

## Original Research Article

### **Diagnostic utility of Bedside Lung Ultrasonography in Neonates with Respiratory Distress**

#### Abstract

**Background:** Lung Ultrasound (LUS) has recently become an important method for diagnostic examination and monitoring of lung disease. Many lung diseases, such as respiratory distress syndrome, transient tachypnea of the newborn, pneumonia and pneumothorax were diagnosed by chest X-ray, but can now easily be diagnosed with lung ultrasound. LUS has many advantages over X-ray and CT scan including accuracy, reliability, low-cost and simplicity, as well as the fact that ultrasound incurs no risk of radiation damage.

**Objective:** The aim of this study was to evaluate role of LUS in neonates with respiratory distress (RD) within 4 hours of life and to calculate the sensitivity, specificity, and negative and positive predictive value of LUS for RDS and TTNB, using an external reader blinded to the clinical condition.

**Design and Methods:** Neonates born at a gestation from 28 weeks to up to 40 weeks born in the hospital and developing RD on first 4 hours of life were enrolled. Neonates were managed as per standard NICU guidelines on the basis of clinico-radiological features. The diagnosis based on clinico-radiological features as ascertained by the treating neonatologist was considered gold standard. Just before LUS, the RD was objectively scored using Modified Silverman Andersen score. LUS was performed as soon as possible, and within 4 hours of life. The images were captured and stored and interpreted by the Radiologist who was blinded to the neonate's clinical condition and chest radiograph. Chest radiograph was done using portable X Ray machine within 4 hours of life. LUS was performed at bed-side with a high-resolution linear transducer and interpreted according to observational index included pleural A lines, B lines, Air bronchogram and Lung consolidation. Based on LUS findings, differentiation between RDS, TTNB, MAS and Pneumonia were made. Sn, Sp, PPV, and NPV were calculated. The agreement between LUS and clinico-radiological diagnosis were observed.

**Results:** 100 neonates were studied (mean gestational age:  $245.83 \pm 20.90$  days), mean birth weight:  $2.258 \pm 0.63$ kg). 22 infants had a final diagnosis of RDS and 64 of TTNB. LUS showed a Sn of 100% and Sp of 89.7%, with a PPV of 73.3% and a NPV of 100 % for RDS, and a Sn of 82.8% and Sp of 100% with a PPV of 100% and a NPV of 76.6% for TTNB.

**Conclusion:** LUS is a reliable method to diagnose RDS and TTNB in newborns with RD. It showed high sensitivity and specificity in diagnosing RDS and TTNB.

**Keywords:** LUS, TTNB, RDS

## INTRODUCTION

Respiratory distress in neonates continues to be one of the most important causes of morbidity and mortality in premature infants and term infants in neonatal intensive care unit (NICU)<sup>1</sup>. Respiratory distress is the commonest cause of NICU admission which may be because of many reasons. The causes of respiratory distress in neonates include Respiratory distress syndrome (RDS), Transient tachypnea of newborn (TTNB), Pneumonia, Meconium aspiration syndrome (MAS), Pneumothorax, and Congenital diaphragmatic hernia<sup>2</sup>. The risk of developing RDS decreases with both increasing gestational age and birth weight. The incidence rate is 80% in infants < 28 weeks' gestation, 60% at 29 weeks, 15-30% at 32-34 weeks, and declines with maturity to 5% at 35-36 weeks. Accordingly, the RDS incidence rate is estimated to be 80% for infants weighing < 750 g at birth and 55% for infants weighing 750-1000 g<sup>1</sup>. However, in recent years, with the application of antenatal corticosteroids and delivery room pulmonary surfactant, both typical and severe RDS in premature infants have greatly declined<sup>3</sup>. The diagnosis of RDS is usually based on clinical manifestations, arterial blood gas analysis and chest radiograph. Preterm and term neonates are also at risk of TTNB. Lung ultrasound (LUS) is typically not included in the diagnostic work-up of neonatal RDS and TTNB, however, recently LUS has recently been found to be of value in diagnosis and follow up of these neonates<sup>4</sup>. LUS is a simple, practical and low-cost method in diagnosing neonatal respiratory conditions. Ultrasound is non-ionizing and gives no hazard to the patient. It is essential to use the ALARA (as low as reasonably achievable) principle when imaging with a modality that uses ionizing radiation, keeping radiation exposure as low as reasonably achievable<sup>5</sup> whereas LUS can be done numerous times without any risk of radiation exposure. Portable chest radiographs are easily available, though it has issues of radiation exposure. Chest CT scan poses greater hazards and potentially high risks of DNA damage and cancer<sup>6</sup>. Some authors have recommended bedside LUS as a preferred imaging modality in evaluation of lung diseases due to its greater accuracy, reliability, ease of performance and lack of potential adverse effects (i.e., radiation). In NICUs, bedside LUS has the potential to replace chest radiograph and become the first-line approach used for the diagnosis and differential diagnosis of various neonatal lung diseases<sup>7</sup>. LUS has become an important tool in the diagnosis and follow-up of lung diseases in newborn period in recent years. Emerging data suggests that neonatal lung diseases such as Pneumonia, TTNB and RDS can be diagnosed with LUS. More evidence is

needed before its routine use can be justified in a general hospital setting. Therefore, we planned this prospective study to evaluate the diagnostic utility of LUS in neonates with respiratory distress.

**TABLE 1: Clinico-radiological criteria for diagnosing different types of respiratory distress-**

| Types of RD | Clinical criteria  | Radiological criteria   |
|-------------|--|---|
| RDS         | Onset within the first few hours of life, gestation less than 34week, progressive distress, good response to surfactant administration.  | Presence of diffuse atelectasis, 'ground glass' appearance of the lung fields, low lung volumes and diffuse air bronchograms, reticulogranular pattern. |
| TTNB        | Onset at birth, progressively decreasing with time. Resolution within the first 48 to 72 h of life.  | Prominent peri-hilar vascular markings, edema of the inter-lobar septae, fluid in the fissures, and hyperinflation.                                     |
| PNEUMONIA   | Onset at birth or at any time during the first 24 h of life, presence of risk factors such as PROM, maternal fever, foul smelling liquor and Urinary tract infections in the mother. | Patchy or asymmetrical opacities.   |

**Aim:** To evaluate the diagnostic utility of lung ultrasonography as a diagnostic modality in neonates with respiratory distress compared to clinico-radiographic criteria.

**Objectives:** To determine the diagnostic accuracy of lung ultrasonography for identifying the etiology of respiratory distress (RD) in neonates compared to clinico-radiological criteria.

To compare the LUS findings with clinical severity of respiratory distress.

**MATERIALS AND METHODS:** After the approval of Institutional Ethical Committee and Scientific Committee, written informed consent was obtained from all patients participating in the study.

**Study Design:** Prospective observational study.

**Study Duration:** Sept 2019 to July 2020.

**Study setting:** Department of Paediatrics, Holy Family Hospital, Delhi.

**Sample size:** Almost 35% babies admitted to NICU have respiratory distress. They could be either having HMD or TTNB or MAS or any other lung condition<sup>8</sup>. Previous studies on LUS have shown a sensitivity of above 90% and specificity around 80%. Using these values of sensitivity and specificity, precision of 10%, and power of 80%, the minimum required sample size was calculated to be 98, rounded off to 100.

Putting the above values in the undermentioned formula:

$$\begin{aligned} TP+FN &= Z^2 \times SN(1-SN) / d^2 \\ &= 1.96^2 \times 0.9 \times 0.1 / 0.1 \times 0.1 \\ &= 34.57 \end{aligned}$$

$$N(Sn) = \frac{TP+FN}{PREVALANCE} = 34.57/0.35 = 98 \text{ (approx.)}$$

$$\begin{aligned} FP+TN &= Z^2 \times SP(1-SP) / d^2 \\ &= 3.84 \times 0.80 \times 0.2 / 0.1 \times 0.1 \\ &= 61.4 \end{aligned}$$

$$N(Sp) = \frac{FP+TN}{1-PREVALANCE} = 61.4 / (1-0.35) = 94 \text{ (approx.)}$$

**Inclusion Criteria:** Neonates with gestational age 28 weeks to 40 weeks presented with Respiratory distress - grading is defined by using Modified Silverman Andersen score (1-Upper chest retraction, 2-Lower chest retraction, 3-Xiphoid retraction, 4-Nasal flaring, 5-Expiratory grunt), score >6 is indicative of impending failure.

**Exclusion Criteria:** Neonates with chest deformity, Multiple congenital anomaly and Gestational age less than 28 weeks and more than 40 weeks.

**Methods:** Informed consent of the parents of neonates included in the study was taken after providing written patient information sheet in Hindi/English. All cases which satisfied the inclusion criteria were taken into the study. Patient enrolment was started after institutional ethical clearance was obtained.

**Basic Information:** Gestational Age (in days), Sex, Apgar score, Mode of delivery, Need of surfactant administration, Modes of respiratory support, were obtained. Apgar score was recorded at birth. Surfactant administration was required neonates who presented with RDS as per clinico-radiographic criteria assessed by the attending neonatologist. Various modalities of respiratory support were utilized as dictated by the clinical condition of the neonates including oxygen support, CPAP, high flow nasal cannula (HFNC) or mechanical ventilation.

Neonates born at a gestation from 28 weeks to up to 40 weeks born in the hospital and developing respiratory distress on first 4 hours of life were enrolled. The neonates were managed as per standard NICU guidelines on the basis of clinico-radiological features. The diagnosis based on clinico-radiological features as ascertained by the treating neonatologist was considered gold standard. Just before lung ultrasound, the respiratory distress was objectively scored using Modified Silverman Andersen score. LUS was performed as soon as possible, and within 4 hours of life. The images were captured and stored and interpreted by the Radiologist who was blinded to the neonate's clinical condition and chest radiograph.

Chest radiograph was done using portable X Ray machine within 4 hours of life. LUS was performed at bed-side with a high-resolution linear transducer and interpreted according to observational index included pleural A lines, B lines, Air bronchogram and Lung consolidation. Based on LUS findings differentiation between Respiratory distress syndrome, Transient tachypnea of newborn, Meconium aspiration syndrome and Pneumonia were made. The agreement between Lung ultrasound and clinico-radiological diagnosis were observed.

**Lung Ultrasound**<sup>9</sup>: We selected a high-frequency linear probe ( $\geq 9.0$  MHz) for LUS to ensure high resolution. Infant kept in a quiet state and swaddled to expose only the area to be examined. Placement of the infant done in the supine, prone or side position before and during the process of examination. Sedatives were not used while pacifier used wherever needed. Supine positioning used for scanning of the anterior and lateral chest. Each lung into three regions: anterior, lateral and posterior lung area using the anterior axillary line and the posterior axillary line as boundaries. B-mode was used mode in obtaining LUS images. Placed the transducer perpendicular to the ribs and slid it from the midline to the lateral side along the wide axis to perform the perpendicular scanning. After initial area of the lung was scanned, the transducer was moved from up to down and scanned the remaining areas until all the lung fields were examined. Perpendicular scanning was the most important scanning method. Keeping the

transducer perpendicular to the ribs was the key to obtaining accurate and reliable results. Rotate the transducer 90° after finishing the perpendicular scanning. Keep the transducer parallel to the ribs and slide it along the narrow axis to realize the parallel scanning. After the initial area of the lung is scanned, move the transducer from up to down to scan the remaining areas until all the lung fields were examined.

### **Lung Ultrasonography Terminology**

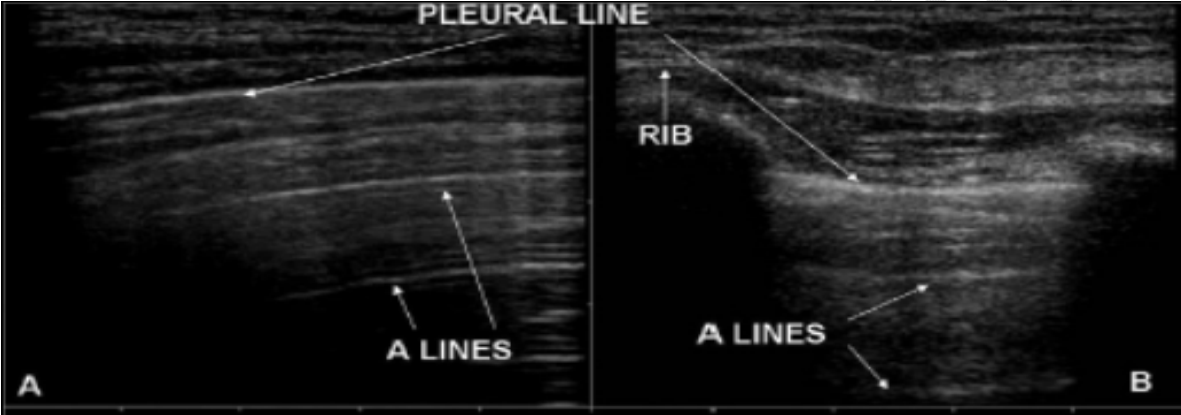
A **pleural line** is a hyperechoic reflection over the pleural lung surface interface. It appears as a smooth, regular and relatively straight hyperechoic line. The pleural line moves in a to- and fro-pattern, synchronized with respiratory movement-called lung sliding. **A-lines** are hyperechoic, arranged in parallel and equidistant from one each other<sup>10</sup>. **B Line** is a type of linear hyperechoic reflection of an artifact. B-lines are roughly vertical to the pleural line. Alveolar-interstitial syndrome (AIS) is defined as two or more than B-lines in any scanning area<sup>11</sup>. When the probe is put to scan perpendicular to the ribs, the presence of concentrated B-lines may cause the acoustic shadow of the ribs to disappear within the entire scanning zone. This type of B-line is called a **coalescent B-line**. A **white lung** is present when each scanning zone on both sides of the lung presents as coalescent B-lines. Coalescent B-lines and a white lung are manifestations of severe pulmonary edema<sup>12</sup>. **Lung consolidation** presents as areas of consolidation with presence of air bronchograms or /and fluid bronchograms<sup>13</sup>.

**Table 2 Criteria for diagnosing different etiologies of respiratory distress-**

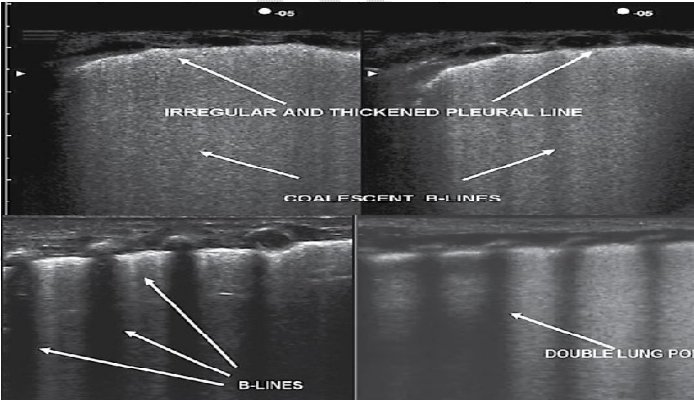
| <b>Diagnosis</b>   | <b>LUS finding</b>   |
|--------------------|--|
| <b>Normal lung</b> | Pleural A-lines are smooth, regular and straight. A-line echoes diminish to the deep part of the lung fields, not more than one or two B-lines in a normal lung, no pleural effusion or lung consolidation.  |
| <b>RDS</b>         | Lung consolidations accompanied by air-bronchograms and often observed in the posterior parts of the lungs.<br>In mild RDS, consolidations are limited only to the region beneath the pleura and if the areas of consolidation may extend to deeper parts of the lung fields, it denotes more severe RDS.<br>Consolidated areas show an uneven hypoechoic quality and Bilateral white lung (coalescent B-lines from base to apex), thickned and irregular pleural A line <sup>12</sup> . |
| <b>TTNB</b>        | Lung edema without lung consolidations.<br>Mainly >3 broad and unsharp compact B-line are seen.  |

|                  |  |
|------------------|--|
|                  | A-line disappearance, no consolidation and no air bronchogram <sup>14</sup> .  |
| <b>PNEUMONIA</b> | Lung consolidation with irregular margins and air bronchograms, pleural line abnormalities <sup>15</sup> .                                 |
| <b>MAS</b>       | Coalescent B-lines, irregular sub-pleural consolidations with more prominence on one side and white out lung in severe MAS <sup>16</sup> . |

**Figure 1: Normal LUS showing Pleural line, Horizontal A lines equidistance from each other**



**Figure 2: LUS image show thickened and irregular pleural line and coalescent B lines suggestive of RDS.**



**DATA ENTRY AND STATISTICAL ANALYSIS:**

The collected data was transformed into variables, coded and entered in Microsoft Excel. Data was analyzed and statistically evaluated using Stata Statistical Software (version 12).

Quantitative data was expressed in mean  $\pm$  standard deviation (SD) and depending upon normality of distribution, difference between two comparable groups were tested by student's t-test (unpaired) or Mann Whitney 'U' test while qualitative data were expressed in percentage and statistical differences between the proportions were tested by chi square test or Fisher's exact test. Sensitivity was defined as the number of true positives/(number of true positives + number of false negatives); specificity as the number of true negatives/(number of false positives + number of true negatives); positive predictive value (PPV) as the number of true positives/(number of true positives + number of false positives), and negative predictive value (NPV) as the number of true negatives/(number of true negatives + number of false negatives). Cohen's Kappa value was calculated to assess percentage agreement between LUS and clinic-radiological and concordance. 'P' value of less than 0.05 was considered statistically significant. **RESULTS:** During the study period, 100 patients fulfilling the inclusion criteria were enrolled. The baseline characteristics of the enrolled infants are presented in (Table. 3).

**Table 3: Demographic table**

| <b>Parameters</b>                            | <b>n (%)</b>       |
|--|--------------------|
| Male gender                                  | 61 (61)            |
| APGAR score at 1 minute, Median (IQR)        | 7 (7-8)            |
| APGAR score at 5 minutes, Median (IQR)       | 9 (8-9)            |
| Birth weight, kg, mean $\pm$ SD              | 2.258 $\pm$ 0.63   |
| Gestational age, days, mean $\pm$ SD         | 245.83 $\pm$ 20.90 |
| Early preterm (28 wk to 32+6 wk)             | 20 (20)            |
| Late preterm (33 wk to 36+6 wk)              | 39 (39)            |
| Term (37 wk to 40 wk)                        | 41 (41)            |
| <b>Mode of delivery</b>                      |                    |
| LSCS   | 65 (65)            |
| NVD  | 35 (35)            |
| <b>Time of onset of respiratory distress</b> |                    |
| Within 1 hours                               | 96 (96.0)          |
| Within 2 hours                               | 4 (4.0)            |
| SA score at Chest Radiography, mean $\pm$ SD | 3.25 $\pm$ 1.24    |

|                                |                 |
|--------------------------------|-----------------|
| SA score at LUS, mean $\pm$ SD | 3.03 $\pm$ 1.19 |
| Sepsis                         | 11(11)          |

Mean age of neonates enrolled in this study was 245.83 $\pm$ 20.90 days. More than half of were males (61%). APGAR score at 1 minute 7 (7-8). APGAR score at 5 minutes 9 (8-9). 20% were early preterm, 39% were late preterm and 41% were term. Most of the infants were term and late preterm. Overall, 12 neonates required surfactant administration. Most of the neonates were in between 1.5kg to 2.49kg (44%), 43% neonates were  $\geq$  2.5 kg and only 13% neonates were < 1.5 kg. Most of the neonates were delivered by LSCS (65%). 96 neonates developed respiratory distress (as assessed by Silverman Score) within one hour of life. At the time of chest radiograph, 49 neonates were oxygen support, 20 neonates were HFNC, 9 neonates were on CPAP and 22 neonates were on ventilator. At the time of LUS procedure, 48 neonates were on oxygen support, 21 neonates were on HFNC, 9 neonates were on CPAP and 22 neonates required ventilation. The LUS finding in the form of A Lines which were present in 14% neonates, Air Bronchogram were present in 30% neonates and Lung consolidation present in 31%. On the basis of B lines 13% were present with few narrow and sharp, 54% were present with >3 broad unsharp compact and 33% were present with coalescent white out lung.

**Table 4: Distribution of final diagnosis based on clinico-radiological assessment (n=100)**

| Final diagnosis              | n  | %    |
|------------------------------|----|------|
| Normal                       | 11 | 11.0 |
| RDS                          | 22 | 22.0 |
| TTNB                         | 64 | 64.0 |
| Pneumonia                    | 1  | 1.0  |
| Meconium aspiration syndrome | 2  | 2.0  |

Over all from the clinical scenario and radiological finding, which was considered as gold standard, the final diagnosis was RDS in 22 neonates, TTNB in 64 neonates, pneumonia in 1 neonate and meconium aspiration syndrome in 2 neonates.

**Table 5: Diagnostic accuracy of LUS for RDS**

| Clinico-radiological diagnosis<br>(Gold Standard) | LUS               |                    | Total |
|---|-------------------|--------------------|-------|
|   | Suggestive of RDS | Not suggestive RDS |       |
| RDS present                                       | 22                | 0                  | 22    |
| RDS absent  | 8                 | 70                 | 78    |

Compared to clinico-radiographic criteria (gold standard), LUS showed a sensitivity of 100%, a specificity of 89.7%, a PPV of 73.3%, and a NPV of 100%.

|     | Observed Agreement | Expected agreement | Kappa       | Std Error | Z    | P value          |
|-----|--------------------|--------------------|-------------|-----------|------|------------------|
| RDS | 92.0%              | 61.9%              | <b>0.79</b> | 0.06      | 8.11 | <b>&lt;0.001</b> |

LUS and clinico-radiological diagnosis for detection of RDS had an observed agreement of 92%, Cohen's kappa of **0.79** and p value (**<0.001**).

**Table 6: Diagnostic accuracy of LUS for TTNB**

| Clinico-radiological diagnosis<br>(Gold standard) | LUS                |                        | Total |
|---|--------------------|------------------------|-------|
|   | Suggestive of TTNB | Not suggestive of TTNB |       |
| TTNB present                                      | 53                 | 11                     | 64    |
| TTNB absent                                       | 0                  | 36                     | 36    |

Compared to clinico-radiographic criteria (gold standard), LUS showed a sensitivity of 82.8%, a specificity of 100%, a PPV of 100%, and a NPV of 76.6% for TTNB group.

|      | Observed Agreement | Expected agreement | Kappa       | Std Error | Z    | P value          |
|------|--------------------|--------------------|-------------|-----------|------|------------------|
| TTNB | 89.0%              | 52.1%              | <b>0.77</b> | 0.06      | 7.96 | <b>&lt;0.001</b> |

LUS and clinico-radiological diagnosis for detection of TTNB had an observed agreement of 89%, Cohen's kappa of **0.77**, p value (**<0.001**).

**Table 7: Diagnostic accuracy of LUS for RDS group (Radiological diagnosis as gold standard)**

| Radiological diagnosis | LUS               |                       | Total |
|------------------------|-------------------|-----------------------|-------|
|                        | Suggestive of RDS | Not suggestive of RDS |       |
| RDS present            | 23                | 1                     | 24    |
| RDS absent             | 7                 | 69                    | 76    |

Compared to Radiographic criteria (gold standard), LUS showed a sensitivity of 95.8%, a specificity of 90.7%, a PPV of 76.6%, and a NPV of 98.5%.

**Table 8: Diagnostic accuracy of LUS for TTNB group (Radiological diagnosis as gold standard)**

| Radiological diagnosis | LUS                |                     | Total |
|------------------------|--------------------|---------------------|-------|
|                        | Suggestive of TTNB | Not suggestive TTNB |       |
| TTNB present           | 46                 | 9                   | 55    |
| TTNB absent            | 7                  | 38                  | 45    |

Compared to Radiographic criteria (gold standard), LUS showed a sensitivity of 83.6%, a specificity of 84.4%, a PPV of 86.7%, and a NPV of 80.8%.

|      | Observed Agreement | Expected agreement | Kappa       | Std Error | Z    | P value          |
|------|--------------------|--------------------|-------------|-----------|------|------------------|
| RDS  | 92.0%              | 61.9%              | <b>0.79</b> | 0.06      | 8.12 | <b>&lt;0.001</b> |
| TTNB | 84.0%              | 56.2%              | <b>0.68</b> | 0.07      | 6.94 | <b>&lt;0.001</b> |

Observed agreement between LUS and Radiological diagnosis for detection of RDS and TTNB group were 92% and 84% respectively. Cohen's kappa for agreement between LUS and Radiological diagnosis for detection of RDS group and TTNB group was 0.79 and 0.68 respectively (p value **<0.001** for both).

Table 9 shows the relationship between LUS findings and SA scores for the enrolled neonates. Neonates with A lines had significantly lower SA score compared to those without A lines ( $2.21 \pm 0.57$  vs  $3.16 \pm 1.21$ ,  $p=0.001$ ). Types of B lines (few, narrow, sharp; > 3 broad and unsharp; and coalescent white out lung) were compared for the SA scores. It was observed that B lines had

significantly different SA scores with being highest for coalescent white out lung ( $3.84 \pm 1.4$ ) followed by  $> 3$  broad and unsharp ( $2.72 \pm 0.78$ ). Few, narrow and sharp has the lowest SA scores ( $2.23 \pm 0.59$ ). Neonates with air bronchogram had significantly higher SA score compared to those without air bronchograms ( $3.8 \pm 1.47$  vs  $2.7 \pm 0.87$ ,  $p < 0.001$ ). Neonates with lung consolidation had significantly higher SA score compared to those without lung consolidation ( $3.77 \pm 1.45$  vs  $2.69 \pm 0.87$ ,  $p < 0.001$ ).

**Table 9: Relationship between LUS findings and SA Score**

| Lung USG finding                 | SA Score |          | P value          |
|----------------------------------|----------|----------|------------------|
|                                  | Mean     | $\pm$ SD |                  |
| <b>A-lines</b>                   |          |          |                  |
| Present                          | 2.21     | 0.57     | <b>0.001</b>     |
| Absent                           | 3.16     | 1.21     |                  |
| <b>B-lines</b>                   |          |          |                  |
| Few, narrow, sharp               | 2.23     | 0.59     | <b>&lt;0.001</b> |
| $>3$ , broad & Unsharp (compact) | 2.72     | 0.78     |                  |
| Coalescent White Out Lung        | 3.84     | 1.4      |                  |
| <b>Air Bronchogram</b>           |          |          |                  |
| Present                          | 3.8      | 1.47     | <b>&lt;0.001</b> |
| Absent                           | 2.7      | 0.87     |                  |
| <b>Lung consolidation</b>        |          |          |                  |
| Present                          | 3.77     | 1.45     | <b>&lt;0.001</b> |
| Absent                           | 2.69     | 0.87     |                  |

**Discussion-**Respiratory distress is the commonest cause of NICU admission. We enrolled all consecutive neonates admitted to NICU with respiratory distress. Point of care LUS is a feasible and convenient diagnostic method that can be performed in the NICU at the bedside. Our prospective observational study was conducted in a tertiary NICU to evaluate the role of LUS in diagnosis of neonates with respiratory distress compared with clinico-radiological criteria (considered as gold standard). Newborns developing respiratory distress within 4 hours were enrolled. A total of 100 neonates were enrolled. Diagnostic accuracy of LUS was compared to clinico-radiographic diagnosis for diagnosis of RDS. In neonates with a clinico-radiographic diagnosis of RDS, LUS was observed to have a sensitivity, specificity, PPV and NPV of 100%, 89.7%, 73.3%, and 100% respectively. The signs of lung disease on LUS among the neonates with RDS in our study were: Absence of A-lines (100%), B Line Coalescent White Out Lung (100%), presence of lung consolidation (95.4%) and air bronchograms (95.4%) respectively. Our

findings are consistent with earlier studies by many authors. **Ahuja, et al. (2012)** evaluated the role of Trans abdominal USG of lung bases HMD in premature neonates with respiratory distress soon after birth. They reported 85.7% sensitivity, 75% specificity, 88.88% positive predictive value, and 69.2% negative predictive value for the diagnosis of HMD<sup>17</sup>. **Liu et al. (2013)** reported the common ultrasonic findings of RDS as lung consolidation with air bronchograms (100%); in addition, pleural line abnormalities, the disappearance of A-lines, and interstitial syndrome were also reported<sup>18</sup>. **Rachuri et al. (2017)** 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%<sup>19</sup>. Diagnostic accuracy of LUS was compared to clinico-radiographic diagnosis for the diagnosis of TTNB, In neonates with a clinico-radiographic diagnosis of TTNB, LUS was observed to have a sensitivity, specificity, PPV and NPV of 82.8%, 100%, 100%, and 76.6% respectively. The signs of lung disease on LUS among the neonates with TTNB in our study were: A-line disappearance (93.8%), Absence of lung consolidation (87.5%) with air bronchograms (89.1%) and most important feature was >3, broad & Unsharp (compact) B lines (81.2%). Our findings are consistent with earlier studies by many authors. **Ibrahim et al. (2018)** was performed LUS in 65 near and full-term neonates presented with RD within the first 12:24 hours of admission in NICU. Among the 65 neonates 73.8% were diagnosed to have TTN, 18.5% were diagnosed to have pneumonia, 4.6% had meconium aspiration syndrome (MAS) and 3.1% had respiratory distress syndrome (RDS). The Double lung point has 69.6% sensitivity, 100% specificity, 100% PPV and 39.1% NPV for detecting TTN<sup>20</sup>. **Gupta et al. (2018)** evaluated 77 neonates with respiratory distress within 6 hours of life, the main ultrasonic imaging features of TTN include double lung point, interstitial lung syndrome/ white lung, pleural line abnormalities, and A-line disappearance. Double lung point was only observed in infants with TTN and not in infants with RDS; therefore, the sensitivity and specificity of double lung point for the diagnosis of TTN was 76.7%, but the specificity was 100%. Double lung point is a specific feature of TTN and lung consolidation is observed only in patients with RDS. Double lung point and lung consolidation with air bronchogram are the most important features for differentiating TTN from RDS using LUS<sup>21</sup>.

In neonatal population, the role of LUS in diagnosis of pneumonia has not been studied much. The LUS findings were large areas of lung consolidation with irregular margins and air

bronchograms, pleural line abnormalities. **Liu et al. (2014)** evaluated 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. They concluded that LUS is a reliable tool for diagnosing neonatal pneumonia<sup>22</sup>.

In our study, two infants were diagnosed as Meconium aspiration syndrome as clinic-radiologically and by LUS. The LUS finding were coalescent B-lines, irregular subpleural consolidations with more prominence on one side and white out lung in severe MAS. **Piastra et al. (2014)** 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<sup>23</sup>.

In pneumonia, lung consolidation had irregular margin, and air bronchograms. MAS could be regarded as a special type of pneumonia, with its main signs on LUS being quite similar to pneumonia. Clinical history is contributory in making a diagnosis of MAS.

To summarize, some findings on LUS are associated with increased clinical severity. Studies have used scores to objectively quantify the lung findings. LUS has the potential to be used for follow up and decision making for weaning off from respiratory support.

**Conclusion-** LUS is a feasible, convenient, time saving, low cost modality, can be performed in the NICU at the bedside and also avoids harmful radiation exposure seen with the use of chest radiography. Our study shows a high sensitivity and a specificity of LUS in diagnosis of RDS and TTNB compared to clinico-radiographic criteria as gold standard. Observed agreement between LUS and clinico-radiological diagnosis for detection of RDS and TTNB were 92% and 89% respectively. LUS is a reliable method to diagnose RDS and TTNB in newborns with respiratory distress. Bedside LUS performed by trained pediatric residents can be utilized routinely in neonatal units for diagnosis and severity assessment. Due to distinct neonatal lung sonographic patterns, even novice interpreters with brief training in are able to distinguish RDS, TTNB, normal lung, and other conditions. The findings from this prospective study suggests

utility and high diagnostic accuracy of LUS in NICU for respiratory distress especially by physicians attending neonates.

**Recommendations**-LUS is a feasible and convenient diagnostic method that can be performed in the NICU at the bedside. LUS can also be used for severity assessment and further studies can be done to devise protocols for management of neonates with respiratory distress based on LUS scores. As with lots of ultrasonic applications, this modality is operator dependent, therefore, it is expected that operators acquire sufficient training and practice with this modality. LUS should be part of a curriculum of residents and fellows caring for newborns.

**Limitations**-The sample size of the study was small. LUS is operator dependent, therefore, it should be ensured that operators acquire sufficient training and practice with this modality. In our study, we did not evaluate inter-observer agreement for chest radiography, and future research has to address this topic, comparing the reliability of chest radiography and lung sonography. Surfactant treatment and respiratory support may have affected LUS findings, which was not evaluated in this study.

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