

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

Thesis

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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/  $\mu$ L). 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 thrombocytopenia

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

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ  
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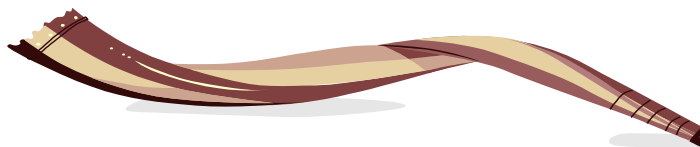
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# LIST OF CONTENTS

Title	Page No.
List of Tables.....	I
List of Figures .....	II
List of Abbreviations .....	IV
Protocol .....	—
Introduction .....	1
Aim of the work .....	4
Review of Literature	
Chapter I: Anatomy and development of the spleen .....	5
Chapter II: Physiology Of The Spleen .....	14
Chapter III: Thrombocytopenia in chronic liver disease .....	21
Chapter IV: Hypersplenism.....	34
Chapter V: Splenic artery embolization (SAE) .....	46
Patients and methods .....	65
Results.....	80
Discussion .....	90
Summary .....	102
Conclusions .....	107
Recommendations.....	109
References .....	111
Arabic summary .....	—

## LIST OF TABLES

Tab. No.	Title	Page No.
<b>Table (1):</b>	Age and Sex of the Studied and Control groups: .....	81
<b>Table (2):</b>	Descriptive Data of the Clinical Presentation of the studied groups:.....	82
<b>Table (3):</b>	Ultrasound & upper Endoscopic Findings before partial splenic embolization of the studied patients: .....	83
<b>Table (4):</b>	Laboratory findings of the studied group before partial splenic embolization:.....	84
<b>Table (5):</b>	Comparison between the studied group and the Control group according to the thrombopoietin and platelet levels. ....	86
<b>Table (6):</b>	Changes in Thromboprotein Level and Platelets Level among Studied group: .....	87
<b>Table (7):</b>	Correlation between thromboprotein level and different parameters:.....	88
<b>Table (8):</b>	Validity of thromboprotein in prediction of thrombocytopenia:.....	89

# LIST OF FIGURES

Fig. No.	Title	Page No.
<i><u>Figures in the review of literature</u></i>		
<b>Figure (I):</b>	Anatomical relations of the spleen.....	6
<b>Figure (II):</b>	Histological structure of the spleen.....	9
<b>Figure (III):</b>	The segments of splenic artery .....	11
<b>Figure (IV):</b>	The termination of an arteriole.....	12
<b>Figure (V):</b>	Functional structure of the spleen .....	14
<b>Figure (VI):</b>	Multiple factors can cause or contribute to the development of thrombocytopenia in patients with chronic liver disease.....	24
<b>Figure (VII):</b>	Thrombopoietin role in megakaryopoiesis and thrombopoiesis. ....	27
<b>Figure (VIII):</b>	Selective partial splenic arterial embolization.....	54
<b>Figure (VIII A):</b>	Arteriograms obtained before embolization show normal splenic anatomy .....	54
<b>Figure (VIII B):</b>	Postembolization arteriogram shows complete occlusion of the targeted splenic artery upper segment.....	55
<b>Figure (IX):</b>	Drawing of nonselective partial splenic arterial embolization shows patchy changes in perfusion (brown areas) throughout the splenic parenchyma.....	55
<b>Figure (IX A):</b>	Transverse CT scan of the abdomen shows splenomegaly before embolization .....	56
<b>Figure (IX B):</b>	Transverse CT scan, obtained 4 months after embolization, shows massive necrosis (arrows) of the splenic parenchyma.....	56
<b>Figure (X A):</b>	Splenic arteriogram, obtained before embolization, shows normal anatomy and parenchymal enhancement pattern .....	57

## LIST OF FIGURES (Cont...)

Fig. No.	Title	Page No.
<b>Figure (XB):</b>	Splenic arteriogram, obtained after nonselective embolization shows abrupt occlusion (arrows) of many splenic arterial branches and patchy remnants (10%–20%) of parenchymal blush .....	57
 <i><u>Figures in the results</u></i>		
<b>Figure (1):</b>	Age and Sex Distribution of the studied cases. ....	81
<b>Figure (2):</b>	The state of esophageal varices in the studied patients. ....	83
<b>Figure (3):</b>	Comparison between thrombopiotien level at Level 0, 1 and 2. ....	85
<b>Figure (4):</b>	Comparison between Platelet level at Level 0, 1 and 2. ....	85
<b>Figure (5):</b>	Comparison between the Studied group and Control group according to the thrombopoiten level (A) and platelet level (B).....	86
<b>Figure (6):</b>	Roc curve of the thrombopiotien level.....	89

## **LIST OF ABBREVIATIONS**

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

## **LIST OF ABBREVIATIONS (Cont...)**

<b>Abbrev.</b>	<b>Full term</b>
<b>OV</b>	Oesophageal varices
<b>PC\SD</b>	Platelet count/splenic diameter
<b>PHG</b>	Portal hypertensive gastropathy
<b>PPV</b>	Positive predictive value
<b>PSE</b>	Partial splenic arterial embolization)
<b>PTT</b>	Partial thromboplastin time
<b>PV</b>	Portal vein
<b>SAE</b>	Splenic artery embolization
<b>T.bil</b>	Total bilirubin
<b>TPO</b>	Thrombopoietin
<b>TPO-R</b>	Thrombopoietin receptor
<b>vWF</b>	von Willebrand factor
<b>WBC</b>	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/  $\mu$ L). 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 ( $>75,000/\mu\text{L}$ – $<150,000/\mu\text{L}$ ) is minimal and usually does not interfere with treatment or management decisions.

Moderate thrombocytopenia (50,000 / $\mu$ L–75,000 / $\mu$ L) is observed in approximately 13% of cirrhotic patients. Severe thrombocytopenia (<50,000/ $\mu$ L) 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

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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)*.