CHANGES OF BLOOD PROTEIN 'C" AND FIBRIOLYSIS FOLLOWING ENDOSCOPIC INJECTION SCLEROTHERAPY

THESIS

Submitted for partial fulfilment of
Master Degree In **Internal Medicine**

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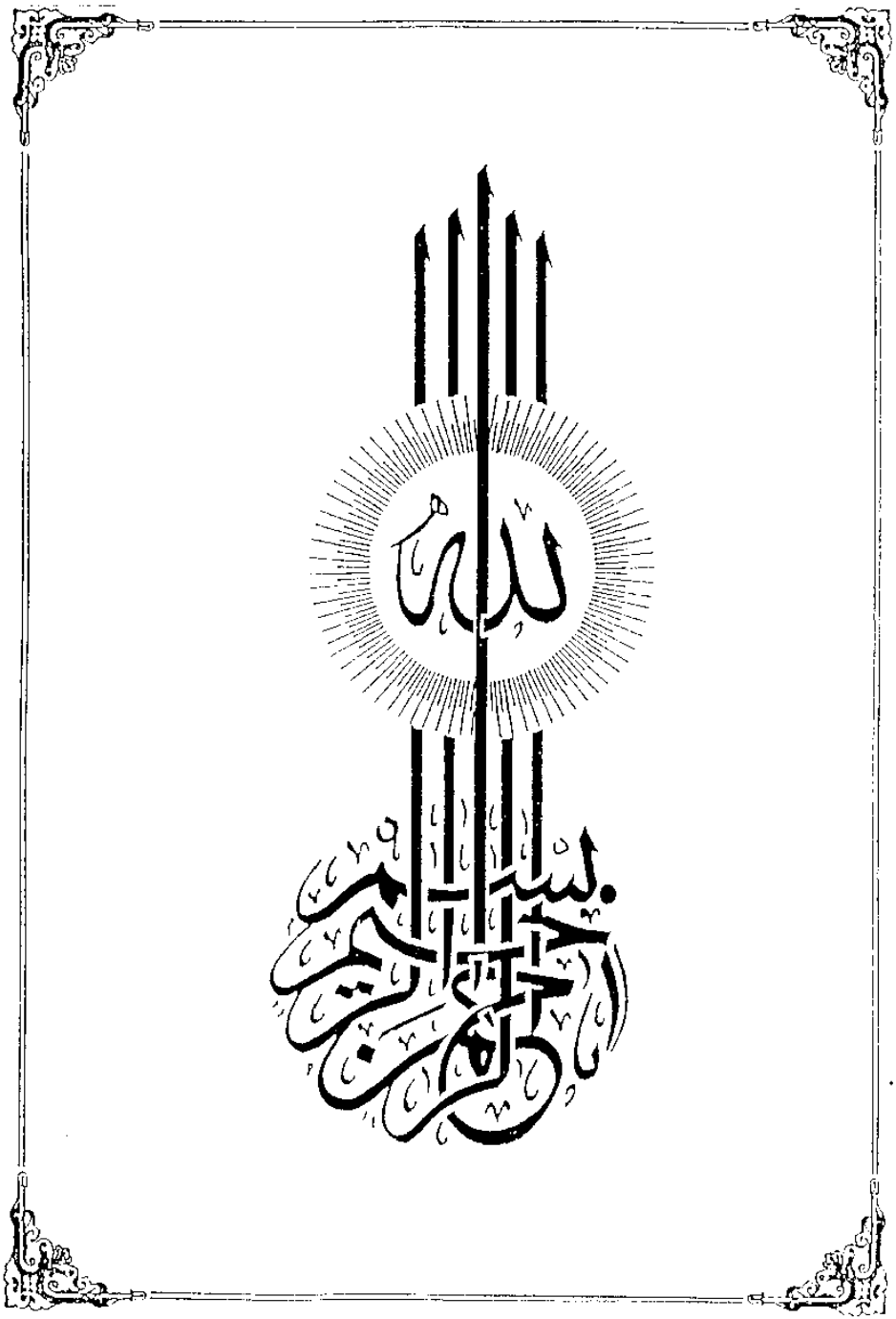
بسم الله الرحمن الرحيم

سُبْحَانكَ لاَ علْمَ لَنَا إلا ما عَلمْتَنَا
إنَّكَ أنتَ العَليمُ الحكيمُ

(سورة البقرة : آية ٣٢)

دار الصداقة



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To ...

The Soul Of My Dear Sister

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Ahmed

List of Abbreviations

AA	amino acid
APC	activated protein C
APCI	activated protein C inhibitor
APTT	activated partial thromboplastin time
AT III	antithrombin III
BHF	Bilharzial hepatic fibrosis
C4BP	C_4binding protein
DIC	disseminated intravascular coagulation
DWBCLT	dilute whole blood clot lysis time
EACA	E-amino caproic acid
ELP	eosophageal luminal pressure
EPI	extrinsic pathway inhibitor
F	coagulation factor
FDPs	fibrinogen/fibrin degradation products
GLa	glutamic acid
HMW-K	High molecular weight kininogen
HRG	Histidine-rich glycoprotein
ICTH	Internal Committee of Thrombosis and Haemostasis
Ka	Kallikrein
LES	lower eosophageal sphincter
PA	plasminogen activator
PAI	plasminogen activator inhibitor
PC	Protein C
PCI	Protein C inhibitor
PEPG	Portal venous-eosophageal luminal pressure gradient.
PL	Platelet phospholipid
Pre-K	Pre-Kallikrein
PT	Prothrombin time
PTT	Partial thromboplastin time
PVP	portal venous pressure
TF	tissue factor
tPA	tissue plasminogen activator
TT	Thrombin time
uPA	urinary plasminogen activator
VWF	VonWillebrand factor

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Introduction And Aim of The Work

INTRODUCTION AND AIM OF THE WORK

Endoscopic injection sclerotherapy has become the principal method for treatment of oesophageal variceal bleeding *(Brakyo et al., 1985).* Bleeding from esophageal varices have been attributed to portal hypertension aided by a variety of hemostatic abnormalities that may associate liver disease.

Protein C was discovered by *Stenflo in (1976)* and was isolated from human plasma by *Kisiel in (1979),* it is a Vit. K dependent glycoprotein *(Griffin et al., 1982).* However, in contrast to Vit K dependant coagulation factors protein C when activated by thrombin is not a procoagulant but a potent anticoagulant *(Kisiel et al., 1977).*

Functions of activated protein C are *(Taylor and Lockhart, 1985).*

1. Inactivation of coagulation factor V, VIII.
2. Inactivation of platelet prothrombin activity.
3. Induction of fibrinolysis.

The clinical importance of protein C has been deduced from the finding of reduced levels of this protein in patients

with congenital thrombotic diseases and in those with acquired conditions resulting in activation of coagulation system as in DIC, also in cases of esophageal varices resulting from liver cirrhosis reduced protein C level would occur *(Clouse & Comp, 1986).*

AIM OF THE WORK:

The aim of this work is to study the effect of injection seclerotherapy using (5% ethanolamine oleate) on selected hemostatic parameters of blood coagulation and fibrinolysis e.g. protein C and F.D.Ps.

OESOPHAGEAL VARICES

Definition:

Oesophageal varices result from anastomosis between the left gastric (coronary) and short gastric veins of the portal system with the intercostal, azygos and diaphragmatic veins of the caval system. Deviation of blood into these channels leads to varicosities in the submucous layer of the lower end of the oesophagus *(Sherlock, 1989).*

Venous anatomy of the lower oesophagus:

Four distinct layers of veins were identified:

1. Surface intra-epithelial channels, consist of fine vessels running all within the mucosa of the oesophagus. They join the superficial venous plexus at right angles immediately below the epithelium.

2. Superficial venous plexus, form a rich network or plexus which communicates freely with the equivalent venous plexus of the stomach.

3. Deep intrinsic veins, they constitute three to five major trunks. They have communications with the superficial venous plexus and counterpart veins in the stomach,

perforating veins lie in the area above the oesophagogastric junction connect the deep intrinsic veins with the deeper veins.

4. Adventitial veins consisted of numerous small veins in the perioesophageal area.

In patients with portal hypertension, all the venous channels reported latter are significantly dilated. Three to five markedly dilated and tortuous deep intrinsic veins form the major varices. Deep intrinsic veins (Variceal channels) and the superficial venous plexus connect across the oesophago-gastric junction with their counterparts in the stomach. Large dilated adventitial veins were seen to communicate with the deeper veins via large perforating veins *(Kitano et al., 1986).*

Pathogenesis of varix formation:

Varices are generally caused by increased blood flow through a vein and the inability of the muscular and elastic tissues in the walls of that vein to withstand the increased intraluminal pressure *(Butler, 1951).*

In portal hypertension, anastomotic channels between the portal and systemic circulation are opened and blood is shunted through these channels, from the portal to systemic

circulation, they readily become converted into thin-walled veins and undergo varicosities *(Leibowtz, 1959).*

Many factors are incriminated to have a role in pathogenesis of variceal formation. The exact mechanism is uncertain. Possible factors are:

1. Portal hypertension.
2. The splanchnic portal venous collaterals.
3. Hypervolaemia.
4. The diaphragmatic action.
5. The lower oesophageal sphincter.
6. Superior vena caval obstruction *(Sherlock, 1989).*

Incidence:

Varices do occur in 80-90% of patients with liver cirrhosis, but oesophagogram with barium shows them only in 66% *(Brick and Palmer, 1964).*

The endoscopic incidence of oesophageal varices in bilharzial hepatic fibrosis varies from 40% *(Khalil and Fadali, 1962)* to as high as 78% *(El-Rooby, 1967).*

The incidence of gastro-intestinal haemorrhage in patients with liver cirrhosis was reported by *(Chiles et al., 1953)* as 25% while *(Franco et al., 1977)* found that, in bleeding

cirrhotics 52% bled from varices and 48% from non variceal sources.

The mortality due to variceal bleeding, without surgery is about 42% varying from 22-84% *(Graham and Smith, 1981).*

Predictors for variceal bleeding:

Sometimes mucosal lesions overlying oesophageal varices are seen at autopsy. However, more often than not, no such lesions are found and, if a bleeding site is identified, usually a "Pinhole" into a varix may be detected *(Reynolds, 1982).*

Ponce and co-workers (1981) looked for microscopical evidence of reflux oesophagitis in bleeding varices. They found no morphometric changes to suggest reflux oesophagitis in the 11 patients examined. Other studies of oesophageal pH and lower oesophageal sphincter pressure likewise have failed to show an unusual incidence of reflux in patients with bleeding varices *(Eckhardt and Grace, 1979),* also patients with achlorhydria from pernicious anaemia have been known to bleed from varices *(Reynolds, 1982).* From the previous reports, it appears that there is little evidence to support the erosive theory of pathogenesis of varix haemorrhage.

Salicylates may precipitate bleeding from varices and should not be used *(Franco et al., 1977).*

Common sense suggests that a larger varix is more liable to bleed than a smaller one. *(Sarin et al. 1989),* found that many factors which could be objectively assessed and have been known to be directly or indirectly associated with variceal bleeding. These include in the order of decreasing importance- variceal size, intravariceal pressure, presence of cherry red spots over the varices, colour of varices, presence of red wale markings and haematocystic spots over the varices.

Reynolds (1980) agreed that, there is no relation between portal pressure and variceal bleeding in patients with established portal hypertension. A portal pressure of 12 mm Hg seems to be the critical pressure, at which the incidence of bleeding rises sharply, above this pressure, the incidence of bleeding from oesophageal varices is not necessarily linearly related to the height of portal pressure.

El-Zayat (1990) reported significant impairment in PT., PTT., FDP., Fibrinogen level, antithrombin 111 and platelet count in patients with bleeding oesophageal varices when compared to non bleeders during active bleeding.