

A Study of Pulmonary Functions in Patients with Cirrhosis of Liver and its Correlation with the Severity of the Disease

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Abstract

Background: Liver cirrhosis may develop as a terminal consequence of a wide range of diseases including alcohol-related liver disease, infections of the liver, metabolic derangements, etc. About 5 - 32% of patients with cirrhosis experience a significant vascular complication of liver disease known as hepatopulmonary syndrome (HPS). In cirrhotic individuals, HPS significantly increases the mortality and morbidity. The present study compared the pulmonary functions and the degree of arterial hypoxaemia with the severity of liver disease.

Methods: The study was performed in Sharda Hospital, department of General Medicine and department of Pulmonary Medicine, School of Medical Sciences and Research, Greater Noida, Uttar Pradesh. A total of 50 patients with a confirmed diagnosis of liver cirrhosis, above the age of 18 years, were included. Patients with co-existing pulmonary diseases, heart disease, and with life-threatening complications of cirrhosis like active upper gastrointestinal haemorrhage, hepatic encephalopathy were excluded from the study.

Results: PFT findings of Restrictive lung disease were seen in 14 patients and Obstructive lung disease was seen in 1 patient in total. Out of 12 patients with CTP class C, 10 patients had restrictive findings and 1 patient showed obstructive findings. Out of 17 patients in CTP class B had 4 patients with restrictive pattern. Patients with CTP class C had a higher occurrence of restrictive pattern of lung disease compared to class A and B and the difference was found to be statistically significant.

Conclusion: Our study concludes that there is a significant correlation between pulmonary functions and the severity of liver cirrhosis. Patients with Child-Pugh class C when compared to patients with class A and B cirrhosis, had significantly lower PaO₂, SaO₂ values in ABG. Also, patients with Child-Pugh class C had lower FEV₁ and FVC values in pulmonary function tests. Restrictive lung disease was more common than obstructive lung disease in patients with cirrhosis of liver.

Key words: Pulmonary function test, Child-Pugh class, deranged liver function, portal hypertension.

Introduction

The histological growth of regenerating nodules encircled by fibrous bands in response to chronic liver injury, which leads to portal hypertension and end-stage liver disease, is known as cirrhosis. Liver cirrhosis may develop as a terminal consequence of a wide range of diseases including alcohol-related liver disease, infections of the liver, toxicity, metabolic derangements, or autoimmune (AI) diseases¹.

Disease of liver leads to portal hypertension, which results from a variety of pathological conditions that increase the resistance to the portal blood flow into the liver. Due to significant structural changes brought on by fibrosis and increased vascular tone in the hepatic microcirculation, cirrhosis is primarily responsible for portal hypertension. Collateral vessel development and arterial vasodilation advance as portal hypertension worsens, increasing blood flow to the portal circulation. Eventually, the hyperdynamic circulatory syndrome develops, leading to oesophageal varices, ascites, splenomegaly, HPS and HRS⁵⁻⁷.

In the absence of cardiac illness, arterial hypoxaemia frequently coexists with liver cirrhosis. Up to 45 - 50% of individuals with cirrhosis may experience impaired pulmonary function and decreased gas exchange. Generally speaking, restrictive pulmonary anomalies are seen, including an increase in the alveolar-arterial oxygen difference, airway blockage, impaired diffusion capacity, and a reduction in total lung capacity⁸. Hypoxaemia in individuals with CLD alters the course of treatment and impacts the prognosis. The link between liver illness and hypoxaemia cannot be explained by a single component alone, and its aetiology is likely to be complex⁹.

About 5 - 32% of patients with cirrhosis experience a significant vascular complication of liver disease known as hepatopulmonary syndrome (HPS). In cirrhotic individuals, HPS increases mortality and may impact the incidence and seriousness of portal hypertension complications^{10,11}. The age-adjusted alveolar-arterial oxygen gradient (AaPO₂) is increased, there is evidence of intrapulmonary vasodilatation, and there is an indication of liver illness or

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portal hypertension. If there is significant hypoxaemia, orthotopic liver transplantation may be considered a treatment for HPS.

The present study evaluated the pulmonary functions by spirometric evaluation, estimated the degree of arterial hypoxaemia by Arterial Blood Gas analysis, and correlated the pulmonary functions with the Child-Pugh score.

Materials and methods

The study was performed at Sharda Hospital, Department of General Medicine and Department of Pulmonary Medicine, School of Medical Sciences and Research, Greater Noida. The patients attending Outpatient Department (OPD) and those admitted were considered for the study. Total study participants were 50.

Inclusion criteria

Patients with a confirmed diagnosis of liver cirrhosis and above the age of 18 years.

Exclusion criteria

1. Patients with co-existing diseases like COPD, bronchial asthma, ILD.
2. Patients with heart diseases like CAD, CHF.
3. Patients with life-threatening complications of cirrhosis like active upper gastrointestinal haemorrhage, hepatic encephalopathy, and HRS.
4. Patients with a history of smoking.

Sample size: There were 50 cases for the study who will be similar to each other in terms of age, sex, and other demographic terms.

Study design

- Observational
- Cross-sectional in nature

Study duration

This was a one-and-half-year study starting from January 2021 to June 30, 2022.

Study conduct

A total of 50 cases were taken for the study. An informed consent was taken from all the subjects included in the study. A thorough history was taken and clinical examination was done. As per protocol, CBC was sent for all patients being admitted along with relevant investigations. Arterial blood gas analysis was done by a single radial puncture under local anaesthesia, while the patient was in the supine

position breathing room air, breathing 100% oxygen. Arterial blood gas was analysed using ABL 800 blood analyser. The ABL 800 FLEX blood gas analyzer allows you to measure a full panel of up to 18 STAT parameters on the same blood sample. This supports fast diagnosis of critically ill patients and reduces the risks and patient discomfort associated with repeated sampling.

- pH (7.35 - 7.45)
- PaO₂ (75 - 100 mmHg)
- PaCO₂ (35 - 45 mmHg)
- HCO₃ (22 - 26 meq/L)
- Base excess/deficit (-4 to +2)
- SaO₂ (95 - 100%)

All patients were subjected to pulmonary function tests using EASYPRO (spirometer) in the standing position according to standard procedures. Forced expired volume in one second (FEV₁) and forced vital capacity (FVC) were measured. Predicted values for each of the parameters were obtained from standardised references.

Method of measurement of outcome of interest

Standard statistical methods were used to measure the outcome.

Statistical analysis

Master chart of data from entire study population was created using their clinical and laboratory records. All the data obtained was analysed statistically using software like Microsoft Excel and IBM SPSS V20. Appropriate standard statistical analysis methods were used to determine factors associated with the outcome. Graphs, tables and flowcharts were used wherever appropriate. A 'p' value of < 0.05 was considered significant.

Results

The study consisted of a total of 50 subjects in which 39 were male and 11 were female.

21 subjects were CTP class A with 18 males and 3 females. 17 were CTP class B, 13 males and 4 females. 12 subjects were CTP class C, 8 males and 4 females. The distribution of subjects based on gender in CTP classes A, B, and C did not differ significantly.

The average age of patients with CTP class A was 40.86 ± 7.8 years, class B was 52.94 ± 11.52 years and class C was 52.42 ± 15.74 years.

The mean ages in CTP classes A, B, and C did not differ significantly (p value 0.052).

Table I: Distribution of study population according to gender.

Gender	Child-Turcotte-Pugh class			Total
	A	B	C	
Male	18	13	8	39
	85.7%	76.5%	66.7%	78.0%
Female	3	4	4	11
	14.3%	23.5%	33.3%	22.0%

p value = 0.438.

Table II: Distribution of the study participants according to age.

	Age (years)			p-value
	Mean	Std. Deviation	F-value	
A	40.86	7.80	2.383	0.052
B	53.94	11.52		
C	52.42	15.74		

Out of 50 subjects in the study, a total of 35 subjects had normal PFT across all the CTP classes, whereas 15 subjects showed abnormal PFT. Of these 15 subjects, 14 showed a pattern of restrictive lung disease whereas 1 showed obstructive lung disease.

Upon further comparison we found that all patients with CTP class A had a normal PFT. Out of 17 patients with CTP Class B, 4 patients had PFT suggestive of restrictive lung disease while the rest were normal. And out of 12 patients with CTP Class C, 10 patients had PFT findings suggestive of restrictive lung disease while 1 patient showed obstructive lung disease.

Patients with CTP class C had a higher occurrence of lung disease compared to class A and B and the difference was significant. Restrictive lung disease was more common than obstructive lung disease (*p value 0.001*).

Table III: Distribution of study population according to PFT and its correlation with CTP class A, B and C.

PFT findings	Child-Turcotte-Pugh class			Total
	A	B	C	
Normal	21	13	1	35
	100.0%	76.5%	8.3%	70.0%
Obstructive lung disease	0	0	1	1
	0.0%	0.0%	8.3%	2.0%
Restrictive lung disease	0	4	10	14
	0.0%	23.5%	83.3%	28.0%

*p value = 0.001**

The mean FEV1 (% of predicted) in subjects with CTP class C disease was $68.92 \pm 7.09\%$ whereas patients with CTP class A and B had FEV1 of $77.43 \pm 5.16\%$ and $70.88 \pm 7.08\%$ respectively. The mean FEV1 was lower in Child-Turcotte-Pugh class C compared to class A and B and the difference was found to be significant (*p = 0.001*).

The mean FVC (% of predicted) in subjects with CTP class C disease was $76.58 \pm 8.34\%$ whereas patients with CTP class A and B had FEV1 of $86.43 \pm 2.17\%$ and $83.47 \pm 5.11\%$ respectively. The Mean FVC was lower in Child-Turcotte-Pugh class C compared to class A and B and the difference was found to be significant (*p = 0.001*).

Table IV: Distribution of study population according to FEV1 and FVC and its correlation with CTP class A, B, and C.

	CTP class	Mean	Std. Deviation	F value	p value
FEV1 (% predicted)	A	77.43	5.16	8.551	0.001*
	B	70.88	7.08		
	C	68.92	7.09		
FVC (% predicted)	A	86.43	2.71	13.152	0.001*
	B	83.47	5.11		
	C	76.58	8.34		

The mean partial pressure of oxygen (PaO2) in subjects with CTP class C disease was 71.42 ± 6.53 mmHg whereas patients with CTP class A and B had PaO2 of 86.29 ± 4.16 mmHg and 81.88 ± 5.89 mmHg, respectively. The mean PaO2 was lower in Child-Turcotte-Pugh class C compared to class A and B and the difference was found to be significant (*p = 0.001*).

The mean arterial oxygen saturation (SaO2) in subjects with CTP class C disease was $86.17 \pm 3.66\%$ whereas patients with CTP class A and B had SaO2 of $95.86 \pm 2.22\%$ and $93.59 \pm 4.47\%$, respectively. The mean SaO2 was lower in Child-Turcotte-Pugh class C compared to class A and B and the difference was found to be significant (*p = 0.001*).

Table V: Distribution of study population according to partial pressure of arterial oxygen (PAO2) and arterial oxygen saturation (SAO2) and its correlation with Child-Pugh score A, B and C.

	CTP Class	Mean	Std. Deviation	F-value	p-value
PaO2 (mmHg)	A	86.29	4.16	29.133	0.001*
	B	81.88	5.89		
	C	71.42	6.53		
SaO2 (%)	A	95.86	2.22	30.488	0.001*
	B	93.59	4.47		
	C	86.17	3.66		

Out of the total 50 subjects who participated in the study 4 gave history of platypnoea of the 4 patients who had history of platypnoea 3 had CTP class C while 1 had CTP class B disease (Table VI).

Table VI: Distribution of study population according to platypnoea.

Platypnoea	Child-Turcotte-Pugh class			Total
	A	B	C	
No	21	16	9	46
	100.0%	94.1%	75.0%	92.0%
Yes	0	1	3	4
	0.0%	5.9%	25.0%	8.0%

*p value = 0.036**

On examination of X-ray, 10 patients out of 50 had findings suggestive of pleural effusion. Of these, 9 patients had CTP class C while 1 had CTP class B disease. None of the patients with CTP class A had evidence of pleural effusion on chest X-ray.

Table VII: Distribution of study population according to chest X-ray findings.

Chest X-ray	Child-Turcotte-Pugh class			Total
	A	B	C	
Normal	21	16	3	40
	100.0%	94.1%	25.0%	80.0%
Pleural effusions	0	1	9	10
	0.0%	5.9%	75.0%	20.0%

*p value = 0.001**

Discussion

In the absence of cardiac illness, arterial hypoxaemia frequently co-exists with liver cirrhosis⁵⁶. Additionally, up to 45 - 50% of individuals may experience changes in pulmonary function and decreased gas exchange¹². A significant vascular consequence of liver cirrhosis illness called hepatopulmonary syndrome (HPS) affects 5 - 32% of cirrhotic individuals¹⁶. There is disagreement over which parameters are more significant⁵⁸, despite the fact that proposed causes of hypoxaemia include a ventilation-perfusion imbalance, an intra- or extra-pulmonary shunt, and alveolar capillary diffusion restriction.

In our study, which was carried-out at the department of General Medicine and department of Respiratory Medicine at Sharda hospital, we evaluated a total of 50 subjects of liver cirrhosis and their PFT findings. Of the 50 total subjects 39 were male and 11 were female. Our study population was further divided into 3 categories based on the Child-Turcotte-Pugh score. We had 21 subjects who were in CTP

class A with 18 males and 3 females. 17 were in CTP class B, 13 males and 4 females. 12 subjects were in CTP class C, 8 males and 4 females. The distribution of subjects based on gender in CTP classes A, B, and C did not differ significantly (p value 0.438).

In our study population, the average age of subjects with CTP class A was 40.86 ± 7.8 years, class B was 52.94 ± 11.52 years and class C was 52.42 ± 15.74 years. CTP classes A, B, and C did not significantly differ in mean age in our study ($p = 0.052$). This was similar to other studies that were reviewed^{22,23}.

When we compared the pulmonary functions of our study population to the severity of liver disease we found that a total of 15 subjects showed abnormal pulmonary function. Of these 15, 14 showed a pattern of restrictive lung disease whereas 1 showed obstructive lung disease on the PFT. Restrictive lung disease was significantly more than obstructive lung disease. Patients with CTP class C had a higher occurrence of lung disease compared to class A and B and the difference was significant. Restrictive lung disease was more common than obstructive lung disease (p value 0.001). In a similar study conducted by Chaitra *et al*¹⁶ it was found that the most common abnormality in pulmonary function tests in patients with cirrhosis of liver was restriction (35%) and only 7% had obstructive changes. The severity of hypoxaemia also correlated positively with the severity of liver disease assessed by CTP score.

In another study by Awad *et al*¹⁵ it was found that the restrictive ventilatory function predominates. In this study, restricted ventilation affected 23 patients (46%) of all patients, obstructive ventilation affected 5 patients (10%), and combined obstructive and restrictive ventilation affected 16 patients (32%) of all patients.

The findings of the current study are also consistent with a study by Hourani *et al*¹¹ that looked at pulmonary dysfunction in advanced liver disease and found that 25% of patients had ventilatory limitation while only 3% had airflow obstruction. In 35% of patients, a restrictive ventilatory defect was present in addition to a diffusion anomaly. About 27% of individuals had an unusually low FEF (25 - 75%). The study also showed that numerous other causes, such as pleural effusion, ascites, or abnormalities of the interstitial lungs, were the cause of limitation in addition to the low incidence of significant abnormalities in maximal static respiratory pressure.

In the current study, FEV1 and FVC was significantly decreased among Child-Turcotte-Pugh score C compared to score A and B. The mean FEV1 in Child-Turcotte-Pugh class C was $68.92 \pm 7.09\%$ whereas patients with CTP class A and B had FEV1 of $77.43 \pm 5.16\%$ and $70.88 \pm 7.08\%$ respectively. When compared, the difference was found to

be significant among the three classes ($p = 0.001$).

The mean FVC in Child-Turcotte-Pugh class C was $76.58 \pm 8.34\%$ whereas patients with CTP class A and B had FEV1 of $86.43 \pm 2.17\%$ and $83.47 \pm 5.11\%$ respectively. The FVC was significantly reduced in patients with CTP class C when compared to CTP class A and B ($p = 0.001$). In a study conducted by Chaitra *et al*¹⁶, it was observed that FEV and FVC values in the Child-turcotte-pugh C group were found to be lower than those in the Child-pugh A and B group. With increasing degree of hepatic dysfunction, the severity of hypoxaemia also rose proportionately. In another study, Awad *et al*¹⁵ found that in group III (child C) patients forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were substantially lower than those in group II (I and II). Additionally, when group (I) and group (II) were examined, forced expiratory flow at 25% to 75% and forced vital capacity (FEF 25 - 75%) revealed a statistically significant difference (II and III).

In our study, we found that the mean partial pressure of oxygen (PaO₂) in subjects with CTP class C disease was 71.42 ± 6.53 mmHg whereas patients with CTP class A and B had PaO₂ of 86.29 ± 4.16 mmHg and 81.88 ± 5.89 mmHg, respectively. We also found that the mean arterial oxygen saturation (SaO₂) in subjects with CTP class C disease was $86.17 \pm 3.66\%$ whereas patients with CTP class A and B had SaO₂ of $95.86 \pm 2.22\%$ and $93.59 \pm 4.47\%$, respectively. The difference among the three classes for both PaO₂ and SaO₂ was significant. The findings of our investigation were in agreement with those of Medha *et al*²², who investigated arterial hypoxaemia in patients with liver cirrhosis and found that patients with chronic liver disease and cirrhosis had lower arterial oxygen tension and oxygen saturation. Awad *et al*¹⁵ also reported that the mean partial arterial carbon dioxide pressure (PaCO₂) in group III (Child C) was significantly lower when compared to group I (Child A) and group II (Child B). In the study conducted by Chaitra *et al*¹⁶, it was observed that there was progressive decrease in PaO₂ and SaO₂ values as the child-pugh score increased. Konstantinos *et al*⁸ discovered that decreased PaO₂ and SaO₂ levels were closely connected to advanced liver cirrhosis and higher grades of ascites.

In our study 4 patients gave a history of platypnoea. Out of the 4 patients 3 had CTP class C while 1 had CTP class B disease. Anand *et al*²⁸ in his study at Haryana reported significantly higher incidence of dyspnoea, platypnoea in patients with HPS.

In our study, on examination of X-ray, 10 patients out of 50 had findings suggestive of pleural effusion. Of these, 9 patients had CTP class C while 1 had CTP class B disease. None of the patients with CTP class A had evidence of pleural effusion on chest X-ray. This difference was

statistically significant. In the study conducted by Awad *et al*¹⁵, it was found that pleural effusion was the commonest clinical finding in examination of the respiratory system of 11 (18.3%) patients which was followed by consolidation in (3.4%) patients.

Conclusion

Our study concludes that derangements in pulmonary functions are seen in patients with cirrhosis of the liver. PFT findings of restrictive lung disease were more frequent than obstructive lung disease. Also severity of cirrhosis correlates directly with the incidence of lung disease. In our study, patients with CTP class C cirrhosis had significantly deranged pulmonary function when compared to patients with CTP class A and B.

We also found that patients with CTP class C cirrhosis had significantly lower PaO₂, SaO₂ values in ABG when compared to CTP class A and B. Also, patients with child-pugh class C had lower FEV1 and FVC values in pulmonary function tests. Significant decreases in PaO₂, SaO₂, FEV1 and FVC are associated with restrictive pulmonary function patterns in patients with severe liver cirrhosis and ascites. These Patients are more susceptible to infection and adult respiratory distress syndrome (ARDS) as a result of reduced pulmonary resistance. Accordingly, depending on combined hepatic and pulmonary disorders, the prognosis for those individuals is poor.

Based on the findings of our study we recommend that a patient with cirrhosis of the liver should also be evaluated for pulmonary function with pulmonary function tests and arterial blood gas analysis. This would help to quantify the compromise in the pulmonary function so that remedial measures may be taken which would help to prevent pulmonary complications in such patients.

Limitations: This study has a small sample size. It is a single-centre study. Being a hospital-based study, there is a bias factor in selection of subjects. Only symptomatic patients who presented to hospital were studied.

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MEDICAL COUNCIL OF INDIA (MCI)/NATIONAL MEDICAL COMMISSION (NMC) GUIDELINES FOR AUTHORS (AMENDED), 2020

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