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*Research Article*

## STUDY TO KNOW THE ASSOCIATION BETWEEN LIVER CIRRHOSIS AND PULMONARY FIBROSIS IN PATIENTS VISITED TERTIARY CARE HOSPITAL

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**Abstract:**

**Objective:** To know the association between pulmonary fibrosis and liver cirrhosis in various cirrhosis groups according to the age classification.

**Study design:** This is a descriptive study.

**Place and Duration:** Study conducted in the medicine department of Mayo Hospital, Lahore for the duration of Six Months from October 2019 to March 2020.

**Methodology:** Fifty patients were included in the study. All patients over 20 years of age are offered in the outpatient department, accident and emergency department and admitted to the medical unit. Patients were comparable in terms of age, sex, and physical characteristics, and the frequency of pulmonary fibrosis and child's classes were observed.

**Results:** The prevalence of hepatitis C is higher than that of hepatitis B. The causes of cirrhosis are the same as fibrosis. In developed countries, most cases are caused by chronic alcohol abuse or chronic hepatitis C. In some parts of Asia and Africa, cirrhosis is often due to chronic hepatitis B. Pulmonary fibrosis is an important component of many common parenchymal or interstitial lung diseases. Fifty patients included in the study were with mean age of  $36.67 \pm 8.35 \pm SD$  between 20-25 years of age. Fifty-six percent were male patients and 44% were female and female / male ratio was 1.27: 1. 18 (38%), mean  $\pm SD$  was  $1.31 \pm 0.21$  and only 1 (2%) patient left the study. There were 9 patients in class A (18%), 16 children in class B (32%) and 22 patients in class C (44%). Each patient's class was assigned according to two clinical criteria and three laboratory criteria as defined in the CTP system. Twenty-two (44%) of 50 patients had laboratory or clinical criteria for pulmonary fibrosis in cirrhosis. Twenty-six (52%) were missing and only 2 (4%) were missing due to error in studies. The ultrasound findings of portal hypertension, ie the reduction of liver span was 50 (100%) time and portal vein dilatation was 10 (20%). Splenomegaly was absent in 9 patients (18%) and 5 patients (10%) had present and ascities in 13(26%) patients and absent in 4(8%). Pulmonary fibrosis and liver cirrhosis were statistically significant. The difference of the test was significant ( $p < 0.05$ ).

**Conclusion:** There is a significant relationship between pulmonary fibrosis and liver cirrhosis and it increases the incidence of pulmonary fibrosis with the progression of child's classification.

**Key words:** liver cirrhosis, pulmonary fibrosis and Childs classification.

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**INTRODUCTION:**

Pulmonary fibrosis is an important component of many common interstitial or parenchymal lung diseases.<sup>1</sup> T cells (CD4 +) are specialized in the production of soluble factors (cytokines) that can be profibrotically effective (IL-4, IL-13, TGF- $\beta$ ), but this functional specialization is not rigid; CD8 + can also function as an important source of cytokines and CD4 +. In the United States; the most important causes of chronic liver disease is Hepatitis C virus (HCV) and interpretations for about fifteen percent of viral hepatitis<sup>2</sup>. Cirrhosis is one of the major causes of mortality worldwide. It is the main cause of cirrhosis in Pakistan. Hepatitis C is more than hepatitis B. As of fibrosis, the causes of cirrhosis are the same<sup>3</sup>. Most cases are due to chronic hepatitis C or chronic alcohol abuse. In some parts of Africa and Asia, chronic hepatitis B is the cause of cirrhosis<sup>4</sup>. Cirrhosis of unknown etiology (cryptogenic cirrhosis) is becoming less common because many specific causes (eg steatohepatitis, chronic hepatitis C) have been identified<sup>5</sup>. It can also cause cirrhosis, such as bile duct injury, the bile duct mechanical obstruction or primary biliary cirrhosis<sup>6</sup>. These include loss and damage of type I alveolar epithelial cells followed by type II cells hyperplastic expansion; predominantly T helper (Th) 2 cytokine profile; Variable chronic inflammatory cell infiltration; stimulation of proinflammatory cytokines such as tumor necrosis factor TNF- $\alpha$  and interleukin (IL) -8<sup>7</sup>. Idiopathic pulmonary fibrosis is advanced interstitial lung disease that seriously conciliations lung function<sup>8</sup>. The possible consequences of IPF for an abnormal healing response to alveolar surface injury and disease development are characterized by progressive accumulation of collagen and fibroblast hyperplasia that destroy normal lung tissue. In the world; one of the most common causes of chronic liver disease is Hepatitis C virus (HCV). Chronic hepatitis C is a form of insidiously progressive liver disease that progresses continuously but silently with cirrhosis for 10 to 30 years in 20 to 50% of cases. Hepatitis C-induced cirrhosis is estimated at 5% to 10% and is one of the leading causes of death, especially in Japan. Chronic HCV infection has been associated with various extrahepatic complications<sup>9</sup>.

**MATERIALS AND METHODS:**

This descriptive study was held in the the medicine department of Mayo Hospital, Lahore for the duration of Six Months from October 2019 to March 2020. Fifty patients were included in the study. All patients over the age of 20 are presented in the outpatient department, accident and emergency department and admitted to the medical unit. Patients were comparable in terms of age, sex, and physical characteristics, and the frequency of pulmonary fibrosis and child's classes were observed. Data collection procedure: patients were evaluated for clinical, acidic, jaundice and hepatic encephalopathy. Laboratory tests were performed to identify the child's class, such as serum albumin, bilirubin and prothrombin time. All patients underwent chest X-ray and ultrasound to check liver, portal vein dilatation, spleen size, and average clavicular line for the presence or absence of ascites. Pulmonary function tests were performed to determine the restrictive pattern of lung diseases. For the presence or absence of pulmonary fibrosis, all patients underwent HRCT testing.

**Statistical analysis:** All information collected was entered into 16 versions of SPSS software and analyzed with statistical program. Descriptive statistics were calculated. Age, quantitative variables were presented as mean and standard deviation. Qualitative variables such as gender, pulmonary fibrosis and ultrasound findings, ie splenomegaly, portal vein dilatation, and ascites were presented as frequency and percentage in tabular forms.  $P < 0.05$  was considered significant.

**RESULTS:**

Fifty patients of both sexes were included in the study. The mean age of the patients was  $36.67 \pm 8.35$  years. Of the 56 patients, 8 (16%) were in the 20-35 age group, 22 (44%) between 36 and 51 years, 30% between 52 and 67 years, and only 5 (10%) were older than 67 years. The difference was not statistically significant. Fifty-six male patients and female were 44% with male to female ratio of 1.27: 1 (Table 1).

Table 1: Frequency distribution of demographic variables of patients (n=50)

	Frequency	%age
Male	28	56.0
Female	22	44.0
<b>Age range (yrs)</b>		
20 – 35	8	16.0
36 – 51	22	44.0
52 – 67	15	30.0
>67	5	10.0

Mean $\pm$ SD 36.67 $\pm$ 8.35

Table 2 shows that 50 patients had pulmonary function tests, 35 (70%) were restrictive, 12 (24%) were obstructive, and 3 (6%) had no PFT, and an interstitial lung disease, such as IPF.

**Table 2: Frequency of pulmonary function test**

Pulmonary test	Frequency	%age
Restrictive	35	70.0
Obstructive	12	24.0
Missing	3	6.0

Table 3 shows the distribution of child's group. In group A were  $\pm 22$  (44%) with mean  $\pm$  SD  $1.52 \pm 0.29$ , in group B 9 (18%) with mean  $\pm$  SD  $1.02 \pm 0.62$  and 18 (36%) in group C with mean  $\pm$  SD  $1.31 \pm 0.21$  and only 1 (2%) patient disappeared.

**Table 3: Distribution of Child's group and Child's Classes of patients**

Child Group	Child Group			Child's Class	
	Frequency	%age	Mean $\pm$ SD	Frequency	%age
A	22	44.0	1.52 $\pm$ 0.39	9	18.0
B	9	18.0	1.02 $\pm$ 0.62	16	32.0
C	18	36.0	1.31 $\pm$ 0.53	22	44.0
Missing	1	2.0		3	6.0

Table 3 also shows that the child's class A had patients 9(18%), in B 16 (32%), and C has 22 patients (44%). Each patient's class was assigned according to two clinical criteria and three laboratory criteria as defined in the CTP system. Twenty-two (44%) of 50 patients had clinical and laboratory criteria for pulmonary fibrosis in cirrhosis. Twenty-six (52%) were missing and only 2 (4%) were missing due to incomplete studies (Table 4).

**Table 4: Frequency of pulmonary fibrosis cirrhosis**

Pulmonary test	Frequency	%age
Present	22	44.0
Absent	26	52.0
Missing	2	4.0

The ultrasound findings of portal hypertension, ie the reduction of liver span was 50 (100%) time and portal vein dilatation was 10 (20%). Splenomegaly was absent in 9 patients (18%) and 5 patients (10%) had present and ascities in 13(26%) patients and absent in 4(8%). Pulmonary fibrosis and liver cirrhosis were statistically significant. The difference of the test was significant ( $p < 0.05$ ) (Table 5).

**Table 5: Ultrasonography findings of portal hypertension features**

Features	Present	Absent
Splenomegaly	9 (18%)	5 (10%)
Portal vein dilatation	10 (20%)	6 (12%)
Ascities	13 (26%)	4 (8%)
Reduced liver span	50 (100%)	0 (0%)

Liver biopsy is the gold standard procedure for the diagnosis of liver cirrhosis. Most patients with liver cirrhosis have an irregular clotting profile and thrombocytopenia. Biopsy is contraindicated in most of these patients, so we have to rely on clinical evaluation and laboratory and radiological examinations to prove cirrhosis. Idiopathic pulmonary fibrosis is also a fatal progressive disease. In view of the above facts, it is believed that cytokines involved in the stimulation of liver cells to produce collagen should stimulate the lungs from the bloodstream to produce collagen in the lungs as in the liver. This will help treat IPF with drugs used to treat cirrhosis. Therefore, we will demonstrate this relationship through tissue cultures and additional research study cells. In addition, early detection and treatment of IPF in cirrhosis population will have an impact on survival.

**DISCUSSION:**

In a study conducted by Puoti, the mean age was 32 years. In this study, the  $\pm$  mean age of the patients was  $36.67 \pm 8.35$  years, male patients were 28 (56%), women were 22 (44%) patients and M:F ratio found to be 1.27: 1. In a study by the American Thoracic Society Joint Declaration (ATS) in the United States, the European Respiratory Society reported more men than women with IPF<sup>10</sup>. Another study by Watters, men and women was equally influenced. This study shows the incidence of pulmonary fibrosis in patients with liver cirrhosis (44%) compared to the incidence in the general population (3%)<sup>11</sup>. The risk of developing pulmonary fibrosis increases with the number of years of occupational exposure. Powder containing steel, rice, lead and pine wood is more specifically linked to the development of pulmonary fibrosis<sup>12</sup>. Unfortunately, most studies that attempt to identify environmental risks for the development of pulmonary fibrosis are limited to the confidence in clinical diagnosis without an HRCT scan or confirmation<sup>13</sup>. The frequency of interstitial lung disease in chronic liver disease of different etiologies varies between 13-60% in the published literature. The present study shows that the frequency of IPF is high and the frequency of liver cirrhosis may be higher. Mediators producing chronic inflammation play a key role in the accumulation of collagen fibers. Mediators also reach the lungs through circulation, so the weather causes this agent to accumulate collagen in the lungs, causing fibrosis. According to the results of pulmonary function tests, the patient with obstructive PFT may also have fibrosis, so PFT is not a reliable indicator of interstitial lung disease in patients with liver cirrhosis<sup>14</sup>. The results of my study also showed that Pediatric Class A 9 (18%) patients had a lower incidence of pulmonary fibrosis than Pediatric Class B 16 (32%) and had a lower frequency than Pediatric Class C 22 (44%). This increases as the accumulation of collagen in the liver increases<sup>15</sup>.

**CONCLUSION:**

There is a significant relationship between pulmonary fibrosis and liver cirrhosis and it increases the incidence of pulmonary fibrosis with the progression of child's classification.

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