

Examine the Association between Patients of Liver Cirrhosis and Pulmonary Dysfunctions

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ABSTRACT

Background: Cirrhosis is a condition in which the liver does not function properly due to long-term damage. It is the end stage of chronic liver disease clinically characterized by progressive liver failure, development of portal hypertension or hepatocellular carcinoma. Fibrosis occurs due to interaction between different cell types and cytokines. Profibrotic agents include type-2 CD4 positive lymphocytes, CD40 receptor, interaction and cytokines like IL-4, TGF beta, platelet derived growth factor.

Aim: To evaluate the relationship of liver cirrhosis and pulmonary fibrosis according to child's classification.

Duration and Place of Study: Six months from 01-07 2016 to 30-01-2017 at University College of Medicine and Dentistry, University of Lahore.

Methods: This is a case series description study. Seventy patients were included according to inclusion and exclusion criteria.

Conclusion: A significant relationship between cirrhosis of liver and pulmonary fibrosis and with advancement of child class, frequency of pulmonary fibrosis increases.

Keywords: Liver Cirrhosis, Pulmonary fibrosis, High resolution CT scan.

INTRODUCTION

Pulmonary fibrosis occurs due to interaction between different cell types and cytokines. It may be a secondary effect of other diseases.^{1,2} The word *cirrhosis* is from Greek, *kirrhos* "yellowish" and *-osis* meaning "condition", describing the appearance of a cirrhotic liver. The liver cirrhosis affected about 2.8 million people and resulted in 1.3 million deaths in 2015. These, alcohol caused 348,000, hepatitis C caused 326,000, and hepatitis B caused 371,000. Cirrhosis and chronic liver disease were the tenth leading cause of death for men and the twelfth for women in the United States, more men die of cirrhosis than women.³

The viral hepatitis is major cause of liver cirrhosis in Pakistan. The prevalence of hepatitis C is more than hepatitis B.⁴ Hepatitis B and C viruses are common causes of acute and chronic hepatitis.⁵ Hepatitis C is an infectious disease caused by the hepatitis C virus (HCV) that primarily affects the liver.⁶ In western world alcoholic liver disease accounts for 60 to 70% cases of cirrhosis. Other causes of cirrhosis include cryptogenic cirrhosis (10-15%), biliary diseases (5-10%), genetic hemochromatosis (5%). Wilson's disease and alpha-1 antitrypsin deficiency are rare causes of cirrhosis. In cirrhosis there is increase deposition of collagen type I & II) and stimuli for deposition of collagen come from cytokines produced by chronic inflammation, like TNF alpha, TNF beta and IL-1 & by injured endogenous cells⁷.

Patients with primary biliary cirrhosis develop interstitial lung disease with moderately restrictive lung function test. Idiopathic pulmonary fibrosis is associated with cirrhosis due to hepatitis C virus.⁸ Interstitial lung disease appears medially 4.5±3.2 SD years after clinical onset of chronic hepatitis. Abnormalities in pulmonary function have been reported in association with chronic liver disease of varied etiology e.g. in one study most commonly affected test of lung function was reduced lung capacity for carbon mono-oxide (DLco), followed by ventilatory restriction (25%) and air flow obstruction (3%). Pulmonary functions are further impaired in cirrhosis and ascities cause further deterioration. In another study obstructive air way disease was found in 11%, restrictive lung disease in 17% and reduced diffusion capacity in 43%.^{9,10}

RESULTS

This study includes 70 patients of both sexes. Out of 70 patients 48 (69%) were males and 22 (31%) were females (Figure 1). Most of the patients were of age range between 36-55 years (63%). Minimum age was 15 years and maximum age of patients was 70 years. The mean age was 29.79±5.30SD (Table 1).

Pulmonary function tests were performed on 51 (73%) patients out of these 51 patients 40 (57%) showed restrictive pattern of pulmonary function tests (PFT's) which was suggestive of interstitial lung disease like idiopathic pulmonary fibrosis (IPF). Twelve patients (17%) showed obstructive pattern of PFT's, while PFT's of 18 patients (26%) were missing (Figure 2).

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Child's class was assigned to each patient based on two clinical and three laboratory criteria as defined in CTP system. Twenty four patients (34%) were of Child's class A, 21 patients (30%) were of Child's class B, 23 patients (33%) were of Class C while 2 patients (3%) could not have been assigned Child class due to incomplete workup (Table 2). High resolution computed tomography (HRCT) scan of lungs was performed on 54 patients (77%) out of 70 while HRCT results of 15 patients (21%) were missing. Out of 54 patients 26 (37%) showed evidence of pulmonary fibrosis. On HRCT while 29 patients (42%) did not showed any evidence out of 26 patients which showed presence of pulmonary fibrosis (Figure 3). Five patients (19%) belongs to Child class A, 11 patients (42%) belong to Child class B while 10 (39%) belongs to Child class C showed pulmonary fibrosis on HRCT (Table 3). The limitations of this study, as we know that gold standard to diagnose cirrhosis is liver biopsy but most of the patient with cirrhosis have deranged co-agulation profile and thrombocytopenia. So biopsy is contraindicated in majority of these patients, so we have to rely on clinical assessment as well as laboratory and radiological investigations to establish cirrhosis. The frequency of ILDs in liver disease of different etiologies (like HCV, PBC) has been discussed but no similar study is available.

Idiopathic pulmonary fibrosis is also a progressive fatal disease but much less research work to develop drugs for IPF is being done. Taking into consideration the above facts it is thought that as the cytokines involved in stimulation of cells in liver to produce collagen reach the lungs through blood circulation so they might stimulate the fibrogenic cells in the lungs to produce collagen in the same way as in liver.

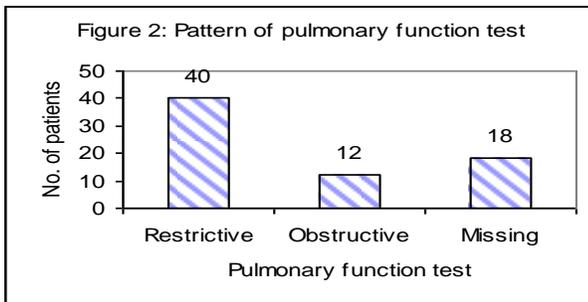
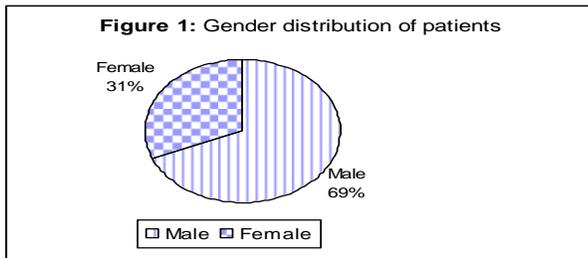


Table 1: Age distribution of patients (n=70)

Age (years)	n	%age
15-35	5	7.0
36-55	44	63.0
56-70	21	30.0

Table 2: Child's group distribution

Tests	n	%age
Child's A	24	34.0
Child's B	21	30.0
Child's C	23	33.0
Missing	02	3.0

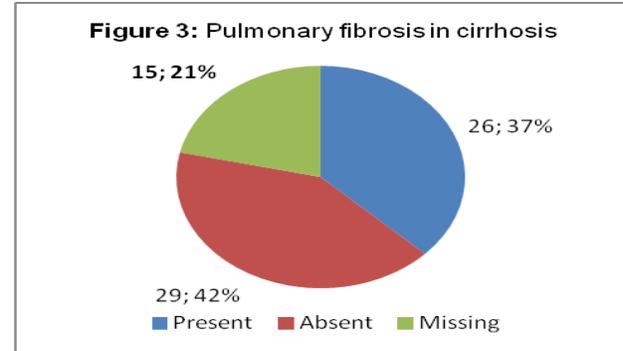


Table 3: Frequency of pulmonary fibrosis in different Child Classes

Classes	n	%age
Child's A	5	19.0
Child's B	11	42.0
Child's C	10	39.0

DISCUSSION

This study shows that frequency of pulmonary fibrosis in patients with cirrhosis of liver much more (49%) as compared to frequency in general population (3% in Western population).

The frequency of interstitial lung disease in chronic liver disease of different etiologies varies between 13-60% in the literature published. In view of the higher frequency of IPF in my study may be due to higher incidence of liver cirrhosis in this part of world⁹.

The mediators produced chronic inflammation plays key role in deposition of collagen fibers. The mediators also reach the lungs through circulation, so weather these mediator produces deposition of collagen in lungs to produce fibrosis. This is the hypothesis, which can be made on the facts and results of my study. On the basis of results of pulmonary function tests it is also seen that patient with obstructive picture of PFT's can also have fibrosis, so in patients with cirrhosis of liver PFT's is not a reliable indicator of interstitial lung disease¹¹.

It is also seen in the results that patients with Child class A have less frequency of pulmonary fibrosis as compared to Child's class B and B has less frequency as compare to Child class C. It means that as deposition of collagen increase in the liver. It also increases in lungs so frequency of interstitial lung disease (ILD) is maximum in Child class C¹².

This hypothesis is strongly supported by previous one that Hepatitis C virus (HCV) is a trigger for ILD¹³. The frequency of pulmonary fibrosis in patients with restrictive pattern of PFT's is 85% and this is also significant as compared to the study conducted by Chen & Yand¹⁴.

Hepatitis C virus antibodies was also found in significant proportion of patients in my study which is very much similar to results in literature.¹⁵

CONCLUSION

It is concluded that a significant relationship between cirrhosis of liver and pulmonary fibrosis and with advancement of child class, frequency of pulmonary fibrosis increases.

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