Screening for Hepatopulmonary Syndrome in Child C Cirrhotic Patients Candidate for Liver Transplantation

Thesis by

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Submitted for partial fulfillment of
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2009-2010

Abstract

Background: Hepatopulmonary syndrome (HPS) is one of the pulmonary complications of liver cirrhosis. This syndrome is characterized by a triad of liver cirrhosis, hypoxemia and intrapulmonary vascular dilatation confirmed by contrast enhanced echocardiography. **Aim:** To screen for HPS in Child C cirrhotic patients candidate for liver transplantation. **Methods:** For all the patients arterial blood gases, abdominal ultrasound, and transthoracic contrast echocardiography was done. **Results &conclusions:** 9.7% of patients had the criteria of HPS, there is a direct relation between hepatitis C virus as an etiology of chronic liver disease and HPS, there was a positive correlation between PVD, splenic diameter and HPS. Also there was positive correlation between dyspnea, cyanosis, spider nevi and HPS.

Key words:- Liver cirrhosis , hypoxemia, hepatopulmonary syndrome.

Acknowledgment

t is a great thing to feel success and have the pride of achieving all what is always aspired. First of all, Thanks to God who gave me everything including the ability to fulfill this work. One must not forget all those who usually help and push him onto the most righteous way that inevitably ends with fulfillment and perfection.

When the instant comes to appreciate all those kind hearted people, I soon mention Prof. **Waheed Radwan** , Professor of Critical Care Medicine, Cairo University, the person who gave me the honor to be his student. He really helped me by his precious opinions and contributive comments that served much in the construction of this work.

Great thanks are also to Prof. **Mervat El Damarawy**, professor of Internal Medicine, TBRI . She was always there to care, support, encourage and provide constructive pieces of advice in every possible way.

Thanks also to **Dr. Ahmed Samir** , lecturer. Of Critical Care Medicine, Cairo University, who was the real guide, his endless support was behind the progress of this work.

I cannot forget the help of the medical staff and nursing team of the Critical care unit in our institute for their cooperation in the practical part of this work.

I would also like to record my thanks and sincere gratitude to my family for their great help and support throughout the work.

Abbreviations

A-a 0_2 : Alveolo-Arterial Oxygen

ACR : Acute Cellular Rejection

AIDS : Acquired Immunodeficiency Syndrome

Alb : Albumin

ALP : Alkaline Phosphatase

ALT : Alanine Transaminase

ANA : Antinuclear Antibody,

ANCA : Antineutophil Cytoplasmic Antibody

ASMA : Antismooth Muscle Antibody

AST : Aspartate Transaminase

AVMs : Arteriovenous Malformations

BIL : Bilirubin

CBC : Complete Blood Count

CAD : Coronary Artery Disease

COPD : Chronic Obstructive Pulmonary Disease

CT : Computed Tomography

CTP : Child-Turcotte-Pugh Classification

DIC : Disseminated Intravascular Coagulopathy

ET : Endothelin

F_iO_2 : Fraction of Inspired Oxygen

GGT : Gamma Glutamic Transpeptidase

HAT : Hepatic Artery Thrombosis

HCC : Hepatocellular Carcinoma

HCV : Hepatitis C Virus

HCO3 : Bicarbonate

HBV : Hepatitis B Virus

HH : Hereditary Hemochromatosis.

HIV : Human Immune Deficiency Virus

HPS : Hepatopulmonary Syndrome

HRCT : Thoracic High Resolution Computed Tomography

HRS : Hepatorenal Syndrome

H.S : Highly Significant

ICU : Intensive Care Unit

IPVDS : Intrapulmonary Vascular Dilatations Syndrome

INR : International Normalized Ratio

LFTs : Liver Function Tests

LT : Liver Transplantation

MAA scan : Technetium 99m Macroaggregated Albumin Lung Perfusion Scan

MELD : Model For End -Stage Liver Disease

NASH : Non Alcoholic Steatohepatitis

NOS : Nitric Oxide Synthase

N.S : Non Significant

NO : Nitric Oxide

OLT : Orthotopic Liver Transplantation

PAH : Pulmonary Arterial Hypertension

PaO_2 : Arterial Oxygen Tension

PAO2 : Alveolar Oxygen Tension

P_B : Barometric Pressure

PC : Prothrombin Concentration

PCO_2 : Carbon Dioxide Tension

PCR : Polymerase Chain Reaction

P_{H2O} : Water Vapor Pressure

PLT : Platlets

PGI2 : Prostaglandin I2

PGE1 : Prostaglandin E1

PNF : Primary Non Function

PT : Prothrombin Time

PVD : Portal Vein Diameter

P value : Significance Level

SAAG : Serum-Ascites Albumin Gradient

SBP : Spontaneous Bacterial Peritonitis

SO2 : Oxygen Saturation

S.D. : Standard Deviation

SGOT : Serum Glutamic Oxaloacetic Transaminase

SGPT : Serum Glutamic Pyruvic Transaminase

TBRI : Theodor Belharz Research Institute

TECE : Transesophageal Contrast Echocardiography

TTCE : Transthoracic Contrast Echocardiography

TIPS : Transjugular Intrahepatic Portosystemic Shunt

TPO : Thrombopoietin

UNOS : United Network for Organ Sharing

VIP : Vasoactive Intestinal Peptide

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INTRODUCTION

The hepatopulmonary syndrome is characterized by a defect in arterial oxygenation induced by pulmonary vascular dilatation in the setting of liver disease; 4-27.6% of these patients of all ages can be affected. *(Lang et al, 2007)*

A classification of the severity of the hepatopulmonary syndrome based on abnormalities in oxygenation is vital because severity influences survival and is useful in determining the timing and risks of liver transplantation. *(Berthelot et al., 2000)*

The defect in oxygenation is due to a ventilation–perfusion mismatch characterized by increased blood flow while alveolar ventilation is uniformly preserved. *(Akira et al., 2006)*

Enhanced pulmonary production of nitric oxide has been implicated as a key priming factor for the development of pulmonary vascular dilatation. *(Arguedas et al., 2005)*

Arterial hypoxemia is common in the context of hepatic disease; its cause is often multifactorial (e.g., ascites, hepatic hydrothorax, and chronic obstructive pulmonary disease). *(Miguel et al., 2005)*

A diagnosis of HPS is established when the following three points are fulfilled *(Umeda et al., 2006):*

1. Chronic liver disease, usually complicated by portal hypertension.
2. Arterial hypoxaemia, defined by a reduced partial pressure of arterial oxygen (PaO_2) or more accurately by an increased alveolar-arterial gradient A-a gradient. The latter includes determination of

the partial pressure of arterial carbon dioxide ($PaCO_2$) which is often low in cirrhotic patients as a result of hyperventilation.

3. Intrapulmonary vascular dilatation, detected either by two dimensional contrast echocardiography or macroaggregated albumin lung perfusion scan.

Currently, no effective medical therapies for the hepatopulmonary syndrome exist, and liver transplantation is the only successful treatment. *(Fallon and Abrams, 2000)*

Studies have shown a greater median survival rate in patients without hepatopulmonary syndrome. Survival was significantly worse among patients with a partial pressure of oxygen of less than 60 mmHg at the time of diagnosis. *(Rodriguez et al., 2004)*

Because of the poor outcome without liver transplantation, the diagnosis of the hepatopulmonary syndrome is considered to be an indication for liver transplantation, and patients with this syndrome are given a higher priority for transplantation than patients with other disorders and on the otherhand patients with HPS and preoperative partial pressure of oxygen of 60 mm Hg or less can be considered uneligable for transplantation as mortality rate is higher and reversibility rate is low. *(Gupta et al., 2001)*

Aim of the work

The aim of this work is to screen for Hepatopulmonary syndrome in child C cirrhotic patients candidate for liver transplantation using full history taking, clinical examination, several laboratory investigations including arterial oxygenation and transthoracic contrast echocardiography for re-estimating the priority, early listing and prognosis of those patients.

Chapter I

Liver Cirrhosis

Cirrhosis is the end result of chronic liver injury from a variety of causes. It is defined by marked disruption of hepatic architecture with extensive fibrosis and fibrotic encirclement of regenerative nodules. There are a large number of conditions that can lead to cirrhosis. The development of portal hypertension and its complications contribute substantially to the morbidity and mortality associated with cirrhosis. Consequently, the prevention and treatment of these complications is one of the cornerstones of the management of the cirrhotic patient. *(Kozak et al. 2005)*

Definition:

Cirrhosis is a slowly progressive disease, causing irreversible scarring and nodularity of the liver in response to chronic injury from a variety of causes *(Rimola et al. 2000)* This process distorts the normal liver architecture, interferes with blood flow through the liver and disrupts the biochemical functions of the liver *(Mathews et al. 2006).*

Etiological classification of cirrhosis:

1- Hepatitis and other viruses: (Post hepatitis)

Worldwide, hepatitis B is the most common causes of cirrhosis, but in Egypt and in the United States hepatitis C is a more common cause *(Gebo et al. 2002).*

2- Drugs, Toxins, and infections:

This is rare. Long-term infections with various bacteria or parasites can damage the liver and cause cirrhosis *(Scott et al, 2004).*

3- Bile duct obstruction (Biliary cirrhosis):

In adults, the most common cause is primary biliary cirrhosis, a disease in which the ducts become inflamed, blocked, and scarred *(Jones, 2003).* Secondary biliary cirrhosis can happen after gallbladder surgery if the ducts are injured, gall stones or sclerosing cholangitis *(Giorgini et al. 2005).* In adults, gallstones are a common cause of bile duct blockage. Surgery to remove the gallbladder also blocks the bile ducts *(Prince et al. 2001).*

4- Autoimmune cirrhosis:

In autoimmune hepatitis, the body's immune system attacks the liver, causing cell damage that leads to cirrhosis *(Al varez et al. 2002).*

5- Obstruction of outflow of blood from the liver (i.e. Budd-Chiari syndrome).

6- Cardiac cirrhosis.

7- Inherited disease: (metabolic):

They include Wilson disease, cystic fibrosis, alpha-1 antitrypsin deficiency, hemochromatosis, galactosemia, and glycogen storage disease *(NDDIC, 2003).*

8- Chronic alcoholism: (Alcoholic):

Is the most common form of cirrhosis in the United States. The severity of the process depends on how much you drink and how long you have been abusing alcohol. The amount of alcohol needed to injure the liver varies widely from individual to individual *(Sheth et al. 2002).*

9- Nonalcoholic Steatohepatitis (NASH):

This is a condition in which fat builds up in the liver, eventually causing scar tissue to form *(Petrides et al. 1994).* This kind of cirrhosis is linked to diabetes, obesity, coronary artery disease, protein malnutrition