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Role of Ultrasound in Evaluation of Pulmonary Manifestations of COVID-19 Using Computed Tomography as A Gold Standard

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ABSTRACT
Background: In critical care medicine, lung ultrasonography (LUS) has become more widely utilized as a trustworthy method for assessing lung diseases. Since COVID-19 pneumonia lesions have a predominant peripheral distribution, LUS detection is more appropriate.
Objective: This study was aimed to assess the role of LUS in early diagnosis of COVID-19, as well as severity assessment of COVID-19 patients using CT chest as a gold standard.
Patients and methods: Patients in this prospective cohort study were complaining of symptoms raising suspicion of SARS-CoV-2 infection and referred from chest emergency departments. Ultra-sound and CT were done for all patients and finding were correlated in the two modalities with estimation of the severity score.
Results: out of 242 patients with CT chest findings positive for COVID-19 infection, 232 patients demonstrated positive LUS findings for COVID-19. Our study revealed the sensitivity of LUS up to (99.15%), specificity (100%), PPV (100%), NPV (80%) and accuracy (99.17%).
Conclusion: It could be concluded that LUS could show pulmonary manifestations indicative of COVID-19 in symptomatic patients with high diagnostic accuracy comparable to CT chest.
Keywords: CT, US, COVID-19, Diagnosis.

INTRODUCTION

By the end of 2019, China had become a global for the SARS-CoV-2 virus, which causes severe acute respiratory syndrome, causing a unique interstitial pneumonia outbreak. Even in the most developed and wealthy nations, the COVID-19 outbreak is causing the healthcare systems a great deal of trouble.

The SARS-CoV-2 infection's most common negative effect, interstitial pneumonia, must be swiftly diagnosed during the pandemic surge. New patients must be isolated. The frontline relies heavily on chest imaging. Lung CT was deemed the gold standard chest imaging method and is highly advised in suspected instances among the commonly used chest imaging technologies [1, 2].

Investigations have shown that CT is very sensitive in detecting the early stages of interstitial pneumonia, even in COVID-19 patients who are asymptomatic and in patients whose first rapid test (RT-PCR) swab results were negative. A systematic use of CT during the pandemic surge is impossible due to the biological and monetary costs, the lack of availability in areas with low resources, and the increased risk of in-hospital cross-infections when infected patients referred to the radiology units. Social norms concur with the proposal to restrict the use of CT scans during a pandemic spike [3]. Chest radiography (CXR) and lung ultrasonography (LUS) are reliable alternatives that may be used in this field. LUS demonstrated good feasibility and sensitivity for COVID-19 pneumonia, with a specificity that increases during the peaks of occurrence. When utilizing LUS properly, it's also crucial to take into account the different COVID-19 pneumonia risk categories and correlate LUS patterns with the patient's clinical phenotype at the time of emergency department presentation. Lung ultrasound (LUS) has therefore been suggested as a substitute imaging tool for suspected COVID-19 pneumonia patients [3].

In symptomatic COVID-19 patients who reported to the emergency department (ED) in the spring of 2021, when the COVID-19 pandemic was at its worst, this research was outlined to evaluate the accuracy and diagnostic rule of ultrasound (US) compared to computed tomography (CT) in detecting lung affection.

PATIENTS AND METHODS

This prospective cohort study was carried out at the Radiodiagnosis Department, Zagazig University Hospitals, Radiodiagnosis Center, Suez General Hospital and Radiodiagnosis Department, El-Mouneera General Hospital. It included a total of 242 patients with clinically suspected SARS-CoV-2 infection, referred from chest emergency Departments.

The included 242 patients were 143 men and 99 women, their average age was (47.94 ±13.47) years ranged from 20 to 78 years.

Inclusion Criteria: All genders, any patient with clinically suspected COVID-19 infection, and individuals who presented to the emergency department (ED) with symptoms raising suspicion of SARS-CoV-2 infection.

Exclusion Criteria: Women who were pregnant, and patients who dropped out of the trial (US or CT not available).

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Ethical consent:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University Research Ethics Board (ZU-IRB#6920/13-6-2021). Written informed consent was taken from all participants. The study was conducted according to the Declaration of Helsinki.

All patients were subjected to General examination; (Personal history (name, age, occupation, contact with a positive case of COVID-19) and present history (complaints) Fever, cough, sputum production, dyspnea, sore throat, rhinorrhea, and nasal obstruction). All patients did routine RT-PCR. Imaging modalities including Chest CT (Non-contrast) and Lung Ultrasound were done for all cases.

Imaging Analysis:

Lung Ultrasound: Major Criteria including three or more B-lines/lung rockets per lung zone, multifocal fused B-lines/waterfall sign in any lung zone and white lung sign. Minor criteria including C-line sign, pleural line thickening or irregularity, shred sign/ lung consolidation and air bronchogram sign, any major criteria alone was sufficient to raise suspicion COVID-19 infection. Minor criteria alone are not specific for COVID-19 infection.

CT Chest: Major criteria including unilateral patches of ground glass opacity, bilateral patches of ground glass opacity, lung consolidation and ground glass opacity and consolidation. Minor criteria: linear opacities, rounded opacities, septal thickening, reticular shadows under pleura and cloudy shadows under pleura. Any major criteria alone was sufficient to raise suspicion of COVID-19 infection. Two or more minor criteria were considered suspicious in the current pandemic; however, they were not specific for COVID-19 infection.

Severity Score:

Disease was classified into 4 categories as regarding CT and US findings: Mild, moderate, severe and critical groups.

Lung Ultrasound Severity Score [4]:

The 12 lung zones, including the upper and lower portions of the anterior, lateral, and posterior sides of both lungs, were examined using the LUS methodology. According to four ultrasonic aeration patterns, each zone was graded. We assigned points for each location of interest based on the worst ultrasonography pattern seen in each zone of the 12 examined zones. The ultimate total LUS score, which ran from 0 to 36 was made (1–7 mild, 7–11 moderate, 11–18 severe, and 18–36 critical) [5].

Zero points = A lines or one or two isolated B lines together with lung sliding are present. One point = three to four B lines and a considerable reduction of lung aeration (septal rockets). Two points= significant aeration loss in the lungs with five or more B lines (Diffuse coalescent B lines). Three points= the existence of a tissue that is hypoechoic and poorly defined and exhibits a total lack of lung aeration (consolidation).

CT Chest severity score [6]:

The level of anatomic involvement was taken into consideration while calculating a semi-quantitative CT severity score for each of the 5 lobes following **Pan *et al.*** [7], as shown: scores 0,1, 2,3, 4 and 5 when no involvement, less than 5% involvement; from 5 to 25% involvement, from 26 to 50% involvement, from 51-75% involvement, and when more than 75% involvement, respectively. Each individual lobar score and the resulting global CT score were added together (0 to 25).

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level, Chi-square test For categorical variables, to compare between different groups. Fisher's Exact or Monte Carlo correction: Correction for chi-square when more than 20% of the cells have expected count less than 5. The capacity of the test to correctly identify diseased individuals in a population "TRUE POSITIVES". The greater the sensitivity, the smaller the number of unidentified case "false negative.

RESULTS

There were 242 patients that participated in the trial, 143 men and 99 women; their average age was (47.94 ±13.47) years ranged from 20 to 78 years.

Table 1 shows that 232 patients (95.9%, 232/242) had positive findings by lung US. The following results were the most common ones: B-lines (95.9%, 232/242) (fig.1), C-line sign (80.6%, 195/242) (fig.2), and a thickened pleural line (88.8%, 215/242) (fig.3). In severe and critical cases, pulmonary consolidations (fig. 1) were more common than in mild cases, and individuals who were complaining for a longer time had thicker pleural lines than those who had it for a shorter time.

Table (1): LUS different findings in studied cases (n = 242)

Ultrasound findings	No.	%
Thickening of pleural line	215	88.8
Pleural line irregularity	203	83.9
Blurred pleural line	10	4.1
Discontinuous pleural line	174	71.9
B line, rocket sign	232	95.9
Partially diffused B-line	225	93.0
Completely diffused B-line (white lung)	139	57.4
Waterfall sign	139	57.4
Large consolidation	16	6.6
Lung sliding		
Absent	43	17.8
Reduced	194	80.2
Normal	5	2.1
A lines	213	88.0
C-line sign	195	80.6
Negative findings (normal)	10	4.1

Regarding CT findings: Ground glass opacity (fig. 2) was the most common finding detected in 96.7% of our patient and 95.5% had mainly peripheral distribution (Table 2).

Table (2): CT different findings in the studied cases (n = 242)

CT findings	No.	%
GGO	**234**	**96.7**
Consolidation	**70**	**28.9**
GGO & Consolidation	**77**	**31.8**
Linear opacities	**167**	**69.0**
Rounded opacities	**221**	**91.3**
Crazy Paving Pattern	**95**	**39.3**
Reverse halo sign	**6**	**2.5**
Central distribution	**148**	**61.2**
Peripheral distribution	**231**	**95.5**
Bronchial wall thickening	**138**	**57.0**
Pulmonary nodules	**7**	**2.9**
Air bronchogram	**76**	**31.4**
Lymphadenopathy	**12**	**5.0**
Reticulations under pleura	**175**	**72.3**
Negative findings (normal)	**8**	**3.3**

Table 3 shows that Particularly in the severe and critical stages of the disease, the severity of COVID-19 pneumonia as determined by LUS was closely correlated with the severity of the chest scan as determined by CT.

Table (3): Comparison between CT and US according to severity (n = 242) (% from total)

	CT									
	No COVID-19 (n = 8)		**Mild disease (n = 27)**		**Moderate disease (n = 117)**		**Severe disease (n = 72)**		**Critical disease (n = 18)**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
US										
No COVID-19	**8**	**3.3**	**2**	**0.8**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**
Mild disease	**0**	**0.0**	**25**	**10.3**	**6**	**2.5**	**0**	**0.0**	**0**	**0.0**
Moderate disease	**0**	**0.0**	**0**	**0.0**	**111**	**45.9**	**0**	**0.0**	**0**	**0.0**
Severe disease	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**72**	**29.8**	**0**	**0.0**
Critical disease	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**18**	**7.4**
χ^2 (p)	**χ^2=519.977 (MCp<0.001*)**									
κ (Level of agreement)	**κ =0.951 (Level of agreement: very good)**									

Patchy consolidation (fig. 1) was seen in CT chest in 55/242 patients and in LUS in 38/242 patients. It was observed mainly in severe and critical stage of disease. Pleural effusion is a rare finding in COVID-19, seen in only 16/242 patients in both CT chest and LUS.

There was a high agreement between number of affected lobes in both CT chest and LUS. Moreover, both LUS and CT findings showed the lesions of COVID-19 were more likely to occur in the lower lobes of lungs with bilateral distribution: 190/242 patients according to CT chest compared to 188/242 patients in LUS.

Table 4 shows that out of 234/242 patients with CT chest findings positive for COVID-19 infection, 232 patients demonstrated positive LUS findings for COVID-19. Our study revealed the sensitivity of LUS was (99.15%), specificity (100%), PPV (100%), NPV (80%) and accuracy (99.17%).

Table (4): Agreement (sensitivity, specificity and accuracy) for diagnosis of COVID-19 pulmonary infection (n = 242) (% from total)

Diagnosis	CT				Sensitivity	Specificity	PPV	NPV	Accuracy
	Non COVID-19 (n = 8)		COVID-19 (n = 234)						
	No.	%	No.	%					
US									
Non COVID-19	**8**	**3.3**	**2**	**0.8**	**99.15**	**100.0**	**100.0**	**80.0**	**99.17**
COVID-19	**0**	**0.0**	**232**	**95.9**					
χ2 (FEp)	**χ2=191. 945 (FEp<0.001*)**								

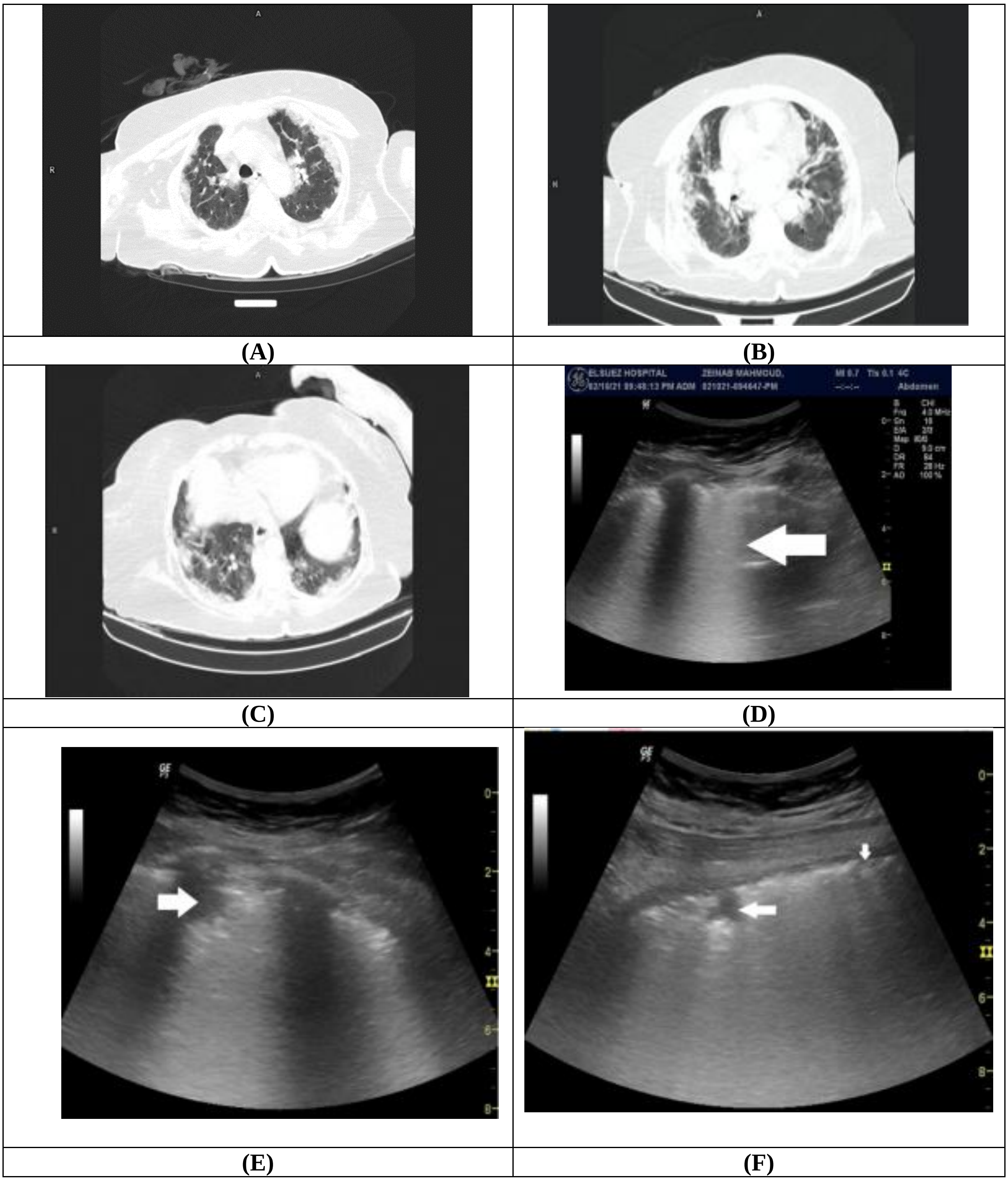

Figure (1): A 63-year-old female patient with COVID-19 symptoms science 21 days, HRCT **(figure a to c)** shows bilateral upper and lower lung lobes subpleural sheets of irregular consolidation with interstitial septa thickening. US reveals **d)** Completely fused B-lines (arrow). **e)** Subpleural echogenic area (tissue pattern) representing consolidation patch (arrow). **f)** Subpleural echogenic area (tissue pattern) representing consolidation patch (long arrow). The pleural line was thickened and interrupted (short arrow).

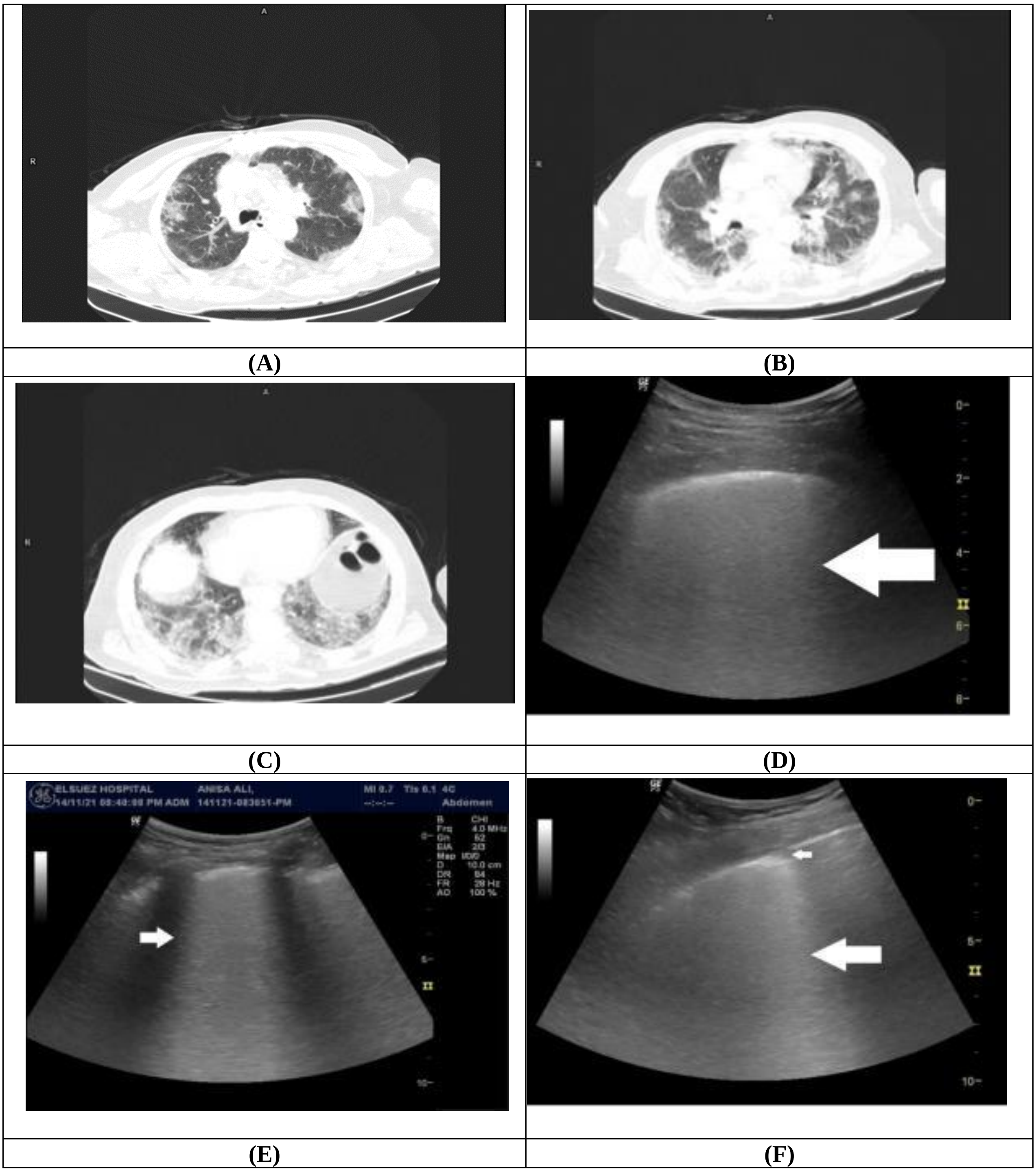

Figure (2): A 34-year-old male with COVID-19 symptoms started 14 days earlier.
HRCT **(figure a to c)** shows bilateral peripheral patches of ground glass opacity with crazy paving pattern and interstitial reticular thickening involving all lobes. LUS shows: **d)** Completely fused B-lines (compact B-lines). **e)** Partially fused B-lines (waterfall sign). **f)** Partially fused B-lines (large arrow) with small sub-pleural consolidations (C-line) (small arrow).

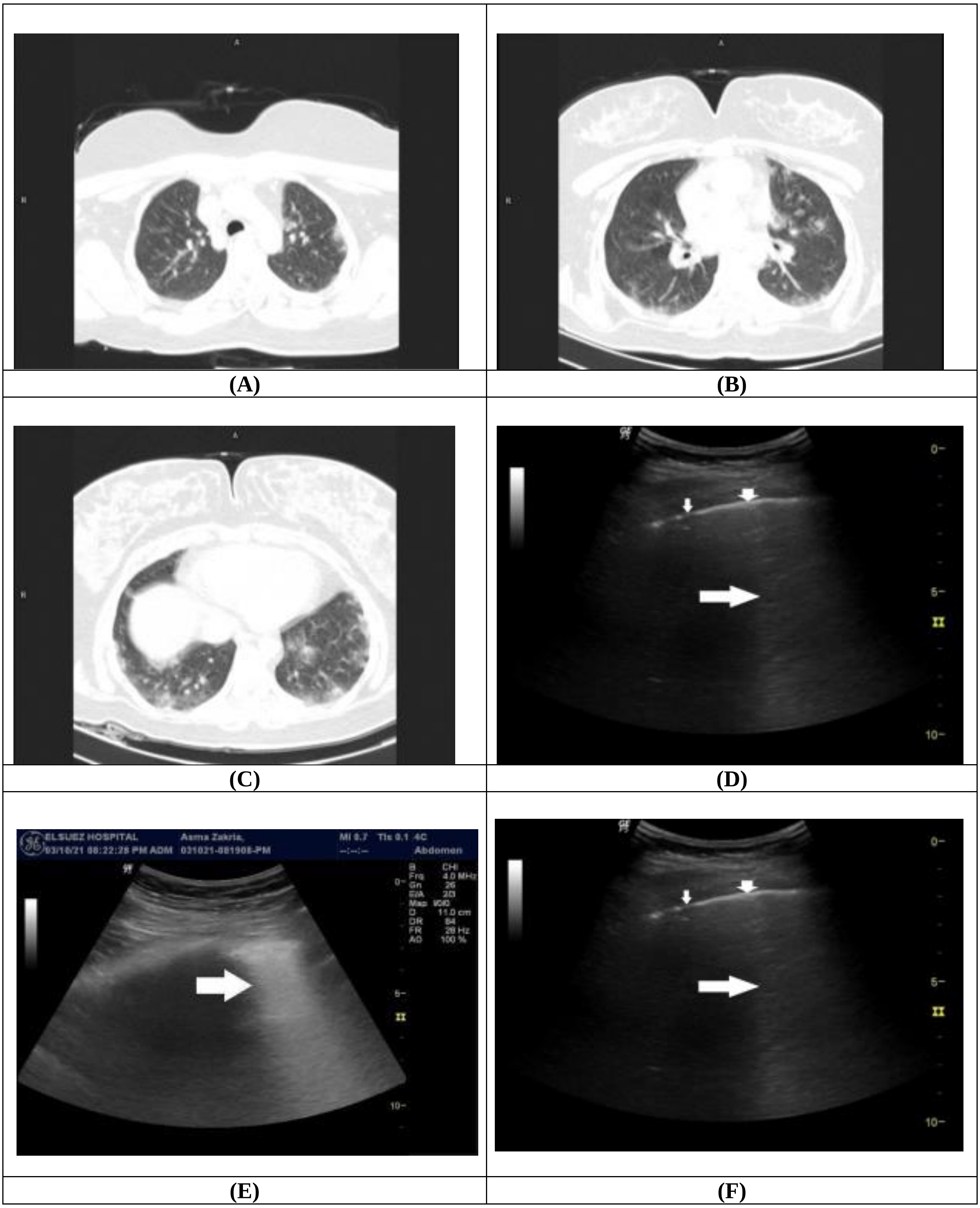

Figure (3): A 24-year-old female with fever and cough started 6 days earlier. HRCT **(figure a to c)** showed bilateral multiple scattered ill-defined areas of ground glass opacity in all lung lobes with mainly peripheral distribution. LUS shows: **d&e)** Partially fused B lines (waterfall sign) (arrow) in multiple lung zones. **f)** Focal B-lines (big arrow). The pleural line was thickened and irregular (small arrows).

DISCUSSION

This recently identified virus that causes the 2019 coronavirus illness (COVID-19) has spread incredibly swiftly throughout the whole planet [11].

Although there are still many unanswered problems surrounding SARS-CoV-2 infection, imaging plays a crucial part in this epidemic. To evaluate patients with pathological results who would need hospitalization, both CT and LUS modalities can be utilized as triage tools, helping health systems across the world to make the most use of their limited resources [10]. Our study included 242 patients, 143 men and 99 women; their average age was (47.94 ±13.47) years. The main findings by US in COVID-19 patients were B-lines (focal 95.9%, partially diffused 93% or completely diffused 57.4%) which agreed with **Tan *et al.*** [8] results who found disperse B-line and rocket sign in 33.3%, partially diffused B-lines in 100% and completely diffused B-lines or white lung in 83.3%. We were in the same line only in the ratio of partially diffuse B line and differ in that of focal and complete forms. The main differences between the two studies were that our study had larger sample volume (242 patients with 234 confirmed COVID-19 patients), while the other study had small sample volume (32 patients with only 12 confirmed COVID-19 patients). We also agreed with **Zieleskiewicz *et al.*** [9] as they revealed that the main finding of LUS was interstitial syndrome (B lines or lung rockets), as well as, **Zhu *et al.*** [10] study who showed B lines in (89.5%) of patients.

Patients with severe COVID-19 disease frequently had pulmonary consolidations or subpleural localized lesions (typically smaller than 1.0 cm), which were seen in 41.7% of patients (39). We found higher parentages of small sub-pleural consolidation (C-line) reaching up to (80.6%) accompanied by B-line abnormality whether focal or diffuse, this may be due to larger sample size and variable stages of the disease included in our study.

We agreed with **Yi *et al.*** [11] study who described the pleural line using high-frequency ultrasonography as rough, unsmooth, and interrupted, mostly due to the reduced gas content and sound wave reflection in the subpleural alveoli and interstitial lesions. This is in the same line with us as, the pleural line changes in our study were thickening in 88.8% and irregularity in 83.9% which were observed more in severe and critical patients. Individuals with a longer course of the disease are more likely to have a thicker pleural line than patients with a shorter course of the disease. **Zhu *et al.*** [10] reported pleural line changes in only 26.3% of their patients and **Zieleskiewicz *et al.*** [9] who showed pleural irregularity in only 32% of their patients. Both studies disagree with our study probably due to smaller sample size and lower stage of the disease severity, for example; in **Zhu *et al.*** [10] study among the 48 patients who underwent LUS, only 38 patients had COVID-19 pneumonia. Rare or less common LUS findings in our study were large consolidation 6.6% and pleural effusion 6.6%. **Tan *et al.*** [8] agreed with our study and showed pleural effusion in only 8.3% of patients**. Zhu *et al.*** [10] also detected consolidations in 15.8% of their patients and pleural effusions in only 5.3%. However, neither our investigation nor the aforementioned studies reported any cases of empyema or pneumothorax.

The most common CT chest findings in our study were ground glass opacities (96.7%), rounded opacities (91.3%), linear opacities (69%) and reticulations (72.3%). Mixed GGO and consolidation were detected in (31.8%) and solitary consolidation patches were seen in (28.9%) with air bronchogram sign seen in (31.4%). Crazy paving pattern was seen in (36.8%). Bronchial wall thickening was noted in (57%). Atypical findings like reverse halo sign were observed in (2.5%). Lymph node enlargement and Pleural effusion were seen in (5%) and (6.6%) respectively.

Wu *et al.* [12] revealed that GGO (91%) and consolidation were the most common CT abnormalities seen (63 percent), which agreed with our findings except for consolidation which has lower incidence in our study. Additionally, 6 percent of patients had pleural effusion, 4 percent of patients had enlarged lymph nodes, and 29 percent of patients exhibited crazy paving sign, which is consistent with our findings. A triangular or angular GGO under the pleura with enlarged internal interlobular septa appeared as the "spider web sign," which was first observed and termed in the **Wu *et al.*** [12] research and was recorded in (25%) of patients. The surrounding pleura was pulled, creating the appearance of a spider web in the corner. That indication was not found in the current investigation.

The pulmonary manifestations of the disease by US are mainly B lines (whether focal or diffuse) which were bilateral in 77% of patients in the current study. **Zieleskiewicz *et al.*** [9] found that interstitial syndrome (B lines or lung rockets) was bilateral in 85% of their patients which matched us. This study revealed that the positive US finding for COVID 19 were more prominent in lower lung lobes mainly in the lower lobes as well as right middle lobe (middle-lower predominance). The lesions were distributed as following: RUL = 162/232, RML = 194/232, RLL = 217/232, LUL = 132/232, LLL = 184/232.

Yi *et al.* [11] found that ultrasonic manifestations of COVID-19 were mainly observed in the posterior and inferior areas of the lung. The distribution of lung lesions nearly matched our distribution.

The pulmonary lesions in CT chest in our study showed peripheral distribution in (95.5%) of cases and central distribution in (61.2%). The disease showed bilateral distribution in (78.5%) of cases. The distribution of lesions in lung lobes showed a middle-lower lobe predominance with the majority of lesions seen in both lower lobes and right middle lobe.

In Wu *et al.* [12] study, Lesions had a subpleural (peripheral distribution) pattern in 53% of patients, a diffuse pattern in 9% of cases, a peribronchial pattern in 4% of cases, and a mixed pattern in 30% of cases. The majority of the lesions occurred in the periphery, which is consistent with our findings. The right lower lobe dorsal segment (69/80), the right lower lobe posterior basal segment (68/80), the right lower lobe lateral basal segment (64/80), the left lower lobe dorsal segment (61/80), and the left lower lobe posterior basal segment (65/80) were the lung segments most often affected. The distribution often demonstrates a lower lobe preponderance, which is consistent with our results.

In our study disease was classified into 4 groups as regarding LUS and CT chest severity score. We found a high correlation between severity score of COVID-19 pneumonia assessed by LUS and severity score as assessed by CT chest especially in severe and critical stage of the disease with an agreement at = 0.951 (very good).

Zhu *et al.* [10] used similar methods for assessing the severity in CVOID-19 patients by US and CT. A positive correlation between the LUS and CT scores was found (r = 0.82, 95% CI: 0.66–0.91, p < 0.001), which is in the same line with us.

The accuracy of lung ultrasound in diagnosis of COVID-19 in our study was calculated to be 99.17% with 99.15% sensitivity. **Alrifai *et al.*** [13] agreed with our study and revealed that, ultrasound gives nearly similar accuracy (85%) as CT in diagnosis of pulmonary changes in pneumonic COVID-19 with 87.93% sensitivity. Therefore, ultrasound is nearly as effective as CT in diagnosis of COVID-19 pneumonia.

A study by **Lieveld *et al.*** [14] also agreed with our study, they found that For COVID-19 pneumonia, LUS and CT had equivalent diagnostic accuracy, with an agreement of 0.65. with LUS demonstrated a sensitivity up to 92%.

LIMITATIONS

Difficulty to assess 12 lung zones properly of LUS scan protocol in mechanically ventilated patients. We did not correlate the LUS or CT findings with patient outcomes including disease progression and different stage of the disease in the same patient. Because of the overlying bone structures and that part of the lung is not adherent to the pleural surface, part of the chest is not visible to the ultrasound probe. Therefore, LUS can examine more extensively the posterior-lateral lower areas than posterior superior areas. Also the interposition of lung air content may hinder full visibility of even large lesions by US.

CONCLUSION

It could be concluded that LUS could show pulmonary manifestations indicative of COVID-19 in symptomatic patients with high diagnostic accuracy comparable to CT chest. LUS has the advantage of being low cost, easy access, short scan time compared to CT chest, it also limits exposure to COVID-19 infection since patients are not required to be transferred to the radiology unit but instead LUS can be performed bedside during any stage of the disease. Furthermore, the lack of ionizing radiation makes diagnosis of COVID-19 in pregnant women easier and the scan can be performed as many times as required. All of these advantages plus the high accuracy of LUS in the diagnosis of COVID-19 allows LUS to be an alternate imaging modality for the diagnosis and severity assessment of the disease, besides being a useful tool in screening for COVID-19 pneumonia.

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