Lung Ultrasound to Diagnose Infectious Pneumonia of the Newborns: A Prospective Multicenter Study

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Abstract

Background: Whether Lung ultrasound (LUS) can be used for pathogenic diagnosis is still controversial. This was conducted to test the accuracy and reliability of ultrasound in the diagnosis of pneumonia and to clarify whether ultrasound has diagnostic value for the etiology. *Methods:* A total of 135 neonatal pneumonia patients with an identified pathogen and 50 newborns with normal lungs in the newborn intensive care unit of 10 tertiary hospitals in China were enrolled. The study ran from November 2020 to December 2021. The infants were divided into various groups according to pathogens, the time of infection, the gestational age, the severity of the disease. The distribution of pleural line abnormalities, pulmonary edema, and pulmonary consolidation, as well as the incidence of air bronchogram and pleural effusion based on LUS, were compared between the above groups and between the pneumonia and healthy control groups. *Results:* There were significant differences in pulmonary consolidation. The sensitivity and specificity of the diagnosis of severe pneumonia based on the extent of pulmonary consolidation were 83.3% and 85.2%, respectively. The area under the receiver operating characteristic curve for the identification of mild or severe pneumonia based on the distribution of pulmonary consolidation was 0.776. *Conclusion:* Lung ultrasound has good performance in differentiating the severity of neonatal pneumonia, but cannot be used for pathogenic diagnosis.

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What's Known on This Subject

Lung ultrasound has been successfully used to diagnose neonatal pneumonia, but whether lung ultrasound can be used for pathogenic diagnosis is still controversial.

What This Study Adds

Lung ultrasound has good performance in differentiating the severity of neonatal pneumonia, but cannot be used for pathogenic diagnosis.

Background: Whether Lung ultrasound (LUS) can be used for pathogenic diagnosis is still controversial. This was conducted to test the accuracy and reliability of ultrasound in the diagnosis of pneumonia and to clarify whether ultrasound has diagnostic value for the etiology.

Methods: A total of 135 neonatal pneumonia patients with an identified pathogen and 50 newborns with normal lungs in the newborn intensive care unit of 10 tertiary hospitals in China were enrolled. The study ran from November 2020 to December 2021. The infants were divided into various groups according to pathogens, the time of infection, the gestational age, the severity of the disease. The distribution of pleural line abnormalities, pulmonary edema, and pulmonary consolidation, as well as the incidence of air bronchogram and pleural effusion based on LUS, were compared between the above groups and between the pneumonia and healthy control groups.

Results: There were significant differences in pulmonary consolidation. The sensitivity and specificity of the diagnosis of severe pneumonia based on the extent of pulmonary consolidation were 83.3% and 85.2%,

respectively. The area under the receiver operating characteristic curve for the identification of mild or severe pneumonia based on the distribution of pulmonary consolidation was 0.776.

Conclusion: Lung ultrasound has good performance in differentiating the severity of neonatal pneumonia, but cannot be used for pathogenic diagnosis.

Key words: Lung ultrasound; Neonatal pneumonia; diagnosis.

Word counts: abstract: 218; text: 3341;

1. Background

Pneumonia is one of the main causes of death in infants and young children, especially in developing countries[1, 2]. Pneumonia has the greatest risk of death in the neonatal period, causing approximately 750,000-1.2 million neonatal deaths each year, accounting for 10% of the global child mortality[3]. A survey showed that pneumonia was the leading cause of death in ultralow-birth-weight infants, at approximately 22.5%[4]. As an auxiliary tool, lung ultrasound (LUS) has been increasingly used in the diagnosis of pneumonia in recent years and has good diagnostic performance[5-9]. It has become an international consensus method for the diagnosis of neonatal pneumonia [10, 11]. Compared with chest X-ray, LUS has the advantages of no radiation, low cost, convenience, speed, and accuracy[12-14] and has a higher diagnostic efficacy for pneumonia[15-18].

The current problems with LUS and pneumonia are as follows: (1) To the best of our knowledge, the studies on the diagnosis of neonatal pneumonia using LUS are all small, single-center, retrospective studies, so large, multicenter, prospective studies are needed. (2) There is considerable controversy as to whether LUS can differentiate the etiology of pneumonia. Some studies suggest that LUS imaging can make pathogenic judgments about bacterial vs. non-bacterial pneumonia[19, 20], but our experience is quite different. Therefore, we conducted this multicenter prospective study to try to clarify these problems, thereby contributing to the better clinical application of LUS.

2. Methods

2.1 Research subjects

This study was a multicenter, prospective, descriptive study. Eighteen tertiary hospitals in China signed up to participate in this study, but eight hospitals could not meet the requirements of this study (seven hospitals provided case collection data that did not meet the requirements, and the images of one hospital did not meet the requirements). Neonatal pneumonia patients from the newborn intensive care unit of the other 10 tertiary hospitals were included in the study. The study ran from November 2020 to December 2021. Participating hospitals and personnel had to meet the following requirements: 1) The ultrasound examination personnel received more than 3-6 months of professional training at the professional training base for LUS and passed the assessment. 2) The quality of the provided LUS images was good enough. 3) The hospital did LUS examinations for more than 1 year.

The inclusion criteria of the study subjects were as follows: 1. Patients with a confirmed diagnosis of neonatal pneumonia. The diagnostic criteria were as follows: (1) presence of cough, fever, or dyspnea; (2) fine, moist rales on auscultation; (3) significantly increased or decreased white blood cell count, increased neutrophil concentration or immature/total neutrophil ratio, high erythrocyte sedimentation rate, or high C-reactive protein level; and (4) patchy, blurred shadows of uneven density in the lung fields on chest radiograph or lung consolidations accompanied by air bronchograms or fluid bronchograms; the pleural line was abnormal and the A-lines disappeared, while B-lines or alveolar-interstitial syndrome was visible in the nonconsolidated areas; different degrees of unilateral or bilateral pleural effusion were visible in some infants on LUS. 2. Patients with complete LUS examination and related necessary auxiliary examinations within 1-2 hours after clinical diagnosis of pneumonia. 3. Patients with clear etiological evidence. The etiological diagnosis came from a positive result in any of the following tests: 1) blood culture; 2) sputum culture (the same bacterium more than two times); 3) polymerase chain reaction; 4) the tuberculosis test (T-spot) was positive

and sputum smears were positive for acid-fast bacilli twice; and 5) gene sequencing. Exclusion criteria: 1. severe congenital malformations; 2. chromosomal or genetic diseases; 3. no consent from family members; 4. incomplete data, or the ultrasound image collection did not meet the criteria.

The newborns enrolled in the study were still treated according to the local diagnosis and treatment plan. LUS images of five newborns with normal lungs were selected from each hospital as the control group, including at least one preterm infant. This study was approved by the Ethics Committee of Maternal and Child Health Care Hospital, Chaoyang District, Beijing (No. 2011-LC-Ped-01), and the participating hospitals. Informed consent was obtained from the baby's guardian before collecting the data.

2.2 Demographic and clinical data of study subjects

In this study, the general information of the study subjects, such as gestational age, sex, delivery method, and birth weight, were analyzed. The time interval between clinical examination and the acquisition of LUS images was no more than 2 hours. After collection, the study subjects were divided into groups by different criteria: 1. According to the pathogen(s) detected, the subjects were divided into the bacterial infection group, the viral infection group, the atypical pathogen (mycoplasma or chlamydia) group, the fungal infection group, and the mixed infection group (with two or more pathogens). After the patient was discharged from the hospital, the final diagnosis of the pathogen was made based on the clinical data and the test results. 2. The infants were divided into the full-term group and the preterm group according to their gestational age. 3. According to the time of infection, the newborns were divided into congenital infectious pneumonia (within 48 hours after birth), nosocomial infectious pneumonia (48 hours after hospitalization), and community-acquired pneumonia. 4. According to the criteria (adapted from the Pediatric Infectious Diseases Society–Infectious Diseases Society of America criteria[21]) in Table S1, the patients were divided into the mild pneumonia group and the severe pneumonia group .

2.3 LUS

LUS examinations were performed by physicians who had performed LUS examinations for more than 1 year. Before the start of the study, three 12-region LUS images were collected from each participating center and sent to an ultrasound expert for review (J.L). The personnel collecting the images were further trained until they met the requirements of image acquisition. Those who eventually could still not meet the requirements were not included in the multicenter study. The doctor who performed the LUS examination and the doctor who supervised the patient were different doctors, and the doctor who performed the LUS was blinded to the results of the clinical examination and etiological examination. Instrument and equipment probe selection and operation methods strictly followed relevant guidelines [10, 22]. At the time of examination, the bilateral lungs were divided into 12 regions based on the anterior axillary line, the posterior axillary line, and the nipple line. Patients were examined in the decubitus, lateral, and prone positions using the longitudinal and transverse approaches[22].

For the description of the LUS findings in each of the 12 regions, we referred to the *Protocol and Guidelines for Point-of-Care Lung Ultrasound in Diagnosing Neonatal Pulmonary Diseases Based on International Expert Consensus* [10]. In this study, the abnormal LUS signs were as follows: 1. abnormal pleural lines, including a broken, thickened, blurred, and disappeared pleural line; 2. pulmonary edema signs, including the B-line, confluent B-line, alveolar-interstitial synthesis, compact B-line, and white lung; 3. pulmonary consolidation and air bronchogram; 4. comorbidities such as pleural effusion and pneumothorax.

According to the 12-region method, the total number and distribution of pleural line abnormalities, pulmonary edema signs, and pulmonary consolidation in each subject was counted. For example, if the total number of regions involved in pulmonary consolidation was 3, it was recorded as 3. The incidence of air bronchogram and pleural effusion was analyzed. Then, the incidence and the number of regions in which LUS images were distributed were compared between different groups. The LUS images that were distributed in the unilateral or bilateral lungs were compared between patients with pneumonia caused by different pathogens. According to the area involved in the pulmonary consolidation, the size of the pulmonary consolidation was divided into mild pulmonary consolidation (the consolidation extent was limited to the pleural

line, involving only one intercostal space, see Figure 1), moderate pulmonary consolidation (the consolidation involved 2-3 intercostal spaces, see Figure 1), and extensive lung consolidation (involving more than three intercostal spaces, see Figure 1). The correlation between the number of areas involved in pulmonary consolidation and the presence of mild or severe pneumonia was analyzed. The correlation between extensive pulmonary consolidation and mild and severe pneumonia was analyzed.

3. Statistical analysis

Bacterial pathogens are easy to detect relative to other pathogens and, based on previous experience, account for approximately 70% of all pathogens that can be detected. Assuming that bacterial pneumonia can be distinguished from other pathogenic pneumonia by lung ultrasound, AUC values of 0.7–0.79 is a fair test[23], and the lowest value of 0.7 is taken to estimate the sample size. In this case, considering alpha = 0.05 and beta = 0.10, n=96.

All data were statistically analyzed with SPSS version 25.0 (IBM Inc., Chicago, IL, USA). Continuous data were evaluated for normality and homogeneity of variances by the Kolmogorov–Smirnov test and analysis of variance, respectively. The data did not satisfy the normal distribution or the homogeneity of variances so they were compared by the Kruskal-Wallis H test or the Mann-Whitney U test. Categorical data were compared by the chi-squared test or Fisher's exact test. The specificity and sensitivity of the extensive lung consolidation for distinguishing mild and severe pneumonia were calculated based on this test. The relationship between the number of areas involved in pulmonary consolidation and mild or severe pneumonia was analyzed using the receiver operating characteristic curve (ROC), and the Youden index of the curve was calculated.

We present summary statistics as median (interquartile range [IQR]) for continuous variables and frequencies (percentages) for categorical variables. All tests were two-sided, and a p value <0.05 was considered a significant difference.

4. Results

4.1 Demographics and general information

A total of 135 cases of neonatal pneumonia with confirmed pathogens were collected, with a gestational age of 25-42^{+4} weeks, birth weight of 700-4350 g. Fifty newborns with normal lungs were enrolled as a control group (Figure 1), with gestational age of 25^{+4} to 41^{+1} weeks, birth weight of 750-4010 g, A comparison of demographic characteristics between two groups is presented in Table 1. In the pneumonia group, there were 135 patients with abnormal pleural lines, and the involved areas were in 1-12 regions; 126 patients had pulmonary edema signs, which were in 1-12 regions; 135 patients had pulmonary consolidation, which were in 1-12 regions; and there were 37 patients with air bronchogram and 19 patients with pleural effusion. In the control group, there were no patients with pleural line abnormalities, pulmonary consolidation, air bronchogram, or pleural effusion, though six patients had pulmonary edema signs in regions 1-3. The basic demographic data of children with pneumonia and healthy newborns were not significantly different, but the distribution of LUS images was significantly different (Table 2)

4.2 Comparison of lung ultrasound in different groups

Among the 135 children, 72 were infected with bacteria, 20 had mixed infections, 19 had viral infections, 12 had atypical pathogen infections, and 12 had fungal infections (Figure 2). There was no significant difference in the distribution of the LUS images between the groups after pairwise multiple comparison (Table 2).

The bacterial infection group was divided into the bacillus group (49 cases, Figure 2) and the coccus group (23 cases, Figure 2). There was no significant difference in LUS images between the two groups (Table 2).

There were 61 patients with community-acquired pneumonia, 37 patients with congenital pneumonia, and 37 patients with nosocomial pneumonia (Figure 2). The LUS images were similar between the three groups (Table 2).

There were 69 full-term infants and 66 premature infants (Figure 2). The differences in LUS manifestations between the two groups were not significant (Table 2).

There were 108 patients in the severe group (Figure 1, 2) and 27 patients in the mild group (Figure 1). There were no significant differences in pleural line abnormalities, pulmonary edema signs, or pleural effusion between the severe group and the mild group, but there were significant differences in pulmonary consolidation and air bronchogram between two groups. The ROC curve of pulmonary consolidation (total number of regions) to distinguish severe and mild pneumonia had an area under the curve of 0.776. The Youden index was 3.5, the sensitivity was 77.8%, and the specificity was 63% (Table S2). The sensitivity of LUS images of extensive pulmonary consolidation to distinguish severe and mild pneumonia was 83.3%, and the specificity was 85.2% (Table 3).

There were 68 patients with bilateral pleural line abnormalities in the bacterial infection group, 18 patients in the mixed infection group, 16 patients in the viral infection group, 10 patients in the atypical pathogen infection group, and 12 patients in the fungal infection group. There were four patients with unilateral pleural line abnormalities in the bacterial infection group, two in the mixed infection group, three in the viral infection group, two in the atypical pathogen infection group, and zero in the fungal infection group. There were 58 patients with bilateral pulmonary edema signs in the bacterial infection group, 16 in the mixed infection group, 14 in the viral infection group, 10 in the atypical pathogen infection group, and 10 in the fungal infection group. There were 11 patients with signs of unilateral pulmonary edema in the bacterial infection group, two in the mixed infection group, three in the viral infection group, one in the atypical pathogen infection group, and one in the fungal infection group. There were 53 patients with bilateral pulmonary consolidation in the bacterial infection group, 16 in the mixed infection group, 12 in the viral infection group, nine in the atypical pathogen infection group, and 11 in the fungal infection group. There were 19 patients with unilateral pulmonary consolidation in the bacterial infection group, four in the mixed infection group, seven in the viral infection group, three in the atypical pathogen infection group, and one in the fungal infection group. There was no significant difference in unilateral or bilateral distribution between groups based on the pairwise multiple comparison (Figure S1).

5. Discussion

To the best of our knowledge, this is the first multicenter prospective ultrasound study of neonatal pneumonia based on the identification of the pathogen. We compared neonatal pneumonia with different pathogens, different degrees of infection, different infection times, and different gestational ages. The results showed that (1) LUS can well diagnose neonatal pneumonia, but there was no difference in the LUS signs of neonatal pneumonia between different pathogens, different infection times, or different gestational ages. (2) The size and extent of the pulmonary consolidation has a high sensitivity (83.3%) and specificity (85.2%) for the distinction of severe and mild neonatal pneumonia.

With the widespread application of LUS, Tsung et al.[24] proposed that pulmonary consolidation combined with air bronchogram suggested bacterial infectious pneumonia. In contrast, in the study by Öktem et al.[25], 50 cases (100%) of viral pneumonia all had pulmonary consolidation combined with air bronchogram. In the study by Buonsenso et al.[19], among the 76 cases of viral pneumonia and 43 cases of atypical pathogenic pneumonia, 25 (32.9%) and 26 cases (60.5%) were associated with air bronchogram. In this study, the differences in the incidence of air bronchogram between pneumonia patients with different pathogens was not significant. Unlike the above studies based on other auxiliary examinations, this study was based on the study of the clear etiology and may therefore be more accurate. Air bronchogram is the presence of air in bronchioles and terminal bronchioles in pulmonary consolidation .[26]. It is only associated with pathological changes at different stages of disease development[27], not a sign of bacterial or viral infection. For example, the typical LUS manifestations of neonatal respiratory distress syndrome are pulmonary consolidation and air bronchogram[28, 29].

Some studies suggest that bilateral pulmonary consolidation mostly occurs in viral pneumonia while unilateral pulmonary consolidation mostly occurs in bacterial pneumonia[19, 20]. In the study by Buonsenso et al.[19],

bilateral pulmonary consolidation was found in 0.09% of bacterial pneumonia, 46.15% of viral pneumonia, and 31.58% of atypical pneumonia cases. In contrast, Malla et al.[30] found that bilateral pulmonary consolidation occurred in 35.6% of bacterial pneumonia cases and 11.1% of viral pneumonia cases. The study of coronavirus disease 2019 (COVID-19) by Zieleskiewicz et al.[31] found that 17% of pulmonary consolidation occurred in one of the lungs, and 15% of pulmonary consolidation occurred in both lungs. The size of pulmonary consolidation has also been used to distinguish between bacterial pneumonia and viral pneumonia. Malla et al.[30] believed that pulmonary consolidation of viral pneumonia was <0.5 cm. Berce et al.[20] set the threshold of 2.1 cm of pulmonary consolidation for the identification of bacterial vs. viral pneumonia. In a study of bronchitis, Biagi et al.[32] found that when pulmonary consolidation was greater than 1 cm, the likelihood of bacterial bronchitis was high. Buonsenso et al.[19] found that 55.22% of bacterial pneumonia, 35.38% of viral pneumonia, and 44.74% of atypical pneumonia had pulmonary consolidation of 1.5-4 cm. The three cases of COVID-19 reported by Hernández et al.[33] each had multiple pulmonary consolidations with diameters ranging from 2 to 24 mm. According to the above reports, due to differences between subjects, the location and size of pulmonary consolidation in patients with viral or bacterial pneumonia are not specific. The extent of pulmonary consolidation and the total area of the lung involved are only related to the severity of the disease and are not affected by the etiology of the infection. This study did not find differences in pleural lines, pulmonary edema signs, distribution of pulmonary consolidation, or the involved areas between bacterial infection, atypical pathogen infection, viral infection, mixed infections, and fungal infections. Pulmonary consolidation is caused by alveolar exudate[34]. Its size depends on the degree of air loss from the alveoli[35]. It is only a nonspecific sign of pneumonia. Pneumonia caused by any etiology or pathogen can result in pulmonary consolidation. In addition, LUS sometimes has difficulty measuring the actual size of each pulmonary consolidation[36]. Therefore, it is difficult to distinguish the etiology of neonatal pneumonia from the size and distribution of pulmonary consolidation.

Through this multicenter, prospective study, we have confirmed that the degree and extent of pulmonary consolidation in neonatal pneumonia with different pathogens were only related to the severity of the disease, and extensive pulmonary consolidation could be used to well distinguish between severe and mild neonatal pneumonia. The size of pulmonary consolidation only represents the degree of lung tissue damage by pneumonia, which is consistent with the pathology of pulmonary consolidation. The area under the ROC curve correlating the area of pulmonary consolidation and the severity of pulmonary consolidation was 0.776. When the area of pulmonary consolidation was [?] 4, the sensitivity was 77.8%, and the specificity was 63%. Bitar et al.[37] found that the number of pulmonary consolidations in pneumonia was correlated with the degree of PO_2/F_iO_2 deterioration, and the results of this study were similar. Mafort et al.[38] believed that pulmonary consolidation was related to the severity of pneumonia. Kong et al.[39] found that pulmonary consolidations were significantly more numerous in severe pneumonia. However, Alharthy et al.[40] found that by the time patients with severe pneumonia were discharged, the LUS signs of pulmonary consolidation had been significantly reduced. This evidence indicates that the imaging manifestations of pulmonary consolidation in pneumonia can only represent the disease process of neonatal pneumonia, and it is difficult to distinguish the pathogens of neonatal pneumonia based on pulmonary consolidation.

The shortcomings of this study are as follows: First, the pathogens were unevenly distributed, being mainly bacteria, and the sample size of some pathogens, such as mycoplasma, chlamydia, and fungi, was small. More experiments containing a larger number of these pathogens are needed to confirm the above findings. Second, there were more severe pneumonia patients than mild patients, which may have influenced the specificity of distinguishing mild from severe pneumonia based on the extent of pulmonary consolidation. In the future, more mild pneumonia patients need to be included to confirm the conclusions of this study.

6. Conclusion

LUS is a radiation-free, convenient, efficient auxiliary tool for the diagnosis of neonatal pneumonia. However, LUS has difficulty distinguishing neonatal pneumonia with different pathogens, different gestational ages, and different infection times. The size and extent of pulmonary consolidation has good performance in judging the severity of neonatal pneumonia. These LUS features will help clinicians more accurately manage

patients.

Contributors' Statement:

Dr Jing Liu conceptualized and designed the study, drafted the initial manuscript, obtained funding and take responsibility for the integrity of the data and the accuracy of the data analysis.Dr Hai-Ran Ma conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript.Drs Peng Jiang, Yan-Lei Xu, Xiu-Yun Song, Jie Li, Li-Han Huang, Ling-Yun Bao and Rui-Yan Shan designed the study, collected data, carried out the initial analyses, and reviewed and revised the manuscript.All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Abbreviation List

AB: air bronchogram

APL: abnormal pleural lines

IQR: interquartile range

LUS: Lung ultrasound

PE: pleural effusion

PES: pulmonary edema signs

PS: pulmonary consolidation

ROC: receiver operating characteristic curve

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Table 1. Demographic and Descriptive Information

Variable	Pneumonia (N=135)	control subjects (N=50)	*P* values
Demographic information			
Gestational Age, wk	37.8(5.6)	37.1(8.4)	0.72
Birth Weight, g	3(1.7)	2.7(1.9)	0.99
Sex[b]			
Male	84(62)	26(52)	0.24
Female	51(38)	24(48)	
Delivery method[b]			
Cesarean delivery	58(43)	26(52)	0.32
Vaginal delivery	77(57)	24(48)	

a, Data are presented as median (IQR)

b, Data are presented as No. (%).

Table2. Comparison of the LUS manifestations in different groups.

	median (IQR)	median (IQR)	median (IQR)		No. (%)	No. (%)
Group	APL	PES	PC	PC	AB	PE
Pneumonia (N=135)	8(6)	7(7)	4(5)	4(5)	37(27)	19(14)
Control subjects (N=50)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
P values	<0.001	<0.001	<0.001	<0.001	<0.001	0.004
Bacteria (N=72)	10(6)	8(8)	4(5)	4(5)	17(22)	8(10)
Mixed infections (N=20)	8(6)	6(5)	5(6)	5(6)	7(35)	4(20)
Viral infections (N=19)	8(8)	4(5)	3(5)	3(5)	5(26)	2(11)
Atypical pathogen (N=12)	9(6)	7(8)	7(6)	7(6)	3(25)	3(25)
Fungal infections (N=12)	8(7)	8(7)	5(2)	5(2)	5(42)	2(17)
P values	0.62	0.10	0.49	0.49	0. 64	0.55
bacillary pneumonia(N=49)	10(6)	8(7)	4(4)	4(4)	14 (29)	6 (12)
coccal pneumonia(N=23)	12(7)	8(8)	4(5)	4(5)	3 (13)	2 (9)
P values	0.82	0.89	0.50	0.50	0.23	>0.99
community-acquired pneumonia (N=61)	8(8)	6(5)	4(6)	4(6)	15(25)	12(20)
Congenital pneumonia(N=37)	8(6)	8(5)	4(3)	4(3)	8(22)	3(8)
Nosocomial pneumonia(N=37)	11(6)	7(8)	6(4)	6(4)	14(38)	4(11)
P values	0.22	0.51	0.10	0.10	0.25	0. 24
Full-term(N=69)	8(7)	6(5)	4(5)	4(5)	17(25)	11(16)
Preterm(N=66)	10(6)	7 (5)	5(4)	5(4)	20(30)	8(12)
P values	0.23	0.33	0.25	0.25	0.56	0.52
Severe pneumonia(N=108)	10(6)	7(7)	5(4)	5(4)	35(32)	16 (15)
Mild pneumonia(N=27)	6(8)	6(5)	2 (2)	2 (2)	2(7)	3 (11)
P values	0.15	0.37	<0.001	<0.001	0.01	0.76

Abbreviations: APL, abnormal pleural lines; PES, pulmonary edema signs; PS, pulmonary consolidation;

AB, air bronchogram; PE, pleural effusion.

Table3. The sensitivity and specificity of LUS images of extensive pulmonary consolidation to distinguish severe and mild pneumonia

Extensive pulmonary consolidation	Severe pneumonia	Mild pneumonia	Total	Sensitivity (a/a+c)	Specific
Present	90(a)	4(b)	94(a+b)	83.3%	85.2%
Not present	18(c)	23(d)	41(c+d)		
Total	108 (a+c)	27(b+d)	82(a+b+c+d)		

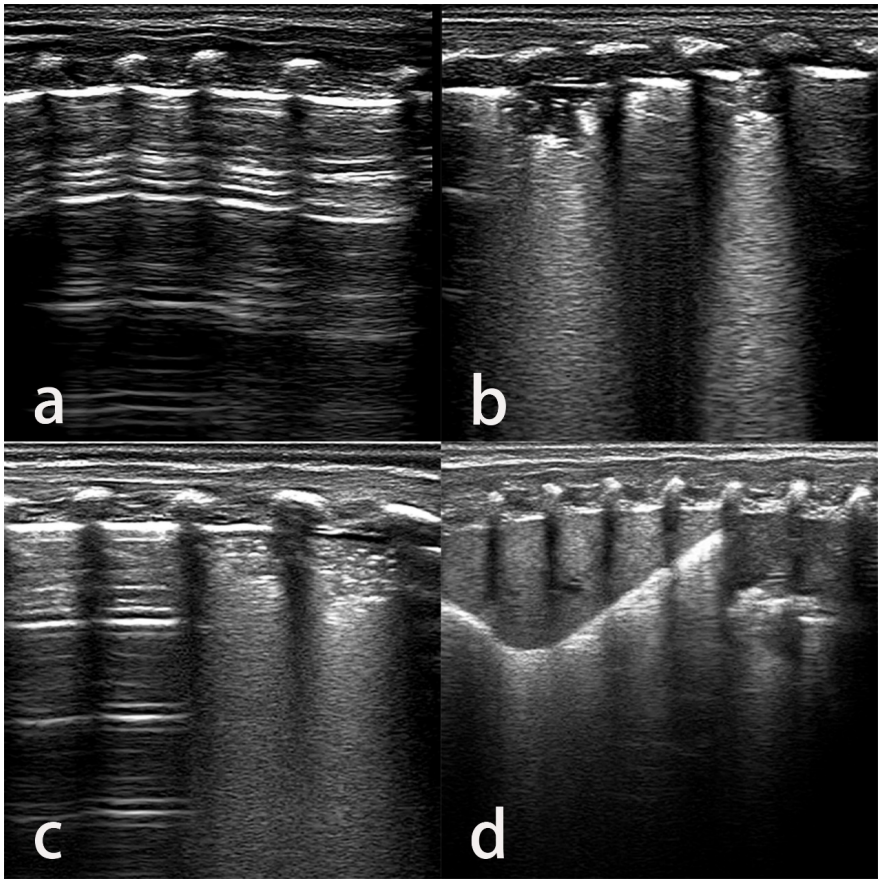


Figure1: Lung ultrasound findings of normal lung and pneumonia in neonates: a. Normal lung b. Mild pulmonary consolidation (mild pneumonia): the consolidation extent was limited to the pleural line, involving only one intercostal space; c. Moderate pulmonary consolidation (mild pneumonia): the consolidation involved 2-3 intercostal spaces. d. Extensive lung consolidation (severe pneumonia): involving more than three intercostal spaces.

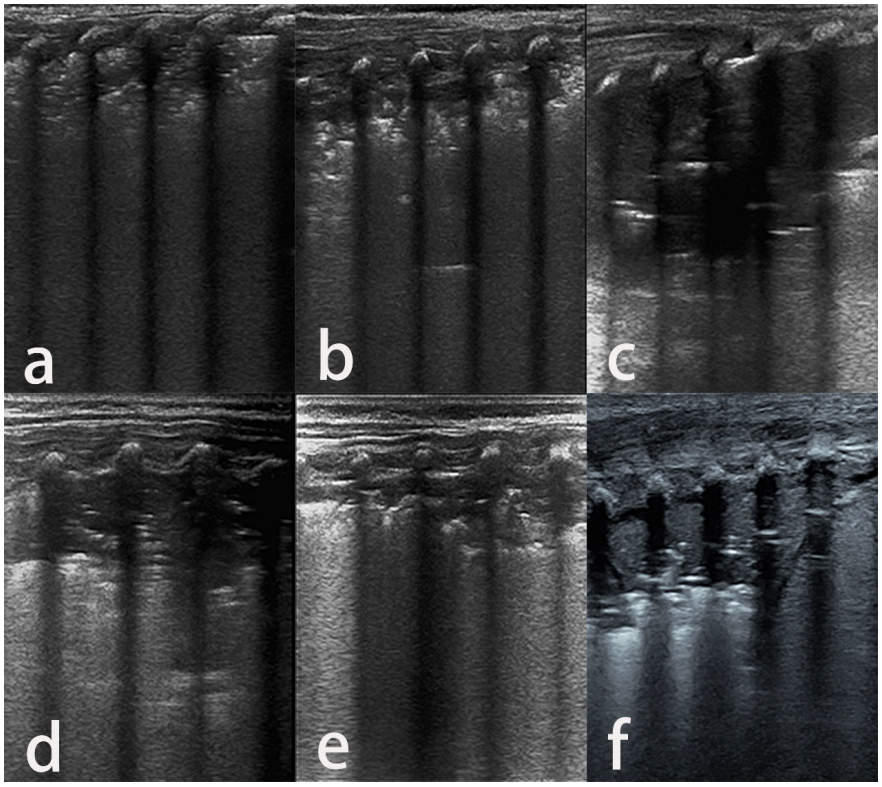
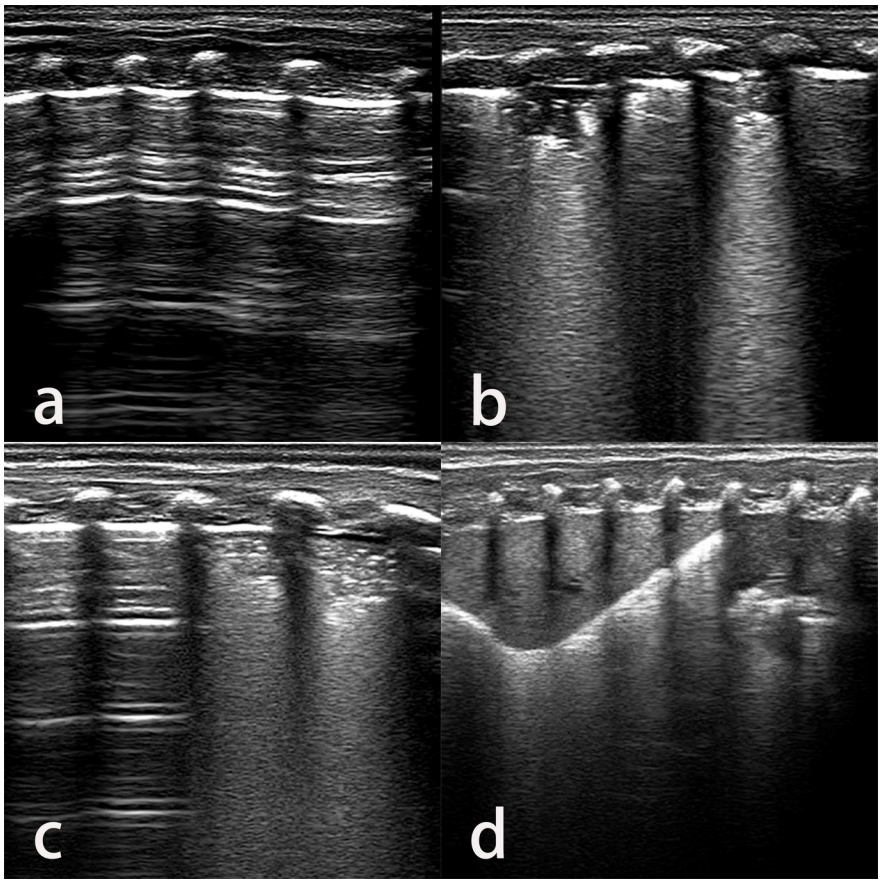


Figure2: Lung ultrasound findings of severe pneumonia in neonates: a. Pseudomonas aeruginosa Pneumonia (nosocomial pneumonia); gestational age, 28 wk plus 3 d; b. Streptococcus pneumonia (congenital pneumonia); gestational age, 41 wk plus 3 d; c. Pneumonia infected by Staphylococcus aureus and Escherichia coli (nosocomial pneumonia); gestational age, 28 wk; d. Respiratory syncytial virus pneumonia (community-acquired pneumonia); gestational age, 40 wk; e. Chlamydia trachomatis pneumonia (community-acquired pneumonia); gestational age, 38 wk plus 2 d; f. Candida albicans pneumonia (nosocomial pneumonia) gestational age, 27 wk plus 6 d.



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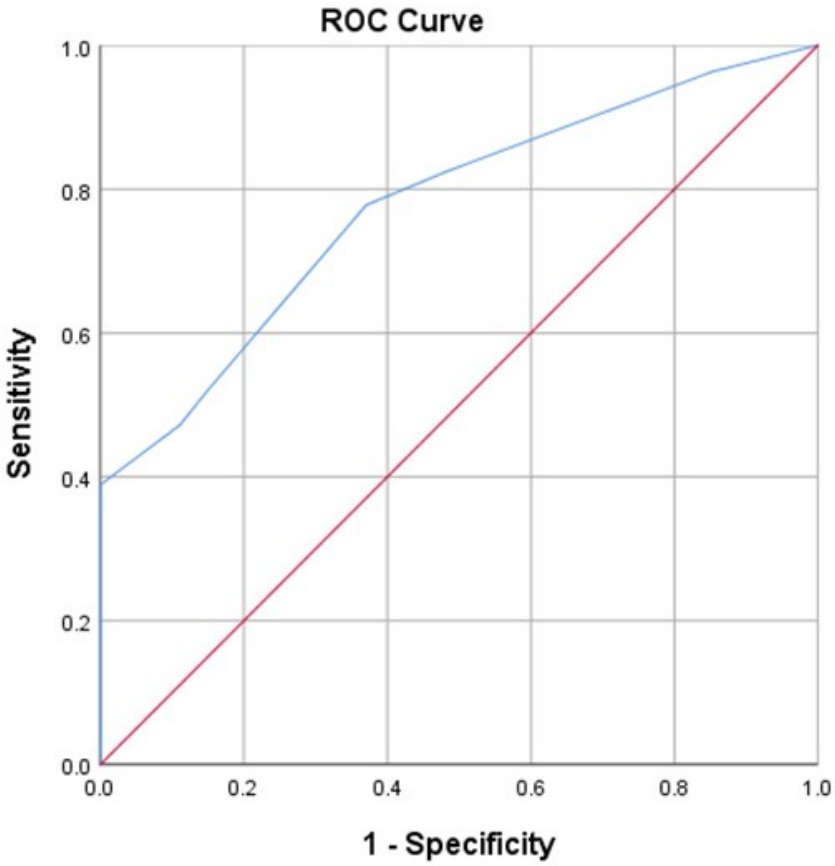

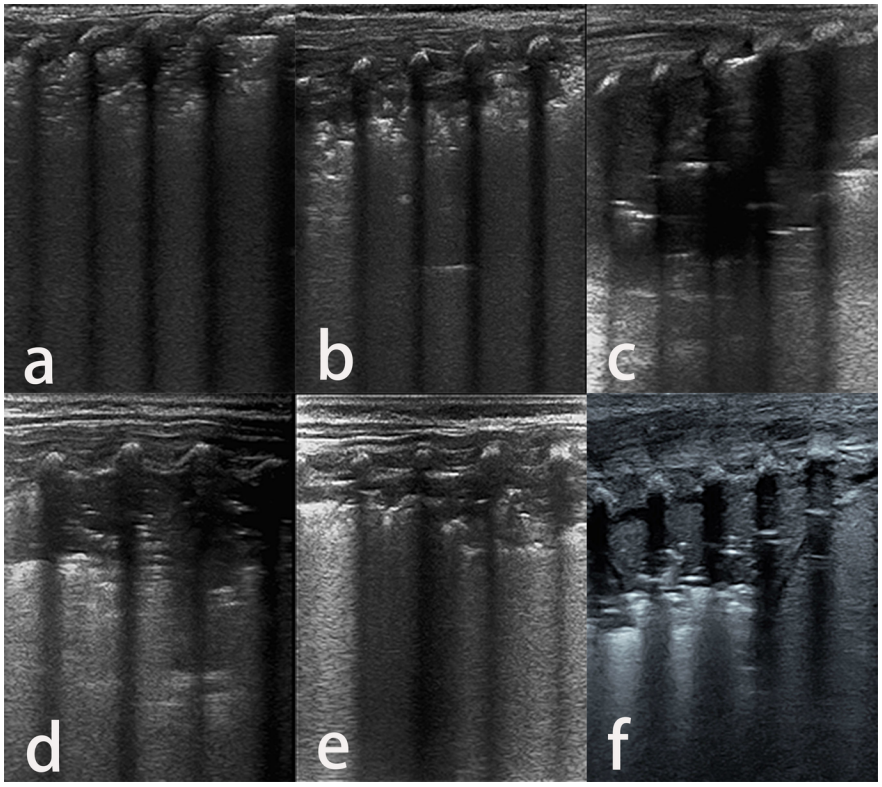

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