Point-of-care lung ultrasound in three neonates with COVID-19

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Abstract
Since March 2020, the world is involved in the COVID-19 pandemic, a disease caused by a novel virus called SARS-CoV-2. Some authors have described the ultrasonographic findings of COVID-19 pneumonia in adults and children, but data on neonates are lacking. Our objective was to describe the ultrasonographic lung pattern on newborns with SARS-CoV-2 infection during the COVID-19 pandemic. Newborns who tested positive for SARS-CoV-2 PCR in respiratory samples and were evaluated with point-of-care lung ultrasound (LU) from March to April 2020 were included. LU was performed bedside by a single investigator at the time of diagnosis and every 48 h during the first week following diagnosis. Six areas were studied. Three neonates were included. Infants’ comorbidities included meconium aspiration syndrome, bronchopulmonary dysplasia, and Hirschsprung’s disease. One required mechanical ventilation. No deaths occurred. LU showed B-lines, consolidation, and spared areas. No pneumothorax or pleural effusion was observed.

Conclusions: LU could be of value when managing COVID-19 neonates. We describe the findings of lung ultrasound monitoring during the first week following diagnosis in three neonates with SARS-CoV-2 infection.

What is known:
• Lung ultrasound (LU) is a useful tool in COVID-19 management in adults. To date, no report on LU and neonates with SARS-CoV-2 infection has been published.

What is new:
• This study adds evidence about LU findings in neonates with SARS-CoV-2 infection.

Keywords Lung ultrasound · Neonate · COVID-19 · SARS-CoV-2 · Point-of-care ultrasound · Ultrasonography · Coronavirus

Introduction
Since December 2019, a novel virus called SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) has been described as responsible for a life-threatening disease: COVID-
19 (coronavirus disease 2019) declared by the World Health Organization (WHO) as a pandemic on March 11, 2020 [1].

In the neonatal period, only a few cases have been reported positive, the largest series coming from a report of 33 pregnant woman with SARS-CoV-2 infection and three neonates with a positive polymerase chain reaction (PCR) result in China [2]. These three children had a mild course of the disease except from the one born prematurely. No deaths or vertical transmission have been reported to date.

Lung ultrasonography (LU) has been previously described as a safe tool to study respiratory and cardiac diseases in neonates [3–5]. Some authors have already suggested that LU would be of interest in COVID-19 adult patients at various points of healthcare structure [6–8]. Peng et al. first described the characteristic LU findings in COVID-19 pneumonia in 20 adults, stating that thickening of pleural line, a variety of B-line patterns, and consolidation appeared, together with spared areas. Pleural effusion was uncommon, and A-lines appeared during the recovery phase [9]. These findings were consistent with previous reports on viral pneumonia [10], but, to date, no international consensus on its practical implications has been published. Similar findings have been reported in children [11].

Although some institutions, including the Chinese Neonatal 2019-nCoV Expert Working Group, the American Academy of Pediatrics (AAP), and the Spanish Society of Neonatology (SENeo), had established guidelines to manage this infection in the neonatal population, there is little experience regarding the diagnosis and evolution of the disease in this vulnerable population [12–14]. To our knowledge, there is no previous report about LU findings in newborns developing SARS-CoV-2 infection.

The objective of this study is to describe the ultrasonographic lung pattern in newborns with SARS-CoV-2 infection during the COVID-19 pandemic. We hypothesize that findings in neonates could be similar to those described in adults and children.

**Materials and methods**

**Study design, setting, and participants**

Consecutive case series including newborns was admitted to a single tertiary neonatal unit with SARS-CoV-2 infection and evaluated by point-of-care LU from March to April 2020. Patients were included if they had a positive result for SARS-CoV-2 PCR in a respiratory sample (nasopharyngeal swab or bronchoalveolar aspirate), regardless of their respiratory and clinical situation. Cases were classified following international definitions for fetal, perinatal, and neonatal COVID-19 [15].

Patients were managed according to the SENeo and Spanish Healthcare Ministry guidelines for COVID-19 [13, 16] and the unit’s protocol. Babies were isolated inside incubators in a separate room with a single nurse in charge, but no negative-pressure room was available. The results of the ultrasounds did not modify the patients’ management, as they were performed by a neonatologist not involved in these patients’ treatment. Data from the clinical history and informed consent from the parents were obtained.

**Lung ultrasound**

Point-of-care lung ultrasound exams were performed by a sole neonatologist experienced in the use of this technique, using a broadband high-frequency linear transducer (6–11 MHz) and the General Electrics LOGIQ 6Q portable ultrasound machine. Depth was adjusted to 4 cm, and focus was set at the pleural line. No harmonics were used. Video images and photographs were taken. The patients were examined inside an incubator, in supine position and at resting state. Swaddling and sucking were offered by the nurse. The ultrasound was repeated every 48 h during the first week following diagnosis (days 0, + 2, + 4, + 6), maintaining all the safety and cleaning measures established by Spanish Healthcare Ministry guidelines (transducer covered by sterile protection and operator fully equipped with personal protection equipment). Longitudinal and transversal images were obtained. The findings were described qualitatively and semiquantitatively according to previously described Brat’s LU score [17]. The LU score ranged from 0 to 18 points (each area with values from 0 to 3 points): 0 points: A-pattern, 1 point: ≥ 3 B-lines, 2 points: crowded and coalescent B-lines, and 3 points: extended consolidation. Total score ranged from 0 to 18 points. Three areas were studied in each hemithorax:

- Anterior: between medioclavicular and anterior axillary lines.
- Lateral: between anterior and posterior axillary lines.
- Posterior: between paravertebral and posterior axillary lines.

**Results**

During the study period, three patients were included. Clinical and epidemiological characteristics of the patients are described in Table 1. Patients 1 and 2 had lung comorbidities: meconium aspiration syndrome (MAS) and bronchopulmonary dysplasia (BPD) respectively. All samples obtained were nasopharyngeal swab except for a bronchoalveolar aspirate in patient 1 (Table 2).

This newborn was studied for SARS-CoV-2 infection because of his mother’s results (she was tested because of postpartum fever, no respiratory symptoms), and the other two patients were discovered positive during an extended and active investigation including all patients in the unit after the first case (patient 1) was diagnosed, despite their asymptomatic status. The mother of patient 2 was also asymptomatic, despite a positive result. The three patients were classified as “probable postpartum
acquired neonatal infection” (positive PCR ≥ 48 h of life in a neonate not tested at birth). No serology study was performed, as it was not mandatory to confirm the diagnosis.

All three had negative PCR result before discharge (obtained 6–8 days after diagnosis) (Table 2). At least three lung ultrasound exams were obtained on each infant during the study period, at 48-h intervals. LU score evolution can be seen in Fig. 1. See electronic supplementary material (ESM) to find some LU videoclips. Findings observed in the sample can be summarized as follows:

**Patient 1**

Term newborn requiring mechanical ventilation, nitric oxide, cooling therapy, inotropes, and antiepileptic drugs because of severe hypoxic-ischemic encephalopathy in a MAS context. At the start of the LU follow-up (3 days of life, DOL), despite the MAS diagnosis, no extended consolidation was seen in any areas, but a thin pleural line with conserved lung sliding and no coalescent B-pattern were shown. However, in the evolution, coalescent B-lines and some consolidation appeared in both lateral and posterior areas, diameters ranging from 5 to 24 mm (Fig. 2, ESM 1). This patient needed mechanical ventilation for the first 6 DOL and afterwards, nasal cannula for 16 more days. Maximum LU score was 10 points at day + 4.

**Patient 2**

This was a preterm infant with a postmenstrual age (PMA) of 39 + 3 weeks (78 DOL) when SARS-CoV-2 infection was

### Table 1 Clinical and epidemiological characteristics of the patients included

|                        | Patient 1                  | Patient 2                | Patient 3               |
|------------------------|----------------------------|--------------------------|-------------------------|
| Birth weight (g)       | 3700                       | 1135                     | 3550                    |
| Sex                    | M                          | M                        | M                       |
| Mode of delivery       | Vaginal                    | Vaginal                  | Vaginal                 |
| Previous diagnosis     | Severe hypoxic-ischemic encephalopathy, meconium aspiration and multiorgan failure | Prematurity, BPD (28 weeks) | Hirschsprung’s disease |
| Parents tested         | Yes. Mother positive       | Yes. Mother positive     | Yes. Parents negative   |
| Time on MV since birth (d) | 6                         | 0                        | 0                       |
| Time on NIV or nasal cannula since birth (d) | 16                        | 70                       | 0                       |
| Respiratory support at diagnosis | MV                        | Room air                 | Room air                |
| Fever                  | No                         | No                       | No                      |
| Minimum lymphocyte count (× 10^9/L) | 11.4                      | 7.9                      | 3.7                     |
| Maximum CRP (mg/L)     | 57                         | < 1                      | < 5                     |
| Maximum PCT (ng/mL)    | 0.82                       | -                        | 0.1                     |
| Maximum ferritin (ng/mL) | 491                       | -                        | 1000                    |
| Maximum D-dimer (ng/mL) | 5317                      | -                        | 1891                    |

d, g, m, M male, BPD bronchopulmonary dysplasia, MV mechanical ventilation, NIV non-invasive ventilation, CRP C-reactive protein, mg milligrams, mL millilitre, ng nanogram, PCT procalcitonin

### Table 2 Samples obtained at diagnosis and follow-up of the patients included

|                        | Patient 1                  | Patient 2                | Patient 3               |
|------------------------|----------------------------|--------------------------|-------------------------|
| At diagnosis           |                            |                          |                         |
| DOL (d)                | 2                          | 78                       | 6                       |
| PMA (wk+ d)            | 38 + 3                     | 39 + 3                   | 39 + 6                  |
| Sample obtained        | Bronchoalveolar aspirate   | Nasopharyngeal swab      | Nasopharyngeal swab     |
| PCR result             | Positive                   | Positive                 | Positive                |
| At follow-up           |                            |                          |                         |
| DOL (d)                | 10                         | 84                       | 13                      |
| PMA (wk + d)           | 39 + 3                     | 40 + 2                   | 40 + 6                  |
| Days after diagnosis   | 8                          | 6                        | 7                       |
| Sample obtained        | Nasopharyngeal swab        | Nasopharyngeal swab      | Nasopharyngeal swab     |
| PCR result             | Negative                   | Negative                 | Negative                |

d, wk weeks, PCR polymerase chain reaction
confirmed. He was still hospitalized because of oxygen dependence from birth in the context of BPD diagnosis. He had several LU performed before the infection, and, despite showing an improvement from birth, he still presented no coalescent B-pattern with more than three B-lines in all lung areas (Fig. 3). Along the course of the infection, B-pattern turned more crowded, especially in posterior areas, and consolidation appeared in both sides, diameters ranging from 2 to 13 mm (Fig. 3). The pleural line appeared blurred and thick in almost all areas, but with normal lung sliding. Despite this worsening, he tolerated weaning off respiratory support (nasal cannula) in a few days following the onset of the infection and was discharged home at 85 DOL (40 + 3 PMA) on room air. Maximum LU score was 8 points at day + 6.

Patient 3

This was a term newborn admitted to the hospital because of Hirschsprung’s disease. He did not need any respiratory support during the admission. At diagnosis (6 DOL), LU showed a majority of areas with A-pattern and a thin pleural line with normal lung sliding and isolated B-lines. However, in posterior areas, the pleural line was thick and blurred and B-lines were coalescent in some intercostal spaces. Millimetric “subpleural consolidation” was seen. In the follow-up, these findings rapidly disappeared and the whole lung presented with an A-pattern and a fine pleural line (Fig. 4). Maximum LU score was 4 points at day 0.

No pleural effusion or pneumothorax was observed in any patient.

Discussion

We report the lung ultrasonography evolution of three neonates with SARS-CoV-2 infection.

Several reports confirm that it seems to be a mild infection in the majority of cases in children [18–20]. In the neonatal field, evidence is sparse [21]. The SARS-CoV-2 infection can range from asymptomatic infection to severe respiratory distress in neonates and children. Many reports have described CT scan in COVID-19 pneumonia [22]. However, CT scan availability is sparse in several settings, especially in a pandemic context, which implies a lack of resources and requires a rational use of them. There is also a concern regarding ionizing radiation implications in the neonatal population [23].

International guidelines had validated lung ultrasonographic imaging in several neonatal respiratory diseases, as in meconium aspiration syndrome, respiratory distress syndrome, transient tachypnea, etc. [3, 24]. As stated in Chinese and Spanish Societies’ recommendations on SARS-CoV-2 infection, LU is suitable to study even the asymptomatic neonatal patients with a confirmed infection [12, 13]. However, to date, only a few reports have been published about LU findings in COVID-19, the majority of them being adult case series and clinical recommendations [8]. To our knowledge, there is no report of newborns evaluated with lung ultrasound after testing positive for this new virus. Furthermore, we are not aware of any report addressing the evolution of the ultrasonographic findings in these patients.

Our results show the ultrasonographic lung pattern in three newborns with SARS-CoV-2 infection during this 2019–2020 pandemic. We present three neonates with very different
backgrounds, one with an acute lung disease (MAS), another with a chronic lung disease (BPD), and the third patient with no lung disease. This diversity allows for comparison of the evolution of the three. Previous literature has described the ultrasound scan pattern of MAS and BPD [3, 24–26]. We cannot state that the origin of the findings described in our patients is due solely to SARS-CoV-2 infection, but we consider it important to describe the ultrasonographic and clinical course of the infection in these patients, given that newborns with different conditions will suffer from this infection. Surprisingly, the emergence of some consolidation and areas with coalescent B-lines was not accompanied by a respiratory deterioration, in contrast with adult reports [8]. This is important to note, since LU is a clinical tool, always integrated in the clinical context of the patient, and decisions regarding treatment should always keep the clinical condition in mind.

Even the patient without any previous lung disease (patient 3) showed some isolated B-lines. The significance of this finding is worth noting, since it has been reported that even neonates without any respiratory disease can show B-lines up to 19 days after birth [27].

Regarding LU score, all the three patients had an initial score of 3–4 points, proving that some degree of alveolar-interstitial syndrome is very common in newborns. Patients 1 and 2 scores increased to 8–10 points during the course of the disease process. The patient with the worst respiratory evolution (patient 1) had the highest scores, and patient 3 (no need for respiratory support) had the lowest, although the evolution was different between them (Fig. 1). This score was modified from an index proposed for adult patients. It correlates with extravascular lung water and has been demonstrated useful in predicting mechanical ventilation or surfactant needs in preterm population [28, 29].

Our findings are consistent with those previously described in adults and children: thick pleural line, spared areas, B-lines, consolidation, and no pleural effusion [11, 30].

Limitations of our report are that two of the newborns had respiratory diseases in addition to SARS-CoV-2 infection, and this may cause confusion about the significance of the findings. However, we compared the findings with a previous LU in the patient with BPD and also presented a term neonate with no lung disease. The patients described had mild courses of the respiratory disease, seen as consistent with the ultrasonographic appearance. However, it is of interest to study this group of patients due to the possibility of oligosymptomatic infection in infants and neonates [31]. Lung ultrasonography is a feasible complementary test with clear benefits in triage, diagnosis, and management without the risks of patient transfer or ionizing radiation [8]. Further reports are needed to evaluate the usefulness of LU in the study of newborns with COVID-19.

**Conclusion**

We show the findings of lung ultrasound monitoring after SARS-CoV-2 infection in the three neonates. The findings are nonspecific, and more evidence is needed to determine the significance of lung ultrasonography in the practical approach to this disease.
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Authors’ contributions R.G.H. designed the study, performed the acquisition and analysis of the data and drafted the text. A.B.E.I., J.C.P. and A.M.G. made contributions to the conception of the work and revised it critically. All the authors revised and approved the final version of the text.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from the legal guardians of all individual participants included in the study.

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