

Review Article



Budd Chiari Syndrome in Children

Mukesh Khadga¹, Mahmudul Hasan², AZM Raihanur Rahman³, Nazmul Ahamed⁴,
Md. Benzamin⁵, Mohammad Ahmadur Rahman⁶, A S M Bazlul Karim⁷.

Abstract

Budd-Chiari syndrome (BCS) is a rare disorder presenting with hepatic venous outflow obstruction from the level of the hepatic veins to the junction of the inferior vena cava (IVC) with the right atrium. It is rare in infants and children so, delay in diagnosis or misdiagnoses are very commonly seen. It results from either primary or secondary cause. Hypercoagulable state can be identified in majority of the cases. The clinical presentations may vary from asymptomatic to fulminant liver failure. A high index of suspicion and imaging findings may help in early diagnosis of this condition. Doppler ultrasonography can be the initial diagnostic investigation of choice. The treatment options include medical therapy along with surgical measures including liver transplantation for end-stage liver disease.

Keywords: Budd-Chiari syndrome, Children, Doppler ultrasonography, Hepatic venous outflow obstruction.

Date of received: 15.11.2019.

Date of acceptance: 05.01.2020.

KYAMC Journal. 2020;11(1):46-49.

DOI: <https://doi.org/10.3329/kyamcj.v11i1.47151>

Introduction

Budd-Chiari Syndrome (BCS) is a heterogenous group of clinical conditions that is associated with hepatic venous outflow obstruction.¹ Budd-Chiari syndrome (BCS) was first recognized by Budd and Chiari in 1845 and 1899, respectively.² It is characterized by a triad of ascites, hepatomegaly and right upper quadrant pain. It is rare in children and infants.³ It may have a wide range of presentation from being asymptomatic to acute liver failure.⁴ Depending on the cause of obstruction, BCS may be primary due to thrombosis/web or secondary when the lesion is outside the venous system (tumor, abscess, etc.).⁵ It can also be classified as (i) acute, develops usually within 1 month or symptomatic for less than 6 month (ii) subacute, insidious onset, it may take as long as 3 months time, usually having minimal/trace or no ascites and (iii) chronic with disease duration of 6 or more months or signs of portal hypertension present.^{6,7,8} It can be diagnosed by radiological imaging and liver biopsies.⁹ Appropriate anticoagulation along with regular follow-up may have a good outcome.¹⁰

Epidemiology

BCS is a rare condition with varying prevalence geographically. The estimated incidence of BCS in Western countries is 1 in 2.5 million person year.¹¹ Data from outside of the Western world, however, vary significantly. Japan had an estimated incidence of 0.13 per million per year in 1989.¹² In Nepal, BCS had an incidence of 2.50 per million per year that accounted for 17% of the patients presenting with chronic liver disease with.¹³ BCS occurs in 1/100 000 of the general population worldwide.¹³ Men are affected more in Asia whereas women are commonly affected in Europe.^{14,15,16}

Etiology and Pathogenesis

BCS may be primary due to thrombosis/web or secondary when the lesion is outside the venous system (tumor, abscess).¹⁷ In the Western countries, thrombosis of hepatic vein is the common cause of primary BCS, whereas in Asians, the cause is idiopathic or related to anatomical anomalies, like-membranous obstruction.¹¹

1. Resident, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
2. Resident, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
3. Resident, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
4. Resident, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
5. Resident, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
6. Resident, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
7. Chairman and Professor, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

Correspondent: Dr. Mukesh Khadga, Resident, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, Email: coolmuks0@gmail.com, Mobile: 01731698009

Irrespective of the cause, hepatic venous outflow tract obstruction results in increased hepatic sinusoidal pressure leading to portal hypertension. The hepatic venous stasis and congestion results in hypoxic damage and ischemic necrosis of adjacent hepatic parenchymal cells.¹⁷ The long term hepatic congestion leads to sinusoidal thrombosis and increased pressure, which ultimately promotes hepatic fibrosis.¹⁸ If no measures are taken to relieve the sinusoidal pressure, then nodular regeneration, fibrosis and ultimately cirrhosis occur.¹⁹

Several multicenter data showed a combination of several prothrombotic conditions in 25% to 46% of the patients with primary BCS,^{15,20-22} which was more than expected in the general population. The prothrombotic conditions found in BCS, in particular the classical type, include: Factor V Leiden mutation, protein C deficiency, protein S deficiency, prothrombin (PT) gene mutation, antithrombin deficiency, antiphospholipid syndrome and paroxysmal nocturnal haemoglobinuria.²³ BCS may also be associated with systemic inflammatory diseases, such as Behçet' disease, vasculitis, sarcoidosis and other connective tissue diseases.²³

Clinical Presentation

Patients may have a wide range of presentation from being asymptomatic to acute liver failure.⁴ One study has shown that about 15% of the patients remain asymptomatic with preservation of some hepatic venous outflow.²⁴ Patients of BCS commonly present with abdominal pain (61%), ascites (83%) and hepatomegaly (67%).¹⁵ Other clinical features include jaundice, splenomegaly, oesophageal bleeding (5%) and hepatic encephalopathy (9%).^{10,15}



Fig 1: Ascites in BCS



Fig 2: Doppler USG showing thrombus in proximal IVC (arrow).

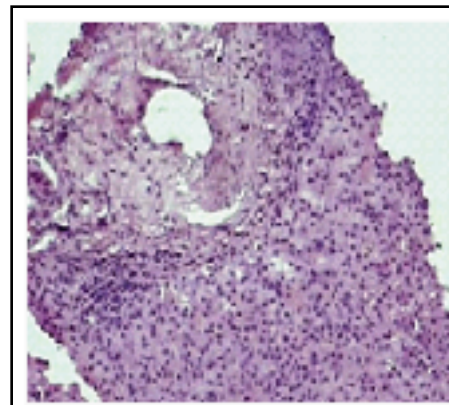


Fig 3: Histopathologic features thrombus in proximal IVC (arrow). of BCS with centrilobular congestion, perivenular fibrosis (H and E stain)

Diagnosis

In most of the cases, Doppler USG can confirm the diagnosis of BCS. One study showed that Doppler USG established the diagnosis of BCS in 95% cases.¹⁰ A similarly high diagnostic accuracy (>80%) of Doppler has been shown by others.^{8,25} Doppler ultrasonography shows the specific findings in the hepatic or caval veins, such as stenosis, thrombosis, fibrotic cord, or insufficient recanalization of the vessel, along with caudate lobe hypertrophy which are highly specific for Budd-Chiari syndrome.²⁶

Some other imaging findings for BCS may include hepatic veins without flow signal, and with spider-web appearance, reversed or turbulent flow, collateral hepatic venous circulation. Non-visualization or tortuous hepatic veins are common but these are non-specific sonographic findings of BCS.¹

Contrast-enhanced CT, MRI scans, Magnetic resonance venogram (MRV) and Hepatics cintigraphy may be useful for determining the presence of any thrombus or detect the site and cause of obstruction.³ It is seen that thrombosis may be the inciting event for membranous web formation, so all patients should be investigated for the underlying hypercoagulative states.² Venography is done when diagnosis is uncertain or to see the anatomy prior to treatment plan.⁴

If imaging fails to show the obstruction then liver biopsy is the other investigation option and it shows congestion, liver cell loss and fibrosis predominantly located in the centrilobular area which can differentiate BCS from veno-occlusive disease.²⁷

BCS and some cardiac disorders, like tricuspid regurgitation and constrictive pericarditis may have similar clinical manifestations. So, in such patients, echocardiography is helpful to differentiate from BCS.¹ Other routine tests to see hepatic involvement include- Serum bilirubin, Serum aminotransferase levels, Serum alkaline phosphatase and Serum albumin.

Management

The management options for BCS patients include supportive medical treatment, anticoagulation therapy whereas surgical measures include balloon angioplasty, decompressive portosystemic shunt procedures-transjugular intrahepatic portosystemic shunt (TIPS), and liver transplantation for end-stage liver disease.^{28,29} If patients have a contraindication to warfarin or progressive disease, Rivaroxaban can be a reasonable alternative anticoagulant.³⁰

Despite the high efficacy of Rivaroxaban, the risk of bleeding still occurs during its use.³¹

The prognostic indicators are ascites, elevated prothrombin time, encephalopathy, and altered serum levels of sodium, albumin, creatinine, and bilirubin, cirrhosis and the presence of portal hypertension.³²

Conclusion

BCS is often misdiagnosed as a case of chronic liver disease. Doppler ultrasonography can confirm the diagnosis. A timely diagnosis along with appropriate treatment with oral anticoagulant like-Rivaroxaban may prevent the need of operative procedures of major surgery and liver transplantation.

Acknowledgement

We are grateful to Assistant Professor Dr. Rubaiyat Aalm, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

References

1. Aydinli M, Bayraktar Y. Budd-Chiari syndrome: Etiology, pathogenesis and diagnosis. *World J Gastroenterol* 2007;13:2693-2696.

2. Horton JD, SanMiguel FL, Membreno F, Wright F, Paima J, Foster P, et al. Budd-Chiari syndrome: illustrated review of current management. *Liver Int* 2008;28:455-456.
3. Rajani R, Melin T, Björnsson E, Broomé U, Sangfelt P, Danielsson Å, et al. Budd Chiari syndrome in Sweden: epidemiology, clinical characteristics and survival-an 18?year experience. *Liver International* 2009;29:253-259.
4. EASL Clinical Practice Guidelines. Vascular diseases of the liver. *J Hepatol.* 2016; 64:179-202.
5. Okuda K, Kage M, Shrestha SM. Proposal of a new nomenclature for Budd-Chiari syndrome: hepatic vein thrombosis versus thrombosis of the inferior vena cava at its hepatic portion. *Hepatology* 1998; 28:1191-1198.
6. Valla DC. Hepatic vein thrombosis (Budd-Chiari syndrome). *Semin Liver Dis* 2002; 22: 5-14.
7. Hector Ferral, George Behrens and Jorge Lopera. Budd-Chiari Syndrome. *American Journal of Roentgenology* 2012; 199: 737-745.
8. Dilawari JB, Bambery P, Chawla Y, Kaur U, Bhusnurmath SR, Malhotra HS. Hepatic outflow obstruction (Budd-Chiari syndrome). Experience with 177 patients and a review of the literature. *Medicine (Baltimore)* 1994;73:21-36.
9. Gentil-Kocher S, Benard O, Brunelle F, Hadchouel M, Maillard JN, Valayer J et al. The Budd-Chiari syndrome in children: a report of 22 cases. *J Pediatr* 1988; 113: 30-38.
10. Kathuriaa R, Srivastavaa A, Yachhaa S K, Poddara U, Baijalb S S. Budd-Chiari syndrome in children: clinical features, percutaneous radiological intervention, and outcome. *European Journal of Gastroenterology and Hepatology.* 2014; 26:1030-1038.
11. Valla DC. Hepatic venous outflow tract obstruction etiopathogenesis: Asia versus the West. *J Gastroenterol Hepatol* 2004; 19: 204-211.
12. Okuda H, Yamagata H, Obata H, Epidemiological and clinical features of Budd Chiari syndrome in Japan. *J Hepatol* 1995;22:1-9.
13. Shrestha SM, Okuda K, Uchida T, Endemicity and clinical picture of liver disease due to obstruction of the hepatic portion of the inferior vena cava in Nepal. *J Gastroenterol Hepatol* 1996;11:170-179.
14. Valla DC. The diagnosis and management of the Budd-Chiari syndrome: consensus and controversies. *Hepatology* 2003; 38: 793-803.

15. Darwish MS, Plessier A, Hernandez Guerra M, Etiology, management, and outcome of the Budd-Chiari syndrome. *Ann Intern Med* 2009;151:167-175.
16. De Leve LD, Valla DC, Garcia, Tsao G. American association for the study liver diseases. Vascular disorders of the liver. *Hepatology* 2009;49: 1729-1764.
17. Menon KV, Shah V, Kamath PS. The Budd Chiari syndrome. *N Engl J Med* 2004;350:578-585.
18. Simonetto DA, Yang HY, Chronic passive venous congestion and hepatic fibrogenesis via sinusoidal thrombosis and mechanical forces. *Hepatology* 2015;61:648-659.
19. Cazals Hatem D, Vilgrain V, Genin P, Arterial and portal circulation and parenchymal changes in Budd-Chiari syndrome: a study in 17 explanted livers. *Hepatology* 2003;37:510-519.
20. Denninger MH, Chait Y, Casadevall N, Cause of portal or hepatic venous thrombosis in adults: the role of multiple concurrent factors. *Hepatology* 2000;31:587-591.
21. Janssen HL, Meinardi JR, Vleggaar FP, Factor V Leiden mutation, prothrombin gene mutation, and deficiencies in coagulation inhibitors associated with Budd-Chiari syndrome and portal vein thrombosis: results of a case control study. *Blood* 2000;96:2364-2368.
22. Primignani M, Barosi G, Bergamaschi G, Role of the JAK2 mutation in the diagnosis of chronic myeloproliferative disorders in splanchic vein thrombosis. *Hepatology* 2006;44:1528-1534.
23. Mac Nicholas R, Olliff S, Elias E, Tripathi D. An update on the diagnosis and management of Budd Chiari syndrome. *Expert Rev. Gastroenterol. Hepatol* 2012;6:731-744.
24. Hadengue A, Poliquin M, Vilgrain V, The changing scene of hepatic vein thrombosis: Recognition of asymptomatic cases. *Gastroenterology* 1994;106: 1042-1047.
25. Bolondi L, Gaiani S, Li Bassi S, Zironi G, Bonino F, Brunetto M, et al. Diagnosis of Budd-Chiari syndrome by pulsed Doppler ultrasound. *Gastroenterology* 1991; 100:1324-1331.
26. Boozari B, Bahr MJ, Kubicka S. Ultrasonography in patients with Budd-Chiari syndrome: diagnostic signs and prognostic implications. *J Hepatol* 2008;49:572-580.
27. Misra V, Verma K, Singh D K, Misra S P. The Case Report Budd-Chiari Syndrome in a Child: A Case Report and Review of the Literature. *Journal of Clinical and Diagnostic Research* 2012; 6:1783-1785.
28. Sherlock S, Dooley J. *Diseases of the Liver and Biliary System*, 11th edn. Oxford: Blackwell Publishing 2002;192-198.
29. Nagral A, Hasija R, Marar S, Nabi F. Budd-Chiari syndrome in children: experience with therapeutic radiological intervention. *J Pediatr Gastroenterol Nutr.* 2010; 50:74-78.
30. Pedersen MR, Molloy P, Wood D, Seetharam A. Direct intrahepatic portocaval shunt for treatment of portal thrombosis and Budd-Chiari syndrome. *Annals of hepatology* 2016; 15:127-130.
31. Beyer-Westendorf J, Förster K, Pannach S, Ebertz F, Gelbricht V, Thieme C, et al. Rates, management, and outcome of rivaroxaban bleeding in daily care: results from the Dresden NOAC registry. *Blood, The Journal of the American Society of Hematology* 2014; 124:955-962.
32. Murad SD, Valla DC, de Groen PC, "Determinants of survival and the effect of portosystemic shunting in patients with Budd-Chiari syndrome". *Hepatology* 2004; 39: 500-508.