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Original Research Article

Lung ultrasound as modality in diagnosis of respiratory distress syndrome in newborn infants

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ABSTRACT

Background: The aim of this study was to evaluate the value of lung ultrasound in the diagnosis of respiratory distress syndrome (RDS) in newborn infants.
Methods: From April 2019 to March 2020, all newborns admitted in neonatal intensive care unit within 72 hours of life having suspection of RDS on the basis of clinical features were enrolled in study. A total of 59 newborns were included in our study irrespective of gestational age and birth weight.
Results: According to the findings of chest X-ray, there were 10 cases of grade I RDS, 16 grade II cases, 12 grade III cases, and 6 grade IV cases. Lung ultrasound was performed at bedside by a single expert. The ultrasound indexes observed in this study included pleural line, A-line, B-line, lung consolidation, air bronchograms, bilateral white lung, interstitial syndrome, lung sliding, lung pulse, comet tail artifacts etc. In our study it was found that ultrasound sonography (USG) chest has a sensitivity of 100% and specificity of 93.33% in diagnosing RDS which is consistent with other studies. In our study it was found that USG chest has a positive predictive value of 97.78%, negative predictive value of 100% and diagnostic accuracy of 98.31% for diagnosis of RDS.
Conclusion: This study indicates that using an ultrasound to diagnose neonatal RDS is accurate and reliable tool. A lung ultrasound has many advantages over other techniques. Ultrasound is non-ionizing, low-cost, easy to operate, and can be performed at bedside, can be repeated several times in a day making this technique ideal for use in NICU.

Keywords: Lung ultrasound, Neonatal respiratory distress syndrome, Newborn, Chest X-ray

INTRODUCTION

Neonatal respiratory distress syndrome (RDS), also known as hyaline membrane disease, is a condition commencing at or shortly after birth and increases in severity until progressive resolution among the survivors, usually between the 2nd and 4th day. Edema is frequently seen on 2nd day due to fluid retention and capillary leak.[1] The underlying pathogenesis of the disease involves developmental immaturity of the lungs, leading to the absence of pulmonary surfactant.[2] 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 gm at birth and 55% for infants weighing 750-1000 gm.[1]

The central feature of RDS is surfactant deficiency due to lung immaturity, commonly a result of premature birth or delayed lung maturation associated with maternal diabetes or male gender. Surfactant dysfunction can also be caused by perinatal asphyxia, pulmonary infection, or

excessive fetal lung liquid due to delivery without labour.[3]

However, in recent years, with application of antenatal corticosteroids and delivery room surfactant, both typical and severe RDS in premature infants have greatly declined. Greater awareness of RDS has led to a more frequent diagnosis in term neonates. The diagnosis of RDS is usually based on clinical manifestation, arterial blood gas analysis and chest X-ray.[3] Chest radiography has been considered to be the standard radiological diagnostic tool for the RDS. It has been found that all the four-stage scale of RDS severity based on radiological findings correlates closely with actual disease severity. Radiographies are used not only for the diagnosis of RDS but also for evaluating the effectiveness of therapy, so multiple radiographs are used which carries the risk for long term adverse effects. The risk of the effect of ionizing radiation is higher the younger the child is, with the same dose of ionizing radiation a 1 year old is 10-15 times more at risk of developing carcinoma than adult. Thus, the continuous search for the balance between the potential benefits and the potential delayed adverse effects which may arise is inevitable when working with the children. Reduction of the dose of ionizing radiations is one of the main goals of pediatric radiology. Ultrasound imaging is increasingly being used as a non-invasive routine procedure at NICUs for diagnosis of the central nervous system, abdominal cavity, heart, and hip joints.

Recently, ultrasound has been used extensively and successively in diagnosis of many kinds of lung disease and few studies have addressed RDS.[2] This is supported by the fact that neonates have thinner thoracic wall, smaller width of thorax and lung volume and these features enables better imaging quality and visualization of almost the entire surface of the lung when compared to adults. Lung ultrasound at birth may detect infant with RDS before clinical deterioration and even before PaO_2/FiO_2 changes.[1] Recently, ultrasound has been used extensively and successfully in the diagnosis of many kinds of lung disease and a few studies have addressed neonatal RDS.[2,6-15] This study aims to further evaluate the value of an ultrasound in the diagnosis of RDS in newborn infants.

METHODS

Study design

The study was hospital based prospective observational study conducted for one year, from 1st April 2019 to 31st March 2020 the study was approved by ethical committee of govt. medical college Srinagar.

Settings

The study was conducted at post graduate department of pediatrics, at GB pant hospital, an associated hospital of govt. medical college Srinagar, Jammu and Kashmir, Northern India. The hospital has a catchment area of both rural and urban population and is a referral tertiary care hospital.

Criteria for RDS

Progressive respiratory distress occurring shortly after birth, tachypnea, expiratory grunting, nasal flaring, subcostal retractions, cyanosis, reduced or absent breath sounds, or severe dyspnea requiring continuous positive pressure ventilation support for at least 72 hours.

Typical chest X-ray abnormalities such as hypoexpansion, diffuse, fine granular densities, air bronchogram signs, ground-glass opacities, blurred cardiac borders, or white lungs (white-out appearance).

Arterial blood gas analysis showing hypoxia, hypercapnia, and an oxygen/fraction of inspired oxygen ratio (PaO_2/FiO_2) less or equal to 26.7 kPa.

Inclusion criteria

All newborns admitted in NICU with suspection of RDS on the basis of clinical features as described above were enrolled in study.

Exclusion criteria

Those patients whose dyspnea was caused by diseases other than RDS like severe infection, meconium aspiration, major congenital abnormalities, life threatening chromosomal alterations etc. were excluded.

Approach

All newborns admitted in NICU within 72 hours of life having suspection of RDS on the basis of clinical features were enrolled in study. Informed consent was obtained from the parents prior to enrolling the neonate in the study. The neonate admitted to the NICU had undergone detailed physical examination and relevant investigations including complete blood count, arterial blood gas, renal function tests, chest radiograph and ultrasound chest.

A conventional antero-posterior chest X-ray was performed at the bedside of all clinically suspicious RDS patients immediately after admission. After diagnosis of RDS was established (clinically and radiologically), its stage of severity was determined on the basis of four stage radiographic scale (Figure 1). The initial analysis of radiographs was carried out by the team of clinicians working in the NICU, as this enabled prompt implementations of respective treatment measures. However, the final evaluation of chest radiographs was performed by a radiologist. A lung ultrasound was then performed on all RDS patients at bedside by a single expert (another radiologist) within 24 hours of admission using both transthoracic and transabdominal approaches

respectively, however the expert was blinded of previous X-ray results. Stages of severity on ultrasound chest were determined on the basis of three stage USG scale. Correlation of stages of chest radiography and USG chest for RDS was performed.

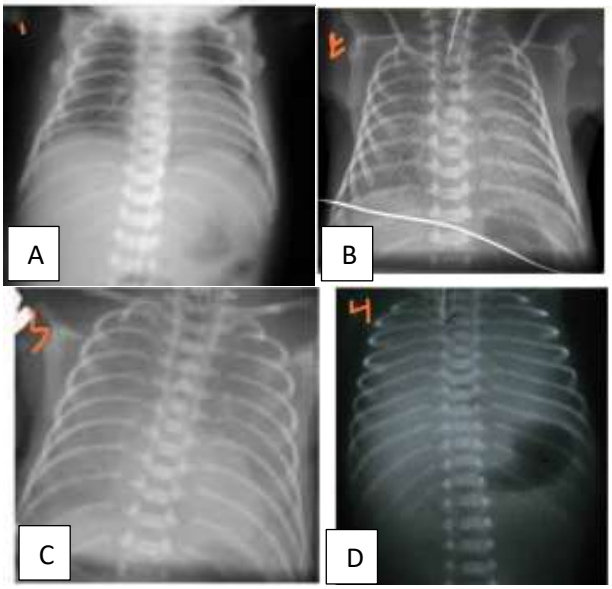

Figure 1: Grades of RDS on chest X-ray. (A) grade I, (B) grade II, (C) grade III, (D) grade IV.

A high-resolution USG machine LOGIQ-Qe using linear transducer of 7.5 MHZ frequency was used in the study. The ultrasound execution cut-off time was 3-5 minutes.

Ultrasound indexes used in this study

Pleural line: The regular echogenic line under the superficial layers of the thorax moving continuously during respiration, while abnormal pleural lines refer to pleural line disappearance, indistinct or thicker in width more than 0.5 cm.

A-line: A series of echogenic, horizontal, parallel lines equidistant from one another below the pleural line, which are the reverberation artifacts of the pleural line

B-lines: Also known as ultrasound lung comets, hyperechoic narrow-based artifacts spreading like laser rays from the pleural line to the edge of the screen.

Lung consolidation: Defined as areas of hepatization (tissue pattern) with presence of air bronchograms or fluid bronchograms.

Pleural effusion: Defined as anechoic-dependent collections limited by the diaphragm and the pleura.

Comet-tail artifact: Sonographic artifact with an appearance similar to that of the ring-down, artifact but more attenuated, shorter, and tapering in depth as in the tail of a comet. The mechanism underlying comet tail artifact formation is reverberation.

Interstitial syndrome: Defined as the presence of more than 3 B-lines or the presence of areas of 'white lung' in every examined area.

Bilateral white lung: defined as the presence of compact B-line in the 6 areas without horizontal reverberation.

Lung pulse: Lung sliding is replaced by a kind of pulsation, synchronized with heart activity, which is the early specific ultrasound sign of complete atelectasis.

Statistical analysis

Data was entered in Microsoft excel. Bar charts and box plots were used for geographical representation of data. Descriptive statistics for the group of studied neonates was calculated including mean values, standard deviation. Sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy and confidence interval were estimated by using statistical formulas.

In our study it was found that all the cases diagnosed as RDS by X-ray chest were detected by USG chest and only one patient not having features of RDS on X-ray chest was found to had findings of RDS on lung USG (p value=0.480). We used McNemar chi-square test to analyze the difference between X-ray chest and USG chest for the diagnosis of RDS in newborn infants. Data analyses were done by using SPSS version 20.0.

RESULTS

This study was hospital based prospective observational study conducted for one year, from 1st April 2019 to 31st March 2020. All newborns admitted in NICU within 72 hours of life, with suspection of RDS on the basis of clinical features and accepting the inclusion criteria were enrolled in study. A total 59 newborns were included in our study irrespective of gestational age and birth weight. In our study the number of male babies were more as compared to females {33 males (55.9%), 26 females (44.1%)}. It was found that number of preterm were more as compared to term {preterm 49 (83.1%), term 10 (16.9%)}. It was found that maximum number of newborns admitted in our study were between 3-11 hours (69.7%). In our study maximum number of newborns were between 31 to 37 weeks of gestational age (73%). In our study the number and percentage according to birth weight was with extreme low birth weight 1.7% (n=1), very low birth weight 10.2% (n=6), low birth weight 49.2% (n=29), normal weight 39% (n=23). In our study number of cases born via lower segment caesarean section (LSCS) were more than NVD born {LSCS n=39 (66.1%), NVD n=20 (33.9%)}.

In our study all the patients who were diagnosed on X-ray chest were also detected by lung ultrasound and only one

patient not having features of RDS on X-ray chest was found to had findings of RDS on lung ultrasound (p value=0.480).

Table 1: Comparison of X-ray and lung ultrasound.

Variables		X-ray		Total
		Positive	Negative	
USG	Positive	44	1	45
	Negative	0	14	14
Total		44	15	59

Table 2 showing number and percentage of patients showing I-IX respectively on lung ultrasound and table 3 showing designation of lung ultrasound. The maximum number of the patients diagnosed RDS were having I, II, III, V and only few had IV, VI, VIII, IX on lung ultrasound.

Table 2: Percentage of patients showing features on lung ultrasound.

Findings on lung ultrasound	Number	Percentage (%)
I	38	84.4
II	32	71.1
III	30	66.7
IV	5	11.1
V	32	71.1
VI	3	6.3
VII	6	13.7
VIII	8	17.8
IX	3	6.7

Table 3: Designation of lung ultrasound.

Findings on lung ultrasound	Designation
Pleural line	I
Lung consolidation	II
Interstitial syndrome	III
B-lines	IV
Bilateral white lung	V
Pleural effusion	VI
A-line	VII
Lung pulse	VIII
Comet tail artifacts	IX

In our study all extremely low birth weight (ELBW), very low birth weight (VLBW) and maximum number of low birth weight (LBW) were having RDS.

In our study it was found that number of cases diagnosed RDS were more who were born LSCS as compared to NVD.

Table 5: Mode of delivery and RDS on X-ray.

Variables	LSCS	NVD
X-ray positive	28	16
X-ray negative	11	4
Total	39	20

In our study there were 39 preterm patients who were X-ray positive and 10 pre-term patients were X-ray negative while 5 term newborns were X-ray positive and 5 were X-ray negative.

Table 6: Gestational age and RDS.

Variables		Preterm	Term	Total
Stages on X-ray chest	Nil	10	5	15
	I	9	1	10
	II	13	3	16
	III	11	1	12
	IV	6	0	6
Total		49	10	59

In our study it was found that patients having stage I on X-ray chest were having stage I on USG chest and patients having stage II were having stage II on USG chest, but patients having either stage III or IV on X-ray chest were having stage III on USG chest. Lung ultrasound cannot differentiate stage III and stage IV of X-ray chest. Therefore, in our study it was found that number of patients having stage I, II, on X-ray chest and USG chest were equal that is 10, 16. The number of patients having stage III, IV on X-ray chest were 12, 6 respectively and the number of patients having stage III, on USG chest were 19. In our study one of the patients who was not having features of RDS on X-ray chest was having features of RDS on USG chest (stage III of USG), so total number of patients having stage III on USG chest were 19 in comparison to 18 (12+6) of X-ray stage and IV.

In our study significant correlation between severity of stages of RDS assessed by chest ultrasound and by chest radiography was observed within all stages.

Table 7: Correlation between chest USG and chest X-ray.

Variables		X-ray					Total
		Negative	I	II	III	IV	
USG	Negative	14	0	0	0	0	14
	I	0	10	0	0	0	10
	II	0	0	16	0	0	16
	III	1	0	0	12	6	19
Total		15	10	16	12	6	59

In our study it was found that in comparison to X-ray chest, lung USG has sensitivity of 100% and specificity of 93.33% positive predictive value of 97.78%, negative predictive value of 100%, diagnosis of RDS in newborn infants.

Table 8: Comparison between USG chest and chest X-ray.

Variables	Percentage (%)	95% CI
Sensitivity	100	(91.97, 100)
specificity	93.33	(70.18, 98.81)
Positive Predictive Value	97.78	(88.43, 99.61)
Negative Predictive Value	100	(78.47, 100)
Diagnostic Accuracy	98.31	(91, 99.7)

DISCUSSION

The results of this study confirm that lung ultrasonography has a very high sensitivity and specificity in the diagnosis of neonatal RDS. In our study it was found that lung ultrasound had sensitivity 100% and specificity 93.33% as compared to El-Malah et al were it was found that lung ultrasonography had sensitivity 98% and specificity 92% in detection of pulmonary manifestations of RDS.[4] In our study 59 neonates were enrolled in study as compared to 55 in Cattarossi et al and 100 in Liu et al.[1,2] Therefore, a sample size of 59 would be statistically appropriate to derive any conclusion.

The mean gestational age in our study group was 33.29±3.887 weeks as compared to 27.2±2.7 weeks in a study by Cattarossi et al while mean gestational age was 34.9±2.7 weeks in a study by Liu et al which was almost consistent with our study.[1,2] In our study number of patients having gestational age 24 to 40 weeks at time of admission were 2, 2, 2, 4, 2, 1, 4, 2, 4, 5, 9, 12, 7, 2, 1 respectively showing maximum no. of patients in our study were between 31-37 weeks gestational age. No other study has discussed number of patients and their corresponding gestational age.

In our study minimum birth weight was 600 gm and maximum birth weight was 3700 gm. The mean birth weight was 2225.42±666.331 gm as compared to study done by Bober et al were minimum birth weight was 500 gm and maximum birth weight was 4400 grams, in a study done by Liu et al minimum birth weight was 1000 gm and maximum birth weight was 4120 gm.[2,5] both results were consistent with our study. In our study number of males were 33 and number off males were 26, male to female ratio was 1.27:1,this was consistent with study done by Liu et al (M:F=1.1428:1) and study done by El-Malah et al (M:F=1.5:1).[2,4] In our study there was variation in age of presentation as compared to other studies because of referral from distant hospitals, transportation etc. In our study ratio of LSCS:NVD was 1.95 as compared other studies done by Liu et al (LSCS: NVD=2.1), Cattarossi et al (LSCS: NVD=12.3).[1,2] In our study number of patients with ELBW were 1, VLBW were 6, LBW were 29, and those with normal birth weight 23. None of studies conducted previously classified newborn on basis of ELBW, VLBW, LBW and normal birth weight.

In our study we used both transthoracic and transabdominal approach to examine all lung fields for the purpose of diagnosis of RDS and accessing its severity. Although different approaches were used in other studies for diagnosis of RDS their results were consistent with our study. In our study out of total number of RDS patients, 28 were born by LSCS mode and 16 were born by NVD. Among all RDS positive, 10 had stage-I, 16 had stage II, 12 had stage-III and 6 had stage IV RDS on X-ray chest. Among LSCS born (28-patients) 8 had stage I, 9 had stage-II, 8 had stage III and 3 had stage IV RDS on X-ray chest and among NVD born (16 patients) 2 had stage I, 7 had stage II, 4 had stage III, and 3 had stage IV RDS on chest X-ray. Our results were consistent with study done by Liu et al.[2] In our study number of preterm having RDS on X-ray chest were 39 and number of terms having RDS on chest X-ray were 4, our results were consistent with studies done by Liu et al and by Cattarossi et al.[1,2]

In our study number of patients who showed pleural line, lung consolidation, interstitial syndrome, B lines, bilateral white lung, pleural effusion, A line, lung pulse, comet tail artifacts on USG chest were 38, 32, 30, 5, 32, 3, 6, 8, 3 and there percentage were 84.4, 71.1, 66.7, 11.1, 71.1, 6.7, 13.3, 17.8, 6.7 respectively. In our study maximum number of the patients diagnosed RDS were having pleural line, lung consolidation, interstitial syndrome, and bilateral white lung, only few patients were having B lines, pleural effusion, A line, lung pulse, ang comet tail artifacts on lung USG. Therefore, pleural line, lung consolidation, interstitial syndrome and bilateral white lung are more sensitive in detecting RDS in newborn infants as compared to B lines, pleural effusion, A line, lung pulse and comet tail artifacts. Results of our study were consistent with studies by Leu et al and by Cattarossi et al.[1,2] In our study it was found that having stage I on X-ray chest were having stage I on USG chest and patients having stage II were having stage II on USG chest, but patients having either stage III or IV on X ray chest were having stage III on USG chest. In our study one of patient who was not having features of RDS on X-ray chest was having features of RDS on USG chest. Significant correlation between severity of stages of RDS assessed by chest ultrasound and by chest X-ray was observed within all stages. There was no difference between right and left lung on USG findings.

As compared to other studies positive predictive value, negative predictive value and diagnostic accuracy for RDS were more in our study.

Limitations

A sample size of 59 was small for study and might not be appropriate. For such a study large sample size is required so that sensitivity and specificity of lung ultrasound for diagnosis of RDS could be accurately determined. Ultrasound chest is not able to pick up some acute complications of RDS like pneumomediastinum, interstitial emphysema, pneumopericardium, small pneumothorax.

CONCLUSION

Both clinical features and chest X-ray are sensitive but there are some limitations. Clinical assessment varies depending upon observer's experience, variable presentation in extreme preterm and extremely low birth weight. Interpretation of location and nature of opacity on chest X-ray is sometimes difficult. Multiple radiographs are required to reach the diagnosis which poses the risk of radiations to infants. In such cases lung ultrasound is very useful both for rapid diagnosis and to avoid risk of hazards of radiation. There is no need to manipulate the baby as in case of X-ray chest particularly when newborn is in ventilator.

Taking consideration to all the above features it was found that USG is a reliable and accurate tool for the diagnosis of RDS in newborns. A lung ultrasound has many advantages over other techniques. Ultrasound is non-ionizing, low cost, easy to operate, can be performed at bedside, can be repeated several times in a day without hazards to operator and to patients making this technique ideal for use in NICU.

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