



Pregnancy Outcome in Patients with Budd Chiari Syndrome: A Single Centre Experience

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللَّهِ عَلَيْكَ
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List of Contents

Title	Page No.
List of Tables	5
List of Figures	7
List of Abbreviations.....	8
Protocol.....	
Introduction.....	- 1 -
Aim of the Work	14
Review of Literature	
▪ Budd–Chiari Syndrome (BCS)	15
▪ Pregnancy and Budd- Chiari Syndrome	54
Patients and Methods	69
Results	78
Discussion.....	101
Summary	108
Conclusion	111
Recommendations	112
References	113
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Tables of Review&patients and methods		
Table (1):	Estimates of incidence of Budd–Chiari syndrome	16
Table (2):	Approximate prevalence of major risk factors in patients with primary BCS Prevalence (%) Europe China.	19
Table (3):	Proposed workup for investigating underlying risk factors of Budd–Chiari syndrome	20
Table (4):	Proportion of patients with JACK2-V617F mutation in unselected patients with BCS in non-European countries or Turkey.	27
Table (5):	Proportion of patients with factor V Leiden mutation in unselected patients with BCS in non-European countries or Turkey:	28
Table (6):	Characteristics at presentation in Western patients with BCS/HVOTO	29
Table (7):	Child-Pugh scoring system	75
Table (8):	(Rotterdam) Murad’s BCS prognostic classification	75
Tables of Results		
Table (9):	Demographic and obstetric characteristics of the studied cases	79
Table (10):	Budd Chiari disease characteristics of the studied cases.....	81
Table (11):	Anticoagulation used among the studied cases.....	82
Table (12):	: Clinical findings of the studied cases at baseline.....	84
Table (13):	Laboratory findings of the studied cases at baseline.....	87
Table (14):	US findings of the studied cases at baseline	88

List of Tables *cont...*

Table No.	Title	Page No.
Table (15):	Upper endoscopy findings of the studied cases at baseline	84
Table (16):	Pregnancy outcome of the studied cases	89
Table (17):	Comparison according to pregnancy fate regarding demographic and obstetric characteristics	91
Table (18):	Follow up events among the studied cases	92
Table (19):	Comparison according to pregnancy fate regarding Budd Chiari disease characteristics...	93
Table (20):	Comparison according to pregnancy fate regarding given treatment.....	94
Table (21):	Comparison according to pregnancy fate regarding clinical findings	96
Table (22):	Comparison according to pregnancy fate regarding laboratory findings.....	97
Table (23):	Comparison according to pregnancy fate regarding US findings.....	98
Table (24):	Comparison according to pregnancy fate regarding Upper endoscopy findings.....	99
Table (25):	Follow up events among the studied cases	100
Table (26):	Logistic regression for factors affecting abortion.....	100

List of Figures

Fig. No.	Title	Page No.
Figures of Review		
Fig. (1):	Occlusion of upper part of IVC	37
Fig. (2):	CT in a 28-year-old female with idiopathic acute Budd-Chiari syndrome demonstrates hepatomegaly with diffuse patchy enhancement due to hepatic congestion and necrosis	38
Fig. (3):	A 42-year-old female patient with chronic Budd-Chiari syndrome demonstrates large enhancing regenerative nodule (arrow) as well as ascites and lack of hepatic opacification due to congestion and necrosis	40
Fig. (4):	Short segment obstruction in inferior vena cava	41
Fig. (5):	Collateral veins in Budd-Chiari syndrome.	42
Fig. (6):	Proposed algorithm for management of patients with Budd-Chiari syndrome (BCS)/ hepatic venous outflow tract obstruction (HVOTO).....	53
Fig. (7):	Shows prevalence of pregnancy related BCS among different countries.....	60
Figures of Results		
Fig. (8):	Anticoagulation given in 1 st trimester among the studied cases.	83
Fig. (9):	Pregnancy outcome of the studied cases	90
Fig. (10):	Comparison according to pregnancy fate regarding given treatment.....	95

List of Abbreviations

Abb.	Full term
A.....	<i>Aorta</i>
AFP.....	<i>Alpha feto protein</i>
ALT.....	<i>Alanine aminotransferase</i>
ANA	<i>Antinuclear antibody</i>
APL	<i>Antiphospholipid</i>
AST.....	<i>Aspartate aminotransferase</i>
AZ	<i>Azygos vein</i>
BCS.....	<i>Budd chiari syndrome</i>
BCSG	<i>Budd chiari study group</i>
CALR	<i>Calreticulin gene</i>
CI.....	<i>Confidence interval</i>
CS	<i>Caesarean section</i>
CT.....	<i>Computed tomography</i>
DM	<i>Dibetes mellitus</i>
DNA	<i>Deoxyribonucleic acid</i>
DVT	<i>Deep venous thrombosis</i>
ET	<i>Essential thrombocytosis</i>
FDA.....	<i>Food and drug administration</i>
FVLM.....	<i>Factor v leiden mutation</i>
GA	<i>Gestional age</i>
GI.....	<i>Gastrointestinal</i>
HELLP.....	<i>H : hemolysis – el :elevated liver enzymes – lp: low platlets</i>
Hb	<i>Hemoglobin</i>
HBV	<i>Hepatitis b virus</i>
HCC.....	<i>Hepatocellular carcinoma</i>
HCV	<i>Hepatitis c virus</i>
HVOTO.....	<i>Hepatic venous outflow tract obstruction</i>
ICU	<i>Intensive care unit</i>
INR.....	<i>International normalization ratio</i>
IRHV.....	<i>Inferior right hepatic vein</i>

List of Abbreviations cont...

Abb.	Full term
<i>IUD</i>	<i>Intrauterine device</i>
<i>IVC</i>	<i>Inferior vena cava</i>
<i>IVF</i>	<i>In vitro fertilization</i>
<i>LFT</i>	<i>Liver function tests</i>
<i>LIPV</i>	<i>Left inferior phrenic vein</i>
<i>LL</i>	<i>Lower limb</i>
<i>LMWH</i>	<i>Low molecular weight heparin</i>
<i>LRV</i>	<i>Left renal vein</i>
<i>MELD</i>	<i>Model for End-Stage Liver Disease</i>
<i>MPL</i>	<i>Myeloproliferative leukemia virus oncogene</i>
<i>MPN</i>	<i>Myeloproliferative neoplasms</i>
<i>MRI</i>	<i>Magnetic resonance</i>
<i>MTHFRD</i>	<i>Methyl tetrehydro folate reductase</i>
<i>NA</i>	<i>Not applicable</i>
<i>NICU</i>	<i>Neonatal intensive care unit</i>
<i>OCP</i>	<i>Oral contraceptive pills</i>
<i>PAP</i>	<i>Pulmonary artery pressure</i>
<i>PD</i>	<i>Protein deficiency</i>
<i>PH</i>	<i>Pulmonary hypertension</i>
<i>PHG</i>	<i>Portal hypertensive gastropathy</i>
<i>PLT</i>	<i>Platlats</i>
<i>PT</i>	<i>Prothrombin</i>
<i>PTT</i>	<i>Partial thromboplastin time</i>
<i>PVT</i>	<i>Portal vein thrombosis</i>
<i>RUQ</i>	<i>Right upper quadrant</i>
<i>SAAG</i>	<i>Serum ascites albumin gradient</i>
<i>SD</i>	<i>Standard deviation</i>
<i>SLE</i>	<i>Systemic lupus erythromatosis</i>
<i>Smv</i>	<i>Superior mesenteric vein</i>
<i>SPSS</i>	<i>Statistical package for social sciences</i>
<i>SV</i>	<i>Splenic vein</i>

List of Abbreviations *cont...*

Abb.	Full term
<i>TIPSS</i>	<i>Transjugular intrahepatic portosystemic shunt</i>
<i>UFH</i>	<i>Unfractionated heparin</i>
<i>US</i>	<i>Ultrasound</i>
<i>US</i>	<i>United states</i>
<i>UTI.....</i>	<i>Urinary tract infection</i>
<i>WBC</i>	<i>White blood cells</i>

INTRODUCTION

Budd-Chiari syndrome (BCS) is a rare disorder caused by hepatic venous outflow obstruction and resulting hepatic dysfunction due to sinusoidal congestion, ischaemic injury to the liver and portal hypertension (*Valla, 2003*). The main mechanism for BCS is thrombosis of the hepatic veins or of the terminal portion of the inferior vena cava (*Janssen et al., 2003*). The diagnosis of BCS is based on the demonstration of a hepatic venous outflow tract obstruction. This obstruction can be accurately documented by non-invasive imaging such Doppler ultrasonography, computed tomography (CT) or magnetic resonance imaging (MRI). Doppler ultrasonography is regarded as the initial technique of choice and offers a high sensitivity and specificity (*Bolondi et al., 1991*).

The exact prevalence of BCS is unknown but has been estimated as 1 per 100000 of the general population worldwide (*Valla, 2003*), with a higher prevalence being evident in developing countries such as India, Nepal, South Africa (*Wang and Jones, 1996*). BCS affects all races, usually during the third or fourth decades of life, and is more common in females (*Valla, 2002*).

In Egypt the epidemiology of BCS showed that the presentation was chronic in 79.8% of patients, acute or subacute in 19.1% and fulminant in 1.1%. Factor V Leiden mutation (FVLM) was the most etiological cause of the disease

(53.1%) followed by mutation of the gene encoding for methyl tetra hydro folate reductase (MTHFR) (51.6%). Current or recent hormonal treatment was documented in 15.5% of females, aetiology couldn't be determined in 8.5% of patients. Males had significantly higher rates of MTHFR gene mutation and Bechet's disease, while females had significantly higher rates of secondary antiphospholipid antibody syndrome (*Sakr et al., 2011*).

The management using stepwise regimens is largely successful with anticoagulation and interventional radiology alone. Stepwise regimen includes; anticoagulant therapy for an indefinite period; angioplasty or stenting for stenosis of hepatic veins; and decompressive techniques [surgical shunt or trans jugular intrahepatic portosystemic shunts (TIPSS)] for patients who are nonresponsive to medical treatment or not candidates for angioplasty/Stenting (*EASL, 2016*). TIPSS has a lower morbidity and mortality rate than surgery and is a preferred approach. The outcomes are favourable with 10-year survival approaching 90% (*Tripathi et al., 2017*).

Patients with BCS usually have risk factors for venous thromboembolism. Pregnancy is a hypercoagulable state and earlier studies reported that women with BCS could be at risk of developing severe exacerbation of their underlying disease during pregnancy (*Dilawari et al., 1994*). Several previously reported observations suggest that pregnancy in BCS women in the West could cause deterioration of the liver disease and

pregnancy was associated with development of ascites in several women with known BCS (*Martinelli et al., 2006*).

The desire for pregnancy is increasingly expressed by those young patients once their condition has greatly improved.

Data concerning pregnancy in women with BCS is scarce and thus there are no clear-cut guidelines for the outcome and management of pregnancy in patients with BCS (*Valla, 2008*).

AIM OF THE WORK

To assess the maternal and foetal outcome in a group of women who became pregnant while having BCS.

Chapter 1

BUDD–CHIARI SYNDROME (BCS)

Budd–Chiari syndrome (BCS) has been defined as an obstruction of the hepatic venous outflow tract without any cardiac disorder. The obstacle causing BCS may be located in the small or large hepatic veins or on the suprahepatic portion of inferior vena cava (IVC), but does not include sinusoidal obstruction syndrome/ hepatic veno-occlusive disease (*Valla, 2009*).

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 Mediterranean, and Europe share many characteristics including of the level of obstruction and individual causal factors. However, in China, involvement of the IVC may be common. Availability of the experts in noninvasive imaging techniques are essential for diagnosis of cases in different populations and to obtain reliable epidemiological data (*Valla, 2009*).

Table (1) shows that prevalence of BCS in Europe has been relatively consistent [0.35–0.8 cases per million (pmi) per