Study Of P-selectin Glycoprotein Ligand 1 (PSGL-1) And Soluble P-selectin In Chronic Liver Disease And Their Correlation With Bleeding Or Thrombosis

THESIS

Submitted In Partial Fulfillment For Master Degree In Clinical And Chemical Pathology

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2008

ABSTRACT

Bleeding and thrombotic complications are common problems in patients with chronic liver disease. P-selectin is platelet activation marker that has been shown to be involved in thrombogenesis as well as bleeding disorders and may represent a possible link between inflammation and thrombosis through its adhesion to P-selectin glycoprotein ligand-1(PSGL-1, CD162) on leukocytes. PSGL-1 is a disulfide-bonded homodimeric mucin-like glycoprotein on leukocytes that interacts with P-, L-, and E-selectin. Thrombomodulin is a trasmembrane endothelial receptor involved in protein C pathway and may play a role in regulation of coagulation and inflammation processes. In order to investigate the clinical and pathogenic role of sP-selectin, CD162 and serum thrombomodulin in chronic liver disease, they were measured in 35 patients with chronic liver disease divided into; portal vien thrombosis group (PVT)(n=14), hematemesis group (n=11) and conservative treatment group (n=10). sP-selectin was significantly elevated in all patient groups as a part of inflammatory and immunological reactions that take place in patients with chronic liver disease. However among the 3 studied groups, the patients with hematemesis showed the highest elevation, may be due to hyperactivity of platelets, while in the PVT the lowest increase in sP-selectin level was recorded. This could be due to consumption of sP-selectin during clot formation. However, decrease surface expression of CD162 on neutrophils was detected in all our studied groups; this may be due to leukocyte activation and endtoxemia occurring in chronic liver disease. Thrombomodulin was significantly elevated in all patient groups and portal PVT showed the highest increase due to its hypersecretion from the activated endothelium with thrombus

formation. However, marked elevation of thrombomodulin in patients with chronic liver disease could be one of hepatoma markers.

Key wards:

sP-selectin, thrombomodulin, P-selectin glycoprotein ligand-1 (PSGL-1, CD162), chronic liver disease, portal vein thrombosis, hematemesis and hepatocellular carcinoma.

ACKNOWLEDGEMENT

"All the Praises and Thanks be to Allah,
The Lord of the Alamin"

I wish to express my deepest gratitude to **Professor Dr. Hoda Sadeek**, Professor of Clinical Pathology, Faculty of Medicine, Cairo University, for her effective guidance, valuable suggestions, unlimited help and unfailing support.

I wish to express my deep appreciation and profound gratitude to **Professor Dr. Bothaena Madkour,** professor of Hematology, Theodor Bilharz Research Institute, for her indispensable guidance, instructive supervision, and continuous support since the very beginning of this research work.

I would like to extend my thanks to **Professor Dr. Salwa Toeima**, Professor of Haematology and Head of Hematology Theodor Bilharz Research Institute, for providing all the facilities possible for the success of this work.

I am greatly honored to express my sincere gratitude and deep appreciation to **Dr. Eman Abd-El Mohesn**, lecturer of Clinical Pathology, Faculty of Medicine, Cairo University for her gracious help and support.

I would like to extend my thanks to **DR. Abia Fouad** lecturer of Haematology, Theodor Bilharz Research Institute, for her help and support.

Many thanks go to my colleagues and the staff members of Hematology Department, Theodor Bilharz Research Institute, for their kind help and moral support.

I dedicate this work to my parents who have done and still doing a lot to me without waiting for anything in return and I hope I can pay even a small part of my debt to them.

Finally, I wish to thank my dear husband for his support, love and patience.

List of ABBREVIATIONS

Abbreviation	The full term
5-HT	5-hydroxytryptamine
ADP	Adenosine diphosphate
ADPase	Adenosine diphosphatase
AICF	Accelerated intravascular coagulation and fibrinolysis.
AIH	Autoimmune hepatitis
ALD	Autoimmune liver disease
ALT	Alanine aminotransferase.
AMA	Antimitochondrial antibodies
ANA	Anti nuclear reactivities
APC	Activated protein C
AST	Aspartate aminotransferase
AT III	Antithrombin III
BCS	Budd-Chiari syndrome
β-TG	Beta thromboglobulin
C4b	Complement system
Ca^{++}	Calcium
c-AMP	Cyclic adenosine monophosphate
c DNA	Complementary deoxyribonucleic acid
CD	Cluster of differentiation
cGMP	Cyclic guanosine monophosphate
COX-1	Cyclooxygenase-1
CR	Consensus repeat
CTL	Cytotoxic T lymphocyte
DIC	Disseminated intravascular coagulation
EDRF	Endothelial derived relaxing factor
EGF	Epidermal growth factor
ECs	Endothelial cells
ENA-78	Extractable nuclear antigen-78
EPCR	Endothelial cell protein C receptor
ERK	Extracellular signal-regulated kinase
F1+2	Fragments 1+2
Fmlp	*N*-formyl-methionyl-leucyl-phenylalanine
FucT-VII	Fucosyltrasferase enzyme
GAG	Glycosaminoglycans
gla	γ-carboxyglutamic acid
GlyCAM-1	Glycosylation-dependent cell adhesion molecule 1
GP	Glycoprotein
Hb	Hemglobin concentration.
HBV	Hepatitis B virus

HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HMWK	High-molecular-weight kininogen
HPC	Hematopoietic progenitor cells
HRG	Histidine-rich glycoprotein
ICAM-1	Intercellular adhesion molecule–1
LC1	Liver cytosol type 1
LFA- 1	Leukocyte function-associated antigen–1
LKM1	Liver kidney microsomal antibody type 1
IL	Interleukin
LPS	Lipopolysaccharide
Ma	Maximum amplitude
Mac-1	Leukocyte integrin alpha M beta2
MAPK	Mitogen activated protein kinases
MOH	The Egyptian Ministry of Health
mRNA	Messenger ribonucleic acid
NF-Kb	Nuclear Factor κB
NO	Nitric oxide gas
OCS	Open Canalicular System
PAF	Platelet activating factor
PAI-1	Plasminogen activator inhibitor-1
PAIg	Platelet- associated immunoglobulin
p-ANCA	Anticytoplasmic neutrophil antibodies with perinuclear pattern
PAR1	protease-activated receptor-1
PC	Protein C
PF3	Platelet factor 3
PF4	Platelet factor 4
PFA-100	Platelet function assay
PGI_2	Prostaglandin
PIVKA	Proteins Induced by Vitamin K Absence
PMA	Phorbol 12-myristate acetate
PS	Protein S
PSC	Primary sclerosing cholangitis
PSGL-1	P-selectin glycoprotein ligand 1
PT	Prothrombin time
PTT	Partial thromboplastin time
PVT	Portal vien thrombosis
RANTES	Regulated upon activation normal T cell expressed presumed secreted
RBCs	Red blood cells.
scu-PA	Single-chain urokinase-type plasminogen activator
SERPINS	Serine protease inhibitors
SMA	Anti smooth muscle antibodies

TAFI	Thrombin-activatable fibrinolysis inhibitor
TAT	Thrombin-antithrombin III complex
TBRI	Theodor Bilharz Research Institute
tcu-PA/T	Thrombin-cleaved 2-chain urokinase-type plasminogen activator
tPA	Tissue plasminogen activator
TEG	Thromboelastography
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
Th1	T helper 1
Th2	T helper 2
TIPS	Transjugular intrahepatic portosystemic shunt
TM	Thrombomodulin
TMLeD/LeD	Lack the N-terminal lectin-like domain of TM
TNF-α	Tumor necrosis factor- α
Tpa	Tissue plasminogen activator
TPO	Thrombopoietin
TT	Thrombin time
TXA2	Thromboxane A2
VEGF	Vascular endothelial growth factor
VLA-4	Very late activation–4
vWF	von Willebrand Factor
WBCs	White blood cells

LIST OF CONTENTS

LIST OF FIGURES

PAGE

PAGE

LIST OF TABLES

PAGE

PAGE