation, irregular linear opacity, parenchymal bands, and pericatricial emphysema. [18]

Using the above CT grading, a Korean study evaluated the correlation between microbiological yield and radiographic activity on chest CT, in suspected PTB patients. The culture rates of each radiographic activity were 61.6%, 60.7%, 4.3% and 0%, respectively. However, with regards to the diagnostic performance of definite and overall PTB, the radiographic activities showed high sensitivity and NPV when the definitely and probably active grades were considered as active PTB. These findings suggest that radiographic activity can be used for the diagnosis of PTB, and in the initial guidance of anti-TB therapy, for presumptive PTB, in clinical practice.[21]

A research done in Tehran to assess the role of HRCT in diagnosing active pulmonary TB done on 76 patients showed that endobronchial spread of TB was picked by HRCT in 96-98 % of cases in comparison to the figure of 19 -58 % on chest radiography. Cavitation was also seen in a mean of 50 % of cases of active secondary TB whereas a significantly higher proportion displayed the same finding on HRCT even in cases complicated by parenchymal fibrosis and architectural distortion. [22] The same research concluded that HRCT had a sensitivity of 96 % in diagnosing active TB though it lacks in specificity.[22] A more recent research done in Brazil published in 2017 showed that findings included the presence of a tree-in-bud pattern in 93% of cases, ill-defined nodules in 84% of cases, consolidation in 77% of cases, architectural distortion in 71% of cases, cavitary lesions in 62% of cases and bronchial dilatation and wall thickening in 93% of cases with confirmed active pulmonary TB.[19]

Literatures regarding diagnostic delay point out that our medical care suffers from a significant lag in diagnosis. Yimer et al's study found that in Ethiopia patients with TB symptoms contact an educated health worker on average after just 25% of the total delay period. Thus, there is a fourfold-difference in the time of first contact and diagnosis. Also in this study , patients who first visited a qualified medical provider experienced a 21 day delay before initiation of treatment [23] where as others had a diagnostic delay of upto 80 days. A 2014 audit on diagnosis and treatment of TB done at 2 hospitals and 2 health centers in Addis Ababa concluded that only 25 % of smear negative active TB cases were correctly diagnosed by chest radiography.[25] The core problem in delay of diagnosis and treatment seemed to be a vicious cycle of repeated visits at the same healthcare level, resulting in nonspecific antibiotic treatment and failure to access specialized TB services. [24]

Objectives

General objective

To compare the reliability of CXR in the diagnosis of ‘active’ pulmonary TB in comparison to chest CT.

Specific objective

Determine reliability of CXR as a diagnostic tool for active TB in the evaluated cases.

3. Methods and Materials

3.1 Study area and period

3.1.1 Study area

The study was conducted at radiology department of SPHMMC in Addis Ababa, Ethiopia. St. Paul's Hospital was built in 1969 G.C. by Emperor Haile Selassie in collaboration with the German Evangelical Church, as a source of medical care for underserved populations. It's the second largest hospital in the country with a catchment population of more than 5 million. Currently it has an annual average of 200,000 patients. Approximately 75% of the patients receive medical services free of charge. There are over 1300 clinical and nonclinical staff in over 13 departments. It is under supervision of Federal Ministry of Health (FMOH) and has affiliations with foreign universities including Tulane and Michigan University. It is capable of giving services for 24 hrs a day. The medical school opened in 2007 GC during the Ethiopian calendar millennium, hence the name, and yearly provides much needed medical professionals to Ethiopia.[26]

The radiology department has state of the art digital X ray , CT and MRI machines capable of producing quality images and no less than 30 competent radiographic technologists with adequate years of experience obtaining images. The department has a total of 15 senior radiologists and around 60 residents in different levels of specialty training. The department is divided in to different units including chest imaging, body imaging , ultrasound imaging, neuroradiology, MSK imaging and interventional radiology headed by respective sub specialized consultant radiologists and fellows. Around 2000 chest X ray and 200-300 chest CT images are interpreted monthly by the responsible residents and seniors.

3.1.1 Study period

A retrospective review of the X ray and CT images of patients imaged over the past 12 months from April 2018 to March 2019 was done in the 4 months period from April – July 2019.

3.2 Study design

Retrospective record review was done by a chest subspecialist senior radiologist and two senior radiology residents.

3.3 Study population

Presumptive pulmonary TB cases with imaging of both chest CT and CXR at SPHMMC in the 12 months from April 2018 to the end of March 2019.

Pulmonary TB (PTB)		Second imager		
		Active PTB Present (Positive)	Active PTB Absent (Negative)	Total
First imager	Active PTB Present (Positive)	A	B	A+B
	Active PTB Absent (Negative)	C	D	C+D
	Total	A+C	B+D	A+B+C+D

3.4 Inclusion criteria

Cases not started with anti-TB therapy in the interval between CT and CXR

3.5 Exclusion Criteria

Temporal interval of more than 15 days between the CT and X ray images.

The X ray image of the patient is poor quality and not readable

Patients with an HRCT assessment of indeterminate activity and inactive TB

3.6 Sample size

All eligible cases (definitely active and probably active) from April 2018 to March 2019 were enrolled in the study.

3.7 Data collection

The data abstraction template was prepared in a manner to answer the questions set out in the objective of the study. The questions were organized in a pattern to preserve the flow of documentation, with branching types of questions utilized.

The template was prepared in English language. First the primary investigator gave a tutorial to the data abstractors and a pilot testing was done with a few images to preserve the intra and inter-rater reliability of the data abstracted. The data abstractors were two second year Radiology residents familiar with the terminology used in the template and also with the PACS system. The data abstraction template was revised following the pre testing to preserve the intra and inter-rater reliability.

The primary investigator identified CT images of patients with the diagnosis of active TB from the RIS archive log. The next step was extraction of these CT images from the PACS system by the primary investigator and they were re evaluated by a Senior Radiologist, subspecialized on chest imaging with greater than 10 years experience, for the confirmation of active TB diagnosis. Any records that didn't fulfill the inclusion criteria were cleaned, as clearly described in the data abstraction template, by the primary investigator and data abstractors.

Subsequently digital X rays of the patients fulfilling the inclusion criteria were interpreted by two senior radiology residents for characterization of the radiographic appearance in the X rays of these patients during the weekends of the study period. In the meantime the data was abstracted utilizing the above template by the data abstractors based on the interpretation of the senior residents. Percentage agreement was calculated to check for the inter reader reliability to assess the agreement between the readings of the two senior residents. [27,28] . The senior radiologist supervised the interpretation of the X ray images. The primary investigator was not involved with interpretation of images to avoid bias. Rather supervision of the data abstraction and overall activities was the role of the principal investigator. Further medical records and presence of concurrent illnesses was obtained from medical charts of patients by the primary investigator as deemed necessary.

3.8 Data quality assurance

The principal investigator with the aid of continuous supervision from the clinical supervisor will review and check the relevance and completeness of the collected data. The X ray interpreters are final year residents and the data abstractors are second year residents both knowledgeable on the topic. The data abstractors are trained on the data abstraction template and neutral to the outcome of the study. These conditions shall be maintained to maintain the validity and reliability of the acquired data. Data shall be cleaned before any analysis.

3.9 Data processing and analysis

After data collection, data was entered in to SPSS version 23. Percentage agreement and Cohens Kappa statistics was calculated.[27,28]. The inter-reader agreement amongst the imaging physicians was assessed using the kappa statistic. Agreement was defined as two readings being either radiologically TB positive or TB negative. The following interpretation was used to define the strength of agreement for the kappa coefficient : <0.21 = poor, $0.2 - 0.4$ = fair, $0.4 - 0.6$ = moderate, $0.61 - 0.8$ = good and $0.8 - 1.0$ = very good agreement

3.10 Ethical considerations

The research was conducted with the recognition and endorsement of the research board of SPHMMC. The patient's identities was kept anonymous at all times with confidentiality of information acquired from medical records and collected data was not transferred to a third party.

3.11 Result dissemination plan

Data was analyzed and important conclusions and recommendations generated. The results of the research will be presented to department of radiology. Findings may also be presented on different conferences and professional society meetings like Ethiopian Radiologic Society, Ethiopian public health association and Ethiopian Medical association annual meetings after review by the department. The data shall also be used as a base line for future studies and interventions.

Operational definitions

Active pulmonary TB (Positive) on CT – will be operationalized in this study to include the definitively active and probably active groups defined by the findings of tree in bud opacities, ill-defined nodules, consolidations, cavitation and bronchial wall dilatation & thickening with surrounding air space nodules.[2,30]

Active PTB (Positive) on chest X ray – Primary active tuberculosis will be characterized by lymphadenopathy, consolidation, pleural effusion, and miliary nodules.

Post primary tuberculosis characterized by consolidations that are predominant in the apical and upper lung zones, nodules, and cavitation.[4]

Bronchiectasis - irreversible dilatation of a bronchus / bronchi, often with associated thickening of the bronchial wall

Bulla - A round, focal air space, 1cm or more in diameter, demarcated by a thin wall.

Cavity - thick walled abnormal gas filled spaces within the lungs.

Centrilobular nodules - Nodules following the central tubular structures in a secondary pulmonary lobule (ie, the centrilobular artery and bronchiole)

Consolidation - Homogeneous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls

Ground glass opacification - Hazy increased attenuation of lung, but with preservation of bronchial and vascular margins;

Inactive disease - demonstrates radiographic or clinical evidence of previous tuberculosis but no evidence of currently active tuberculosis

Linear opacity - An elongated, thin line of soft-tissue attenuation.

Parenchymal band - Elongated opacity, usually several mms wide and up to about 5-cm long, often extending to the pleura.

Parenchymal fibrosis – presence of excessive fibrotic tissue within the interstitium of the lung following a previous pulmonary pathology.

Presumptive TB cases – cases with suspicion of active TB disease based on their clinical evaluation, presenting with signs and symptoms of TB.

Pulmonary TB negative on CT – these cases do not meet the inclusion criteria of the study.

Pulmonary TB negative on CXR – cases which fulfill the CT diagnosis of TB disease but do not show characteristic X ray features of active TB disease based on the agreement of the interpreters or simply not in line with the operational definition of CXR pulmonary TB positive.

Reticulation - Innumerable, interlacing line shadows that suggest a mesh.

Senior Radiologist – consultant level radiology professional. For this study, a subspecialist in chest imaging, with experience of more than 10 years in general radiology.

Senior Radiology Residents – final year radiology residents

Smear negative – Negative yield for acid fast bacilli on sputum smear.

Tree in Bud appearance – Nodular dilatation of centrilobular branching structures that resembles a budding tree and represents exudative bronchiolar dilatation

5. Results

Of the 42 CXRs, 2 had to be excluded from further analysis due to poor image quality preventing reliable image interpretation. Of the remaining 40 CXRs, 32 (80 %) were classified as “abnormal TB suggestive” and 8 (20 %) as “normal” or “abnormal but not TB suggestive” (Table 1).

Table 1

The first imager's final assessment * The second imager's final assessment
Crosstabulation

Count

		The second imager's final assessment		Total
		Suggestive of active TB	Not suggestive of active TB	
The first imager's final assessment	Suggestive of active TB	23	4	27
	Not suggestive of active TB	5	8	13
Total		28	12	40

5.1 Inter-reader agreement

Percentage agreement and Cohen’s Kappa was calculated to assess the inter reader agreement between the readings of the two senior residents. The percentage agreement was 77.5 % and the Cohen’s Kappa value calculated to assess the non chance agreement between the two imagers was found to be 0.477 suggesting a moderate agreement. (Table 2)

Table 2

Pair-wise unweighted Cohen's kappa statistic comparing chest radiographs rated as "abnormal TB" or "normal/abnormal not TB".

Symmetric Measures

	Value	Asymptotic Standardized Error ^a	Approximate T ^b	Approximate Significance
Measure of Agreement	.477	.149	3.020	.003
N of Valid Cases	40			

5.2 Agreement for specific disease pattern

Agreement for the predominantly present specific disease patterns was assessed separately. A specific disease pattern was defined as present if at least one of the senior residents identified the disease pattern in at least one zone of the lung on the CXR. Agreement was defined if both senior residents identified that pattern as present. The Cohens Kappa agreement between the senior residents for the findings of cavitory lesions, bronchopneumonic pattern (infiltration) and fibrocystic change was less marked but much better for patterns like pleural effusion and consolidative opacities. (Table 3)

Table 3 : Reading agreement (Percentage agreement and Cohen's Kappa) between the two imagers for specific disease patterns.

Comparison	Consolidation		Bronchopneumonic Pattern		Cavitation		Pleural effusion		Lymphadenopathy		Fibrocystic changes	
	PA (%)	Cohen's Kappa	PA (%)	Cohen's Kappa	PA (%)	Cohen's Kappa	PA (%)	Cohen's Kappa	PA (%)	Cohen's Kappa	PA (%)	Cohen's Kappa
Imager 1 Vs Imager 2	82.5	0.776	82.5	0.551	87.5	0.479	92.5	0.826	87.5	0.61	87.5	0.490

6. Discussion

Despite the identification of a particular disease presentation (e.g., infiltration, cavitation, and distribution zones), there is no intrinsic algorithm of disease patterns leading the reader to a final radiological diagnosis. The reader still has to subjectively decide the final radiological diagnosis based on his/her findings, experience, and knowledge. In the absence of a specific agreement between all readers on which findings constitute a positive radiological finding of TB, individual readers may agree on the disease presentation and distributable zone, but end up with a different final diagnosis. Alternatively, they could disagree on the individual disease findings yet still end up with the same final radiological diagnosis.

The high prevalence within the study cohort may have led the imagers to assume any abnormalities whether real or perceived to be suggestive of TB and explain their high sensitivity. The agreement between the two imagers for specific disease patterns such as broncho-pneumonic pattern, cavitation and fibrocystic changes was moderate (0.4-0.6) based on Cohens statistics but the agreement was higher, showing good agreement (0.6-0.8), for the more obvious disease patterns like pleural effusion, consolidation and lymphadenopathy. These results highlight the problem that even experienced imagers may show disparity on the specific radiological signs of TB on chest X ray.

A potential limitation of the present study was that a significant portion of the CXRs were marked as “not good but readable” by the readers, suggesting that outcomes may have been different if film quality had been better. Many of the images showed significant radiographic errors from poor acquisition techniques, which is not uncommon in resource constrained settings. Therefore the principal investigator and the readers deemed it necessary to include the poor quality but readable images in this study and its outcome.

The overall poor quality of CXRs compounds the difficulty of interpreting subtle findings in particular, which no doubt contributed to lack of agreement between readers. But still this fact is not purely a limitation but also a strength of the study as most of the X rays in general practice in our country do have this problem.

HRCT was used as the reference standard and the X rays were reviewed retrospectively possibly eliminating more obvious disease patterns such as miliary nodules and classic cavitary lesions of TB which are likely picked on the initial screening CXR without a further recommendation of HRCT. Additionally most of the images displayed prior parenchymal distortion possibly limiting the readers identification of specific disease patterns and hence their agreement.

Strengths of the study

1. The utilization of digitalized X ray images which allowed for better image visualization and manipulation.
2. The image interpreters were well trained senior residents who have adequate knowledge on the imaging features of TB and also familiar with the PACS system and image manipulation.
3. The results of the study can serve as a baseline data for further studies.

Limitations of the study

1. The study was a retrospective review amenable to bias
2. A rather limited sample size due to deleted images from the source PACS system.
3. The study did not differentiate between the reliability of CXR for the primary or secondary forms of TB but rather the diagnostic reliability for any form of active TB disease.
4. Inadequate clinical data on some of the studied cases.
5. More accurate diagnostic tools such as sputum culture and Gene Xpert were not utilized in the study.

7. Conclusion and recommendations

7.1 Conclusions

This study found a moderate agreement between the two image interpreters on the final diagnosis of active TB with a Cohen's statistic value of 0.477. The specific disease pattern with the highest degree of agreement between the readers was pleural effusion with a Cohen's value of 0.826 and the lowest for fibrocystic changes of TB. Most previous studies, actually find only a "fair" to "moderate", sometimes "good" inter-reader agreement and this study also demonstrated result in line with those findings. The limited sample size, suboptimal image quality and retrospective nature of the study may be responsible for the decreased agreement of the final diagnosis of active TB disease prompting a further prospective study with a larger sample size.

7.2 Recommendations

1. Accurate reporting of CXRs for TB is a complex and challenging task. This is true, even amongst expert readers, in patients with presumptive TB in resource-constrained settings where suboptimal CXR quality is common. The more subtle X-ray findings of active pulmonary TB are less picked and agreed upon even by the experienced readers therefore HRCT can be utilized for these difficult cases.
2. Prospective studies with larger sample sizes and more complete data can further support the results of this study.

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Annex

Data abstraction template

Type in the number of the appropriate answer in the data entry column or specify in writing on the blank spaces.

No.	Data item	Data entry
1	Identification of the patient (Initials only)	
2	MRN	
3	Age of the patient	
4.	Sex of the patient	
5	. Chest CT available in the PACS system - 1. YES 2 .NO	
6	Chest CT Image No.	
7	Chest CT was suggestive of active pulmonary TB- 1.YES 2.NO IF answer ‘2 ’ discard patient from study	
8.	CXR available in the PACS system – 1.YES 2.NO	

	If answer '2' discard patient from study	
9	CXR ID	
10	X ray quality 1. Optimal 2. Suboptimal for interpretation If answer '2' discard from study	
11.	Finding on CXR 1. Normal 2. Pathology detected If answer '2' move on to the next question	
12.	What was the pathologic finding on CXR ? 1. Fibrotic bands likely inactive disease 2. Consolidation 7. Atelectasis 3. Air space nodules 8. Reticulonodular opacity 4. Cavitation 9. Lymphadenopathy 5. Miliary nodules 10. Pleural effusion 6. Bronchiectasis 99. Other finding	
13	If answer to previous question is ' 11' list all in the data entry field	
14.	If answer to question No.12 is '99', Is the finding suggestive of	

	active TB? 1. Yes 2. No 3. Cannot decide	
15	If bronchiectasis seen, which lung zone 1. left upper lung zone 3. right upper lung zone 2. left mid and lower lung zone 4. right mid and lower lung zone	
16.	If consolidation seen 1. left upper lung zone 3. right upper lung zone 2. left mid and lower lung zone 4. right mid and lower lung zone	
17.	If cavitation seen, specify which lung zone 1. left upper lung zone 3. right upper lung zone 2. left mid and lower lung zone 4. right mid and lower lung zone	
18	In the presence of cavities , characterize 1. Thin walled 4. Air fluid level 2. Thick walled 5. With surrounding air space opacity 3. Irregular wall 6. Multiple of the above features	
19	If answer to the above is ‘ 6’ , specify the numbers of all on the entry field	

20	If air space nodules seen, specify which lung zone 1. left upper lung zone 3. right upper lung zone 2. left mid and lower lung zone 4. right mid and lower lung zone	
21	If Lymphadenopathy seen 1. Hilar 2. Paratracheal 3. Both hilar and paratracheal	
22	If answer to above question '1', hilar lymphadenopathy seen 1. Unilateral 2. Bilateral	
23.	If pleural effusion seen 1. Unilateral 2. Bilateral	
24.	If answer to above '1' specify which side 1. Left 2. Right	
25.	Xray characteristic of the Pleural fluid 1. Simple 2. Loculated 3. With associated pleural thickening	
26.	The summation of the X ray findings is suggestive of active TB 1. Yes 2. No 3. Inconclusive 4. Other diagnosis	

RESEARCH APPROVAL

This research by ----- (**principal investigator**) is accepted in its presented form by examiners in satisfying research requirement for the Specialty certificate in radiology.

EXAMINERS

1. _____
FULL NAME RANK SIGNATURE DATE