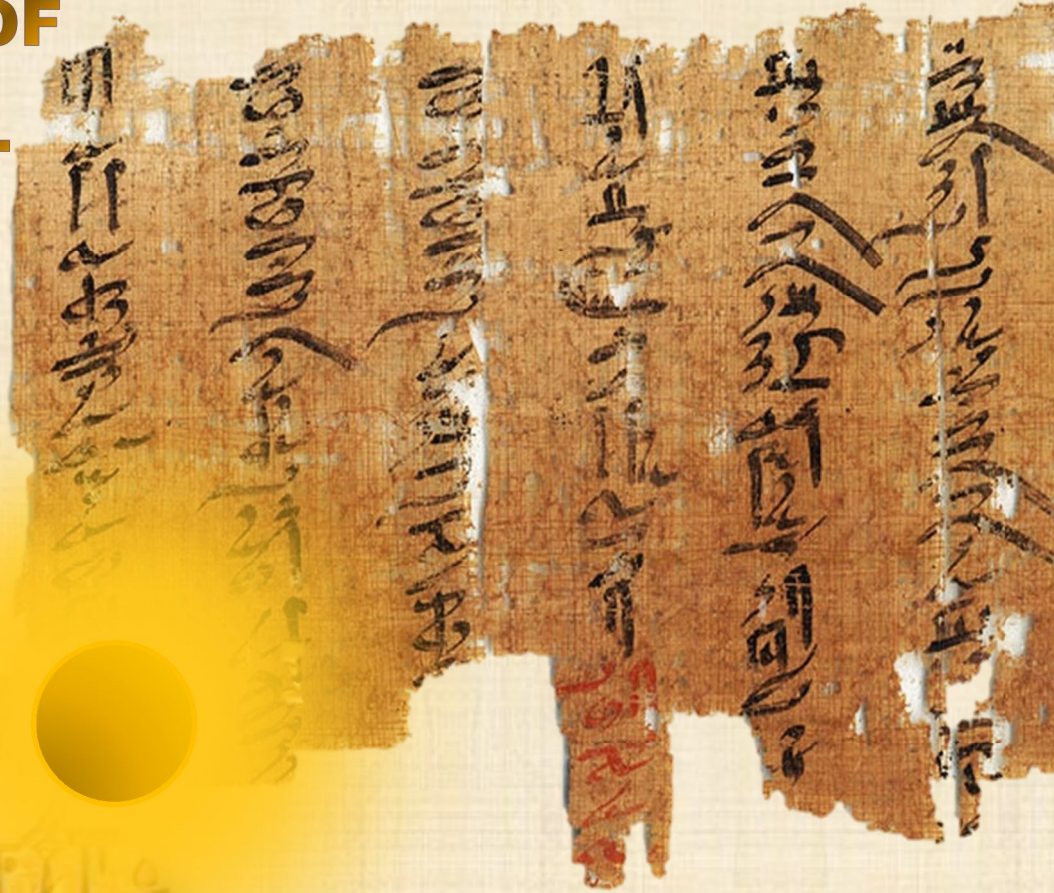


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Original article

Ultrasound in Suspected Pneumonic COVID-19: Our Experience

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ABSTRACT

Background: Coronavirus disease-19 [COVID-19] is a pandemic spreading all over the world. The novel corona virus has a specific tropism for the low respiratory airways causing viral pneumonia. Early diagnosis of suspicious COVID-19 pneumonia represents a pillar for immediate management. Computed tomography [CT] scan is considered the gold-standard screening tool, but it has several limitations. A chest ultrasound could play a role in COVID-19.

Aim of the work: To evaluate the role of lung ultrasound [LUS] in diagnosis of suspicious COVID-19 pneumonia.

Patients and Methods: Sixty patients with suspected COVID-19 pneumonia were included. They were initially evaluated in triage and initial diagnosis [Al-Azhar University Hospital; Damietta] and followed up by the surveillance and infection control team till the final diagnosis or discharge from isolation hospitals. All were evaluated clinically, by imaging modalities [LUS, chest computed tomography [CT]] and diagnosis confirmed by polymerase chain reaction. Data of LUS and chest CT compared to results of PCR.

Results: LUS had sensitivity of 88.2%, specificity of 11.5%, PPV of 56.6%, NPV of 42.8% and overall diagnostic accuracy of 55.0%. on the other side, CT scan had 94.1%, 3.85, 56.14%, 33.33% and 57.0% for sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy, successively. Results of LUS are slightly lower than CT.

Conclusion: US is a useful screening and monitoring tool in suspected COVID-19. It is feasible, portable with an accepted rate of sensitivity. However, it is advisable to be used as an integrated diagnostic tool.

Keywords: COVID-19; Lung Ultrasound; Pneumonia; Screening; Diagnosis.

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* Main subject and any subcategories have been classified according to research topic.

INTRODUCTION

Coronavirus disease-19 [COVID-19] is an infectious pandemic caused by a new coronavirus, known as severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]^[1]. Clinically, it presents by non-specific manifestations of fever, fatigue and dry cough. But, it could be completely asymptomatic or complicated by severe pneumonia^[2]. Treatment is mainly supportive. However, available medical treatments for COVID-19 pneumonia [a severe complication of the disease] include different anti-viral drugs, drugs blocking the inflammatory cascade [e.g., anti-interleukin-6], chloroquine, mechanical ventilation [MV] and extracorporeal membrane therapy. Available evidence recommends early treatment, as it is concomitant by better and rapid improvement^[3,4]. This elucidate the significance of diagnostic methods early in the course of the disease.

Computed tomography [CT] is extensively used as an initial screening and diagnostic tool of viral pneumonia [including COVID-19]^[5]. The real-time, polymerase chain reaction [RT-PCR] is then used to confirm the diagnosis of COVID-19 by amplification of nucleic acid particles, detected from respiratory tract or blood specimens^[6]. Unfortunately, RT-PCR had multiple limitations: first, the results are false negatives when viral load in the specimen is low leading to low detection rate; Second, it could not reflect the disease severity or predict its progression; Third, shortage of reagents supply, and new reagents awaits extensive studies and improvement; Fourth, it takes time to obtain the results. For these reasons, researchers recommend the usage of CT as the main and initial tool for diagnosis of COVID-19^[7]. Additionally, if there is a patient with suspicion of COVID-19 [on clinical basis] with positive CT findings, but negative PCR, such patient must be isolated and managed as a positive case as soon as possible^[8]. Computed tomography is not readily available in all health care facilities, especially in developing countries. Thus, another, readily available, relatively cheap initial diagnostic and screening tool is mandatory. Ultrasound could represent such tool. **Soldati et al.**^[4] reported that, a chest ultrasound could have a role in COVID-19 pandemic and they advocated the spread of its use.

The main advantages of thoracic ultrasound include wide availability, easily use, ease and rapid

disinfection, and the ability of its use at patient's bedside. In addition, it is more sensitive than X-ray chest in diagnosis of different pneumoniae^[9,10]. However, the ultrasound role as a sole or complementary diagnostic modality in COVID-19 pandemic is still questioned.

AIM OF THE WORK

The aim of the present work is to investigate the diagnostic ability of thoracic ultrasound in suspicious COVID-19 infection and/or COVID-19 pneumonia. Also, to compare its findings to CT and SARS COV2 PCR.

PATIENTS AND METHODS

The present study is a prospective cohort study, carried out at Al-Azhar University hospital [New Damietta] during the period from April to June 2020. Sixty patients with suspicious COVID-19 clinically were recruited. Included patients were selected from those attending triage room and emergency department. The diagnosis was confirmed or excluded by PCR. The study protocol was approved by the local and research ethics committee of Damietta Faculty of Medicine [Al-Azhar University].

As a tertiary care hospital, our hospital developed its own triage for COVID-19 with its nomination as a pandemic. At emergency department entry, a team of [chest disease specialist, general practitioner and high nurse] who had been trained for handling of suspicious COVID-19 cases checked all attendants and divide them into two suspicious and non-suspicious groups according to the case definition of COVID-19 launched by Egyptian Ministry of Health [MOH] in April 2020. Suspected cases are admitted to a special department of the hospital [which is totally away from and secured to prevent transmission of infection other departments of hospital] to fulfill the case definition. Suspected cases were subjected to analysis of complete blood count [CBC] and arterial blood gases [ABG]. Chest ultrasound was performed under standard precautions of infection control. Suspected cases directly referred to isolation hospitals in Damietta governorate, for further management. Chest ultrasound examination had been completed in the special department of isolation, under strict precautions to minimize exposure to infection according to WHO recommendations, with portable ultrasound machine. The lung had been scanned as described previously by **Buonsenso et al.**^[11].

A convex sensor [3.5 MHz] connected to a tablet was used for lung ultrasound. This system has been selected to mitigate the chance of infection and the resulting nosocomial spread. Two operators, an ED doctor [pulmonary intensivist] and an ED nurse [operator 2] entered the insulation room. Lung ultrasound was conducted by Operator 1 who reached the patient. Operator 2 was responsible for freezing and saving images/videos, but the patient did not touch anyone else in the room. The two operators shared and agreed this procedure before entering the room to minimize the risk of contamination. The tablet and the sensor have been sterilized in a certain area at the end of the procedure and are placed in two new sterile plastic bags. In the next, the thorax was scanned at bedside in the following 12 lung areas: anterior higher and lower, lateral higher and lower, posterior higher and lower on both sides of the lung. 'B-lines' are a hallmark of alveolo-interstitial US syndrome and their semi-quantification helps in determining its duration. Although a recent consensus discusses some aspects of B-line image acquisition, research are sparse on reproducibility between raters and transducers^[12]. **CT examinations** had been performed as described by **Xu X. et al.**^[13]. Image analysis carried by an-independent radiologist described lesion characteristics [e.g., distribution, number of lobes, lesion's pattern and involvement of adjacent structures]. Consolidation confirmed if there is an opacity which obscured bronchial structures and pulmonary vessels. Crazy paving defined as ground glass opacity associated with interlobular septal thickening ^[14]. Our infection control and surveillance team was able to follow up those 60 patients. Then, patients were subdivided into covid-19 positive and negative subgroups according to results of SARS-CoV2 PCR.

Statistical analysis of data: by statistical package for social sciences [SPSS], version 16 [SPSS Inc., Chicago, USA], all statistical tests had been carried out. Qualitative data presented in frequency and percentage distribution, while quantitative data presented as mean [for central tendency] \pm standard deviations [SD; for dispersion]. The yield of studied tools had been determined by Wilsons score method. Groups had been compared by student samples [t] test, Chi square, Mann Whitney tests according to type of data. $P < 0.05$ had been considered significant. A receiver operating characteristic curve (ROC curve) (Wilson score

method) was used to test the validation and accuracy of the chest CT scan and LUS in COVID19 screening considering SARS COV2 Polymerase chain reaction (PCR) (Wilson score method) as a gold confirmatory standard. Also, a receiver operating characteristic curve (ROC curve) (Wilson score method) was used to test the validation and accuracy of the LUS in COVID19 pneumonia screening considering chest CT scan as a gold confirmatory standard.

RESULTS

The present study included 60 patients with clinical and imaging suspicion of COVID-19 pneumonia. The diagnosis was confirmed in 34 patients [56.7%] and 26 patients [43.3%] yielded negative 3 PCR examination results. Males represented 67.6% of positive and 53.9% of negative group with no significant difference between groups. The age ranged between 19 and 69 years and the mean age of positive group was 43.97 ± 12.5 years, while it was 44.58 ± 9.67 years. Both positive and negative groups were comparable as regard to different comorbid diseases [chronic obstructive pulmonary disease [COPD], diabetes mellitus, hypothyroidism and neuromyopathy], except significant increase of hypertension and liver diseases among positive [73.5%, 17.6%] when compared to negative group [46.2%, 0.0% respectively] [Table 1]. The clinical and laboratory data were presented in table [2]. No significant difference was reported between positive and negative groups as regard any of clinical or laboratory data, except significant decrease of albumin in negative when compared to positive group [3.45 ± 0.84 vs 4.03 ± 1.01 respectively]. The ultrasound findings in relation to the CT characters among the studied patients are presented in table [3], 11.7% was free of any LUS characters but 100% of them showed ground glass opacity in the chest CT. Only 20% of the patients revealed Thick pleural line by ultrasound; majority 66.7% of them was ground glass opacity in the CT. Multiple B line ultrasonographic character presented among 15.0% of patients and 33.3%, 33.3% of them showed ground glass opacity and combined ground glass opacity & consolidation in the CT respectively. Majority 30.0% of the patients revealed lung rocket in the pulmonary ultrasound 33.3% of them showed crazy paving and 27.8% of them showed consolidation in the CT.

According to results of ultrasound scan, COVID-

19 positive patients were assigned to positive or negative groups and their results were compared to final PCR results to test sensitivity and specificity of both modalities and results had been presented in table [4]. CT scan had 94.1%, 3.85, 56.14%, 33.33% and 57.0% for sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy, successively; while LUS had sensitivity of 88.2%, specificity of 11.5%, PPV of 56.6%, NPV of 42.8% and overall diagnostic accuracy of 55.0%. Results of LUS are slightly lower than CT in diagnosis of COVID19 infection. COVID-19 positive patients were assigned to pneumonic or non-pneumonic groups and their results were compared to chest CT scan to test sensitivity and specificity of LUS in diagnosis of COVID19 pneumonia in comparison to chest CT scan as a gold standard and results had been presented in table [6]. LUS had 87.93%, 0.0 %, 96.23%, 0.0% and 85% for sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy, successively.

Results of CT scan in the current study were normal among 5.9%, revealed consolidation among 20.6%, ground glass opacity [GGO] among 35.3%, crazy paving among 17.6%, GGO with consolidation among 11.8%, GGO with crazy paving among 8.8%, while no patients had lymph-adenopathy or pleural effusion. These data were compared to previous studies and results showed great variability [Table 5].

Mortality among COVID-19 patients was presented in figure [1]. Two patients out of 34 positive cases [5.9%] were died.

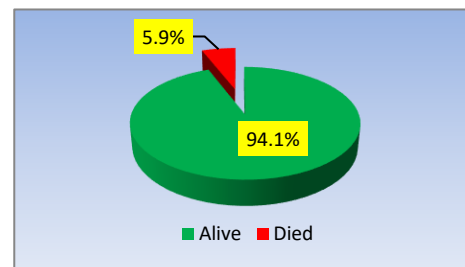


Figure [1]: Mortality among the COVID-19 patients

Table [1]: Demographic and comorbid conditions variability among the studied group

Variable		COVID 19 cases [N=34]	Non COVID 19 [N=26]	P- value
Age	Mean± SD	43.97± 12.5	44.58±9.67	0.835
Sex	Male	23 [67.6%]	14 [53.9%]	0.197
	Female	11 [32.4%]	12 [46.1%]	
Comorbidities				
Hypertension		25[73.5%]	12 [46.2%]	0.031*
COPD		2 [5.9%]	4 [15.4%]	0.224
Diabetes Mellitus		22 [64.7%]	15 [57.7%]	0.580
Hepatic disorder		6 [17.6%]	0 [0.0%]	0.024*
Hypothyroidism		3 [8.8%]	3 [11.5%]	0.728
Collagen disorder		0 [0%]	0 [0%]	-
Neuromyopathy		3 [8.8%]	1 [3.8%]	0.444

N: number of subjects, SD: standard Deviation, COPD: chronic obstructive pulmonary disease. *Statistical Significance was defined as P <0.05.

Table [2]: Clinical and laboratory data of the patients suspected with COVID-19

Variable	COVID 19 cases [N=34]	Non COVID 19 [N=26]	P- value
BMI	27.88 ± 5.37	28.73 ± 3.81	0.835
HR	115.15 ± 14.7	113.27 ± 11.64	0.594
SO2	88.85 ± 2.69	87.27 ± 4.81	0.111
HGB	13.71 ± 1.70	12.90 ± 1.57	0.063
TLC ×10 ³	12.18 ± 5.56	12.25 ± 4.79	0.959
Lymphocytes×10 ³	2.198 ± 0.82	3.92 ± 0.69	0.172
Albumin	4.03 ± 1.01	3.45 ± 0.84	0.019*
Urea	66.94± 41.02	85.65 ± 45.95	0.103
Creatinine	1.76 ± 1.22	1.92 ± 0.59	0.545
Na	134.47 ± 8.26	130.61 ± 6.52	0.055
K	4.40 ± 0.91	4.15 ± 1.07	0.341
CRP	45.12 ± 22.03	47.15 ± 26.55	0.747
D-dimer	1661.17 ± 952.17	1496.92 ± 811.23	0.484

N: number of subjects, SD: standard Deviation, BMI: Body mass index, HR: heart rate, SO₂: oxygen saturation, HGB: hemoglobin, TLC: total leucocyte count, CRP: C-reactive protein. *Statistical Significance was defined as P <0.05.

Table [3]: Distribution of LUS findings in relation to the chest CT scan characters among the studied patients

LUS		Chest Computed Tomography						Total*
		Normal	GGO	Consolidation	Crazy Paving	GGO, Consolidation	GGO, Crazy Paving	
Normal	N	0	7	0	0	0	0	7
	% ^α	0.0%	38.9%	0.0%	0.0%	0.0%	0.0%	11.7%
	% [Ⓞ]	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	100.0%
Thick pleural line	N	1	8	0	0	2	1	12
	% ^α	50.0%	44.4%	0.0%	0.0%	15.4%	20.0%	20.0%
	% [Ⓞ]	8.3%	66.7%	0.0%	0.0%	16.7%	8.3%	100.0%
Multiple B line	N	0	3	2	0	3	1	9
	% ^α	0.0%	16.7%	14.3%	0.0%	23.1%	20.0%	15.0%
	% [Ⓞ]	0.0%	33.3%	22.2%	0.0%	33.3%	11.1%	100.0%
Lung Comet	N	0	0	7	2	5	0	14
	% ^α	0.0%	0.0%	50.0%	25.0%	38.5%	0.0%	23.3%
	% [Ⓞ]	0.0%	0.0%	50.0%	14.3%	35.7%	0.0%	100.0%
Lung Rocket	N	1	0	5	6	3	3	18
	% ^α	50.0%	0.0%	35.7%	75.0%	23.1%	60.0%	30.0%
	% [Ⓞ]	5.6%	0.0%	27.8%	33.3%	16.7%	16.7%	100.0%
Total	N	2	18	14	8	13	5	60
	% ^α	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	% [Ⓞ]	3.3%	30.0%	23.3%	13.3%	21.7%	8.3%	100.0%

*[Pearson Chi-Square = 53.6, P value = 0.000], GGO: Ground Glass Opacity, ^α percentage within CT, [Ⓞ] percentage within LUS

Table [4]: Evaluation of validation and accuracy of CT vs LUS for COVID-19 epidemics screening when Polymerase chain reaction (PCR) is a gold standard using Wilson score method

Variable	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	Diagnostic accuracy
CT scan	94.1% [80.91- 98.37]	3.85% [0.68-18.89]	56.14% [43.28- 68.23]	33.33% [6.15-79.23]	57% [41.36-68.42]
LUS	88.2% [73.38-95.33]	11.5% [4.03-28.98]	56.6% [43.27- 69.0]	42.8% [15.82-74.95]	55% [42.49-66.91]

CT: computed tomography, US: ultrasonography, CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value

Table [5]: Comparison of CT findings with some papers published during 2020

Variable	Current study	Xu X.,et al. ^[13]	Chen et al. ^[15]	Chung M. et al. ^[14]	Song et al. ^[16]
Normal	3.3%	23%	N/A	N/A	N/A
Consolidation	30.0%	13%	100%	29%	59%
GGO	23.3%	72%	14%	86%	77%
Crazy Paving	13.3%	12%	N/A	N/A	N/A
GGO, Consolidation	21.7%	N/A	N/A	N/A	N/A
GGO ,Crazy Paving	8.3%	N/A	N/A	N/A	N/A
Lymphadenopathy	N/A	1%	N/A	0.0%	6%
Pleural Effusion	N/A	4%	N/A	0.0%	6%

CT: computed tomography, GGO: Ground Glass Opacity

Table [6]: Evaluation of validation and accuracy of LUS for screening of COVID-19 pneumonia epidemics when chest CT scan is a gold standard using Wilson score method

Variable	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	Diagnostic accuracy
LUS	87.93% [73.38 - 95.33]	0.0 % [0.0 - 65.76]	96.23% [87.25 - 98.96]	0.0% [0.0 - 35.43]	85% [73.89 - 91.9]

CT: computed tomography, US: ultrasonography, CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value

DISUCSSION

Although, about nine months had been passed since the documentation of the first COVID-19 case, the world still fight to find a curative treatment or a vaccine for the disease. All countries tailored their daily activity to adopt live with the disease, and some countries no longer considered it as a high consequence infection disease, although world health organization still report progressive increase of recorded cases allover the globe^[17].

The importance of a screening test or tool becomes more and more significant with time. Computed tomography, lung ultrasound, and viral swabs had been used as a screening tools. However, CT imaging had the drawbacks of being slow, expose patient to ionizing radiation, and exposes the other medical team members to COVID-19 infections^[18].

On the other side, lung ultrasound is readily available, had no risk or exposure to ionizing radiation and relatively simple when compared to CT [no need for staff or time as CT]. But, it carries the same risk exposure to COVID-19 of the treating physician^[9].

We here presented our experience with LUS. Results revealed that, ultrasound is nearly as effective as computed tomography in diagnosis of Pneumonic COVID-19. **Soldati et al.**^[4] advocated the use of lung ultrasound use as a screening tool in COVID-19 pandemic on the basis of animal studies and its role in acute respiratory distress syndrome^[19] and its diagnostic role in H1N1 pandemic^[20].

Soldati et al.^[4] strongly proposed the diagnostic benefits of lung ultrasound for: triage [pneumonic/non-pneumonic COVID-19], diagnostic suspicion in emergency situation, follow up and monitoring [either in wards or intensive care unit] and reduction of exposed health care professionals to risk of infection [single clinician].

In addition, **Vetrugno et al.**^[9] concluded that, the use of lung ultrasound permitted the identification of patients with lung involvement. Disease severity had been documented and serial thoracic ultrasound were used to document the course of the disease. A significant reduction of chest x-ray and CT scans had been observed with the introduction of ultrasound.

Fox and Dugar^[21] challenged the use of ultrasound in COVID-19 due to non-specific manifestations of the disease which resembles picture of other viral pneumonia and acute respiratory distress syndrome in its severe form. However, they recommended the use of LUS to increase sensitivity, for proper allocation of medical service and monitoring of patients. This reflected their orientation to the important role of LUS in COVID-19 irrespective of non-specific manifestations [the tool could not blamed for this findings].

Regarding CT findings in the current work, it lies with previous studies showed that, main changes on CT depends on the study of the disease and usually presented as patchy or segmental GGO with vascular dilatation. Very small number of patients had normal CT findings, early in the disease. With disease progression, the GGO increased with involvement of multiple lobes, appearance of consolidations, both GGOs surrounding consolidations [which is characteristic for severe stages]. In addition, septal thickening and crazy paving are usually present. In advanced stages, CT lung revealed consolidation with GGO around consolidated areas accompanied by bands of parenchymal origin with small amount of effusion [i.e. lung whiteout]^[7].

Hamer et al.^[22] also reported that, the most common manifestations of pneumonic COVID-19 on CT are GGO, followed by a mixed picture of GGO and consolidation, and then consolidation alone.

In addition, the sensitivity of CT in the current work lies with the range of reported in previous studies. For example, **Cheng et al.**^[23], **Caruso et al.**^[24], **Ai T, et al.**^[25], and **Fang et al.**^[26] reported that, the sensitivity of chest CT for COVID-19 pneumonia detection [diagnosis] has been reported to be [97%], the specificity [25% to 56%], and the overall accuracy [68% to 72%].

Results of the current work revealed that, ultrasound give nearly similar accuracy as CT in diagnosis of pulmonary changes in pneumonic COVID-19. One study compared different imaging modalities in intensive care unit revealed high agreement between LUS and CT. The same authors appreciate the role of LUS in exclusion of other pulmonary diseases [e.g., pneumothorax and effusion]^[27].

Poggiali et al.^[28] also reported a strong concordance between LUS and CT when carried out simultaneously in patients with flu-like manifestations and recommended its use instead of CT in early diagnosis of COVID-19.

Liu et al.^[29] through an international webinar concluded that, LUS appears to be a promising first line, comprehensive diagnostic tool in both suspected and diagnosed COVID-19.

Istvan-Adorjan et al.^[30] carried a mini-review about LUS in COVID-19 and concluded that, In COVID-19, pulmonary lesions determine the clinical course and prognosis of the disease and LUS is an easy imaging modality, considered a significant tool for diagnosis and follow up, which help timely and proper therapeutic decisions.

More recently [June 2020], **Boero et al.**^[31] evaluated the role of LUS in COVID-19 management and concluded that, a growing evidence supports the use of LUS in COVID-19. However, no data of multicenter studies are available. LUS could play a strategic roles in the management of the disease from presentation, at hospitalization and event after discharge. They advocated rapid research to set a protocol for LUS as a single or integrated tool in management of COVID-19.

One limiting step of the current work is the small sample size of the included patients and absence of control group. However, a strength point is the use of PCR as a reference for diagnosis of COVID-19. Another strength point is comparing LUS to CT [CT considered as a gold-standard for diagnosis in suspected cases], which reflected the power of LUS as a diagnostic tool.

We could conclude that, LUS could be a useful screening and follow up tool in COVID-19 infection epidemic or even COVID-19 pneumonia and similar conditions; especially in low-resources medical facilities. It is feasible, portable and revealed an accepted rate of sensitivity.

Financial and Non-Financial Relationships and Activities of Interest

Authors declare that, there was no competing interest

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