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Original Article

Internal Medicine Section

Focused Ultrasonography in COVID-19: A Prospective Cross-sectional Study

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ABSTRACT

Introduction: The Coronavirus disease-2019 (COVID-19) pandemic requires adaptation of the care delivery process. Since the point of care ultrasonography (USG) is an essential diagnostic tool that aids in making clinical management decisions in a short time, wider adoption of USG by general health practitioners dealing with COVID-19 patients across the country could improve the care delivery process in a pandemic scenario. A simple diagnostic algorithm of USG limited to two echo views was proposed for ease of training and broader adoption of the technique. The study analysed the efficacy of focused USG in COVID-19 using this approach for diagnosing and managing critically ill COVID-19 patients.

Aim: To determine the concordance between ultrasonographic diagnosis based on a focused algorithm and clinical diagnosis in COVID-19 patients.

Materials and Methods: A prospective cross-sectional study was conducted on 58 COVID-19 positive patients admitted to the COVID-19 Intensive Care Unit (ICU) of a tertiary care hospital, in Kerala, India from October 2020 to March 2021. The inclusion criteria were age 18 years or above, hypoxaemia (SpO_2 <94%) and hypotension (systolic blood pressure <90 mmHg). Apical four chamber and subcostal views were captured using a phased array probe (1.7-4 Hz). The cause of hypoxaemia or hypotension was diagnosed based on an algorithm constructed with Echocardiographic (ECHO) findings in COVID-19. A clinical diagnosis was made, laboratory data, and chest radiograph. Agreement between ultrasonographic and clinical diagnosis was assessed using the Cohen's Kappa inter-rater coefficient. Statistical Package for the Social Sciences (SPSS) version 20 was used for the statistical analysis.

Results: Mean age of the population was 65.6±17.3 years, and the male to female ratio was 1.5:1. Clinical diagnoses were categorised into six groups. The agreement between the ultrasonographic and the clinical diagnoses was substantial (95.1%), with Kappa 0.905 (0.851-0.959). The median time taken for image acquisition was 30 seconds (IQR 30, 60). Additional views performed for lungs and vessels did not change the clinical diagnosis or management.

Conclusion: The proposed technique is simple yet effective for clinical management decisions. It has the potential for improving patient care delivery on a larger scale, since it reduces the time lag in instituting therapy.

Keywords: Coronavirus disease-2019, Critical illness, Diagnostic imaging, Pandemic, Ultrasound

INTRODUCTION

In mid 2020, the sudden influx of patients due to the COVID-19 pandemic overwhelmed the surge capacity of the limited health resources across the country. The care delivery process had to be adapted to deal with this crisis. A problem oriented bedside USG helps acquire relevant diagnostic information, enabling management decisions [1-3]. Furthermore, it reduces the risk of disease transmission [4]. Most of COVID-19 patients who require ICU admission, have hypoxaemia, along with bilateral infiltrates in Chest X-ray (CXR). In addition, most of them have multiple comorbidities. Hypoxaemia may be caused by factors other than COVID-19 pneumonia, such as cardiogenic pulmonary oedema or fluid overload as in kidney failure. It is essential to quickly screen for these factors to administer precise treatment. Point of care USG, including heart and Inferior Vena Cava (IVC), aids in rapid differentiation between pulmonary and other causes of hypoxaemia on admission [5,6].

As the pandemic surged, doctors from different specialities managed COVID-19 patients in the ICU, along with physicians and intensivists. USG was already part of the bedside decision making process, and it became essential to train all doctors involved in ICU patient management in USG to make timely decisions. A consistent and systematic approach of USG examination had to be developed to ensure that all patients received optimal treatment. The learning process involved: image acquisition and interpretation; a standardised algorithm to rule out causes of hypoxaemia and hypotension other than COVID-19 pneumonia. A brief core USG examination which could be taught in a few short training sessions and reinforced by repetition during daily rounds, was necessary.

The standard intensive care USG includes apical four chamber (4C), parasternal long axis, short axis and subcostal views, and multiple views for lung, abdomen, and vessels. However, a quick screening of the heart and IVC using one or two views is often employed in ICU during an emergency to derive critical information [5-7]. In this study, apical 4C and subcostal views were chosen for the core USG examination. These two views, which essentially look at the size and function of all four chambers of the heart and IVC, were presumed to provide information to distinguish the cause of hypoxaemia and hypotension in COVID-19 patients and guide fluid therapy [5,6]. A similar approach using the subcostal view alone for ten seconds is currently being practised for determining the cause of cardiac arrest in advanced cardiac life support [8]. A systematic review on training in point of care USG found that studies conducted with simplified imaging goals to address specific clinical questions with binary outcomes like abnormality present or absent had increased accuracy in the hands of trainees [6]. Successful mastering of the technique and reducing errors depended upon the experience of repetition of limited learning parameters [7,9,10].

An algorithm was constructed based on ECHO features reported in COVID-19 to rule out the possible aetiologies for hypoxaemia and hypotension in COVID-19. Hypoxaemia and hypotension in COVID-19 may be caused by coronary or pulmonary thrombosis, myocarditis, diarrhoea, shock and renal failure. However, COVID-19 primarily affects the pulmonary system causing pneumonia or Acute Respiratory Distress Syndrome (ARDS) [11]. There is abundant literature on USG in COVID-19 [12-15]. ECHO features of COVID-19 in the published studies include Left Ventricle (LV) systolic or diastolic dysfunction, Regional Wall Motion Abnormality (RWMA) suggestive of Acute Coronary Syndrome (ACS), acute myocarditis, Right Ventricle (RV) dilatation and dysfunction (McConnell's sign) in Pulmonary Thromboembolism (PTE) and stress induced cardiomyopathy characterised as RWMA or apical ballooning of LV [16].

This study looked into the efficacy of an approach limited to two views, apical 4C and subcostal, to determine the cause of hypoxaemia and hypotension in COVID-19, guided by an algorithm. The study's primary objective was to determine the concordance between the ultrasonographic diagnosis using the proposed technique and diagnosis based on clinical and laboratory data.

MATERIALS AND METHODS

This was a hospital based prospective cross-sectional study, conducted between October 2020 to March 2021, at Pushpagiri Medical College hospital, Kerala, India. It is a tertiary care teaching hospital in Kerala, with a critical care residency program that includes bedside ultrasound training. The study was approved by the Institutional Review Board and Ethics Committee (no. II/27/2020) and was registered at the clinical trials registry India (ICMR no.2020/10/037526).

Inclusion criteria: COVID-19 positive (RT-PCR or antigen assay) patients with moderate and severe respiratory involvement as per the Disease Classification by the COVID-19 National Task Force, Government of India [17] or other critical illnesses were admitted into a designated COVID-19 ICU where isolation precautions were taken. From these patients admitted in the COVID-19 ICU, those who met the inclusion criteria were included in the study. COVID-19 positive (RT-PCR or antigen assay), age ≥18 years, hypoxaemia (SpO_2 <94%) or hypotension (systolic blood pressure <90 mmHg) or both.

Exclusion criteria: Patients who did not give consent or in whom image acquisition was impossible and patients with indefinite clinical diagnosis was excluded.

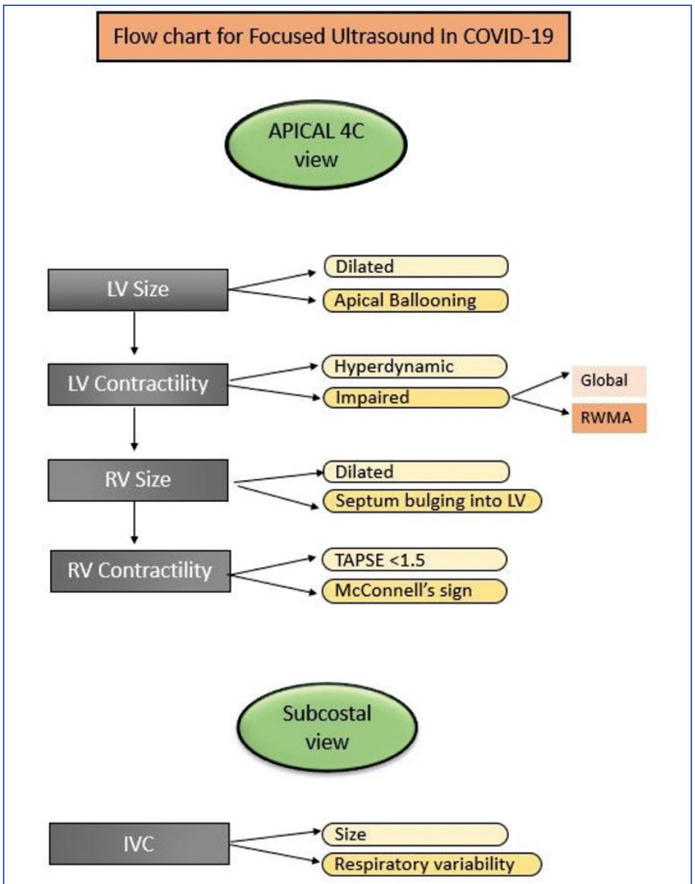
Sample size calculation: Sample size was determined by the formula

$$n=\frac{(Z^2_{1-\alpha/2})pg}{d^2}$$

The minimum sample size calculated using the above formula was 47 using z=1.96, α_error 5%, 10.0 precision and 14% prevalence. Here, prevalence refers to the proportion of hospitalised COVID-19 patients admitted to the ICU [18].

Study Procedure

Focused USG, based on a charted algorithm [Table/Fig-1], was performed in this group ensuring adequate isolation precautions, by a certified intensivist with eight years of experience in performing USG on the critically ill. A dedicated portable ultrasound machine (Vivid E by Wipro GE healthcare limited, China, 2016, version 6.0.4) with phased array, curvilinear and linear array probes were used for procuring images. Apical 4C and subcostal views were captured and recorded with the phased array probe (1.7-4 Hz). Both views were used for assessment by visual estimation of: a) RV size and function; and b) LV size and function/RWMA. A long axis view of the IVC for maximum diameter and the presence of respiratory variability was obtained with the subcostal view. These were used for assessment of volume status. Subcostal 4C served as an alternate view when the apical 4C view was poor. The images were then reviewed immediately to reach an USG based diagnosis for the cause of hypoxaemia or hypotension, which was documented [Table/Fig-2]. When required these images were saved to allow remote interpretive assistance from cardiologists. Image acquisition was done for 3-4 cardiac cycles, and the time taken was documented. The time required for image acquisition was defined as the time point from when the physician started using the probe for image acquisition of the apical 4C view, subsequently proceeding to the subcostal view and the end time point was when these two images were captured.



[Table/Fig-1]: Algorithm for focused ultrasonography in COVID-19.
4C Four chamber, RV: Right ventricle; LV: Left ventricle; RWMA: Regional wall motion abnormality; IVC: Inferior vena cava; TAPSE: Tricuspid annular plane systolic excursion

Diagnosis	Ultrasonographic findings
Septic shock	It may be associated with a normal or hyperdynamic LV and IVC ≥0.5 cm with or without respiratory variability
Hypovolemic shock	Hyperdynamic LV with papillary muscle kissing sign, small size IVC (<0.5 cm) with respiratory variability
Cardiogenic shock/pulmonary oedema	LV enlargement and dysfunction (global/RWMA)
Obstructive shock	RV enlargement, dysfunction and tricuspid valve regurgitation and interventricular septum protruded to the left ventricle showing the "D sign" and dilated IVC (≥2 cm) with no respiratory variability
Hypoxaemia because of kidney failure with fluid overload	Normal LV and IVC size ≥1 cm with no respiratory variability

[Table/Fig-2]: Ultrasonographic diagnosis based on findings.
RV: Right ventricle; LV: Left ventricle; RWMA: Regional wall motion abnormality; IVC: Inferior vena cava

Additional views taken were documented, and findings were assessed to see their contribution to the diagnosis or treatment. Clinical diagnosis was decided by two intensivists treating the patient, based on the clinical details, laboratory data, imaging, and consultative calls documented. All patients had CXR and Electrocardiogram (ECG).

The primary outcome was agreement between ultrasonographic diagnosis and clinical diagnosis. Secondary outcomes were to estimate the time required for the acquisition of images as per the study protocol and to evaluate whether additional views of the heart, lung, leg veins, abdomen when acquired, aided in gaining critical information for immediate management. Informed written consent for the use of personal data was taken when the patients were deemed competent. In cases where patients could not give consent while in the ICU, informed consent was taken later from the patient or his immediate next of kin.

STATISTICAL ANALYSIS

Assessment of the level of agreement between ultrasonographic diagnosis and clinical diagnosis was done by employing the cohen's kappa inter-rater coefficient. Value assumed by the coefficient was reported with the 95% confidence intervals, and p-value <0.01 was considered significant. Statistical Package for the Social Sciences (SPSS) version 20 was used for the statistical analysis.

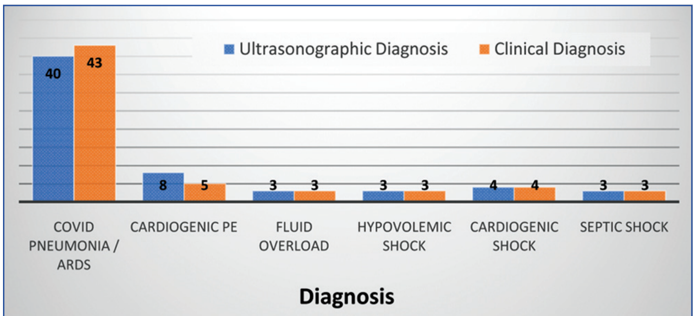
RESULTS

Out of the 104 patients admitted to the COVID-19 ICU during the study period, 62 met the inclusion criteria. A total of 49 had only hypoxaemia, seven had only haemodynamic instability and six had both. One patient who did not give consent was excluded. Two patients were excluded as image acquisition was impossible. Another patient with an indefinite clinical diagnosis was excluded from the analysis. Data of 58 patients were analysed. Pre-existing heart disease was present in five patients. Common co-morbidities were diabetes mellitus, hypertension, Chronic Kidney Disease (CKD), chronic Obstructive Airway Disease (OAD), Obstructive Sleep Apnea (OSA),coronary artery disease and Left Ventricular Dysfunction (LVD). Male to female ratio was 1.5:1. The mean age was 65.6±17.3 years. Clinical diagnoses were categorised into six groups. Ultrasonographic findings are shown in [Table/Fig-3].

Ultrasonographic findings	Number of patients
Dilated LV size and LV dysfunction/RWMA	10
Dilated RV size and/or RV dysfunction	3
IVC <1cm and with respiratory variability	15
IVC ≥1cm and with respiratory variability	35
IVC >1 cm with no respiratory variability	8

[Table/Fig-3]: Ultrasonographic findings in the study group.
RV: Right ventricle; LV: Left ventricle; RWMA: Regional wall motion abnormality; IVC: Inferior vena cava; A single patient had more than one finding

The agreement between ultrasonographic and clinical diagnosis of cardiogenic pulmonary oedema was 62.5% (k=0.743). The overall agreement between the ultrasonographic and clinical diagnosis was substantial (95.1%), with Kappa coefficient of 0.905 (0.851-0.959) [Table/Fig-4,5]. The median time taken for image acquisition was 30 seconds (IQR 30, 60). Additional views, performed on 11 patients, did not change the clinical diagnosis or management.



[Table/Fig-4]: Comparison of ultrasonographic diagnosis with clinical diagnosis.
PE: Pulmonary oedema; Numerical data for this graph is provided in [Table/Fig-5]

DISCUSSION

This study demonstrated that a problem oriented approach of sonography limited to two ECHO views with the phased array probe by the treating physician could provide sufficient information to make critical management decisions in COVID-19 patients with hypoxaemia or hypotension. The protocol effectively guided fluid therapy based on cardiac and IVC findings. The novelty of study's novelty is in the emphasis on a core USG examination with limited views for easy mastering of a basic skill set, taking into consideration the lack of trained personnel in the wake of the pandemic. Point of care USG requires a new perspective in the setting of the emergence of COVID-19 for several reasons. Firstly, widespread adoption of USG could be helpful in increasing the efficiency of the healthcare system in the event of a disaster of this kind. Secondly, USG by the clinical personnel who might already be in the isolation room with the patients can restrict additional personnel like sonographers thus ensuring optimal use of PPE kits in the pandemic situation.

From early 2020, the literature showed the utility of USG in managing COVID-19. Lung Ultrasound (LUS) was found useful in the early diagnosis of COVID-19 [12,14,15,19]. It is useful for monitoring lung recruitment in ARDS and troubleshooting complications like pneumothorax. However, COVID-19 affects multiple organs [11]. In this context, multiorgan USG might yield better diagnostic performance [13]. The standard multiorgan USG involves acquisiting multiple views using the curvilinear, phased array and vascular probes for imaging lungs, heart, vessels and abdomen. A vascular probe is helpful to rule out Deep Vein Thrombosis (DVT). However, pulmonary thrombosis in COVID-19 is more likely due to pulmonary vascular and endothelial inflammation than the classical thromboembolism from leg veins [20]. More than half of the patients with pulmonary thrombi were not associated with DVT [21] and a computer tomography with pulmonary angiography scan is required to rule out pulmonary thrombosis. The benefits concurred by an additional vascular probe to rule out DVT in all COVID-19 cases is thereby limited. The Lung Ultrasound (LUS) requires advanced expertise for interpretation. Considering the above mentioned diagnostic complexities, currently, the skills required for performing a multiorgan USG are part of the repertoire of trained intensivists, thus limiting the practical application. The simple two view approach with phased array probe, if widely accepted, can be a framework on which further knowledge in performing a multiorgan protocol can be acquired later [9,10].

Several USG based protocols are available for rapid evaluation of aetiology of shock and hypoxaemia [2,22,23]. A simplified algorithm for diagnosis of both hypoxaemia and hypotension was used in this study, which was based on previously reported ECHO features of COVID-19 [16]. The cause of shock in COVID-19 may be sepsis, hypovolemia, cardiac or obstructive (PTE or tension pneumothorax). the IVC maximum diameter and presence of respiratory variability were used as a dynamic method for preload responsiveness and for guiding fluid therapy [24,25]. There are several causes of respiratory failure in these patients other than COVID-19 related pneumonia

Diagnosis	USG diagnosis	Clinical diagnosis	Agreement (%)	Cohen's kappa (κ)	p-value
COVID pneumonia/ARDS	40	43	93	0.887 (0.824-0.950)	<0.001
Cardiogenic pulmonary ooedema	8	5	62.5	0.743 (0.603 - 0.883)	<0.001
Fluid overload	3	3	100	1	<0.001
Hypovolemic shock	3	3	100	1	<0.001
Cardiogenic shock	4	4	100	1	<0.001
Septic shock	3	3	100	1	<0.001

[Table/Fig-5]: Agreement between ultrasonographic and clinical diagnoses.
Cohen's kappa=0.905 (0.851-0.959); p<0.001; Agreement=95.1%; Data given in the table can overlap

and ARDS, such as acute pulmonary oedema due to fluid overload or cardiac failure, acute exacerbation of OAD, OSA or complications like pneumothorax or pulmonary embolism.

A study by Volpicelli G et al., found high a level of concordance (k 0.971) between the clinical and ultrasonographic diagnosis in patients admitted to the emergency department with hypotension [2]. In comparison, the present study looked into the aetiology of hypoxaemia and hypotension in COVID-19. This study used a combination of USG findings similar to that used by Volpicelli G et al., to diagnose different types of shock and causes of hypoxaemia, except hypovolemic and septic shock.

The ultrasonographic features of hypovolemic and septic shock overlap, making it difficult to differentiate [2]. The diagnosis of septic shock was applied to COVID-19 patients with hypotension and normal heart on ECHO. Three patients with hypotension with IVC <0.5 cm with respiratory variability and hyperdynamic LV were grouped under the ultrasonographic diagnosis of hypovolemic shock [22]. Another group with difficulty in reaching a diagnosis was patients with pre-existing ECHO abnormalities. They posed a challenge in determining the exact cause of hypoxaemia and shock. In these cases, it was found that the immediate clinical cause of deterioration was not necessarily cardiac. A group of four patients clinically diagnosed with ACS presented with pulmonary oedema or shock. ECHO findings of RWMA and LVD suggested cardiogenic aetiology in this group.

COVID-19 pneumonia was diagnosed based on clinical features and CXR pattern. Troponin I, brain natriuretic peptide and ECG were done in all patients to rule out ACS or LVD as the cause of hypoxaemia or hypotension. The IVC size and respiratory variability guided fluid management in these patients. In patients with CKD, who presented with pulmonary oedema, fluid overload was diagnosed as the cause of hypoxaemia once a cardiac cause was ruled out.

Compression Ultrasound (CUS) performed with a vascular probe to rule out DVT was most common additional view documented in this study. The CUS did not show findings suggestive of DVT in any of the patients in the study group. The LUS was done in a few cases, and a short axis view of the heart was done in one case with suspected RWMA. These additional views would have increased the certainty of diagnosis for the treating doctor but did not change the final management of the patient in this study.

The USG is an affordable, portable, easy to operate, and non ionising imaging modality that can work on battery and is ideally suited for remote and rural places [26,27]. There is enough data on its utility and implementation in various parts of the world like Haiti, Kenya and rural parts of Canada, Australia and New Zealand [26,28]. Surveys from these areas reveal mainly two problems, need for training and quality assurance [29]. Technological advancement in the last decade has provided affordable machines with better image quality [30]. The USG training has some learning considerations to be addressed. Acquisition of the image is the first step of USG training. It has been shown that repetition of fewer trainable parameters will reduce the chance of technical and interpretive error by novice trainees [6]. This idea of using limited views has been exploited by institutions in countries that are already implementing USG training for junior doctors and in rural practice [10]. A short memorable USG examination based on two views described in this present study can be the backbone structure for USG training in India. Advanced, specialised imaging can then be expanded upon this knowledge framework.

Despite the indisputable advantages of USG in COVID-19, it is not yet used in the most wanted areas where alternate diagnostic modalities are seldom available [26]. The COVID-19 pandemic has created an opportunity for training and adopting newer tools that could continue in the future. Availability of platforms for data transfer, further increases this tool's desirability for remote settings. The advantage of the proposed technique with limited number of views which can provide maximum information is that it will ease the learning curve leading to wider acceptability and adoption of point of care USG in clinical practice. From an economic standpoint, portable machines with a single probe are more affordable. In addition, this approach which takes less than thirty seconds to two minutes, reduces the time of close contact and risk compared to the standard multiorgan ICU protocol, further encouraging health practitioners to take up this modality in the pandemic setting [4].

Limitation(s)

This was a single centre study limiting the generalisability of the result. Another pitfall of USG is that, respiratory variability of IVC may not be reliable in ARDS patients who are mechanically ventilated with high Positive End Expiratory Pressure (PEEP).

CONCLUSION(S)

Point of care USG has immense practical utility in critical care delivery in a pandemic scenario. It is well recognised that training in this modality needs to be encouraged. The approach used in this study based on an algorithm using the apical 4C and subcostal views was effective in diagnosing the complications in critically ill COVID-19 patients and managing them. This approach makes training and adoption of this technique simple and less time consuming.

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