Introduction

Patients with chronic liver disease have an increased prevalence of pulmonary vascular disorders. Two forms of pulmonary vascular disorders can complicate chronic liver disease: the hepatopulmonary syndrome and portopulmonary hypertension. Both tend to occur in patients with chronic and late-stage liver disease ***(Badesch and Rubin, 2005).***

Recognition of the importance of pulmonary vascular complications of hepatic disease states has increased due to the increasing practice of orthotopic liver transplantation. These liver-induced pulmonary vascular disorders namely, hepatopulmonary syndrome and portopulmonary hypertension influence survival and candidacy for orthotopic liver transplantation ***(Rodriguez-Roisin et al., 2004).***

The differing incidence is primarily due to heterogeneity of the applied diagnostic criteria. This syndrome is a well defined cause of hypoxaemia in patients who have liver disease due to abnormal intrapulmonary vascular dilatation, which results in an excess perfusion for a given state of ventilation. This complication is characterised by anatomical shunting and a diffusion-perfusion abnormality (***Naeije, 2003***) .

Patients with liver cirrhosis have hyperdynamic circulation and hyperventilation. In spite of this fact, mild hypoxemia is seen in 70% of these patients (***Gadour et al., 2001***).

In 1884, Fluckiger studied the interaction between lung and liver, when he first saw a woman with cirrhosis, and digital clubbing. "Hypoxemia of cirrhosis" was clarified by Sneel, who recognized a decreased arterial saturation in three patients with cirrhosis in 1935 and described what is currently called "hepatopulmonary syndrome". In 1977, Kennedy firstly suggested this term ***(Lange and Stoller, 1995.)***

Hepatopulmonary syndrome, is a life-threatening condition defined as the triad of liver disease, pulmonary gas exchange abnormalities leading to arterial deoxygenation, and widespread pulmonary vascular dilatation. The prevalence of hepatopulmonary syndrome in cirrhotic patients varies from 4% to 19%, and this variation is due to varying cut offs for the abnormal alveolar-arterial gradient and partial pressure of oxygen that are used to define gas-exchange abnormalities, while the prevalence in series of patients awaiting orthotopic liver transplantation ranges from 5 to 32%. Clinical manifestations include dyspnea, which is the predominant presenting symptom, while digital clubbing, cyanosis, spider navi, and severe hypoxemia strongly suggest hepatopulmonary syndrome. Diagnosis of hepatopulmonary syndrome is practically confirmed by contrast-enhanced transthoracic echocardiography ***(Rodriguez-Roisin and Krowka, 2008).***

Hepatopulmonary syndrome affects 10% - 30% of patients with cirrhosis and portal hypertension and significantly increases mortality (***Roberts et al., 2010***).

Hepatopulmonary syndrome can affect patients with a wide spectrum of liver diseases including viral and non-viral hepatitis, granulomatous liver

disease including sarcoidosis, hepatocellular carcinoma, inferior vena cava obstruction, Budd-Chiari syndrome and is reported in patients with non cirrhotic portal hypertension and periportal fibrosis. HPS due to schistosomaisis was first reported in 1997. Pulmonary abnormalities and especially HPS are described in association with celiac disease and nodular regenerative hyperplasia (***Cancado et al., 2006***). Both acute and chronic liver diseases have been associated with hepatopulmonary syndrome, but most commonly it presents in patients with cirrhosis. Portal hypertension seems to be the predominant factor related to this syndrome ***(Benjaminov et al., 2003).***

The pathogenesis of HPS remains unknown (***Moller et al., 2007***) . The pathophysiologic basis for the shunting is a combination of vasodilatation and vascular remodeling in the lung resulting in vascular diversion away from the alveolus at levels that range from the microscopic to shunts. The extent of vasodilatation can result in demonstrably increased intrathoracic blood volumes (***Joshi et al., 2009***). There is also evidence of an increase in lung capillary density and an accumulation of monocytes in the microvasculature (***Zhang et al., 2009***) Alveolar nitric oxide production is increased and this correlated with HPS but not with arterial oxygen impairment (***Degano et al., 2009***) implying a specific role in the pathogenesis of the condition rather than a secondary phenomenon. Other implicated mediators include heme oxygenase, tumor necrosis factor and vascular endothelial growth factor-A (***Yeshua, 2009***)

Recent Studies suggesting that genes involved in the regulation of angiognesis (***Roberts et al., 2010***) . Genetic alteration has not, as yet, been defined in this syndrome; however, cytokines and chemokines have been suggested to play a role. (***Rovin et al., 1999***).

To date many medical therapies have been tried for HPS, including indomethacin, aspirin, almitrine, somatostatin and garlic but none has been clearly beneficial. The only successful, long-term treatment currently available is liver transplantation. Eighty-five percent or more of patients with HPS who receive liver transplantation experience either significant improvement or complete resolution of hypoxemia (***Swanson et al., 2005***).

Patients with HPS have better outcomes after transplant surgery if their resting PaO2 (partial pressure of oxygen in arterial blood) is greater than 50 mm Hg breathing room air and/or a scintigraphic shunt fraction less than 20%. Greater degrees of hypoxemia and/or intrapulmonary shunting are associated with unacceptably high perioperative mortality (***Krowka et al ., 2004***)