



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



HANAA ALY



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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**ADAMTS13 and von Willebrand Factor Levels
in Patients with Chronic Hepatitis C:
Relations to Hemostatic Imbalance
and Bacterial Infection**

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسببائك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
ADAM	: A Disintegrin and Metalloprotease
ADAMTS13	: A dis-integrin and metalloproteinase with a Thrombospondin type-1 motif
AF	: Ascitic fluid
ALT	: Alanine amino transferase
ANC	Absolute neutrophil count
aPTTs	: Activated partial thromboplastin times
AST	: Aspartate amino transferase
AT	: Antithrombin III
CRP	: C reactive protein
CUB	: Complement component C1r/C1s, Uegf, and bone morphogenic protein 1 domain.
cys-rich	: Cysteine-rich domain
dis-like	: Disintegrin-like domain
EDTA	: Ethylenediaminetetraacetic acid
EGF	: Epidermal growth factor
GP Ib	: Glycoprotein Ib
GP Ib-IX-V	: Glycoprotein Ib-IX-V
Hb	: Hemoglobin
HCT	: Hematocrit value
HMWM	: High molecular weight multimers
HSCs	: Hepatic stellate cells
LBP	Lipopolysaccharide binding protein
MCV	: Mean cell volume

mRNA	: Micro ribonucleic acid
PAI-1	: Plasminogen activator inhibitor-1
PAI-2	: Plasminogen activator inhibitor-2
PC	: Proteins protein C
PH	: Portal hypertension
PHT	: Portal hypertension
PMN	: Polymorphonuclear
pro-VWF	: Von Willebrand factor propeptide
PS	: Protein S
PT	: Prothrombin times
PVT	: Portal vein thrombosis
RBCs	: Red cell count
ROC	: Receiver operating characteristics
RT-PCR	: Reverse transcriptase-polymerase chain reaction
SBP	: Spontaneous Bacterial Peritonitis
SP	: Signal peptide
TAFI	: Thrombin Activatable Fibrinolysis Inhibitor
TM	: transmembrane domain
tPA	: Tissue plasminogen activator
TSP1	: Thrombospondin type-1 motifs
TTP	: Thrombotic thrombocytopenic purpura
UL-VWF	: Ultra large Von Willebrand factor
VWF	: Von Willebrand factor
VWF Ag	: Von Willebrand factor antigen
WBCs	: White blood cell count

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Introduction

Von Willebrand factor (VWF) is a multimeric glycoprotein that is primarily secreted by activated endothelial cells. It supports platelet adhesion and aggregation in a high shear stress environment (**Van Mourik *et al.*, 1999**). VWF levels are not only markers of portal hypertension but are also independently linked to bacterial translocation, inflammation and procoagulant imbalance. Their levels also predict most clinical events and mortality independently of the severity of portal hypertension (**Mandorfer *et al.*, 2018**).

The hemostatic and thrombogenic potential of VWF depends on its multimer size, which is regulated by ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type-1 motif, that cleaves VWF multimers to smaller forms less capable of activating platelets (**Soejima *et al.*, 2001**). Decreased ADAMTS13 activity is a feature of thrombotic thrombocytopenic purpura associated with the abundance of unprocessed, ultra-large VWF in plasma facilitating a prothrombotic state (**Tsai *et al.*, 2003**).

ADAMTS13 mRNA is primarily expressed in the liver (**Levy *et al.*, 2001; Zheng *et al.*, 2001**). The hepatic stellate cells are considered a major source of the circulating enzyme (**Zhou *et al.*, 2005; Uemura *et al.*, 2008**). Activation of quiescent stellate cells to activated liver myofibroblasts