


ORIGINAL ARTICLE: IMAGING

Chest ultrasound compared to chest X-ray for pediatric pulmonary tuberculosis

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Abstract

Introduction: Chest ultrasound is increasingly used to radiologically diagnose childhood pneumonia, but there are limited data on its use for pulmonary tuberculosis (PTB).

Aim: Compare chest ultrasound with a chest X-ray (CXR) findings.

Methods: Children (up to 13 years) with suspected PTB were enrolled. Bedside chest ultrasound findings were compared to CXR. The analysis was stratified by PTB category: confirmed PTB (microbiologically confirmed), unconfirmed PTB (clinical diagnosis with negative microbiological tests), or unlikely PTB (other respiratory diseases with improvement without tuberculosis treatment).

Results: One hundred fifty-nine children were enrolled (57% boys, median age 26.6 months [interquartile range 15.1-59.3]). Ultrasound detected abnormalities in 72% (n = 114), CXR in 56% (n = 89), $P < .001$. Pleural effusion was detected on ultrasound in 15% (n = 24) compared 9% (n = 14) on CXR, $P = .004$, more in confirmed PTB (33%, n = 12 vs 8%, n = 4 unlikely PTB, $P = .013$). Ultrasound detected enlarged mediastinal lymph nodes more commonly (22%, n = 25) than CXR (6%, n = 10, $P = .001$); the size of lymph nodes in the unlikely category (1.0 cm) was smaller than the other two PTB categories (1.4 and 1.5 cm, $P = .001$). Inter-reader agreement (kappa Cohen) was higher for ultrasound than CXR for several findings (consolidation 0.67 vs 0.47, pleural effusion 0.86 vs 0.56, enlarged lymph nodes 0.56 vs 0.27).

Presentation: Preliminary data were presented at the 66th Annual Meeting of the American Society of Tropical Medicine and Hygiene in Baltimore, United States of America (November 5-9 2017).

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Conclusion: Ultrasound detected abnormalities more frequently than CXR with the higher inter-reader agreement; ultrasound abnormalities were most common in children with confirmed PTB. Ultrasound is a promising modality for detecting abnormalities in PTB. Further studies should evaluate the diagnostic accuracy of ultrasound against a gold standard.

KEYWORDS

chest ultrasound, CXR, diagnostics, pediatric pulmonary tuberculosis

1 | INTRODUCTION

Tuberculosis (TB) remains a global major public health issue in children with an estimated one million incident cases in 2017.¹ Pulmonary TB (PTB) is the most common presentation but diagnosis can be challenging due to nonspecific signs and symptoms, paucibacillary disease, and difficulties in obtaining adequate samples.² Chest X-ray (CXR) is the imaging tool of choice, with perihilar or mediastinal lymphadenopathy being the most characteristic findings.³⁻⁵ However, the intra- and inter-reader agreement for lymphadenopathy on CXR is poor (κ 0.00-0.40).⁵⁻⁷ Other common CXR findings described in children with PTB are consolidation or pleural effusion,^{3,5} but these are common findings in other respiratory infections as well.

Chest ultrasound is increasingly used for the diagnosis of pediatric lung disease including pneumonia, bronchiolitis, or respiratory distress syndrome.⁸ Advantages of chest ultrasound are that it is free of ionizing radiation; can be performed by the clinician at the bedside and is easily reproducible; making it a suitable tool for diagnosis, prompt management decisions, and monitoring of treatment response. Training in chest ultrasound is relatively easy, and clinicians can be expected to perform good quality chest ultrasounds after 30 supervised examinations.⁹ Furthermore, due to the recent development of portable, low-cost ultrasound machines, bedside chest ultrasound may become a cost-effective tool especially in resource-limited settings.

Data on the use of chest ultrasound for the diagnosis of PTB in children are limited.¹⁰⁻¹³ Previous studies showed that chest ultrasound demonstrated pleural effusion more commonly in children with microbiologically confirmed PTB than in children with other respiratory diseases.¹³ Mediastinal ultrasound was feasible in visualizing lymphadenopathy,¹⁰⁻¹² and children with confirmed PTB had larger lymph nodes than children with other respiratory diseases.¹³ Consolidation was as common in children diagnosed with PTB compared to those with other respiratory diseases, but the resolution of consolidation was slower in children with confirmed PTB.¹³

The aim of this study was to compare chest ultrasound findings with CXR findings in children with suspected PTB.

2 | METHODS

This was a prospective study of children hospitalized with suspected PTB at a tertiary children's hospital in Cape Town, South Africa from

July 2014 to October 2015. Children from up to 13 years (the maximum age of children being admitted in our hospital) with suspected PTB were consecutively enrolled. Inclusion criteria were cough plus one of the following: (a) weight loss or failure to thrive over the last 3 months; (b) a positive tuberculin skin test; (c) a CXR suggestive of PTB; or (d) a household TB contact. Children on TB treatment or TB prophylaxis for more than 72 hours, those unable to provide an adequate sample, or when parents were unable to provide informed consent, were excluded. Children with exclusively extrapulmonary TB (EPTB) or if the time between chest ultrasound and CXR was more than 7 days were excluded from this analysis.

The study was approved by the Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town. Written informed consent was obtained from a parent or legal guardian; assent was obtained in children older than 7 years.

2.1 | Investigations

Two induced sputum samples were collected for liquid mycobacterial culture (BACTEC MGIT; Becton Dickinson, Sparks, MD) and Xpert MTB/RIF (Xpert, Cepheid, Sunnyvale, CA), HIV testing, chest ultrasound, and CXR were performed on all enrolled children. Children were categorized into one of three PTB categories¹⁴; (a) confirmed PTB, *Mycobacterium tuberculosis* detected by either culture or GeneXpert; (b) unconfirmed PTB, clinically diagnosed but microbiological testing negative; or (c) unlikely PTB, not clinically or microbiologically diagnosed, and improvement of respiratory disease without TB treatment.¹⁴

All children underwent chest ultrasound, including mediastinal ultrasound, and had an anterior-posterior and lateral CXR.

2.2 | Chest ultrasound

A portable, low-cost, greyscale ultrasound machine (Mindray DP10, Mindray, Shenzhen, China) with a 5 to 10 MHz linear probe was used to scan the chest. A clinician (CCH) without prior ultrasound experience, who attended 4-day ultrasound training before the start of the study, performed the ultrasound scans. The children were scanned either sitting or supine plus in left and right lateral decubitus position, to examine the lungs and pleura. The chest was divided into 14 regions; the left and right, anterior, lateral and posterior, superior

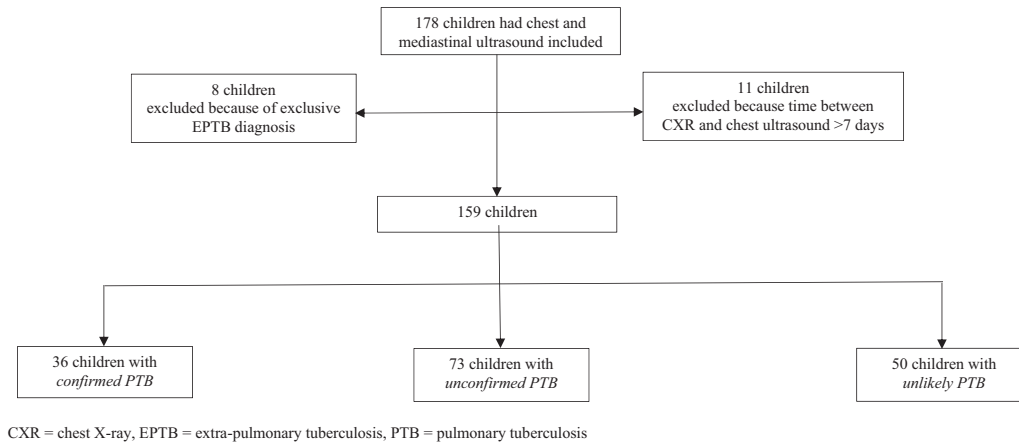


FIGURE 1 Flow diagram of participant enrolment

and inferior region, and the two apices. All regions were scanned in the longitudinal and transverse (intercostal) planes.¹⁵ In addition, mediastinal ultrasound was performed through the suprasternal notch with a 5.0 to 8.5 MHz micro-convex probe. The child was placed in the supine position with the neck slightly extended to improve access to the suprasternal notch: transverse and oblique views were obtained.¹⁶ All cine clips were saved. The clinician performing the ultrasound recorded the findings “consolidation less than 0.5 cm” (E-Image 1), “consolidation ≥ 0.5 cm” (E-Image 2a), “pleural effusion” (E-Image 3a), “enlarged mediastinal lymph nodes ≥ 1.0 cm” (E-Image 4a) on a standardized reporting form. Another clinician (SB), with 1 year of pediatric ultrasound experience, reviewed the saved ultrasound cine clips and independently reported on these using the same standardized reporting form. In case the sonographer and the clinician reviewing the saved ultrasound cine clips disagreed on a chest ultrasound finding, the saved cine clips were reviewed by both clinicians again and their findings were discussed to come to an agreement. If no consensus was met the findings of the sonographer were used for comparison with CXR. A senior ultrasound specialist was consulted to resolve any disagreement on mediastinal ultrasound.

2.3 | CXR

To ensure the highest achievable quality of CXR reports, the posterior-anterior and lateral CXRs were independently reviewed by two pediatric radiologists reporting on a standardized record sheet “consolidation” (E-Image 2b), “pleural effusion” (E-Image 3b), “enlarged mediastinal lymph nodes” (E-Image 4b), and “final diagnosis”: TB or no TB. In case of disagreement on the final diagnosis, a third pediatric radiologist was consulted, and the final diagnosis was based on majority opinion. In case of disagreement for the other findings (consolidation, pleural effusion, or enlarged mediastinal lymph nodes), the finding of the most experienced TB radiologist (SA) was used for comparison with ultrasound. The inter-reader agreement of clinicians analyzing the chest ultrasound was

compared with the inter-reader agreement between the first two pediatric radiologists reporting on the CXRs.

The sonographer, the clinician reviewing the saved ultrasound clips, and the radiologists were blinded to each other’s findings and clinical or microbiological data.

2.4 | Data analysis

Ultrasound findings were compared to CXR findings for the presence of consolidation, pleural effusion, or enlarged mediastinal lymph nodes. Descriptive statistics were used for participant characteristics; mean and standard deviation (SD) were used for normally distributed data, median and interquartile range (IQR) were used for nonnormally distributed data. McNemar’s test or χ^2 test was used to calculate the *P* value.

Cohen’s kappa coefficient (κ) was used to analyze the inter-reader agreement for chest ultrasound and for CXR. The following interpretation of the result was used: less than zero no agreement, 0 to 0.20 slight, 0.21 to 0.40 fair, 0.41 to 0.60 moderate, 0.61 to 0.80 substantial, and 0.81 to 1 almost perfect agreement.¹⁷ STATA 14.2 (StataCorp; 2015, TX) was used for analysis.

3 | RESULTS

3.1 | Demographics

One hundred seventy-eight children underwent chest ultrasound and CXR. Eight children were excluded from analysis because of an exclusive EPTB diagnosis, and a further 11 children were excluded because the interval between chest ultrasound and CXR was more than 7 days. Of the 159 children remaining, 36 (23%) had confirmed PTB, 73 (46%) had unconfirmed PTB, and 50 (31%) had unlikely PTB, Figure 1. Ninety children (57%) were boys; median age was 26.6 months (IQR = 15.1–58.1) and 14% (*n* = 22) were HIV infected, Table 1.

TABLE 1 Demographics

	Male, n (%)	Median age (IQR), in mo	HIV infected, n (%)	Mean interval chest US and CXR, d (SD)
All enrolled patients, n = 159	90 (57)	26.6 (15.1-58.1)	22 (14)	2.3 (1.7)
Confirmed PTB, n = 36	23 (64)	48.6 (18.3-65.9)	6 (17)	2.3 (1.6)
Unconfirmed PTB, n = 73	42 (58)	25.0 (14.0-43.0)	10 (17)	2.4 (1.6)
Unlikely PTB, n = 50	25 (50)	23.9 (16.4-56.2)	6 (12)	2.1 (1.8)

Abbreviations: CXR, chest X-ray, d, day; HIV, human immunodeficiency virus; IQR, interquartile range; mo, month; n, number; PTB, pulmonary tuberculosis; SD, standard deviation; US, ultrasound.

The mean time between chest ultrasound and CXR was 2.3 days (SD 1.7 days). The mean duration for performing a chest ultrasound was 6 minutes (SD 5-8 minutes).

3.2 | Chest ultrasound vs CXR findings

One hundred fourteen (72%) children had an abnormal finding (consolidation ≥ 0.5 cm, pleural effusion, or enlarged mediastinal lymph node ≥ 1 cm) on chest ultrasound vs 89 (56%) children who had an abnormal finding on CXR, $P < .001$. Children in the confirmed PTB category had the highest proportion with an abnormal finding on ultrasound (83%) compared to 72% in the unlikely PTB category, $P = .220$, Table 2.

Consolidation was the most common abnormal finding, with a consolidation ≥ 0.5 cm occurring in 75 (47%) children on chest ultrasound and in 83 (52%) on CXR, $P = .267$, Table 3. Consolidation was as common in children with confirmed PTB (56%) as in children with unlikely PTB (52%, $P = .744$). CXR and chest ultrasound performed similarly for detecting large consolidation (≥ 0.5 cm) across the three PTB categories, Table 3. In contrast, a small consolidation (< 0.5 cm) was reported on chest ultrasound in 78 (49%) children (15/36 confirmed PTB, 41/73 unconfirmed PTB, 22/50 unlikely PTB, $P = .250$). CXR reported consolidation of any size in 44 (28%) of those children. In six (five unlikely PTB and one unconfirmed PTB) children, a consolidation was reported on CXR but no consolidation (not ≥ 0.5 cm nor < 0.5 cm) was seen on chest ultrasound. In three of those six children, the radiologists did not agree on this finding, a third radiologist was consulted.

Pleural effusion was found on ultrasound in 24/159 (15%) children compared to 14/159 (9%) children on CXR, $P = .004$, Table 3. Both chest ultrasound and CXR detected pleural effusion in 13 children; chest ultrasound detected 11 (7%) additional children with a pleural

effusion that was not seen on CXR, mainly in the confirmed PTB category where eight additional children were detected (in 7/8 children the pleural effusion was accompanied by a consolidation; in five of those seven children CXR reported only a consolidation; in the remaining children the CXR was reported to be normal). In one of the 14 children with a reported pleural effusion on CXR, a large consolidation was reported on chest ultrasound rather than a pleural effusion. Pleural effusion on ultrasound was significantly more commonly detected in children with confirmed PTB (33%) than in children with unlikely PTB (8%), $P = .013$. In the confirmed PTB category the pleural effusion was accompanied by consolidation in 8/12 (75%) children, in the unconfirmed PTB category in 4/8 (50%) children and in the unlikely PTB category in 1/4 (25%) children.

Pediatric Pulmonology Mediastinal ultrasound could be evaluated in 112/159 (70%) children as the clips were of poor quality or ultrasound could not be performed due to poor compliance in 30%. Enlarged mediastinal lymph nodes were detected in 25/112 (22%) children on ultrasound (of whom 10 were in the unlikely PTB category) and in 10/159 (6%) children on CXR, $P = .001$, Table 3. CXR did not detect any enlarged lymph nodes in the unlikely PTB category. The enlarged lymph nodes in the unlikely PTB category were significantly smaller than in the other two categories (median size enlarged lymph nodes unlikely PTB 1.0 cm [range 1.0-1.1 cm], unconfirmed PTB category 1.4 cm [range 1.0-2.8 cm], confirmed PTB category 1.5 cm [range 1.0-1.6 cm], $P = .001$).

Twenty-two children were HIV infected; ultrasound detected abnormalities in similar numbers of HIV infected (73%) and uninfected children (58%), $P = .181$, Table 4.

Chest ultrasound had "substantial" and "almost perfect" inter-reader agreement for consolidation ≥ 0.5 cm ($\kappa = 0.67$) or pleural effusion ($\kappa = 0.86$), respectively, and a moderate agreement for enlarged mediastinal lymph nodes ($\kappa = 0.56$). The inter-reader

TABLE 2 Abnormal chest ultrasound and chest X-ray findings by TB category

	Abnormal ultrasound ^a n/N (%)	Abnormal CXR ^b n/N (%)	Abnormal CXR or ultrasound n/N (%)	P value Ultrasound vs CXR
Total	114/159 (72)	89/159 (56)	130/159 (82)	<.001
Confirmed PTB	30/36 (83)	22/36 (61)	32/36 (89)	.021
Unconfirmed PTB	49/73 (67)	37/73 (51)	55/73 (75)	<.001
Unlikely PTB	36/50 (72)	30/50 (60)	44/50 (88)	.201

Abbreviations: CXR, chest X-ray; n, number of children with abnormal finding; N, number of children investigated; PTB, pulmonary tuberculosis.

^aAbnormal CXR means: consolidation, pleural effusion, or enlarged mediastinal lymph nodes detected.

^bAbnormal chest ultrasound means: consolidation ≥ 0.5 cm, pleural effusion, or enlarged mediastinal lymph nodes detected.

TABLE 3 Positive findings on chest ultrasound findings versus chest X-ray

Finding PTB category	Positive chest ultrasound finding n/N (%)	Positive CXR finding n/N (%)	Agreement chest ultrasound and CXR positive n/N (%)	Positive chest ultrasound or CXR finding n/N (%)	P value Ultrasound vs CXR
Consolidation (≥ 0.5 cm)	75/159 (47)	83/159 (52)	53/159 (33)	105/159 (66)	.267
Confirmed PTB	20/36 (56)	20/36 (56)	15/36 (42)	25/36 (69)	1.000
Unconfirmed PTB	29/73 (40)	33/73 (45)	18/73 (25)	44/73 (60)	.433
Unlikely PTB	26/50 (52)	30/50 (60)	20/50 (40)	36/50 (72)	.317
Pleural effusion	24/159 (15)	14/159 (9)	13/159 (8)	25/159 (16)	.004
Confirmed PTB	12/36 (33)	4/36 (11)	4/36 (11)	12/36 (33)	.005
Unconfirmed PTB	8/73 (11)	7/73 (10)	6/73 (8)	9/73 (12)	.564
Unlikely PTB	4/50 (8)	3/50 (6)	3/50 (6)	4/50 (8)	.317
Enlarged mediastinal lymph nodes ≥ 1 cm	25/112 (22)	10/159 (6)	3/112 (3)	29/159 (18)	.001
Confirmed PTB	7/24 (29)	4/36 (11)	0/24 (0)	11/36 (31)	.206
Unconfirmed PTB	8/51 (16)	6/73 (8)	3/51 (6)	8/73 (11)	.257
Unlikely PTB	10/37 (27)	0/50 (0)	0/37 (0)	10/50 (20)	.002

Abbreviations: CXR, chest X-ray; n, number of children with a positive finding; N, number of children who underwent the investigation; PTB, pulmonary tuberculosis.

agreement for a consolidation less than 0.5 cm on chest ultrasound was fair ($\kappa = 0.39$). The inter-reader agreement for CXR was fair to moderate for consolidation ($\kappa = 0.47$), pleural effusion ($\kappa = 0.56$), and enlarged mediastinal lymph nodes ($\kappa = 0.27$), Table 5.

4 | DISCUSSION

In this study of children with suspected PTB, an abnormal finding was seen more frequently on chest ultrasound than on CXR for all three PTB categories. Children in the confirmed PTB category had an abnormal finding on chest ultrasound more frequently. Furthermore, ultrasound had a higher inter-reader agreement than CXR for

consolidation ≥ 0.5 cm, pleural effusion, or enlarged mediastinal lymph nodes. The ultrasound had the additional advantages in that it could be performed relatively easily as a bedside investigation, was quick to perform and was done by a clinician.

This is the first study comparing chest ultrasound findings with CXR findings in children with suspected PTB. A recent systematic review showed that there are limited data on the use of chest ultrasound in patients with PTB.¹⁸ This review identified 12 small (1–87 participants) studies, of which three were pediatric (each with 30–57 participants), using mediastinal ultrasound.^{10–12} We found that a large consolidation (≥ 0.5 cm) was nearly as commonly detected on ultrasound as on CXR and that a small consolidation (< 0.5 cm) was predominantly identified on chest ultrasound. This is consistent with previous pneumonia studies,^{19,20} in which a consolidation less than 1 cm was more commonly detected on chest ultrasound than CXR.^{19,20} A study performed in adults with PTB reported that subpleural nodules (consolidation < 1 cm, close to the pleural line) were present in almost all patients²¹; however, a control group was lacking. In our study, a small consolidation was found on ultrasound in 49% of children and was present in all three TB categories,

TABLE 4 Positive chest ultrasound and CXR findings in HIV infected and noninfected children with suspected PTB

Imaging finding	HIV+ (n = 22)	HIV- (n = 137)	P value
Abnormal chest ultrasound, n (%)	16 (73)	79 (58)	.181
Consolidation ≥ 0.5 cm, n (%)	14 (64)	61 (45)	.096
Pleural effusion, n (%)	5 (23)	19 (14)	.281
Enlarged mediastinal lymph nodes, n/N (%)	3/16 (19)	22/96 (23)	.711
Abnormal CXR, n (%)	14 (64)	75 (55)	.435
Consolidation, n (%)	14 (64)	69 (50)	.247
Pleural effusion, n (%)	1 (5)	13 (9)	.448
Enlarged mediastinal lymph nodes, n (%)	0 (0)	10 (7)	.191

Abbreviations: CXR, chest X-ray; HIV, human immunodeficiency virus; PTB, pulmonary tuberculosis.

TABLE 5 Inter-reader agreement of chest X-ray and chest ultrasound

Imaging finding	Kappa Cohen chest X-ray	Kappa Cohen chest ultrasound
Consolidation < 0.5 cm	...	0.39
Consolidation ≥ 0.5 cm	0.47	0.67
Pleural effusion	0.56	0.86
Enlarged mediastinal lymph nodes	0.27	0.56

including the unlikely PTB category. The clinical importance of small consolidation is unclear, as this may represent early disease, but has also been reported in healthy people. Further, the inter-reader agreement for a small consolidation was only fair. Further studies are needed to evaluate the clinical relevance and natural history of a small consolidation.

Pleural effusion was significantly more common on ultrasound than on CXR, especially in the confirmed PTB category. This is consistent with prior studies that have shown ultrasound to be superior to CXR for pleural effusion,^{22,23} and for differentiating consolidation from pleural effusion.²⁴ In the confirmed PTB category, pleural effusion was often accompanied by a consolidation. Although pleural effusion and consolidation can occur in children with pneumonia caused by other bacteria or viruses, PTB should be considered as a possible diagnosis when a pleural effusion is detected in the right setting and accompanied by a consolidation.

Enlarged mediastinal lymph nodes, the diagnostic hallmark for PTB in children,³⁻⁵ were more commonly detected by ultrasound but were also found in the unlikely PTB category, but the size of nodes was smaller than in the other two categories. In contrast, CXR did not detect enlarged lymph nodes in unlikely TB; as the size of lymph nodes in the unlikely PTB category ranged from 1.0 to 1.1 cm, these might have been too small to be detected on CXR. A previous study in children with a positive tuberculin skin test showed that mediastinal ultrasound detected enlarged lymph nodes in 67% of the children with a normal CXR.¹⁰ It can be difficult to detect enlarged mediastinal lymph nodes on the posterior-anterior CXR as vascular and thymic structures might be confused for enlarged lymph nodes and vice versa. In addition, the wide inter-reader variability of reporting enlarged lymph nodes on CXR makes the interpretation difficult. Detection of enlarged mediastinal lymph nodes on ultrasound in the unlikely PTB category makes it difficult to distinguish PTB from other respiratory infections of other causes; based on the difference in size measured between the two PTB category and the unlikely PTB category, we recommend that future studies should determine the cut-off for enlarged lymph nodes in children with TB on ultrasound.

Chest ultrasound had a better inter-reader agreement for consolidation, pleural effusion, or enlarged mediastinal lymph nodes than CXR. This is in line with previous studies showing poor inter-reader agreement for the detection of mediastinal lymphadenopathy on CXR⁵⁻⁷ and a higher inter-reader agreement amongst chest ultrasound readers compared to CXR readers for the detection of consolidation in children with pneumonia.²⁵

Limitations of this study include comparing chest ultrasound with CXR. We found a limited inter-reader agreement on CXR findings; therefore, we considered CXR as an imperfect comparison to ultrasound. Because of that, we chose not to calculate the sensitivity or specificity of ultrasound vs CXR. Until advances in technology make CT or MRI a safe, ethical choice, we are limited to using CXR. A further limitation was the lack of prior ultrasound experience by the sonographer; previous chest ultrasound studies on children with pneumonia found that the diagnostic accuracy was higher when the sonographer was more experienced.⁸

Chest ultrasound is limited as only findings close to the pleural line can be detected, as the ultrasound beam will be scattered and impeded by the aerated lung. Therefore, abnormalities that do not reach the pleural line may be missed by ultrasound. Mediastinal ultrasound could not be evaluated in 30% of the children, due to low-quality imaging or noncompliance. This is a known limitation inherent in the use of mediastinal ultrasound especially in young children with short necks.

A further limitation is that a third radiologist was only consulted when there was a disagreement on the final diagnosis. Finally, ultrasound images were interpreted by clinicians, whereas CXR images were interpreted by pediatric radiologists; despite this, an ultrasound revealed abnormalities more commonly and with a higher inter-reader agreement.

Further prospective, larger-scale, multicenter studies evaluating the diagnostic accuracy of chest ultrasound compared to a gold standard such as CT or MRI should be conducted, using experienced sonographers.

5 | CONCLUSIONS

Chest ultrasound detected abnormalities more frequently than CXR, and ultrasound abnormalities were most common in the confirmed PTB category. Chest ultrasound also showed higher inter-reader agreement between clinicians for all categories of findings than CXR read by subspecialist pediatric radiologists. Chest ultrasound may, therefore, be useful to identify lung disease including PTB and other respiratory diseases. Lymph node size appears to differentiate PTB from other lower respiratory tract infections. However, microbiologic diagnosis remains important for confirming the diagnosis. Further studies should evaluate if chest ultrasound detects enlarged mediastinal lymph nodes in children with other respiratory diseases, and evaluate the diagnostic accuracy and significance of chest ultrasound compared to a valid imaging gold standard, like chest CT or MRI.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

AUTHOR CONTRIBUTIONS

CCH, SB, MPG, and HJZ conceived the ultrasound protocol. CCH performed and recorded chest and mediastinal ultrasound. SB reviewed the saved ultrasound cine clips. SA, HL, and HM recorded the CXRs. CCH analyzed the data and prepared the manuscript. MPG and HJZ supervised CCH; HJZ designed and oversaw the TB diagnostic study. CCH drafted the manuscript. CCH, SB, SA, MPG, and HJZ were involved in data interpretation and manuscript revision. All authors contributed to and approved the final version of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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