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REVIEW ARTICLE

Role of chest ultrasound in neonatal lung disease: a review of current evidences

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ABSTRACT

Among the common causes of neonatal admission to NICU, respiratory distress is one of the important causes. The neonatal respiratory distress is end result of various pulmonary and non-pulmonary causes. Differentiation of pulmonary causes of respiratory distress is important for the neonatologist as treatment differs with different etiologies. Conventionally, chest X-ray and sometimes CT scan have been used to identify the etiology of respiratory distress but these modalities have several limitations which make their use in NICU doubtful. In recent decades, there has been use of lung ultrasound (LUS) to identify and differentiate the etiologies of respiratory distress. The current available evidence show that LUS has good sensitivity and specificity to identify all the common causes of neonatal distress like respiratory distress syndrome, transient tachypnea of newborn, pneumothorax, and pneumonia. This review will cover the various uses of LUS in neonatal care with current available evidence.

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Chest X-ray; lung ultrasound; neonate; point of care; respiratory distress syndrome

Introduction

Identification of etiology of neonatal respiratory distress is often a diagnostic dilemma for the neonatologist because of the low sensitivity and specificity of the clinical signs and symptoms. Lung ultrasound (LUS) for the diagnosis of various neonatal lung diseases has been introduced recently in neonatal care and is slowly gaining popularity [1]. The studies have shown that LUS is an accurate and reliable point of care for diagnosis of neonatal lung pathology. LUS is also low cost, simple, results are obtained immediately, the operator is easily trainable for both operation of machine and interpretation of images and radiation free, thus making it a promise-able bedside tool to be used in NICU. Conventionally chest X-ray (CXR) and CT scan have been used to identify lung pathology and for finding the cause of respiratory distress in neonates. There is radiation exposure of the neonates with them, there is large turnaround time for both and shifting a sick neonate for CT scan is worrisome for the neonatologist. If there is need for sequential monitoring of the neonate with multiple CXR, then the neonate is exposed to multiple radiation exposure, whereas LUS can be done numerous times without any risk of radiation exposure [2–4]. This review will cover the various uses of LUS in various neonatal respiratory diseases and the current evidence over it.

Technique of lung ultrasound (LUS)

LUS in neonates requires a high-frequency linear array probe, which is usually more than 7.5 MHz. The neonate is examined in quiet state and is examined in supine, prone, and side position. The lung is divided in three areas based on the imaginary anterior and posterior axillary lines (anterior area between parasternal and anterior axillary line, lateral area between anterior and posterior axillary line, and posterior area beyond posterior axillary line). Longitudinal and transversal sections are obtained of both the lungs keeping probe vertical and parallel to the ribs.

Normal echographic lung appearance

Pleura is seen as a regular echogenic line in normal lung which is moving continuously to and fro during inspiration and expiration. This is known as pleural line and is smooth regular hyperechogenic line. This movement is known as lung sliding [5]. The abnormalities associated with pleural line include disappearance, a significantly thickening, evidence of small subpleural

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consolidation, and irregular or coarse appearance of the pleural line [6]. Beyond the pleura, lung appears black as it is filled with air, therefore, it does not allow further visualization of normal lung parenchyma.

A-line

The A-line is seen as a series of echogenic parallel lines distally, equidistant from one another, below pleural lines. These lines appear with large change in acoustic impedance at the pleura–lung interface and are type of reverberation artifact caused by the pleural line [7].

B-line

The B-lines are oriented vertically, project from pleural lines to edge of the screen, erase A lines, and move with inspiration and expiration. These lines are produced when ultrasound wave encounters the alveolar gas–liquid interface, thus the presence of lines indicates either an abnormality in the interstitial or alveolar compartment and correlate with lung interstitial fluid content [8]. These lines are usually not seen in normal pediatric and adult population but can be seen in normal neonate in initial 48 h because sometimes there is delay in absorption of lung fluid [9]. The comet-tail artifact on LUS is seen as gradually weakening and parallel lines that resemble the tail of a comet. This artifact is result of an ultrasound wave that, upon encountering the alveolar gas–liquid interface, produces multiple reflections from the pleural line [8].

Alveolar-interstitial syndrome (AIS)

The presence of more than three B-lines or the presence of areas of "white lung" in every examined area [6].

Spared areas

These are the areas having normal pattern on LUS, and are surrounded by areas of AIS and extending for at least one intercostal space in the longitudinal scan [6].

Bilateral "white lung"

The presence of compact B-lines in all the examined areas of lung (six areas), without spared regions [6].

Lung pulse

This is early LUS sign of complete atelectasis. In this lung, sliding is replaced by a kind of pulsation that is synchronized with heart activity [10,11].

Lung point

This is specific LUS sign of pneumothorax. In it fleeting appearance of a normal lung pattern is replaced by an abnormal lung pattern in a particular location on the chest wall [12].

Double lung point (DLP)

This sign is seen when there is difference in severity or nature of pathological changes in different areas of the lung. It is defined as sharp cut-off point between the upper and the lower lung field seen on longitudinal scan [9].

Thus, in summary: in LUS images, the normal lung is "black", moderately diseased lung (with interstitial water) is "black and white" (with white lines corresponding to B-lines) and markedly diseased lung (with alveolar edema) is "white" (diffusely bright)

Respiratory distress syndrome (RDS)

Neonatal RDS, earlier known as hyaline membrane disease (HMD), is characterized by increasing respiratory distress, starting at birth and gradually worsening [13]. The LUS finding of RDS is "black and white" with white lines correspond to B lines in the moderately diseased lung with interstitial water and "white" with diffusely bright appearance in the markedly diseased lung with alveolar edema, presence of AIS; pleural lines abnormalities; presence of "spared areas"; presence of large consolidations [7]; bilateral evidence of echographic white lung without spared areas, associated with thickened and irregular pleural line [6]. The severity of RDS can be assessed by the appearance of normal areas within 24–48 h indicating a mild disease while persistent white lung indicates a moderate or severe RDS. Vergine et al. studied the role of LUS in 59 neonates admitted with respiratory distress. The results of the study showed that LUS had a sensitivity of 95.6% and a specificity of 94.4%, with a positive predictive value (PPV) of 91.6% and a negative predictive value (NPV) of 97.1% for RDS [14]. Copetti et al. studied LUS in 40 newborn infants with radiological and clinical signs of RDS and in 15 preterm infants without RDS. The results showed that LUS had 100% sensitivity and specificity in diagnosis of RDS and it can be used as bed side screening tool for diagnosis of RDS, and for early administration of surfactant in preterm infants with respiratory distress [6]. Liu et al. studied 45 newborn infants with RDS and 30 neonates without lung disease. The finding showed that LUS signs of lung consolidation, pleural line abnormalities, bilateral

"white lung", and A-line disappearance were seen in 100% of RDS patients whereas these were present in none of the controls ($p < .001$). LUS showed 100% sensitivity and specificity when ultrasonic signs of lung consolidation, pleural line abnormalities, and bilateral "white lung" coexisted or when lung consolidation, pleural line abnormalities and A-line disappearance coexisted [15]. In other studies too, Liu et al. showed that simultaneous demonstration of lung consolidation, pleural line abnormalities and bilateral white lung, or lung consolidation, pleural line abnormalities and A-line disappearance had sensitivity and specificity of 100% for diagnosis of RDS [16,17]. Rachuri et al. studied role of LUS in identifying the etiology of respiratory distress in neonates. The results showed that LUS had sensitivity and specificity of 98.4% and 100%, respectively, in the diagnosis of respiratory distress. The PPV for RDS on LUS was 96.6% whereas NPV was 100% [18]. Hiels et al. recently published systematic review seeking role of LUS or CXR in diagnosis of RDS. This review included 480 neonates and result showed that the pooled sensitivity and specificity of lung ultrasound were 97% (95% CI 94–99%) and 91% (95% CI: 86–95%), respectively, thus showing that LUS is highly sensitive for the detection of neonatal RDS, although there is potential to miss comorbid air-leak syndromes [19]. Sawires et al. showed good role of LUS in the early detection and follow-up of RDS in NICU [20]. Chen et al. in his study enrolled 3405 neonates and showed that LUS has clinical value for the diagnosis of lung disease and for differentiating the causes of long-term oxygen dependency in premature infants, particularly for the diagnosis and identification of RDS and transient tachypnea of newborn (TTN) [21].

TTN

TTN often follows an uneventful delivery at (or close) to term with major presenting symptoms being persistently high respiratory rates [11]. The ultrasound features suggestive of TTN are the presence of normal pleural line and pleural sliding, very compact B-lines in the inferior pulmonary fields, and less compact B-lines in the superior fields (double lung point) in both lungs, or bilateral numerous non-compact B-lines indicating interstitial engorgement [9]. Vergine et al. conducted study to calculate the sensitivity, specificity, NPV, and PPV of LUS for TTN. Fifty-nine neonates with respiratory distress admitted in NICU for respiratory distress underwent LUS within 1 h of admission. The ultrasound images were saved and sent to external reader. Thirty neonates were diagnosed as having TTN and the results showed that LUS had a sensitivity of 93.3%, a specificity of 96.5% with a PPV of 96.5%, and a NPV of 93.4% for TTNB, thus showing LUS having good sensitivity and specificity in diagnosis of TTN [14]. Liu et al. studied role of LUS in diagnosis of TTN and its differentiation from RDS. The study enrolled 60 infants diagnosed with TTN based on medical history, clinical manifestations, arterial blood gas analysis, and chest radiography, 40 hospitalized neonates with non-lung diseases and 20 patients with RDS. The LUS findings of TTN were double-lung point (DLP), interstitial syndromes or white lungs, pleural line abnormalities, A-line disappearance, and pleural effusion, whereas the main LUS manifestation of RDS was lung consolidation with air bronchograms. The sensitivity and the specificity of DLP for the diagnosis of TTN were 76.7% and 100%, respectively [22]. Liu et al. in another study enrolled 1358 infants including 228 neonates with TTN. The results showed that primary ultrasonic characteristic of TTN was pulmonary edema. Severe cases of TTN showed "White lung" or a "compact B-line", whereas TTN primarily presented as pulmonary interstitial syndrome or "double lung point". The white lung or a compact B-line exhibited a sensitivity of 33.8% and a specificity of 91.3% in diagnosing TTN, whereas double lung point exhibited a sensitivity of 45.6% and a specificity of 94.8% in diagnosing severe TTN [23]. Rachuri et al. showed that LUS had 100% PPV and NPV for diagnosis of TTN [18]. Thus, current evidence support the role of LUS in diagnosis of TTN and differentiating TTN from RDS, the two most common cause of respiratory distress.

Meconium aspiration syndrome (MAS)

MAS is a common cause of severe respiratory disease in full-term and post-term infants. In MAS, the images seen by LUS are coalescent B-lines, irregular subpleural consolidations with more prominence on one side along with few spared areas and white out lung in severe MAS [24]. Piastra et al. studied six patients with MAS and showed the presence of B-pattern (interstitial) coalescent or sparse; consolidations; atelectasis; and bronchograms as LUS features of MAS [25]. Liu et al. conducted study to see the role of LUS in diagnosis of MAS in newborn. This study enrolled 117 newborns with MAS and 100 controls. The results of the study showed that the LUS findings in MAS were pulmonary consolidation with air bronchogram (100%); pleural line anomalies and the disappearance of the A-line (100%); alveolar-interstitial syndrome or B-line in the non-consolidation area (100%); severe massive atelectasis and visible lung pulse (16.2%); and pleural effusion (13.7%). The authors concluded that LUS can

be used routinely to diagnose MAS in an accurate, reliable, convenient, and non-invasive manner [26].

Air leak syndrome

Air leak syndrome is characterized by leakage of air from the alveoli into the extra-alveolar space. The most common types of air leak syndrome are pneumothorax, pneumomediastinum, pneumopericardium, and pulmonary interstitial emphysema (PIE). Pneumothorax (PTX) is the most common type of air-leak syndrome in infants and seen in approximately 2–10% of VLBW [27–29]. LUS has been used as point of care in NICU for the diagnosis of PTX. USG finding suggestive of PTX are the absence of lung sliding, the absence of B lines, the absence of lung pulse, and the presence of lung point. In LUS, for diagnosis of PTX, the neonate should be kept in a reclining position for letting air collection within the anterior non-dependent portions of the pleural space [30]. There is enough evidence in adult population seeking role of LUS in the detection of PTX, but in neonates, there are very few studies [31–33]. Cattarossi et al. conducted first study to see diagnostic accuracy of lung USG in neonatal pneumothorax. This study compared lung USG, CXR, and chest transillumination (CTR) for diagnosis of PTX in neonates having confirmed the presence of air in the pleural space. This study enrolled 49 neonates with respiratory distress. Twenty-three neonates had PTX requiring aspiration or chest drainage, and 26 had respiratory distress without PTX. Both groups underwent LUS, CTR, and CXR. The results of the study were promising as LUS was consistent with PTX in all 23 patients requiring chest aspiration. In this group, CXR missed one case and CTR missed three cases of PTX. The sensitivity and the specificity in diagnosing PTX were 100% for LUS, 96% and 100% for CXR, and 87% and 96% for CTR. This study thus showed that in newborns, LUS is at least as accurate as CXR in the diagnosis of PTX and CTR had lower accuracy [34]. Liu et al. recently published study seeking the reliability and accuracy of LUS for diagnosing neonatal PTX. The study was conducted in two phases, with 40 neonates in the first phase with confirmed PTX underwent LUS to identify the USG findings of neonatal PTX and in the second phase, 50 neonates were enrolled with severe lung disease who were suspected of having pneumothorax. The results showed that main LUS features of PTX were lung sliding disappearance (100%); the existence of the pleural line and the A-line (100%); lung point (75% of the infants with mild-moderate pneumothorax, absent in 25% severe pneumothorax); absence of B-lines in the area of the pneumothorax (100%); and absence of lung consolidation in the area of the pneumothorax (100%). The accuracy and reliability of the lung sonographic signs of lung sliding disappearance as well as the existence of the pleural line and the A-line in diagnosing pneumothorax were as follows: 100% sensitivity, 100% specificity, 100% PPV, and 100% NPV. Thus the authors concluded that LUS is an accurate and reliable in diagnosing and ruling out neonatal PTX and was equally accurate to CXR [35].

Pulmonary hemorrhage (PH)

PH is a common severe and critical disease in neonates with clinical features varying from blood tinged tracheal or pharyngeal secretions, on one hand, to massive intractable bleeding, on the other hand. PH is end result of various etiologies, having rapid progression and having high mortality rate [36–38]. The role of LUS has been sought in one study that evaluated LUS for diagnosis of PH. The study enrolled 157 neonates who were divided into two groups namely 57 neonates diagnosed with PH as per the medical history, clinical manifestations and chest X-ray findings, and a control group of 100 neonates with no lung disease. All neonates underwent bedside LUS in a quiet state in a supine, lateral, or prone position followed by comparison of LUS findings between the two groups. The LUS findings associated with PH were lung consolidation with air bronchograms (82.5%), shred sign (91.2%), pleural effusion (84.2%), atelectasis (33.3%), pleural line abnormalities, as well as disappearing A-lines (100%) and alveolar-interstitial syndrome (11.9%). The shred sign exhibited a sensitivity of 91.2% and a specificity of 100% for diagnosing PH. The authors thus concluded that LUS is useful and reliable for diagnosing PH [39]. Liu et al. similarly conducted study in 142 neonates, 42 neonates were diagnosed with pulmonary hemorrhage according to their medical history, clinical manifestations and chest X-ray findings, and 100 neonates acted as control with no lung disease. The results of the study showed main findings associated with pulmonary hemorrhage were shred sign (95%), lung consolidation with air bronchograms (83%), pleural effusion (81%), atelectasis (33%), pleural line abnormalities and disappearing A-lines (100%), and AIS (12%). The above signs were not seen in normal controls (all $p < .01$) with normal lung mainly manifesting with clear pleural line and A-lines under ultrasound. Thus the author concluded that LUS is accurate and reliable for diagnosing PH and can be used for routine application for the diagnosis in NICU [40].

Neonatal pulmonary atelectasis (NPA)

NPA is seen secondary to many neonatal diseases, such as RDS, pneumonia, and MAS. The LUS features of atelectasis are large lung consolidation with air bronchograms, paralleled air bronchogram, pleural line abnormalities, and A-line disappearance [41]. Liu et al. studied role of LUS in diagnosis of NPA. The study enrolled 80 neonates with NPA and 50 neonates without lung disease. Each lung of every infant was divided into the anterior, lateral, and posterior regions by the anterior and posterior axillary lines. Each region was scanned carefully with the probe perpendicular or parallel to the ribs. The LUS findings were confirmed by CXR or CT scan. The study showed that the main LUS findings were large areas of lung consolidation with clearly demarcated borders, air bronchograms, pleural line abnormalities, and absence of A-lines, as well as the presence of lung pulse and absence of lung sliding. The sensitivity of LUS for the diagnosis of NPA was 100%, whereas the sensitivity of CXR was 75%, thus showing that LUS was an accurate and reliable method for diagnosing NPA [42].

Neonatal pneumonia

LUS has been used in diagnosis of pneumonia in adult patient with the typical features being hypoechoic areas of varying size and shape, irregular and serrated margins, heterogeneous echo texture, air bronchograms, dynamic air bronchograms, pleural effusion, and hepatization of lung tissue [43–45]. In neonatal population, the role of LUS in diagnosis of pneumonia has not been studied much. Liu et al. conducted study to see the role of LUS in diagnosis of pneumonia in neonatal population. The study enrolled 40 neonates with severe pneumonia according to their medical history, clinical manifestations, and chest radiograph findings and 40 normal neonates. The LUS findings were large areas of lung consolidation with irregular margins and air bronchograms, pleural line abnormalities, and interstitial syndrome. A large area of lung consolidation with irregular margins had 100% sensitivity and 100% specificity for the diagnosis of neonatal pneumonia. Thus, this study showed that LUS being a reliable tool for diagnosing neonatal pneumonia [46].

Prediction of need for mechanical ventilation

Respiratory distress is among the commonest cause for neonatal admission and, in preterm neonates, it is the most common cause of respiratory failure requiring mechanical ventilation. The neonatal clinical and CXR features are often not accurate for guiding the clinical course of respiratory distress [47]. Rodríguez-Fanjul et al. conducted study to see the role of LUS for prediction of need for mechanical ventilation in neonates >32-week gestation. This study enrolled 105 neonates who were admitted for respiratory distress. LUS was performed by neonatologist and ultrasound images were analyzed by second neonatologist, who was not aware of the patient's clinical condition. The LUS findings were classified into the following two groups according to the potential risk of a bad respiratory outcome: low risk (normal or transient tachypnea of the newborn) or high risk (respiratory distress syndrome, meconium aspiration syndrome, pneumothorax, or pneumonia). The same type of classification was made after reading CXR. Respiratory failure was defined as a need for mechanical ventilation during the first day of life. In the study population, 20% of infants had respiratory failure requiring intubation, and was seen more frequently in the high risk group (RR = 17.5; 95% CI 4.3–70.9, $p < .01$). As predictors of respiratory failure, lung ultrasound and chest X-ray showed a high index of agreement (κ coefficient = 0.91; 95% CI 0.83–1, $p < .01$) and good accuracy (LUS: 95% sensitivity, 82.5% specificity, and a NPV of 98.5%). Thus, the authors concluded that LUS can be used as bedside for determining the neonates admitted with respiratory distress requiring mechanical ventilation, thus helping clinician to carrying out appropriate transfers of such neonates to higher center [48].

Congenital diaphragmatic hernia (CDH)

CDH is defined as the presence of intestinal viscera (stomach, liver, and intestine) in the thoracic cavity secondary to defect in the diaphragm. CDH is a life-threatening condition with an incidence of approximately 1 in 2500 live births [49,50]. LUS has been used in the diagnosis of CDH postnatally in pediatric population. On LUS, diaphragm appears as bright curved lines that move with respiration. The pleural lines are seen as a bright or hyperechoic line just deep to the ribs. In case of left CDH, there will be normal lung sliding in right side in all intercostal spaces. The heart is not visualized in the expected location, but rather seen in the right hemi-thorax. In the left chest, lung sliding is seen only in superior one-third of the chest. A transition point is seen where normal lung sliding is replaced by loops of bowel. The remainder of the left hemi-thorax shows a static pleural line and loops of bowel beneath the parietal pleura with visible

peristalsis and dirty shadowing, which is seen as bright echoes from intraluminal air with indistinct posterior shadowing [51]. Rankin et al. reported a 12 days old infant who presented with respiratory distress. LUS helped in excluding cardiac disease and pneumothorax, and expedited the identification of CDH [52]. Desjardins et al. reported that 20 days old infant was diagnosed as CDH with the help of LUS in emergency department and underwent repair surgery [53]. Thus, LUS can be used in the diagnosis of CDH, although still it needs large study to confirm usefulness of LUS in the diagnosis.

Conclusions

LUS can be used in NICU for the diagnosis of etiology of neonatal respiratory distress. LUS has shown good sensitivity and specificity for the diagnosis of respiratory distress syndrome, transient tachypnea of newborn, neonatal pneumonia, pneumothorax, neonatal pulmonary atelectasis, and congenital diaphragmatic hernia. The neonatologist should be trained both for doing and interpreting LUS images so that it can be used for the point of care of neonate and CXR and CT scan can be avoided in them.

Disclosure statement

No potential conflict of interest was reported by the authors.

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