ORIGINAL ARTICLE

Concordance of Chest Ultrasonography with Contrast-Enhanced Chest Computed Tomography in the Detection of Mediastinal Lymphadenopathy among Pediatric Patients Clinically Diagnosed with Tuberculosis

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ABSTRACT

Objective:
To determine the agreement of chest sonography with contrast-enhanced chest computed tomography scan in the detection of mediastinal lymphadenopathy in children with clinically diagnosed tuberculosis (TB)

Design setting and participants:
Twelve patients (5 females and 7 males) with age range of 8–17 years old, and with clinically diagnosed TB disease were prospectively recruited and underwent chest ultrasound using standard sonographic protocol. Computed tomography (CT) was used as gold standard to confirm the presence of mediastinal lymphadenopathy. The images were interpreted blindly by two pediatric radiologists.

Results:
Sonographic zones showing the highest concordance with CT include those taken in the transverse suprasternal and left parasternal views namely, zones B (prevascular/left upper paratracheal, 91.7%), C (subaortic/AP window, 100%), G (prevascular, 100%) & H (pericardial, cardiophrenic, 100%). The sonographic zones that show lower concordance are zone A (83.3%), as well as those taken in the suprasternal oblique views namely, zone E (retrotracheal, 75%) and zones D (prevascular) and F (retrotracheal/subcarinal), both at 83.3% concordance. Overall, the level of agreement of ultrasound findings with CT findings is moderate (89.6%, 95% CI Concordance = [0.835, 0.957] Cohen's Kappa = 0.535), and was statistically significant.

Conclusion:
Chest sonography shows moderate agreement with CT in detecting mediastinal lymphadenopathy in children with TB. Ultrasound may be used as an initial tool to detect enlarged lymph nodes in children clinically diagnosed with TB and to assess for disease progression.

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INTRODUCTION

Tuberculosis (TB) remains to have a significant burden worldwide. In 2015, the World Health Organization (WHO) declared TB to be responsible for more deaths than any other single infectious disease [1]. Children are included among the high-risk groups for developing TB and often pose a challenge to the clinicians in making a definitive diagnosis. Despite the global drop in the number of newly diagnosed TB cases as reported by the recent 2021 WHO report, children still accounted for 8% of all TB cases. The Philippines remains to be in the top 30 list of countries with high disease burden, which constitutes 6% of the total global TB cases [2].

On chest radiography, mediastinal lymphadenopathy with or without parenchymal involvement is the single most important diagnostic feature [3] and is regarded as the radiological hallmark of primary TB. Lymphadenopathy is also the most common abnormality noted in children with primary TB. However, this is not pathognomonic of TB because other infectious processes can also present with lymphadenopathy [4].

Marcet et al. generally recommend pediatric patients with a positive tuberculin skin test to undergo a chest radiographic study and mediastinal sonography. If both examinations are unrevealing, no additional imaging studies are needed. If radiographic findings are inconclusive and sonography is normal or confirms the presence of a hyperplastic thymus, no other diagnostic studies are needed [5]. In another study done in 2004 wherein they compared ultrasound with plain radiography and computed tomography scan for the detection of mediastinal TB lymphadenopathy in children [6], it showed that in 90.5% of children with chest x-ray images compatible with TB, coincident findings were also found in the mediastinal ultrasound study. In those with normal chest radiography, 66.7% had evidence of mediastinal lymphadenopathy on ultrasound. In all cases but one, ultrasound and computed tomography (CT) findings agreed. They concluded that mediastinal US is useful for the detection of enlarged lymph nodes in children with a positive tuberculin reaction and normal chest radiography.

In a study by Wernecke et al. in 1990, different proportion of diagnostic sonographic examinations varied for the different mediastinal compartments ranging from 85% (subcarinal region) to as high as 96% (supraaortic region). These results showed that sonography is superior to chest radiography in the diagnosis of mediastinal tumors. In certain mediastinal regions (supraaortic, pericardial, prevascular, and paratracheal), sonography was found to be more sensitive than that of CT [7]. Several more recent literatures depict that chest CT with contrast is the measure modality of choice to adequately assess mediastinal lymphadenopathies and/or masses and that chest sonography has good concordance with chest CT in detecting mediastinal lymphadenopathies.

However, sonography has limitations in assessing hilar involvement, because the hilum is surrounded by air in the lungs. Other limitations of using ultrasound include operator dependence and subjectivity, but these can be overcome with experience and procedure standardization [8]. Evaluation of primary progressive TB remains to be a combination of clinical, laboratory and imaging parameters. CT with contrast remains to be the gold standard and superior to all other imaging modalities in the detection of mediastinal lymphadenopathies, which is the imaging hallmark of primary progressive TB. The objective of this study is to determine the agreement of chest sonography with contrast-enhanced chest CT in the detection of mediastinal lymphadenopathy in children with clinically diagnosed TB disease.

METHODS

The legal guardians of all subjects participated voluntarily, and the participants/ representatives have provided written informed consent to participate in this study. This study was approved by the Institutional Review Board.

Eligible children aged 5–17 years old with clinical manifestations of TB (suspects/newly diagnosed untreated Category III pulmonary TB) who were referred for Chest CT for the evaluation of TB were prospectively enrolled. Such population was chosen since children in this age group can follow simple instructions, thereby waiving the need for sedation.

Children who have history of exposure to a patient with known active TB disease, positive Mantoux / tuberculin skin test, signs and symptoms suggestive of TB and/or abnormal chest X-ray were included. Meanwhile, children who were referred for other primary causes such as blood dyscrasia, autoimmune disease, other infections, neoplasms or who has moderate to high risk of developing iodinated contrast-media adverse reaction (e.g. renal disease/abnormal creatinine, allergy to contrast, food or medication allergy, asthma, congestive heart failure, thyroid disease, diabetes, seizure disorder, sickle cell trait and any pre-existing medical problem) were excluded in the study.

Prior to the CT procedure, serum creatinine and calculation of estimated glomerular filtration rate (eGFR) were obtained from all the participants to ensure adequate renal function. Computed tomography was performed on Siemens Somatom Force dual-source, dual-energy CT system. CT settings were adjusted to a low mAs and kVP, with less than 1 mm collimation, single breath hold and fast table speed. Scanning was performed from thoracic apex to the upper abdomen with ultra-high pitch and kVp of 120 (for body weight of more than or equal to 20 kg) and automated mAs. Non-ionic iodinated contrast media was administered at a dose of 1.2 cc/kg. Study was sent to a picture archive and communication system (PACS) for storage and interpretation.

The reference standard for the primary analysis was the presence of enlarged lymph nodes in chest CT, taken as any node measuring more than 1 cm in transverse or short axis dimension.

After performing the CT procedure, patients proceeded to ultrasound. A grey-scale and color doppler ultrasound machine (Hitachi Hi Vision Preirus) was utilized with small aperture phased array transducer having a center frequency of approximately 7.5 MHz (5.0 – 8.8 MHz) to access the mediastinum through the window of the suprasternal notch and the intercostal space left of the sternum. An experienced pediatric radiologist performed the ultrasound study, and the techniques are adapted from the study of Pool et. al. that was published in 2017 [9].

The four-view technique used the thymus as the acoustic window in all four predefined zones. The first predefined zone is noted in the transverse suprasternal view (Figs. 1–3) labeled as Zones A, B and C. Zone A is anterior to the right and left brachiocephalic vein within the thymic region, Zone B is seen between the left brachiocephalic vein and the aorta, while Zone C is between the aorta and the pulmonary trunk. The second predefined zone is obtained at the oblique suprasternal view (Fig. 4), and are labeled as Zone D, which is anterior to the left brachiocephalic vein within the thymic region, Zone E which is lateral to the arch of the aorta and posterior to the left subclavian artery, and Zone F is seen inferior and posterior to the aortic arch. The third predefined zone is seen at the transverse left parasternal view (Fig. 5) as represented by Zone G, which is anterior and to the left of the pulmonary trunk within the thymic region. The fourth predefined zone is identified in the longitudinal left parasternal view (Fig. 6), depicted as Zone H, which is seen at the anterior and to the left of the right atrium and ventricle within the thymic region.

The imaging studies were independently reviewed by two pediatric radiologists who are at least 8 years in practice. The official results of both ultrasound and CT were forwarded to the attending pediatrician's clinic for proper management.

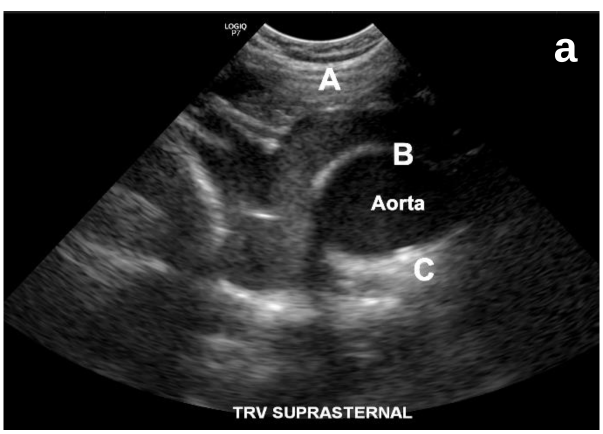
Statistical analysis using SPSS software was utilized. Concordance rate (number of positive and negative concordance) using number and percent (%) with 95% confidence interval (CI) was calculated. Agreement between ultrasound and CT was measured using Kappa correlation coefficient.

RESULTS

A total of 12 patients (5 girls and 7 boys) were included with age ranging from 8 years old to 17 years old, with mean age of 11 years old (Table 1). 7 of 12 patients have 100% concordance rate, while 2 patients have only 5 of 8 concordant zones (Table 2).

Table 1 Descriptive statistics: Patient profile

Profile	Frequency	Percentage
Age (in years)		
8	2	16.7
9	4	33.3
10	2	16.7
12	1	8.3
15	1	8.3
17	2	16.7
Sex		
Female	5	41.7
Male	7	58.3
TOTAL	**12**	**100.0**



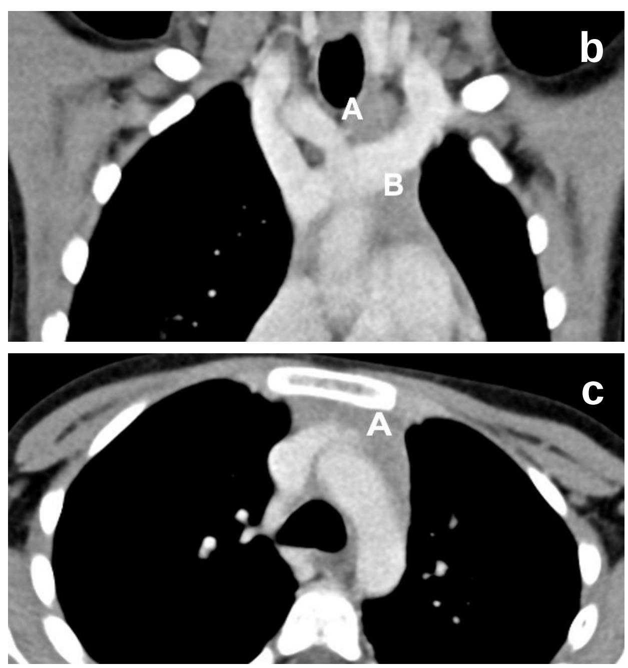


Fig. 1a-c Predefined zones in the transverse (TRV) suprasternal view in ultrasound (**a**) and computed tomography (CT) (**b, c**). A - anterior to the right and left brachiocephalic veins within the thymic region corresponding to prevascular space on CT; B - between the left brachiocephalic vein and the aorta corresponding to prevascular/left upper paratracheal region on CT; C - between the aorta and the pulmonary trunk corresponding to the subaortic/aortopulmonary window on CT

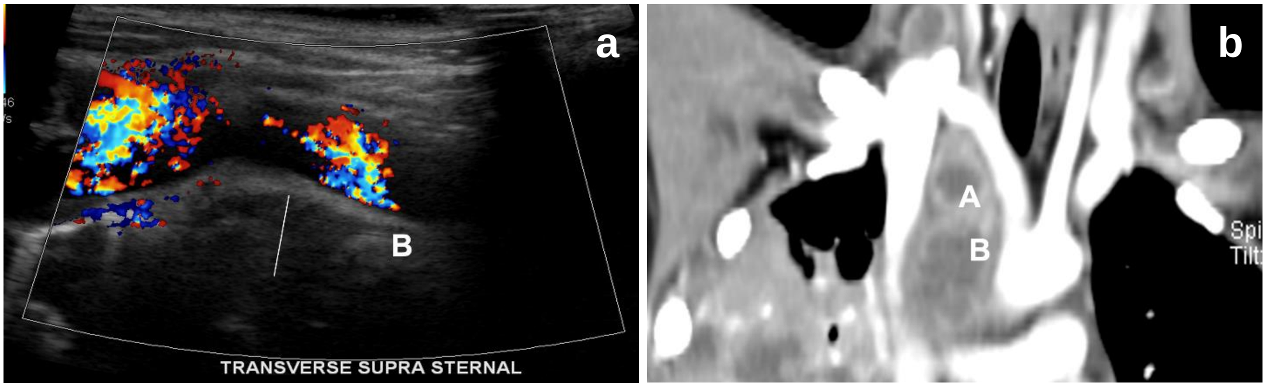


Fig. 2a–b Predefined zones in the transverse suprasternal view in ultrasound (**a**) and computed tomography (**b**). An enlarged lymph node (white line behind the colored brachiocephalic veins) is noted in zones A & B, with corresponding coronal CT image in soft tissue window setting

Table 2 Descriptive statistics: per patient finding

Patient # (Age in years)	No. of Concordant Zones (total of 8)	Concordant Zones	Concordance Rate (%)
Patient 1 (17)	8	A to H	100
Patient 2 (17)	8	A to H	100
Patient 3 (9)	5	A, C, F to H	62.5
Patient 4 (9)	8	A to H	100
Patient 5 (9)	8	A to H	100
Patient 6 (8)	8	A to H	100
Patient 7 (10)	6	A to D, G, H	75.0
Patient 8 (9)	8	A to H	100
Patient 9 (15)	8	A to H	100
Patient 10 (10)	7	B to H	87.5
Patient 11 (8)	7	A to D, F to H	87.5
Patient 12 (12)	5	B, C, F to H	62.5

Concordance rate was computed (Table 3). In Zone A, 5 patients were found positive for mediastinal lymphadenopathy in CT, but only 3 were positive in ultrasound. All 7 patients that were found negative in CT were properly identified in ultrasound but 2 patients were classified as “false negatives”. Hence, concordance rate was computed to be equal to 83.3% (CI: 62.2 to 100%). The level of agreement of ultrasound findings with CT findings in Zone A using Cohen’s Kappa statistic was equal to 0.636, which is classified as “substantial agreement”, and was found to be statistically significant.

In Zone B, 2 patients were found positive for mediastinal lymphadenopathy in CT, but only 1 of them were positive in ultrasound. All 10 patients that were found negative in CT were properly identified in ultrasound but 1 patient was classified as “false negative”. Hence, concordance rate was computed to be equal to 91.7% (CI: 76 to 100%). The level of agreement of ultrasound findings with CT findings in Zone B using Cohen’s Kappa statistic was equal to 0.625, which is classified as “substantial agreement”, and was found to be statistically significant.

In Zone C, all twelve (12) patients were found negative for mediastinal lymphadenopathy in CT and all were also found negative in ultrasound. Hence, concordance rate was at 100% (12 of 12 patients).

In Zone D, 3 patients were found positive for mediastinal lymphadenopathy in CT, but only 1 of them were positive in ultrasound. All 9 patients that were found negative in CT were properly identified in ultrasound but 2 patients were classified as “false negatives”. Hence, concordance rate was computed to be equal to 83.3% (CI: 62.2 to 100%). The level of agreement of ultrasound findings with CT findings in Zone D using Cohen’s Kappa statistic was equal to 0.429, which is classified as “moderate agreement”, but was found to be not statistically significant.

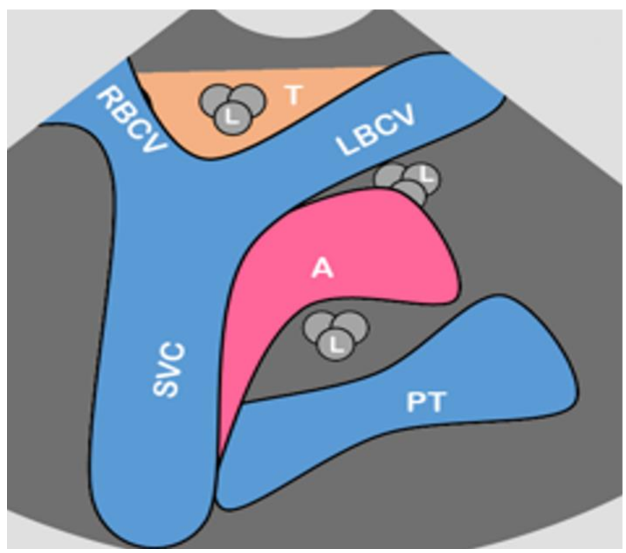


Fig. 3 Predefined zones in the transverse suprasternal view in ultrasound. A - aortic arch; L - lymph node; LBCV - left brachiocephalic vein; PT - pulmonary trunk; RBCV - right brachiocephalic vein; T - thymic region

Table 3 Zone A: Agreement of ultrasound (US) findings with computed tomography (CT) findings. * - not significant; † - significant at 5%; ‡ - significant at 1%

US Zones		CT Positive	CT Negative	Statistics
A	**Positive**	3	0	Concordance Rate = 83.3% 95% CI [0.622, 1.000]
	Negative	2	7	Cohen's Kappa = 0.636†
B	**Positive**	1	0	Concordance Rate = 91.7% 95% CI [0.760, 1.000]
	Negative	1	10	Cohen's Kappa = 0.625†
C	**Positive**	0	0	Concordance Rate = 100.0% 95% CI [1.000, 1.000]
	Negative	0	12	Cohen's Kappa = n/a
D	**Positive**	1	0	Concordance Rate = 83.3% 95% CI [0.622, 1.000]
	Negative	2	9	Cohen's Kappa = 0.429*
E	**Positive**	0	0	Concordance Rate = 75.0% 95% CI [0.505, 0.995]
	Negative	3	9	Cohen's Kappa = n/a
F	**Positive**	0	0	Concordance Rate = 83.3% 95% CI [0.622, 1.000]
	Negative	2	10	Cohen's Kappa = n/a
G	**Positive**	1	0	Concordance Rate = 100.0% 95% CI [1.000, 1.000]
	Negative	0	11	Cohen's Kappa = 1.000‡
H	**Positive**	1	0	Concordance Rate = 100.0% 95% CI [1.000, 1.000]
	Negative	0	11	Cohen's Kappa = 1.000‡

In Zone E, 3 patients were found positive for mediastinal lymphadenopathy in CT, but none of them were positive in ultrasound. All 9 patients that were found negative in CT were properly identified in ultrasound but 3 patients were classified as "false negatives". Hence, concordance rate was computed to be equal to 75.0% (CI: 50.5 to 99.5%).

In Zone F, 2 patients were found positive for mediastinal lymphadenopathy in CT, but none of them were positive in ultrasound. All 10 patients that were found negative in CT were properly identified in ultrasound but 2 patients were classified as "false negatives". Hence, concordance rate was computed to be equal to 83.3% (CI: 62.2 to 100%).

In Zone G, 1 patient was found positive for mediastinal lymphadenopathy in CT, and this was also found positive in ultrasound. All 11 patients that were found negative in CT were also properly identified in ultrasound. Hence, concordance rate was computed to be equal to 100% (12 of 12 patients). The level of agreement of ultrasound findings with CT findings in Zone G using Cohen's Kappa statistic was equal to 1.000, which is classified as "perfect agreement", and was found to be statistically significant.

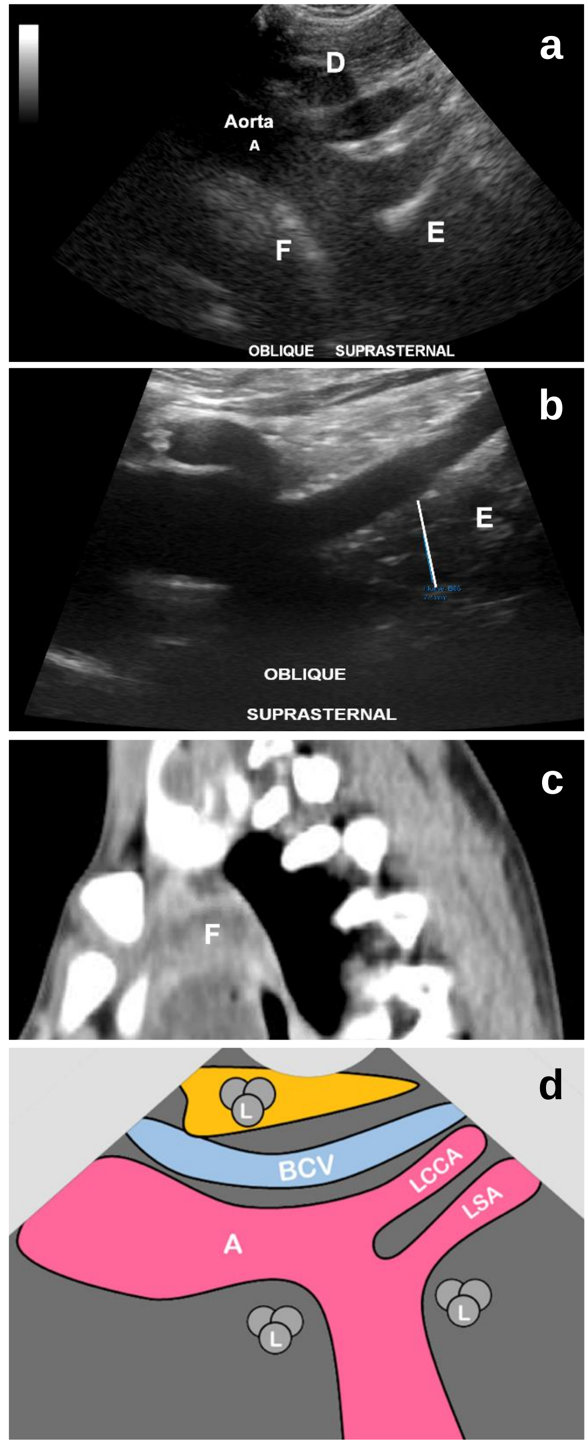


Fig. 4a–d Predefined zones in the oblique suprasternal ultrasound view (**a, b**), computed tomography (**c**) and in a schematic diagram (**d**). Enlarged lymph nodes are noted in a different patient (white line in **b**, and zone F in **c**). A - aortic arch; BCV - brachiocephalic vein; D - anterior to the left brachiocephalic vein within the thymic region corresponding to prevascular space; E - lateral to the arch of the aorta and posterior to the left subclavian artery corresponding to retrotracheal region; F - inferior and posterior to the aortic arch seen in the retrotracheal/subcarinal region; L - lymph node; LCCA - left common carotid artery; LSA - left subclavian artery

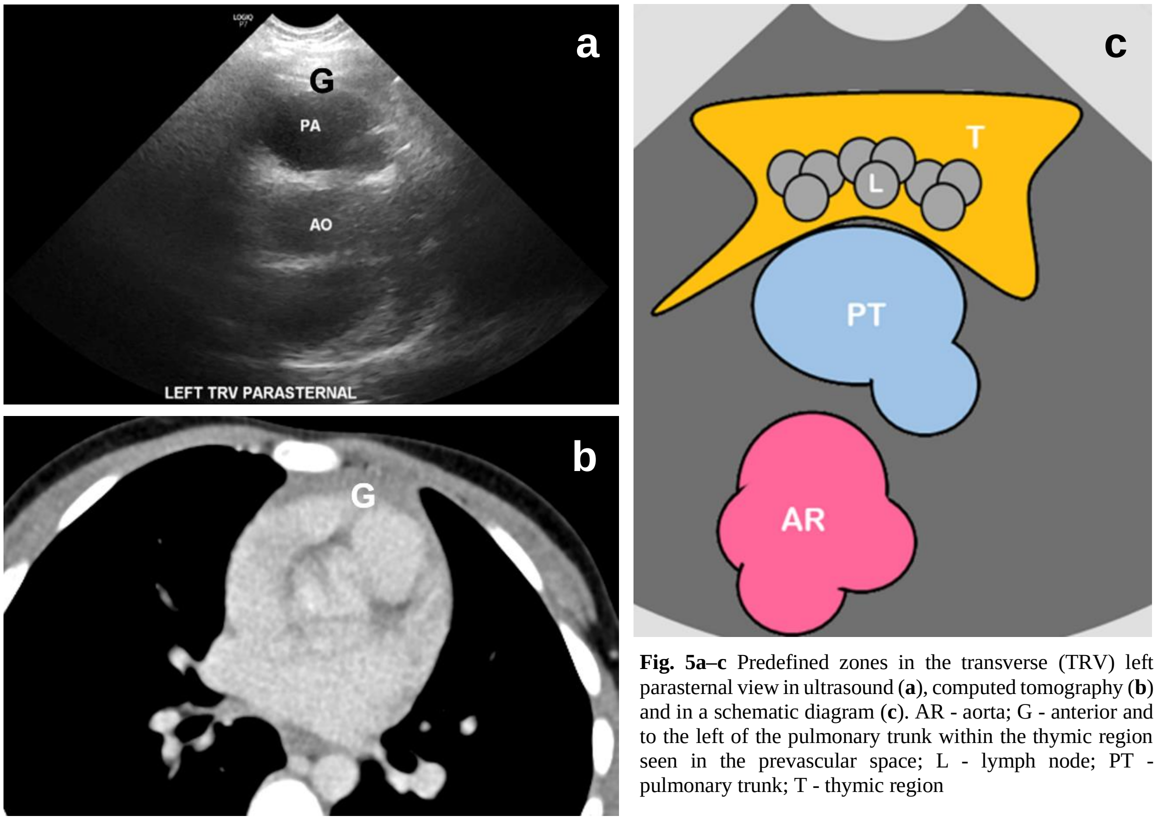


Fig. 5a–c Predefined zones in the transverse (TRV) left parasternal view in ultrasound (**a**), computed tomography (**b**) and in a schematic diagram (**c**). AR - aorta; G - anterior and to the left of the pulmonary trunk within the thymic region seen in the prevascular space; L - lymph node; PT - pulmonary trunk; T - thymic region

In Zone H, 1 patient was found positive for mediastinal lymphadenopathy in CT, and 1 was also found positive in Ultrasound. All 11 patients that were found negative in CT were also properly identified in Ultrasound. Hence, concordance rate was computed to be equal to 100% (12 of 12 patients). The level of agreement of ultrasound findings with CT findings in Zone H using Cohen's Kappa statistic was equal to 1.000, which is classified as "perfect agreement", and was found to be statistically significant.

The level of agreement of ultrasound findings with CT findings in Zone C, E, F using Cohen's Kappa statistic were not computed, due to insufficient information.

Overall (Table 4), 17 zones were found positive for mediastinal lymphadenopathy in CT, but only 7 of them were positive in ultrasound. All 79 zones that were found negative in CT were properly identified in ultrasound but 10 zones were classified as "false negatives". Hence, concordance rate was computed to be equal to 89.6% (CI: 83.5 to 95.7%).

Overall, the level of agreement of ultrasound findings with CT findings using Cohen's Kappa statistic was equal to 0.535, which is classified as "moderate agreement", and was found to be statistically significant.

Table 4. Overall agreement of ultrasound (US) findings with computed tomography (CT) findings. ***** - not significant; † - significant at 5%; ‡ - significant at 1%

	CT			Statistic
US	**Positive**	**Negative**	**TOTAL**	
Positive	7	0	**7**	Concordance Rate = 89.6.0%
Negative	10	79	**89**	95% CI [0.835, 0.957]
TOTAL	**17**	**79**	**96**	Cohen's Kappa = 0.535‡

DISCUSSION

In this cross-sectional study, the researchers determine the agreement of chest sonography with contrast-enhanced chest CT in the detection of mediastinal lymphadenopathy in children with clinically diagnosed TB. By adapting the standardized sonographic views developed by Pool et al. [9], the investigators were able to view the mediastinal lymph nodes and correlate to its corresponding CT planes. The sonographic zones showing the highest concordance with CT include those taken in the transverse suprasternal and left parasternal views namely, zones B (prevascular/ left upper paratracheal, 91.7%), C (subaortic/AP window, 100%), G (prevascular, 100%) & H (pericardial, cardiophrenic, 100%). The identification of these zones is most likely due to the accessibility of acoustic windows and lesser artifacts using the ultrasound techniques.

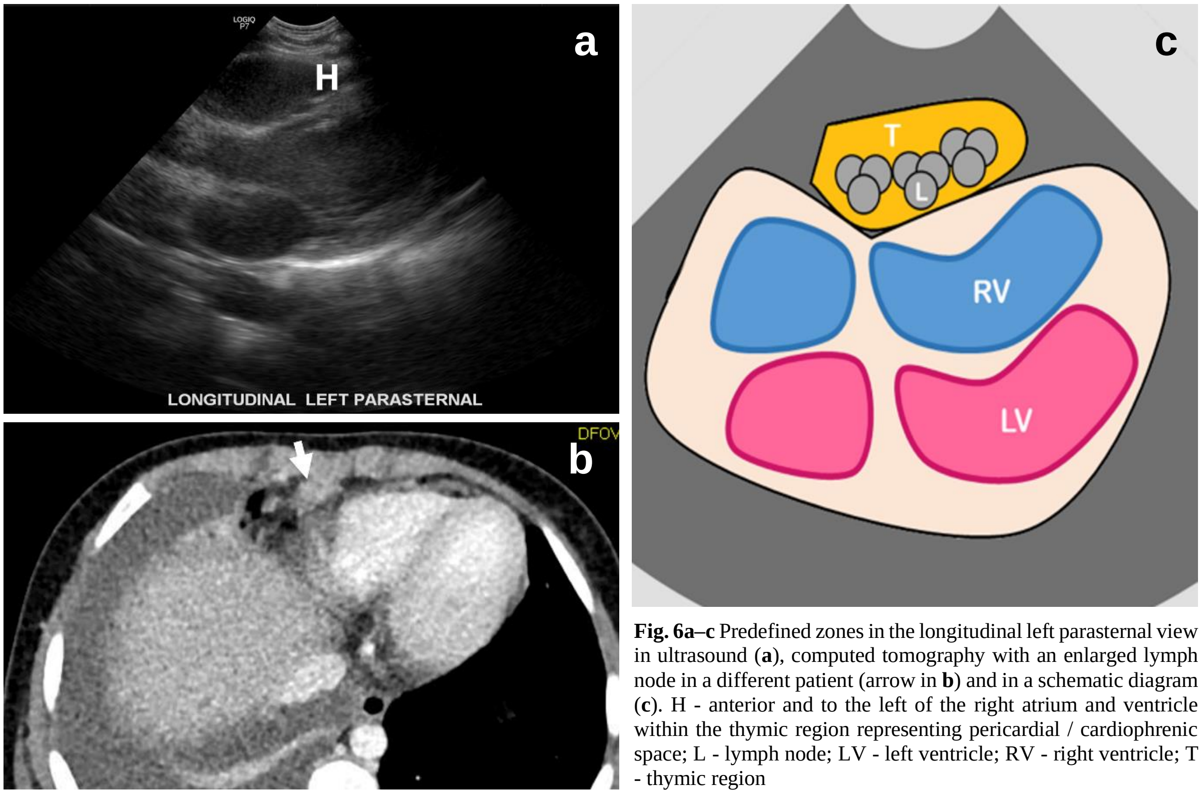


Fig. 6a–c Predefined zones in the longitudinal left parasternal view in ultrasound (**a**), computed tomography with an enlarged lymph node in a different patient (arrow in **b**) and in a schematic diagram (**c**). H - anterior and to the left of the right atrium and ventricle within the thymic region representing pericardial / cardiophrenic space; L - lymph node; LV - left ventricle; RV - right ventricle; T - thymic region

Meanwhile, sonographic zones which showed lower concordance include zone A (83.3%) as well as those taken in the suprasternal oblique views, namely, zone E (retrotracheal, 75%) and zones D (prevascular, 83.3%) and F (retrotracheal/subcarinal, 83.3%). These may be attributed to the limited views mostly due to poor acoustic window (zone D and zone A both corresponds to same prevascular spaces), deeper region of the mediastinum, and obscuration of the vascular landmarks in cases where lymph nodes are confluent and/or too large. Most of the discordant zones were negative on ultrasound but positive on CT. However, most of the positive findings on ultrasound were concordant with CT.

In a similar study by Wernecke [7] where ultrasound was compared with X-ray and CT for non-specific mediastinal masses, ultrasound also demonstrated high sensitivity at the paratracheal (89%), AP window (81%) and pericardial regions (100%), while ultrasound of the subcarinal region (69%) and posterior mediastinum (6%) also appears less sensitive. The prevascular (92%) space, meanwhile, yielded slightly higher sensitivity in the study.

Overall, the level of agreement of ultrasound findings with CT findings is "moderate" (89.6%), and was found to be statistically significant. This is congruent to the study done by Marcet [6] in a smaller group of six patients, which showed a concordance of (83.3%) between results of mediastinal ultrasonography and CT examination.

Despite the advances in modern medicine, diagnosis of childhood tuberculosis remains a challenge. The chest radiograph is one of the most commonly used tests in the diagnosis of TB, but it has its own inherent problems, as there is a high intra and inter-observer variability in interpretation of the radiograph. Furthermore, it is repeatedly stated in previous studies that although it achieves a moderate specificity of 74%, its sensitivity is low at 39% [10]. Computed tomography scan is an imaging tool with high accuracy and is considered the gold standard imaging test for primary pulmonary TB, capable of demonstrating abnormalities not readily seen in other imaging modalities [11, 12]. CT, however, is expensive and is not readily in low resource areas where TB is endemic. CT also poses radiation concerns especially in children.

The major factor encountered that decreased concordance of ultrasound findings with CT findings is obscuration of vascular landmarks (e.g., brachiocephalic vein, left common carotid and subclavian arteries) if the lymph nodes are too large or exhibits confluence. Operator expertise, dependence and subjectivity also come into play but may eventually be lessened with more experience.

A limitation of this study is its relatively small sample size. However, being a pilot study in the local setting, this can serve as a model for future research endeavors on this field.

CONCLUSION

Mediastinal ultrasound can be used as an initial imaging tool to detect enlarged lymph nodes in children clinically diagnosed with TB disease and to assess for progression. However, if found negative and clinically indicated, CT may still be done for further evaluation.

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