



● *Original Contribution*

USE OF LUNG ULTRASOUND IN DETECTION OF COMPLICATIONS OF RESPIRATORY DISTRESS SYNDROME

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Abstract—Repeated chest radiography is required for the diagnosis and follow-up of neonates with respiratory distress syndrome (RDS) and carries the risk of radiation hazards. Lung ultrasound (LUS) is a non-invasive bedside diagnostic tool that has proven to be effective in the diagnosis of RDS. Our aim was to assess the role of LUS with respect to the standard chest X-ray (CXR) in the detection of complications of RDS in neonates. Ninety premature newborns of both genders with RDS (mean gestational age = 29.91 ± 1.33 wk) and 40 premature babies as a control group were involved in this study. All patients underwent initial clinical assessment as well as CXR and LUS. Those who presented with respiratory distress and/or exhibited deterioration of oxygenation parameters were followed by CXR and, within 4 h, by LUS. Alveolo-interstitial syndrome and pleural line abnormalities were detected in all cases (100%) in the initial assessment, patchy consolidation was detected in 34 cases and white lung was detected in 80 cases. Alveolo-interstitial syndrome was detected in 19 controls. In follow-up of the patients, LUS was superior to CXR in detection of consolidation and sub-pleural atelectasis, but not in detection of pneumothorax. We concluded that bedside LUS is a good non-hazardous alternative tool in the early detection and follow-up of RDS in the neonatal intensive care unit; it could be of value in reducing exposure to unnecessary radiation. (E-mail: happy7_kd@yahoo.com) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: Respiratory distress syndrome, Premature newborns, Lung ultrasonography, Chest X-ray.

INTRODUCTION

Neonatal respiratory distress syndrome (RDS) starts at or shortly after birth and increases in severity until progressive resolution among its survivors. RDS usually occurs between the second and fourth days after birth. It is due, at least in part, to insufficiency of pulmonary surfactant and is confined mainly to preterm infants (Copetti et al. 2008).

The incidence rate is 80% in infants <28 wk of gestation, 60% at 29 wk and 15%–30% at 32–34 wk and declines with maturity to 5% at 35–36 wk (Liu et al. 2014a). RDS also is observed in term infants, in whom its incidence varies between 3.6% (Liu et al. 2010) and 6.8% (Bouzir et al. 2007). The risk factors for occurrence of RDS in term infants include selective cesarean section, severe birth asphyxia and maternal–fetal infection (Liu et al. 2014c).

The diagnosis of RDS is usually based on clinical manifestations, arterial blood gas analysis and chest

X-ray findings (Liu et al. 2014a). Repeated chest radiography is required for diagnosis and follow-up of patients with RDS and carries the risk of radiation hazards (Lichtenstein and Mauriat 2012). Lung ultrasonography (LUS) is a non-invasive bedside diagnostic tool that has proven to be effective in the diagnosis and follow-up of RDS and almost all its complications in neonates (Copetti and Cattarossi 2008). The availability of skilled neonatologists able to perform bedside LUS and eliminate the wait for a radiologist is another reason to emphasize the utility of LUS.

The aim of this study was to assess the role of LUS with respect to the standard chest X-ray (CXR) in the detection of complications of RDS in neonates.

METHODS

Ninety premature newborns of both genders with RDS (mean gestational age = 29.91 ± 1.33 wk) and a control group of 40 premature newborns (mean gestational age 34.22 ± 1.05 wk) without respiratory distress (lung diseases were excluded by clinical examination and CXR) were involved in this case–control prospective study. All patients were recruited into the study and

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managed in the neonatal intensive care unit (NICU) of Children's Hospital, Cairo University, between September 2012 and January 2014. This tertiary-care unit admits neonates born in the obstetric unit of the same hospital. The number of deliveries in this unit reaches as high as 1,000 to 1,500 per mo; the total number of NICU admissions throughout the study period was 350, with an average of 50 newborns per mo. The diagnosis of RDS was based on clinical and radiologic findings.

It should be noted that the infants in the control group had been admitted for other reasons (low birth weight, $N = 27$; maternal chorioamnionitis, $N = 7$; jaundice, $N = 4$; hypoxic ischemic encephalopathy, $N = 2$). Newborns with gestational age ≥ 37 wk, patients with congenital chest or heart diseases and neonates with hypoxic ischemic encephalopathy were excluded from this study ($N = 24$).

Approval was obtained from the research ethics committee of the Pediatric Unit at Cairo University. Data were confidentially preserved according to the Revised Helsinki Declaration of Bioethics. Informed written consent was obtained from the parents of the patients. Parents of 17 infants refused to have their children involved in the study.

The diagnosis of RDS was based on clinical, laboratory and radiologic criteria: clinical criteria (onset of symptoms within 6 hours of birth) included a respiratory rate >60 /min, dyspnea characterized by intercostal, subcostal or suprasternal retraction, grunting or cyanosis; laboratory criteria included arterial blood gas levels indicating respiratory acidosis ($\text{pH} < 7.25$, $\text{PaCO}_2 > 60$ mm Hg, $\text{PaO}_2 < 50$ mm Hg); radiologic criteria included CXR findings graded as follows: grade I = mild ground glass veiling; grade II = bilateral well-evident reticulonodular pattern; grade III = air bronchogram; grade IV = bilateral symmetric parenchymal opaqueness (white lung).

We encountered 14 patients who were grade I by CXR but did not fulfill other criteria for diagnosis of RDS, so they were excluded from the study. We also had 22 patients categorized as grade II, 22 patients as grade III and 46 patients as grade IV.

Gestational age, sex, mode of delivery, Apgar score at 1 and 5 min, birth weight, whether surfactant was required, whether positive pressure support was required (and method of positive pressure support), duration of stay and fate (death or discharge) were recorded.

All patients underwent an initial assessment when they presented with respiratory distress. This assessment comprised (i) clinical assessment of respiratory distress, auscultation of chest and exclusion of other systems affected; (ii) radiologic assessment by CXR and LUS (LUS was done within 4 h after CXR); (iii) collection

of a venous blood sample for complete blood count and qualitative assessment of C-reactive protein and another arterial sample for measurement of arterial blood gases; and (iv) echocardiography to exclude congenital heart diseases and persistent pulmonary hypertension.

Patients were followed clinically during their stay in the NICU according to our unit protocol. CXR was performed for the following clinical indications: development of dyspnea, respiratory rate >60 /min, grunting and cyanosis and/or worsening of oxygenation parameters. After establishment of proper respiratory status, LUS was performed within 4 hours of a supine anteroposterior CXR by another investigator (radiologist) who was blinded to the CXR findings. The CXR was performed with the Philips Mobile Medical X-ray system D-22335 (Philips, Hamburg, Germany).

Lung ultrasonography technique

Lung ultrasonography was performed with a Toshiba Diagnostic Ultrasound System Nemio XG SSA-580A, using a linear 7-MHz probe (Toshiba, Tokyo, Japan). Lung regions that were explored by auscultation were also examined by ultrasonography. The sonographer scanned the anterior, lateral and posterior chest walls. Images of longitudinal and transverse sections were obtained. On the anterior chest, transverse sections were obtained by positioning the probe transversally, from the second to the fifth intercostal spaces; longitudinal sections were obtained by positioning the probe longitudinally, along the parasternal, mid-clavicular, anterior axillary and mid-axillary lines. On the posterior chest wall, transverse sections were obtained by positioning the probe on the intercostal spaces below the scapular spine; longitudinal sections were obtained along the para-vertebral, scapular and posterior-axillary lines.

Definitions of pathologic lung ultrasound findings

1. A pleural line is an echogenic line that lies between the two shadows of the ribs and represents the pleural surface (Gardelli et al. 2012). Pleural line abnormalities are defined as thickening (>0.5 mm), irregularity or coarsening or the presence of small sub-pleural consolidation patches (Fig. 1a) (Copetti et al. 2008).
2. The quad sign (Fig. 1b), anechoic pleural fluid trapped between the echogenic pleural line and the roughly parallel lung surface (Lichtenstein and Mauriat 2012), indicates pleural effusion.
3. The tissue-like sign indicates lung consolidation (Fig. 1), in which the airless sub-pleural, consolidated lung appears as a large, iso-echoic, wedge-shaped area with an internal-branching, echogenic, linear air bronchogram. An echogenic branching air bronchogram that appears parallel, crowded or condensed suggests

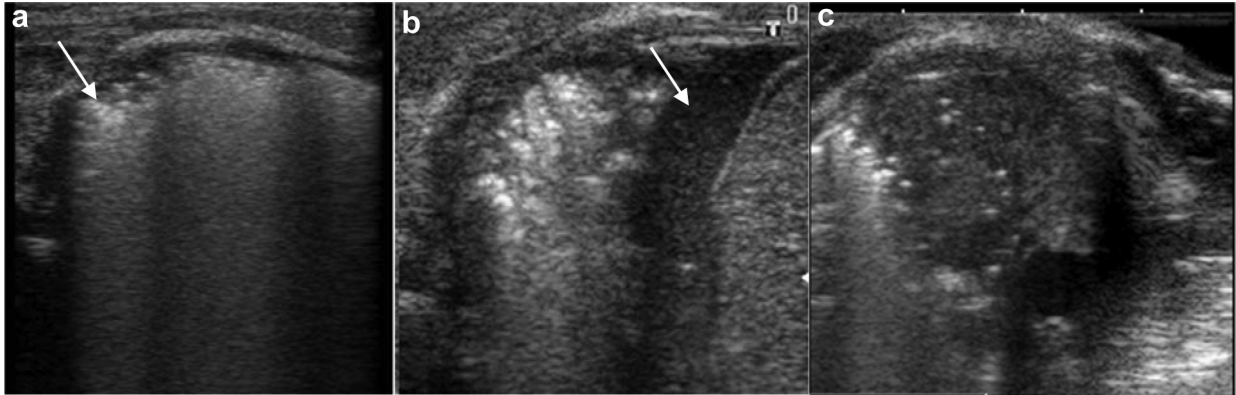


Fig. 1. Ultrasound images of pleural line abnormalities, pleural effusion and sub-pleural lung consolidation. (a) Pleural line abnormalities (thick, irregular with small sub-pleural patch of consolidation [arrow]) with a scattered echogenic air bronchogram (arrow). (b) Quad sign: Note the anechoic fluid between the consolidated lung and pleural line (arrow). (c) A large sub-pleural patch of consolidation appears iso-echoic with branching echogenic air bronchogram.

atelectasis (Lichtenstein and Mauriat 2012; Lovrenski 2012).

- On LUS, parenchymal micro-abscesses appear as rounded or oval hypo-echoic areas within the consolidation patch (Fig. 2) (Lovrenski, 2012).
- B-Line artifacts and lung rockets (indicating AIS) are echogenic comet tail artifacts 7 mm apart arising from the pleural line and represent edematous inter-lobular septa (Copetti *et al.* 2008). It is possible to observe B-lines in normal term neonates, especially after cesarean section, but these tend to disappear within 24–36 d as the fluid gradually is cleared from the fetal lungs (Copetti and Cattarossi 2007; Dexheimer Neto *et al.* 2012). Confluent lines <3 mm apart represent diffuse areas of white lung parenchyma and indicate

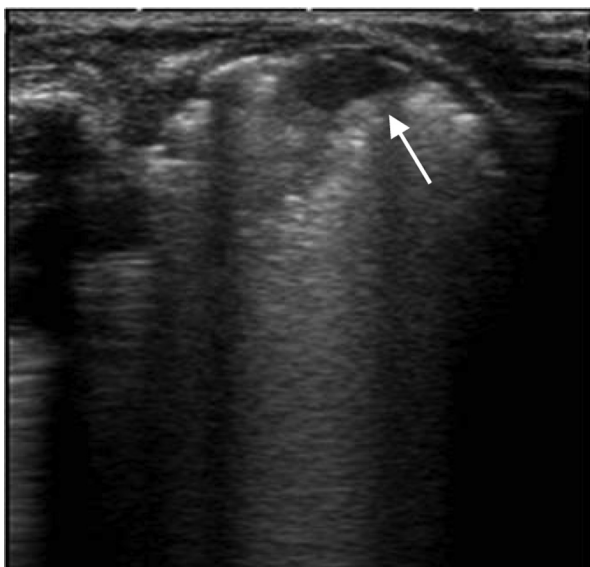


Fig. 2. Early developing parenchymal micro-abscess appears as a hypo-echoic area within consolidated lung (arrow).

alveolar edema as well as echographic white lung (Fig. 3) (Copetti *et al.* 2008; Lichtenstein *et al.* 1997, 2005).

- Among these confluent B-lines, the seashore sign and lung sliding sign indicate absence of a pneumothorax. The lung sliding sign represents the normal sliding motion of the pleural line during breathing, and the seashore sign refers to the granular pattern below the pleural line in M-mode images. Abolished lung sliding (stratosphere sign) suggests pneumothorax, in which the normal granular pattern seen in M-mode is absent (Fig. 4) (Husain *et al.* 2012).

Statistical analysis

Quantitative (numerical) data are expressed as the mean \pm standard deviation. Qualitative (categorical) data are expressed as frequencies and percentages. An independent *t*-test was used to compare results between cases and controls. χ^2 and McNemar tests were used to compare results of CXR and LUS, as well as sonographic findings, between cases and controls. The significance level was set at $p < 0.05$. Statistical analysis was performed with SPSS 16.0 (SPSS, Chicago, IL, USA) for Windows.

RESULTS

This study included 90 premature newborns (36 males and 54 females) with a mean gestational age of 29.91 ± 1.33 wk and mean birth weight of 1384.22 ± 176.46 g. As a control group, we included 40 premature newborns (22 males, 18 females) with a mean gestational age of 34.22 ± 1.05 wk and mean birth weight of 1580.6 ± 204.44 g. All included patients were negative for C-reactive protein. Characteristics of the studied newborns are summarized in Table 1.

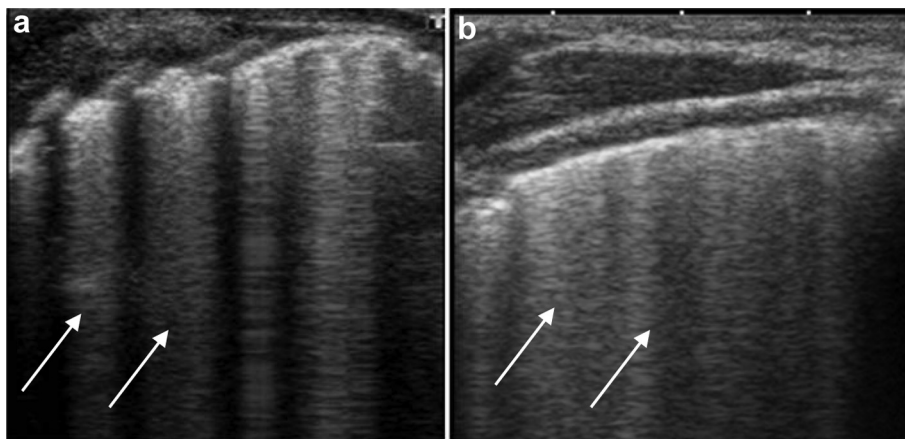


Fig. 3. Ultrasound images of alveolar interstitial syndrome. (a) Interstitial edema with comet tail artifacts 7 mm apart (*arrows*). (b) Alveolar edema with wide comet tail artifacts <3 mm apart (*arrows*).

In the control group, AIS was detected in 19 premature newborns (47.5%). There were no other sonographic findings. In the initial assessment of cases, AIS and pleural line abnormalities were detected by LUS in all cases (100%), whereas consolidation was detected in 34 cases (37.8%) and echographic white lung was detected in 80 cases (88.9%) (Table 2). The sensitivity of LUS in the detection of AIS was 100%, and its specificity was 52.5%. There was a statistically significant ($p < 0.001$) difference between cases and controls with respect to initial sonographic findings. There was a statistically significant difference between grades of RDS as detected by CXR and cases diagnosed as consolidation and white lung by LUS (Table 2).

In follow-up, LUS was superior to CXR in the detection of consolidation and sub-pleural atelectasis, but not in the detection of pneumothorax (Table 3, Fig. 5). In the first follow-up (see follow-up 1 in Table 3) ($N = 46$), LUS was successful in the detection of pleural effusion in six cases (13%) and parenchymal micro-abscesses

in two patients (4.3%). These pathologies were not observed by CXR.

DISCUSSION

As a bedside tool, LUS could be useful in the evaluation of critically ill neonates and has progressively gained wide acceptance in recent years, owing to its lack of ionizing radiation and the ease with which the basic normal and pathologic LUS patterns can be mastered (Bedetti et al. 2006; Copetti and Cattarossi 2008). Other advantages of LUS include reliable image quality and the ability to visualize the whole neonatal lung surface with high sensitivity and specificity (Bober and Swietliński 2006; Copetti et al. 2008; Iuri et al. 2009; Lichtenstein et al. 2004; Lovrenski 2012; Pieper et al. 2004). To date, despite its high diagnostic validity, the use of bedside LUS as part of routine examination is not widespread.

In the present study, the initial LUS examination of preterm neonates with RDS revealed AIS and pleural line

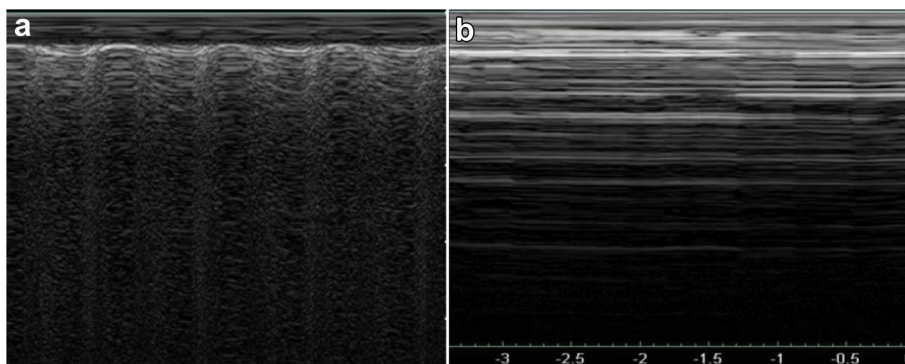


Fig. 4. M-Mode images. (a) Normal lung sliding motion revealed by the granular pattern. (b) Abolished lung sliding motion evidenced by loss of the normal granular pattern, indicating pneumothorax.

Table 1. Demographic data of patient and control groups

	Patients (N = 90)	Controls (N = 40)	<i>p</i> value
Gestational age (wk)	29.91 ± 1.33	34.22 ± 1.05	0.002
Gender			0.081
Male	36/90 (40%)	22/40 (55%)	
Female	54/90 (60%)	18/40 (45%)	
Mode of delivery			0.185
Normal delivery	38/90 (42.2%)	21/40 (52.5%)	
Cesarean section	52/90 (57.8%)	19/40 (47.5%)	
Birth weight (g)	1384.22 ± 176.46	1580.6 ± 204.44	<0.001
Apgar at 5 min	6.6 ± 1.08	6.2 ± 0.08	0.029
Onset of symptoms (h)	2.6 ± 1.19 (min 1, max 5)	N/A	
Complete blood count		N/A	
Hemoglobin (g/dL)	16.41 ± 1.85		
Total leukocyte count (× 1000/mm ³)	8.04 ± 1.40		
I/T ratio	0.06 ± 0.026		
Platelets (× 1000/mm ³)	298.33 ± 85.61		
Duration of stay (d)	21.64 ± 3.57 (min 3, max 61)	N/A	
Cases received surfactant		N/A	
Yes	58 (64.4%)		
No	32 (35.6%)		
Cases required positive pressure support			
No	12 (13.3%)	N/A	
Yes			
Continuous positive airway pressure	47 (52.2%)		
Intermittent mandatory ventilation	31 (34.5%)	N/A	
Fate		N/A	
Discharge	54 (60%)		
Died	36 (40%)		
Initial clinical findings		N/A	
Respiratory distress	90 (100%)		
Diminished air entry	56 (62.2%)		
Crepitations	6 (6.7%)		
Wheezes	2 (2.2%)		

abnormalities in all patients. Despite the statistically significant difference between cases and controls with respect to AIS, several studies have found that AIS and pleural line abnormalities can be present in other lung diseases such as pneumonia and are not specific to RDS (Liu 2014; Soldati *et al.* 2009). Pieper *et al.* (2004) and Liu *et al.* (2014b) found pleural line abnormalities and patchy consolidations in preterm infants with neonatal atelectasis as well as in those with severe neonatal pneumonia. Therefore, initial LUS findings encountered in different cases of neonatal respiratory distress cannot be considered specific for RDS and thus cannot replace initial chest radiography in establishing an initial diagnosis of RDS.

Alveolo-interstitial syndrome was found in preterm newborns not diagnosed with RDS owing to impaired clearance of fluid from the fetal lungs (Raimondi *et al.* 2012). Therefore, in agreement with Liu *et al.* (2014a), we suggest that RDS can exist with pulmonary edema and not only atelectasis.

Statistically significant differences were observed between patients with large areas of consolidation detected by LUS, as well as those with echographic white lung, and patients with grade III and IV RDS, in agreement with previous studies (Copetti *et al.* 2008; Liu *et al.* 2013). Initial X-rays taken early after birth for neonates

with clinical signs of RDS revealed three basic radiographic patterns of RDS: bilateral white-out lungs, bilateral parenchymal granular infiltration and diffuse air bronchogram. These patterns guided the grading of RDS. The statistically significant difference found between large areas of consolidation and echographic white lungs enables LUS to reveal a reproducible imaging pattern that parallels respiratory status and, thus, can be used to predict the need for respiratory support (Raimondi *et al.* 2012).

During follow-up studies for clinically indicated patients, LUS was statistically significantly more accurate

Table 2. Initial assessment of patients with chest X-ray and lung ultrasound

Chest X-ray grade	Lung ultrasound (consolidation)		<i>p</i> value
	Yes	No	
II (N = 22)	2	20	0.001
III (N = 22)	8	14	
IV (N = 46)	24	22	
	Lung ultrasound (white lung)		
	Yes	No	
II (N = 22)	12	10	<0.001
III (N = 22)	22	0	
IV (N = 46)	46	0	

Table 3. Comparison between CXR and US during follow-up of patients

	Imaging method			p value
		Yes	No	
Follow-up 1 (N = 46)				
Consolidation (9.14 ± 2.17)*	CXR	24	22	0.007
	LUS	40	6	
Subpleural atelectasis (10.42 ± 4.22)*	CXR	8	38	0.008
	LUS	16	30	
Pneumothorax (7.02 ± 1.49)*	CXR	8	38	1.00
	LUS	8	38	
Pleural effusion (9.27 ± 2.74)*	CXR	0	46	†
	LUS	6	40	
Follow-up 2 (N = 26)				
Consolidation (14.64 ± 4.12)*	CXR	10	16	0.002
	LUS	20	6	
Sub-pleural atelectasis (15.07 ± 3.53)*	CXR	6	20	0.125
	LUS	10	16	
Pneumothorax (12.82 ± 2.07)*	CXR	8	18	0.500
	LUS	6	20	
Follow-up 3 (N = 26)				
Consolidation (19.40 ± 2.74)*	CXR	20	6	0.008
	LUS	14	12	
Subpleural atelectasis (19.86 ± 4.41)*	CXR	2	24	0.500
	LUS	4	22	
Pneumothorax (17.80 ± 5.04)*	CXR	8	18	1.00
	LUS	8	18	
Follow-up 4 (N = 14)				
Consolidation (24.17 ± 3.31)*	CXR	2	12	0.031
	LUS	8	6	
Subpleural atelectasis (23.44 ± 1.07)*	CXR	0	14	†
	LUS	4	10	
Pneumothorax	CXR	0	14	†
	LUS	0	14	

CXR = chest X-ray; LUS = lung ultrasound.

* Mean age (post-natal day) of patients for a particular complication.

† No statistics are computed because at least one variable is constant.

than chest radiography in the detection of patchy consolidation and atelectasis, as reported in previous studies (Bober and Swietliński 2006; Cortellaro et al. 2012;

Lichtenstein et al. 2004; Liu et al. 2013). This proves the superiority of LUS to radiography in the detection of lung consolidation and atelectasis.

Given the thinner thoracic walls and smaller lung volumes of neonates and the ability of LUS to visualize the whole lung surface, parenchymal micro-abscesses and small amounts of pleural effusion were efficiently detected and followed up with LUS in cases in which chest radiographs failed to detect these findings (Zanobetti et al. 2011).

In contrast to Volpicelli et al. (2012), who stated that LUS has become more accurate than supine anterior chest radiography in diagnosing pneumothorax, we did not find any significant difference between LUS and CXR in the detection of pneumothorax during follow-up of our patients. We could attribute this discrepancy to the small number of pneumothorax cases (eight patients) diagnosed in our study.

This study was conducted on a large number of patients with RDS; however, there are some limitations. First, there was no comparison with other causes of respiratory distress in newborns, such as pneumonia and transient tachypnea of newborn. Second, we were unable to perform some scheduled CXRs because of limitations in our unit's management protocols.

CONCLUSIONS

Bedside LUS is a good non-hazardous alternative tool for the early detection and follow-up of RDS in the NICU. Also, LUS is superior to CXR in the detection of complications of RDS, particularly consolidation, atelectasis and micro-abscesses. This could be of value in reducing exposure to unnecessary radiation doses.

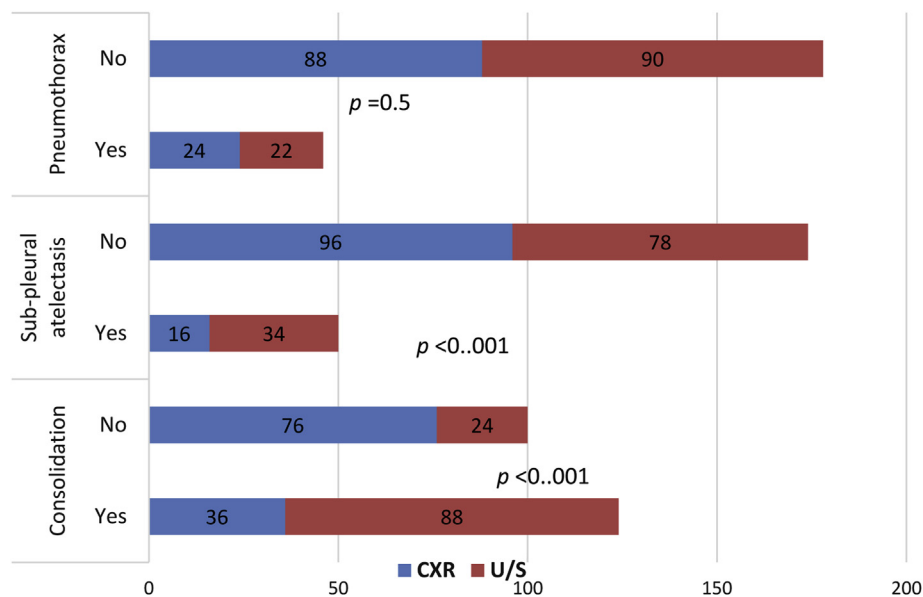


Fig. 5. Comparison between chest X-ray and ultrasound throughout the whole study.

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