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Research Article

Frequency of Restrictive Pulmonary Function and Its Association with Cardiac Dysfunction in Patients with Different Stages of Chronic Hepatitis C Infection

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ABSTRACT

Background: Chronic hepatitis C virus (HCV) infection is a systemic disease, and its effect on the lung and cardiovascular system has been reported.

Objective: To determine the frequency of restrictive pulmonary function and its association with cardiac dysfunction in patients with different stages of chronic hepatitis C infection.

Materials and Methods: This cross-sectional, observational study was carried out in the HBS General Hospital Islamabad for a total period of six months, from November, 2025 to April, 2026. The total number of patients who were enrolled was 150, who were divided into three groups: mild fibrosis, significant fibrosis, and cirrhosis based on the results of the non-invasive fibrosis assessment. The data was analyzed using SPSS version 25, with a p-value of less than 0.05 used as a criterion for statistical significance.

Results: Restrictive pulmonary function was found in 31.3% of patients. The prevalence rose with greater severity of hepatitis C (HC) liver disease, with cirrhosis being the highest prevalence ($p<0.001$). In all patients, cardiac dysfunction was detected in 26.7%, and was significantly more frequent than in patients with normal pulmonary function ($p<0.001$).

Conclusions: Impaired pulmonary function is prevalent in people with chronic hepatitis C infection and is strongly linked with cardiac dysfunction, particularly in the more advanced stages of liver disease.

Keywords: Chronic Hepatitis C, Restrictive Pulmonary Function, Cardiac Dysfunction, Liver Fibrosis, Spirometry.

INTRODUCTION

Chronic systemic disease often produces changes in the physiology of other organs, such as the respiratory and cardiac systems, in addition to the primary organ of disease. In the context of COVID-19, Kurmanova et al. demonstrated that the clinical presentation of people with chronic obstructive pulmonary disease was significantly affected, suggesting that COVID-19 stressors could alter the trajectory of chronic respiratory disease (1). Similarly, Ratiu et al. reported that chronic hepatitis C virus (HCV) infection remained a systemic burden, even in hemodialysis patients, despite recent improvements in virological treatment of HCV infection, and that HCV-related organ effects could persist (2). Gonzalez-Aldaco et al. also discussed the metabolic dysfunction that frequently occurs with chronic hepatitis C, such as steatotic liver changes, that have been observed to affect overall disease course and clinical management (3).

Other populations have also examined the correlation between chronic viral infection and pulmonary function. Cordero et al. reported that the epigenetic measure, the "GrimAge" was associated with impaired pulmonary function measures such as airway function and blood-based lung function measures in

individuals with HIV (4), and Rodriguez-Sabogal et al. reported that recovery from respiratory viral infection was associated with changes in baseline pulmonary function measures and 1-, 6-, and 12-month follow-up pulmonary function measures in people with HIV (5). More recently, Awadh et al. demonstrated that comorbid conditions and prescribed chronic medications were significant factors in the treatment plan of patients with chronic HCV infection, echoing the systemic nature of the disease (6).

Cardiac involvement has also been noted in a chronic viral infection setting. In a series of studies, Stachel et al. showed that HCV viremia in the donor heart is correlated with measurable long-term rejection outcomes in patients who receive a cardiac transplant (7). Zhao et al. demonstrated that serum bilirubin, blood uric acid, and C-reactive protein levels are correlated with the severity of the disease in patients with chronic obstructive pulmonary disease, thus indicating that biochemical abnormalities originating in the liver extend to the pulmonary status (8), while Iovănescu et al. presented a wide range of cardiac abnormalities associated with chronic viral illness (9).

There is a well-defined description of restrictive pulmonary disease as a feature of other chronic diseases. Jozef et al.'s paper described the pathophysiology of a classic and progressive restrictive lung disease, idiopathic pulmonary fibrosis, which has important diagnostic and prognostic implications (10), and Huang et al. reported a close correlation between sociodemographic factors and the burden of comorbidities in patients with chronic obstructive pulmonary disease in a large national survey (11). A health-systems perspective of the high costs of disease progression of untreated chronic hepatitis C in the United States was described by Jang et al. (12), highlighting the clinical and economic significance of detecting extrahepatic complications earlier and at a point where they can be modified.

Restrictive ventilatory abnormalities are also described in the non-pulmonary disease setting. In children with ß-thalassemia, Eltagui and colleagues observed that there was also a background of silent restrictive lung disease even when the children did not have any clinical symptoms of their respiratory disease (13), suggesting that similar pulmonary changes may be underappreciated in other chronic hemolytic or hepatic diseases. In their study of prosthetic joint infection after total knee arthroplasty, Weinstein et al. showed how chronic disease states may be complicated by other systemic derangements that can easily be overlooked if an organized multi-organ assessment approach is not used (14) and Yang et al. demonstrated the relationship of systemic derangements (e.g. insulin resistance, as measured by the triglyceride-glucose index), to lung function parameters in the general population, suggesting a plausible metabolic link between systemic derangement and pulmonary mechanics (15).

Finally, current practice guidance reviewed by Karvellas et al. highlights the need for diagnosis of extrahepatic organ dysfunction, such as pulmonary and cardiac involvement, in the treatment of the critically ill cirrhotics (16). Teng et al. demonstrated the benefits of structured pulmonary rehabilitation even in the elderly and multimorbid population who had chronic respiratory limitation, highlighting the importance of early recognition of restrictive pulmonary impairment, while Mitrani et al. showed that even long-term cardiac surveillance following COVID-19 infection identified persistent cardiac abnormalities in a subset of patients reinforcing that chronic viral illness can leave a measurable cardiac footprint long after the acute insult (17, 18).

Although evidence is accumulating of a link between chronic systemic illness and both pulmonary and cardiac dysfunction, few studies have focused on restrictive pulmonary dysfunction and its association with cardiac dysfunction within the various phases of chronic hepatitis C disease. In view of the above, the present study was designed to explore the prevalence of restrictive pulmonary function and its correlation with cardiac dysfunction in patients having various stages of chronic hepatitis C infection, and as a bedside assessment tool, spirometry and echocardiogram are easy to perform in a resource-limited setting like Pakistan.

Objective: To determine the frequency of restrictive pulmonary function and its association with cardiac dysfunction in patients with different stages of chronic hepatitis C infection.

MATERIALS AND METHODS

Study Design: Cross-sectional observational study.

Setting: HBS General Hospital Islamabad.

Study Duration: Six months, from November, 2025 to April, 2026.

Sample Size: Using the rule of thumb of about 30% restrictive pulmonary function (RPF) among patients infected with chronic hepatitis C (cHC), a sample size of 150 was calculated using OpenEpi, with a 95% confidence interval and 5% margin of error.

Inclusion Criteria: Adult patients (more than 6 months anti-HCV and HCV RNA positive) who could perform spirometry.

Exclusion Criteria: patients with known primary pulmonary disease (COPD, asthma, interstitial lung disease); primary cardiac disease other than hepatitis C; active pulmonary infection; co-infection with HIV or hepatitis B; and incomplete clinical/procedural data.

Methods: All enrolled patients were clinically assessed, laboratory tested, and non-invasive fibrosis staged (transient elastography/APRI score) into mild fibrosis, significant fibrosis, and cirrhosis. Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and the FEV1/FVC ratio were measured by standard spirometry. Restrictive pulmonary function was characterized as FVC <80% of predicted FVC, and the FEV1/FVC ratio was not significantly decreased. A transthoracic echocardiogram was performed to obtain left ventricular ejection fraction (LVEF) and parameters of diastolic function. The data were analyzed with SPSS-25 software. Data for continuous variables were presented as mean ± standard deviation, and for categorical variables as frequencies and percentages. Independent t-test and a chi-square test were used to compare groups as appropriate. A p-value ≤0.05 was considered statistically significant.

RESULTS

A total of 150 patients with chronic hepatitis C infection were included in the study. The mean age of the study subjects was 47.6 years ± 10.9 years; there was a slight male predominance (54.7%).

Table 1: Baseline Demographic and Clinical Characteristics (n = 150)

Variable	Frequency (%) / Mean ± SD
Age (years)	47.6 ± 10.9
Male	82 (54.7%)
Female	68 (45.3%)
Diabetes Mellitus	41 (27.3%)
Hypertension	38 (25.3%)
BMI (kg/m²)	25.4 ± 3.8

Patients were divided based on liver disease, and pulmonary function testing showed a progressive trend in the prevalence of restrictive pulmonary function, the most common being in patients with cirrhosis.

Table 2: Frequency of Restrictive Pulmonary Function across Stages of Chronic Hepatitis C

Disease Stage	Restrictive Pattern n (%)	Normal Pattern n (%)
Mild Fibrosis (n=54)	9 (16.7%)	45 (83.3%)
Significant Fibrosis (n=58)	19 (32.8%)	39 (67.2%)
Cirrhosis (n=38)	19 (50.0%)	19 (50.0%)

Overall p-value <0.001 (chi-square test for trend across disease stages).

The results of cardiac assessment revealed that patients with restrictive pulmonary function had a significantly higher frequency of cardiac dysfunction than patients with normal pulmonary function.

Table 3: Comparison of Cardiac Parameters between Restrictive and Normal Pulmonary Function Groups

Variable	Restrictive (n=47)	Normal (n=103)
LVEF (%)	48.9 ± 8.2	56.3 ± 6.5
Diastolic Dysfunction	21 (44.7%)	18 (17.5%)
Cardiac Dysfunction (overall)	24 (51.1%)	16 (15.5%)

p<0.001 for all comparisons between groups.

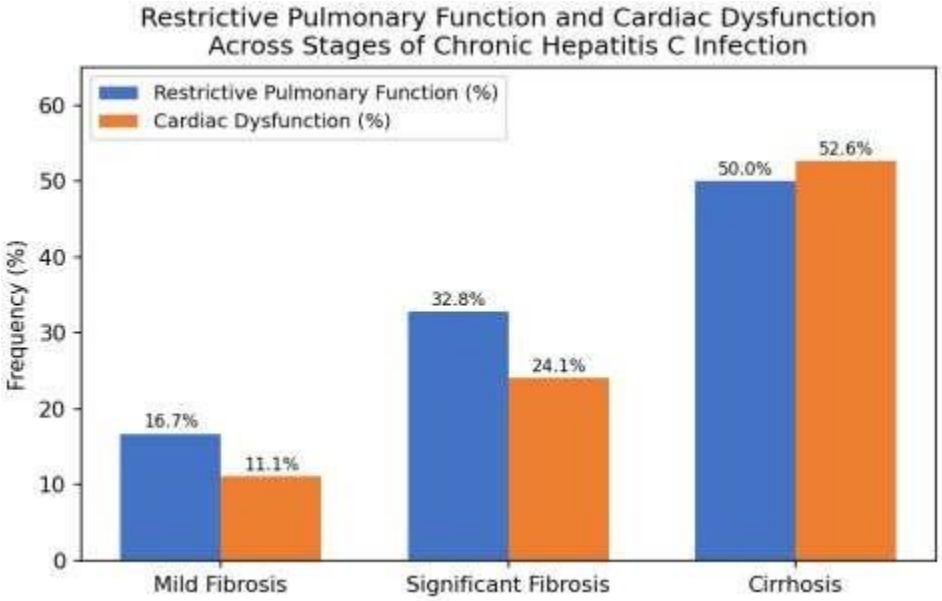
Table 4: Association of Cardiac Dysfunction with Stage of Chronic Hepatitis C Infection

Disease Stage	Cardiac Dysfunction n (%)	Normal Cardiac Function n (%)

Mild Fibrosis (n=54)	6 (11.1%)	48 (88.9%)
Significant Fibrosis (n=58)	14 (24.1%)	44 (75.9%)
Cirrhosis (n=38)	20 (52.6%)	18 (47.4%)

Overall p-value <0.001.

Graph (Bar Chart): Restrictive Pulmonary Function and Cardiac Dysfunction Across Stages of Chronic Hepatitis C



As demonstrated by the graphic, the frequency of restrictive pulmonary function and the frequency of cardiac dysfunction increase step-wise with disease progression of the chronic hepatitis C infection and are highest for the patients with cirrhosis. In total, 47/150 patients (31.3%) had restrictive pulmonary function, and 40/150 (26.7%) had cardiac function. Restrictive pulmonary function and cardiac dysfunction were progressive with increasing stage of liver disease, and a significant relationship was found between the presence of restrictive pulmonary function and cardiac dysfunction ($p<0.001$).

DISCUSSION

The present study aimed to evaluate the prevalence of restrictive pulmonary function (RPF) and the relationship between RPF and cardiac dysfunction in cases of various stages of chronic hepatitis C infection. In our 150 patients, restrictive pulmonary function was found in 31.3% and was more common with increasing degrees of fibrosis and cirrhosis (50% in those with cirrhosis). Cardiac dysfunction was also present in 26.7% of patients overall, and was significantly more prevalent in patients with restrictive pulmonary function. Based on these findings, it is possible to conclude that the chronic hepatitis C infection is chronic in nature and it is stage-dependent; that both the pulmonary and cardiovascular extrahepatic involvement may be progressive aspects of the same disease; and that both extrahepatic processes may be mechanistically linked.

Our results are similar to the general literature on pulmonary manifestations of chronic systemic disease. Our findings support the idea that the clinical phenotype of those with chronic viral hepatitis was also significantly modified during the COVID-19 pandemic, as suggested by Kurmanova et al., who showed that the clinical features of patients with chronic obstructive pulmonary disease were significantly altered during the COVID-19 pandemic, and that the respiratory system is vulnerable to systemic insults (1). Both Ratiu et al. and Gonzalez-Aldaco et al. reported the systemic burden of hepatitis C, even in patients on hemodialysis undergoing direct-acting antiviral treatment (2, 3), which supports the notion that organ effects of HCV infection may persist despite the progress made in virological therapies and may be responsible for some of the systemic metabolic changes observed in our cohort, as mentioned by Gonzalez-Aldaco et al. (3), including the frequent occurrence of steatotic liver disease (3).

Other populations have been examined for the relationship between chronic viral infection and pulmonary function. Both of these observations support the plausibility of pulmonary and cardiac implications during the virus infection, as we observed in chronic hepatitis C (4, 5), and are in line with the fact that comorbidity and chronic medication use affect the overall treatment plan of people with chronic hepatitis C (6).

The results of our study corroborate those from other chronic viral and post-viral diseases. Stachel et al. showed direct evidence of hepatitis C virus (HCV) impact on cardiac tissue and function by establishing measurable long-term outcomes of rejection in hepatitis C (HC) transplant recipients (7). Zhao et al. identified that there was a correlation between biochemical tests (bilirubin, uric acid, and C-reactive protein) and severity of chronic obstructive pulmonary disease (8), a finding that is similar to ours, where we have seen an increasing burden of cardiac dysfunction with worsening liver disease in our cohort, and Iovănescu et al. reviewed the burden of cardiovascular disease in HIV patients (9), which is also similar to our observation of a progressive increase in cardiac dysfunction with worsening liver disease.

Other chronic non-primary-pulmonary diseases can also be associated with restrictive lung disease. In a large national survey, Huang et al. found that there was a close association between sociodemographic and comorbidity factors with pulmonary outcomes in a large national survey, underscoring the importance of identifying at-risk subgroups, including our cirrhosis stratum, as Jozef et al. have done in their review of the pathophysiology of idiopathic pulmonary fibrosis, a classic restrictive lung disease, and the mechanisms of progressive fibrosis that may share pathways with the metabolic and inflammatory milieu of chronic hepatitis C (10). The significant health care burden caused by the progression of untreated chronic hepatitis C (12) highlights the clinical and economic value of detecting extrahepatic complications earlier, when they may have a modifiable cause.

Our finding of a restrictive pulmonary function in the absence of routine screening for respiratory involvement in these hepatitis C-positive patients is similar to what Eltagui et al. observed in children with ß-thalassemia without any overt respiratory symptoms (13). The chronic disease states may be complicated by further systemic derangements that must be carefully monitored in multi-system fashion, as Weinstein et al. illustrated in an illustrative, although clinically different, example, chronic disease states may be complicated by further systemic derangements that must be carefully monitored in multi-system fashion, as Weinstein et al. illustrated in an illustrative, although clinically different, example (14), and Yang et al. illustrated an association between the triglyceride-glucose index, an index of insulin resistance, and lung function parameters in a general population, suggesting that the metabolic derangements frequently seen in advanced chronic disease state of hepatitis C may plausibly extend to pulmonary and cardiac function as observed in our study (15).

Our emphasis on combined pulmonary and cardiac assessment is in keeping with the AASLD practice guidance on combined organ assessment of patients with advanced liver disease and acute-on-chronic liver failure (16), and the value of pulmonary rehabilitation even in the elderly, multimorbid patient with chronic respiratory limitation (17), as well as the finding that long-term cardiac monitoring after COVID-19 infection showed that in a proportion of patients, cardiac abnormalities persisted (18), which parallels the stage-dependent cardiac dysfunction that we observed in our cohort with chronic hepatitis C.

Our results overall confirmed that chronic hepatitis C infection not only damages the liver, but is linked to a progressive and stage-dependent impact on restrictive pulmonary function and cardiac dysfunction, and that this latter finding was strongly correlated with the former. The present study was, however, performed in one center over a limited period of time, and there was a lack of long-term follow-up; large, multi-center, longitudinal studies are needed to confirm the present findings and to elucidate the underlying mechanistic pathways that link chronic hepatitis C, pulmonary restriction, and cardiac dysfunction.

CONCLUSION

Restrictive pulmonary function is common among patients with chronic hepatitis C infection and increases significantly with advancing stage of liver disease. It is also strongly linked with cardiac insufficiency, especially in those with cirrhosis. Simple spirometric and echocardiographic assessment should be integrated into the routine evaluation of the patient with chronic hepatitis C infection,

particularly patients in the advanced fibrosis stage, to identify at-risk patients for systemic extrahepatic complications and to institute multidisciplinary management as soon as possible. Larger, multicenter, longitudinal studies are suggested to confirm these findings and to help elucidate the underlying pathophysiological mechanisms.

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