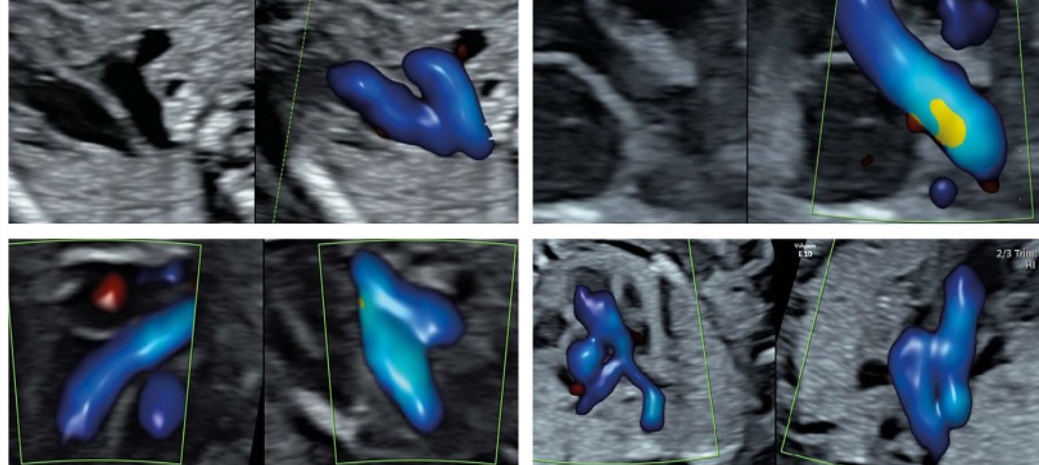


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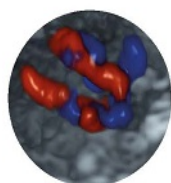
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Clinical role of lung ultrasound for diagnosis and monitoring of COVID-19 pneumonia in pregnant women

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KEYWORDS: COVID-19; lung ultrasound; POCUS; pregnancy

ABSTRACT

Lung ultrasound has been suggested recently by the Chinese Critical Care Ultrasound Study Group and Italian Academy of Thoracic Ultrasound as an accurate tool to detect lung involvement in COVID-19. Although chest computed tomography (CT) represents the gold standard to assess lung involvement, with a specificity superior even to that of the nasopharyngeal swab for diagnosis, lung ultrasound examination can be a valid alternative to CT scan, with certain advantages, particularly for pregnant women. Ultrasound can be performed directly at the bed-side by a single operator, reducing the risk of spreading the disease among health professionals. Furthermore, it is a radiation-free exam, making it safer and easier to monitor those patients who require a series of exams. We report on four cases of pregnant women affected by COVID-19 who were monitored with lung ultrasound examination. All patients showed sonographic features indicative of COVID-19 pneumonia at admission: irregular pleural lines and vertical artifacts (B-lines) were observed in all four cases, and patchy areas of white lung were observed in two. Lung ultrasound was more sensitive than was chest X-ray in detecting COVID-19. In three patients, we observed almost complete resolution of lung pathology on ultrasound within 96 h of admission. Two pregnancies were ongoing at the time of writing, and two had undergone Cesarean delivery with no fetal complications. Reverse transcription polymerase chain reaction analysis of cord blood and newborn swabs was negative in both of these cases. Copyright © 2020 ISUOG. Published by John Wiley & Sons Ltd.

CASE SERIES

We assessed four pregnant women with symptoms suspicious for COVID-19. Reverse transcription polymerase chain reaction (RT-PCR) analysis of nasopharyngeal swabs gave positive results for all four women at first evaluation. Lung ultrasound (LUS) was performed at admission, before the RT-PCR results were available. Clinical and ultrasound parameters, treatment and outcome data are shown in Table 1. The median age of the women was 38.5 (range, 31–42) years and the gestational ages at admission ranged from 17 to 38 weeks. In all four cases, the medical history was unremarkable. At the time of admission to hospital, all four patients were symptomatic; all four presented with cough, one with ageusia/anosmia and three with fever ($\geq 38^{\circ}\text{C}$).

Laboratory investigations showed relative lymphocytopenia and elevated C-reactive protein in all cases and raised lactic dehydrogenase levels in two cases. Three women were breathing spontaneously at admission, while one patient, at 24 weeks' gestation, required intensive care unit (ICU) admission for non-invasive ventilation. At the time of writing, two pregnancies were ongoing, and two had delivered with no fetal complications; Patient 2 delivered at 40 weeks' gestation by planned Cesarean delivery, while Patient 4 underwent emergency Cesarean section at 36 weeks' gestation due to fetal bradycardia. RT-PCR analysis of cord blood and newborn swabs (performed on days 1 and 4, respectively) was negative in both cases, and both newborns were discharged in good clinical condition.

Two of the patients underwent chest X-ray at first evaluation (Figures S1 and S2) and no patient underwent computed tomography (CT). All of them underwent LUS

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at admission and throughout the course of the disease (every 24–48 h), which showed in all cases signs of lung involvement. In particular, the woman requiring ICU admission (Patient 1) presented the most severe LUS findings, with pleural-line abnormalities and multiple

subpleural consolidations in all 14 lung areas¹. In this case, considering the clinical and laboratory data, the young gestational age and risk of severe premature delivery, together with the LUS findings (Figure 1a), which showed diffuse lung disease, the multidisciplinary team

Table 1 Main clinical, laboratory and radiological findings in four pregnant women with COVID-19 monitored with lung ultrasound (LUS) examination

	Patient 1	Patient 2	Patient 3	Patient 4
MA (years)	31	42	39	38
GA (weeks)	24	38	17	35
Clinical presentation	Fever Cough SpO ₂ 96% SoB	Fever Cough SpO ₂ 98% Breathing normal	Cough Ageusia Anosmia SpO ₂ 99% Breathing normal	Fever Cough SpO ₂ 97% Breathing normal
Main lab findings	WBC 700/mm ³ L 540/mm ³ * LDH 395 IU/L CRP 38.5 mg/L	WBC 8300/mm ³ L 800/mm ³ * LDH 228 IU/L CRP 15.6 mg/L	WBC 6710/mm ³ L 1115/mm ³ * LDH 154 IU/L CRP 5.9 mg/L	WBC 5370/mm ³ L 750/mm ³ * LDH 468 IU/L CRP 91.3 mg/L
Chest X-ray findings	Basal interstitial disease (<i>n</i> = 1)	NP	NP	Bilateral, basal, hyperlucency (<i>n</i> = 1)
LUS findings				
First exam	Irregular pleural line White lung Large subpleural consolidations Multiple vertical artifacts (NoA, 14/14)	Irregular pleural line Multiple confluent vertical artifacts Patchy areas of white lung (NoA, 6/14)	Irregular pleural line Multiple vertical artifacts (NoA, 2/14)	Irregular pleural line Isolated vertical artifacts (NoA, 2/14)
At 48 h	Irregular pleural line White lung Large subpleural consolidations Vertical artifacts (NoA, 14/14)	—	—	—
72–96 h	Irregular pleural line White lung Consolidations Multiple vertical artifacts (NoA, 12/14)	Irregular pleural line Multiple vertical artifacts (NoA, 5/14)	Irregular pleural line Isolated vertical artifacts (NoA, 2/14)	Irregular pleural line Multiple, confluent vertical artifacts Patchy area of white lung (NoA, 5/14)‡
> 96 h	Irregular pleural line White lung Small subpleural consolidations Vertical artifacts (NoA, 10/14)	Regular pleural line Isolated vertical artifacts (NoA, 2/14)	Regular pleural line Isolated vertical artifacts (NoA, 1/14)	Regular pleural line Normal A-lines (NoA, 0/14)§
Treatment	Hydroxychloroquine Lopinavir/ritonavir Tolilizumab†	Hydroxychloroquine Lopinavir/ritonavir	Hydroxychloroquine Lopinavir/ritonavir	Hydroxychloroquine Lopinavir/ritonavir
Ventilation support	CPAP	Nothing	Nothing	Nothing
ICU	Yes	No	No	No
Pregnancy status	Uncomplicated ongoing pregnancy Stable maternal condition	CS at 40 weeks Good maternal condition	Uncomplicated ongoing pregnancy Good maternal condition	CS at 36 weeks due to fetal bradycardia Good maternal condition

Vertical artifacts correspond to so-called ‘B-lines’, as initially named by Volpicelli *et al.* during 2012 consensus conference¹¹; however, recent evidence suggests that vertical lines are heterogeneous entities providing different information, and the term ‘vertical artifacts’ may be more appropriate^{5,6}. *Lower threshold of absolute lymphocyte count is 1000 in third trimester of pregnancy¹⁰; although all women had relative lymphocytopenia, only three had absolute lymphocytopenia (normal value in our laboratory: 2800–9700/mm³). †Tolilizumab added based on lung involvement documented on LUS. ‡Slight worsening of clinical condition on same day; patient began coughing. §Improved clinical condition, no more fever or cough. CPAP, continuous positive airway pressure; CRP, C-reactive protein (normal level in our laboratory: > 5 mg/L); CS, Cesarean section; GA, gestational age; ICU, intensive care unit; L, lymphocytes; LDH, lactic dehydrogenase (normal level in our laboratory: < 250 IU/L); MA, maternal age; NoA, number of lung areas involved on lung ultrasound, i.e. number with at least one of 14 potential pathological areas; NP, not performed; SoB, shortness of breath; WBC, white blood cells.

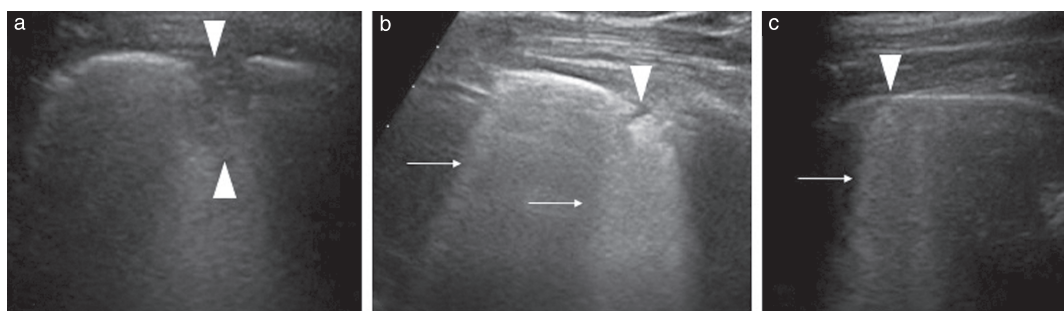


Figure 1 Lung ultrasound images from patient with COVID-19 pneumonia who required admission to intensive care unit (Patient 1). (a) Initial examination showed subpleural consolidations (arrowheads) with posterior white areas. (b,c) During follow-up imaging at 72–96 h and on day 14, consolidation size reduced progressively (arrowheads) and vertical artifacts appeared (arrows).

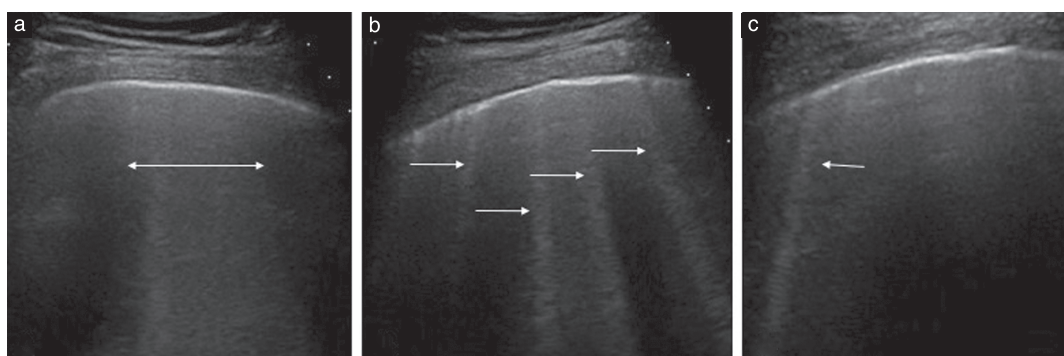


Figure 2 Lung ultrasound images from patient with COVID-19 pneumonia (Patient 2). (a) Initial examination showed patchy area of white lung (double-headed arrow) and normal A-pattern was not visible. During follow-up at 72–96 h, concomitant with patient improvement, multiple vertical artifacts (arrows) were visible (b), which had become progressively more isolated by day 5 (c).

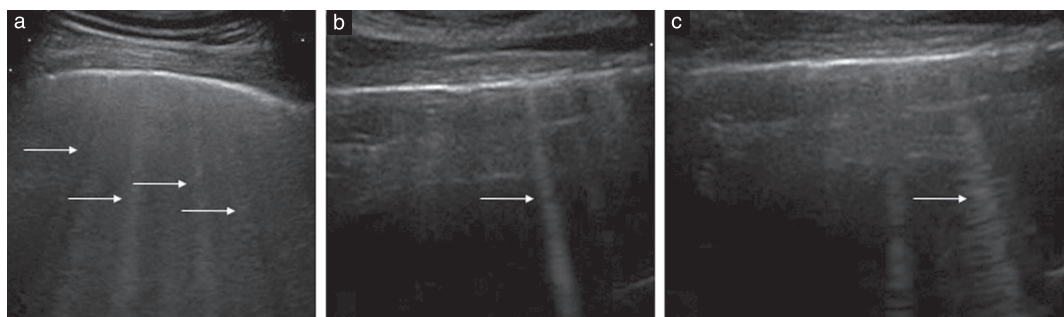


Figure 3 Lung ultrasound images from patient with COVID-19 pneumonia (Patient 3). (a) Initial examination showed areas with multiple vertical artifacts (arrows). (b,c) During follow-up at 72–96 h and on day 5, concomitant with patient improvement, vertical artifacts became more isolated.

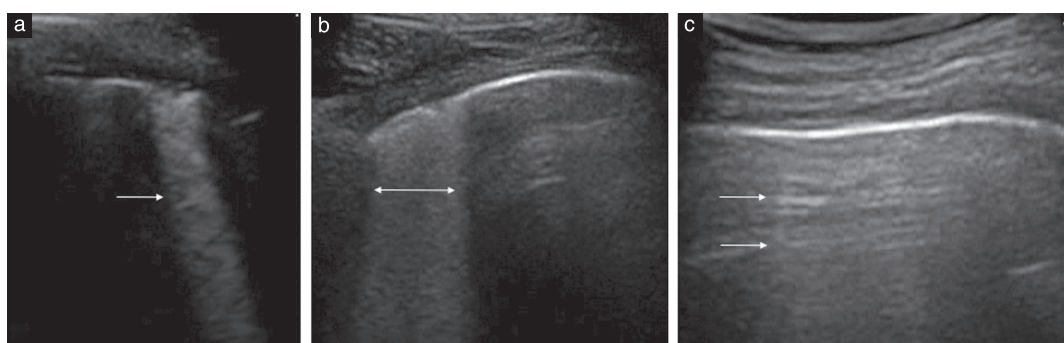


Figure 4 Lung ultrasound images from patient with COVID-19 pneumonia (Patient 4). (a) Initially, isolated thick vertical artifacts were visible (arrow). (b) During follow-up at 72–96 h, patient developed transitory clinical worsening, and lung ultrasound showed patchy area of white lung (double-headed arrow). (c) Patient then improved and lung pattern normalized by day 5, with A-lines visible (arrows).

taking care of the patient decided to begin treatment with tocilizumab. During the course of the disease, LUS monitoring every 24–48 h showed a slow but progressive improvement of lung pathology, characterized by a progressive reduction in the number of lung areas showing pathological findings (Figure 1b,c). Patients 2 and 3 had milder disease, based on both clinical and LUS findings, that improved progressively during the course of the disease (Figures 2 and 3). Patient 4 had mild worsening of clinical condition, characterized by the onset of a severe cough on day 3 following admission, and this was reflected in the LUS pattern, which showed a greater number of lung areas involved (Figure 4a,b). Two days later, however, LUS showed almost complete resolution of lung pathology and the woman was in better clinical condition (Figure 4c).

DISCUSSION

In this observational series, we found LUS to be a useful tool with which to assess and monitor lung involvement in pregnant women with COVID-19 and, in one case, it played a significant role in the treatment decision. All patients showed ultrasound features indicative of COVID-19 pneumonia at admission and three patients had almost complete resolution of lung pathology at LUS within 96 h from admission.

Pathological lung findings have also been described in a study evaluating serial CT scans in non-pregnant adults with COVID-19 pneumonia; these indicated slow improvement of the disease². CT scan is the gold standard for assessing COVID-19 pneumonia³, and should be used whenever clinically indicated and logistically feasible; it should always be considered in order to check the lung status in cases with severe conditions or sudden, unexplained clinical worsening and in the presence or on suspicion of other complications, such as emboli. However, an alternative imaging method, such as LUS, may be considered, particularly for pregnant women. LUS is radiation-free, and can therefore be used safely multiple times for serial examinations⁴. It has been proved capable of detecting COVID-19 pneumonia^{5–7}. Moreover, in emergency situations, such as the current pandemic, performed by appropriately trained gynecologists/obstetricians¹, it may

be incorporated quickly and easily into a routine fetal ultrasound examination. Kalafat *et al.*⁸ described positive LUS findings in a COVID-19 pregnant woman with an initial negative RT-PCR result. Their LUS findings correlated with CT findings, highlighting the usefulness of LUS in pregnant women with suspected COVID-19. Conversely, chest X-ray has low sensitivity in detecting COVID-19 pneumonia⁹. LUS, also being a safer option, might therefore be preferable to chest X-ray in pregnant women.

In conclusion, LUS examination by a physician experienced in LUS should be considered for monitoring pregnant women, even those with no or mild symptoms, as long as the proper use of personal protective equipment and sterilization procedures⁴ can be guaranteed.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:



Figure S1 Chest X-ray (left image) in pregnant woman with COVID-19 (Patient 1), showing bilateral basal bronchial thickening (black arrows), without evident consolidations. Conversely, lung ultrasound (right image) showed multiple, bilateral subpleural consolidations (white arrows), pleural line irregularities (yellow arrow) and vertical artifacts (B-lines) in all lung areas explored.

Figure S2 Chest X-ray (left image) in pregnant woman with COVID-19 (Patient 4), showing bilateral basal hyperlucency ‘of unclear significance, to be related to clinical/laboratory findings’ (black arrows), without evident consolidations. Lung ultrasound (right image) showed pleural line irregularities with thick vertical artifacts (B-lines) (white arrow) in basal posterior left and right lung.