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New Insight in The Use of Thoracic Ultrasonography in The Diagnosis of Interstitial Lung Diseases.

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Abstract:-

Background: The ultrasonographic evaluation of Interstitial lung diseases (ILD) depends on the appearance and the quantification of multiple B-lines; which are produced by the reflection of the ultrasonographic beams from the subpleural thickened interlobar septa on the lung surface interface.

Aim:- This study was conducted to assess the usefulness of Thoracic Ultrasonography (TUS) in the diagnosis of ILD, and to assess the correlations of the ultrasonographic features with radiological and functional parameters of ILDs.

Patient and method:- Forty-six patients with ILD were included in this prospective study; each patient underwent Lung Ultrasonography (LUS), Multi-Detector CT chest (MDCT), and spirometry.

Results:- The ultrasonographic findings in ILD patients were B lines in 96%, pleural line irregularity in 70%, fragmentation in 26%, thickening in 91% of cases, subpleural lesions was present in 26% of cases, diminished lung sliding was in 17% of cases. Increasing the distance between B lines was negatively correlated with both ground-glass opacities and Forced Vital Capacity (FVC), and positively correlated with disease duration and reticular opacities in High-Resolution Computed Tomography (HRCT).

Conclusion:-TUS can be used as a complementary imaging technique for the diagnosis of ILD besides HRCT. The B-lines distance is considered as a sign of pulmonary function deterioration and a sign of disease severity.

Keywords: Lung ultrasonography, interstitial lung diseases, multidetector computed tomography.

Introduction:-

LUS depends on the principle that every chronic or acute disease decreases lung aeration, generating lung surface changes and producing distinct patterns. This permits the diagnosis of different conditions and the assessment of therapeutic interventions *(1)*.

Many years ago, thoracic ultrasound was exclusively limited to the examination of pleural effusions. However, during the past few years, the scope of practical applications of LUS has been significantly widened in a variety of conditions, especially in emergency cases *(2)*.

ILD is defined as pulmonary interstitium thickening (space between the alveolar epithelium and the capillary endothelium) leading to gas exchange impairment because of different causes (3).

ILD is a heterogeneous collection of disorders with various causes, clinical manifestations, radiographic features,

and histological changes that affects the lung parenchyma (the airspaces, the interstitium, the vessels, and the peripheral airways). Diagnosis of ILD is challenging and needs a combination of the clinical, the histological, the radiological, and the functional data [4].
Because it is not reasonable to use a CXR for early detection of ILD (which may be normal in early stages in most cases), MDCT is considered the "gold" standard imaging method for detecting, diagnosing, and monitoring patients with ILD. However, the LUS scores utility had been validated by numerous studies, in addition to its correlation with CT findings in chronic and acute respiratory diseases [5].
However, some studies have found that thoracic ultrasonography, as a consequence of its distinguished advantages (cost-effectiveness, ready availability, and absence of exposure to radiation), can successfully play a complementary role in the diagnosis of ILD, especially when CXR or MDCT is not available or undesirable as in pregnancy [6].
Current data has demonstrated that TUS, a non-invasive approach, can be helpful in ILD diagnosis by detecting B-lines, which is considered the sonographic sign of alveolar interstitial syndrome [7].
In this study, We intended to highlight the new insight in the diagnosis of ILDs from the view of ultrasonography for many pulmonologists and radiologists who are not aware of this promising role and limited the diagnosis of ILDs only to HRCT.

Aim of the study:

This study was conducted to:-
1- Assess the usefulness of LUS in the diagnosis of ILDs.
2- Assess the correlations of the ultrasonographic features with radiological and functional parameters of ILD.

Patients and methods

This prospective observational study was conducted in Sohag University Hospital on 46 patients. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Sohag University, and informed consent was obtained from all patients.
All the patients were subjected to a detailed history, careful clinical examination, pulmonary function test, laboratory investigations included arterial blood gases, radiological investigations included CXR, MDCT, and TUS.

Inclusion criteria:-
- Those who were suspected of ILD (exertional dyspnea, chronic cough, and dry crepitation in chest examination and restrictive pulmonary function tests)
- Those with a known medical history of ILD.

Exclusion criteria:-
- Pregnant or children.
- The cases with pulmonary edema of different causes because B-lines may be detected in these cases.

Spirometry:-
- Pulmonary function tests were done using a Spirometer with computer processing (the device is Jaeger Master Screen Diffusion, Gmbh, Hochberg, Viasys Healthcare, Germany).
- The values were recorded at the time the patient did the maximum effort to avoid any expected errors. The percentages and the absolute values of the spirometric measurements predicted from the patient's sex, weight, height, and age were calculated.

- **Ventilatory defect of the restrictive pattern** was defined by spirometric parameters of FEV1/FVC is greater than 70% predicted but FVC is less than 80% predicted [8].
- Grading the severity of the restrictive dysfunction as follows;

- Mild : FVC >70% (%predicted)
- Moderate: 60-69%
- Moderately severe: 50-59%
- Severe: 35-49%
- Very severe: <35%.[8].

Multidetector computed tomography (MDCT):-

- The device used was Toshiba Alexion 16 slice CT scanner.
- MDCT pattern was recorded as regards the predominant pattern either reticular, ground glass, cystic, nodular, crazy paving, mosaic, honeycombing or mixed.

Thoracic ultrasound:-

- It was performed for all patients using Mindray Bio-Medical Electronics Co., Shenzhen, China ultrasound machine using a grayscale (B-mode), or time-motion mode (M-mode). Cases were examined by oblique and longitudinal scans both on the posterior and anterior chest in the supine and seated positions using high and low-frequency probes.

The following were assessed:

B-lines. As regards the International Consensus Conference on Lung and Pleural Ultrasonography, B-lines are hyper-echoic vertical lines, laser-like, starting from the pleural line, moving with lung sliding and obliterating most of A-lines [9]

The distance between the two adjacent B-lines near to pleural line is measured and recorded in milliliters, B3 and B7 indicate that the distance between two adjacent B lines was respectively 3 and 7 mm.

B-lines indicate **partial** loss of pulmonary aeration and represent the thickening of subpleural septa either by inflammatory cells, pulmonary edema, or fibrous tissues [10].

A positive region: means the presence of three B-lines or more between two ribs in the longitudinal plane which is known as" Alveolar Interstitial syndrome" **The positive examination** means the presence of two positive regions or more on both sides[11].

Lung sliding: is defined as the" to and fro" dynamic movement of the lung during respiration, which was seen at the pleural line [12].

Assessment of pleura as regards pleural thickness and pleural surface (either regular, irregular, or fragmented).

Statistical analysis

Data were analyzed by using SPSS program version 25.0. Quantitative data was recorded as mean, median, and range. Qualitative data were recorded as numbers and percentages, in addition to the bivariate correlation between variables was done using the Pearson correlation test.

Results:-

This prospective study was done on 46 patients diagnosed as having ILD. Their ages ranged from 28 to 60 years old. They were 14 male and 32 female patients, with 12 smokers. The most presenting symptom was exertional dyspnea and cough in all cases, followed by chest pain in 22% of cases and wheezes in 9% of cases ***(Table1)***. Regarding the HRCT patterns found in the studied population, a reticular pattern was the most frequent, followed by ground-glass pattern, mosaic appearance, equal percentage of honeycombing and nodular cases, then cystic and crazy paving respectively. There was more than one HRCT pattern in the same case ***(Table2).*** Regarding the sonographic features among cases of ILDs. It was demonstrated that B-lines were present in 96% of cases, B- line distance was 7 mm in 73 % of cases, 3 mm in 27% of cases, pleural line abnormalities in the form of irregularity was in 70%, fragmentation in 26%, thickening in 91% of cases, subpleural lesions were present in 26% of cases, lung sliding was preserved in 83%, diminished in 17% of cases ***(Table 3).*** Regarding the correlation between TUS features and either the spirometric pulmonary functions or the MDCT pattern, there was a significant positive correlation between B-line distance in LUS and both the reticular pattern in MDCT((r=0.7, P=<0.0009), and the disease duration (r=0.6, P<0.0006) as shown in ***figure (1,4)***. There was a significant negative correlation between the B-line distance and both the FVC by spirometry (r=−0.76, P<0.0002) and the GGO pattern (r=−0.53, P<0.0007) in MDCT as shown in ***figure(2,3) and(Table4).***

Table (1) The demographic data of the studied populations(n=46**)**

Variables	**N (%)**
Age (Mean + SD)	44 $\pm$ 16
Gender Male	14(30%)
Female	32(70%)
Smoking Cigarette	8(17%)
Goza	4(9%)
Non smoker	34(74%)
Symptoms	
Exertional dyspnea	46(100%)
Cough - Productive - Dry	46(100%) 34(74%) 12(26%)
Chest pain	10(22%)
Wheezes	4(9%)

Table (2) HRCT findings in the ILD group(n=46)

HRCT Pattern	**Column N**	**%**
Reticular	22	48%
Cystic	8	17%
Honeycombing	14	30%
Ground glass	19	41%
Nodular	14	30%
Crazypaving	2	4 %
Mosaic	16	35%

Table (3) Ultrasonographic findings in the ILDs (n=46)

U/S Findings		**No.**	**%**
B Lines	Absent	2	4%
	present	44	96%
B lines distance (m.m)	B3	12	27%
	B7	32	73%
Pleural line	regular	14	30%
	irregular	32	70%
	fragmented	12	26%
Pleural thickness	Normal	4	9%
	Thickened	42	91%
Subpleural lesions (hypo-echoic lesion)	No	34	74%
	yes	12	26%
Lung sliding	Diminished	8	17%
	Normal	38	83%

Table (4) Correlation coefficient between B –Line distance with FVC, HRCT, and disease duration.

Variable	**FVC**		**GGO HRCT pattern**		**Reticular HRCT pattern**		**Disease duration**	
	r	**P**	**r**	**P**	**r**	**P**	**r**	**P**
B-Line distance	**-0.76**	**<0.0002**	**-0.53**	**<0.0007**	**0.7**	**<0.0009**	**0.6**	**<0.0006**

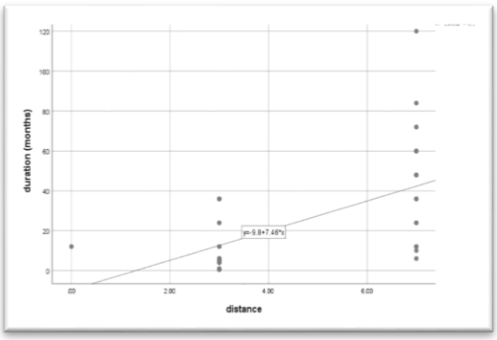


Figure 1: Positive correlation between disease duration and B-line distance in U/S

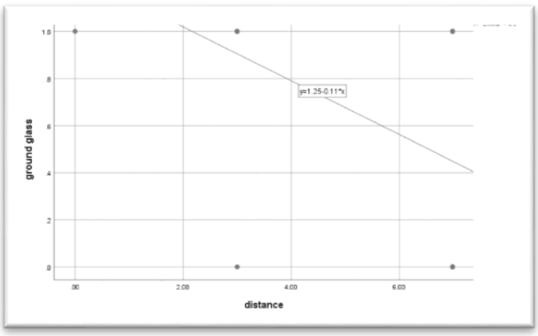


Figure 2: Negative correlation between the ground glass pattern on HRCT and the B-line distance in U/S.

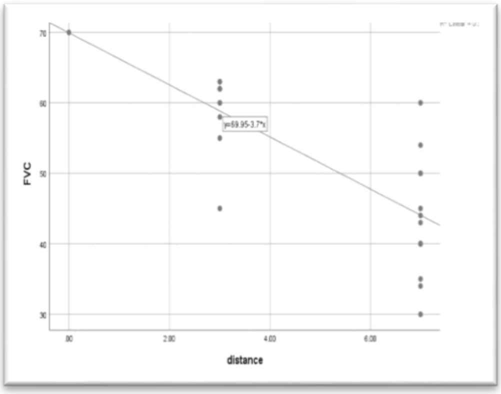


Figure 3: Negative correlation between the FVC and the B-line distance in U/S

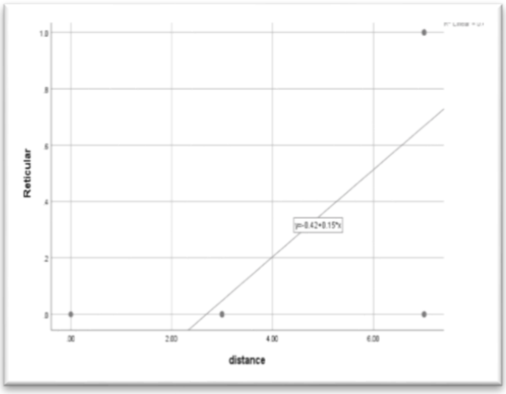
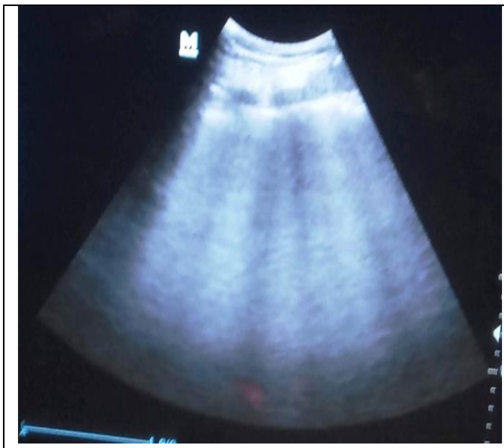
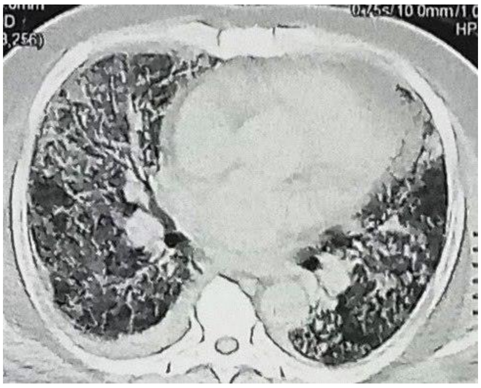


Figure 4: Positive correlation between reticular pattern on HRCT and B-line distance in U/S

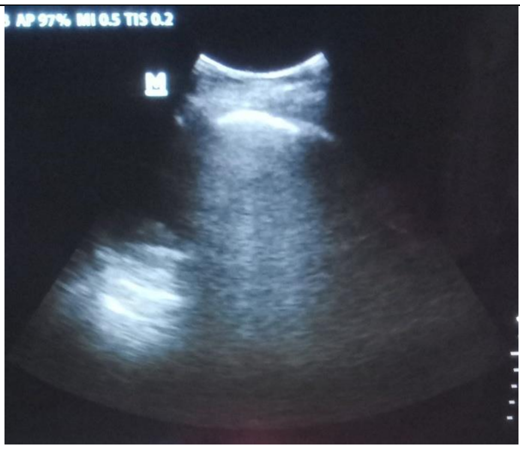


(a)

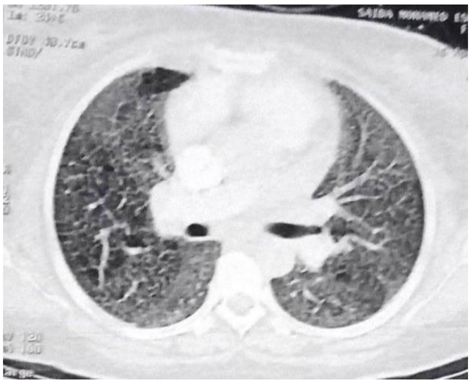


(b)

Figure5:-
a)TUS shows multiple B lines (B7)
b) HRCT shows reticular pattern



c)



d)

Figure6:-
c)TUS shows adherent B lines (B3) "white lung"
d) HRCT shows ground glass pattern

Discussion:-

The ultrasonographic evaluation of Interstitial lung diseases (ILD) depends on the appearance and the quantification of multiple B-lines, which are produced by the reflection of the ultrasonographic beams from the subpleural thickened interlobar septa on the lung surface interface. In ILDs, the interstitial interlobular septa are thickened by the accumulation of collagen tissue, while in patients who have heart failure, the interstitial interlobular septa are thickened by the accumulation of water *(13)*.

Thanks to the ease of its use, its availability, rapidity, reliability repeatability, its cheapness, its noninvasive approach, and its avoidance of ionizing radiation and contrast media, LUS became the “go-to” imaging technique for the lung and the pleura in a safe, and efficient and a cost-effective manner. Furthermore, its useful role as a bedside test in critically ill cases in the ICU is due to its portability *(14)*.

The present study was near to that reported by **El Fatah et al., (2019)** who diagnosed hypersensitivity pneumonitis in half of the cases, IPF in 10 (16.6%), nonspecific interstitial pneumonia (15%), five (8.3%) cases had sarcoidosis, one (1.6%) case had lymphangioleiomyomatosis, one (1.6%) case had pleural parenchymal fibroelastosis, while only four (6.6%) cases had rheumatoid arthritis. In the current study, by using TUS, 96% of the patients had diffuse and multiple B-lines bilaterally reflecting the diffuse fibrosing process *(15)*.

Histologically, the distance between the interlobular septa once they are at the subpleural space, are 7mm apart, and this is approximately the distance between the beginnings of the discrete comet tails at the site of the pleural line *(16)*.

By correlating the sonographic features with the radiological and the functional pattern of ILDs, we reported that there was a significant negative correlation between the B-line distance and the FVC($r=-0.76$, $P<0.0002$). This agreed with the results of **Gargani et al., (2009), Hasan et al., (2013),** and **Agmy et al., (2016)** who reported that the B lines were inversely correlated with the FVC. We also found a positive correlation between the disease duration and the B-line distance ($r=0.6$, $P<0.0006$) *(17-19)*. This is because, the narrower the distances between B lines (B3) the earlier the alveolar wall affection and the less pulmonary function impairment, while the wider the distances between B lines (B7) is a sign of more thickening of interstitial septa and therefore more impairment in lung function.

In the present study, the opacity of the ground glass pattern had a highly significant negative correlation with the B-line distance in LUS ($r=-0.53$, $P<0.0007$) and a significant positive correlation between the B-line distance and the opacity of reticular pattern in MDCT ($r=0.7$, $P<0.0007$). This agreed with the findings of **Mansour et al., (2018), Agmy et al., (2016), Hasan et al., (2013),** and **Assayag et al., (2012)** who found that the distance between every two contiguous B lines is positively correlated with the degree of interstitial affection on MDCT***(18-21).***

According to the pleural line, most cases had thickness in the pleural line (91%, n=42), whereas 9% (n=4) had normal thickness, irregular pleural line in 70 % (n=32), regular pleura in 14 (30%), this was near to **El Fatah et al., (2019)** who reported pleural line thickness in (71.7%, n=43), whereas 28.3% (n=17) had normal thickness, irregular pleural line in (71.7%, n=43) and regular pleural line in (28.3%, n=17) *(15)*.

Subpleural parenchymal lesions in ILD patients are seen in LUS and represent a wide spectrum of pathologic alterations, such as pulmonary metastasis, granuloma, and pulmonary nodules[6].

As regards the presence of subpleural lesions by TUS, in the present study we found that 18% of cases had subpleural lesions, while **Reissig and Kroegel., (2003)** reported that one-third of ILD cases had subpleural lesions, **Agmy et al., (2016)** found that 38% of cases had subpleural alterations [6, 19].

In the current study, assessment of lung sliding revealed that it was present in 83% of the cases and being diminished in 17% of cases. These findings were in agreement with **Mansour et al., (2018)** study in which lung sliding was normal in 82.5% and absent in 17.5% of cases [20].

This may be attributed to the fact that lung sliding is affected late in the advanced stages of fibrosis, as fibrosis reaches the visceral pleura and leads to restriction of lung expansion, which finally impairs lung sliding. [19].

The limitation of the current study is that the diffusion capacity of carbon monoxide was not measured.

Conclusion:-

TUS can be used as a complementary imaging technique for the diagnosis of ILDs besides HRCT. The B-lines distance is considered as a sign of pulmonary function deterioration and a sign of disease severity by the presence of increased reticular pattern on HRCT.

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