Comparison of Lung Ultrasound Findings in Patients with Pulmonary Tuberculosis and Lobar Pneumonia: A Case-control Study

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Abstract

Background: The utility of lung ultrasound (LUS) in diagnosing respiratory disorders is being studied only in recent times. We aimed to describe the ultrasound (USG) features of pulmonary tuberculosis (TB) and compare them with those of lobar pneumonia. In addition, the LUS findings of both diseases were corroborated with chest X-ray findings. **Methods:** The study subjects consisted of adult subjects recently diagnosed with pulmonary TB and those diagnosed with lobar pneumonia. Both subsets of patients underwent LUS evaluation. Results: Ninety-six subjects with 64 microbiologically confirmed TB and 32 lobar pneumonia patients were included. The study subjects' mean age was 46.78 ± 15.75 years and the majority were males (n = 62; 64.6%). LUS showed focal interstitial pattern, cavity, and irregular pleura in TB patients which were significantly different ($P \le 0.001$) from the findings of air bronchogram and/or shred sign seen in patients with lobar pneumonia. The overall sensitivity of LUS compared to X-ray, to identify abnormalities in TB and lobar pneumonia patients, was 88.6%. The LUS and CXR findings were concordant in 93.75% of TB patients and 90.6%) of lobar pneumonia patients. Additional USG abnormalities other than that seen on CXR were demonstrated in 13 (20.3%) TB patients. Conclusion: LUS is a valuable tool to detect TB and lobar pneumonia and can discriminate between the two conditions. LUS performance was on par with CXR in the detection of abnormalities. The lack of radiation exposure and portability of LUS makes it an attractive tool for bedside use as well as in field conditions where radiography may not be readily available.

Keywords: Focal interstitial pattern, lobar pneumonia, lung ultrasound, pulmonary tuberculosis

INTRODUCTION

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There has been a great explosion of information about the application of lung ultrasound (LUS) in clinical practice in recent years. The evaluation of the lung by ultrasound (USG), which can be performed by the treating physicians themselves, has revolutionized clinical practice. The main advantage of LUS is its bedside availability. LUS complements the physical examination and clinical diagnosis and relies on the fact that every pulmonary illness alters lung aeration, especially when the pathology abuts the pleura. LUS is useful in the diagnosis of pulmonary infiltrates, and can reliably differentiate consolidations and interstitial syndrome, mass, and loculated effusions. This differentiation is not always possible by

chest X-ray and may warrant a computed tomography. LUS is a noninvasive, inexpensive, and less risky (no radiation exposure) tool, although training centers and criteria regarding certification are still lacking in some countries. A large body of information on the use of LUS in the critically ill is available, where identification of occult pneumothorax, minimal pleural effusions, diagnosis of interstitial syndromes, differentiation of ARDS from consolidations, and differentiation of interstitial diseases from pulmonary edema have been described.[1]

India harbors one-fourth of the global population of patients with tuberculosis (TB).^[2] Identification of these patients relies

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on microbiological testing with sputum smear examination and/or molecular diagnostics. Chest radiography is an important adjunct tool to identify patients with presumptive TB. LUS can be a value-added tool as it is time-saving, available at the bedside, and less expensive compared to computed tomography. A recent study by Agostinis *et al.* evaluated the use of LUS as a complementary tool in the diagnosis of TB.^[3] There is sparse literature on the use of LUS for pulmonary TB.^[4-6]

A meta-analysis by Chavez *et al.* has shown that LUS can be a valuable tool to diagnose lobar pneumonia.^[7] The sensitivity and specificity of LUS were as high as 88% and 86%, respectively, for the detection of lobar pneumonia.^[8] International evidence-based recommendations for point-of-care LUS state that LUS is superior to chest X-ray to rule in significant interstitial syndrome.^[9] Pulmonary TB usually presents as an interstitial syndrome (B pattern) due to miliary TB or interstitial pattern/subpleural nodules due to consolidation/parenchymal infiltrates.^[10]

There is limited existing data to support the application of LUS in the identification of pulmonary TB. Our primary aim was to describe the sonological features of newly diagnosed pulmonary TB infection. We also attempted to compare the LUS features in TB patients with those diagnosed with acute bacterial lobar pneumonia.

MATERIALS AND METHODS

Cases

Subjects 18–65 years of age and recently suspected or diagnosed with pulmonary TB were taken up for this study. The diagnostic criteria for TB were any person with cough and/or fever of 2 or more weeks duration, significant weight loss, hemoptysis, or any abnormality in the chest radiograph with sputum positive for AFB and/or positive for mycobacteria by cartridge-based nucleic acid amplification test (CBNAAT).

Controls

Subjects 18–65 years of age and recently diagnosed with lobar pneumonia were included as controls. Lobar pneumonia was defined when there was new-onset fever, cough ± chest pain, and crepitations or dullness to percussion on clinical examination and the chest radiography showed a new or progressive infiltrate, seen as a consolidation with air-bronchogram sign. The other features were a new onset of purulent sputum or a change in the character of sputum, isolation of an organism from blood culture, and isolation of the pathogen from a specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy.

Exclusion criteria

Patients clinically diagnosed but who lacked bacteriological confirmation of TB were excluded. Other exclusion criteria were subjects with prior history of TB; smear/CBNAAT negative but turn culture positive for TB; positive for both AFB and any other bacterial organism in culture; other structural lung diseases such as bronchiectasis, chronic obstructive

pulmonary disease, and interstitial lung disease (ILD), body mass index of >35, and a smoking history of >20 cigarettes per day.

The study was conducted in accordance with the Declaration of Helsinki and was initiated after approval from St. John's Medical College and Hospital Ethics Committee (study reference number 14/2018). A written informed consent was obtained from the study subjects.

Study design

All consecutive patients who presented to the pulmonary outpatient department or were admitted as inpatients were taken up for study once they fulfilled the inclusion and exclusion criteria. A sputum Gram stain and culture and sputum for AFB and CBNAAT were done for all patients. The chest X-rays were reported by the radiologist in our institution. Pending the microbiological test reports, all subjects were evaluated by a complete thoracic USG. The USG was assessed by an investigator (UD) who was blinded to the group allocation (cases/controls) and the chest X-ray. The LUS recorded images were scrutinized by another investigator (PR), findings were confirmed and any discordance was recorded. A comparison of X-ray findings and LUS was done by PR. Both the USG operators were proficient in LUS and are certified as Basic LUS providers.

A complete LUS with a Sonosite S-ICU (FUJIFILM Sonosite Inc. P07577) curvilinear probe (3.5-5 MHz) was done within 12 h of inclusion in the study. Each hemithorax was methodically scanned, images were recorded and findings were also noted, from the apex to the base of the lung longitudinally. Each hemithorax was scanned in the anterior, lateral, and posterior areas, and the findings were recorded for upper and lower regions within each area [Figure 1a and b], resulting in a total of 12 regions per subject.[8] LUS was also performed in a transverse view of the area of interest when an abnormality was visualized. The time taken to complete the LUS was noted. The features studied by LUS were lung sliding, focal interstitial pattern, the presence of B lines and number of B lines per LUS region, shred sign, air-bronchogram, cavity, pleural line smoothness, and pleural effusion. The patients were categorized as TB or consolidation based on the LUS characteristics.

Once bacteriological confirmation of TB, or consolidation was available, their diagnosis based on the LUS characteristics was

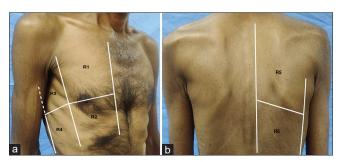


Figure 1: (a and b) Division of the chest regions for ultrasound scan

revisited and compared. The LUS findings were compared with chest x-ray findings.

Statistics

The prevalence of TB in India in 2018 was 190 per 1 lakh population. We estimated a sample size of 102 at 80% power and 5% alpha error. (nMaster version 1.1). Estimating a 10% refusal rate, the final sample size was 112. The demographic details, CXR abnormalities, and the LUS findings were analyzed using descriptive statistics. The LUS abnormalities in patients with lobar pneumonia and TB were compared by the Chi-square test. Nonparametric tests were applied for variables with skewed distribution. P < 0.05 was considered significant. Agreement between the two investigators (UD and PR) on the interpretation of LUS was analyzed by Cohen's kappa coefficient.

RESULTS

A total of 96 subjects were included in the study [64 with TB and 32 with lobar pneumonia; Figure 2]. The study was initiated in June 2018 and data collection was stopped due to the onset of the COVID-19 pandemic. The mean age of the study subjects was 46.78 ± 15.75 years. The majority were males with a male-to-female ratio of 42:22 in TB subjects and 20:12 in subjects with lobar pneumonia. All the cases of TB were confirmed microbiologically by sputum smear examination (n = 56; 87%) and by bronchoalveolar lavage in 8 patients (12.5%). One subject was smear negative but CBNAAT positive. There was no significant difference in the presence of comorbid conditions between the two groups. Diabetes was the most frequent comorbid condition, with 4 patients in the TB group and 3 patients in the lobar pneumonia group afflicted with the condition. One subject in the lobar pneumonia group had coexisting HIV infection and was on treatment for the same.

The comparison of radiological and sonological features is given in Table 1. Upper zone nonhomogenous opacities were more common in TB patients (n = 35, 54.6%) as compared to lobar pneumonia patients (n = 13, 40.6%). Moreover, lower zone opacities were seen more in lobar pneumonia patients (n = 15, 46.9%) in comparison to TB patients (n = 5, 7.8%). Miliary pattern was seen in four TB patients. Three subjects in each group had pleural effusion detected by LUS. Focal interstitial pattern, seen as small rounded or irregular sub-pleural hypodensities [Figure 3], and irregular pleura [Figure 4] were the most frequent USG features seen in TB, significantly more than in patients with lobar pneumonia. Most of the hypodensities were subcentimetric, ranging from 3 mm to 9 mm in size. The

Table 1: Demographic and image characteristics of study subjects

Characteristics	Cases (n=64), n (%)	Controls (n=32), n (%)	P
Mean age (years)	45.5±15.9	50.1 ± 14.8	
Male:female ratio	42:22	20:12	
Chest X-ray			
Effusion	2 (3.1)	3 (9.3)	< 0.001
Cavity	17 (26.6)	0	
Bilateral upper zone opacities	17 (26.6)	5 (15.6)	
Unilateral upper zone opacities	18 (28.1)	8 (25)	
Unilateral lower zone opacities	5 (7.8)	15 (46.9)	
LUS findings			
Focal interstitial pattern	55 (85.9)	14 (43.7)	< 0.001
Shred sign	29 (45.3)	11 (34.4)	
Irregular pleura	7 (10.9)	0	
Cavity	9 (14.1)	0	
Air bronchogram	0	8 (25)	

LUS: Lung ultrasound

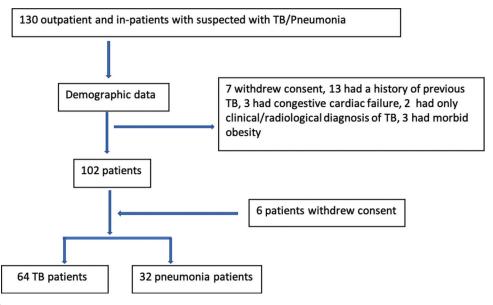


Figure 2: Study flow

classical "shred sign" [Figure 5], seen as a hyperechoic, broken, and irregular line at the deep edge of the sonological image, in the consolidated area of the lung, was also seen more frequently in TB patients.

The LUS findings in lobar pneumonia were characterized by consolidation with dynamic air bronchogram and shred sign [Figure 6]. The presence of an irregular pleura with no other sonological abnormality or presence of a cavity was exclusively seen in patients with TB [Figure 7].

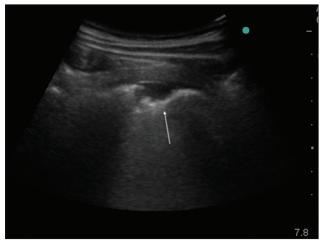


Figure 3: Sub pleural nodules. Arrows: Subpleural nodules, characterized by parenchymal subpleural hypoechoic region with posterior acoustic enhancement



Figure 5: Shred sign. Arrow points to shred sign characterized by hyperechoic, broken, and irregular line at the deep edge of the sonological image, in the consolidated area of the lung

The overall sensitivity of LUS compared to X-ray, to identify abnormalities in TB and lobar pneumonia patients, was 88.6%. The agreement of chest X-ray and LUS findings is given in Table 2. The sensitivity of LUS was 78% in patients with TB and 85% in patients with lobar pneumonia. In addition, it was observed that in 13 (20.3%) of TB patients, LUS was able to detect focal interstitial patterns and/or irregular pleura even in areas that looked normal on the chest radiogram.

The agreement on LUS findings between the two authors was good with a kappa coefficient value of 0.85. The time taken to complete LUS ranged from 3 to 6 min.



Figure 4: Irregular pleura. Arrow: Irregular pleura



Figure 6: Air-bronchogram characterized by hyperechoic branching image within the hypoechoic area with shredded margins. Arrows show the air-bronchogram

Table 2: Agreement of CXR and lung ultrasound findings				
Imaging modality	Pulmonary TB ($n=64$), n (%)*	Pneumonia (n=32), n (%)*		
Concordant areas of CXR and USG abnormalities	60 (93.75)	29 (90.6)		
CXR abnormalities with no USG abnormality	4 (6.2)	3 (9.3)		
Additional USG abnormality other than that seen on CXR	13 (20.3)	4 (12.5)		

^{*}Sum of subjects among TB and pneumonia patients will be >64 and 32, respectively, because row 3 includes those subjects from row 1 with additional USG abnormalities. The sensitivity of LUS was 78% in patients with TB and 85% in patients with lobar pneumonia. USG: Ultrasound, TB: Tuberculosis, LUS: Lung ultrasound, CXR: Chest X-Ray



Figure 7: Cavity characterized by hypoechoic area with surrounding shred sign. Arrow points to the shred sign

DISCUSSION

As knowledge of the use of LUS is gaining widespread application, it is imperative to inculcate the use of LUS in daily practice. Previous studies have reported LUS findings individually similar to the current study in TB^[10-12] and lobar pneumonia patients.^[3,11] However, a systematic comparison of LUS and CXR findings between adult PTB and lobar pneumonia patients has not been reported previously.

Our study showed considerable differences in LUS findings between TB and lobar pneumonia patients. A sizeable proportion of patients with PTB in our cohort had focal interstitial patterns detected on LUS. Although the two groups had overlapping LUS findings, the composite findings of focal interstitial pattern, cavity, and irregular pleura seen in TB patients were significantly different from the findings of air bronchogram and/or shred sign seen in patients with lobar pneumonia. A high proportion (97%) of small subpleural lesions were reported in a study by Agostinis *et al.*^[3] in 60 PTB patients as compared to 85.9% in ours. Consolidations were seen in 41.4% of subjects as opposed to 45.3% of subjects in our study. Consolidations were also reported in 77% of PTB patients in a study by Montuori *et al.*^[13]

In our study, although 17 TB patients had radiographic evidence of a cavity on CXR, USG was able to characterize the cavities in 9 patients. Detection by LUS is limited when a cavity is surrounded by air-filled alveoli. LUS does not detect abnormalities that do not have an air-fluid interface. Thus, LUS detects a cavity when it is thick-walled or has a surrounding consolidation. The presence of a focal interstitial pattern and irregular pleura in the upper regions of the LUS was more in favor of a TB diagnosis. This is consistent with the upper lobe predilection of infection with TB.

A systematic review reported the presence of pleural effusions, pleural thickening, and mediastinal nodes in children as USG features of TB.^[14] In this review, a parenchymal pattern was

reported in one study alone which recruited only miliary TB patients. Our study has demonstrated the utility of LUS in not only identifying parenchymal abnormalities in TB but also in differentiating the abnormalities from those caused by lobar pneumonia. Some LUS features noted in children with TB,[15] such as mediastinal lymph nodes, and pleural effusion are not common in adult patients. The pathologic presentation of TB in adults differs from that seen in children and one has to be mindful of this fact while performing LUS in adults. LUS has high sensitivity (95%) in the diagnosis of lobar pneumonia, especially in the initial 24 h, when lobar pneumonia is evolving and before any abnormality can be detected on the CXR.[16] A systematic review has demonstrated that the sensitivity of the CXR using a scoring system in TB diagnosis was >80% whereas the specificity estimates were low with a median of 42%.[17]

Our study demonstrates that LUS is on par with CXR in the detection of abnormalities in both TB and lobar pneumonia. The LUS and CXR findings were concordant in 90.6% of lobar pneumonia and 93.75% of TB patients. A higher percentage of lobar pneumonia patients had no LUS abnormalities as compared to TB patients [Table 2]. LUS detects artifacts that abut the pleura, therefore, LUS will be normal if lobar pneumonia is in a segment that does not reach the pleural surface. [18] In contrast, the ability of LUS to detect abnormalities in the absence of CXR findings was seen in TB patients, which were evident as a focal interstitial pattern. The reason behind better detection by LUS in TB is that patients may have a disease process more extensive than evident in the CXR, and the process is adjacent to the pleural surface.

LUS is a valuable tool to detect both TB and lobar pneumonia and can discriminate between the two conditions. A composite finding of focal interstitial pattern, irregular pleura, and/or cavity can rule in TB diagnosis as opposed to a composite of shred sign and air bronchogram, which is more suggestive of lobar pneumonia. Moreover, LUS has multiple benefits over CXR, as it can be performed in a dyspneic patient who cannot hold his breath or stand upright for an inspiratory CXR. LUS can be completed rapidly within a few minutes and without delay due to the immediate bedside availability. Similarly, LUS is preferable in pregnant females, as LUS has no harmful radiation. With the advent of hand-held and portable USG machines, LUS can be a valuable tool in field conditions to screen for TB, where the availability of X-ray machines in remote areas may be challenging. Besides, screening with portable or hand-held USG machines is feasible and less time-consuming.

Limitations

LUS was performed by a trained physician in this study. However, a confident diagnosis of lung abnormalities by LUS is possible with adequate training in acquiring and interpreting LUS. The generalizability of USG findings in patients with preexisting lung diseases such as bronchiectasis, ILDs, and chronic obstructive lung disease may be a challenge.^[19] The

presence of the abovesaid comorbidities may themselves yield irregular pleura and subpleural nodules.^[20] Further randomized control trials in the community and the abovesaid comorbidities would pave the way for a definitive role of USG as an important aid in the diagnosis and differentiation of TB and lobar pneumonia.

CONCLUSION

LUS is a valuable addition to the diagnostic evaluation of TB and lobar pneumonia. The presence of focal interstitial pattern, cavity, and irregular pleura helps to identify TB in patients presenting with fever and cough. In comparison, a shred sign or air bronchogram favors a diagnosis of lobar pneumonia in such patients. LUS has better sensitivity in the diagnosis of lung abnormalities in TB and lobar pneumonia. LUS is safe, reliable, portable, and easy to perform.

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INII.

Conflicts of interest

There are no conflicts of interest.

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