Original Article

Pulmonary Dysfunction in Patients with Cirrhosis of the Liver: A Study of Pulmonary Function Tests and Arterial Blood Gases

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Abstract

Background and Aim: Respiratory complications in liver cirrhosis can occur due to various mechanisms, such as ascites causing restricted lung expansion and opening of intrapulmonary vascular shunts due to high portal pressures. We aimed to study the effects of the liver dysfunction on the lungs by evaluating arterial blood gas (ABG) and pulmonary function test (PFT) of all study subjects. **Subjects and Methods:** A cross-sectional study was done between August 2020 and September 2022. Diagnosed cases of the liver cirrhosis were enrolled in the study after informed consent and were subjected to the following investigations: chest X-ray, oximetry, spirometry, diffusing capacity of the lung for carbon monoxide (DLCO), two-dimensional echocardiography, and ABG analysis (ABGA). The cases were divided into three groups based on their Child–Pugh staging, and statistical analysis was done on the collected data. **Results:** A total of 64 (53 males and 11 females) patients with an average age of 49.82 ± 9.89 years were studied. Alcoholism was the most common cause of cirrhosis in males. Breathlessness (65.6%) and pleural effusion (26.6%) were the most common respiratory symptoms and signs, respectively. Seventeen patients had hepatic hydrothorax, eight patients had hepatopulmonary syndrome (HPS), and six patients had portopulmonary hypertension. Low pH (17.2%) and oxygen partial pressure (PaO_2) (20.3%) were the most common ABGA findings. The pH, PaO_2, forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC), and DLCO were significantly low in Child Pugh Stage C ($P < 0.05$). The pH, pO_2, HCO_3, FEV_1, FVC, FEV_1/FVC, and DLCO were significantly lower in patients with HPS ($P < 0.05$). **Conclusion:** Metabolic acidosis and low FEV_1/FVC and DLCO were the common findings in study subjects. Pulmonary dysfunction was common in advanced liver cirrhosis. Patients with HPS had worse ABG and PFT parameters than those without HPS.

Keywords: *Acidosis, hepatopulmonary syndrome, hypoxia, liver cirrhosis*

Introduction

Pulmonary dysfunction can occur in cirrhosis of the liver either due to intrinsic cardiopulmonary disorders which are not liver-specific or due to unique problems occurring in the presence of the liver cell failure and portal hypertension.[1]

Hepatopulmonary syndrome (HPS), portopulmonary hypertension (POPH), and hepatic hydrothorax (HH) are some of the pulmonary disorders unique to chronic liver diseases. POPH is characterized by an elevated mean pulmonary artery pressure (mPAP) secondary to an increased pulmonary vascular resistance (PVR).[2] HPS is a triad of the liver disease, arterial deoxygenation, and pulmonary vascular dilatation.[3,4] Reduction in residual volume, total lung capacity, and diffusion capacity (DLCO) are noted during pulmonary function testing in advanced cirrhosis. Portal hypertension causes intrapulmonary shunting and opening of new arteriovenous shunts in the portopulmonary circulation, which can cause impairment of gas exchange even in the absence of ascites.[5] With the progression of cirrhosis, metabolic functions of the body, including acid-base homoeostasis, are compromised. Respiratory alkalosis with or without metabolic acidosis is the most common disorder in liver cirrhosis.[6]

The current study was carried out on patients with liver cirrhosis with an aim to estimate the effects of the liver dysfunction on the lungs by evaluating arterial blood gas (ABG) and pulmonary function test (PFT) of all study subjects.

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Subjects and Methods

A cross-sectional observational study was conducted at a tertiary care hospital in India between August 2020 and September 2022. A total 64 patients with cirrhosis of the liver were included in the study after the institutional ethics committee approval. Patients above 18 years of age and of either gender with confirmed diagnosis of cirrhosis of the liver by (a) ultrasound (USG) or computed tomography (CT) of the abdomen (showing shrunken, nodular liver with coarse echotexture), (b) with evidence of the liver disease of more than 6 months duration, and (c) evidence of portal hypertension on USG or upper gastrointestinal endoscopy were included in the study after they signed written informed consent.

Pregnant women, cases with bronchial asthma, chronic obstructive pulmonary disease (diagnosed as per the American Thoracic Society criteria),[7] human immunodeficiency virus infection, chronic kidney diseases, primary pulmonary disorders (interstitial or parenchymal), ischemic heart disease, or any other structural heart diseases were excluded from the study as these conditions may cause changes in the PFT parameter values or patients may be unable to perform PFTs.

Detailed history, general and respiratory examination, and routine laboratory investigations such as complete blood count, liver function tests, chest X-ray, two-dimensional (2D) echocardiography, and high-resolution chest tomogram (HRCT) were carried out for all the participants. In addition, the following investigations were carried out on all the study subjects:

- Pulse oximetry: Measurement of O_2 saturation (SaO_2) was performed on all patients on room air, in supine and sitting positions, with a portable pulse oximeter (Dr. Trust, Omron, Philips)
- PFTs (spirometry) were carried out using a spiroanalyzer (Spiro-pro). The best of three consecutive spirometry recordings were used. The measurements included assessments of (a) forced vital capacity in liters (FVC), (b) forced expiratory volume in 1 s in liters (FEV_1), (c) FEV_1/FVC ratio (%), and (d) FEV 25%–75% (forced expiratory flow, 25%–75%)
- Diffusing capacity of the lung for carbon monoxide (DLCO) was measured with ERT Spiro sphere. The method was as follows: the patient took a full inspiration of a gas mixture containing 0.3% carbon monoxide and 10% helium. After a 10-s breath-hold, the patient was asked to exhale. The first portion of the exhaled breath was discarded, and the next liter was collected and analyzed. The difference between the original and final concentrations of carbon monoxide was measured
- ABG analysis (ABGA) was carried out on room air and in supine position. A sample was taken from the radial or femoral artery and analyzed using blood gas analyzer (ABL90 FLEX). The following values were measured: (a) pH, (b) arterial oxygen partial pressure in mmHg (PaO_2), (c) arterial carbon dioxide partial pressure in mmHg, and (d) HCO_3^- (bicarbonate level in mEq/L). Hypoxia was defined as pO_2 of <80 mmHg on ABGA.

The cases were divided into three categories as per the Child–Turcotte–Pugh (CTP) staging into CTP Stage A (score 5–6), CTP Stage B (score 7–9), and CTP Stage C (score ≥10).[8] The CTP score was calculated with the following parameters: serum bilirubin, serum albumin, prothrombin time, ascites, and hepatic encephalopathy. POPH was diagnosed when patients of cirrhosis were found to have pulmonary hypertension with a right ventricular systolic pressure of more than 25 mmHg on 2D transthoracic echocardiography. HPS was diagnosed when there was the presence of both orthodeoxia on oximetry and intrapulmonary vascular dilatations (IPVDs) on CT pulmonary angiogram (CTPA) in a patient who became breathless in sitting position.

The data were analyzed using SPSS version 21 (IBM, Armonk, New York, USA) statistical software. All the continuous variables were expressed as mean ± standard deviation. One-way analysis of variance (ANOVA) test was applied to compare the means of more than two groups. All the tests were two tailed with a confidence interval of 95%. The tests were considered statistically significant if the $P < 0.05$.

Results

Out of 64 patients studied, 53 (82.8%) were male and 11 (17.2%) were female. The male-to-female ratio was 4.8:1. The mean age of the patients was 49.82 ± 9.89 years. Alcoholic liver disease was the most common cause of cirrhosis in male subjects (32/53 males), whereas autoimmune hepatitis was the most common cause of cirrhosis in females (6/11 females). A total of 24 patients were in Child–Pugh Stage A (37.5%), 28 patients were in Child–Pugh Stage B (43.8%), and 12 patients were in Child–Pugh Stage C (18.8%). Among the alcoholics, 43.8% of patients were in Child–Pugh Stage C. Jaundice (93.8%) and abdominal distention (85.9%) were the most common symptoms. Breathlessness was found in 42 (65.6%) cases. Hepatic encephalopathy was present in 12 patients. The remaining 52 patients had no evidence of hepatic encephalopathy.

Table 1 shows the clinical and radiological parameters of the cases. The average pulse and respiratory rate of the patients were different across the CTP stages with CTP Stage C having significantly higher pulse rate and respiratory rate than Stages A and B. The mean oxygen saturation on oximetry was 95.67 ± 2.15% in supine position and 94.60% ± 3.14% in sitting position. The oxygen saturation by pulse oximetry was significantly different across the Child Stages A to C ($P < 0.05$). Thus, patients in Child

Table 1: Clinical and radiological parameters

Parameters	Total (*n*=64)	CTP Stage A (*n*=24)	CTP Stage B (*n*=28)	CTP Stage C (*n*=12)	*P* (ANOVA test)
Vital parameters					
Pulse/min	90.69±23.24	69.75±7.74	100.28±22.38	110.17±11.58	<0.0001
Respiratory rate/min	21.94±4.67	19.92±3.03	21.42±4.80	27.16±3.86	<0.0001
Saturation O_2	95.67±2.15	96.75±2.15	95.36±11.79	94.25±15.49	< 0.05
RS examination					
Normal	38	22	14	2	
Abnormal	26	2	14	10	
Chest X-ray PA					
Normal	46	24	19	3	
Abnormal					
Consolidation	2	0	0	2	
Pleural effusion	17	0	9	8	
HRCT with CTPA					
Normal	9	4	3	2	
Abnormal					
Consolidation/pleural effusion	14	0	9	5	
IPVD present	4				
Not done/not indicated	39	0	1	3	

IPVD: Intrapulmonary vascular dilatations, HRCT: High-resolution chest tomogram, CTPA: Computed tomography pulmonary angiogram, CTP: Child–Turcotte–Pugh, PA: Pulmonary artery, RS: Respiratory system

Stage C had statistically significantly higher pulse rate, higher respiratory rate, and lower oxygen saturation on admission when compared to patients in Child Stage A of the liver cirrhosis. Respiratory system examination was normal in 38 (59.4%) patients. Chest X-ray was normal in 72% of cases. Transudative pleural effusion was the most common finding (26.6%) clinically (on chest X-ray) and microscopically. Average hemoglobin (10.44 ± 1.10 g/dL), total bilirubin (3.95 ± 1.82 mg/dL), aspartate transaminase (105.45 ± 62.92 U/L), alanine transaminase (114.58 ± 64.96 U/L), serum albumin (3.55 ± 0.66 mg/dL), and serum creatinine (1.25 ± 0.58 mg/dL) were significantly different across the CTP Stages A to C ($P < 0.05$ for each parameter). Six (9.4%) patients were diagnosed to have POPH with 50% of them being in CTP stage C of cirrhosis. HRCT thorax with CTPA was done in 25 out of 64 patients. IPVD was found in eight patients, all of whom had orthodeoxia on pulse oximetry and thus were diagnosed to have HPS. Seven out of eight patients with HPS were in CTP Stage C (87.5%). HPS had a significant association with Child–Pugh Stage C (Chi-square $P = 0.001$). Patients in Child–Pugh Stage C, thus, had statistically significantly higher serum creatinine, lower serum albumin, and higher chances of having HPS.

Table 2 shows ABGA and PFT findings in the study subjects as per their CTP stages. ABG of the study subjects showed low pH in 11 patients (pH <7.35 [17.2%]) and hypoxemia in 13 patients (PaO_2<80 mmHg [20.3%]). Low pH and hypoxemia were statistically significantly correlated with worsening CTP scores (ANOVA test $P < 0.05$), with CTP Stage C having the lowest pH and PaO_2. There was also a statistically significant difference in FEV1/FVC, % predicted FEV_1/FVC, DLCO, and % predicted DLCO from CTP Stage A to Stage C (ANOVA test $P < 0.05$).

To study the impact of the presence of HPS on ABG and PFT, patients were categorized into those with HPS ($n = 8$) and those without HPS ($n = 56$). Average pH in the patients with HPS was 7.31 ± 0.04, mean pO_2 was 75.62 ± 6.0 mmHg, and serum bicarbonate was 17.51 ± 3.68 mEq/L. pH, pO_2, and HCO_3 were significantly lower in patients with HPS than in the patients without HPS ($P < 0.05$). The mean FVC (2.44 ± 0.02 L), FEV_1 (1.69 ± 0.04 L), FEV_1/FVC (69.21 ± 0.96), and DLCO (16.69 ± 0.89 ml/min/mmHg) in patients with HPS were significantly altered as compared to the subjects without HPS (ANOVA test $P < 0.05$). However, FEV 25%–75% (2.53 ± 0.08 L/s) was comparable in the patients with and without HPS ($P > 0.05$).

Thus, a majority of the ABG parameters were affected in advanced liver cirrhosis patients (CTP Stage C) due to the presence of IPVDs and severe portal hypertension. A majority of them were hypoxemic and had metabolic acidosis.

Discussion

Liver is the main organ involved in various metabolic, excretory, synthetic, and secretory functions of the body. Chronic liver diseases such as cirrhosis affect these functions, leading to portal hypertension and causing complications such as hepatic encephalopathy, variceal bleeding, hypersplenism, and spontaneous bacterial peritonitis. Hypoxemia and respiratory symptoms such as

Table 2: Arterial blood gas and pulmonary function test parameters as per Child–Turcotte–Pugh stages

Parameters	Mean±SD	CTP Stage A	CTP Stage B	CTP Stage C	*P* (ANOVA test)
pH	7.39±0.05	7.41±0.01	7.41±0.04	7.32±0.04	0.001
$PaCO_2$ mmHg	40.47±6.50	40.21±4.11	40.07±8.16	41.92±6.33	0.69
PaO_2 mmHg	90.81±9.48	95.75±5.22	92.07±8.53	78.00±6.54	0.001
HCO_3 (mEq/L)	22.11±3.44	22.35±1.62	23.4±3.58	21.24±4.74	0.15
FVC (L), mean±SD	2.68±0.15	2.77±0.08	2.70±0.18	2.69±0.09	0.11
Percentage predicted FVC	84.8±8.36	84.63±8.41	84.4±8.32	83.41±8.5	0.12
FEV_1 (L), mean±SD	1.98±0.19	2.11±0.08	2.04±0.15	2.04±0.09	0.07
Percentage predicted FEV_1	91.17±7.38	91.95±7.43	91.5±7.4	90.83±8.18	0.11
FEV25%–75% (L/s) (mean±SD)	3.83±0.37	3.96±0.41	3.75±0.31	3.82±0.49	0.15
Percentage predicted FEV25–75	91.6±4.9	91.2±4.88	92.0±4.98	91.9±5.19	0.21
FEV_1/FVC (mean±SD)	73.94±3.56	76.17±2.56	73.90±3.09	69.58±1.90	0.001
% Predicted FEV_1/FVC	79±6.50	83.83±6.53	81.1±6.52	70.41±6.36	0.00001
DLCO (mL/min/mmHg), mean±SD	23.90±4.95	26.00±3.68	24.88±4.29	17.38±2.95	0.001
Percentage predicted DLCO	84.73±21.67	92.04±21.8	89.03±21.70	60.08±21.9	0.0001

CTP: Child–Turcotte–Pugh, DLCO: Diffusion lung capacity for carbon monoxide, SD: Standard deviation, FVC: Forced vital capacity, FEV_1: Forced expiratory volume in 1 s, PaO_2: Oxygen partial pressure, $PaCO_2$: Carbon dioxide partial pressure, HCO_3: Bicarbonate level

breathlessness and cough are often associated with chronic liver diseases.

Male-to-female ratio in the current study was 4.8:1. Few other studies showed similar findings.[9,10] However, in the study by Awad *et al*., there were more female subjects (68%) than males (32%).[11] Alcohol addiction is more prevalent among males (23%–74%) as compared to the females (24%–48%) in India and this may be the reason for the skewed gender distribution in the current study.[12]

Alcoholic liver disease was the most common cause of cirrhosis (50%), followed by hepatitis B infection (15.6%). In a few similar studies carried out outside India, hepatitis B was the most common cause of cirrhosis.[9,10] However, some Indian studies corroborated the finding of alcoholism being the most common cause of cirrhosis in India.[13,14] Interestingly, in a recent study carried out in India on 64 subjects with cirrhosis, nonalcoholic fatty liver disease (43.8%) was the most common cause of cirrhosis, followed by alcoholism (26.6%).[15] This may reflect the changing etiological pattern of cirrhosis of the liver with changes in Indian lifestyle.

Dyspnea (65.6%) was present in nearly two-thirds of the patients on admission. Many similar studies found that dyspnea was a common presenting symptom in cirrhosis patients.[11,16,17] Dyspnea in cirrhosis can occur due to mechanical causes such as basal atelectasis due to IPVD predominantly affecting the lung bases,[18] massive ascites pushing the diaphragm,[19] and HH.[20]

The prevalence of HH (26.6%) in the current study was higher than the average prevalence of 5%–11%.[20] HH is a transudative pleural effusion in a patient with portal hypertension without underlying cardiorespiratory pathology.[20] Pleuroperitoneal communications, negative intrathoracic pressures, and thinning of diaphragm due to malnutrition seen in chronic liver diseases are the causes for HH.[21] Spontaneous bacterial empyema can complicate HH and carries a mortality rate of around 20%.[22] The management of HH includes thoracocentesis, transjugular intrahepatic portosystemic shunt, and video-assisted thoracoscopy for closure of diaphragmatic defects, but recurrence is common in decompensated liver disease. The management strategies aim to reduce the ascitic fluid production and prevention of its transfer to the pleural space, removal of fluid from the pleural space, and obliteration of the pleural space to prevent recurrence and liver transplantation.[23]

Two large studies in the US carried out on patients with cirrhosis awaiting liver transplantation found that the prevalence of POPH was 5.3%–8.5%.[24,25] The prevalence in the current study was again higher than this (9.4%). An Indian study reported a very high prevalence of POPH (35.71%).[26] In our study, the worsening Child scores did not significantly alter the prevalence of POPH, which was in line with the findings of similar studies.[26-30] High mPAP and PVR during right heart catheterization were diagnostic of POPH.[22] 2D echocardiography finding of high right ventricular systolic pressure (>25 mmHg) is also a fairly good indicator of POPH. In the current study, 2D echocardiography criterion was used for the diagnosis of POPH.

The prevalence of HPS in the current study was 12.5%. The global prevalence of HPS in cirrhosis was approximately 4%–19%.[3] An Austrian and an Indian study showed a very high prevalence of HPS in cirrhosis (27.5% and 40.6%, respectively).[3,15] The presence of HPS was significantly more common in patients with poorer CTP score, which was a finding similar to our study.

In the present study, FEV_1/FVC and DLCO (including % predicted FEV_1/FVC and % predicted DLCO) were significantly different across the Child–Pugh stages with

lowest values recorded in Child Stage C. Thus, there was a mixed obstructive and restrictive airflow limitation in patients with advanced CLD. POPH, HH, and HPS could have contributed to this spirometry abnormality. Alkhayat *et al*., in their study, found that both FEV_1, FVC, and FEV_1/FVC values were significantly less in the Child–Pugh Stage C.[16] However, Yigit *et al*. did not find any statistically significant difference in FEV_1/FVC among the three CTP stages.[10] The findings of association of low DLCO with worsening Child scores were found in a study by Park *et al*.[9] However, another study did not find any correlation between the DLCO and Child stages.[31]

In health, the liver contributes to a state of stable acid-base state by albumin synthesis and clearing of lactic acid from the circulation.[32] Usually, respiratory alkalosis is found in patients with stable cirrhosis. However, the pattern of acid-base abnormalities differs in compensated versus decompensated liver diseases. Most of the critically ill cirrhosis patients have demonstrated severe hypoxemia with metabolic acidosis due to hypoalbuminemia, elevated lactate, and unmeasured anions alongside complications such as acute GI bleed and hepatic encephalopathy. Hypoxemia on ABGA was present in 20.3% of cases. In few similar European studies, nearly one-third of the patients with cirrhosis had hypoxemia.[10,11,33] In the study by Helmy and Awadallah, the prevalence of arterial hypoxemia was 14.6%.[17] The current study observed that both the PaO_2 and the pH were statistically significantly lower with worsening CTP scores. This observation was similar to the observation by Helmy and Awadallah.[17]

The study relied upon ABGA, 2D-echocardiography, and HRCT with CTPA for the diagnosis of HPS and did not include some other useful diagnostic tests such as transthoracic contrast echocardiography and right heart catheterization. The sample size was relatively small. Generalizing the outcomes to a larger population may require such a study with a larger sample size. Selection bias, not taking into account the impact of age, medications, and addiction on the pulmonary functions of the study subjects and lack of follow-up were some other limitations of the study.

Conclusion

Thus, pulmonary complications in chronic liver diseases were common, with dyspnea being the presenting symptom and pleural effusion being the common respiratory finding. Patients in Child–Pugh Stage C had more respiratory symptoms than other patients. The presence of HPS significantly altered both the ABG and PFTs. Mixed obstructive and restrictive pulmonary disorders, hypoxia, and metabolic acidosis were found in the patients with advanced CLD.

Physicians should be aware of the possible mechanisms, by which the respiratory system can be affected by chronic liver diseases. A high degree of suspicion and timely investigations for the impending respiratory complications in patients with cirrhosis may offer a survival advantage to these patients.

Ethical statement

The study was approved by the institutional Ethics Committee of Dr. D. Y. Patil Medical college, Hospital and Research centre, Dr. D. Y. Patil Vidyapeeth, Pune (Deemed to be University) Research Protocol No. IESC/PGS/2018/137.

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Conflicts of interest

There are no conflicts of interest.

References

1. Postic C, Dentin R, Girard J. Role of the liver in the control of carbohydrate and lipid homeostasis. Diabetes Metab 2004;30:398-408.
2. Porres-Aguilar M, Altamirano JT, Torre-Delgadillo A, Charlton MR, Duarte-Rojo A. Portopulmonary hypertension and hepatopulmonary syndrome: A clinician-oriented overview. Eur Respir Rev 2012;21:223-33.
3. Schenk P, Fuhrmann V, Madl C, Funk G, Lehr S, Kandel O, *et al.* Hepatopulmonary syndrome: Prevalence and predictive value of various cut offs for arterial oxygenation and their clinical consequences. Gut 2002;51:853-9.
4. Grilo-Bensusan I, Pascasio-Acevedo JM. Hepatopulmonary syndrome: What we know and what we would like to know. World J Gastroenterol 2016;22:5728-41.
5. Soulaidopoulos S, Goulis I, Cholongitas E. Pulmonary manifestations of chronic liver disease: A comprehensive review. Ann Gastroenterol 2020;33:237-49.
6. Ahya SN, José Soler M, Levitsky J, Batlle D. Acid-base and potassium disorders in liver disease. Semin Nephrol 2006;26:466-70.
7. Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, *et al.* Diagnosis and management of stable chronic obstructive pulmonary disease: A clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med 2011;155:179-91.
8. Child CG, Turcotte JG. Surgery and portal hypertension. Major Probl Clin Surg 1964;1:1-85.
9. Park MS, Lee MH, Park YS, Kim SH, Kwak MJ, Kang JS. Abnormal gas diffusing capacity and portosystemic shunt in patients with chronic liver disease. Gastroenterology Res 2012;5:182-9.
10. Yigit IP, Hacievliyagil SS, Seckin Y, Oner RI, Karincaoglu M. The relationship between severity of liver cirrhosis and pulmonary function tests. Dig Dis Sci 2008;53:1951-6.
11. Awad NF, Elbalsha AA, Abo Amer MZ, Ibrahim MH. Study of the relationship between severity of liver cirrhosis and pulmonary function tests. Egypt J Hosp Med 2019;76:4570-6.
12. Alcohol Use Disorder. Alcohol Use Disorder | National Health Portal of India; 2020. Available from: https://www.nhp.gov.in/healthlyliving/alcohol-use-disorder. [Last accessed on 2023 Apr 13].
13. Kaur D, Chhina RS, Goyal O, Goyal P. Etiological profile of cirrhosis in a tertiary care institute in Northern India. J Gastrointest Infect 2018;8:28-31.

14. Mukherjee PS, Vishnubhatla S, Amarapurkar DN, Das K, Sood A, Chawla YK, *et al.* Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. PLoS One 2017;12:e0187033.
15. Khiangte B, Kothakota SR, Sasidharan M, Kareem H, Joshi S, Kumar VV, *et al.* Prevalence and determinants of hepatopulmonary syndrome in decompensated chronic liver disease. Indian J Gastroenterol 2020;39:362-9.
16. Alkhayat K, Moustafa G, Zaghloul A, Elazeem AA. Pulmonary dysfunction inpatients with liver cirrhosis. Arch Med 2017;9:4.
17. Helmy AM, Awadallah MF. Study of pulmonary dysfunctions in liver cirrhosis. Egypt J Chest Dis Tuberc 2014;63:1079-85.
18. Benz F, Mohr R, Tacke F, Roderburg C. Pulmonary complications in patients with liver cirrhosis. J Transl Int Med 2020;8:150-8.
19. Kaltsakas G, Antoniou E, Palamidas AF, Gennimata SA, Paraskeva P, Smyrnis A, *et al.* Dyspnea and respiratory muscle strength in end-stage liver disease. World J Hepatol 2013;5:56-63.
20. Chaaban T, Kanj N, Bou Akl I. Hepatic hydrothorax: An updated review on a challenging disease. Lung 2019;197:399-405.
21. Surani SR, Mendez Y, Anjum H, Varon J. Pulmonary complications of hepatic diseases. World J Gastroenterol 2016;22:6008-15.
22. Machicao VI, Balakrishnan M, Fallon MB. Pulmonary complications in chronic liver disease. Hepatology 2014;59:1627-37.
23. Banini BA, Alwatari Y, Stovall M, Ogden N, Gershman E, Shah RD, *et al.* Multidisciplinary management of hepatic hydrothorax in 2020: An evidence-based review and guidance. Hepatology 2020;72:1851-63.
24. Krowka MJ, Swanson KL, Frantz RP, McGoon MD, Wiesner RH. Portopulmonary hypertension: Results from a 10-year screening algorithm. Hepatology 2006;44:1502-10.
25. Ramsay MA, Simpson BR, Nguyen AT, Ramsay KJ, East C, Klintmalm GB. Severe pulmonary hypertension in liver transplant candidates. Liver Transpl Surg 1997;3:494-500.
26. Balde J, Rao NK, Ballala K, Samanth J, Shetty KR, Patil N, *et al.* Echocardiographic abnormalities in cirrhosis and their correlation with severity of cirrhosis using child-pugh score among patients in a tertiary care hospital. Indian J Med Res 2016;144:935-7.
27. Abd-El-Aziz TA, Abdou M, Fathy A, Wafaie M. Evaluation of cardiac function in patients with liver cirrhosis. Intern Med 2010;49:2547-52.
28. Castro M, Krowka MJ, Schroeder DR, Beck KC, Plevak DJ, Rettke SR, *et al.* Frequency and clinical implications of increased pulmonary artery pressures in liver transplant patients. Mayo Clin Proc 1996;71:543-51.
29. Ghayumi SM, Mehrabi S, Zamirian M, Haseli J, Bagheri Lankarani K. Pulmonary complications in cirrhotic candidates for liver transplantation. Hepat Mon 2010;10:105-9.
30. Kawut SM, Krowka MJ, Trotter JF, Roberts KE, Benza RL, Badesch DB, *et al.* Clinical risk factors for portopulmonary hypertension. Hepatology 2008;48:196-203.
31. Møller S, Krag A, Madsen JL, Henriksen JH, Bendtsen F. Pulmonary dysfunction and hepatopulmonary syndrome in cirrhosis and portal hypertension. Liver Int 2009;29:1528-37.
32. Scheiner B, Lindner G, Reiberger T, Schneeweiss B, Trauner M, Zauner C, *et al.* Acid-base disorders in liver disease. J Hepatol 2017;67:1062-73.
33. Charalabopoulos K, Peschos D, Zoganas L, Bablekos G, Golias C, Charalabopoulos A, *et al.* Alterations in arterial blood parameters in patients with liver cirrhosis and ascites. Int J Med Sci 2007;4:94-7.