



بسم الله الرحمن الرحيم

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15 Years Survival of Budd-Chiari Patients in a Single Center Study

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿قَالُوا سُبْحٰنَكَ لَا عِلْمَ لَنَا

إِلَّا مَا عَلَّمْتَنَا ۗ إِنَّكَ أَنْتَ

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List of Abbreviations

Abb.	Full term
<i>AC:</i>	<i>Anticoagulants</i>
<i>ANA:</i>	<i>Anti- nuclear- antibody</i>
<i>APS:</i>	<i>Antiphospholipid syndrome</i>
<i>AST& ALT:</i>	<i>Serum aspartate and alanine Aminotransferases levels</i>
<i>AT:</i>	<i>Antithrombin</i>
<i>BCS:</i>	<i>Budd-Chiari Syndrome</i>
<i>BIL:</i>	<i>Bilirubin</i>
<i>BM:</i>	<i>Bone Marrow</i>
<i>CBC:</i>	<i>Complete blood count</i>
<i>CT:</i>	<i>Computed Tomography</i>
<i>DDLT:</i>	<i>Deceased donor liver transplantation</i>
<i>DOACs:</i>	<i>Direct oral anticoagulants</i>
<i>ET:</i>	<i>Essential thrombocytosis</i>
<i>FVLM:</i>	<i>Factor V Leiden mutation</i>
<i>GERD:</i>	<i>Gastro-Esophageal reflux disorder</i>
<i>HBV:</i>	<i>Hepatitis B virus</i>
<i>HCC:</i>	<i>Hepatocellular carcinoma</i>
<i>HCV:</i>	<i>Hepatitis C virus</i>
<i>HVOTO:</i>	<i>Hepatic venous outflow tract obstruction</i>
<i>INR:</i>	<i>International normalised ratio</i>
<i>IRHV:</i>	<i>Inferior right hepatic vein</i>
<i>IVC:</i>	<i>Inferior vena cava</i>
<i>JAK2:</i>	<i>Janus Kinase 2</i>
<i>LCF:</i>	<i>Liver cell Failure</i>
<i>LDLT:</i>	<i>Living donor liver transplantation</i>
<i>LFTs:</i>	<i>Liver function tests</i>
<i>LHV:</i>	<i>Left hepatic vein</i>
<i>LMWH:</i>	<i>Low molecular weight heparin</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>LT:</i>	<i>Liver transplant</i>
<i>LTHV:</i>	<i>Left Hepatic vein</i>
<i>MELD:</i>	<i>Model for End-Stage Liver Disease</i>
<i>MPN:</i>	<i>Myeloproliferative neoplasms</i>
<i>MR:</i>	<i>Magnetic resonance</i>
<i>MRI:</i>	<i>Magnetic resonance imaging</i>
<i>MTHFR:</i>	<i>Methyl tetra hydro folate reductase</i>
<i>OLT:</i>	<i>Orthotopic liver transplantation</i>
<i>OV:</i>	<i>Oesophageal varices</i>
<i>PC def:</i>	<i>Protein C deficiency</i>
<i>PGM:</i>	<i>Prothrombin gene mutation</i>
<i>PHG:</i>	<i>Portal Hypertensive Gastropathy</i>
<i>PNH:</i>	<i>Paroxysmal Nocturnal Hemoglobinuria</i>
<i>PS def:</i>	<i>Protein S deficiency</i>
<i>PT:</i>	<i>Prothrombin time</i>
<i>PTFE:</i>	<i>Polytetrafluoroethylene</i>
<i>PV:</i>	<i>Polycythemia rubra vera</i>
<i>PVT:</i>	<i>Portal vein thrombosis</i>
<i>RTHV:</i>	<i>Right hepatic vein</i>
<i>TIPSS:</i>	<i>Transjugular intrahepatic portosystemic shunt</i>
<i>VK:</i>	<i>Vitamin K</i>

INTRODUCTION

Budd-Chiari syndrome (BCS) is defined as the obstruction of hepatic venous outflow regardless of its causative mechanism or level of obstruction. This obstruction can be traced to the small hepatic venules up to the entrance of the inferior vein cava (IVC) into the right atrium (*Valla, 2009*).

Hepatic outflow obstruction related to cardiac disease, pericardial disease or sinusoidal obstruction syndrome have different pathophysiological and clinical implications and are excluded from this definition (*Hernández-Gea et al., 2019*).

Up to 50% of all cases of BCS are due to chronic myeloproliferative disorders like polycythemia vera (PV) (*Valla, 2002*) or coagulopathies like factor V (Leiden) gene mutation (*Deltenre et al., 2001*), and some showed the inherited deficiency of protein C,S and antithrombin 3 (*Valla, 2009*).

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

It was empirical to highlight the Egyptian experience in BCS and evaluate the long term outcome of the disease in a single Egyptian university center in Cairo.

AIM OF THE WORK

The idea of this work was to report the results of a vast clinical experience over 15 years presented by Tropical medicine department Ain Shams University through analysing the patient and disease characteristics, outcome, complications and innovations in therapeutic intervention.

Ultimately this should throw lights on the understanding of the pathophysiology causes and clinical consequences of BCS among Egyptian patients.

Chapter 1**BUDD- CHIARI SYNDROME**

Budd–Chiari syndrome (BCS) is an uncommon condition, caused by obstruction to hepatic venous outflow. It is largely underdiagnosed, and a high index of suspicion is required for any patient with unexplained portal hypertension. The understanding of its etiology and pathology is improving with advances in diagnostic techniques (*Sharma et al., 2021*).

BCS is classified as primary when the obstruction to hepatic venous outflow is related to a primary venous problem, such as thrombosis, stenosis, or webs, and as secondary when it is related to extrinsic compression, such as that caused by abscess, tumor, cyst, or hyperplastic nodules (*Aydinli and Bayraktar, 2007*).

Causes

Common causes of BCS include inherited and acquired hypercoagulable states (*Menon et al., 2004*). Inherited hypercoagulable states such as factor V Leiden mutation, protein C deficiency, protein S deficiency, the prothrombin G20210A mutation, and antithrombin III deficiency are common causes of hepatic vein thrombosis resulting in BCS. Acquired prothrombotic states such as myeloproliferative disorders (e.g., polycythemia vera, paroxysmal nocturnal hemoglobinuria, essential thrombocytosis, agnogenic myeloid metaplasia, and

myelofibrosis) account for more than 50% of BCS cases (*Menon et al., 2004; Plessier et al., 2008 & Cura et al., 2009*). Other conditions have been proposed as risk factors for the development of BCS, including Behçet disease, hypereosinophilic syndrome, and ulcerative colitis (*Plessier et al., 2008*) and pregnancy, malnutrition, and the use of oral contraceptives (*Cura et al., 2009 & Pati et al., 2009*).

Pathophysiology

Once the hepatic veins occlude, the liver venous outflow is compromised, the sinusoidal and portal pressures increase, and the portal flow decreases; if this process continues, it leads to hepatic congestion; formation of ascites; and, in certain cases, portal vein thrombosis (*Menon et al., 2004*). Hepatocytes undergo hypoxic damage that eventually evolves into noninflammatory centrilobular cell necrosis (*Valla, 2002; Aydinli and Bayraktar, 2007*). If this hepatocellular damage is massive, the patient will present with a fulminant form of BCS, which is a potentially fatal condition (*Washburn et al., 2006*).

Epidemiology:

There is no evidence for a difference in incidence of BCS between the West and East. Throughout the world, nearly all cases /HVOTO appear to be caused by hepatic venous obstruction, associated or not associated with involvement of parts of the IVC. India, Pakistan, the Middle East, the