### A STUDY OF LUNGS PROFILE IN CIRRHOSIS OF LIVER

**Medicine**

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### ABSTRACT

**Introduction:** The preclinical phase of liver cirrhosis is usually prolonged over several years; once clinical events occur, such as, ascites, encephalopathy, variceal bleeding or the development of hepatocellular carcinoma the remaining course of the disease is much shorter and usually fatal. For liver cirrhosis there still no curable treatment available except for liver transplantation.

**Methods & Materials:** Total of 100 cases of liver cirrhosis were assessed between June 2013 and November 2015 with their consent. Detailed history, thorough clinical examination and relevant investigations were done and analyzed.

**Result:** It was observed that 25 percent patient of liver cirrhosis associated with hepatopulmonary syndrome (HPS). Conclusion: Early identification of pulmonary complications in cirrhotic patients is crucial as it affects the prognosis and guides the future management in liver cirrhosis.

### KEYWORDS

Cirrhosis, Hepatopulmonary syndrome, Portopulmonary hypertension

In ancient Chinese medicine, the Liver—not the Heart—was considered "the Center" of the body. The word Cirrhosis comes from the Greek word Kirrhos, which means Orange yellow. Laennec gave cirrhosis its name kirrhos in 1819 in a brief footnote to his treatise De l'auscultation mediate.

The definition of Cirrhosis remains morphological, described by a working party for the World Health Organization (WHO) in 1978 as: "a diffuse Process characterized by fibrosis and the conversion of normal liver architectures into structurally abnormal Nodules".

Cirrhosis is a chronic disease of the liver in which diffuse destruction and Regeneration of hepatic parenchymal cells has occurred, in which diffuse increase in connective tissue has resulted in disorganization of the lobular architecture. The triad of parenchymal necrosis, regeneration and scarring is always present regardless of individual clinical manifestations.

In the evolution of many chronic liver diseases cirrhosis is a stage that is considered to be irreversible. Cirrhosis can be stabilized by controlling the primary disease but its presence implies consequences such as portal hypertension, intrahepatic shunting of blood, impaired parenchymal function affecting protein synthesis, hormone metabolism and excretion of bile and bile salts. The most common complications are: gastrointestinal haemorrhage, ascites, encephalopathy, bacterial infections, renal failure, hepatocellular carcinoma and hepatic failure.

Certain reversible components of cirrhosis have been indicated where significant histological improvement have occurred with regression of cirrhosis but complete resolution with a return to normal architecture seems unlikely.

The underlying immunological response has usually been acting fora months or years where inflammation and tissue repairing are in progress simultaneously which leads in the end to fibrosis and cirrhosis.

The main causes of cirrhosis are: alcoholic liver disease (ALD), hepatitis B(HBV), hepatitis C (HCV), non-alcoholic steatohepatitis (NASH) haemochromatosis, auto-immune hepatitis (AIH), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). The natural history of cirrhosis can be divided into a preclinical and a subsequent clinical phase.

The preclinical phase is usually prolonged over several years; once clinical events occur, such as, ascites, encephalopathy, variceal bleeding or the development of hepatocellular carcinoma the remaining course of the disease is much shorter and usually fatal. For liver cirrhosis there still no curable treatment available except for liver transplantation.

**Epidemiology:**

In developing countries viral hepatitis is the leading cause of cirrhosis and in the developed countries ALD, HCV and NASH are the most significant causes of cirrhosis.

In many developed countries the death rates from liver cirrhosis have been declining in the recent years with some exceptions. World-wide death rates from alcohol related liver cirrhosis has been decreasing but an increase has been observed in a few Eastern European countries and England.

In the United States (USA) there has been an increase in the proportion of patients with HCV compared to ALD in the recent years. Studies on patients characteristics at diagnosis show that the mean age is around 60 years and majority of the patients are males with the male/female ratio ranging from 1.3:1. The highest mortality from liver cirrhosis is in the age group 60-70 years.

**Aims & Objectives:**

1) Assessment of Incidence of Pulmonary involvement in patient with Cirrhosis of liver.
2) To Study Clinical profile of Pulmonary involvement in patient with Cirrhosis of liver.
3) To Correlate Pulmonary involvement with Hepatic Functional status with Child Pugh's classification.
METHODS & MATERIALS:

The present study was carried out in the Department of Medicine on 100 patients with liver cirrhosis after written consent. It was carried out during the period between June 2013 and November 2015 at the MGM’s Medical college and Hospital Aurangabad. The study protocol was approved by the Medical Ethics Committee For research on Human Subjects of the MGM University.

The diagnosis of Liver Cirrhosis was made on the basis of clinical examination, Laboratory investigations, Liver Biopsy and abdominal ultrasound examination. The severity of liver cirrhosis was assessed according to the Child-Pugh classification.

Study Design:

Type of Study – Cross Sectional Observational Study.

Number of cases for study – 100

Inclusion Criteria – All cases of cirrhosis of liver as per Child Pugh's classification.

Exclusion criteria– Bronchial asthma, COPD,ILD, significant pulmonary long standing disorders.

All patients were subjected to the following:

Complete Clinical examination including history taking (including Personal history) and clinical examination with special emphasis on Abdominal, and Chest examinations.

Laboratory investigations including:

Complete blood count, ESR, fasting blood sugar, Liver functions tests (Bilirubin total and direct, prothrombin time, serum albumin), INR (International Normalized ratio), Arterial Blood Gas analysis, kidney function tests, anti HCV antibody, HBsAg profile.

Radiological investigations including:

Plain Chest X-ray: Postero-anterior chest radiographs were obtained and interpreted by the radiologist. The radiographs were examined for the presence or absence of pleural effusion and its amount, assessment of peripheral pulmonary vascular dilatation at the base of the right lung (we define the peripheral vessels as the vessels located 2 cm from the pleural surface) we measure the diameter of the peripheral pulmonary arterioles and calculate the arteriole/bronchiole (A/B) ratio.

Abdominal Ultrasonography: Using convex probe 5 MHz of a GE logic 9 machine. We assessed liver morphology, portal vein diameter, splenomegaly and ascites.

CT chest(using GE MDCT 64 slice machine):

Westressed upon findings suggestive of interstitial lung disease (ground glassing, reticulation, nodulation, honey combing and fibrosis), presence/absence of pleural effusion and its amount; assessment of peripheral pulmonary vascular dilatation at the base of the right lung (we define the peripheral vessels as the vessels located 2 cm from the pleural surface) we measure the diameter of the peripheral pulmonary arterioles and calculate the arteriole/bronchiole (A/B) ratio which is the ratio between the diameter of the peripheral arteriole and its adjoining bronchiole, and other CT findings were also documented.

Measurement of O2 saturation (SaO2) withportable pulse oximetry: In all patients, the measurements were performed at room O2 partial pressure in the supine position using a pulse oximeter.

Pulmonary function tests (spirometry): During exacerbation and stable condition before and after bronchodilatation using a Spiro analyzer ST-95, serial number 67011870, Fukuda Sangyo 2013 were performed. The best of three consecutive spirometric recordings were performed. The best of three consecutive spirometric recordings were obtained. The best of three consecutive spirometry recordings were performed. The best of three consecutive spirometry recordings were performed. The best of three consecutive spirometry recordings were performed. The best of three consecutive spirometry recordings were performed.

Arterial blood gas analysis on room air: blood samples were obtained by puncture of radial artery and analyzed using blood gas analyzer.

Contrast 2-D Echo heart (Echocardiography): Using available equipment (GE VIVID 7) with 2.5 MHz transducer using standard views by using agitated saline which creates a stream of microbubbles after intravenous injection.

Under normal circumstances, these microbubbles, 60–90 lm in diameter opacify only the right heart chambers because they are filtered in the pulmonary capillary bed and do not appear in the left side of the heart. In case of the presence of intrapulmonary vascular dilatation, the microbubbles appear in the left-heart chambers 4–6 heart beats after their initial visualization in the right side of the heart. Heptopulmonary syndrome was diagnosed after detection of intrapulmonary vascular dilatation (IPVD) by contrast enhanced echocardiography in cirrhotic patients with arterial hypoxemia.

Portopulmonary hypertension was diagnosed when the mean pulmonary artery pressure measured by Doppler echocardiography is >25 mmHg at rest and >30 mmHg during exercise in the presence of a pulmonary arterial occlusion pressure; or a left-ventricular end diastolic pressure of less than 15 mmHg in patients with coexisting portal hypertension.

Statistical analysis of data

The collected data were organized, tabulated and statistically analyzed using the SPSS software computer package and results were obtained and interpreted by statistician.

RESULTS:

Table 1: Clinical Examination in patients:

<table>
<thead>
<tr>
<th>Clinical Examination</th>
<th>No. of patients [n=100]</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Dyspnoea</td>
<td>Present</td>
<td>68</td>
</tr>
<tr>
<td>Cynosis</td>
<td>Present</td>
<td>16</td>
</tr>
<tr>
<td>Clubbing</td>
<td>Present</td>
<td>49</td>
</tr>
<tr>
<td>Spider Naevi</td>
<td>Present</td>
<td>30</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>Present</td>
<td>54</td>
</tr>
<tr>
<td>Ascites</td>
<td>Present</td>
<td>62</td>
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Table 2: Distribution Patients according to Child Pugh Grading:

<table>
<thead>
<tr>
<th>Grading</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>27</td>
<td>27.0</td>
</tr>
<tr>
<td>B</td>
<td>31</td>
<td>31.0</td>
</tr>
<tr>
<td>C</td>
<td>42</td>
<td>42.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
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Table 3: Distribution Patients according to CT-Chest:

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<thead>
<tr>
<th>Pleural Effusion</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Present</td>
<td>25</td>
<td>25.0</td>
</tr>
<tr>
<td>Absent</td>
<td>75</td>
<td>75.0</td>
</tr>
<tr>
<td>Normal</td>
<td>60</td>
<td>60.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
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Table 4: 2D Echo Examination in patients:

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>No. of patients [n=100]</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPVD</td>
<td>Present</td>
<td>25</td>
</tr>
<tr>
<td>Absent</td>
<td>75</td>
<td>75.0</td>
</tr>
<tr>
<td>Normal</td>
<td>15</td>
<td>15.0</td>
</tr>
<tr>
<td>Mild</td>
<td>90</td>
<td>90.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>68</td>
<td>68.0</td>
</tr>
<tr>
<td>Severe</td>
<td>83</td>
<td>83.0</td>
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DISCUSSION:
Liver cirrhosis is often accompanied by arterial hypoxemia in the absence of cardiopulmonary disease. In addition, abnormalities in pulmonary function and impaired gas exchange may occur in as many as 45–50% of patients. Artificial putative mechanisms of hypoxemia include an intrapulmonary shunt, ventilation-perfusion inequality, and alveolar capillary diffusion limitation, there is a lack of agreement on which factors are the most important. Hepatopulmonary syndrome (HPS) is a serious vascular complication of liver disease that occurs in 5–32% of patients with cirrhosis.

POPH (portal pulmonary hypertension) is best defined as a condition characterized by increased mean pulmonary arterial pressure (mPAP) and pulmonary vascular resistance (PVR), resulting in an increased pulmonary arterial hypertension (PAH) in association with portal hypertension, whether or not portal hypertension is related to underlying chronic liver disease.

Fluid in the chest (pleurisy) may be found in at least 10 percent of patients with cirrhosis, being more common on the right side influencing when in large quantities the VA/Q ratio. The present study found an 54% prevalence of arterial hypoxemia in patients with liver cirrhosis. This prevalence different from those reported by Hakanet al. 2007 and Florence et al. 2007 who showed a prevalence of 43.8%, 13.9% and 14% respectively. This wide variability in the prevalence may be explained by the difference in number of patients enrolled in each study as well as the difference in the clinical profiles of the population studied. The present study showed a positive correlation between the presence of arterial hypoxemia and the severity of liver disease assessed by the Child-Pugh score and showed that the severity of hypoxemia is positively correlated with the severity of liver disease. These findings agree with those done by Florence et al. 2007 who showed that, cirrhotic patients with hypoxemia have a higher Child Pugh score than nonhypoxemic patients and the severity of hypoxemia is positively correlated with the Child Pugh score and he stated that, the role of decompensated cirrhosis in the development of hypoxemia explains the improvement in cirrhosis-associated hypoxemia following liver transplantation. The present study showed a statistically significant decrease in serum albumin and increase in prothrombin time in hypoxic patients in comparison to non hypoxemic patients. These results agree with Melot et al. 2007 who showed a decreased serum albumin in hypoxic patients. Low serum albumin may contribute to hypoxemia through causing subtle interstitial edema which leads to impaired diffusion of alveolar O2.

Also hypoalbuminemia predisposes to ascites and hydrothorax leads to hypoxemia. Hakan G. et al. 2007 showed no statistically significant decrease in serum albumin in hypoxic patients which do not agree with this study. The present study showed no statistically significant difference in serum transaminases (AST, ALT) and hemoglobin levels in both groups. These results do not agree with Hakanet al. 2007 who showed a statistically significant decrease in serum AST in cirrhotic patients with hypoxemic. The present study showed a statistically significant decrease in O2 saturation and PaO2 in both supine and erect positions in patients with hypoxemia, but other parameters of ventilator functions showed no statistically significant difference between both groups. These results agree with Konstantinset al. 2007, and Hakanet al. 2007 who showed similar results.

These results could be explained by the fact that we exclude patients with intrinsic pulmonary disease and long standing pulmonary disorders. The present study showed that the severity of hypoxemia assessed by PaO2 and SaO2 is positively correlated with the presence of intrapulmonary vascular dilatation in HPS. These results agree with the study done by Succiveamet al. 2007 who showed a positive correlation between decreased SaO2 detected by pulse oximetry and the presence intrapulmonary vasodilatation characteristic of HPS.

The present study showed a 25% prevalence of HPS in cirrhotic patients. This result is different from that done by Kariet al. 2007 and Thevenet al. 2007 who showed a prevalence of 24% and 20% respectively. But this result agrees with Zhang and Fallon 2007 who stated that, the prevalence of HPS in cirrhotic patients is 5–32%. The present study showed a statistically significant increase in the diameter of peripheral pulmonary arterioles as well as the arteriole/bronchiolone ratio detected by CT chest in patients with HPS in comparison to HPS negative hypoxemic patients. These results do agree with McAdamset al. 2007 who showed that CT chest in patients with HPS showed distal vascular dilatation which mainly concentrated in the lower lung zones. In the present, CT chest showed no evidence of pulmonary fibrosis or other parenchymal lung disease among patients with hypoxemia, which confirms that hypoxemia, was attributed to liver cirrhosis. The result of the study done showed that the sensitivity of CT chest in diagnosis of IPV of HPS is 80%. This result agrees with Michael et al. 2007 who showed that, the sensitivity of CT chest in diagnosis is 86.4% in contrast to the sensitivity of CEE which is considered the gold standard method for the diagnosis of HPS.

In the present study PPHT was diagnosed in 19 patients. Echocardiography aids in diagnosis by detection of raised pulmonary artery pressure and by exclusion of intrinsic heart diseasecausing pulmonary hypertension. CT chest helps induction by exclusion of intrinsic pulmonary disease as intestinal lung disease and obstructive airway disease. This study showed a 19% prevalence of PPHT in liver cirrhosis which is in the same range of most studies who showed a prevalence between 2% and 10% as shown by Maruis et al. 2007.

CONCLUSION:
Liver cirrhosis is associated with unique pulmonary complications. The early identification of pulmonary complications in cirrhotic patients is crucial as it affects the prognosis and guides the future management by speeding up orthotopic liver transplantation (OLT) recommendations.

Pulse oximetry is a simple non-invasive method that can be used as an initial screening modality for early detection of hypoxemia in cirrhotic patients. CEE with color Doppler is a simple non-invasive method with high sensitivity in diagnosis of HPS as well as PPHT.

CT chest has an important role in diagnosis by detection of IPV characteristic of HPS as well as by exclusion of intrinsic pulmonary pathology.

Conflict of interest :
There are no conflicts of interest.

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