

Role of lung ultrasound patterns in monitoring coronavirus disease 2019 pneumonia and acute respiratory distress syndrome in children

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Background: During the coronavirus disease 2019 (COVID-19) pandemic, lung ultrasonography (US) has been gaining importance in pediatric intensive care and emergency settings for the screening, diagnosis, and monitoring of pulmonary pathology.

Purpose: To describe the pattern of lung US changes in patients with COVID-19 pneumonia and its potential role in monitoring ventilated patients.

Methods: This prospective observational study included children aged 1 month to 12 years with a confirmed diagnosis of COVID-19. Lung US was performed using a high-frequency linear probe (5–12 MHz) in all children with moderate/severe respiratory symptoms within 24 hours of admission and then daily until the patient required oxygen therapy. Lung involvement severity was assessed using lung US scores, while lung aeration improvement or deterioration was measured using lung ultrasound reaeration scores (LUSReS).

Results: Of 85 children with moderate to severe disease, 54 with pulmonary disease were included. Of them, 50 (92.5%) had an interstitial pattern, followed by pleural line abnormalities in 44 (81.5%), reduced or absent lung sliding in 31 (57.4%), and consolidation in 28 (51.8%). A significantly higher lung US score (median, 18; interquartile range [IQR], 11–22) was observed in ventilated versus nonventilated patients (median, 9; IQR, 6–11). LUSReS improvement after positive end-expiratory pressure titration was positively correlated with improved dynamic lung compliance and oxygenation indices and negatively correlated with the requirement for driving pressure. Successful weaning could be predicted with 100% specificity if loss of LUSReS ≤ 5 .

Conclusion: Interstitial syndrome, fragmented pleural line, and subpleural microconsolidation were the most prevalent lung US findings in children with COVID-19 pneumonia. Thus, lung US may have the ability to monitor changes in lung aeration caused by mechanical ventilation and predict its successful weaning in children with COVID-19.

Key words: Lung ultrasound, COVID-19, Pneumonia, Monitoring

Key message

Question: Potential role of patterns of lung ultrasonography (US) in monitoring changes in mechanically ventilated patients with coronavirus disease 2019 (COVID-19) pneumonia.

Finding: Interstitial syndrome, an irregular pleural line, and peripheral microconsolidation were the most prevalent findings. Changes in lung aeration after mechanical ventilation correlated with improved oxygenation. A fall in lung ultrasound reaeration score ≤ 5 may predict successful weaning.

Meaning: Lung US is gaining wider utility for monitoring COVID-19 pneumonia.

Introduction

The global community is undergoing austerity due to the catastrophic effect of coronavirus disease 2019 (COVID-19) since the emergence of pandemic. Most COVID-19 cases occur in adults, and a subset may progress to severe respiratory illness due to COVID-19-associated hyperinflammatory syndrome.¹⁾ Severe COVID-19 pneumonia after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure is less common in young adults and children. In a systematic review of 7,480 pediatric patients with confirmed COVID-19, only 2% were severe (e.g., dyspnea, central cyanosis, and hypoxemia), and 0.7% were critical (e.g., acute respiratory distress syndrome [ARDS], respiratory failure, and shock).²⁾

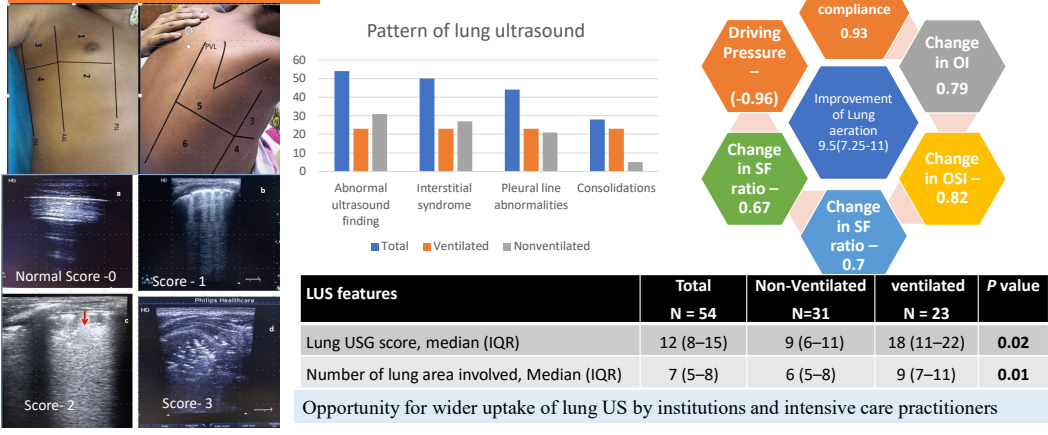
Among adults, chest computed tomography (CT) has been shown to be an effective tool for the diagnosis of COVID-19 pneumonia, as well as a screening tool for the diagnosis of COVID-19 infection in epidemic settings.³⁾ But in children, Chest CT is not recommended as a screening test in suspected COVID-19 infection. The probable risks include radiation ex-

Question - Pattern of lung ultrasound (US) changes in patients with COVID-19 pneumonia and its potential role in monitoring of the ventilated patients.

Method and Pattern – 6 areas of each side scanned with Linear probe – (4-15 Hz)

Result – 54 patients – 23 ventilated, 31 Non-ventilated

Pearson Correlation Coefficient



Graphical abstract

posure, risk of transport of sick patients, COVID-19 exposure to radiology staff, a potentially nondiagnostic study, and increased imaging equipment/room turnaround time for appropriate cleaning and air turnover.⁴⁾

Lung ultrasound (LUS) is a useful diagnostic tool in determining both lung involvement and its severity, thus conceivably plays a role in treatment decisions.⁵⁾ Indeed, LUS is a user-friendly, noninvasive real-time tool available at the patient's bedside.⁶⁾ Pulmonary changes in COVID-19 are predominantly located peripherally in the lower lobes and thus easily persuadable to evaluation by ultrasound, especially in children owing to their thinner chest wall and better image quality.⁷⁾ Several studies draw attention to the applicability of lung US in adults with COVID-19,^{8,9)} however little published evidence exists regarding its clinical usefulness in children.¹⁰⁾

Considering efficacy of lung US in various pulmonary pathologies we incorporated the practice of this imaging modality in routine management of COVID-19 associated pneumonia in children in our tertiary care COVID referral center. In this study, we describe the lung US pattern of COVID-19 infected children and evaluate its role in daily monitoring and weaning of ventilated patients.

Methods

It was a prospective observational study conducted in a tertiary care COVID referral center from September 2020 to June 2021. Children in the age group of 1 month to 12 years with respiratory symptoms on admission in the emergency department, a diagnosis of COVID-19 based on the detection of SARS-CoV-2 by real-time polymerase chain reaction (RT-PCR) from the nasopharyngeal and oropharyngeal swab were

included in the study. Institutional Ethics Committee approval (Ref no – MC/KOL/IEC/NON-SPON/776/09/20) was obtained for conducting the study. Informed consents were taken from the parents/legal guardian of the patients.

Patients with preexisting pulmonary pathology like bronchopulmonary dysplasia, bronchiolitis obliterans, active pulmonary tuberculosis, cystic fibrosis were excluded to minimize the possible interference on the LUS evaluation. Patients with confirmed coinfection by other viral or bacterial pathogen detected by culture or multiplex PCR of respiratory samples were also excluded. Children fulfilling the diagnostic criteria of multisystem inflammatory syndrome (MIS-C) with myocardial dysfunction in echocardiography were also excluded as interstitial edema may be contributed by myocardial dysfunction.¹¹⁾

LUS was performed in all children with pulmonary symptoms and moderate/severe/critical disease severity within 24 hours of admission and then daily till the patient required oxygen therapy.¹²⁾ Chest x-ray was also done in the first 24 hours of hospitalization. Blood culture, sputum or bronchoalveolar fluid culture, and multiplex PCR for other respiratory pathogens were performed. Patients' demographic, clinical, and laboratory data were captured. Severity of respiratory distress, requirement of oxygen, high flow nasal oxygen, noninvasive ventilation, invasive ventilation, duration of respiratory support, oxygenation status, requirement of antiviral, steroid, other treatments, length of pediatric intensive care unit (PICU) stay, and hospital stay were recorded. Acute severe respiratory distress syndrome was defined and categorized according to the pediatric acute lung injury definition.¹³⁾

1. LUS examination

Transthoracic lung ultrasonography was performed by 4 pediatricians trained in method and practicing point of care

LUS for more than 5 years. High-frequency linear probe (4 to 15 MHz) was used to perform LUS. Imaging was done in the supine position and sitting position for patients with moderate severity whereas supine and lateral decubitus position in very sick patients. The depth and frequency were adjusted to set the focal point on the pleural line. By using the anterior & posterior axillary lines, 3 areas per hemithorax were identified (anterior, lateral, posterior). Each area is divided into two, superior and inferior. So, each hemithorax is systemically divided into 6 regions: 2 anterior, 2 lateral, 2 posterior. Finally, for individual patients, 12 chest areas

were analyzed. The anterior scans were performed through the midclavicular line, whereas the lateral scans were done through the midaxillary line, and the posterior scans were performed through the scapular line (Fig. 1).

As stated by the International Consensus Conference on LUS for each area we analyzed the following features: presence of interstitial syndrome (B-lines, not confluent or confluent vertical artifacts with white lung), distribution of B-lines (homogeneous or inhomogeneous with spared areas), consolidations and their distribution, pleural line abnormalities (irregular/fragmented, thickened, and/or with subpleural microconsolidation) and their distribution, pleural effusion, and presence of lung sliding (normal, reduced, or absent).¹⁴⁾

1) LUS score

Assessment of severity of lung involvement was done by LUS score.¹⁵⁾ The maximum score could be 36 and the minimum score zero. (Supplementary Table 1A) (Fig. 2)

2) Lung ultrasound re-aeration score

On daily monitoring of children improvement or deterioration of lung aeration was measured by lung ultrasound re-aeration score (LUSReS) proposed by Bouhemad et al.¹⁶⁾ (Supplementary Table 1B). These measurements were performed daily as routine monitoring and also during significant change in oxygenation and ventilation (oxygen saturation [SpO₂] fall >5% and/or end tidal carbon dioxide rise >10). For ventilated patients, 2 hours after achieving optimum positive end-expiratory pressure (PEEP)

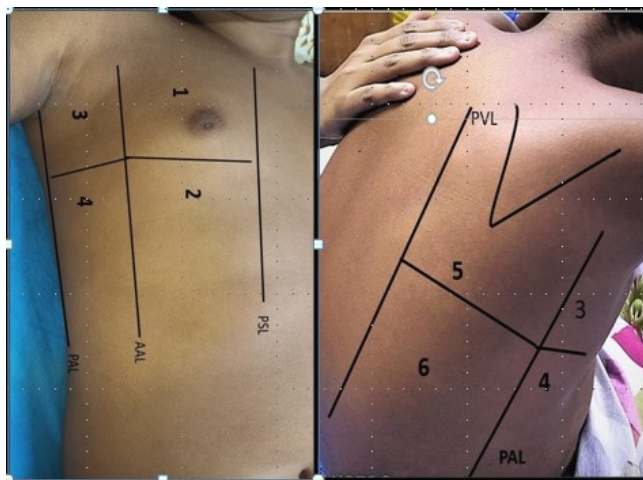


Fig. 1. Anatomical landmark and 6 areas of transthoracic lung ultrasound of right side. AAL, anterior axillary line; PAL, posterior axillary line; PSL, parasternal line; PVL, paravertebral line.

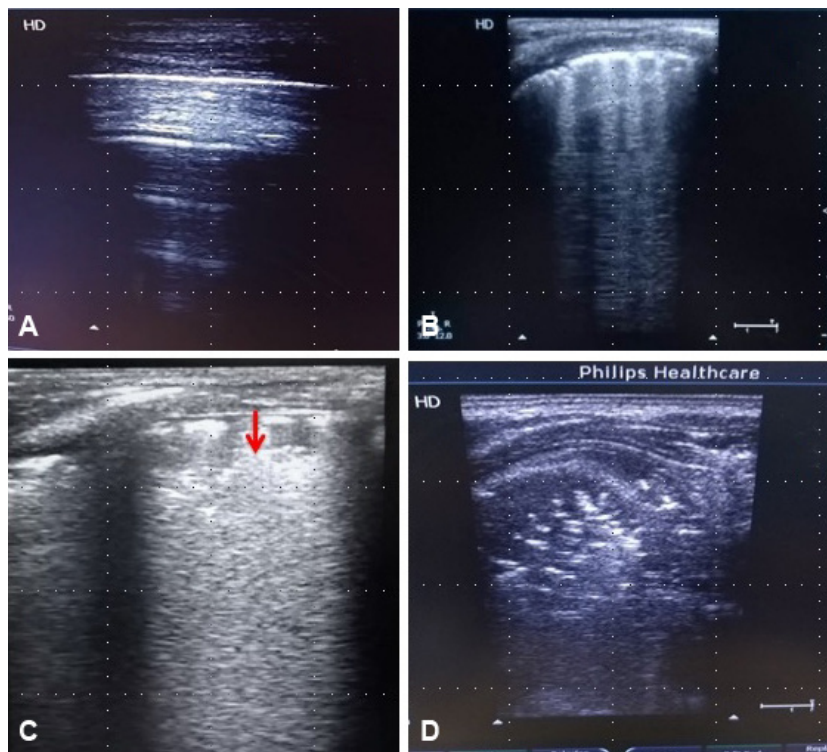


Fig. 2. (A) Normal lung ultrasound – A profile. (B) Clear number of visible B-lines with horizontal spacing between adjacent B-lines. (C) Multiple B-lines indicative of "white lung" with an irregular pleural line and subpleural microconsolidation (arrow). (D) Pulmonary consolidation – C profile.

titration and stable saturation (92%–96%), simultaneously LUSReS, change in dynamic lung compliance, improvement of oxygenation index (OI), oxygen saturation index (OSI), partial pressure of oxygen (PaO₂)/fraction of inspired oxygen (FiO₂) ratio (PF), SpO₂/FiO₂ ratio (SF) and driving pressure were measured.¹³⁾ Dynamic lung compliance was measured by Open lung tool software in Maquet Servo-I ventilator. Loss of LUS aeration score was monitored during weaning and spontaneous breathing trial (SBT), along with other weaning predictors like respiratory rate (RR), heart rate, blood pressure, PaO₂, partial pressure of carbon dioxide, tidal volume, rapid shallow breathing index [RSBI] (breaths/min/mL/kg).¹⁷⁾ RSBI ≤ 8 breaths/min/mL/kg body weight was cutoff for successful weaning. Weaning failure was defined as failed SBT or the need for reintubation within 48 hours following extubation.¹⁸⁾

3) Outcome parameters

The primary objective was to describe and compare the pattern of LUS between ventilated and nonventilated group of children suffering from COVID-19 pneumonia and ARDS.

Secondary objectives were – (1) to find the correlation between improvement of LUSReS and lung compliance, oxygenation indices, driving pressure requirement, 2 hours after PEEP titration; (2) to determine the performance of loss of LUS aeration score to predict successful weaning.

2. Statistical analysis

Data were entered and analyzed using the IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA). Continuous variables were expressed as median with interquartile range (IQR) and mean with standard deviation, while categorical variables, as numbers and percentages. Comparison of demographics, clinical, laboratory test, and lung imaging data (LUS and x-ray) between the 2 group of patients – required mechanical ventilation (MV) (ventilated) and did not require ventilation (nonventilated)

category were analyzed by Fischer, χ^2 , or Mann-Whitney tests. Correlation between improvement in LUSReS and dynamic compliance and oxygenation indices were tested by Pearson rank correlation test. The receiver operating characteristic (ROC) curve was analyzed to assess the predictability of the loss of lung aeration to discriminate between weaning success and failure. Youden index was calculated in MedCalc statistical software to determine the optimal cutoff points of loss of lung aeration score. The area under the curve (AUC) ranges between 0 and 1, and the proximity of AUC to 1 was considered as better performance of that variable. A *P* value <0.05 was considered statistically significant.

Results

During the study period out of 473 admitted children with COVID-19 RT-PCR positive results, 85 children had moderate or severe respiratory symptoms. Thirty-one patients were excluded (Fig. 3). Out of 54 included patients, 23 (42.6%) required MV and termed as ventilated group, whereas the rest 31 patients were termed as nonventilated group.

Demographic, clinical, laboratory, treatment, and outcome parameters of the whole cohort as well as comparison of the parameters between the 2 groups are shown in Table 1. The median age of the study population was 5.5 years (IQR, 1–9). Thirty-one of the cohort (57.4%) were male. Among the clinical characteristics, breathlessness was presenting complaint of 37 patients (77%). Prevalence of comorbidity was greater in the ventilated group (*P*=0.013). The median duration of fever was 6 days (IQR, 3–9.5). RR was significantly high in ventilated patients (42 [IQR, 30–56] vs. 32 [IQR, 24–46], *P*=0.022). Significant low SpO₂ was noted in the ventilated cohort (87 [IQR, 80–92] vs. 92 [IQR, 84–96], *P*=0.013). All patients who required ventilator support fulfilled the criteria of ARDS as

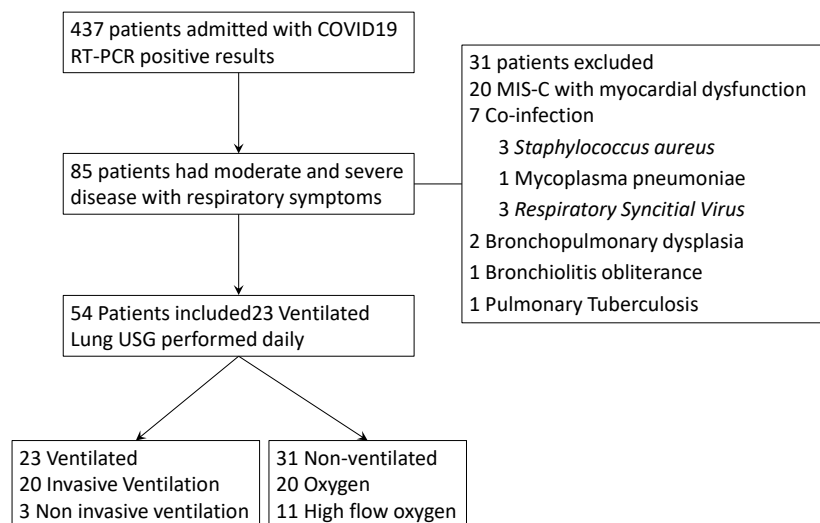


Fig. 3. Study flow. Patients with respiratory symptoms and categorization according to need for mechanical ventilation. COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children; USG, ultrasonography.

Table 1. Demographic, clinical, laboratory, treatment and outcome parameters of the whole cohort and by study group

Characteristic	Total (N=54)	Nonventilated (N=31)	Ventilated (N=23)	P value
Age (yr)	5.5 (1-9)	5.5 (1.5-10)	4.5 (0.8-8)	0.524
Male sex	31 (57.4)	17 (54.8)	14 (61.0)	0.783
Fever duration (day)	6 (3-9.5)	6 (3-10)	5.5 (2.5-9)	0.542
Cough	39 (72.7)	21 (67.7)	18 (78.2)	0.245
Breathlessness	37 (68.5)	14 (45.2)	23 (100)	0.001
Comorbidity, 2 or more	22 (40.7)	8 (25.8)	14 (60.9)	0.013
No. of organ involvement	2 (1-4)	2 (1-3)	3 (2-5)	0.171
PIM III score	12 (8-15)	9 (6-11)	16 (13-20)	0.001
Heart rate	124 (110-146)	122 (108-146)	132 (118-158)	0.063
Respiratory rate	36 (26-48)	32 (24-46)	42 (30-56)	0.022
Temperature (C°)	37.7 (36.9-38.5)	37.5 (37.0-38.4)	37.8 (37.2-38.6)	0.815
SpO ₂ , in room air	90 (82-94)	92 (84-96)	87 (80-92)	0.012
ARDS	33 (61.1)	11 (35.4)	22 (95.6)	0.001
Mild	11	10	1	
Moderate	8	1	7	
Severe	14	0	14	
WBC (×10 ⁹ /L)	8.7 (6.4-11.5)	8.6 (6.0-12.8)	8.9 (6.5-15)	0.923
Lymphocytes (×10 ⁹ /L)	1.1 (0.6-2.2)	1.17 (0.7-1.49)	1 (0.6-1.91)	0.362
Thrombocytes (×10 ⁹ /L)	192 (147-291)	216 (145-288)	172 (115-272)	0.043
Creatinine (mg/dL)	0.7 (0.4-0.9)	0.7 (0.5-0.9)	0.6 (0.4-0.8)	0.737
CRP (mg/dL)	25.8 (12.5-34.5)	21.4 (8.5-30.2)	28.6 (14.4-38.5)	0.067
D-dimer (µg/ml)	4.3 (0.8-10.8)	2.0 (0.7-8.6)	7.1 (1.4-16.3)	0.031
Ferritin (ng/mL)	342 (122-645)	235 (110-456)	543 (240-789)	0.013
Procalcitonin (ng/mL)	0.4 (0.1-0.7)	0.2 (0.1-0.6)	0.6 (0.3-1.3)	0.191
IL-6 (pg/mL) (n=31)	43.0 (12.7-122.0)	18.4 (12.4-69.0)	81.2 (35-200.5)	0.002
Albumin (gm/L)	31.3 (26-34.7)	34.4 (28.7-40.6)	30.2 (24-34.7)	0.124
Treatment				
Remdesivir	28	5 (16)	23 (100)	0.001
Corticosteroid	49	26 (83.8)	23 (100)	0.065
LMWH	22	4 (13)	18 (78)	0.001
Antibiotics >48 hr	19	7 (22.5)	12 (52)	0.041
Prone position	27	7 (22.5)	20 (87)	0.001
PICU admission	43 (79.6)	20 (64)	23 (100)	0.001
Length of PICU stay (day) (n=43)	6.5 (4.5-9.5)	5.0 (3.5-7.0)	8 (5-11)	0.024
Length of hospital stay (day)	8 (7-10)	7.5 (6.0-9.0)	10 (8-13)	0.625
Mortality	2	0	2	

PIM, Pediatric Index of Mortality; ARDS, acute respiratory distress syndrome; WBC, white blood cells; CRP, C-reactive protein; IL, interleukin; LMWH, low molecular weight heparin; PICU, pediatric intensive care unit.

Boldface indicates a statistically significant difference with $P < 0.05$.

compared to 10 patients (32%) in the nonventilated group ($P = 0.001$)

Among the laboratory parameters obtained within first 48 hours of hospital admission, ventilated patients had significantly lower platelet counts compared with nonventilated patients (172 [IQR, 15-272] × 10⁹/L vs. 216 [IQR, 145-288] × 10⁹/L, $P = 0.043$). Serum levels of D-dimer and ferritin were significantly elevated among ventilated study group ($P = 0.031$ and $P = 0.013$ respectively). Statistically significant difference in median interleukin-6 level was noted between ventilated and nonventilated cohort of patients (81.2 [IQR, 35-200.5] pg/mL vs. 18.4 [IQR, 12.4-69] pg/mL, $P = 0.002$).

Remdesivir was used in 28 patients (54%): 23 (100%) in ventilated group versus 5 (16%) in nonventilated group ($P < 0.001$). Corticosteroids and low molecular weight heparin were administered more often in the ventilated group ($P < 0.05$ for both). Prone positioning was performed in 20 (87%) of ventilated patient. Awake proning was done for 7 patients (22.5 %) in the nonventilated group. Early proning was practiced in patients with predominant posterior and lateral lung area involvement. Forty-three patients (79.6%) needed PICU admission. Median PICU length of stay was significantly prolonged in ventilated cohort (8 [IQR, 5-11] vs. 5 [IQR, 3.5-7], $P = 0.024$). Two patients in the ventilated group expired.

1. Pattern of LUS and chest x-ray (CXR) findings (Table 2)

Interstitial syndrome (B-lines) was the most common ultrasound abnormality noticed in 50 patients (92.5%). Bilateral involvement was predominant in the ventilated patients as compared to the nonventilated group: 23 (100%) vs. 6 (19.3%) ($P<0.001$). Inhomogeneous distribution with spared areas was present in 31 (58%). White lung areas were found in 19 subjects and all were in the ventilated group. Pleural line abnormalities were detected in 44 patients (81.5). It was significantly high in ventilated cohort 23 (100%) versus 21 (67%) ($P=0.003$). Fragmented pleural line, thickened pleural line, and subpleural microconsolidation were present in 29 (53.7%), 24 (44.4%), and 39 patients (72.2%), respectively. Eighteen patients (86%) in the ventilated group had reduced lung sliding as compared to 3 (9.6) in nonventilated group ($P<0.001$). Two patients with pneumothorax had absent lung sliding. Consolidation (C profile) was observed in 28 patients (51.8%), with bilateral distribution in 13 patients (24%). Twenty-three ventilated patients (100%) had consolidation, whereas 5 (16.13%) in the nonventilated patient ($P<0.001$). Pleural effusion was present in 12 patients (22.2%) and 7 had bilateral in distribution.

Median LUS score was significantly higher in the ventilated group compared to nonventilated patients (18 [IQR, 11–22] vs. 9 [IQR, 6–11], $P=0.022$). Significantly wider lung area was involved in ventilated patients 9 (IQR, 7–11) vs. 6 (IQR, 5–8) in the nonventilated group ($P=0.015$).

Overall abnormal CXR findings were observed in 47 of patients (87%). Interstitial pattern, ground glass opacities, and consolidations were detected in a significantly higher percentage in the ventilated group compared to the nonventilated group. Perihilar peribronchial wall thickening pattern was noted in 15 of patients (27.7%) and it was present more frequently in nonventilated patients (12 vs. 3) but did not differ at a statistically significant level.

2. Relationship of lung reaeration score to dynamic lung compliance, driving pressure, and oxygenation indices

Among ventilated patients, the median improvement of lung reaeration score was 9.5 (IQR, 7.25–11). Improvement of median lung dynamic complex was 2.74 (IQR, 2.15–3.6) mL/cmH₂O after PEEP titration and it had a strong correlation (Pearson correlation coefficient 0.93, $P<0.001$) with the LUSReS.

Table 2. Lung US patterns in the whole cohort and by study group

LU features	Total (N=54)	Nonventilated (N=31)	Ventilated (N=23)	P value
Abnormal ultrasound finding	54 (100)	31 (100)	23 (100)	
Interstitial syndrome (B-lines)	50 (92.5)	27 (87.1)	23 (100)	0.127
Unilateral interstitial syndrome	21 (38.8)	21 (67.7)	0 (0)	
Bilateral interstitial syndrome	29 (53.7)	6 (19.3)	23 (100)	<0.001
Nonconfluent B-lines (spared area)	31 (57.4)	27 (87.1)	4 (17.4)	<0.001
Confluent B-lines (white lung area)	19 (35.1)	0 (0)	19 (82.6)	
Pleural line abnormalities	44 (81.5)	21 (67.7)	23 (100)	0.003
Fragmented pleural line	29 (53.7)	14 (45.2)	15 (65.2)	0.175
Thickened pleural line	24 (44.4)	14 (45.2)	10 (43.5)	0.655
Subpleural micro consolidation	39 (72.2)	23 (74.2)	16 (69.6)	0.735
Normal lung sliding	21 (38.8)	21 (67.7)	0 (0)	0.001
Reduced lung sliding	31 (57.4)	10 (32.2)	21 (91.3)	0.001
Abolish lung sliding	2 (3.7)	0 (0)	2 (8.7)	0.177
Consolidations	28 (51.8)	5 (16.1)	23 (100)	<0.001
Bilateral distribution	13 (24.1)	0 (0)	13 (56.5)	0.001
Pleural effusion	12 (22.2)	7 (22.6)	5 (21.7)	0.893
Bilateral localization	7 (12.9)	3 (9.6)	4 (17.4)	0.884
Pneumothorax	2 (3.7)	0 (0)	2 (8.6)	0.177
Lung US score	12 (8–5)	9 (6–11)	18 (11–22)	0.022
Number of lung area involved	7 (5–8)	6 (5–8)	9 (7–11)	0.015
CXR findings				
Abnormal CXR findings	47 (87)	24 (77.4)	23 (100)	0.016
Interstitial pattern	29 (53.7)	8 (25.8)	21 (91.3)	0.001
Ground glass opacities	22 (40.7)	7 (22.6)	15 (65.2)	0.002
Perihilar peribronchial opacities	15 (27.7)	12 (38.7)	3 (13.0)	0.064
Consolidation	14 (25.9)	1 (3.2)	13 (56.5)	0.001
Pleural effusion	12 (22.2)	7 (22.5)	5 (21.7)	0.605
Pneumothorax	2 (3.7)	0 (0)	2 (8.7)	0.177

Values are presented as number (%) or median

US, ultrasonography; CXR, chest x-ray.

Boldface indicates a statistically significant difference with $P<0.05$.

Table 3. Correlations between lung ultrasound reaeration score, dynamic lung compliance, oxygenation indices, and driving pressure

Variable	Median (IQR)	Pearson correlation coefficient	<i>P</i> value
Improvement in LUSReS score	9.5 (7.25- 1)		
Improvement of lung dynamic compliance (mL/cmH ₂ O)	2.7 (2.2-3.6)	0.93	<0.001
Change in OI	3.0 (2.6-3.8)	0.79	<0.001
Change in OSI	2.7 (1.9-3.2)	0.82	<0.001
Change in SF ratio	58.0 (23.5-62.0)	0.7	<0.001
Change in PF ratio	59.0 (29.6-65.5)	0.67	0.001
Driving pressure (cmH ₂ O)	13.5 (12.5-15.0)	-0.96	<0.001

IQR, interquartile range; LUSReS, lung ultrasound reaeration score; OI, oxygenation index; OSI, oxygenation saturation index; SF ratio, ratio of oxygen saturation to fraction of inspired oxygen; PF ratio, ratio of partial pressure of oxygen to fraction of inspired oxygen. Boldface indicates a statistically significant difference with *P*<0.05.

All oxygenation indices like OI, OSI, SF ratio, and PF ratio had a good positive correlation with change in lung reaeration score (*P*=0.001 for all). The median requirement of driving pressure after 2 hours of PEEP titration was 14 (IQR, 11.5–18). Driving pressure requirement had a strong negative correlation with improvement of LUSReS (Pearson correlation coefficient: 0.96, *P*<0.001 (Table 3).

Duration of MV before weaning was significantly longer in weaning failure group as compared to the successful group (7.7±2.5 vs. 5.1±2.0, *P*=0.033). Weaning failure cohort had greater median loss of LUSReS during SBT (9 [IQR, 7–12] vs. 5 [IQR, 3–7], *P*<0.001). Other monitored parameters during weaning process like PO₂, FiO₂, P/F ratio, SpO₂, RR, RSBI, PEEP, and pressure had no significant difference between the 2 groups (Table 4). The ROC curve analysis showed that the AUC of the loss of lung aeration for discrimination between successful or failed weaning was 0.94, (95% CI, 0.85–1.00; *P*=0.001), and the cutoff value of 5 or less had a sensitivity of 79% and specificity of 100% to predict successful weaning in the study population.

Discussion

During the COVID-19 pandemic, there has been a paradigm shift from traditional clinical methods to bedside, noninvasive, rapid, and repeatable imaging-based identification, severity assessment, and prospective monitoring of pulmonary pathology. LUS is being increasingly utilized in adults suffering from COVID-19 pneumonia in critical care settings, triaging, and general inpatient settings.^{8,9,19)}

In this study, we observed that all patients with lower respiratory symptoms had abnormal LUS findings. The most prevalent abnormality was interstitial syndrome found in 50 patients (92.5%), followed by pleural line abnormalities 44 (81.5%), reduced or absent lung sliding 31 (57.4%), and consolidation 28 (51.8%) respectively. Severe LUS patterns like bilateral confluent interstitial pattern, abolished or reduced lung sliding and consolidation were frequent findings in patients who required MV and it was corroborated by significantly higher LUS score 18 (IQR, 11–22) in this group as compared to the nonventilated group 9 (IQR,

Table 4. Loss of lung aeration versus other weaning predictors by weaning failure versus success status

Parameter	Weaning failure (N=6)	Weaning successful (N=14)	<i>P</i> value
Duration of MV (day)	7.7±2.5	5.1±2.0	0.033
Loss of lung aeration	9 (7-11)	5 (3-8)	0.001
Comorbidity, n (%)	5 (83)	9 (64)	0.612
SpO ₂ (%)	96.2±2.5	97.2±1.7	0.507
RR (breaths/min)	34 (29-40)	31 (26-35)	0.435
PaO ₂ (mmHg)	100.6±22.4	109.7±22.3	0.273
FiO ₂	0.4±0.1	0.4±0.1	0.415
OI	6.0 (4.5-7.0)	5.5 (4.0-7.0)	0.761
PCO ₂ (mmHg)	47.0±5.4	43.0±4.9	0.074
Tidal volume (mL/kg)	6.2±0.6	6.4±0.8	0.126
Rapid Shallow breathing index (breaths/min/mL/kg)	5.6±2.4	4.8±1.9	0.071
Positive end-expiratory pressure (cmH ₂ O)	5.5±0.5	6.0±0.5	0.544
Pressure support (cmH ₂ O)	10±0	9±1	0.622

Values are presented as mean±standard deviation or median (interquartile range).

MV, mechanical ventilation; SpO₂, oxygen saturation; RR, respiratory rate; PaO₂, partial pressure of oxygen; FiO₂, fraction of inspired oxygen; OI, oxygenation index; PCO₂, partial pressure of carbon dioxide.

Boldface indicates a statistically significant difference with *P*<0.05.

6–11). Improvement in lung USG reaeration score after PEEP titration had a positive correlation with improvement of dynamic lung compliance, OI, oxygenation saturation index, SpO₂/FiO₂ ratio, and PaO₂/FiO₂ ratio, whereas a strong negative correlation was detected with the requirement of driving pressure. Successful weaning could be predicted with 100% specificity if loss of lung aeration scores at or below 5.

In one of the preliminary studies, Musolino et al.¹⁰⁾ from Italy described LUS findings in 10 children with COVID-19 pneumonia. Distinct B-lines (70%), pleural irregularities (60%), areas of white lung (10%), and subpleural consolidations (10%) were major findings of the study. The relevance of LUS as a diagnostic tool in the evaluation of children with (COVID-19) was studied by Hizal et al.²⁰⁾ Out of 40 patients in this cohort, 10 patients had mild pneumonia and 2 were severe/critical. LUS findings were consistent with a chest CT scan. The performance of LUS as a diagnostic test was found to be good; AUC=0.88

(95% CI, 0.75–1.01), sensitivity=83.33%, specificity=93.75%.

Adult studies on lung US in patients with COVID-19 identified similar patterns - interstitial edema, subpleural microconsolidation in an asymmetric multilobar distribution with spared areas involving mainly the lower lobes. Those findings were highly consistent with the CT findings of bilateral, peripheral, and/or subpleural ground glass opacity and/or consolidation on CT.^{9,16,21,22} Similarly in a small group of pediatric patients, *Giorno et al.*²³ showed both the findings and topography of lung compromise on the CT were consistent with the information obtained by lung US.

The frequency of LUS abnormalities was higher in our study population as compared to other pediatric studies. One possible reason is that, we did not screen for asymptomatic patients or patients with only upper respiratory tract symptoms. Chest CT was not done in the study population in acute stage as all patients with lower respiratory tract symptoms had ultrasound changes and also to avoid the risk of transport of sick patients, risk of contamination, avoid unnecessary radiation exposure and difficulty to obtain a good quality image in children.

LUS can play an important role in daily bedside monitoring of ARDS patients in the intensive care unit to assess lung recruitment during PEEP titration. Ultrasonographic assessment of the nonaerated lung area and improvement in aeration score at different levels of PEEP titration and subsequent association with an increase in arterial oxygen partial pressure has been shown in adult study.²⁴ In a prospective study in 40 ARDS patients, *Bouhemad et al.*¹⁶ found a significant correlation between PEEP-induced lung recruitment measured by pressure-volume curves and ultrasound re-aeration score ($Rho=0.88, P=0.001$).

As far as we know, the study on daily sonographic monitoring of COVID-19 pneumonia and ARDS patients has not been done previously. Our data revealed that improvement in lung re-aeration score had a significant correlation with improvement of dynamic lung compliance and oxygenation indices, whereas a negative correlation was noted with driving pressure requirement. Thus, transthoracic lung sonography might be considered a useful clinical tool in COVID-19 ARDS management. LUS can also guide early prone positioning of patients if lesions are distributed in posterior and lateral lung regions. Clinical assessment and respiratory monitoring by the physicians and nurses are basic fundamental need for tailoring therapy and support to individual patient and LUS can aid in the process in greater way in future. In the COVID-19 era with challenges to perform chest CT and repeated CXR opens the opportunity to explore the utility of LUS.

Weaning from MV is a challenging decision, and more so in patients suffering from COVID-19 infection because both extubation and reintubation are high aerosol-generating procedures and requiring special precautions. In a large pediatric study on 106 children, authors concluded the addition of diaphragmatic and lung US improves the performance for prediction of weaning from invasive MV in PICU patients. At total lung score cutoff at 12, AUC for predicting failure of weaning was

0.934, sensitivity, 85.7%; and specificity, 81.2%.²⁵ Another study by *Soummer et al.*²⁶ found loss of aeration determined by LUS during SBT may accurately predict postextubation distress. We observed that loss of lung aeration score at or below 5 was associated with successful weaning.

Being the only tertiary care referral center of the state, we were able to study all moderate to severe COVID-19 infected children, thus our study population represents the whole cohort of the state. We are presenting the data on the LUS pattern of the largest pediatric population. We excluded patients with chronic pulmonary pathology and myocardial dysfunction to eliminate potential confounders. We explored the possible role of this promising tool in prospective monitoring and weaning from MV of severe/critical COVID-19 infected children, which have not been studied previously.

But there are few limitations of LUS – (1) It cannot detect consolidations central in location and perihilar lesions, (2) overdistention of lung during PEEP titration and recruitment cannot be detected. Therefore, we may miss these lesions. We did not assess diaphragmatic function during weaning, which may be associated with weaning failure.

In conclusion, the study revealed that there is opportunity for wider uptake of LUS by institutions and intensive care practitioners. Interstitial syndrome, fragmented pleural line, and subpleural microconsolidation were the most prevalent LUS finding in children affected by COVID-19. In the PICU, LUS may be utilized to identify areas of poor lung aeration, prospectively monitor changes in lung aeration caused by ventilation and recruitment maneuvers as well as predict successful weaning.

Footnotes

Supplementary material: Supplementary Table 1A and B can be found via <https://doi.org/10.3345/cep.2021.00955>.

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