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Association of CT hounsfield unit value of pleural effusion with pleural fluid analysis

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Abstract
Background: Pleural effusion is defined as an abnormal fluid collection in the pleural cavity. In healthy people, pleural cavity contains a small amount of fluid secreted by the parietal pleura (0.25 ml/kg). As the fluid amount increases, lung compliance reduces due to the increased lung capillary pressure. It may lead to patient dyspnea. Pleural effusion can be transudate or exudate. Differentiation between the transudate and exudate is important for clinical management. Abnormal fluid accumulation in the pleural space results from increased permeability of the capillary bed. Thoracentesis is an invasive diagnostic method for obtaining pleural fluid for analysis. This procedure is associated with iatrogenic complications. With the help of computed tomography (CT) density of pleural fluid can be assessed by measuring Hounsfield unit (HU). Type of pleural fluid can be predicted based on HU value of the pleural fluid. Also assessing features like pleural thickening and septation within pleural effusion. This study was conducted with an aim to differentiate between exudative & transudative pleural effusion based on the CT Hounsfield unit.
Methodology: An observational cross-sectional study was conducted in the department of radiodiagnosis consisting of 48 patients with the pleural effusion after clearance from the institutional ethical committee. CT Thorax was performed by a 16 slice MDCT machine. HU value of pleural effusions were measured at three different locations on three different axial slices on the mediastinal window, mean of three HU was calculated and correlated to pathological report.
Results: The median HU value of exudate was 17.94 and transudate was 8.03. The median CT HU value was higher in exudate than that of transudate. The p-value found was 0.001. There was a statistically significant difference in the HU value between the exudate and transudate. According to the Light's criteria, out of 48(100%) patients with pleural effusions, 36(75%) pleural effusions were exudate and the remaining were transudate. The overall relationship between the pleural fluid protein/total protein and CT HU was found using Spearman's rho correlation coefficient. As the pleural fluid protein/total protein ratio increased, the CT HU value also increased. There was a moderate positive correlation between the pleural fluid protein/total protein ratio and CT HU value (rho=0.55, p=0.001).
Conclusion: The exudative and transudative effusion showed a significant difference in the CT HU value. Therefore, the CT HU value can help the radiologist to predict the type of pleural effusion which will further help in the final diagnosis of disease condition along with associated findings in lung and mediastinum. Also, thoracocentesis can be considerably avoided in patients who are at risk of developing pneumothorax and hemothorax.

Keywords: computed tomography (CT), hounsfield unit (HU) pleural effusion, transudate and exudate

Introduction

Background

Pleural effusion results from an abnormality of the pleural fluid dynamics caused due to alteration of colloid osmotic pressure, hydrostatic pressure, lymphatic drainage and capillary permeability [1]. Though the type of pleural effusion is diagnosed based on biochemical analysis, radiographical investigation can also aid in the detection and diagnosis [1].

Pleural effusion is classified as transudate and exudate depending upon composition [1]. Exudative effusion results from the presence of a pleural disease which is related to elevated permeability of the capillaries of the pleura [1]. This type of effusion has high protein content. The differentiation criteria used to separate the type of pleural effusion is called 'Light's criteria' [2, 3]. Pleural fluid is determined as exudate if, a) the ratio of pleural fluid protein to serum protein >0.5 and the pleural fluid lactate dehydrogenase (LDH) to serum LDH ratio >0.6 or the pleural fluid LDH level >2/3rd the upper limit of normal serum LDH [1]. The most common causes of exudative effusion are empyema, tuberculosis, neoplasm, pleuritis, pneumonia and pulmonary embolism [5]. Transudative effusion is associated with systemic diseases and due to an imbalance between osmotic and hydrostatic pressure controlling the formation of pleural fluid [5]. Congestive heart failure, kidney disease, pericardial effusion, cirrhosis of the liver and hypoalbuminemia are common causes of transudative effusion [1].

Thoracocentesis is the most common invasive method for the collection of pleural fluid for biochemical analysis and cytology [6, 7]. Various risks associated with diagnostic thoracocentesis are pneumothorax, haemothorax and laceration of lung. Pneumothorax is the most common complication [6]. Relative contraindications for the

procedure are a small volume of pleural fluid and coagulopathy. Therefore, a non- invasive method to differentiate between transudative and exudative pleural fluid will be an ideal and valuable method to avoid any risks and complications associated with thoracocentesis [8].

Exudate contains a high level of protein, LDH, bilirubin and cholesterol [8]. Pleural fluid analysis is a gold standard for exudative and transudative classification of pleural fluid [9]. CT is the ideal modality for the evaluation of pleural disease [10]. Indeed, CT can be used for the evaluation of pleural effusion and the density of the fluid can be assessed based on HU values and avoid the complications of thoracocentesis [5]. Depending on the HU value of the fluid one can predict the type of pleural fluid [4]. CT can show associated findings like pleural nodules, pleural thickening, loculation or empyema which further helps to support the diagnosis of pleural effusion and these findings play a major role in management of the underlying disease condition [8, 7]. In this regard, the objective of our study was to find the association of CT Hounsfield unit value of pleural effusion with pleural fluid analysis.

Material and Methods

Forty-eight patients with pleural effusions on thoracic CT who underwent diagnostic thoracocentesis within 2 weeks from 2020 to 2021 were prospectively studied. The study protocol was approved by ethics committee of our hospital. The pleural effusions were classified as exudate or transudate according to the Light's criteria. Patients were excluded from study if they had pleural tubes prior to CT imaging and had trauma.

All CT examinations were performed with 16 slice MDCT-GE Bright Speed Elite scanner. A region of interest was placed for measurement of Hounsfield unit (HU) values in the area of greatest amount of effusion on each slice of the three slices used. The average of the three HU values was calculated and correlated with pleural fluid analysis.

The SPSS software was used for statistical analysis. The Unpaired "t" test and Mann Whitney U test were used to compare the variables between the two groups. The nonparametric correlation between two variables was performed using Spearman's rank correlation coefficient. Significance was set at $p<0.05$.

Results

In our study, we included 48 patients diagnosed with pleural effusion. Among the 48 patients 27 patients were males (56.3%) and 21 patients were females (43.8%). The majority of the patients were male (54±17.84, age range 17-89 years old). According to the light's criterion, out of 48(100%) patients with pleural effusions, 36(75%) pleural effusions were exudate and the remaining were transudate.

Table 1: Comparison of CT HU value between exudate and transudate.

Type of pleural fluid	Median HU value	IQR of HU
Exudate	17.94	15.40, 20.06
Transudate	8.03	5.68, 9.59

*IQR: Inter Quartile Range

The median HU value in exudate was 17.94 and in transudate was 8.03. The median CT HU value was higher in exudate than that of transudate.

Table 2: Test Statistics

Mann-Whitney U	30.00
Wilcoxon W	108.00
Z	-4.43
P	0.001

The p-value found was 0.001. There is a statistically significant difference in the HU value between the exudate and transudate.

Table 3: Pleural fluid protein/total protein ratio in two types of pleural fluid.

Pleural Effusion	N	Mean	Standard Deviation	T	P	95% confidence interval of the difference	
						Lower	Upper
Exudate	36	0.70	0.17	6.32	0.001	0.23	0.44
Transudate	12	0.37	0.09				

The 36 exudative pleural effusions had a mean pleural fluid protein/total protein ratio of 0.704(±0.1733). The 12 transudative pleural effusions had the pleural fluid protein/total protein ratio of 0.373(±0.0867). As the p-value is less than 0.05(p=0.001), there is a significant difference in pleural fluid protein/total protein ratio in exudate and transudate.

Table 4: Descriptive Statistics of the patients.

	N	Minimum	Maximum	Mean	Standard deviation
Pleural fluid protein/total protein ratio	48	0.25	1.50	0.62	0.21
HU	48	-25.60	24.53	13.87	9.06

In our study, the minimum pleural fluid protein/total protein ratio was 0.25 and the maximum was 1.50(0.62±0.21).

Table 5: Relationship between the ratio of pleural fluid protein/total protein and CT HU in transudative and exudative effusion using spearman's rho correlation coefficient.

	Overall Total number of patients: 48	Transudative effusion Total number of patients: 12	Exudative effusion Total number of patients: 36
Correlation coefficient	0.55	0.81	0.04
P	0.001	0.001	0.838

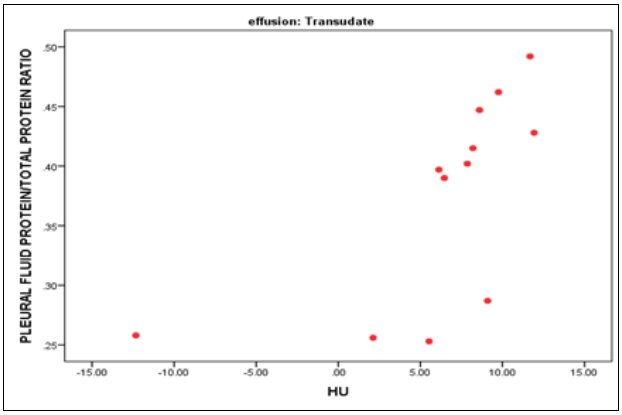

Fig 1: The scatter plot showing the association between the ratio of pleural fluid protein/total protein ratio and CT HU value in transudative effusion.

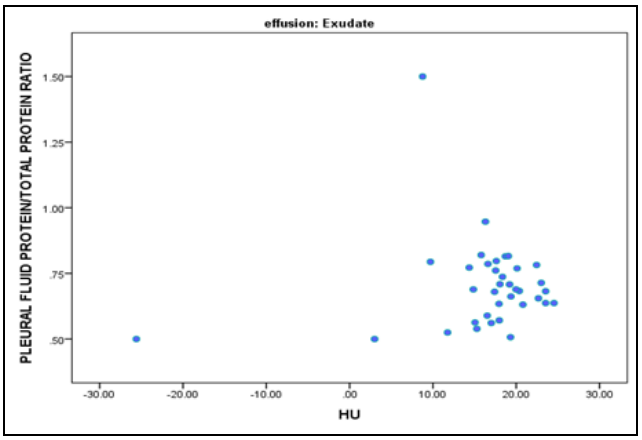

Fig 2: The scatter plot showing the association between the ratio of pleural fluid protein/total protein and CT HU value in exudative effusion.

Representative Images

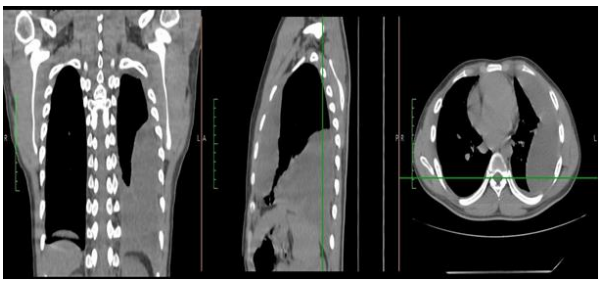

Fig 3: Unenhanced multiplanar reformatted axial CT thorax image showing pleural effusion.

Fig 4: Unenhanced CT thorax axial image showing transudative effusion (L).

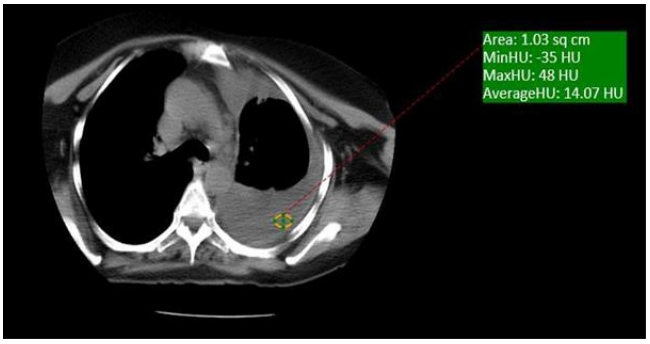

Fig 5: Unenhanced CT thorax axial image showing exudative effusion (L).

Discussion

In a healthy individual, pleural cavity contains a few milliliters of pleural fluid [2]. The abnormality caused due to alteration of colloid osmotic pressure, hydrostatic pressure, lymphatic drainage, and capillary permeability of the pleural fluid dynamics results in pleural effusion. Pleural effusion is further classified as exudative or transudative effusion using Light's criteria [1]. Thoracocentesis is the ideal procedure for collecting the pleural fluid sample for cytological and biochemical analysis of pleural effusion. However, it is associated with various complications, mainly pneumothorax [4]. CT is a non-invasive imaging modality helpful in differentiating the transudative and exudative pleural fluid.

Distinguishing an exudative effusion from a transudative effusion can be of paramount importance in clinical management, especially in patients with malignancy and infection. The classification of a pleural effusion as exudative or transudative is mostly based on the results of the pleural fluid analysis. According to the generally used Light's criteria, exudative effusions are those with a pleural fluid/serum total protein ratio >0.5, a pleural fluid LDH/serum LDH ratio >0.6, or an absolute pleural fluid LDH > 2/3rd of the normal values of serum LDH [2, 5].

In the current observational cross-sectional study, we evaluated a total of 48 cases of pathologically confirmed pleural effusion, who underwent CT thorax examination in our center from April 2020 to March 2021. Patients with clinical suspicion of pleural effusion based on physical examination were referred for CT examination. Cases were Selected after satisfying inclusion and exclusion criteria. CT thorax was performed by GE Brightspeed Elite 16 multislice CT machine and unenhanced 5 mm axial images were acquired and 1.2 mm multiplanar reformatted images were obtained before further evaluation by the radiologist. HU value of pleural effusion was measured using specific software available in the workstation. HU values were recorded along with a radiological report. Subsequently, patients underwent Thoracocentesis for pathological pleural fluid analysis. Finally, the HU values of the pleural effusion were correlated with the pleural fluid analysis report. The statistical data analysis was performed. Association between the categorical variables was tested by using the Unpaired 't' test, Mann-Whitney U test, and Spearman's rank test. p-value (<0.05) was considered as statistically significant. SPSS software was employed for data analysis.

In our study consisting of a total of 48 cases (100%) of pleural effusions, 27 (56.3%) were males, constituted the

majority and 21 (43.8%) were females.

According to Light's criterion, out of 48 patients with pleural effusions, 36 were exudate and 12 were transudate. The pleural fluid protein/total protein ratio was the major biomarker employed for the differentiation of pleural fluid [3]. The 36 exudative pleural effusions showed a mean ratio of pleural fluid protein/serum total protein 0.70 (±0.17) and 12 transudative pleural effusions showed 0.37 (±0.09). There was a significant difference in pleural fluid protein/serum total protein ratio in exudative and transudative effusion (p=0.001). The mean ratio of pleural fluid protein/serum total protein was 0.62 (±0.21).

In our study, we retrospectively correlated the CT HU value of pleural effusion with the pleural fluid analysis. The median CT HU value in exudate was 17.94 HU (range: 15.4-20.06) and in transudate 8.03 HU (range: 5.6-9.59 HU). The median CT HU value was higher in exudate than transudate and statistically significant difference was observed (p=0.001). This is almost similar to observation by Sharma K *et al* Where there was a significantly higher mean CT HU value of exudate (8- 17.1HU) compared with transudate (2-12.5HU). The overall correlation between pleural fluid protein and CT HU value was found using Spearman's rank correlation coefficient. We found out that as the pleural fluid protein/total protein ratio is increasing, the CT HU value also increased. There was an overall moderate positive correlation between the ratio of pleural fluid protein/total protein and CT HU value (rho=0.54, p=0.001). Kiran R Nandalur *et al* identified a moderate but significant positive relationship between mean CT HU and pleural fluid protein/total protein (rho=0.57) [8]. Also, a study conducted by Abramowitz *et al* showed a mild but significant positive relationship (rho=0.14) [5]. The relationship between the pleural fluid protein/total protein ratio and CT HU in 12 transudative effusions was also analyzed. There was a high positive correlation in the ratio of pleural fluid protein/total protein and CT HU value in transudative effusion and it was statistically significant (rho=0.81, p=0.001). Similarly, the relationship between the pleural fluid protein/total protein ratio and CT HU in 36 exudative effusions was analyzed. There was a weak correlation and was statistically insignificant (rho=0.035, p=0.838). Abramowitz *et al* found a high degree of overlap in HU values in differentiating transudate and exudate [8, 5]. Similarly, our study showed considerable overlap in values for transudates and exudates for a majority of effusions in the 8 –13 HU range. On pleural fluid analysis, out of total patients 36 had exudative effusions and 12 had transudative effusions, whereas on CT, 31 patients were exudative excluding 4 patients which showed variable values when considering a cut-off value of ≥10 HU for exudative effusion. While 10 patients were transudative excluding 2 patients which showed overlapping values when considering a cut-off value for transudative effusion ≤10 HU.

In our study, we correlated pleural fluid protein/total protein ratio with CT HU value in exudative and transudative effusion, whereas most of the studies have analyzed the overall relationship between the pleural fluid protein/total protein ratio and CT HU value, which is the strength of our study. The limitation of our study is a small sample size.

Conclusion

The 48 cases of pleural effusion were included in this study after fulfilling inclusion and exclusion criteria. Cases were differentiated as exudate and transudate based on pathological analysis of pleural fluid. The exudative and transudative effusion showed a significant difference in the CT HU value. Here type of pleural effusion can be predicted on CT based on the mean HU value with a cut-off of ≥10 HU for exudative effusion and ≤10 HU for transudative effusion. Therefore, the CT HU value can help the radiologist to predict and diagnose the type of pleural effusion which will further help in the final diagnosis of disease condition along with associated findings in lung and mediastinum. Also, Thoracocentesis can be considerably avoided in patients who are at risk of developing pneumothorax and hemothorax.

Conflicts of interest

The authors do not have any conflict of interest to declare.

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