ASSESSMENT OF SERUM THROMBOPOIETIN LEVEL IN PATIENTS WITH HCV LIVER CIRRHOSIS AND THE IMPACT OF PARTIAL SPLENIC EMBOLIZATION

Thesis

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Master Degree in **Tropical Medicine**

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تقييم معدل الثرومبوبيوتين فى مرضى الألتهاب الكبدى الفيروسى (سى) و تأثير الحقن
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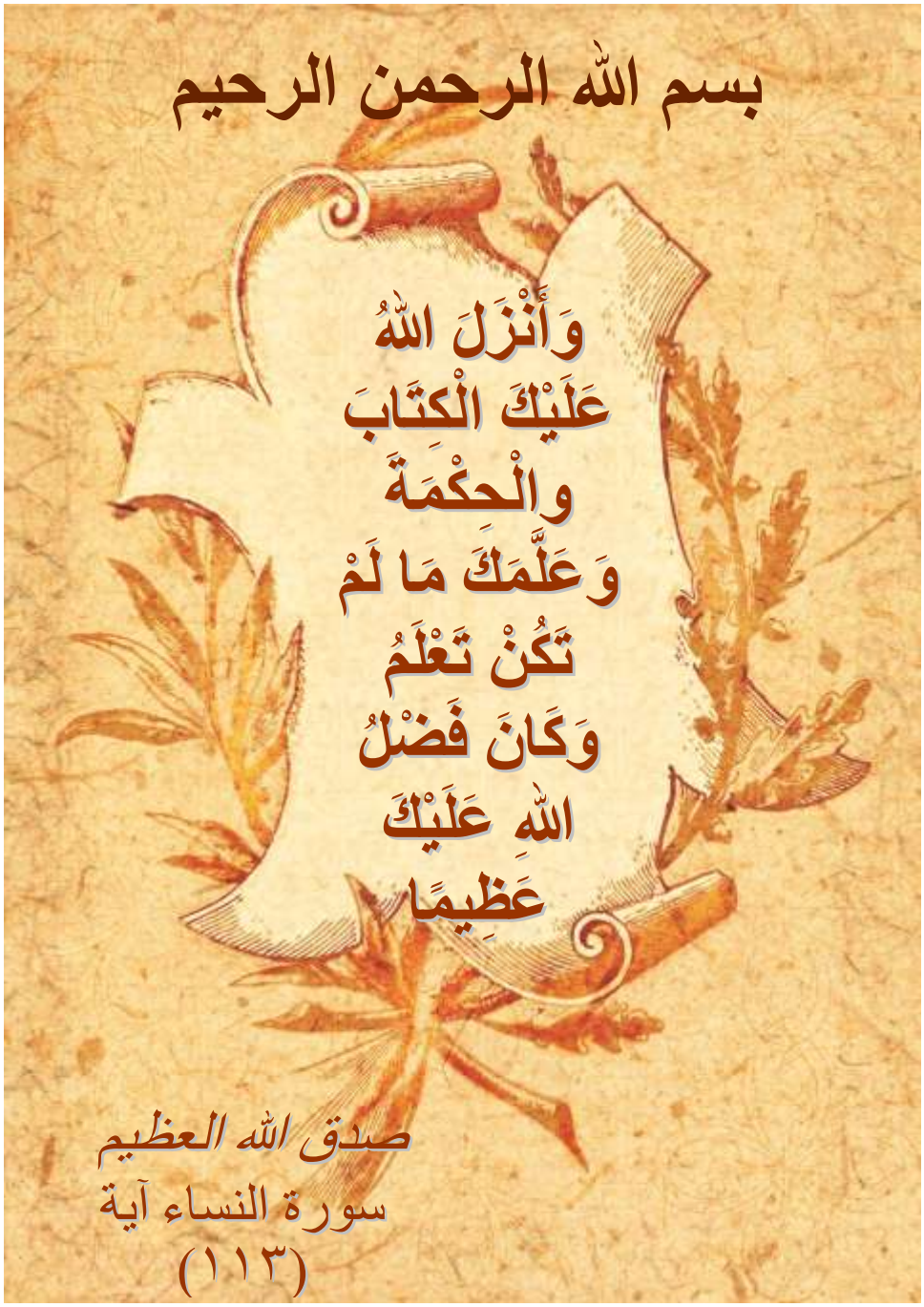
SUMMARY

One of the most frequent complications in patients with chronic liver disease is thrombocytopenia, as it has been observed in up to 76% of patients. Thrombocytopenia is defined as a subnormal number of platelets in the circulating blood (below the normal range of 150,000 to 400,000/ μL). It is the most common cause of abnormal bleeding.

Decreased thrombopoietin ***(TPO)*** production in the cirrhotic liver has been emphasized as an important factor in many patients with cirrhosis and thrombocytopenia. Cirrhotics with thrombocytopenia have significantly lower thrombopoietin levels than do cirrhotics without thrombocytopenia, suggesting inadequate thrombopoietin production in the failing liver**.** Cirrhotics also appear to have a blunted thrombopoietin response to induced thrombo-cytopenia

Partial splenic embolization ***(PSE)*** represents a potential alternative therapeutic method to splenectomy when ablation of the splenic parenchyma is desired, particularly in compromised patients, where splenectomy carries significant morbidity and mortality rates. Hematologic changes after embolization have been observed, especially in platelet values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LIST OF ABBREVIATIONS

Abbrev.	Full term
ALT	Alanine aminotransferase
ANA	Anti nuclear antibody
AST	Aspartate aminotransferase
BSB	Blood Spleen Barrier
BUN	Blood Urea Nitrogen
CBCs	Complete blood counts
CLD	Chronic liver disease
Cr	Creatinine
D.Bil	Direct bilirubin
DCs	Dendretic cells
G-CSF	Granulocyte colony-stimulating factor
GM-CSF	Granulocyte-macrophage colony-stimulating factor
HCV	Hepatitis C Virus
Hb	Hemoglobin
IFN-a	Interferon alfa
Ig	Immunoglobulin
IL	Interleukin
INR	International randomization ratio
ITP	Idiopathic thrombocytopenia purpura
K+	Potassium
Na+	Sodium
NCCLS	National Committee for Clinical Laboratory Standards
NPV	Negative predictive value
OLT	Orthotopic Liver Transplantation

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
OV	Oesophageal varices
PC\SD	Platelet count/splenic diameter
PHG	Portal hypertensive gastropathy
PPV	Positive predictive value
PSE	Partial splenic arterial embolization)
PTT	Partial thromboplastin time
PV	Portal vein
SAE	Splenic artery embolization
T.bil	Total bilirubin
TPO	Thrombopoietin
TPO-R	Thrombopoietin receptor
vWF	von Willebrand factor
WBC	White blood cell count

INTRODUCTION

Introduction:

Chronic liver diseases and their complications constitute a major health problem all over the world especially in our country. Major complications of chronic liver diseases include varices and variceal bleeding, ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, portal hypertension, thrombocytopenia, and hepatorenal syndrome ***(Aref et al., 2004).***

One of the most frequent complications in patients with chronic liver disease is thrombocytopenia, as it has been observed in up to 76% of patients ***(Afdhal et al., 2008).*** Thrombocytopenia is defined as a subnormal number of platelets in the circulating blood (below the normal range of 150,000 to 400,000/ µL). It is the most common cause of abnormal bleeding ***(Bandara et al., 2005).***

Thrombocytopenia can impact routine care of patients with chronic liver disease (CLD), potentially postponing or interfering with diagnostic and therapeutic procedures including liver biopsy, antiviral therapy, and medically indicated or elective surgery.

The clinical significance of mild thrombocytopenia (>75,000/µL–<150,000/µL) is minimal and usually does not interfere with treatment or management decisions.

Moderate thrombocytopenia (50,000 /µL–75,000 /µL) is observed in approximately 13% of cirrhotic patients. Severe thrombocytopenia (<50,000/µL) can be associated with significant morbidity ***(Giannini, 2006).***

The pathogenic mechanisms leading to this disorder were incompletely understood ***(Bashour et al., 2000)***. Several mechanisms had been suggested as a contributing cause to thrombocytopenia in liver diseases such as increased pooling in the enlarged spleen ***(Cardin et al., 2002),*** but thrombocytopenia might even persist after splenectomy in some cases ***(Chaudhary et al., 1994)***. Also it was seen in hepatic patients with normal splenic size ***(Chu et al., 2002).*** Also, inappropriate production of platelets in the bone marrow may present ***(Clarkson and Thmpson, 2000).*** Moreover, reduced half-life of platelets immunologically by increased platelet associated immunoglobulin IgG (auto antibodies) may participate in the induction or aggravation of thrombocytopenia ***(Draper and Hadley, 1990).***

One of the recently postulated causes is reduced production of ***thrombopoietin (TPO) (Chu et al., 2002).*** Thrombopoietin is the major hormone controlling platelet production which is primarily produced by the liver; the predominant thrombopoietin producing organ ***(El-Sokkary et al., 2002).***

Because ***TPO*** was the physiologic regulator of platelet production, circulating levels of ***TPO*** would be

expected to vary inversely with changes in platelet demand ***(Goulis et al., 1999)***. Measurement of serum ***TPO*** has been recently emerged as a new laboratory test for evaluation of patients with thrombocytopenia ***(Hidaka et al., 2002)***

Splenectomy has been the treatment of choice for portal hypertension in patients with liver cirrhosis, but can cause severe complications, including sepsis. ***Transcatheter partial splenic arterial embolization (PSE)*** for hypersplenism was first carried out by ***Maddison in (1973)***. Subsequently, this procedure has been reported to achieve long-term increases in the numbers of platelets and leukocytes in patients with hypersplenism ***(Noguchi, 1995).***

Used prophylactically, splenic artery embolization can improve thrombocytopenia in patients with HCV-induced cirrhosis and hypersplenism, thus facilitating anti-viral therapy ***(Palsson and Verbaan et al., 2005).***

Plasma ***TPO*** levels increased significantly 2 months after ***PSE*** in the cirrhotics ***(Hidaka et al., 2002).*** Few studies have examined the mechanism by which ***PSE*** improves thrombocytopenia in hypersplenism ***(Noguchi et al., 1995).*** However**,** the relation between ***TPO*** and thrombocytopenia in liver cirrhosis remains unclear. Therefore, we need to study the relation between ***TPO*** serum level and thrombocytopenia before and after ***PSE*** in patients with liver cirrhosis.

AIM OF THE WORK

The aim of this study is to evaluate the relation between serum ***thrombopoietin (TPO)*** level and thrombocytopenia in patients with HCV cirrhosis before and after ***partial splenic embolization (PSE).***