



EVALUATION OF PERFORMANCE OF LUNG ULTRASOUND (LUS) IN PAEDIATRIC PNEUMONIA

Chirtrarasan Paraman	Professor, Department of Radiodiagnosis, Government Stanley Medical College, Chennai- 600 001.
Bharathi Priya Raju	Assistant professor, Department of Radiodiagnosis, Government Stanley Medical College, Chennai- 600 001.
Jayavarma Rajendran	Assistant professor, Department of Radiodiagnosis, Government Stanley Medical College, Chennai- 600 001.
Thanga Meena Muthukumar*	Assistant professor, Department of Radiodiagnosis, Government Stanley Medical College, Chennai- 600 001. *Corresponding Author
Thivakaran Thamilarasan	Junior Resident, Department of Radiodiagnosis, Govt Stanley Medical College, Chennai - 600 001.
Amarnath Chellathurai	Professor and Head of the Department, Department of Radiodiagnosis, Govt Stanley Medical College, Chennai - 600001.

ABSTRACT

OBJECTIVES: The purpose of this study is to evaluate the agreement between Lung Ultrasound and Chest radiograph in diagnosing paediatric pneumonia. The secondary objective is to assess if Lung

Ultrasound could be a viable alternate first line imaging modality for evaluation of suspected paediatric pneumonia and to assess if Lung Ultrasound can be used as an imaging modality for serial imaging and follow up of patients with pneumonia and in detecting the complications of pneumonia.

BACKGROUND: Community-acquired pneumonia is the major cause of under-five mortality in children. The high mortality rate in low-income countries and the increasing incidence of complicated pneumonia in developed countries emphasize the need for early diagnosis and proper treatment in order to improve the outcome. There has been some inconsistency regarding the role of imaging techniques in the diagnosis of Community-acquired pneumonia. Although inexpensive and widely available, Chest radiograph has some significant limitations like radiation exposure with high inter-observer and intra-observer variations. Lung ultrasound has shown promising results in this aspect with less inter and intra observer variations with the added advantage of performing at the bedside besides being free from radiation.

MATERIALS AND METHODS: A prospective study of 160 children between 1 and 12 years of age referred by the paediatrician for chest X-ray for suspected pneumonia are included, after getting informed consent from the parent. Clinically unstable patients were excluded from the study. Lung Ultrasound was done in patients and the Lung Ultrasound findings obtained were compared with those of Chest radiograph.

RESULTS: Chest radiograph showed consolidation in 127 patients (79.4%), Peri bronchial thickening was found in 19 (11.9%) patients and Synpneumonic pleural effusion was identified in 13 (8.1%) patients. Chest radiograph was negative for pneumonia in 15 (9.4%) patients. Lung ultrasound showed sub pleural consolidation in 123 (76.9%) patients, confluent B-lines and pleural line abnormalities in 59 (36.87%), and pleural effusion in 18 (11.2%) patients. 5 patients with negative LUS had abnormal CXR. Follow up LUS characteristic were also evaluated by follow up of the consolidation size. The size of consolidation steadily declined on subsequent follow-up Lung Ultrasound consistent with clinical improvement. The Receiver Operator Characteristic (ROC) curve analysis of Lung ultrasound with chest radiograph were AUC (Area Under the ROC curve) = 0.949, $p=0.0005 < 0.01$ which shows highly statistically significant difference with Sensitivity=96.6%, Specificity=93.3%, PPV=99.3%, NPV=73.7% and Accuracy=96.3%.

CONCLUSION: Lung ultrasound shows high accuracy in the detection of pneumonia and possibility of a follow-up of the dynamic pleuropulmonary changes in the natural course of pneumonia and any complications that could arise in the course of its treatment without exposure to ionizing radiation.

KEYWORDS : Paediatric pneumonia, lung ultrasound, consolidation, B-lines, pleural effusion.

INTRODUCTION:

Community-acquired pneumonia (CAP) is the major cause of under-five mortality in children. According to World Health Organization (WHO), Pneumonia accounts for 15% of all global deaths of children under 5 years old, killing 808 694 children in 2017 of which 185429 (22%) occurred in India alone.¹ The high mortality rate in low-income countries and the increasing incidence of complicated pneumonia in developed countries emphasize the need for early diagnosis and proper treatment in order to improve the outcome.² There has been some inconsistency regarding the role of imaging techniques in the diagnosis of CAP. As per WHO and other recommendations, diagnosis and classification of CAP is largely clinical and chest radiography is recommended in severe and complicated cases only.³ According to the British Thoracic Society (BTS) guidelines, clinical symptoms and

signs are usually sufficient to diagnose CAP in children.⁴ Thus, the BTS guidelines do not recommend performing chest radiograph (CXR) in all children with typical pneumonia signs and symptoms. But for a definitive diagnosis, physicians are mostly dependent on chest radiographs (CXR).

Recent BTS Paediatric Pneumonia Audit revealed that in many children suspected of CAP chest radiograph had been done to confirm the diagnosis. It has been shown that clinical signs and symptoms of lower respiratory tract infections are relatively non-specific and that the correlation between clinical and radiological findings in CAP is low.⁵ Since The clinical signs and symptoms do not predict CAP accurately, treating CAP without knowing the extent of underlying pathology and diagnostic confirmation can lead overuse of antibiotics. Therefore, physicians order for CXR in cases of

CAP and the need to prove the pneumonia by imaging methods seems to be, at least somewhat, justified.

Although inexpensive and widely available, CXR has some significant limitations. Firstly, imaging methods associated with radiation exposure should be avoided, particularly in neonates and young children. Children have a 3 to 5 times higher radiation-induced morbidity and mortality risk in comparison to adults. Even though plain radiographs have small amounts of radiation dose exposure about 0.01-1.5 mSv, children are more susceptible to non-deterministic stochastic effects of radiation than adults. Secondly, the interpretation of radiological findings could be challenging not only for clinicians but also for radiologists causing high inter-observer and intraobserver variations.^{6,7} Moreover, subsequent follow-up radiographs were commonly overused, causing unnecessary radiation exposure. CXR is not a perfect diagnostic test for CAP. To explore all lung anatomy, at least two projections are needed. If only the postero-anterior/ antero-posterior projection is used, some lung areas can be obscured by the heart, mediastinum and diaphragm.

The two projections approach leads to substantial exposure to ionizing radiation and a potential risk of cancer and gene mutation development, particularly in the youngest patients. Therefore, CXR is not advisable as a routine in children with suspected CAP.

As a consequence, there is a need for a novel, easily accessible, radiation-free, sensitive and specific imaging technique that could be used as a diagnostic tool in childhood pneumonia. The LUS holds this promise. Recent data showed that in this context lung ultrasound (LUS) may present an attractive alternative for CXR. LUS is a relatively smaller device that makes point of care more feasible. LUS is easy, rapid, portable and repeatable. The non-ionizing property is especially important in children, who carry a higher risk of morbidity due to exposure to radiation than people of other ages. In the recent years, lung ultrasound (LUS) has been demonstrated to be a feasible technique in the evaluation of pneumonia, pneumothorax, atelectasis, pleural effusion and alveolar-interstitial syndrome in adults. In fact, the small body size of these patients, including a small thoracic width and lung mass, allows an easier detection of lung anomalies by LUS, because of a more rapid involvement of the pleura by the disease. Experience with LUS in children has grown in recent years. LUS has shown promise for diagnosis of CAP in children, performing better than chest roentgenogram (CXR).⁸ The LUS has also shown less inter and intra-observer variations. Learning curve of techniques and interpretations of LUS is simple and fast.⁹ The examination is performed at the patient's bedside and it can be repeated without the risk of ionizing radiation.

The aim of this study was to evaluate the role of LUS in the diagnosis of pneumonia in paediatric patients in addition to CXR, and to study its feasibility in the follow-up in hospitalised children with Community Acquired Pneumonia.

MATERIALS AND METHODS:

Study design: After obtaining the ethical committee approval, this prospective observational study was carried out for a period of 3 years between June 2018 and January 2021.

INCLUSION CRITERIA: All children between 1 and 12 years referred by the paediatrician for a chest X-ray for suspected pneumonia were included, after getting informed consent from the parents.

EXCLUSION CRITERIA: Clinically unstable patients were excluded from the study.

METHOD:

All patients underwent a bedside LUS within the first 6 hrs after CXR, and then serially followed up by LUS. LUS was done by an expert with 15 years of experience in paediatric radiology who was blinded to the CXR findings. CXR was evaluated by an expert in the field of paediatric radiology with 20 years of experience. When there was discrepancy between LUS and CXR findings, CT chest was considered goal standard, although not done routinely in view of high radiation and high cost.

LUNG ULTRASOUND (LUS):

LUS was performed using a linear probe with frequencies ranging from 7.5 MHz to 12 MHz Curvilinear probe with frequencies 3-5 MHz was used in obese and to identify deeper lesions. LUS examinations was done according to the methodology described by Copetti and Cattarossi.⁸ To cover the whole lung surface, each hemithorax was divided into three areas:

- The anterior area delimited by parasternal and anterior axillary lines,
- The lateral area between the anterior and posterior axillary lines, and
- The posterior area delimited by the paravertebral and posterior axillary lines.

Each region was scanned in the longitudinal and transverse plane, medial-lateral and up-down respectively. The anterior and lateral regions of the chest were examined with the child in supine decubitus. The posterior region was examined in prone decubitus in infants while sitting position was used to scan the posterior wall in older children. Cephalocaudal dimension of lung consolidation was serially followed up on Day 1, Day 3-6, Day 7-10, Day 11-14 or on the day of discharge, and followed up till whichever time period is earlier.

CLASSIFICATION OF LUS PATTERNS:^[8]

LUS findings were classified according the following patterns:

1. Normal pattern, defined as normal lung sliding with or without A-lines.
2. Presence of focal multiple or confluent B-lines.
3. Pleural line abnormalities, defined as irregular appearance of the pleural line.
4. Presence of subpleural lung consolidations, defined as subpleural echo-poor or tissue-like region, with blurred margins, with or without air-bronchogram (internal hyperechoic punctiform or linear elements).
5. Pleural effusion, defined as anechoic or hypoechoic fluid, with or without floating debris.

CRITERION FOR PNEUMONIA:^[8] The criterion to define pneumonia on LUS is the finding of an hypoechoic area with poorly defined borders and compact underlying artifacts perpendicular to the pleural line, called B lines. The pleural line is less echogenic in the area interested by consolidation and lung sliding is reduced or absent. Bacterial pneumonia is defined as lung consolidation with dynamic air bronchograms. For purposes of analysis, sub-centimetre bacterial pneumonia is defined as focal lung consolidations with air bronchograms with a size of less than one centimetre. As per literature, small subpleural consolidations with no air bronchograms (typically < 0.5 cm) with associated pleural line abnormalities, single or confluent B lines will be considered associated with bronchiolitis or viral pneumonia.

STATISTICAL ANALYSIS: The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used. The Receiver Operator Characteristic (ROC) curve analysis was used to find the Sensitivity, Specificity, PPV and NPV on comparison of LUS

with CXR. In the above statistical tools, the probability value .05 is considered as significant level.

Table 1: Gender distribution

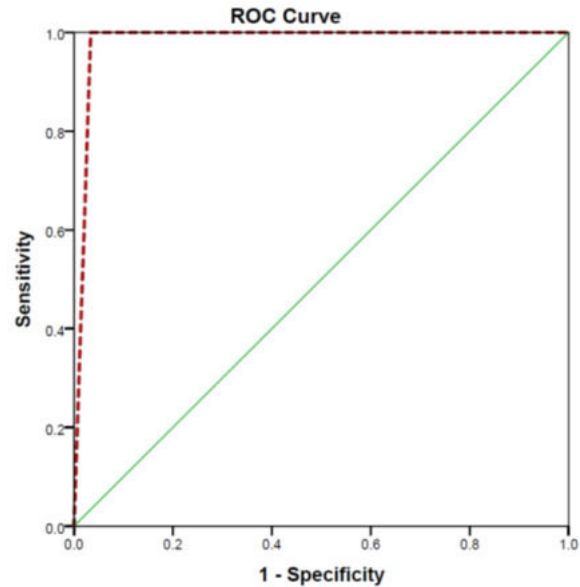
Gender distribution		
	Frequency	Percent
Female	62	38.8
Male	98	61.2
Total	160	100.0

The p value for the gender distribution was <0.004, indicating male children are statistically affected significantly more than female children.

Table 2: Receiver Operator Characteristic (ROC) curve analysis of Pleural Effusion - LUS with CXR

Pleural Effusion - LUS Vs CXR				
		CXR		Total
		Present	Absent	
LUS	Present	13	5	18
	Absent	0	142	142
Total		13	147	160

Area Under the Curve			
Area	p-value	95% C. I	
		LB	UB
.983	0.0005 **	.965	1.000



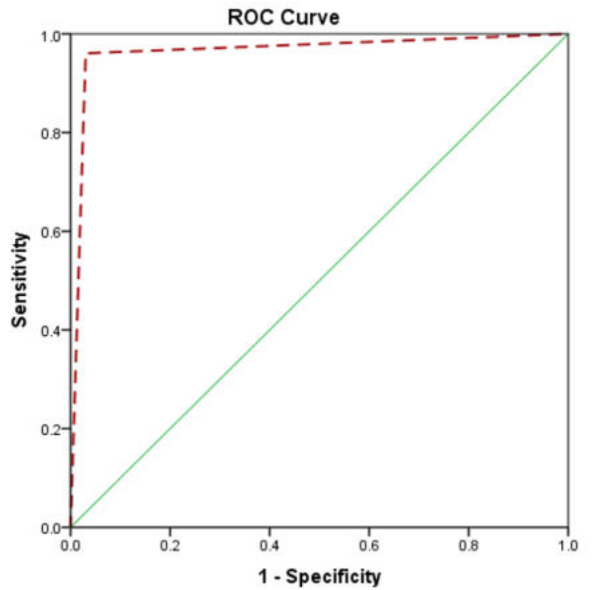
Diagonal segments are produced by ties.

The above table shows Receiver Operator Characteristic (ROC) curve analysis of Pleural Effusion - LUS with CXR were AUC (Area Under the ROC curve) = .983, p=0.0005<0.01 which shows highly statistical significant difference with Sensitivity=100%, Specificity=96.6%, PPV=72.2%, NPV=100% and Accuracy=96.9%.

Table 3: Receiver Operator Characteristic (ROC) curve analysis of Consolidation - LUS with CXR

Consolidation - LUS Vs CXR				
		CXR		Total
		Present	Absent	
LUS	Present	122	1	123
	Absent	5	32	37
Total		127	33	160

Area Under the Curve			
Area	p-value	95% C. I	
		LB	UB
.965	0.0005 **	.926	1.000



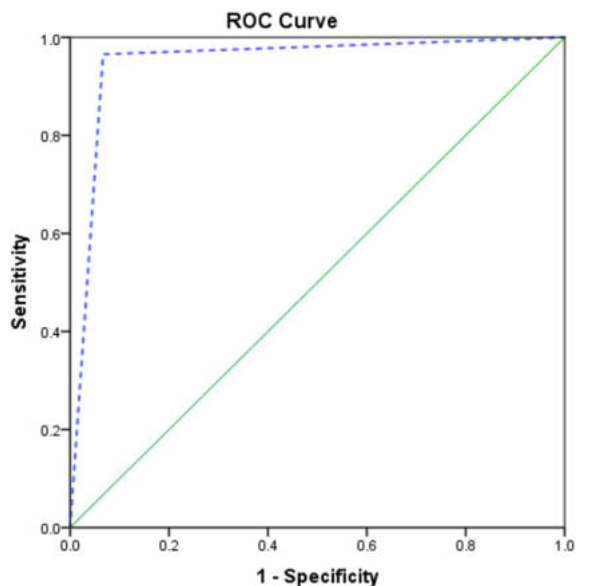
Diagonal segments are produced by ties.

The above table shows Receiver Operator Characteristic (ROC) curve analysis of Consolidation - X-ray with USG were AUC (Area Under the ROC curve) = 0.965, p=0.0005<0.01 which shows highly statistical significant difference with Sensitivity=96.1%, Specificity=97.0%, PPV=99.2%, NPV=86.5% and Accuracy=96.3%.

Table 4: Receiver Operator Characteristic (ROC) curve analysis of LUS with CXR

Positive for pneumonia - LUS Vs CXR				
		CXR		Total
		Present	Absent	
LUS	Present	140	1	141
	Absent	5	14	19
Total		145	15	160

Area Under the Curve			
Area	p-value	95% C. I	
		LB	UB
.949	0.0005 **	.874	1.000



Diagonal segments are produced by ties.

The above table shows Receiver Operator Characteristic (ROC) curve analysis of LUS with CXR were AUC (Area Under

the ROC curve) = 0.949, p=0.0005<0.01 which shows highly statistical significant difference with Sensitivity=96.6%, Specificity=93.3%, PPV=99.3%, NPV=73.7% and Accuracy=96.3%.

Table 5: Follow Up Characteristics Of LUS

Maximum Thickness of Consolidation (mm)	Day 1	Day 3-6	Day 7-10	Day 11-14
<15 mm	48 (30%)	77 (48.1%)	36 (22.5%)	10 (6.25%)
15-29 mm	69 (43.1%)	23 (14.3%)	12 (7.5%)	5 (3.1%)
≥ 30 mm	6 (3.8%)	5 (3.1%)	2(1.3%)	0 (0%)

OBSERVATION AND RESULTS OF THE STUDY: A total of 160 patients admitted with empirical diagnosis of pneumonia based on clinical features were enrolled in the study. CXR showed consolidation in 127 patients (79.4%)[Figure 1]. Peri bronchial thickening was found in 19 (11.9%) patients[Figure 2]. Synpneumonic pleural effusion was identified in 13 (8.1%) patients. CXR was negative for pneumonia in 15 (9.4%) patients.

On day 1 LUS characteristically showed sub pleural consolidation in 123 (76.9%) patients [Figure 3], confluent B-lines and pleural line abnormalities in 59 (36.87%) [Figure 4,5], and pleural effusion in 18 (11.2%) patients. 5 patients with negative LUS had abnormal CXR but 1 patient with negative CXR had LUS findings suggestive of pneumonia with clinical course consistent with pneumonia (p <0.005).

Follow up LUS characteristic are also evaluated by follow up of the consolidation size. On day 1, LUS showed consolidation in 123 (76.9%) with maximum thickness of <15 mm in 48 (30%), between 15-29 mm in 69 (43.1%) while ≥30 mm in 6 (3.8%). During follow up between day 3-6, 7-10, and 11-14 of illness LUS shows consolidation in 105 (65.6%), 50 (31.3%) and 15 (9.3%) patients respectively. The size of consolidation steadily declined on subsequent follow-up LUS consistent with clinical improvement reflected by increase in number of patients with consolidation thickness <15 mm on day 3-6 compared to decrease in the number of patients in the more severe group. All the patients improved clinically. No complications of pneumonia were noted during this study.

DISCUSSION:

Early diagnosis and management of pneumonia in children are important to short- and long-term health outcomes. Clinical examination is highly sensitive but lacks specificity and results in over diagnosis contributing to the overuse of antibiotics.¹⁰ CXR is considered the test of choice for further evaluation for arriving at a definitive diagnosis. CXR is a poor gold standard investigation as it is a two-dimensional imaging technique of three-dimensional anatomy.

The main limitation of radiography is the risk of damage from ionizing radiation with a greater risk than adults because children have more rapidly dividing cells with a potential for more DNA damage and increased life expectancy.¹¹

Other concerns with radiography are great variability in the interpretation lack of reproducibility and delay in availability of the film. Also, in complicated pneumonia CXR is less reliable and chest computed tomography (CT) scan is known to be the gold standard.¹² However, its use has been discouraged due to high radiation, high cost and the need for sedation in young children.

Medical radiation exposure is rapidly increasing. The radiological risk is cumulative in nature and results in stochastic and nonstochastic damage to the cells. The chest is the most frequently evaluated region of the body in children. Although radiation protection measures and guidelines are

stringently adhered to in practice, the risk of radiation hazards still exists. There is research that suggests hepatoblastoma risk may increase due to repeated chest X-rays in intensive care unit patients.¹¹ Unfortunately, paediatricians are often unaware of these risks. It is often possible to significantly reduce medical radiation exposure without compromising patient care.

Weinberg et al first described the use of LUS in evaluating CAP.¹³ Performance of LUS in the evaluation of respiratory pathologies has been studied in detail since then by investigators. Subsequent studies have demonstrated that LUS is able to diagnose pneumonia in adults with high accuracy.¹⁴ Later on studies had demonstrated high efficacy of LUS in diagnosing pneumonia in children.¹⁵ Some technical advantages such as shorter thoracic width, thinner chest wall, and small lung mass theoretically enable LUS examination in children easier than in adults. Recently LUS has been indicated as a clinically useful diagnostic tool in paediatric patients with suspected pneumonia.⁸ The LUS features of pneumonia mainly included sub pleural lung consolidation, pleural line abnormalities, confluent B-lines and synpneumonic pleural effusions.⁹

Tirdia et al, in their study of 139 children showed that LUS was highly accurate for diagnosis as well as follow up of CAP in hospitalized children and in identifying antibiotic failure, directing the course of treatment based on the increase in size of consolidations during treatment.¹⁶

In this study, the various LUS findings are similar to the study by Tirdia et al, and data in the literature. Of the 160 patients enrolled in this study, the detection of pneumonia using LUS (141 patients) compared with chest radiography (145 patients) correlated as defined by the criteria in literature.¹⁶

LUS was able to detect 123 consolidations as compared to 127 locations in CXR of total of 160 patients. LUS was able to identify subcentimeter consolidations that could be missed in conventional radiography. LUS was normal in 5 patients where CXR was positive for perihilar consolidation. The pathology was parenchymal without pleural extension and hence not detected by LUS. While CXR failed to detect abnormality in 1 patient.

In this study, analysis of LUS compared with CXR were AUC (Area Under the ROC curve) = 0.949, p=0.0005<0.01 which shows highly statistical significant difference. LUS performed with a Sensitivity=96.6%, Specificity=93.3%, PPV=99.3%, NPV=73.7% and Accuracy=96.3%. Pereda in their meta-analysis found that LUS had a sensitivity of 96% and specificity of 93%. Other published data also showed that LUS is more sensitive than CXR in the diagnosis of pneumonia in children showing the strength of this investigation.^{14,15}

This study also addresses the follow-up LUS characteristics of pneumonia, showing the dynamic changes of pleuro-pulmonary abnormalities over time determining the effectiveness of LUS in the on-going management of pneumonia over the course of an illness. The size of consolidation and other abnormalities including the B-lines, comet tail artefacts and pleural line abnormalities showed persistent improvement on subsequent follow-up LUS examination that was consistent with clinical improvement. Similar results were found by Caiulo et al and Stefania et al.¹⁵

In this study, follow up LUS did not show increase in the size of consolidation in any of the patients during the course of treatment and all patients went on for full recovery without any complications. All the pleural effusions detected were anechoic indicating transudative reactive effusion without

any features of empyema. This could be attributed to because clinically unstable children were excluded in the study who might have shown features of severe disease with complications.

Thus, this study demonstrates that LUS is safe and accurate for the diagnosis of suspected cases of CAP. It is more sensitive than CXR and also allows a radiation free follow up of patients. It can be easily done at the bedside with the added advantage of having a simple and fast learning curve. Pleural effusion, lung consolidation, interstitial syndrome, and pneumothorax are accessible to LUS. Owing to its capability of dynamic examination and the availability of colour Doppler, LUS is helpful in the evaluation of lung consolidation as it can also differentiate consolidations due to pulmonary embolism, pneumonia, or atelectasis.^{17,18}

LUS also has the potential for diagnosing the nature of the effusion and differentiating bacterial and viral pneumonia. LUS also had a consistently high diagnostic accuracy of pneumonia when compared with chest CT scan as the gold standard.¹⁹

Further research regarding the role of colour Doppler sonography, spectral curve analysis and contrast-enhanced ultrasound is necessary, especially with respect to differential diagnosis of lung consolidations and early detection of complications. Also, while LUS is best performed by trained sonographers, medical students, doctors and other health care workers at the bedside are now being trained in it use, albeit cautiously and there is a considerable increase in the usage of point of care ultrasound making significant improvements in patient evaluation and treatment.

Recent advances in technology have made portable or handheld ultrasonography machines more available. This raises the potential for diagnostic capabilities in rural and remote settings where other imaging modalities are not available.

Limitation of the study is that LUS is able to detect an abnormality only when it reaches the pleural surface but given the small thoracic volumes in children and the nature of the diseases to involve pleura at an early stage LUS is able to detect the disease accurately. If LUS is to be incorporated into the common clinical practice and replace CXR the low sensitivity of LUS in patients with perihilar localization of pneumonia that doesn't reach the pleural surface needs to be kept in mind. LUS missed 5 patients in this study with perihilar consolidation that was detected in CXR. This is a certain degree of limitation of this imaging method.

CONCLUSION:

Lung ultrasound shows high accuracy in the detection of pneumonia and possibility of a follow-up of the dynamic pleuropulmonary changes in the natural course of pneumonia and any complications that could arise in the course of its treatment without exposure to ionizing radiation.



Figure 1: Chest radiograph showing patchy right perihilar consolidation



Figure 2: Chest radiograph showing bilateral peribronchial thickening



Figure 3

LUS in this patient showing consolidation extending to the pleural surface with adjacent synpneumonic effusion which is anechoic without internal echoes suggesting the possibility of an transudative reactive pleural effusion.

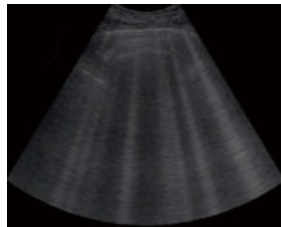


Figure 4

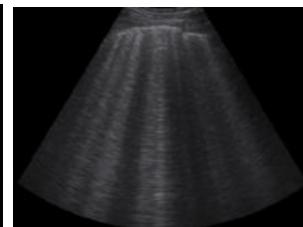


Figure 5

LUS showing Multiple lung rockets/ hyperechoic B- lines are identified in these patients. B- line distribution corresponds with sub-pleural thickened interlobular septa, as demonstrated by CT and are absent under normal conditions.

Abbreviations: CAP - Community-acquired pneumonia, WHO - World Health Organization, BTS - British Thoracic Society, CXR - Chest radiograph, LUS - Lung ultrasound, CT - Computed Tomography, CI - Confidence Interval, ROC - Receiver Operator Characteristic, PPV - Positive predictive value, NPV - Negative predictive value

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