INTRODUCTION

Budd-Chiari syndrome (BCS) represents a spectrum of disease states resulting in hepatic venous outflow occlusion. Obstruction can occur at any level from the hepatic venules to the right atrium of the heart. Anatomic abnormalities including vascular webs or strictures may be present and possibly predispose to venous thrombosis ***(Zimmerman et al., 2006).***

BCS is considered primary or secondary depending on the origin of the obstructive lesion. If obstruction is the result of endoluminal venous lesion like thrombosis, primary BCS is considered. In secondary BCS, the cause originates from neighboring structures like extrinsic compression or tumor invasion ***(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)***

Early diagnosis of Budd-Chiari syndrome is important for establishing appropriate treatment. Because of inhomogeneous distribution of disease in the liver, normal biopsy findings do not exclude this entity ***(Janssen et al., 2003).***

Therefore imaging studies combined with clinical information are often essential for reaching a definitive diagnosis. Evaluation of occlusion of the hepatic veins, inferior vena cava, caudate lobe enlargement, inhomogeneous liver enhancement, presence of intrahepatic collateral vessels and hypervascular nodules is the most important role of imaging examinations of patients with Budd-Chiari syndrome ***(Brancatelli et al., 2007).***

After the documentation of BCS, etiologic factors must be assessed. Hemogram, evaluation of peripheral blood, determination of coagulation factors and inhibitors, genetic tests for factor V and prothrombin, determination of antiphospholipid antibody and lupus anticoagulant, and flow cytometry for paroxysmal nocturnal hemoglobinuria should be performed ***(Aydinli and Bayraktar., 2007).***

Bone marrow biopsy is helpful for diagnosis of primary myeloproliferative disorder and determination of total red cell mass. If available, peripheral blood or bone marrow cultures could be performed for assessment of spontaneous erythroid colony formation, a supportive finding of myeloproliferative disorder ***(Acharya et al., 1995).***

The goals of treatment are to alleviate venous obstruction, prevent extension of thrombosis in the hepatic veins and preserve hepatic function by decreasing the centrilobular congestion. Diagnostic workup to identify the underlying cause should be considered at the time of the initial diagnosis ***(Bayraktar et al., 2007).***

Most patients require an aggressive multidisciplinary approach, including invasive radiologic procedures and surgery, to control symptoms and prevent disease progression. Liver transplantation recently has emerged as the preferred therapy for patients who have fulminant liver failure or cirrhosis ***(Srinivasan et al., 2002)*** and although the cadaveric organ pool is limited, portosystemic shunts remain a therapeutic alternative in patients who have preserved liver function ***(Zimmerman et al., 2006).***

AIM OF THE WORK

The aim of this work is to demonstrate and evaluate the outcome and disease course of patients with Budd-Chiari syndrome after non surgical hepatic decompression techniques in the form of either angioplasty (balloon dilatation with or without hepatic vein stenting) or Transjugular Intrahepatic Portosystemic Shunt (TIPS).

This study will include description of possible procedure related complications and their management as well as clinical, laboratory and radiological assessment of patients.

HEPATIC VASCULAR PHYSIOANATOMIC SPOTLIGHTS

Hepatic circulation:

The vascular system of solid organs has arterial inflow and venous outflow. The liver is unusual in that it derives inflow from both an arterial and venous source. The hepatic artery (HA) contributes 25% of the liver's blood supply and 50% of the hepatic parenchyma oxygen supply. The HA is closely related anatomically to the bile ducts and is critical to these structures in that it is the exclusive supplier of blood flow to the biliary system ***(Deshpande et al., 2002).***

The portal vein (PV) contributes the majority of the liver's blood flow (75%) and accounts for the remaining 50% of the oxygen supply. There are no direct vascular connections between the PV and HA circulations. Blood from both systems enters the hepatic sinusoids at different levels and then unites to empty into central veins (CV_s). From the (CV_s), the circulation enters the principal hepatic venous outflow tracts known as the hepatic veins (HV_s). There are three major HV_s (right, middle, and left). Blood leaves the HV to enter the inferior vena cava (IVC) at a level just below the diaphragm before entering the right atrium **(Fig. 1)** ***(Gilroy and Sorrell, 2006).***

The liver is divided into eight segments. The segmental division is derived from the vascular supply emanating from the major branches of the left and right portal vein. Accompanying

the PV branches to the segments are equivalent first-order divisions of the left and right HAs and bile ducts. The major HVs do not correspond to the segmental division of the liver. The three HVs, also known as the right, middle, and left HV, lie in the fissures between the hepatic segments ***(Gilroy and Sorrell, 2006).***

Figure (2) provides a useful reference for understanding the segmental anatomy of the liver and illustrates common hepatic resection planes ***(Gilroy and Sorrell, 2006).***

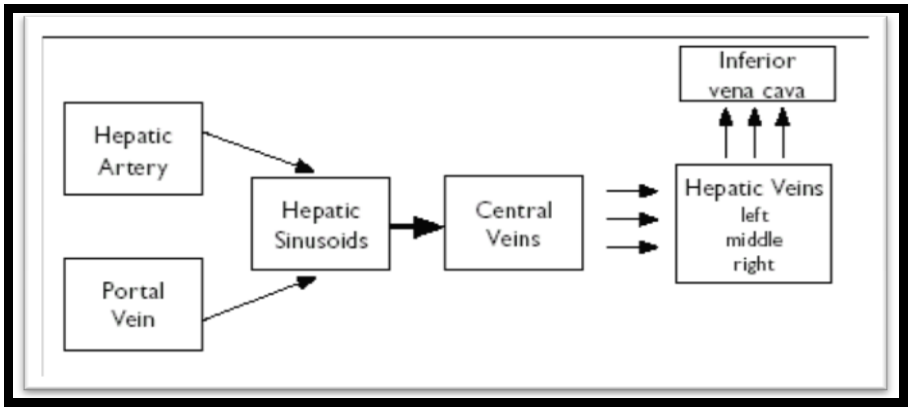

Fig. (1): Hepatic blood flow ***(Gilroy and Sorrell, 2006).***

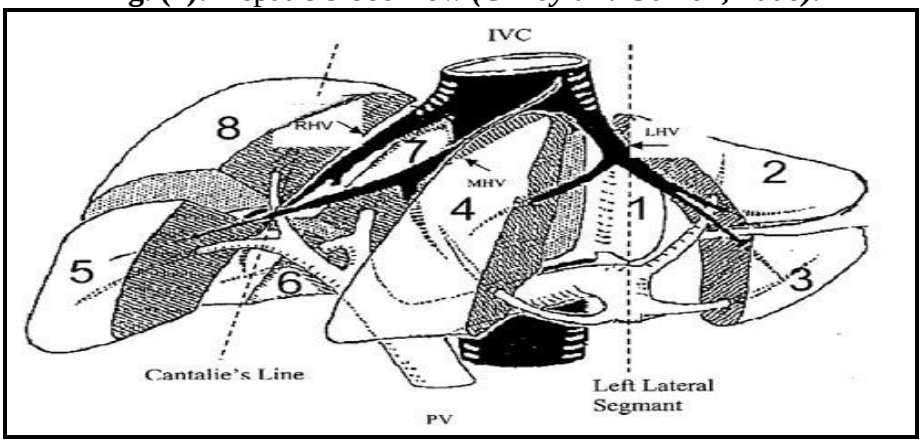

Fig. (2): Segmental anatomy of the liver ***(Gilroy and Sorrell, 2006).***

Histologically, ***Rappaport, (1980)*** divided the liver parenchyma into acini incorporating the terminal hepatic arteriole, portal venule, and bile duct with the adjacent liver parenchyma. The terminal vessels of the portal triad form the center of the acinus, and each acinus interdigitates with those adjacent to form the acinar agglomerates.

Physiologically, a gradient of oxygen and nutrient delivery to the surrounding parenchyma is established by the acinar structure. This gradient allows the liver parenchyma, lying between the portal triad and CV, to be separated into zones **(Fig 3).** Zone 1 contains hepatocytes in close proximity to the sinusoidal inflow and has high oxygen concentrations while zone 3 has lower oxygen tensions and is adjacent to the CV (outflow). These anatomic gradients, by in large, explain the pattern of injury seen in hypoperfusion syndromes where zone 3 hepatocyte injury predominates. With outflow obstruction, hepatocyte loss is also seen in pericentral regions (zone 3); however, in contrast to a hypoperfusion injury, vascular congestion adjacent to the CVs is also present ***(Gilroy and Sorrell, 2006).***

Anatomy of the hepatic veins:

There are three main hepatic veins. The middle and left veins unite before entering the vena cava in 65% to 85% of individuals ***(Honda et al., 1991).***

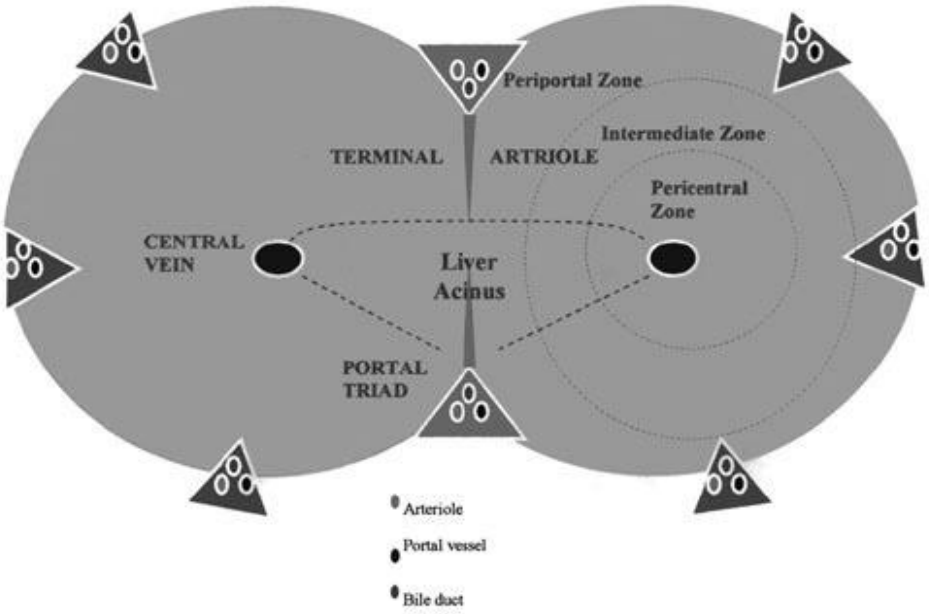

Fig. (3): Zones of the liver parenchyma ***(Gilroy and Sorrell, 2006).***

In 18% of individuals, there are two right hepatic veins draining into the vena cava ***(Cheng et al., 1997).*** In another 23%, there is a separate middle or inferior right hepatic vein draining segments V or VI, respectively. The veins have variable branching patterns. There are axial veins with four to six orders of branches at acute angles, as well as numerous much smaller branches nearly at right angles ***(Wanless, 2007).***

The caudate lobe and adjacent parenchyma are usually drained by one or two small veins directly into the vena cava caudal to the main hepatic veins. When thrombosis of the main hepatic veins occurs, the veins of the caudate lobe are often spared, allowing survival and compensatory hyperplasia of this lobe ***(Wanless, 2007).***

Anastomoses between branches of the hepatic veins are uncommon in the normal liver but may be more frequent in the presence of diseases with portal hypertension ***(Okuda and Takayasu, 1991).***

Anastomoses between branches of the hepatic veins may become enlarged and may be mistaken for the original hepatic veins on Doppler interrogation. Partial recanalization occurs, often leaving webs in the hepatic veins or vena cava. These webs were formerly thought to be congenital, although most are now considered to be acquired ***(Kage et al., 1992).***

Hepatic Collateral Circulation:

Portal hypertension leads to the development of intra- and extrahepatic venous collaterals ***(Okuda and Matsutani, 1991)*** (**Fig.4).** Extrahepatic collaterals are important, because when dilated to form varices, they are susceptible to rupture and cause massive bleeding. Varices in the submucosa of the gastrointestinal tract are most often a problem, especially in the esophagus and stomach ***(Wanless, 2007).***

Dilated umbilical or paraumbilical veins are found in 11% of patients with cirrhosis **(veins of Sappey)**. They may cause a venous hum and caput medusa at the umbilicus **(Cruveilhier-Baumgarten syndrome).** Their presence implies high pressure in the left PV and, therefore, intrahepatic vascular obstruction. The direction of flow in lower abdominal wall

collaterals is caudad if the inferior vena cava is obstructed, as in some patients with Budd-Chiari syndrome ***(Wanless, 2007).***

Varices may be found at sites where the gastrointestinal tract or pancreas becomes retroperitoneal or adherent to the abdominal wall because of pathologic processes. These **"veins of Retzius"** establish connections between the portal bed and the ascending lumbar azygos, renal, and adrenal veins ***(Wanless, 2007)***.

Within cirrhotic parenchyma, shunts are formed by anastomoses between smaller branches of the portal and hepatic veins. These shunts allow blood to bypass the sinusoidal exchange surface, leading to functional impairment. This effect is made worse by the creation of large shunts. In addition, any procedure that decreases portal flow to the sinusoids increases the likelihood of thrombosis, further increasing intrahepatic resistance. Titration of these benefits and liabilities is an important feature of surgical management. Large spontaneous shunts may be beneficial in lowering portal pressure and should not be disturbed without consideration. Portosystemic shunting appears to be responsible for reduced peripheral vascular resistance, possibly through the enhanced release of nitric oxide ***(Bernadich et al., 1997).***

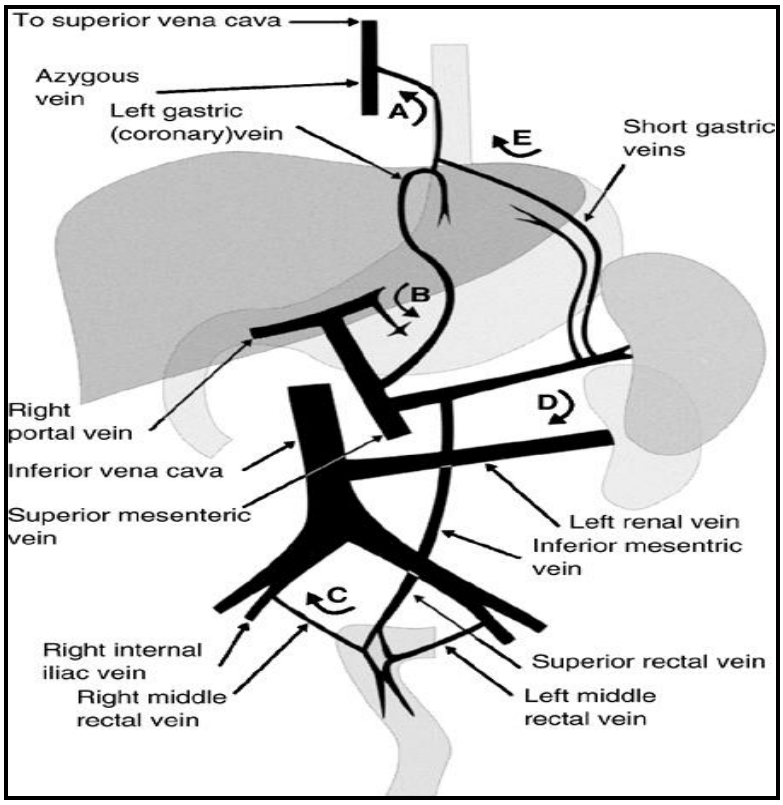

Fig. (4): Diagram of portal circulation ***(Wanless, 1997).***

The most important sites for the potential development of portosystemic collaterals are shown. **A, Esophageal submucosal veins**, supplied by the left gastric vein and draining into the superior vena cava through the azygous vein**. B, Paraumbilical veins,** supplied by the umbilical portion of the left portal vein and draining into abdominal wall veins near the umbilicus. These veins may form a caput medusa at the umbilicus**. C, Rectal submucosal veins,** supplied by the inferior mesenteric vein through the superior rectal vein and draining into the internal iliac veins through the middle rectal veins. **D, Splenorenal shunts:** Created spontaneously or surgically**. E, Short gastric veins** communicate with the esophageal plexus

BCS; DEFINITIONS, CLASSIFICATIONS AND EPIDEMIOLOGY

Definitions:

In *(1857), George Budd* initially described BCS. The syndrome consisted of a triad of hepatomegaly, abdominal pain, and ascites (***Gilroy and Sorrell, 2006).***

Hans Chiari later in ***(1899)*** contributed the characteristic histology of centrilobular injury, sinusoidal congestion, and added obliterating phlebitis of the HVs to the description **(*Gilroy and Sorrell, 2006).***

Several authors who have challenged the term Budd–Chiari syndrome as being ambiguous, have attempted to introduce other nomenclatures, such as hepatic venous outflow obstruction and obliterative hepatocavopathy ***(Ludwig et al., 1990 and Okuda et al., 1998).***

Although important for our understanding of Budd–Chiari syndrome, most of these nomenclatures have not been used in clinical practice. Although the cause, the mechanism and the nature of the vascular obstruction are not given, the term Budd–Chiari syndrome should be retained for two reasons: (a) it has stood the passage of time; and (b) it is more concise than any other terminology to designate the whole spectrum of disorders encompassed by the present definition ***(Janssen, et al., 2003).***

Budd–Chiari syndrome is ***defined as*** hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava and the right atrium, regardless of the cause of obstruction. Outflow obstruction caused by hepatic veno-occlusive disease and cardiac disorders is excluded from this definition ***(Janssen, et al., 2003).***

Veno-occlusive disease (VOD), also referred to as sinusoidal obstruction syndrome, is ***defined as*** a non-thrombotic obstruction of sinusoids or central hepatic veins due to injury of the sinusoidal wall ***(Deleve et al., 2002).*** Veno-occlusive disease occurs following administration of toxic agents and is, at present, encountered almost exclusively in association with bone marrow transplantation ***(Shulman et al., 1994).***

The epidemiology, pathophysiology, treatment and prognosis of veno-occlusive disease are so distinct from other forms of hepatic venous outflow obstruction that its inclusion in future clinical studies on Budd–Chiari syndrome would introduce an unacceptable source of heterogeneity. Obstruction of the small hepatic veins without involvement of the large veins is included in the definition of Budd–Chiari syndrome, while the specific entity of veno-occlusive disease is excluded. The rationale for this distinction has been much debated but is justified by several arguments ***(Janssen, et al., 2003).***

Except for veno-occlusive disease as defined above, the obstruction limited to the small veins is generally due to

thrombosis, allergic phlebitis or granulomatous involvement; all of which are reported causes of large hepatic vein obstruction ***(Valla and Benhamou, 1999).***

Although the manifestations are sometimes difficult to distinguish from those of veno-occlusive disease, the context is usually outside the setting of bone marrow transplantation. A differentiation between isolated small vein thrombosis and veno-occlusive disease can be achieved by means of liver biopsy ***(Janssen, et al., 2003).***

Classifications:

Budd–Chiari syndrome can be classified according to aetiology, site of obstruction, manifestations and duration of the disease as described below ***(Janssen, et al., 2003).***

(1) Aetiology:

Budd–Chiari syndrome is considered primary when obstruction of the hepatic venous outflow tract is the result of an endoluminal venous lesion (thrombosis or web) **(Table 1).** It is considered secondary when the obstruction results from the presence in the lumen of material not originating from the venous system (malignant tumor or a parasitic mass invading the lumen) or from extrinsic compression by a neighboring tumor (abscesses, cysts, benign or malignant solid tumors) ***(Okuda et al., 1998).***

Table (1): Classification of BCS according to aetiology ***(Janssen, et al., 2003).***

Designation	Definition
Primary	Hepatic venous outflow obstruction originating from endoluminal venous lesion (thrombosis, webs, endophlebitis).
Secondary	Hepatic venous outflow obstruction originating from a lesion outside the venous system (tumor, abscess, cysts). The lesion can obstruct outflow by invading the lumen or by extrinsic compression

In practice, Budd–Chiari syndrome is regarded as primary when no causes of secondary obstruction are found. Modern imaging techniques allow easy recognition of these associated lesions. Venous compression can be complicated by thrombosis, particularly when prothrombotic factors are present by chance (inherited thrombophilia) or by association (inflammatory response secondary to an adjacent abscess) ***(Janssen, et al., 2003).***

(2) Site of obstruction:

Obstruction of the hepatic venous outflow tract is classified according to its location: small hepatic veins, large hepatic veins, inferior vena cava and combined obstruction of large hepatic veins and inferior vena cava **(Table 2)** ***(Ludwig et al., 1990).***