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ORIGINAL ARTICLE

Study of pulmonary dysfunctions in liver cirrhosis

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Abstract *Introduction:* End-stage liver disease and its complications are a leading cause of death among adults. The liver plays a central role in health and homeostasis and thus the diseased liver leads to many deleterious effects on multiple organ systems, including the pulmonary system Julie et al. (2007) [1]. A variety of causes for pulmonary dysfunction in liver disease have been identified and include intrinsic cardiopulmonary disorders not specifically related to liver disease as well as unique problems associated with the presence of liver disease and/or portal hypertension Michael et al. (2000) [2]. Liver disease and portal hypertension can be associated with pulmonary vascular complications, including portopulmonary hypertension (POPH), and hepatopulmonary syndrome (HPS) Mateo et al. (2012) [3].

Aim: This study aimed to evaluate the pulmonary dysfunctions complicating liver cirrhosis.

Patients and methods: Fifty patients with liver cirrhosis without intrinsic cardiopulmonary disease were enrolled in this study. All were subjected to complete clinical examination, laboratory investigations, radiological investigations including abdominal ultrasound, chest x ray and CT chest, ECG, contrast enhanced echocardiography with colored Doppler study, gastroscopy, ventilatory function tests, measurement of SaO2 using portable pulse oximetry and arterial blood gas analysis.

Results: The prevalence of arterial hypoxemia in cirrhotic patients was 14.6%. The presence of hypoxemia is increased in patients with advanced liver disease and the severity of hypoxemia was positively correlated with the severity of liver disease assessed by the Child Pugh score. HPS represents 64.1% of causes of hypoxemia. Pulse oximetry is a simple non-invasive method for detection of arterial hypoxemia as an initial screening test for HPS. Contrast enhanced echocardiography (CEE) is the gold standard method for the diagnosis of HPS by detection of intrapulmonary vasodilatation (IPV) characteristic of HPS, while CT chest assists in diagnosis by exclusion of intrinsic pulmonary disease.

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

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Introduction

Pulmonary abnormalities and symptoms are common in patients with chronic liver disease. If questioned, up to 70% of cirrhotic patients undergoing evaluation for liver transplantation complain of dyspnea [4]. Mild hypoxia has been seen in approximately one third of patients with chronic liver disease. Development of hypoxemia in patients with chronic liver disease modifies the line of management and worsens the prognosis of the disease [5].

There is no simple mechanism to explain the association between liver disease and hypoxemia and that probably many factors have a role in its pathogenesis [6]. Although none of them have been proven as the sole reason, nevertheless ascites, hepatopulmonary syndrome, increased closing volume, low albumin levels, anemia, respiratory muscle weakness and extreme hepatomegaly are still considered among the factors implicated in the pathogenesis of hypoxemia in cirrhosis [7].

A variety of causes for pulmonary dysfunction in liver disease have been identified and include intrinsic cardiopulmonary disorders not specifically related to liver disease as well as unique problems associated with the presence of liver disease and/or portal hypertension [2].

Causes of pulmonary abnormalities in chronic liver disease [8]

Intrinsic cardiopulmonary disease	Specific to liver disease
(1) Chronic obstructive pulmonary disease	(A) *Associated with specific liver diseases*. Panacinar emphysema: alpha-1 antitrypsin deficiency Fibrosing alveolitis, pulmonary granulomas: primary biliary cirrhosis
(2) Congestive heart failure	(B) *Fluid retention complicating portal hypertension*. Ascites – Hepatic hydrothorax
(3) Pneumonia	(C) *Pulmonary Vascular abnormalities:* hepatopulmonary syndrome – Portopulmonary hypertension
(4) Asthma	

Hepatopulmonary syndrome (HPS) is a serious vascular complication of liver disease that occurs in 5–32% of patients with cirrhosis [9]. Pulmonary vascular bed abnormalities of HPS can be of two distinct types: diffuse, microscopic precapillary and capillary dilatations, and discrete, macroscopic arteriovenous communications that may resemble classic pulmonary arteriovenous malformations [10]. The presence of HPS increases mortality in cirrhotic patients and may influence the frequency and severity of complications of portal hypertension [11]. The diagnostic features of HPS include evidence of liver disease or portal hypertension, an elevated age-adjusted alveolar-arterial oxygen gradient (AaPO2) and evidence of intrapulmonary vasodilatation. Treatment of HPS consists of supplemental oxygen and consideration of orthotopic liver transplantation if significant hypoxemia is present [12].

PPHT is defined as precapillary pulmonary hypertension accompanied by hepatic disease or portal hypertension in the absence of other known causes of pulmonary arterial hypertension [13]. The reported prevalence of PPHT in cirrhotic patients ranges from 0.25% to 16%, which is influenced by patient characteristics, diagnostic criteria and the diversity of study designs [14].

Although the pathogenesis of PPHT is unknown, causative factors that may lead to the development of structural pulmonary changes include: (1) shear stress in the vascular walls due to increased blood flow in a hyperdynamic state of circulation; (2) a volume phenomenon as a consequence of the increased pulmonary vascular volume; and (3) vasoconstrictive substances such as endothelins (ETs) [15]. Although observations suggest that portopulmonary hypertension is a complication affecting mainly patients with advanced liver disease, no clear relation between the severity of hepatic dysfunction or raised portal venous pressure and the severity of pulmonary hypertension has been conclusively shown [16].

The most common presenting symptom in patients with pulmonary hypertension, irrespective of its cause, is progressive dyspnea on exertion. Other symptoms such as fatigue, palpitations, syncope or chest pain are less frequent. Physical findings indicating pulmonary hypertension are generally subtle and may be completely absent. The most common findings are an accentuated pulmonary component of the second heart sound and a systolic murmur, indicating tricuspid regurgitation [17].

Subjects and methods

This study was conducted on 50 patients with liver cirrhosis after written consent. It was carried out during the period between December 2012 and December 2013 at the Al Madina National Hospital and Al Dar Hospital (Al Madinah Al Munawara). The diagnosis of liver cirrhosis was made on the basis of clinical examination, laboratory investigations and abdominal ultrasound examination. The severity of liver cirrhosis was assessed according to the Child-Pugh classification. Patients were divided into two groups according to the presence of arterial hypoxemia:

Group I: included 9 cirrhotic patients with arterial hypoxemia: 2 patients were Grade A, *2 patients were Grade B and 5 patients were Grade C according to the Child Pugh score*. Patients were subdivided according to the severity of arterial hypoxemia into two subgroups:

Subgroup Ia: included 6 patients with mild to moderate arterial hypoxemia.
Subgroup Ib: included 3 patients with severe arterial hypoxemia.

Group II: included 41 cirrhotic patients with normal arterial oxygen pressure. *12 patients were Grade A, 21 patients were Grade B and 8 patients were Grade C according to the Child Pugh score*.

Arterial hypoxemia was diagnosed when partial pressure of arterial oxygen (PaO2) is less than 80 mmHg at the arterial blood gas analysis. Arterial hypoxemia was considered:

- Mild to moderate hypoxemia: when PaO2 is between 60 and 79 mmHg.
- Severe hypoxemia: when PaO2 is less than 60 mmHg.