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TO DETERMINE THE CORRELATION OF B LINES ON CHEST ULTRASOUND WITH SEVERITY OF IDIOPATHIC PULMONARY FIBROSIS IN PATIENTS PRESENTING AT TERTIARY CARE HOSPITAL, KARACHI

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ABSTRACT

Objective: To determine the correlation of B lines with severity of idiopathic pulmonary fibrosis in patients presenting at Tertiary Care Hospital, Karachi.
Study design: Descriptive cross-sectional study.
Place and duration of study: This study was conducted at Chest Medicine (Ward 12), Jinnah Postgraduate Medical Center (JPMC), Karachi from 01-10-2020 till 31-10-2021.
Material and methods: Data was prospectively collected from patients after taking consent. The sample size for the study will be n=75 patients. Quantitative data was presented as simple descriptive statistics giving mean and standard deviation and qualitative variables was presented as frequency and percentages.
Results: A total of 75 idiopathic pulmonary fibrosis were included in this study. Mean age, duration of symptoms, height, weight and BMI in our study was 51.14±4.49 years, 4.63±2.21 months, 161±6.78 cm, 85.2±8.54 kg and 29.71±2.32 kg/m2. Out of 75 patients with idiopathic pulmonary fibrosis, 12 (16%), 23 (30.7%), 15 (20%) and 25 (33.3%) had normal, mild, moderate and severe idiopathic pulmonary fibrosis severity. Out of 75 patients with idiopathic pulmonary fibrosis, 15 (20%), 20 (26.7%), 29 (38.7%) and 11 (14.7%) belonged to B line quartile 1, 2, 3 and 4. Idiopathic pulmonary fibrosis correlation showed correlation with increasing B lines.
Conclusion: Ultrasound (US) is a promising and valuable tool for screening and assessing interstitial lung disease (ILD). The presence of B-lines on ultrasound has been found to correlate with the severity of idiopathic pulmonary fibrosis (IPF) and may serve as a useful indicator for monitoring treatment outcomes in patients with IPF.

Keywords: B-lines, transthoracic ultrasound, interstitial lung disease.

INTRODUCTION

Interstitial lung diseases (ILDs) encompass a diverse range of lung conditions that can present either acutely or chronically. These diseases are marked by widespread involvement of the lung interstitium and reduced gas exchange efficiency across the alveolocapillary membrane, potentially leading to respiratory failure. [1-2] The underlying causes, clinical symptoms, imaging findings, and tissue histology of ILDs can vary significantly across different types. [3] High-resolution computed tomography (HRCT) is regarded as the current gold standard for diagnosing ILD, as it is a highly sensitive technique for evaluating the extent and patterns of pulmonary fibrosis. [4] Common HRCT indicators of pulmonary fibrosis include a reticular pattern affecting the subpleural areas, ground-glass opacities, nodular and micronodular patterns, and honeycombing. [5]
Recent studies have emphasized that lung sonography is highly sensitive to changes in pulmonary composition and the balance between air and fluid. [6] In a healthy lung, ultrasound (US) waves are entirely reflected by the presence of

air; however, in conditions that reduce alveolar air content and increase fluid in the interstitial or alveolar spaces, specific artifacts are generated. [7-8] Diffuse parenchymal lung diseases, such as pulmonary fibrosis, are identified by the presence of numerous diffuse bilateral B-lines on ultrasound. These B-lines appear as distinct, laser-like vertical hyperechoic artifacts that originate from the pleural line, extend all the way to the bottom of the screen without diminishing, and move in sync with lung sliding. [9-10] The ultrasonographic hallmark of pulmonary fibrosis involves the identification and measurement of these B-line artifacts, also known as the comet tail sign. [11] This artifact is produced by the reflection of the ultrasound beam off the thickened subpleural interlobar septa. [12] The evaluation of ILD via ultrasound is based on the identification and quantification of B-lines, which are reverberation artifacts formed by the reflection of the ultrasound waves from the thickened interlobar septa near the lung surface. [13-14] Transthoracic lung ultrasound offers several advantages over HRCT and pulmonary function tests (PFTs). It is a bedside procedure that is widely accessible, simple to perform, cost-effective, and does not involve ionizing radiation or the use of contrast agents, making it highly acceptable to patients. For critically ill individuals, portable ultrasound machines, even those without Doppler capabilities, can provide a comprehensive and detailed lung evaluation. [15] A study by Mohammadi et al. found a correlation of r = -0.69 between the number of B-lines and the severity of idiopathic pulmonary fibrosis. [15-16]

The rationale of the study is to determine the correlation of B lines with severity of idiopathic pulmonary fibrosis in order to establish the local perspective as there is paucity of local data. Idiopathic pulmonary fibrosis severity has a negative impact on the disease specific health status. Very few international studies are available. These finding are yet to be replicated in a local setting, which can potentially offer new information to clinician that can influence clinical practice and patient outcomes in our local patient population. Moreover, data from this will be helpful in designing interventions with the goal of identify severity through regular screening of suspected patients in order to prevent future disease exacerbations and complications by developing an effective management plan. Finally, ultrasound is useful in situations where HRCT is not available or undesirable, as in pre-hospital emergencies when a patient cannot be transported out of the intensive care unit because of severe disease.

MATERIAL AND METHODS

This cross-sectional study was conducted at the Chest Medicine Ward (Ward 12) of Jinnah Postgraduate Medical Center (JPMC), Karachi, over a six-month period from April 16, 2020, to October 16, 2020, after receiving approval from the institutional review board. A total of 75 patients, aged 30-60 years, were included in the study based on a non-probability consecutive sampling technique. The sample size was calculated using a correlation coefficient of r = -0.69, with a power of 90% and a significance level of 3%. Although the initial calculation required 20 patients, the larger sample size was chosen to ensure adequate representation, as approximately 15 patients with idiopathic pulmonary fibrosis (IPF) were treated monthly at the study site.

Patients with a history of pulmonary embolism, malignancy, tuberculosis, connective tissue disease, congestive heart failure, chronic renal or liver disease, asthma, or chronic obstructive pulmonary disease were excluded. Eligible participants were diagnosed with IPF for more than six months and met at least two of the following criteria: history of nonproductive cough and shortness of breath (NYHA $\geq$ 2) for over three months, HRCT findings of patchy, peripheral, subpleural, bibasilar reticular opacities with subpleural honeycombing of less than 5 mm and ground-glass opacities, pulmonary function tests showing FVC < 75% of predicted, and bronchoalveolar lavage (BAL) showing elevated neutrophils (>5%) or eosinophils (>2%).

Demographic and clinical data were collected at the time of admission. Each patient was examined by the researcher, with supervision from a pulmonologist with over 10 years of experience. Severity of IPF was assessed using HRCT and categorized according to the Warrick score. A lung ultrasound was then performed by a trained pulmonologist using transthoracic sonography with the patient either sitting or supine, arms raised to widen the intercostal spaces. Scanning was conducted in eight regions: upper anterior, lower anterior, upper lateral, and basal lateral areas on both sides of the chest. The presence and number of B-lines were recorded and categorized into quartiles as follows: $\leq$ 5 B-lines (Q1), 6-15 B-lines (Q2), 16-30 B-lines (Q3), and $\geq$ 30 B-lines (Q4).

Data were analyzed using SPSS Version 16. Descriptive statistics, including means and standard deviations, were used to summarize continuous variables such as age, height, weight, body mass index (BMI), and symptom duration. Categorical variables, including gender, were reported as frequencies and percentages. Spearman's correlation coefficient was used to assess the relationship between B-lines quartiles and IPF severity, with a p-value of $\leq$ 0.05 considered statistically significant. Stratification by age, gender, and symptom duration was performed to control for potential confounders, and post-stratification Spearman's correlation analysis was conducted.

RESULTS

A total of 75 patients diagnosed with idiopathic pulmonary fibrosis (IPF) were included in this study. The ages of the patients ranged from 35 to 60 years, with a mean age of 51.14 ± 4.49 years. The average duration of symptoms was 4.63 ± 2.21 months. Additionally, the mean height, weight, and body mass index (BMI) of the patients were 161 ± 6.78 cm, 85.2 ± 8.54 kg, and 29.71 ± 2.32 kg/m², respectively. Regarding the severity of IPF, 12 (16%) of the patients had normal severity, 23 (30.7%) had mild severity, 15 (20%) had moderate severity, and 25 (33.3%) were categorized with severe IPF.

Table 1: Descriptive statistics

Variable	Mean ± SD	Min-Max
Age (Years)	51.14 ± 4.49	35-60
Duration of Symptoms (Months)	4.63 ± 2.21	1-6
Height (cm)	161 ± 6.78	148-168
Weight (kg)	85.2 ± 8.54	68-115
BMI (kg/m²)	29.71 ± 2.32	26-36

The distribution of B-line quartiles showed that 15 patients (20%) were in quartile 1, 20 patients (26.7%) in quartile 2, 29 patients (38.7%) in quartile 3, and 11 patients (14.7%) in quartile 4. The cohort's gender distribution indicated that 52 patients (69.3%) were male, and 23 patients (30.7%) were female. Age-wise, 33 patients (44%) were within the age group of 30-45 years, while 42 patients (56%) belonged to the 46-60 year age group. In terms of symptom duration, 46 patients (61.3%) had symptoms for more than 3 months, while 29 patients (38.7%) reported symptoms lasting less than 3 months.

Stratification based on B-line quartiles and the severity of IPF revealed that in quartile 1, 0 patients (0%) had normal severity, 8 patients (53.3%) had mild severity, 0 patients (0%) had moderate severity, and 7 patients (46.7%) had severe IPF. Similarly, in quartile 2, 4 patients (20%) had normal severity, 12 patients (60%) had mild severity, 0 patients (0%) had moderate severity, and 4 patients (20%) had severe IPF. In quartile 3, 8 patients (27.6%) had normal severity, 3 patients (10.3%) had mild severity, 8 patients (27.6%) had moderate severity, and 10 patients (34.5%) had severe IPF. Quartile 4 revealed that 0 patients (0%) had normal severity, 0 patients (0%) had mild severity, 7 patients (63.6%) had moderate severity, and 4 patients (36.4%) had severe IPF. However, the statistical analysis showed no significant correlation between B-line quartiles and the severity of IPF ($p = 0.11$, $r = 0.133$).

When patients were stratified by age groups (30-45 years and 46-60 years) and IPF severity, similar trends were observed. In the 30-45 age group, patients in B-line quartile 1 had no normal severity cases, 20% had mild severity, and 80% had severe IPF. In the same quartile for the 46-60 age group, 70% had mild severity, and 30% had severe IPF. Across quartiles and age groups, no statistically significant differences were noted, with p-values ranging from 0.09 to 0.15, and r-values close to zero, indicating no significant association between age and IPF severity.

Table 2: Distribution of Idiopathic pulmonary fibrosis

Quartiles	Normal	Mild	Moderate	Severe	Total	% Distribution
B-Line						
Quartile 1	0	8	0	7	15	53.3% Mild, 46.7% Severe
Quartile 2	4	12	0	4	20	20% Normal, 60% Mild, 20% Severe
Quartile 3	8	3	8	10	29	27.6% Normal, 10.3% Mild, 27.6% Moderate, 34.5% Severe
Quartile 4	0	0	7	4	11	63.6% Moderate, 36.4% Severe
Total	12	23	15	25	75	16% Normal, 30.7% Mild, 20% Moderate, 33.3% Severe
Age Group: 30-45 Years						
Quartile 1	0	1	0	4	5	20% Mild, 80% Severe
Quartile 2	3	7	0	1	11	27.3% Normal, 63.6% Mild, 9.1% Severe
Quartile 3	3	1	2	5	11	27.3% Normal, 9.1% Mild, 18.2% Moderate, 45.5% Severe

Quartile 4	0	0	5	1	6	83.3% Moderate, 16.7% Severe
Total	6	9	7	11	33	18.2% Normal, 27.3% Mild, 21.2% Moderate, 33.3% Severe
Age Group: 46-60 Years						
Quartile 1	0	7	0	3	10	70% Mild, 30% Severe
Quartile 2	1	5	0	3	9	11.1% Normal, 55.6% Mild, 33.3% Severe
Quartile 3	5	2	6	5	18	27.8% Normal, 11.1% Mild, 33.3% Moderate, 27.8% Severe
Quartile 4	0	0	2	3	5	40% Moderate, 60% Severe
Total	6	14	8	14	42	14.3% Normal, 33.3% Mild, 19% Moderate, 33.3% Severe

FIGURE-1: IDIOPATHIC PULMONARY FIBROSIS SEVERITY DISTRIBUTION n=75

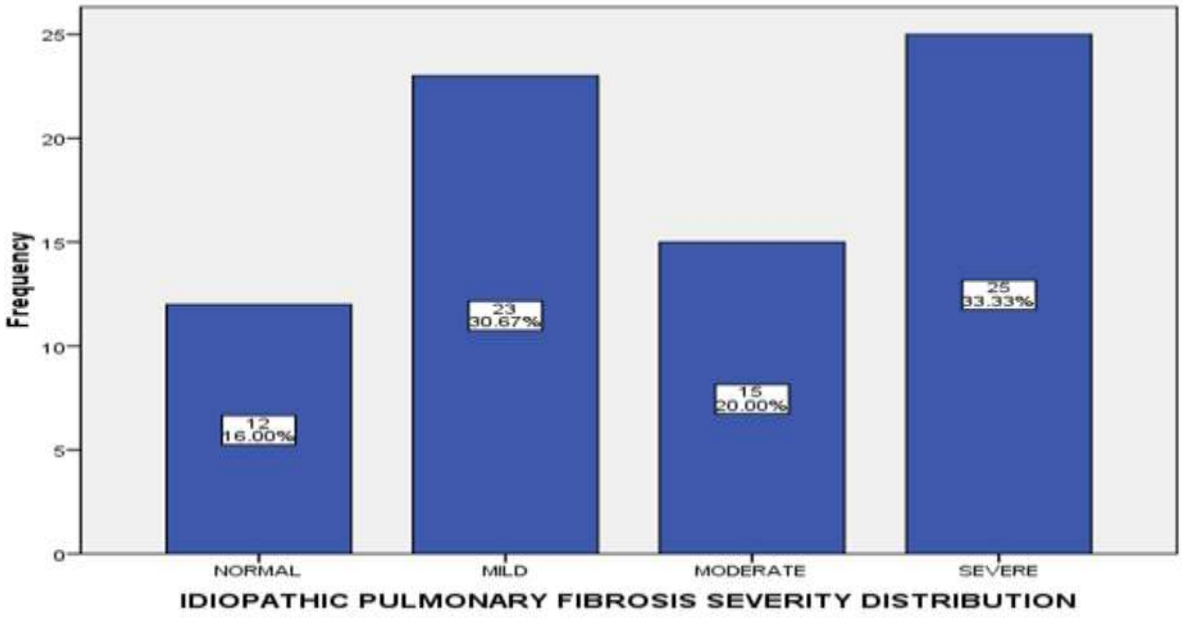
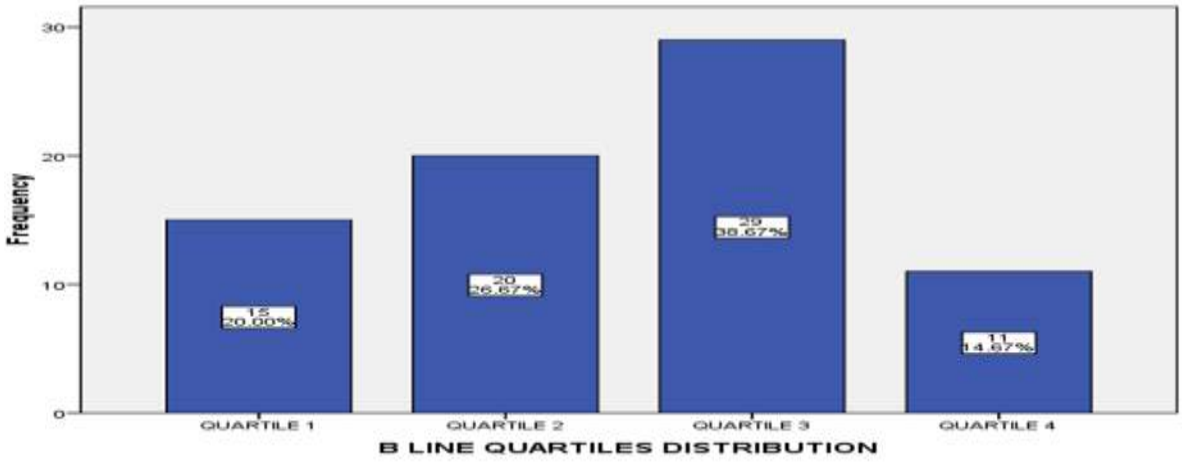
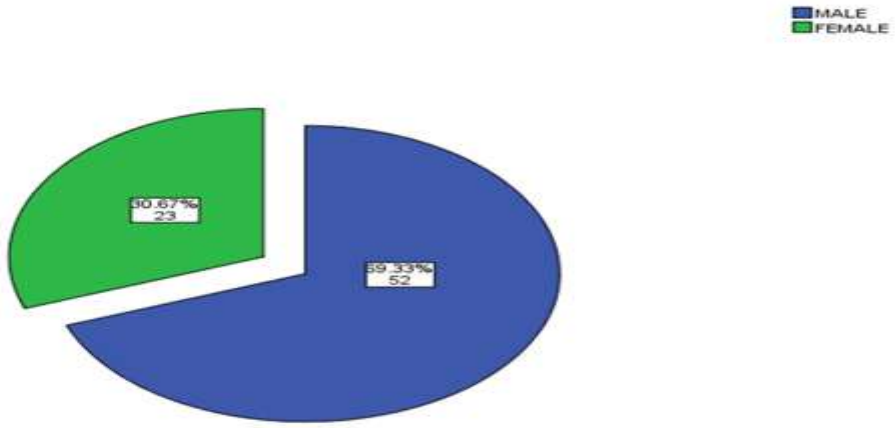


FIGURE-2: B LINE QUARTILES DISTRIBUTION n=75



In terms of gender, male patients in B-line quartile 1 showed that 44.4% had mild severity, while 55.6% had severe IPF. Female patients in quartile 1 had 66.7% with mild severity and 33.3% with severe IPF. Overall, gender did not appear to significantly influence IPF severity, as the p-values for male and female groups were 0.071 and 0.232, respectively. Finally, stratification by symptom duration also showed no significant correlation with IPF severity. Patients with symptoms lasting less than 3 months in quartile 1 had equal distribution between mild and severe IPF (50% each), while patients with symptoms lasting more than 3 months had 55.6% with mild severity and 44.4% with severe IPF. Across all quartiles, no significant association was observed between symptom duration and IPF severity (p-values ranging from 0.129 to 0.145).

FIGURE-3: GENDER DISTRIBUTION n=75



DISCUSSION

Our study found that increased B-line quartiles on lung ultrasound correlated with the severity of idiopathic pulmonary fibrosis, demonstrating a potential non-invasive method for assessing disease progression. These findings are consistent with the study by Hassan et al., which also demonstrated a correlation between the presence of diffuse bilateral B-lines on ultrasound and the severity of idiopathic pulmonary fibrosis as measured by HRCT.[17] Additionally, Singh et al. showed that M-mode ultrasound can differentiate between cardiogenic pulmonary edema and noncardiogenic alveolar interstitial syndrome by evaluating pleural line morphology, further highlighting the diagnostic utility of lung ultrasound in interstitial lung diseases. [18] Santana et al. demonstrated that lung ultrasound can also assess diaphragmatic mobility and thickness, with findings correlating significantly with pulmonary function test results in ILD patients, further emphasizing its role in functional evaluation of these patients. [19] Vizioli et al. compared lung ultrasound with chest X-ray for diagnosing ILD, finding that while LUS had higher sensitivity, chest X-ray showed greater specificity, suggesting that these modalities may be complementary when used together. [20-22] In addition, LUS has been found to correlate with functional and radiological findings in ILD, such as the number of B-lines corresponding to reduced lung function and disease severity, as demonstrated by studies like those by Asano et al. and Zhu et al. These findings suggest that LUS can be a valuable, non-invasive tool for monitoring disease progression and assessing the severity of ILD in clinical practice, particularly in settings where HRCT may not be readily available. [23-24]

Moreover, the correlation between B-line quantification on LUS and disease severity in ILD, as demonstrated in this study, aligns with previous reports that have emphasized the utility of B-lines as markers of interstitial involvement. The presence of diffuse and numerous B-lines has been linked to more severe pulmonary fibrosis, providing clinicians with a practical tool to assess disease burden. This method of evaluation is particularly advantageous as it offers real-time imaging without radiation exposure, making it suitable for repeated use in longitudinal monitoring of ILD patients. A relevant study by demonstrated the utility of LUS in detecting interstitial lung abnormalities, suggesting that it could serve as a reliable alternative in settings where access to HRCT is limited. Additionally, study found that the presence of multiple B-lines on LUS correlated strongly with the extent of lung fibrosis observed on HRCT, further supporting the use of LUS in the non-invasive assessment of interstitial lung disease .[25]

Other studies have emphasized the utility of LUS in identifying viral pneumonia and other forms of interstitial pneumonia. Volpicelli and Testa showed that LUS findings, such as spared lung areas, strongly correlate with viral

pneumonia diagnosed by HRCT. Asano et al. demonstrated that LUS findings, including B-lines and pleural abnormalities, were associated with clinical and functional markers of interstitial pneumonia severity, reinforcing the role of LUS in the assessment of diffuse parenchymal lung diseases. [21-22]

Lung ultrasound (LUS) is emerging as a valuable non-invasive tool for the diagnosis and assessment of idiopathic pulmonary fibrosis (IPF) and other interstitial lung diseases (ILDs). The ability of LUS to detect B-lines, pleural irregularities, and other pathognomonic features offers a promising alternative to traditional imaging modalities such as HRCT, particularly in resource-limited settings or for patients who require frequent monitoring. Our study from Pakistan demonstrated a correlation between the number of B-lines and disease severity, supporting the growing body of evidence regarding the utility of LUS in ILD diagnosis. Further large-scale studies are necessary to validate these findings and establish standardized protocols for LUS in ILD management. The integration of LUS into routine clinical practice could enhance early diagnosis, improve patient outcomes, and reduce the reliance on more invasive or costly imaging techniques.

LIMITATIONS

This study has several limitations that should be acknowledged. First, the sample size was relatively small, comprising only 75 patients, which may limit the generalizability of the findings. Larger, multicenter studies would be needed to confirm the results. Second, the study was conducted at a single center, which may introduce selection bias due to the specific population demographic and geographic characteristics. Additionally, lung ultrasound (LUS) is highly operator-dependent, and variations in experience or technique could affect the accuracy of the results. Although LUS is a promising diagnostic tool, it is still a relatively new method in assessing interstitial lung disease, and there is a lack of standardized protocols, which may affect reproducibility across different settings. Lastly, this study did not compare LUS findings with more invasive diagnostic tools like lung biopsies, which could have provided additional histopathological correlation.

CONCLUSION

US is an attractive and promising technique, which may become an important clinical tool to be integrated with HRCT and PFT in the screening and evaluation of ILD. Transthoracic lung Ultrasound has many advantages over HRCT and PFT; it is a bedside procedure widely available, easily performed, inexpensive, requires neither ionizing radiation nor a contrast medium and is therefore readily and largely accepted by the patient.

In addition, the surface of the lung can be easily studied by US; therefore, the B-lines are quickly detected using either low-frequency (3.5 MHZ) or high-frequency (7.5 MHZ) transducers. In critically ill patients, portable machines even without Doppler power can be sufficient for a complete and detailed lung assessment. Finally, ultrasound is useful in situations where HRCT is not available or undesirable, as in pre-hospital emergencies and in pregnancy and when a patient cannot be transported out of the intensive care unit because of severe disease. B-lines correlated with the severity of idiopathic pulmonary fibrosis and might be useful in monitoring the treatment outcome in IPF patients.

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