INCIDENCE OF CLINICAL AND SUBCLINICAL HEPATIC ENCEPHALOPATHY IN PATIENTS WITH LIVER CIRRHOSIS RECEIVING PROPRANOLOL FOR PREVENTION OF VARICEAL BLEEDING

Thesis
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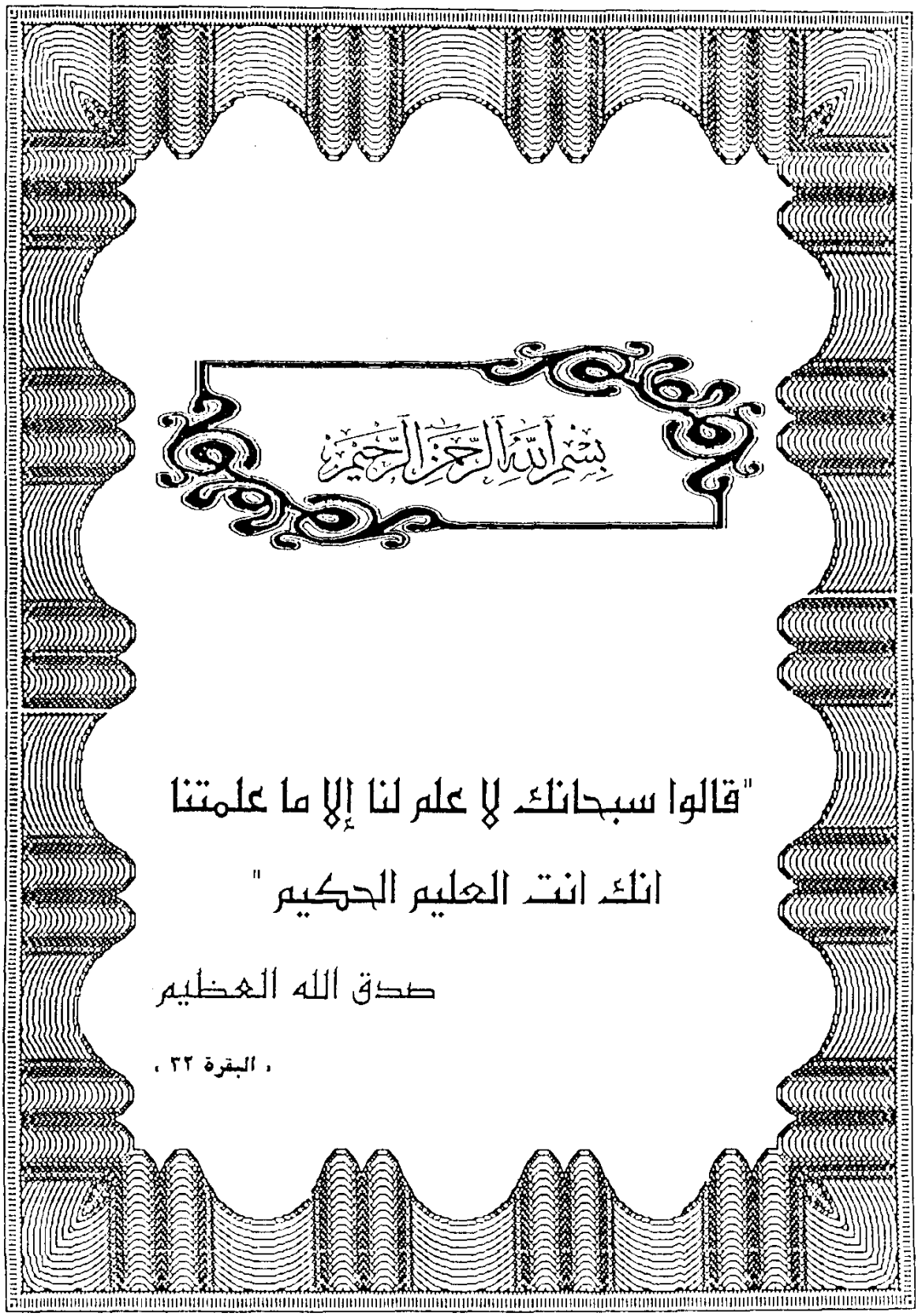

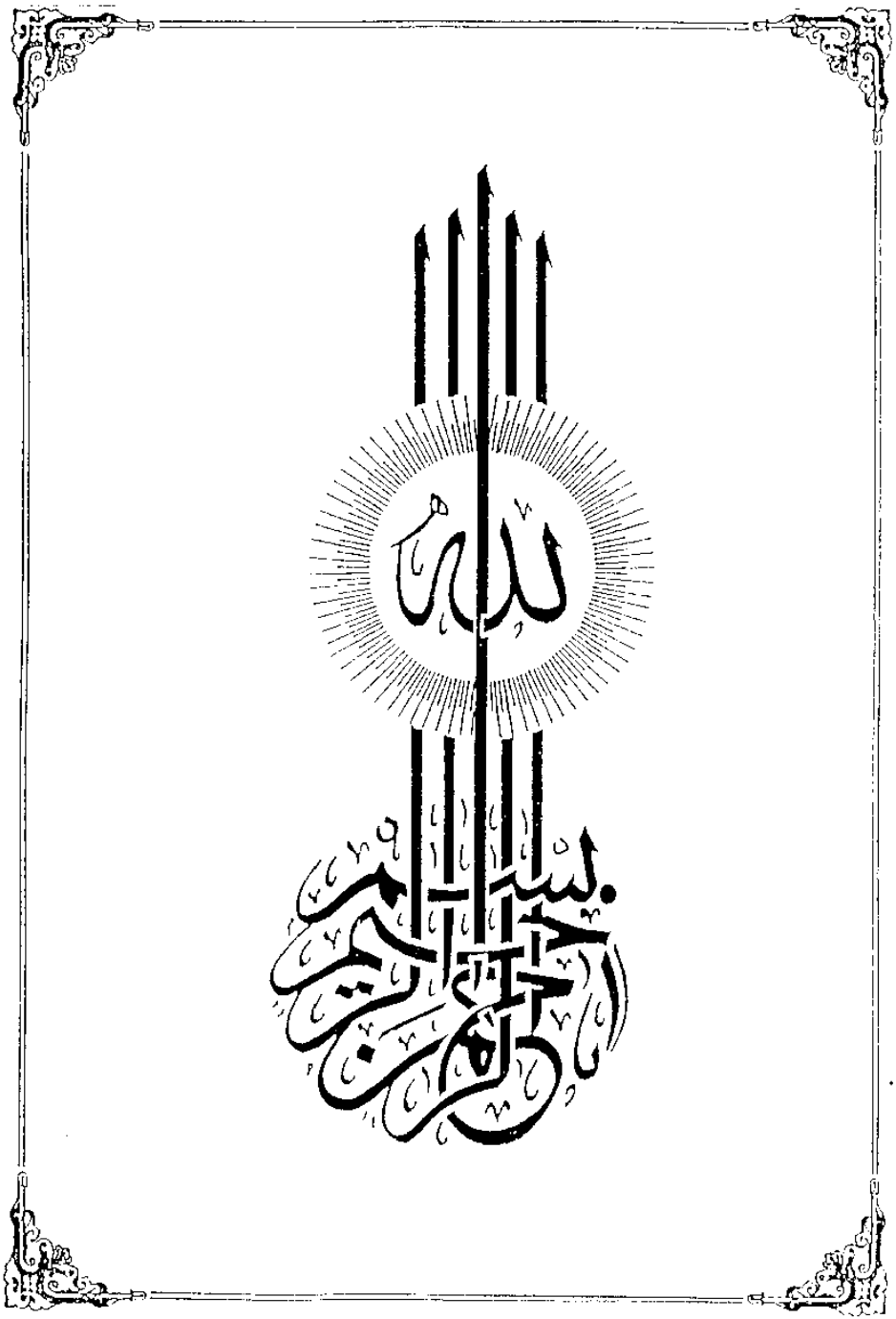

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INTRODUCTION AND AIM OF THE WORK

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AND AIM OF THE WORK

Introduction

Recent attention has been paid to the role of propranolol in prevention of bleeding from oesophageal varices (ELDER, 1992).

The beneficial effect of propranolol on the risk of bleeding from oesophageal varices may be due to reduction of splanchnic arterial inflow and a consequent decrease of portal vein and porto-collateral blood flow (Gaiani, 1991).

It is possible that propranolol through its effects on hepatic blood flow may impair liver functions and precipitate hepatic encephalopathy, and it indicates that this is a potentially major complication of propranolol treatment in patients with liver cirrhosis (Tarver, 1983 & Dunk, 1988).

Aim of the Work

To measure the incidence of clinical and subclinical hepatic encephalopathy that may occur in patients with liver cirrhosis receiving propranolol for prevention of bleeding from oesophageal varices and its relation to liver condition assessed according to modified Child's classification.

REVIEW OF LITERATURE

PORTAL HYPERTENSION

A. Anatomy of the Portal Venous System

The portal system includes all veins which carry blood from the abdominal part of the alimentary tract, the spleen, pancreas and gall bladder **(Sherlock, 1993)**.

Tributaries

Splenic, superior mesenteric and inferior mesenteric veins, also left gastric, right gastric and posterior superior pancreatico duodenal veins. The ligamentum teres and venosum are attached to the left portal vein at the left end of the porta-hepatis **(Douglass, 1979)**.

Porta Caval Anastomosis

When the portal circulation is obstructed, whether it be within or outside the liver, a remarkable collateral circulation develop to carry portal blood into the systemic veins **(Sherlock, 1993)**.

The sites of porta caval anastomosis are as follows **(Douglass *et al.*, 1979)**:-

(a) At the upper end of the gastrointestinal tract: the oesophageal branches of the left gastric vein anastomose with the oesophageal branches of the azygos vein.

(b) At the lower end of the gastrointestinal tract: The superior rectal vein anastomose with the middle and in-

ferior rectal veins and most important of all with the pelvic venous plexus.

(c) Five paraumbilical veins run with the round ligament of the liver from the left portal vein to the umbilicus where they anastomose with the superficial and deep epigastric veins.

(d) Twigs of colic and splenic veins anastomose in the extraperitoneal fat with twigs of the renal vein and with veins of the posterior abdominal wall. Here may be included twigs from the bare area of the liver.

B. Physiology of Portal Venous System

Portal blood flow in man is about 1000-1200 ml/m **(Sherlock, 1993)**.

Portal O_2 Content

The fasting arterioportal O_2 difference is only 1.9 volumes per cent (range 0.4 - 3.3 volumes per cent) **(Smythe, 1951)**. The portal vein contributes 72% of the total oxygen supply to the liver **(Tygstrup *et al.*, 1962)**. The last estimate available indicates that about 2/3 of the hepatic blood flow and about half of the total oxygen consumption is supplied by the portal vein while the hepatic artery contributes the remainder **(Reynolds, 1982)**.

C. Pathophysiology of Portal Hypertension

Eisenberg (1982) described the following factors being responsible for determination of the level of portal pressure:-

(1) The peripheral resistance of the intrahepatic vascular tree.

(2) The inside diameter and the tone of the portal vascular tree (venous wall).

(3) The volume and pressure of the blood flowing via the mesenteric arteries to the portal region.

(4) The capacity and resistance of collateral bypass vessels serving the systemic circulation.

(5) The pressure in the inferior vena cava which can be transmitted to sinusoids via hepatic veins and in a retrograde direction via portacaval anastomosis to the portal system.

PORTAL HYPERTENSION

Definition

Normal portal vein pressure is said to be 5-10 mmHg (Reynolds, 1982).

Portal hypertension is defined as a persistent increase above normal in portal vein pressure. Direct portal system pressure at surgery over 30 cm saline, intrasplenic pressure over 17 mmHg and wedged hepatic vein pressure more than 4 mmHg above inferior venacaval pressure are indicators of portal hypertension (Reynolds, 1982).

Portal hypertension results from increased resistance to the blood flow in the portal vein, inside the liver or hepatic veins (Reynolds, 1982).

Classification of Portal Hypertension

Portal hypertension is divided into three major types:-

- Suprahepatic.
- Intrahepatic.
- Extrahepatic.

based on the location of the presumed increase in vascular resistance (Reynolds, 1982).

Intrahepatic portal hypertension is divided into two types:-

- With normal wedged hepatic vein pressure (presinusoidal portal vein obstruction).
- With raised wedged hepatic vein pressure (post-sinusoidal hepatic vein obstruction).

Sherlock (1993) classified portal hypertension into two groups presinusoidal extrahepatic or intrahepatic and a big group of hepatic causes. This classification depend on a group of techniques such as:-

(a) Intrahepatic pressure to measure pressure in the splenic vein.

(b) Wedged hepatic venous pressure which represents the sinusoidal pressure.

(c) Splenic or portal venography or visceral angiography which shows the site of obstruction and the nature of the collateral circulation.

Classification of portal hypertension (Sherlock, 1993)

Type	*Cause*	*Underlying Disorders*
Presinusoidal		
A. Extrahepatic	- Blocked portal vein or splenic vein	- Intra-abdominal infections.
		- Post-operative.
		- Trauma.
		- Hypercoagulable state.
		- Congenital.
B. Intrahepatic	- Portal zone infiltrates	- Schistosomiasis.
		- Congenital hepatic fibrosis.
		- Lymphomas, myeloid leukaemia
		- Primary biliary cirrhosis
	- Toxic causes	- Inorganic arsenic.
		- Copper
		- Vinyl chloride.
		- Vitamin A intoxication.
		- Cytotoxic drugs.
	- Hepatoportal sclerosis.	
Hepatic		
A. Intrahepatic	- Cirrhosis	- Alcoholic.
		- Chronic active hepatitis.
B. Post sinusoidal	- Blocked hepatic vein	- Veno-occlusive disease
		- Budd chiari syndrome.
		- Tumour invasion.
		- Hypercoagulable state.
		- Oral contraceptives.

Presinusoidal

This includes obstruction to the sinusoids by Kupffer and other cellular proliferation and is usually associated

with relatively normal hepatocellular function. If a patient with this type suffers from haemorrhage due to oesophageal varices liver failure is rarely a consequence (Sherlock, 1993). The obstruction may be at any point in the course of the portal vein (Webb, 1979).

A. Presinusoidal Extrahepatic (Blocked Portal or Splenic Vein)

It may be due to:-

a. Intra-Abdominal Infection

Speticaemia or intra-abdominal infections, umbilical infection may be responsible in neonates (**Thompson *et al.*, 1964**), in older children acute appendicitis and peritonitis may be responsible. Ulcerative colitis and Crohn's disease can be complicated by portal vein block. Portal vein obstruction may be secondary to biliary infection due to gall stones or primary sclerosing cholangitis (Sherlock, 1993).

b. Hypercoagulable States

Especially in older age group. Myeloproliferative diseases especially polycythaemia rubra vera are the commonest association.

c. Tumour Invasion

Carcinoma of the pancreas usually of the body