بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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Factor V Leiden (FVL), Prothrombin G20210A and MTHFR C677T Mutations among Patients of Budd-Chiari Syndrome

Thesis

Submitted for Partial Fulfillment of master Degree in Clinical Pathology

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2021

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH,**
the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Afaf Abdel Aziz Abdel Ghaffar,** *Professor of Clinical Pathology, Faculty of Medicine - Ain Shams University for her keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Prof. Dr. Mohamed Tarif Hamza,** *Professor of Clinical Pathology, Faculty of Medicine - Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am so grateful also for **My Beloved Wife** *for her existence in my life and her continuous support.*

Ahmad Mahmoud

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Abb.	Full term
ACE	Angiotensin-converting enzyme
ACL	Anti-Cardiolipin
ALT	Alanine aminotransferase
ANA	Antinuclear antibody
aPC	Activated Protein
APTT	Activated partial thromboplastin time
ARMS	Amplification refractory mutation system
AST	Aspartate aminotransferase
BCS	Budd Chiari syndrome
COS	Cut-off sample
CT	Computed tomography
DNA	Deoxyribonucleic acid
DVT	Deep vein thrombosis
EASL	European Association for the Study of Liver
FVL	Factor V Leiden
GZ	Gray zone
HBG	Hemoglobin
HCC	Hepatocellular carcinoma
INR	International normalized ratio
IVC	Inferior vena cava
JAK2	Janus kinase 2
MPDs	Myeloproliferative disorders
MRI	Magnetic resonance imaging
MTHFR	Methylene tetrahydrofolate reductase
NC	Negative control
PC	Positive control
PCR	Polymerase chain reaction
PE	Pulmonary embolism
PGM	Phosphoglucomutase
PLT	Platelet
PT	Prothrombin time

List of Abbreviations Cont...

Abb.	Full term
PTT	Partial thromboplastin time
PV	Polycythemia Vera
RBCS	Red blood cells
RFLP	Restriction fragment length polymorphism
rt-PA	Recombinant tissue-type plasminogen activator
SNP	Single nucleotide polymorphism
SVT	Splanchnic vein thrombosis
TIPS	Transjugular intrahepatic portacaval shunt
VTE	Venous thromboembolism
WBC	White blood cell

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INTRODUCTION

BCS is not a primary disease of the liver parenchyma but subsequent liver dysfunction following obstruction of hepatic veins or the suprahepatic Inferior Vena Cava, hepatic venous outflow obstruction results in an elevated sinusoidal pressure and leads to hepatic congestion ***(Oblitas et al., 2020).***

Usually, congestion is followed by subsequent centrilobular fibrosis and nodular regenerative hyperplasia that lead to chronic liver dysfunction and cirrhosis; in some instances, however, it results in fulminant hepatic failure requiring emergency liver transplantation ***(Robertson and Hayes, 2015).***

There is an interesting but not as yet understood difference in the etiology and epidemiology of this condition in the West and East ***(Li et al., 2019).***

The role of the G20210A mutation of the prothrombin gene appears to be negligible in BCS patients ***(Valla, 2017; Qi et al., 2016).***

Other recently identified inherited risk factors have not been extensively studied in BCS patients ***(Li et al., 2019).***

Thrombophilic abnormalities and clonal disorders of hematopoiesis, such as Philadelphia chromosome negative MPNs both overt and occult, are etiological factors in a significant proportion of BCS cases ***(Valla, 2017).***

The prevalence of C677T MTHFR polymorphism appears to be increased in BCS patients worldwide**,** but a causal association has not been clearly established in European patients ***(Qi et al., 2016)***.

Many studies from western countries have revealed that primary BCS can be regarded as a multifactorial disease in which several prothrombotic conditions additively predispose patients to develop thrombosis in hepatic veins ***(Qi et al., 2016).***

Common prothrombotic conditions associated with BCS include inherited and acquired hypercoagulable states ***(Oblitas et al., 2020).***

BCS is a life-threatening group of disorders resulting from hepatic venous outflow obstruction, that may occur at the level of the hepatic venules (hepatic veno-occlusive disease), the large hepatic veins, inferior vena cava (IVC), or the right atrium (congestive hepatopathy) ***(Robertson and Hayes, 2015).***

The clinical presentation is highly variable; from being asymptomatic to fulminate, acute, sub-acute, and chronic subtypes depending on duration of the disease, biochemical disturbance, and liver histology ***(Robertson and Hayes, 2015).***

FVL (**rs6025**) is a variant of human factor V which causes an increase in blood clotting (hypercoagulability). Due to this mutation, Protein C, an anticoagulant protein which