Lung ultrasound an alternative to computed tomography and chest X-ray in the diagnosis of children infected with SARS-CoV-2: a systematic review of literature

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Abstract

Abstract Background: Lung ultrasound (LUS) has become an important tool in diagnosing and following an adult patient with COVID-19; however, the literature for the pediatric age group is limited. Herein, we reviewed the up-to-date literatures on ultrasound use for COVID-19 pediatric patients for better management of COVID-19 in children. Methods and Objectives: The search terms "COVID-19," "SARS-CoV2," "coronavirus," "2019-nCoV," "lung ultrasound," "sonography," "adolescents" "children," "childhood" and "newborn" were searched on the online databases PubMed, Embase and Medline. Articles meeting the inclusion criteria were included in the analysis and review. Results: We identified only fifteen studies to date using LUS to diagnose SARS-CoV-2 infection in children. These studies involved a total of 334 newborns, children and adolescents. Regarding the use of chest X-ray (CXR) and LUS in pediatric patients with COVID-19, we identified six studies with a total of 162 participants, with the following results: 33patients(14.11%) with lung abnormalities on lung US had a normal CXR; however, no patients with normal lung US had abnormalities on the CXR. In addition, regarding the use of computed tomography (CT) and LUS in pediatric patients with COVID-19 infection, we identified five studies with a total of 50 participants and 3 patients(6%) with lung abnormalities on chest LUS had a normal CT. Conclusion: Our findings suggest that LUS is a useful tool in the diagnosis of children and reduction in chest CT assessments may be possible when LUS is used in early diagnosis and follow-up monitoring of COVID-19 pneumonia in the children.

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Results: We identified only fifteen studies to date using LUS to diagnose SARS-CoV-2 infection in children. These studies involved a total of 334 newborns, children and adolescents. Regarding the use of chest X-ray (CXR) and LUS in pediatric patients with COVID-19, we identified six studies with a total of 162 participants, with the following results: 33patients(14.11%) with lung abnormalities on lung US had a normal CXR; however, no patients with normal lung US had abnormalities on the CXR. In addition, regarding the use of computed tomography (CT) and LUS in pediatric patients with COVID-19 infection, we identified five studies with a total of 50 participants and 3 patients(6%) with lung abnormalities on chest LUS had a normal CT.

Conclusion: Our findings suggest that LUS is a useful tool in the diagnosis of children and reduction in chest CT assessments may be possible when LUS is used in early diagnosis and follow-up monitoring of COVID-19 pneumonia in the children.

1 | INTRODUCTION

Since the end of December 2019, coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread worldwide, becoming the first pandemic of the 21st century[1]. Since the beginning of the COVID-19 pandemic, children have been less frequently and severely involved than adults, requiring hospitalization only in 5%–10% of cases[2]. This likely explains the paucity of children-related articles in scientific literature, even with a vertiginous increase in COVID-19 articles. However, recent studies have identified an emerging novel spectrum of the disease in children, including a multisystem inflammatory condition with overlapping features of toxic shock syndrome [3]. To date, the absolute number of those cases with prominent cardiovascular compromise is still low and respiratory symptoms remain the main reason for Pediatric Intensive Care Unit admissions for COVID-19 [4]. The PCR-rapid test is not feasible in all hospitals and a slow turnaround time is an extra burden[5]. Therefore, a rapid, economical and reproducible test to accurately identify the disease in its early stages is critical.

The mild pattern of disease in children's findings is usually subtle compared to adults, and therefore may not be detected on chest X-ray (CXR)[6]. Chest Computed tomography (CT) is undoubtedly the best imaging modality to accurately assess lung involvement in most respiratory illnesses, including COVID-19; however, the cost and possible harmful effects of radiation on a growing child's body must not be ignored, as even low-dose ionizing radiations may increase cancer risk in exposed children [7]. In addition, pathologic findings

are often found later in the disease course, and CT is a poor imaging choice for follow-up or serial imaging [8].

Several studies have shown that lung ultrasound (LUS) is a useful and accurate tool for detecting pneumonia in children[9,10]. Other studies have even shown that LUS can predict more severe pneumonia and monitor antibiotic response. Recently, different LUS patterns have been used to differentiate viral from bacterial pneumonia by defining their etiology in child [11]. Although several studies have investigated LUS in adult COVID-19 patients, the literature for the pediatric age group is limited[12]. This study aimed to review the available evidence of the use of LUS versus CXR and chest CT in children suspected to have COVID-19 pneumonia and sought to identify an alternative diagnostic technique that is less invasive than radiation and more practical in early-stage diagnosis and follow-up monitoring of COVID-19 pneumonia.

2 | MATERIALS AND METHODS

We performed a systematic literature review of published research articles based on a search for the keywords "COVID-19," "SARS-CoV2," "coronavirus," "2019-nCoV," "lung ultrasound (LUS)," "sonography," "adolescents" "children," "childhood" and "newborn" in the online databases PubMed, Embase and Medline. Our systematic review was drafted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 1). The inclusion criteria were English language and publication between 15 May 2019 and 10 October 2021. 181,978 articles were found with "COVID-19" as a keyword. We found 322 articles when limiting the search to lung ultrasound, Adolescents, child and newborn keywords. After reading these 192 manuscripts, we excluded articles that did not concern the study topic or involved an adult population. Among full-text articles assessed for eligibility, we excluded a letter and literature reviews (10 articles).

We included articles on pediatric patients diagnosed with SARS-CoV-2 infection, detected by real-time reverse transcription polymerase chain reaction assay, carried out in upper and lower respiratory specimens taken by nasopharyngeal swab and oropharyngeal swab or respiratory tract aspirates, who underwent at least one time of diagnostic imaging of LUS. Studies enrolling confirmed COVID-19 cases without performing LUS were excluded.

3 | RESULTS

We identified only fifteen studies to date using LUS to diagnose SARS-CoV-2 infection in children and these studies involved a total of 334 newborns and children. These studies used LUS and nasal swabs to diagnose SARS-CoV-2 and show the distribution of different ultrasonic patterns as follows: the presence of B-lines in 73.94% of patients, sub-pleural consolidation in 63.44%, pleural irregularities in29.03%, coalescent B-lines in 27.64% and white lung in11.89% and thickening of the pleuralion in 63.52%. Table1 shows the characteristics of included studies.

Regarding the use of CXR and lung US in pediatric patients with COVID-19 infection, we identified six studies with a total of 126 participants, with the following results: 33patients(14.11%) with lung abnormalities on lung US had a normal CXR; however, no patients with normal lung US had abnormalities on the CXR. Regarding the use of CT and lung US in pediatric patients with COVID-19 infection, we identified five studies with a total of 50 participants, with the following results: 3 patients(6%) with lung abnormalities on chest LUS had a normal CT.

Three studies evaluated the relationship between LUS scores and severity of the disease, and only one study demonstrated the application of LUS in follow-up after discharge on COVID-19 children.

4 | DISCUSSION

There has been limited data regarding the usefulness of LUS in children with COVID-19. Given the paucity of children-related articles in scientific literature, Norbedo et al. reviewed only 2 studies on ultrasound use for COVID-19 suspected pediatric patients and compared them with the published findings in adult patients. They demonstrated that in the context of pediatric patient evaluation use of LUS could aid in

detecting COVID-19 pneumonia, even if a small case series reported encouraging results[8]. Caroselli et al. identified only seven studies using LUS to diagnose SARS-CoV-2 infection in newborns and children and compared it with published findings, including 117 studies describing the use of chest X-ray or chest computed tomography in pediatric patients with COVID-19, and the review indicates that the use of LUS should be encouraged in pediatric patients, who are at highest risk of complications from medical ionizing radiation[28.] To the best of our knowledge, this is the first systematic review study of the pediatric age group to evaluate the use of LUS versus CXR and chest CT in children with COVID-19. In the present study, we identified 33 patients (14.11%) with lung abnormalities on LUS who had a normal chest radiograph, but no patients with normal lung US had abnormalities on the CXR. Therefore, we conclude that lung ultrasound is more accurate than CXR in identifying patients with COVID-19 pneumonia. Moreover, we identified 3 patients(6%) with lung abnormalities on chest LUS who had a normal CT in this review. Feng et al. reported two cases (out of 5 children) and Hizal et al. reported only one case (out of 28 children) of discordance of LUS and chest CT results, respectively, an increased B-line in the lower lobe and normal chest CT findings[17,.21]. All three patients underwent LUS and CT at the time of admission to the hospital with mild to moderate symptoms. Musolino et al. report that more B lines were presented in children in the early stage of the COVID-19 children[20]. Furthermore, the cause of this inconsistency could be that CT scan was suggested as a screening method due to rapid identification of pulmonary images typical of COVID-19 such as the ground-glass opacity; however, it is also demonstrated that the pathological findings are pathological are often found later[29]. Meanwhile, the fact that COVID-19 lung involvement begins predominantly from peripheral regions of the lung creates an advantage in detecting these lesions via LUS. Consequently, the abnormal LUS findings detected in patients with normal CT made us believe that LUS is a sensitive diagnostic tool of child COVID-19 pneumonia, especially in the early stage of the disease and mild cases.

To avoid excessive radiation exposure and contamination of suites, personnel and equipment, the British Paediatric Respiratory Society recommended that chest CT should be reserved for unstable cases with increasingly clinical deterioration or if surgery cannot be postponed[30]. However, as is widely known, the clinical COVID-19 manifestations in children are mild or moderate compared to the adult population; therefore, there is an urgent need to understand the correlation between lung US findings and clinical severity in this desease[31]. In our review, only 3 relevant studies were included. The study of Giorno et al. was the first in the pediatric COVID-19 population to analyze lung US aeration scores and demonstrated that patients that classified as moderate and severe/critical had major abnormalities on lung US and consequently higher lung US aeration scores[15]. They do not have statistical power to confirm the lung US aeration score as a disease severity predictor given the small sample size. Li et al. retrospectively evaluated neonates with confirmed COVID-19 as well as 11 age- and gender-matched controls (control group) simultaneously and the LUSS was significantly higher in the COVID-19 group($P < 0.05$), suggesting that might be an additional tool to help clinicians in risk stratification[18]. However, this was a retrospective study, and few positive cases were not enrolled due to a lack of timely LUS examination. Musolino et al. conducted a prospective observational study, including 30 patients with swab-confirmed COVID-19 infection and the patients were subjected to an LUS within 6 h from admission and after 96 h. The results showed that LUS had a 90.9% sensitivity in detecting signs of lung involvement by COVID-19. Importantly, the LUS allowed differentiating between those with mild or moderate disease[20]. Since the ultrasound aspects described in the study are not pathognomonic of SARS-CoV-2 infection and also found in the course of other lung diseases, the result is still encouraging. In view of this, LUS can be useful to identify patients with lung involvement and in staging their severity in this new disease.

As residual lung fibrosis may develop after viral infections also in children with COVID-19, a longitudinal follow-up study with invasive or less invasive imaging techniques would be of remarkable value. Interestingly, only one study about the application of LUS in longitudinal follow-up on COVID-19 children was founded. This limited use of LUS in children, if reflective of daily clinical practice, contradicts available scientific evidence. Denina et al., using LUS done a follow-up for 28 patients to study the sequelae of COVID-19 in children and lung ultrasound findings correlated with the clinical improvement, showing a complete normalization within 5 weeks from hospital discharge in the majority of patients[14]. Therefore, we believe it

is urgent to prompt further investigation into longitudinal follow-up study with LUS and an extended time follow-up is also necessary.

Finally, research on COVID-19 pneumonia diagnosis is hampered by the difficulties in obtaining a systematic comparison with a CT scan. Despite, we believe that it provides valuable information, as there is limited data regarding pediatric patients with this condition. In addition, all the sonographers from the literatures were not blinded to clinical information because lung US assessment is performed regularly as an extension of the physical examination. Therefore, we recommended that LUS findings always should be interpreted in light of the clinical context.

Consequently, we suggest that LUS is a useful tool in diagnosing children with COVID-19 during the pandemic. When LUS is used in the initial diagnostic steps in early diagnosis and follow-up monitoring of COVID-19 pneumonia in children, reduction in chest CT assessments may be possible.

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None.

Conflict of interests

All authors declare that they have no any conflict of interests.

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Figure legends

Figure 1. The PRISMA flow diagram depicts the flow of information through the different phases of our systematic review

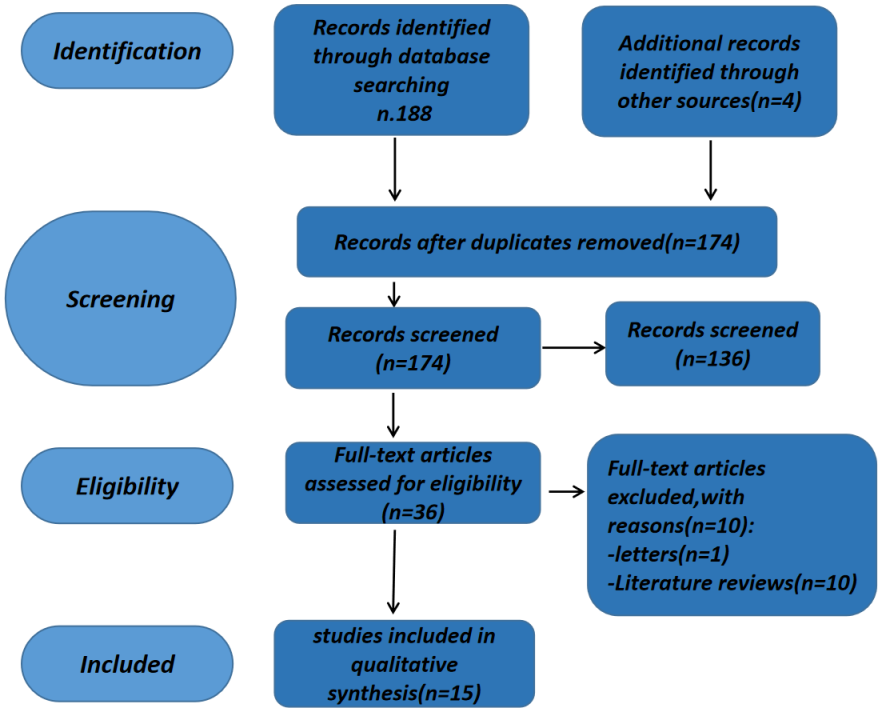

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Table 1Characteristics of included studies.docx available at https://authorea.com/users/738214/articles/712644-lung-ultrasound-an-alternative-to-computed-tomography-and-chest-x-ray-in-the-diagnosis-of-children-infected-with-sars-cov-2-a-systematic-review-of-literature