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RESEARCH ARTICLE

Characteristics of chest ultrasound performed by neonatologists in acute viral respiratory infection and its relationship with respiratory support and mortality

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Abstract

Background: *Respiratory viruses are a frequent cause of infection in neonatology. Point-of-care lung ultrasound (LU) and targeted neonatal echocardiography (TnE) allow pulmonary and hemodynamic assessment at the patient's bedside.* **Methods:** *The aim of this study was to describe the pattern of alterations found by LU and to assess the hemodynamic status in neonates diagnosed with viral infection (reverse transcription polymerase chain reaction) during 2018-2023. LU was performed in 10 regions, and a semi-quantitative scale LU score (LUS) was calculated. TnE was performed if pulmonary hypertension (PH) was suspected. The thymus was measured by ultrasound if there was evidence of increased dimensions on chest X-ray or during LU.* **Results:** *Forty-seven patients were studied (35 severe acute respiratory syndrome coronavirus 2, four respiratory syncytial virus, four rhinovirus, three influenza, and one parainfluenza). LU showed an interstitial pattern of B-lines in 94%, pleural line anomalies in 85%, coalescing B-lines in 60%, and consolidations in 51% (71% posteriorly). About 30% had PH. An increased thymus was shown in 23%. LUS showed a significant median difference between ventilatory support and a positive correlation with FiO_2 used. Consolidations and the presence of PH were associated with mortality; an increased thymus was shown protective.* **Conclusion:** *Ultrasound at the patient's bedside allows the classification and detection of the seriously ill patient (presence of consolidations and PH) allowing timely intervention. As a clinical finding, an increased thymus was shown to be a protective factor against mortality and could represent a marker of adequate immune response.*

Keywords: *POCUS. Severe acute respiratory syndrome coronavirus 2. Lung ultrasound. Respiratory viruses. Thymus. Pulmonary hypertension.*

Características del ultrasonido torácico realizado por neonatólogos en infección respiratoria viral aguda y su relación con soporte respiratorio y mortalidad

Resumen

Introduction: *Los virus respiratorios son causa frecuente de infección en neonatología. El ultrasonido realizado por neonatólogos permite la valoración hemodinámica y por ultrasonido pulmonar (UP) a la cama del paciente.* **Métodos:** *El objetivo*

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fue describir el patrón de alteraciones encontradas por UP y valorar el estado hemodinámico en neonatos con diagnóstico de infección viral (RT-PCR) durante el periodo 2018 a 2023. Se realizó un UP en 10 regiones y se calculó una escala semicuantitativa (ESC), así como ecocardiografía ante la sospecha de hipertensión pulmonar (HP). El timo se midió por ultrasonido si se mostraba con dimensiones incrementadas en la radiografía de tórax o durante el UP. **Resultados:** *Se analizaron 47 pacientes (35 SARS-CoV-2, 4 virus sincicial respiratorio, 4 rinovirus, 3 influenza y 1 parainfluenza). El UP mostró patrón intersticial de líneas-B en un 94%, anomalías de la línea pleural en un 85%, líneas-B coalescentes en un 60% y consolidaciones en el 51% (71% posteriores). Se encontró HP en un 30%. Un timo incrementado en dimensiones se evidenció en el 23%. La ESC mostró una diferencia significativa de medianas entre el soporte ventilatorio y una correlación positiva con la FiO_2 utilizada. Consolidaciones y la presencia de HP se asociaron a mortalidad; el timo incrementado se mostró protector.* **Conclusiones:** *El ultrasonido a la cama del paciente permite la clasificación y detección del paciente gravemente enfermo (presencia de consolidaciones e HP) permitiendo una intervención oportuna. Como hallazgo clínico, el timo incrementado se mostró como factor protector frente a mortalidad, podría ser un marcador de adecuada respuesta inmunitaria.*

Palabras clave: *POCUS. SARS-CoV-2. Ultrasonido pulmonar. Virus respiratorios. Timo. Hipertensión pulmonar.*

Introduction

In developed countries, infants and preschoolers have an average of 6-10 viral infections per year, while schoolchildren and adolescents have about 3-5[1]. Upper airway infections usually do not constitute serious disease but result in missed school days and increased healthcare expenditures. Approximately 6.6 million children under the age of 5 die annually, with pneumonia leading to 1.3 million deaths[2].

Systematic surveillance of nosocomial respiratory viral infections in newborns has proved that they are more frequent than previously assumed, even in asymptomatic infants. Viral infections in neonatology are related to increased length of hospital stay and have been associated to bronchopulmonary dysplasia (BPD) and necrotizing enterocolitis[3,4].

Lung ultrasound (LU) has shown good diagnostic performance for pneumonia in children. According to a recent meta-analysis, LU has sensitivity of 96% and specificity of 93% (area under the curve [AUC] 0.98), superior to traditional radiography, and comparable to the clinical construct[5]. Although some characteristics to differentiate between viral and bacterial pneumonia by LU (extension of the consolidation and the presence of fluid bronchogram) have been described in children, in newborns, the difference is not clear[6]. Hai-Ran and cols demonstrated that LU was useful in newborns to detect pneumonia severity but could not differentiate etiology[7]. In a recent systematic review on viral bronchiolitis, semi-quantitative lung scores (LUS) correlated with the clinical course, were able to predict admission in the intensive care unit, length of hospital stay, and the need for respiratory support[8].

Initial descriptions of LU findings in newborns with respiratory viral infections included pleural line abnormalities (thickening and/or irregularities, smaller "subpleural" consolidations), individual or confluent B-Lines, and usually < 0.5 cm consolidations (although sickest patients showed consolidations that spanned several intercostal spaces)[9]. During the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, viral surveillance increased in our country. Our group previously described 32 newborns with SARS-CoV-2 infections (included in this report) where pleural line abnormalities, B-Line interstitial pattern, confluent B-Lines, and consolidations were found[10]. An extended LU semi-quantitative score (eLUS) was calculated to assess lung involvement that correlated with the degree of disease severity and respiratory support. Given the scarcity of information about the utility of LU in newborn respiratory viral infections, we aim to describe LU findings in our population.

Methods

The study was performed at a Tertiary Level Referral Hospital in Mexico City between January 2018 and July 2023. Newborns with respiratory symptoms and a positive reverse transcription polymerase chain reaction (RT-PCR) for viral infection by nasal swab were assessed by the Hemodynamic Consultation and Ultrasound of the Critically Ill Newborn team[11]. LU and targeted neonatal echocardiography (TnECHO) were performed with the available equipment, either a hand-held equipment protected with a silicone sleeve (Konted™, Beijing China, Linear transducer, 7.5-10.0MHz) or the neonatal intensive care unit (NICU) point of care ultrasound machine available. During 2018-2019, Acuson ×300™ (Siemens Healthcare, Munich, Germany; LU with a 8-14 MHz hockey stick probe and TnECHO with a 9 MHz phased array

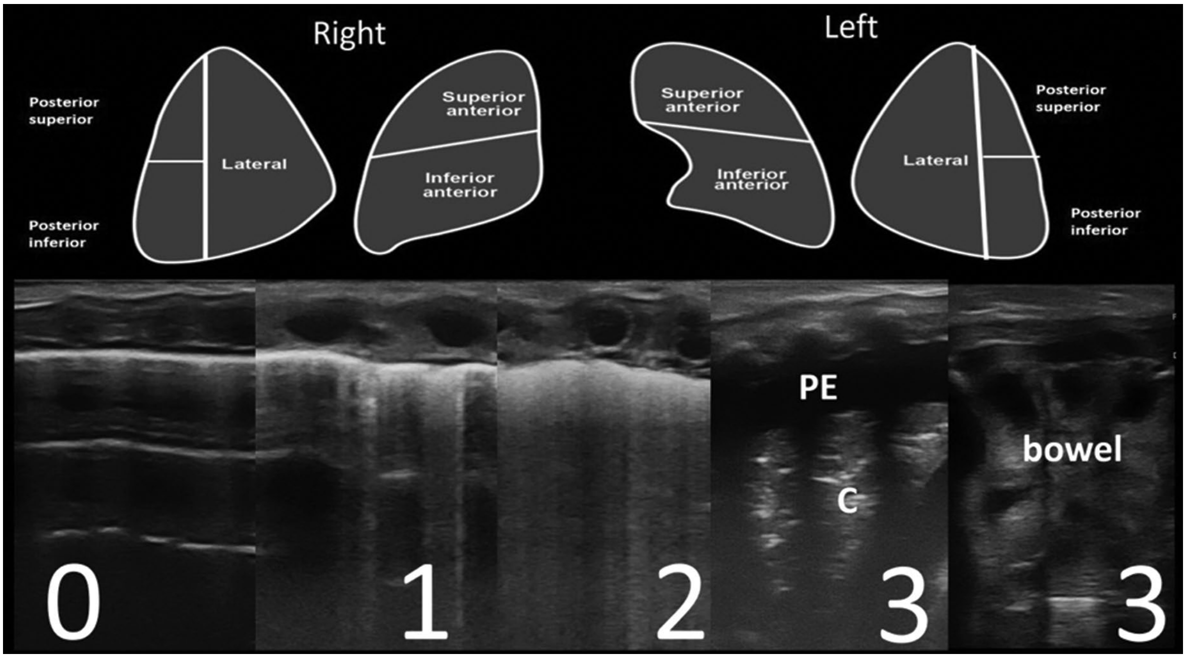

Figure 1. Extended lung ultrasound score. Extended lung ultrasound semi-quantitative score was scored: **0**, defined by the presence of A-lines and pleural sliding; **1**, defined as the presence of ≥ 3 well-spaced B-lines; **2**, defined as the presence of coalescent B-lines or white lung; and **3**, defined as the presence extended consolidations, pleural effusion, or absence of lung in the case of lung malformations.

transducer); and during 2020-2023 Vivid *E90*™ (GE Medical Systems, Milwaukee, WI, USA; LU with a hockey stick probe 8-18 MHz and TnECHO with a 12 MHz phased array transducer).

Ten regions were explored (anterior superior and inferior, lateral, and posterior superior and inferior, right and left)[12]. An extended semi-quantitative LU score (eLUS) was calculated through both transverse and longitudinal scans scoring: 0 (defined by the presence of A-lines and pleural sliding); 1 (defined as the presence of ≥ 3 well-spaced B-lines); 2 (defined as the presence of coalescent B-lines or white lung); and 3 (defined as the presence extended consolidations, pleural effusion, or absence of lung in the case of lung malformations)[13]. Fig. 1 depicts the lung areas and the semi-quantitative scale used described by Loi et al.,[14] adapted from an adult score[15].

Pulmonary hypertension was defined as follows: (a) flattening of interventricular septum in end-systole (short axis view at the level of the papillary muscles) and (b) right ventricular systolic pressure (RVSP), estimated from tricuspid regurgitant (TR) jet, of ≥ 40 mmHg. The pressure gradient between the right ventricle (RV) pressure and the right atrium pressure was estimated using the modified Bernoulli equation ($4 \times TR^2$) if TR was measurable. Right atrium pressure was estimated as 5 mmHg and RVSP was calculated as $4 \times TR^2 + 5$ mmHg. c) Bidirectional or right-to-left shunt through a patent ductus arteriosus or foramen ovale[16]. Ventricular dysfunction was defined for the RV as tricuspid annular plane systolic excursion and/or RV fractional area change under two standard deviations of normal values. For the left ventricle, Simpsons biplane and fractional shortening were considered[17].

If thymic shadow on conventional radiography or ultrasound impressed augmented, transversal diameter as well as the longitudinal areas were measured by ultrasound and the thymic index was calculated[18].

Approval from the Ethics Committee was obtained for the analysis of routinely obtained and anonymized clinical data, so informed consent was waived. Statistical analysis was performed using the Statistical Package for the Social Sciences Version 23.0 (IBM Corp.). Continuous variables showed non-parametric distribution. Statistics are presented as median (interquartile ranges [IQR]) for continuous variables and frequencies (percentage) for categorical variables. A chord diagram with ultrasonographic cardiopulmonary features of viral infection was constructed. Median difference of eLUS between levels of pulmonary support was compared through Kruskal-Wallis test. There correlation between eLUS and FiO_2 was tested with Spearman test. Rank difference between eLUS and FiO_2 needed between survivors and non-survivors was tested with Mann–Whitney U-test. To quantify the association of ultrasonographic findings and mortality odds ratio (OR) with 95% confidence interval (CI) were calculated.

Results

From January 2018 to September 2023, 47 newborns with a positive respiratory viral panel and respiratory symptoms were evaluated. Assessed newborns had a median age at birth (median [IQR]) of 37 (32, 38) weeks of gestation (WOG), with a corrected age at study of 39 (36, 42) WOG and weight of 2,610 (1770 –, 3,000 g. Of the 47 viruses identified, 74% corresponded to SARS-CoV-2, 9% to respiratory syncytial virus (RSV), 9% to rhinovirus, 6% to influenza, and 2% to parainfluenza. The main working diagnosis was term newborn with respiratory distress 34%, preterm newborn 30%, surgical newborn 17%, former preterm with established BPD 9%, congenital heart disease 4%, Down syndrome 4%, and diaphragmatic hernia 2% (Table 1).

Patients were evaluated on mechanical ventilation in 51%, continuous positive airway pressure 8.5%, nasal cannula oxygen in 23.5%, and intermittent (indirect) oxygen in 17%. The symptomatology consisted in the appearance or worsening of respiratory distress in 83% (eight newborns with SARS-CoV-2 were asymptomatic regarding respiratory symptoms). About 32% presented apneas, 28% fever, 19% poor suction, 13% vomiting, 11% lethargy, and 9% seizures. Tachycardia was documented in 49% and hypotension in 17%. Blood count reported an Hb of 14 (12, 16) with 11,500 (9,275, 14, 650) leukocytes, 4,830 (3,395, 6,105) lymphocytes, and 263,000 (149,000, 346,750) platelets.

The pattern found on LU was a pneumogenic (heterogenous) interstitial pattern of B-lines in 94%, pleural line abnormalities (thickened, interrupted) in 85%, coalescing B-lines in 60%, and consolidations in 51% (71% posterior). Seventy-five percentages of the consolidations were considered extended (> 5 mm). Thirty percentages presented pulmonary hypertension in the TnECHO assessment and 4.3% biventricular dysfunction. Figure. 2 depicts LU features of four patients with different viral infections and its corresponding chest

Table 1. Demographic and clinical profile

Demographic variables	n (%) / median (interquartile ranges)
Female	23 (49)
Cesarean section	33 (70)
Maternal age, years	25 (21, 31)
WOG at birth, weeks	37 (32, 38)
Birth weight, grams	2610 (1770, 3000)
Advanced resuscitation at birth	17 (36)
Intubation at birth	13 (27)
Surfactant	14 (29)
Perinatal asphyxia	9 (19)
TPN	24 (51)
TPN days	10 (6, 18)
Main working diagnosis	
Term newborn with RDS	16 (34)
Preterm newborn	14 (30)
Surgical patient	8 (17)
Bronchopulmonary dysplasia	4 (9)
Congenital heart disease	2 (4)
Trisomy 21	2 (4)
Diaphragmatic Hernia	1 (2)
Respiratory support	
Mechanical ventilation	24 (51)
CPAP	4 (8.5)
Nasal cannula oxygen	11 (23.5)
Intermittent indirect oxygen	8 (17)
Clinical findings	
Age at study, WOG	39 (36, 42)
Hb, g/dL	14 (12, 15)
Leukocytes, $10^3/\mu L$	11.500 (9.275, 14.650)
Lymphocytes, $10^3/\mu L$	4.830 (3.395, 6.105)
Neutrophils, $10^3/\mu L$	4.804 (2.950, 8.254)
Platelets, $10^3/\mu L$	263.000 (149.000, 346.750)
Tachypnea/desaturations	39 (83)
Tachycardia	23 (49)
Cyanosis	19 (40)
Apneas	15 (32)
Fever	13 (28)
Rhinorrhea	12 (26)
Poor suction	9 (19)
Hypotension	8 (17)
Conjunctivitis	8 (17)
Vomit	6 (13)
Lethargy	5 (11)
Seizures	4 (9)
Diarrhea	2 (4)
Management	
Antibiotics	22 (46)
Hemodynamic support	12 (25)
Oxygen discharge	11 (23)
Death	6 (13)

WOG: weeks of gestation; TPN: total parenteral nutrition; RDS: respiratory distress syndrome; CPAP: continuous positive airway pressure; Hb: hemoglobin.

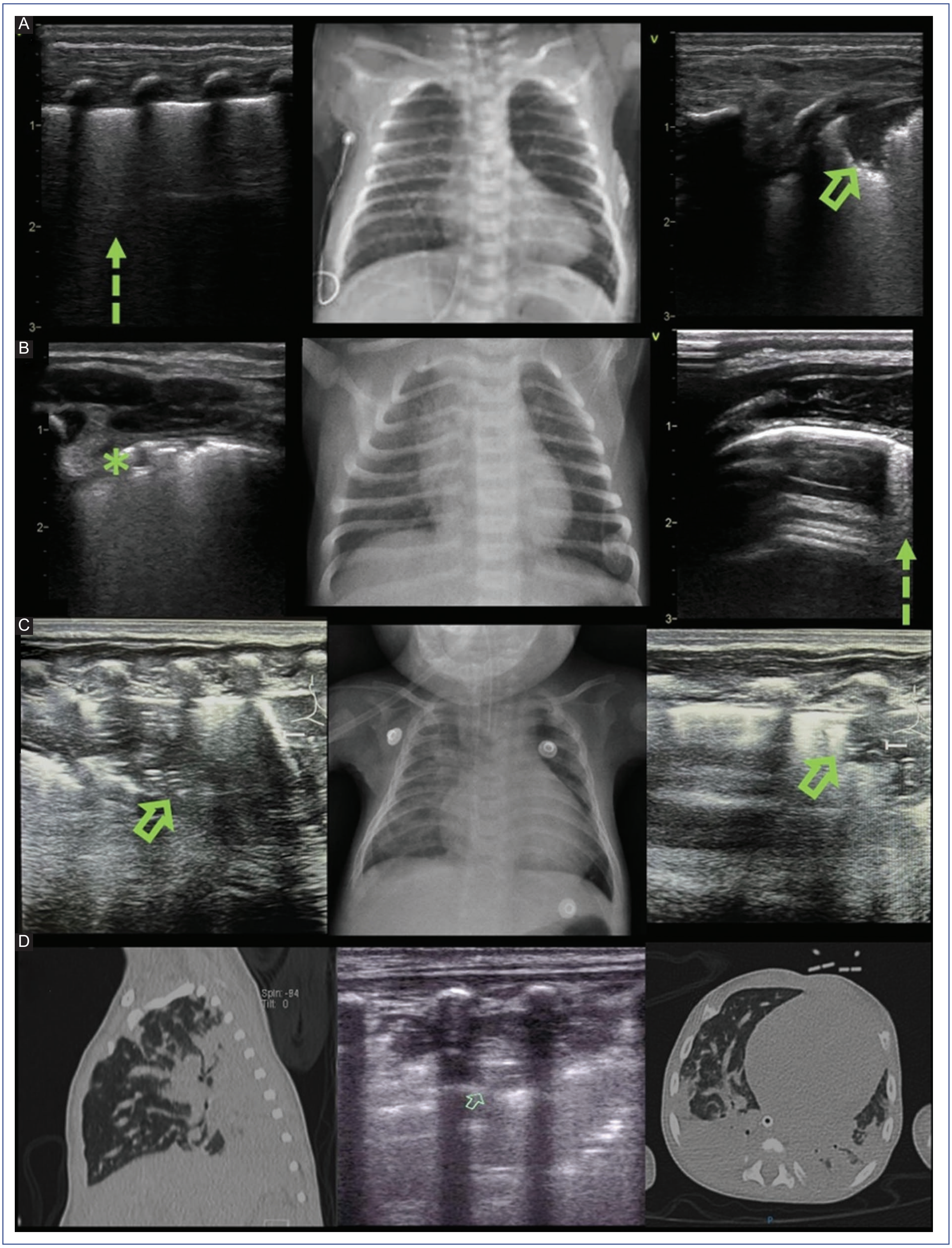

Figure 2. LU features of four patients with different viral infections and its corresponding CXR or CT. **A:** LU and CXR in newborns with SARS-CoV-2, **B:** RSV, **C:** Parainfluenza and **D:** LU and CT in influenza B infection. CT: Competed tomography; CXR: chest radiography; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; LU: lung ultrasound; and RSV: respiratory syncytial virus.

radiography (CXR) or computed tomography (CT). An enlarged thymus was found in 11 patients (nine SARS-CoV-2, one rhinovirus, and one RSV) with an area of 3.8 (3.2, 4.6) cm^2, transverse diameter of 2.4 (2.1, 2.8) cm, and thymic index of 8.68 (7.98, 9.99) cm (Fig. 3). All patients with increased thymus dimensions survived. Figure. 4 depicts a chord diagram with cardiopulmonary features of the hemodynamic consultation and LU assessment.

Significant median differences between levels of pulmonary support and eLUS were demonstrated (Mann–Whitney U, $p = 0.05$). A positive correlation was found between the eLUS and the FiO_2 required at the time of consult ($R^2 = 0.59$, Spearman, $p < 0.0001$) (Fig. 5).

There were 6 deaths (14%) all in patients with comorbidities and none directly related to viral infection. All patients who died had pulmonary hypertension at assessment. A difference in rank eLUS was found between survivors (10 [3, 14]) and non-survivors (21 [19, 22]). At the time of study, non-survivors needed higher FiO_2 (50 [46, 73]) than survivors (25 [23, 35]) (Fig. 6). To quantify the association of ultrasonographic findings and mortality, OR with 95% CI were calculated. As shown in table 2, the presence of consolidations (1.3 [95% CI 1.05-1.68]) and pulmonary hypertension (1.75 [1.1-2.7]) was associated with increased mortality while the presence of an increased thymus was shown protective (0.83 [0.2-0.94]).

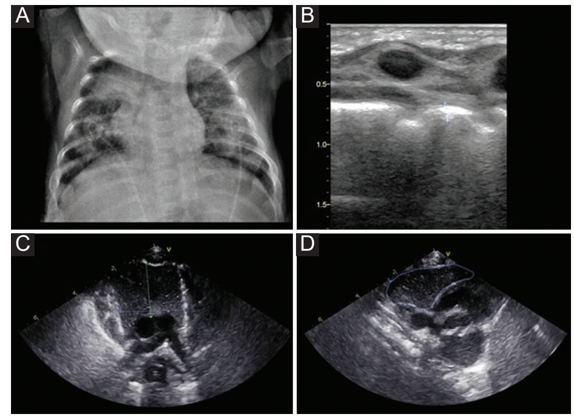

Figure 3. Enlarged thymus. 29-week, male newborn, 44 corrected at discharge with SARS-CoV-2 infection. **A:** enlarged thymic shadow noted on radiography. **B:** LU showed a thick pleural line with a heterogenous B-line interstitial pattern compatible with BPD. **C:** an increased transversal diameter (2.8 cm) and **D:** thymic area (4.6 cm^2) was noted. Thymic index was 12.88 (over the average described).

Discussion

As reported by previous studies, LU findings consisted of pleural line abnormalities, B-line interstitial pattern, confluent B-lines, and consolidations. No pleural effusion was found in our cohort. A recent study of 50 newborns with viral pneumonia in Turkey was conducted with the same findings in LU; also, the disappearance of consolidation and abnormal artifacts with recovery before discharge was demonstrated[19].

From LU findings, only the presence of consolidation was associated with mortality. Consolidations were posterior in 71% of cases demonstrating the importance of using an extended approach (eLUS) interrogating the posterior fields. About 75% of the consolidations were considered extended (depth > 5 mm); a recent study demonstrated that the consolidation index (maximum depth of the biggest consolidation), was not associated with gas exchange, whereas the extension of pathological process (as described by eLUS) was[20]. In our study, an increased eLUS was found in the deceased group with 22 (19, 22) versus 10 (3, 14) in survivals. As demonstrated by Ma et al., in China, in 135 cases of neonatal pneumonia, LU had good performance in diagnosing and differentiating the severity of the pneumonia [in longitudinal scans, they found that consolidations extending more than three intercostal spaces had a sensitivity of 83.3% and specificity of 85.2% (AUC 0.77) to predict severe pneumonia] but was not useful for etiological differentiation. In our patients, almost half of them ended being treated with antibiotics, demonstrating how that to identify patients with concomitant/superimposed bacterial infection especially in severe cases stills challenging. Recently, an algorithm combining procalcitonin and LU was published. It improved the diagnosis of bacterial pneumonia in critically ill children with a sensitivity of 90% (83-94) and specificity of 85% (76-91)[21]. It is important to consider LU as part of a clinical construct that includes the newborns history, physical examination, and laboratory studies.

Most of our patients were screened for SARS-CoV-2 during the pandemic. In pediatrics populations, it has been demonstrated that children with higher LUS are at increased risk of requiring oxygen supplementation[22]. Our group previously reported on 32 newborns with SARS-CoV-2 infections (included in this study); eLUS showed a significant median difference across levels of disease severity and ventilatory support, decreased as clinical improvement occurred. In addition, a positive correlation between eLUS and FiO_2 needed was

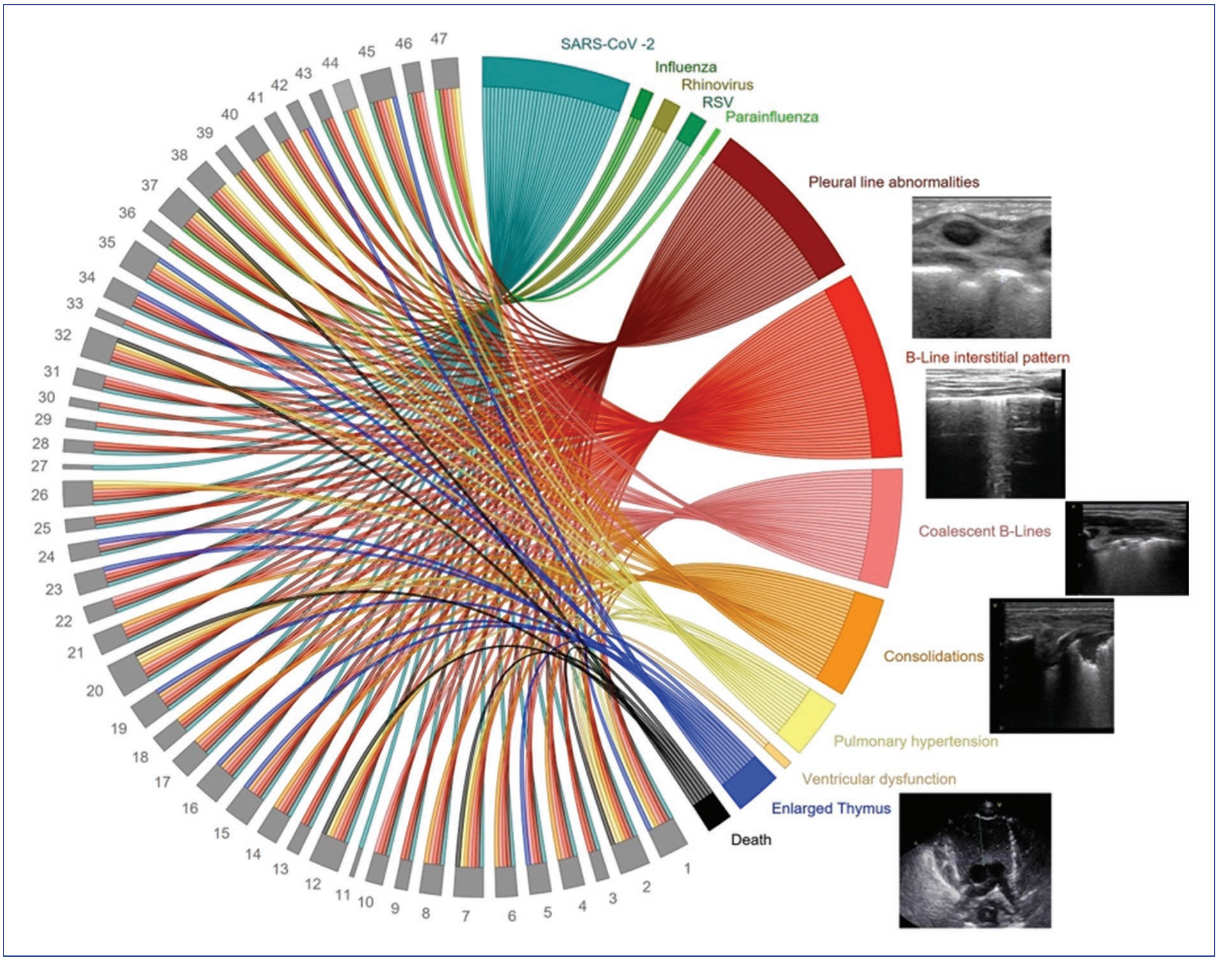

Figure 4. Chord diagram with cardiopulmonary features of the hemodynamic consultation and lung ultrasound assessment.

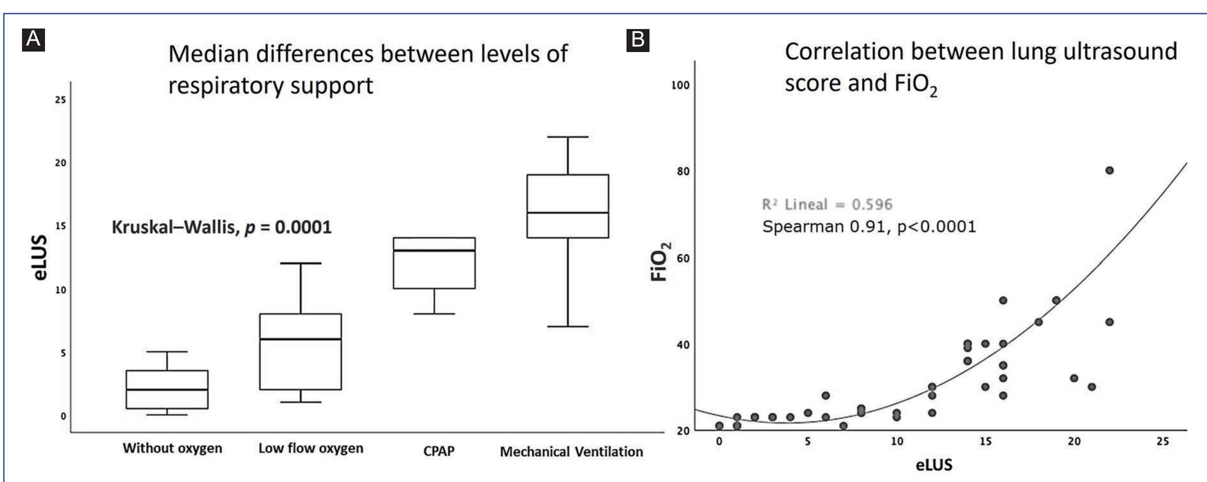

Figure 5. Median differences between levels of respiratory support and correlation between lung ultrasound and FiO_2 needed at the time of consult.

Table 2. Ultrasonographic findings and mortality

Sonographic feature	Survivor		Non-survivors		OR	95% CI
	n	%	n	%		
Pulmonary hypertension*	8	19.50%	6	100.00%	1.75	1.1-2.7
Ventricular dysfunction*	0	0.00%	2	33.30%	1.12	0.9-28
Enlarged thymus*	11	26.80%	0	0.00%	0.83	0.2-0.94
Pleural line abnormalities	34	82.90%	6	100.00%	1.1	1.0-1.3
B-Line interstitial pattern	38	92.70%	6	100.00%	1.15	1.03-1.3
Confluent B-Lines	23	56.10%	5	83.30%	3.9	0.4-36
Consolidation*	18	43.90%	6	100.00%	1.3	1.05-1.68

*X^2 test

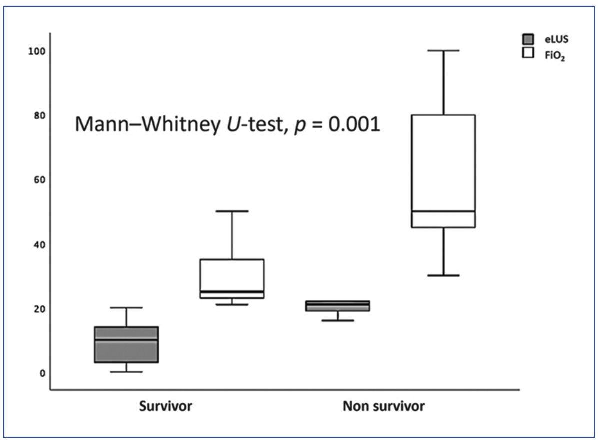

Figure 6. Rank difference between extended lung ultrasound semi-quantitative score and FiO_2 needed between survivors and non-survivors.

observed. This trend persisted even when other identified respiratory viruses were included in the analysis.

As it has been described with several viral infection in the newborn including RSV, LUS correlates with the clinical course and is able to predict admission to the NICU, length of hospital stay, and the need for respiratory support. On TnECHO assessment, the presence of pulmonary hypertension (present in 30% of our population) was associated with mortality. Recently, Kimura et al., described 154 children admitted with RSV bronchiolitis detecting pulmonary hypertension in 29 (19%). Pulmonary hypertension diagnosed by echocardiography was associated with morbidity and mortality[23].

The thymus is a vital organ of the immune system that plays an essential role in thymocyte development and maturation. Thymic atrophy occurs with age (physiological thymic atrophy) or due to viral, bacterial, parasitic, or fungal infection (pathological thymic atrophy). Thymic atrophy directly results in loss of thymocytes and/or destruction of the thymic architecture and indirectly leads to a decrease in naïve T cells and limited T-cell receptor diversity[24]. It has been proposed that in the newborn and toddlers, the young immune system and its efficient T-cells may potentially respond more efficiently to SARS-CoV-2[25] as with aging declining T regulatory cells and increasing memory cells happens[26]. Interestingly, we found increased thymic dimensions (compared to what is reported on the literature) in 23% of discharged patients[27,28]. Thymic size has been positively correlated with gestational age, birth weight, head circumference, and number of lymphocytes in peripheral blood[29]. We hypothesize that it might be related to adequate immune response to the infection.

In our cohort, 23% of patients were discharged on oxygen supplementation. Although reliable prospective studies with large samples are still needed; recently, it has been demonstrated that viral infections are associated with an increased risk of BPD[30].

Our study has several limitations. A portion of the data collection occurred during the SARS-CoV-2 outbreak, which may have introduced bias due to the high prevalence of this specific pathogen. Although multiplex RT-PCR testing was performed in 47% of the cases, a SARS-CoV-2-focused RT-PCR was predominantly used during the pandemic, potentially limiting the identification of co-infections or alternative viral etiologies. In addition, the study population was enrolled over a time span that included pre-pandemic, pandemic, and post-pandemic periods. This temporal heterogeneity likely influenced the seasonal circulation patterns of respiratory viruses. Notably, during the pandemic, there was a significant reduction in the circulation of respiratory viruses other than SARS-CoV-2 and rhinovirus. This shift in viral epidemiology may have impacted on the representativeness of our findings and should be considered when interpreting the result.

Conclusion

LU proved to be a valuable bedside tool in the assessment of newborns with respiratory viral infections, offering insights into disease severity and the need for respiratory support. The extended LUS showed significant correlation with oxygen requirements and clinical outcomes, reinforcing its utility in the neonatal intensive care setting. Furthermore, the presence of pulmonary hypertension, as assessed by TnECHO, was associated with increased mortality, highlighting the importance of comprehensive cardiopulmonary evaluation in this population. Given the dynamic landscape of viral circulation during the COVID-19 pandemic, future prospective studies with larger, more homogeneous cohorts are needed to validate these observations and refine diagnostic and therapeutic algorithms in neonates with viral respiratory infections.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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