

Pulmonary Dysfunction in Patients with Chronic Hepatitis C

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Abstract-

The aim of current study was to find out the frequency of pulmonary dysfunction in patients of hepatitis C and the association of obstructive and restrictive lung disease with HCV. A cross-sectional study was conducted at the Medical ward of Jinnah postgraduate medical center Karachi. To classify on the basis of Child-Pugh scoring, few investigations of all patients were done including abdominal ultrasound, Prothrombin time (PT), activated partial thromboplastin time (APTT), bilirubin, serum albumin level, anti-HCV antibody and PCR for HCV RNA. To detect the lung function, pulmonary function test was performed by using spirometer. Data was entered on Statistical Package for Social Science (SPSS) version-20. Mean age of study participants was 51.7 ± 4.6 . Out of total 150 participants, 58 patients were having restrictive pattern of pulmonary function test while 14 patients were having obstructive pattern of pulmonary function test on spirometry. According to Child-Pugh grading, as the grade increased there was progressive increase in frequency of restrictive lung disease. It can be concluded that chronic HCV has a strong significant association with the lung fibrosis as the disease presents a restrictive type of picture in pulmonary function test and the frequency of restrictive lung disease increase with the advancement of chronic liver disease

Keywords: Hepatitis C virus, Chronic liver disease, Restrictive lung disease, Fibrosis

Introduction

Chronic liver disease (CLD) is one of the most common health problem worldwide. The etiology include viral infection most commonly hepatitis B and hepatitis C, alcohol consumption, autoimmune disease, Wilson's disease, fatty liver disease due to any cause other than alcohol, hereditary hemochromatosis, α -1 antitrypsin deficiency and biliary cirrhosis (1). In western countries the major etiological factor is the alcohol but in Pakistan hepatitis B virus (HBV) and hepatitis C virus (HCV) are the leading cause of CLD (2), out of these two HCV infection is more common (3). HCV belongs to the family of flavivirus and has six different genotypes which are further subdivided into A and B. Genotype I and II are more prevalent in population of United States while subcontinent of South Asia is having genotype III. The recovery rate depends upon the type of genotype (4).

Only 15-20% of cases are reported with acute hepatitis while 80-85% cases develop chronic hepatitis (5). If it is treated timely then can be cured otherwise it develops liver cirrhosis, after that life expectancy decreases to 95% after 5 years and 81% after 10 years. The complication of cirrhosis like ascites develop in 25% of affected individual which further reduces the life expectancy up to 50% after 5 years while hepatocellular carcinoma develop in 2-5% patients per year (6). HCV has multiple extrahepatic complications like include lichen planus, mixed cryoglobulinemia, membranoproliferative glomerulonephritis, autoimmune thyroiditis,

lymphocytic sialadenitis, porphyria cutanea tarda, monoclonal gammopathy, autoimmune idiopathic thrombocytopenia, cardiomyopathies and non-Hodgkin lymphoma (6, 7). Genotype I leads to end stage renal disease while genotype III leads to hepatic stenosis, beside that there are many other pulmonary complications including hepato-pulmonary syndrome, pulmonary interstitial fibrosis and right ventricular systolic dysfunction (8).

The chronic inflammation in HCV causes the lung parenchyma to become hard resulting in scar formation which is called as Idiopathic pulmonary fibrosis. It has been noted that pathophysiology of liver fibrosis is like that of lung, might be because of genetic predisposition. Other possible explanation of lung fibrosis in this case, is viral infections (9, 10). The aim of current study was to find out the frequency of pulmonary dysfunction in patients of hepatitis C and the association of obstructive and restrictive lung disease with HCV.

Material and Methods

A cross-sectional study was conducted at the Medical ward of Jinnah postgraduate medical center Karachi from January 2022 to August 2022. Study got approval from the concerned institute. Those patients were included in the study who were between the age of 30-80 years, presented in medical OPD or admitted in medical ward and were confirmed cases of chronic liver disease on ultrasound and HCV detection by the presence of anti-HCV antibodies and confirmed by PCR. Those patients were excluded who were previously having any lung disease like tuberculosis, chronic obstructive pulmonary disease, lung tumor or metastatic tumor in lung, or having any systemic disease that can affect the lungs like sarcoidosis and rheumatoid arthritis or having connective tissue disease like systemic sclerosis or polymyositis.

Informed consent was taken from the included patients. To classify on the basis of Child-Pugh scoring, few investigations of all patients were done including abdominal ultrasound, Prothrombin time (PT), activated partial thromboplastin time (APTT), bilirubin, serum albumin level, anti-HCV antibody and PCR for HCV RNA. Patients with score less than 7 were included in grade A, score between 7-9 as grade B and score more than 9 was labeled as grade C on Child-Pugh grading system. To detect the lung

function, pulmonary function test was performed by using spirometer and affected patients were categorized on the obstructive or restrictive pattern of lung disease. Patients who were having FEV₁/FVC ratio more than 80%, labeled as restrictive pattern lung disease.

Data was entered on Statistical Package for Social Science (SPSS) version-20. Mean and standard deviation was calculated for all the numerical variables. Student t-test was used to find out the association of Child-Pugh score with the variables of pulmonary function test. p-value less than 0.05 was considered as significant.

Results

Mean age of study participants was 51.7 ± 4.6 , while 52.9 ± 4.7 for males and 49.7 ± 4.5 for females. Majority of the study participants were male (59.2%) followed by female participants (40.8%). Mean with standard deviation of FVC for male was 105.88 ± 19.1 and 103.52 ± 17.4 for females, the FEV₁ was 93.97 ± 25.6 and 93.12 ± 22.7 for males and females respectively as mentioned in Table 1.

Variables	Male	Female
Age (years)	52.9 ± 4.7	49.7 ± 4.5
FVC (L/min)	105.88 ± 19.1	103.52 ± 17.4
FEV ₁ (L/min)	93.97 ± 25.6	93.12 ± 22.7
FEV ₁ / FVC (ratio %)	88.75 ± 1.34	89.9 ± 1.30

Out of total 150 participants, 58 patients were having restrictive pattern of pulmonary function test while 14 patients were having obstructive pattern of pulmonary function test on spirometry. Child-Pugh criteria was used to grade the stages of chronic liver disease, grade A was having 56 patients, grade B 49 patients and Grade C had 45 patients of chronic liver disease. According to Child-Pugh grading 16 patients of grade A, 19 patients of grade B and 23 patients of grade C were having restrictive pattern of lung disease while 4 patients in grade A, 5 in grade B and 5 in grade C fall in the category of obstructive lung disease. Restrictive pattern of lung disease showed a significant association with chronic liver disease (p-value ≤ 0.05),

as the grade increased there was progressive increase in frequency of restrictive lung disease.

Table 2 Association of Child-Pugh grades with the Spirometry results

Grade	n= 150	Restrictive pattern	Obstructive pattern
A	56	16	4
B	49	19	5
C	45	23	5
p-value		0.02	0.462

Discussion

The most common hepatic complications of HCV are cirrhosis and chronic liver disease while known extrahepatic complications are non-Hodgkin lymphoma and cryoglobulinemia, besides, few lung conditions are also reported including exacerbating asthma, chronic obstructive pulmonary disease, interstitial pneumonia and pulmonary fibrosis. The complications due to cirrhosis include hepatopulmonary syndrome, pulmonary hypertension and autoimmune thyroiditis (6, 7, 11). It has been reported that HCV cause inflammation and liver fibrosis, the same mechanism can also occur in lung to cause fibrosis there. Another possible explanation may be the mixing of pulmonary and systemic circulation and accumulation of antigen and antibody complexes in lung glomeruli (12).

One of the study detected anti-HCV antibodies in the patients of idiopathic pulmonary fibrosis with the prevalence of 12.4% (13). Similarly, a study conducted in Egypt, in which recently diagnosed 20 patients of chronic HCV without previous pulmonary disease, were included. Both techniques were used, HRCT and pulmonary function test and reported that out of 20 patients, the 11 patients were having picture of obstructive type of lung disease on pulmonary function test and lung fibrosis on HRCT. The study concluded that PFT can be the substitute of HRCT as it is cost-effective and also prevent from the hazards of radiations (14). Hamid et.al conducted a study on Pakistani population with HCV infection, reported that the cirrhotic patients have some association with lung fibrosis on high resolution computed tomography (HRCT) (7). Another Pakistani study found that the incidence of lung fibrosis increases with the

advancement of CLD (7). Current study reported the same results but instead of using HRCT, pulmonary function test by spirometry, was used. It was noted that as the grade of liver disease rises, the pulmonary function test results became poor and presented the picture of obstructive type of lung disease most probably showing lung fibrosis.

On the other hand Irving et.al conducted a study on 62 patients of idiopathic pulmonary fibrosis and found only two positive cases of anti-HCV antibodies among British population (15). After that the hypothesis was tested in Italy and found anti-HCV antibodies among 60 patients of idiopathic pulmonary fibrosis and 13 patients of control group who did not have idiopathic pulmonary fibrosis so concluded with no association between the two conditions (16). There are few of the explanations for the variation in the results, first is the geographical differences that can't be neglected as the prevalence of HCV vary from region to region, secondly genotyping was not tested as there may be the variations in HCV genome, thirdly interferon administration, commonly used to treat chronic HCV, may has the link with pulmonary fibrosis (4).

Conclusion

It can be concluded that chronic HCV has a strong significant association with the lung fibrosis as the disease presents a restrictive type of picture in pulmonary function test and the frequency of restrictive lung disease increase with the advancement of chronic liver disease.

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