Assessment of Quantitative D-dimer levels in Egyptian Patients with Budd-Chiari syndrome

Thesis

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By

Mohamed Ahmed Bahgat
M.B.B.CH
Faculty of Medicine - Ain Shams University

Supervised by

Professor/ Mohamed Amin Sakr
Professor of Tropical Medicine
Faculty of Medicine- Ain Shams University

Professor/ Manal Fawzy Ghozlan
Professor of clinical pathology
Faculty of Medicine- Ain Shams University

Doctor/ Runia Fouad EL-Folly
Assistant Professor of Tropical Medicine
Faculty of Medicine- Ain Shams University

Faculty of Medicine – Ain shams university
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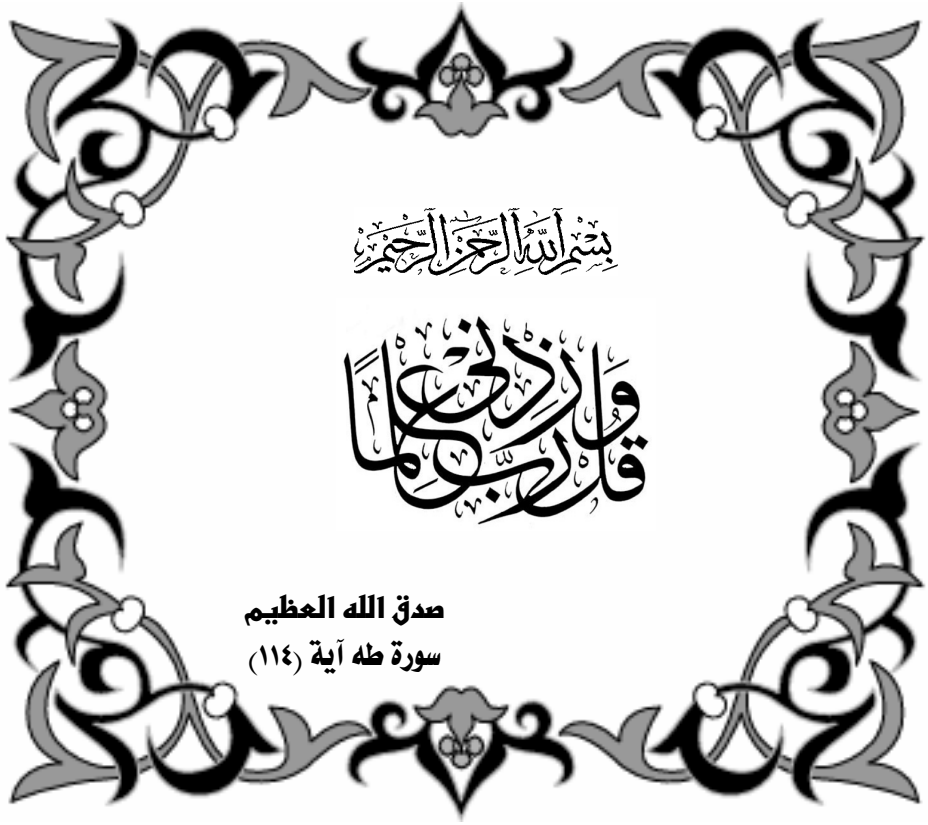

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List of Abbreviations

Abb.	Meaning
a PTT	Activated partial thromboplastin time
ACL	Anti cardiolipin
ALB	Albumin
ALT	Alanin amino-transferase
ANA	Anti Nuclear Antibody
Anti-DNA	Anti double stranded DNA
aPC	Activated protein C
APLAS	Antiphospholipid antibody syndrome
AST	Aspartate amino-transferase
AT III	Anti Thrombin III
BCS	Budd-Chiari syndrome
BCSG	Budd-Chiari Study Group
BK	BradyKinin
BMA	Bone marrow aspirate
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CD	Clusters of differentiation
Cr.	Creatinine
CSF	Cerebrospinal fluid
CT	Computed Tomography
CV	Central vein
D. Bil	Direct Bilirubin
Da	Dalton (unit)
DIC	Disseminated Intravascular Coagulopathy
DVT	Deep Venous Thrombosis
EASVLD	Egyptian Association for the Study of Vascular Liver Diseases
ELFA	Enzyme- linked immunofluorescent immunoassays
ELISA	Enzyme-linked immunosorbent assay
ESR	Erythrocyte sedimentation rate
Fb	Fibrin
FDPs	Fibrin Degradation Products
Fg	Fibrinogen
FVLM	Factor V Lieden Mutation

List of Abbreviations (Cont...)

Abb.	Meaning
GIT	Gastro-Intestinal Tract
Gla	Glutamic acid
HA	Hepatic Artery
Hb	Hemoglobin
HCC	Hepato-cellular Carcinoma
HELLP	Hemolysis, elevated liver enzymes and low platelets
HMWK	High molecular weight kininogen
HS	Highly Significant
HSPG	Heparan sulfated proteoglycans
HV	Hepatic Vein
IgG	Immunoglobulin G
IgM	Immunoglobulin M
INR	International Normalized Ratio
IV	Intravenous
IVC	Inferior Vena Cava
JAK_2	Janus tyrosine kinase-2
K	Kallikrien
K	Potassium
KFT	Kidney function test
LAC	Lupus Anti Coagulant
LL	Lower Limb
LMWH	Low Molecular Weight Heparin
MPD	Myeloproliferative disorders
MPs	Microparticles
MRI	Magnetic Resonance Imaging
MTHFR	Methylenetetrahydro-folate reductase
Na	Sodium
NS	Non Significant
PAI	plasminogen activator inhibitor
PAI-1	plasminogen activator inhibitor-1
PC	Protein C
PE	Pulmonary Embolism
PGM	Prothrombin Gene Mutation
PK	Prekallikrien

List of Abbreviations (Cont...)

Abb.	Meaning
Plt.	Platelets
PNH	Paroxysmal nocturnal hemoglobinuria
PPP	Platelet Poor Plasma
PS	Protein S
PT	Prothrombin time
PTFE	Polytetrafluoroethylene
PTT	Partial thromboplastin time
PV	Portal Vein
PVT	Portal Vein Thrombosis
ROC	Receiver operating characteristic
S	Significant
SC	Subcutaneous
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
T. Bil	Total Bilirubin
TAFI	thrombin activatable fibrinolysis inhibitor
TF	Tissue Factor
TFPI	Tissue factor pathway inhibitor
TIPS	Transjugular Intrahepatic Portosystemic Shunt
TM	Thrombomodulin
t-PA	Tissue Plasminogen Activator
U/S	Ultrasound
VTE	Venous Thrombo-Embolism
vWF	von Willebrand factor
WBCs	White Blood Cells

INTRODUCTION

Budd-Chiari syndrome (BCS) is a rare disorder defined as hepatic venous outflow obstruction at any level between the hepatic veins and the right atrium but generally implies thrombosis of the hepatic veins and/or the intrahepatic or suprahepatic inferior vena cava (IVC) ***(Zahn et al., 2010).***

According to the etiology, BCS can be classified as primary (due to intrinsic intraluminal thrombosis or webs) or secondary (due to intraluminal invasion by a parasite or malignant tumor or extraluminal compression by an abscess, cyst or solid tumor) ***(Aydinli and Bayraktar, 2007).***

Thrombosis is the major cause of hepatic vein obstruction. The combination of one or more thrombogenic disorders and a triggering factor is necessary for venous thrombosis, particularly hepatic vein thrombosis. Most patients with BCS have an underlying condition that predisposes to blood clotting. Obstruction is mainly caused by primary intravascular thrombosis. At least one hereditary or acquired hypercoagulable state could be identified in 75% of patients; more than one etiologic factor may play a role in 25% of patients ***(Denninger et al., 2000)***.

Disorders associated with BCS include the following: hematological disorders including polycythemia rubra vera, paroxysmal nocturnal hemoglobinuria, unspecified myelopro-

liferative disorder, antiphospholipid antibody syndrome, essential thrombocytosis, Inherited thrombotic condition (protein C deficiency, protein S deficiency, antithrombin III deficiency, factor V Leiden mutation), pregnancy, membranous webs, oral contraceptives, chronic infections, chronic inflammatory diseases, tumors, trauma, in addition to the idiopathic cases ***(Murad et al., 2009)***.

The clinical presentation is highly variable but may be categorized as acute and perhaps fulminant hepatic failure, subacute without evidence of cirrhosis or as chronic with evidence of portal hypertension and cirrhosis ***(Zahn et al., 2010).***

Treatment strategy of BCS consists of the following graded approach; (1) anticoagulation, treatment of underlying condition, and symptomatic treatment for complications of portal hypertension in all patients with primary BCS; (2) active search for short-length venous stenoses amenable to angioplasty/stenting; (3) in patients not suited for, or unresponsive to angioplasty/stenting, insertion of a transjugular intrahepatic portosystemic stent shunt (TIPSS) should be considered; (4) and in patients unresponsive to TIPSS, liver transplantation should be considered ***(DeLeve et al., 2009).***

Despite the increasing use of TIPSS and the promising results with regard to technical success, the long-term efficacy

of TIPSS is limited by shunt stenosis or occlusion ***(Pomier-Layrargues et al., 2012).***

D-dimer is a fibrin degradation product, present as a small protein fragment in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two cross-linked D fragments of the fibrinogen protein ***(Adam et al., 2009).***

Quantitative D-dimer assays have a comparably high sensitivity, but a lower specificity, resulting in a more confident exclusion of acute VTE, at the expense of more additional imaging testing ***(Legnani et al., 2010).***

The use of a quantitative D-dimer as a first-line test in the evaluation of patients with intermediate or low clinical probability of having PE is recommended. Appropriate use of the quantitative immunoturbidimetric D-dimer assay can have a substantial influence in reducing health care costs and, more important, reducing unnecessary radiation dose during imaging to patients ***(Gupta et al., 2009).***

When interpreted in conjunction with clinical risk assessment, measurement of D-dimer predicts risk of recurrence of VTE and a positive D-dimer, as well as a negative result, may influence management decisions regarding duration of anticoagulant therapy ***(Baglin et al., 2008).***

AIM OF THE WORK

To assess the level of quantitative D-dimer in patients with BCS having confirmed well established intravascular thrombosis and to identify the possibility of using it as a non invasive method in diagnosis of new thrombotic events (HVs, IVC, PV, DVT, PE or reocclusion of stents).