ORIGINAL ARTICLE

To Find Out the Relationship between Liver Cirrhosis and Pulmonary Fibrosis

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ABSTRACT

Objective: To find out the relationship between cirrhosis of liver and pulmonary fibrosis in different cirrhosis groups according to child's classification.
Study design: It is a descriptive study
Place of study & duration of study: Medical Department at Social Security Hospital, Lahore during the period of six months from 01-01-2010 to 30-06-2010.
Results: Prevalence of hepatitis C is more than hepatitis B. The causes of cirrhosis are the same as those of fibrosis. In developed countries, most cases result from chronic alcohol abuse or chronic hepatitis C. In parts of Asia and Africa, cirrhosis often results from chronic hepatitis B. Pulmonary fibrosis is a major component of many interstitial, or diffuse parenchymal, lung diseases. Fifty patients included in this study between 20-75 years of age with mean±SD 36.67±8.35. Fifty six percent were male patients and 44% were female with male to female ratio 1.27:1. Child group A had 22 (44%) patients with mean±SD 1.52±0.29, group B 9 (18%) patients with mean±SD 1.02±0.62 and Child group C was 18(38%) respectively with mean±SD 1.31±0.21 and only 1 (2%) patient was missing. The Child's class A had 9(18%) patients, Child's class B 16(32%) and Child's class C had 22(44%) patients respectively. Child's class was assigned to each patient based on two clinical and three laboratory criteria as defined in CTP system. Out of 50 patients 22(44%) were present of pulmonary fibrosis in cirrhosis based on clinical and laboratory criteria. Twenty six (52%) were absent and only 2(4%) were missing due to incomplete workup. The ultrasonography finding on features of portal hypertension i.e. reduced liver span 50(100%) were present and portal vein dilation were 10(20%) were present, while 6(12%) were absent splenomegaly were 9(18%) patients were present and 5(10%) were absent and ascities were 13(26%) patients present and 4(8%) were absent. Pulmonary fibrosis and cirrhosis of liver were statistical correlation test difference was significant ($p < 0.05$).
Conclusion: A significant relationship between liver cirrhosis and pulmonary fibrosis and with advancement of Child's class, frequency of pulmonary fibrosis increases.
Key words: Liver Cirrhosis, Pulmonary Fibrosis and Child's Classification

INTRODUCTION

Pulmonary fibrosis is a major component of many interstitial, or diffuse parenchymal, lung diseases. T cells (CD4+) specialize in production of soluble factors (cytokines) that may act profibrotically (IL-4, IL-13, TGF-β[1]. However, such functional specialization is not strict; CD8+ T cells may also serve as a significant source of cytokines, and CD4+[2].

The hepatitis C virus (HCV) is one of the most important causes of chronic liver disease in the United States. It accounts for about 15% of acute viral hepatitis, 60 to 70% of chronic hepatitis, and up to 50% of cirrhosis, end-stage liver disease, and liver cancer. Of the U.S. population, 1.6% or an estimated 4.1 million Americans, have antibody to HCV (anti-HCV), indicating ongoing or previous infection with the virus. Hepatitis C causes an estimated 10,000 to 12,000 deaths annually in the United States[3].

Cirrhosis is a leading cause of death worldwide. Viral hepatitis is major cause of cirrhosis in Pakistan. Prevalence of hepatitis C is more than hepatitis B. The causes of cirrhosis are the same as those of fibrosis. In developed countries, most cases result from chronic alcohol abuse or chronic hepatitis C. In parts of Asia and Africa, cirrhosis often results from chronic hepatitis B. Cirrhosis of unknown etiology (cryptogenic cirrhosis) is becoming less common as many specific causes (e.g., chronic hepatitis C, steatohepatitis) are identified. Injury to the bile ducts also can result in cirrhosis, such as mechanical bile duct obstruction, primary biliary cirrhosis. These include damage and loss of type I alveolar epithelial cells followed by hyperplastic expansion of type II cells[4]; variable chronic inflammatory cell infiltration[5]; a

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predominant T helper (Th)2 cytokine profile; induction of pro-inflammatory cytokines, such as interleukin (IL)-8 and tumor necrosis factor TNF-α and TNF-ß.[6]

Idiopathic pulmonary fibrosis is a progressive interstitial lung disease that severely compromises pulmonary function.[7] IPF likely results from an abnormal healing response to injury of the alveolar surface and development of the disease is characterized by fibroblast hyperplasia and progressive collagen deposition that effaces normal lung tissue.[8] The median survival time for patients with IPF is 3 years from the time of diagnosis, and there is currently no effective treatment[9].

Hepatitis C virus (HCV) is one of the more common causes of chronic liver disease in world. Chronic hepatitis C is an insidiously progressive form of liver disease that relentlessly but silently progresses to cirrhosis in 20%-50% of cases over a period of 10-30 years.[10] Hepatitis C-related cirrhosis is estimated at 5%-10%, and it is one of the major causes of death, especially in Japan. Chronic HCV infection has been associated with a variety of extrahepatic complications. Anti-HCV antibody positivity in patients with idiopathic pulmonary fibrosis (IPF) is significantly higher than that in patients without IPF both in Italy and Japan[11,12].

Methodology: This descriptive study was conducted at Nawaz Sharif Social Security Hospital/University College of Medicine, The University of Lahore during the period of six months. In this study fifty patients were included. All patients above 20 years of age presenting to medical out patient department, accident & emergency department and admitted in medical unit. It was a descriptive study. Patients were comparable with respect to age, sex and physical characters and looked frequency of pulmonary fibrosis and Child's classes.

Data collection procedure: Patients were clinically assessed for ascities, jaundice and hepatic encephalopathy. Laboratory investigations were performed for diagnosis like serum albumin, bilirubin and prothrombin time to define Child's class. Chest X-ray and ultrasound was done for all the patients for reduced liver span, coarse echotexture, portal vein dilatation, size of spleen in cm and mid clavicular line for absence or presence of the ascities. All the patients pulmonary function test was done to find out the restrictive pattern of lung diseases. For the presence or absence of pulmonary fibrosis HRCT test was done all the patients.

Statistical analysis: All information collected from the proforma was entered into SPSS version 16 computer software and analyzed through its statistical programme. Descriptive statistics were calculated. The quantitative variables age, Child group were presented in the form of mean and standard deviation. The qualitative variables like sex, pulmonary fibrosis and ultrasound findings i.e. splenomegaly, portal vein dilation and ascities were presented as frequencies and percentages in tabulated forms. P value of ≤ 0.05 was considered as significant.

RESULTS

Fifty patients of both sexes were included in this study conducted at Nawaz Sharif Social Security Hospital/ Lahore. The mean age of patients was 36.67±8.35 years. Out of 50, 8(16%) patients were in age group between 20-35 years, 22(44%) patients between age range of 36-51 years, 30% patients in 52-67 years of age and only 5(10%) patient was more 67 years of age. The difference was statistically not significant. Fifty six percent were male patients and 44% were female with male to female ratio 1.27:1 (Table 1).

Table 2 shows the pulmonary function tests were performed out of 50 patients 35(70%) were restrictive and 12(24%) patients showed obstructive and 3(6%) were missing patients of PFT's, which was suggestive of interstitial lung disease like IPF. Table 3 shows the distribution of child's group. Child group A had 22(44%) patients with mean±SD 1.52±0.29, group B 9(18%) patients with mean±SD 1.02±0.62 and Child group C was 18 (36%) respectively with mean±SD 1.31±0.21 and only 1(2%) patient was missing. Table 3 also shows the Child's class A had 9(18%) patients, Child's class B 16(32%) and Child's class C had 22(44%) patients respectively. Child's class was assigned to each patient based on two clinical and three laboratory criteria as defined in CTP system.

Out of 50 patients 22(44%) were present of pulmonary fibrosis in cirrhosis based on clinical and laboratory criteria. Twenty six (52%) were absent and only 2(4%) were missing due to incomplete workup (Table 4). The ultrasonography finding on features of portal hypertension i.e. reduced liver span 50(100%) were present and portal vein dilation were 10(20%) were present, while 6(12%) were absent, splenomegaly 9(18%) were present and 5(10%) were absent and ascities were 13(26%) present and 4(8%) were absent. Pulmonary fibrosis and cirrhosis of liver were statistical correlation test difference was significant ($p < 0.05$) (Table 5).

Liver biopsy is a gold standard procedure for diagnosis of cirrhosis of liver. Most of the patients with liver cirrhosis have deranged coagulation profile and thrombocytopenia. 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.

Idiopathic pulmonary fibrosis is also a progressive fatal disease. 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. This will help the treatment of IPF with the drugs used to treat the cirrhosis. So we shall also prove this relationship by tissue and cells cultures of further research work. Also early detection and treatment of IPF in cirrhotic population will have impact on survival.

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

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

Mean±SD 36.67±8.35

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: Distribution of Child's group and Child's Classes of patients

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

Table 4: Frequency of pulmonary fibrosis cirrhosis

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

Table 5: Ultrasonography findings of portal hypertension features

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

DISCUSSION

In a study carried out by Puoti, the mean age was 32 years.[13] In the present study the mean±SD age of patients was 36.67±8.35 years and male patients were 28 (56%) and female were 22 (44%) patients with male to female ratio 1.27:1 of liver cirrhosis and pulmonary fibrosis which is comparable with other studies. A study done in America by Joint Statement of the American Thoracic Society (ATS), European Respiratory Society more males have been reported with IPF than females.[14] Another study carried out by Watters, males and females are equally affected.[15]

The present study shows the frequency of pulmonary fibrosis in patients with cirrhosis of liver (44%) as compared to frequency in general population (3%). The risk of developing pulmonary fibrosis increases with the number of work years of exposure. Dust containing steel, brass, lead, and pine wood are most specifically linked to developing lung fibrosis. Unfortunately, many of the studies attempting to define the environmental risks for developing pulmonary fibrosis are limited by a reliance on the clinical diagnosis without performance of HRCT scanning or confirmation[16].

The frequency of interstitial lung disease in chronic liver disease of different etiologies varies between 13-60% in the literature published. The current study shows the higher frequency of IPF, it may be due to higher incidence of liver cirrhosis[17].

The mediators produced chronic inflammation plays key role in deposition of collagen fibers. The mediators also reach the lungs through circulation, so weather this mediator produces deposition of collagen in lungs to produce fibrosis. 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 disease.

The results of my study also shows that patients with Child class A 9 (18%) have less frequency of pulmonary fibrosis as compared to Child's class B 16 (32%) and B has less frequency as compare to Child class C 22 (44%). It means that as deposition of collagen increase in the liver. It also increases in lungs so frequency of ILD is maximum in Child class C.

This hypothosis is strongly supported by previous one that HCV is a trigger for ILD[18]. The frequency of pulmonary fibrosis in patients with restrictive pattern of PFT's is 70% and this is also significant as compared to the study conducted by Chen & Yand[19] Hepatitis C virus antibodies was also found in significant proportion of patients in my study

which is very much similar to results of a study conducted by Manganelli.[20]

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