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Research Article

Color Doppler Ultrasound: An Effective Tool for Discriminating a Small Pleural Effusion from Pleural Thickening (Study of 875 Cases)

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Received: December 27, 2021; **Published:** January 26, 2022

Abstract

Background: Small pleural effusions are missed several times by grey scale ultrasound and are reported as pleural thickening. Such cases impose a challenge of remaining undiagnosed due to unavailability of samples. Fluid Color Sign of Color Doppler ultrasonography, produces colors for pleural effusion and is capable of detecting minute pleural effusions with significant accuracy, enabling diagnostic sampling and precise diagnosis possible.

Objectives: The main objective was to determine the diagnostic accuracy of Color Doppler Ultrasound over grey scale for differentiating minimal pleural effusion from pleural thickening.

Materials and Methods: This prospective study was conducted from 01-01-2018 to 30-11-2019, at pulmonology-OPD, Gulab Devi Teaching Hospital Lahore. 875 adult, willing patients with radiographic evidence of minimal pleural effusion were included while the patients with large pleural effusion, not willing for pleural aspiration and participation in study were excluded. All patients were subjected to grey scale and Color Doppler scanning for the identification of minimal pleural effusion. The presence of pleural effusion was confirmed by ultrasound guided aspiration and was taken as reference. The findings were summarized, tabulated and SPSS-21 soft-ware was utilized for analysis.

Results: The grey scale ultrasonography detected pleural effusion with 93.26% sensitivity, 100.0% specificity and diagnostic accuracy 93.37%. By Color Doppler technique, sensitivity 99.48%, specificity 100% and diagnostic accuracy 99.49% was obtained. The Fisher exact test statistic value was 0.0015, significant at $p < 0.05$.

Conclusion: Color-Doppler ultrasound is an accurate tool for differentiating minimal pleural effusions from pleural thickening.

Keywords: *Color Doppler; Diagnostic Accuracy; Minimal; Pleural Effusions; Pleural Thickening; Trans-Thoracic Scan*

Abbreviations

PE: Pleural Effusion; CXR: Chest X-Ray; CT: Computerized Tomography; CDU: Color Doppler Ultrasound

Introduction

Accumulation of liquid in pleural space is known as pleural effusion and it is always due to a disease process. It can be due to pulmonary, pleural, chest wall or generalized metabolic or neoplastic disorders. X-ray chest combined with clinical findings is considered the first-line tool for detecting pleural effusion in a pulmonology clinic [1]. The regional and international reports support the usefulness of

trans-thoracic ultrasound in detecting and quantifying pleural effusions with good accuracy [2-4]. On routine chest ultrasound, pleural effusion usually appears as an anechoic space between parietal and visceral pleura, changing shape by change in position and also during respiratory movements [5]. The identification of minimal pleural effusion is a practical issue, especially when it is present on the background of thickened pleura. Because both lesions have anechoic morphology on Gray-scale ultrasonography. This appearance do not guarantee neither for the presence of pleural fluid nor for the pleural thickening [6,7]. Such effusions are missed several times and are reported as pleural thickening. These cases remain undiagnosed and untreated because of non-availability of fluid sample and pose a challenge in future.

Color Doppler ultrasound (CDU) is widely used to determine vascular anatomy and intravascular pathologies including flow pattern by colors produced by moving blood. It was observed that Color Doppler sonography generates colors in moving pleural effusion due to cyclic respiratory and cardiac movements. This phenomenon is known as "Fluid Color Sign" [8]. While colors are not produced by thickened pleura [9]. Fluid color sign is capable of detecting as small as 10 - 20 ml fluid [10,11]. It is easily available, simple to use and can be employed as real-time guidance for thoracentesis, we used this sign for detecting small pleural effusions and differentiating effusions from pleural thickening.

Objectives of the Study

To determine the diagnostic accuracy of Color Doppler Ultrasound over grey scale ultrasound for discriminating between a small pleural effusion and pleural thickening.

Materials and Methods

This analytical cross sectional study was conducted in the Pulmonology OPD of Gulab Devi Teaching Hospital Lahore-Pakistan from January, 2019 to December 2019. Ethical approval was obtained from IRB of the hospital vide No. Admin/GDEC/258/19. Total 875 adult patients with clinical and radiographic evidence of small pleural effusion were included while those with large pleural effusion, not willing for thoracentesis or participation in study were excluded. Informed consent was obtained from every patient.

After history, physical examination and chest x-ray, patients with presumptive diagnosis of small pleural effusion were subjected to transthoracic ultrasonography. Grey scale ultrasonography was performed by Sonovista-*fx* machine (siemens), using 3.5 - 5.5MHZ transducer. All patients were scanned anteriorly, posteriorly and laterally on both sides in sitting and supine positions. On Gray-scale scanning, pleural effusions were diagnosed by anechoic area between visceral and the parietal pleurae, presence of internal echoes or septae and change of shape with change in position. Those hypoechoic areas not changing shape by change in position were declared as pleural thickening. The Doppler filter was set at 50 - 100 Hz and color Doppler gain was adjusted to allow only a few noise specks in the background and scanning was done at low velocity setting (0.25 m/sec). All patients were evaluated with color Doppler imaging, pleural effusions were diagnosed by fluid color signals while pleural thickening was declared in those where no color signal obtained. The fluid moving towards the probe produced red color while moving away from the transducer generated blue color. After detecting pleural effusion by Gray-scale and Color Doppler imaging, the presence of pleural effusion was confirmed by ultrasound guided aspiration and aspirated pleural fluid was considered as gold standard reference.

Results were recorded in case report form. Data was summarized, organized and tabulated. SPSS-21 soft-ware was utilized for statistical analysis. The quantitative variables were expressed by mean ± SD and frequencies were employed for numerical variables. Sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value were calculated. Fisher exact test was utilized for comparison. A p-value < .05 was considered significant. The results were interpreted in the light of statistical results to reach the conclusions.

Results

A total of 875 patients with suspicion of small pleural effusion underwent ultrasonography. 542 (61.94%) patients were male while 333 (38.05%) were female. Male to Female ratio was 1.6:1. Mean age was 42.54 years with SD. ± 18.47 and Std. Error: ± 1.31. All patients

presented with typical symptoms of respiratory illness (Table 1). Chest pain and dry cough were predominant symptoms. All patients had suspicion of small pleural effusion on clinical and radiographic grounds. Gray-scale ultrasound detected pleural effusion in 621/875 cases out of which 553 were successfully aspirated but no fluid came out in 68 cases. 254 cases were declared pleural thickening but in 32 cases fluid could be aspirated and no fluid was found in 222 cases on thoracentesis. For calculating the efficacy for gray-scale sonography, we had true positive cases (TP): 553, False negative (FN): 32, true negative (TN): 222 and false positive (FP) cases were 68. Color Doppler ultrasound detected pleural effusion in 587 cases. Pleural thickening was diagnosed in 288 cases. Pleural aspiration was successful in 585 cases. No fluid came out in two cases. For calculating the efficacy, we had TP cases: 585, FP: 02, TN: 288 and FN: 00. Thoracentesis diagnosed 585 pleural effusion cases on pleural aspiration. Sonographic morphology of pleural effusion and pleural thickening was recorded (Figure 1). The diagnostic yield of CXR, Gray-scale ultrasound, CDU and thoracentesis was tabulated (Table 2). The efficacy of Gray scale and CDU for detecting pleural effusion was calculated, considering aspirated pleural fluid as reference (Table 3).

Gray-scale ultrasound detected 621 cases as pleural effusion and 254 as pleural thickening. CDU diagnosed 587 pleural effusions and 288 pleural thickenings. The Fisher exact test statistic value was 0.0879. The result is not significant at $p < .05$.

Nos	History Findings	Observed cases	Percentage
1.	Dry cough	621	70.97.0%
2.	Productive cough	132	15.08%
3.	High grade fever	207	23.65%
4.	Shortness of breath	158	18.05%
5.	Chest pain	630	72.00%
8.	Weight loss	490	56.00%

Table 1: *Frequency of clinical manifestations in 875 patients.*

Sr. no.	Diagnostic Modality	Pleural Effusion cases *n(%)	Pleural thickening cases *n(%)
1.	Chest X-Ray (CXR)	875 (100.0%)	00 (%)
2.	Gray-scale sonography	621 (70.97 %)	254 (29.02%)
3.	Color Doppler Sonography	587 (67.08%)	288 (32.91%)
4.	Pleural Aspiration	585 (66.85%)	290 (33.14%)

Table 2: *Frequency of radiologic and thoracentesis diagnosis. n = 875.*
**n(%): Number of observed patients with frequency.*

Efficacy of Gray Scale ultrasound		
Statistic	**Value**	**95% Confidence Interval**
Sensitivity	94.53%	92.37% to 96.23%
Specificity	76.55%	71.25% to 81.31%
Positive Predictive Value	89.05%	86.84% to 90.93%
Negative Predictive Value	87.40%	83.12% to 90.72%
Diagnostic Accuracy	88.57%	86.28% to 90.60%
Efficacy of Color Doppler Ultrasound		
Sensitivity	100.00%	99.37% to 100.00%
Specificity	99.31%	97.53% to 99.92%
Positive Predictive Value	99.66%	98.66% to 99.91%
Negative Predictive Value	100.00%	
Diagnostic Accuracy	99.77%	99.18% to 99.97%

Table 3: *Efficacy of gray-scale and color doppler ultrasound with thoracentesis as reference.*

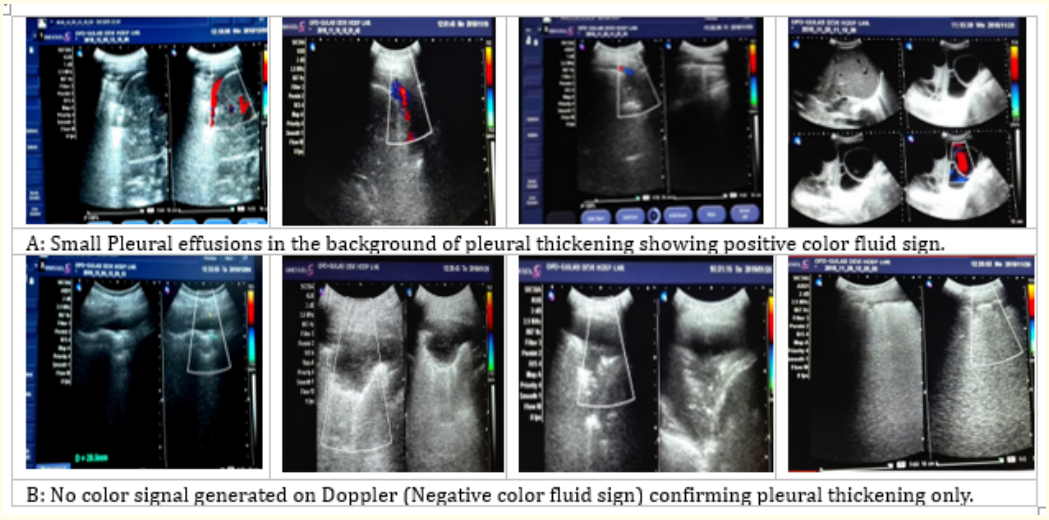

Figure 1: *Sonographic morphology by gray-scale and color doppler ultrasonography.*

Discussion

Pleural effusions are encountered daily in out-patient department. It is always due to some disease process and requires definite detection prior to aspiration for diagnostic work-up. Imaging is considered corner stone for diagnosis and management of pleural effusions. Multiple view radiography is the conventional tool but it has low sensitivity for small pleural effusions. Furthermore, it does not differentiate between effusion and pleural thickening [12,13]. Additionally, some pathologies like pleural thickening, masses or fibrosis also mimic with pleural effusion. CT-scan effectively identifies small pleural effusions but its cost, availability, need for expert radiologist and exposure to ionizing radiations are main constrains. Furthermore, it may not be suitable for pediatric and pregnant patients.

The usefulness of trans-thoracic ultrasonography in pleural diseases is well understood in our region. It is being used primarily for confirmation of pleural effusion in patients with abnormal chest x-ray [14]. Routine gray-scale ultrasonography has an excellent diagnostic yield for pleural effusion but becomes compromised for a small pleural effusion present in the background of pleural thickening [15]. Moving fluid in pleural space, generates color signals by CDU. The pleural fluid associated with pleural thickening moves during cyclic cardiac and respiratory movements and color signals produced indicate the presence of fluid and even loculated fluid can be detected by this modality (Figure-1, image A).

In this study on 875 patients, male to female ratio 1.6:1 conveys that pleural effusions being more frequent in males than in female. This observation is in agreement with reports of Burgess Lesley and colleagues and Luis Valdes., *et al.* [17,18] Mean age of 42 years, is in fair congruence with the reports of Zuberi FF and associates and Bhattacharya S and co-workers [19,20].

The study conveyed that chest x-ray declared pleural effusion in 875/875 cases and was unable to identify pleural thickening (Table 2). So, it cannot be relied for discriminating between pleural effusion and pleural thickening.

This study communicated that out of 875 patients with presumptive diagnosis of small pleural effusion, only 621/875 cases were diagnosed pleural effusion by Gray-scale ultrasound. While 254 were declared pleural thickening. Although it is capable of detecting 100 ml or more fluid with 100% sensitivity [21,22] and can diagnose as small as 05ml effusion [23] but when small pleural effusion is present

on the background of pleural thickening, confusion arises because both have similar appearance on gray-scale ultrasound, thus compromising the efficacy. That is why the study showed sensitivity 94.53%, specificity 76.55% and diagnostic accuracy 88.57%. Gehmacher O, Kopf A., *et al*. and Chen HJ, Tu CY, Ling SJ., *et al*. reported that an echo-free area between the visceral and parietal pleurae is not a reliable sign for fluid on grey scale scanning because it does not differentiate successfully between small pleural effusion and pleural thickening [6,7]. Similarly, Wu RG., *et al*. reported that an anechoic layer in pleural space, raising confusion about pleural effusion or thickening, really requires color Doppler ultrasound to illicit color fluid sign [24].

On applying color Doppler imaging to all cases, CDU successfully differentiated between fluid and pleural thickening and detected 587 cases of pleural effusion and 288 cases of pleural thickening with 100% sensitivity and 99.31% specificity. Of which 585 were successfully aspirated under ultrasound guidance. In two cases, effusion was too small and deep to be aspirated. Because aspirated fluid was considered as the gold standard reference, 585 cases were recorded as true-positive and specificity was reduced to 99.31% while diagnostic accuracy was 99.77%. If we consider the fluid color sign as reference, the specificity will become 100%. In figure 1B, all images created the impression of pleural effusion on routine gray-scale scanning but on applying CD-imaging, no color was generated, thus excluding the possibility of pleural effusion and confirmed the diagnosis of pleural thickening. In this way, 288 cases were declared pleural thickening and the need for putting a needle inside for aspiration was confidently abolished which otherwise would have been inevitable in search of sample. No patient with pleural thickening displayed fluid color sign, indicating 100% specificity. The sensitivity, specificity and diagnostic accuracy of color Doppler imaging is in fair agreement with those of Tirupati S Rajasekhar who reported a specificity of color Doppler ultrasound in discriminating minimal pleural effusion from pleural thickening 98.75%, sensitivity 89.32% and diagnostic accuracy 96% [25]. Similarly, Ali A Hasan., *et al*. reported 90% sensitivity, 100% specificity and diagnostic accuracy of 95.0% [26]. Kalokairinou-Motogna., *et al*. reported specificity 100% sensitivity 96.72% and accuracy 97,57% [27]. Although presence of fluid was shown by color Doppler ultrasound in two cases which were not approachable by needle due to deep location and minute quantity.

The Fisher exact test statistic value equal to 0.0879 for Gray-scale and color Doppler ultrasound is not significant at $p < .05$. It indicates that there is not much difference in the efficacy of the two modalities but CDU is a good aid to gray-scale ultrasound capable of increasing sensitivity, specificity and diagnostic accuracy from 94.53%, 76.55%, 88.57% to 100.0%, 99.31% and 99.77% respectively, for differentiating between pleural effusion and pleural thickening. As it does not involve any ionizing radiation, it can be used with confidence for pregnant and pediatric patients, safely [28]. Additionally, a portable machine also has the edge of usability as point of care tool especially in ICU and non-mobile patients [29]. Because the procedure is so simple, it can be used by an experienced pulmonologist in emergency as an instant problem solving tool thus reducing the work-load on busy radiologists.

In the light of this discussion, we feel justified to comment that just by placing a transducer in intercostal space, ultrasonography enables us to differentiate between a pleural effusion and pleural thickening and helps a lot in decision making about thoracentesis or to refer the patient to thoracic surgeon for consultation. Additionally, it is an amazing guiding tool for thoracentesis. Because the aspiration is done in real-time visualization, it has eliminated the chances of wrong side, wrong site and blood vessel trauma [30].

The main limitation of the study is that it is a single center study, while with multi-center studies and larger sample size, the subject can be explored more effectively. It is an undisputed fact that sonography results depend on the quality of ultrasound machine as well as the skill of the operator, so inter observer variations can be encountered at different centers. Therefore, it is recommended that all pulmonary students must be trained adequately with gray scale and CD-imaging for pleural diseases before going to serve the community. This step may help in reducing inter-observer variations [31].

Conclusion

Color Doppler imaging is a useful diagnostic aid to gray-scale ultrasound for discriminating minimal pleural effusion from pleural thickening with remarkable accuracy.

Acknowledgements

The authors would like to thank Mr. Mehfooz Ahmed, and Muhammad Tahir for their valuable assistance.

Conflict of Interest

There is no conflict of interest among the authors.

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