

Etiological Spectrum of Portal Hypertension in Children-An Experience in a Tertiary Centre of North India.

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ABSTRACT

Background: Portal hypertension is defined by a pathological increase in portal venous pressure. Any condition that interfere with blood flow at any level within the portal system can lead to portal hypertension. For better management, it is important to determine the underlying cause. This Study was done to evaluate the etiology of portal hypertension in children admitted in a tertiary care centre of Lucknow, North India. **Methods:** This cross sectional study was done in the Department of Forensic Medicine in Association with Pediatrics Department, Era's Lucknow Medical College & hospital on 40 consecutive cases of portal hypertension enrolled from Jan. 2014 to Dec. 2014. **Results:** Age of the children was 2-12 years with mean age of 7.2±4.3 years and male: female ratio was 1.5:1. Out of 40 children, 32 (80%) developed portal hypertension due to pre-hepatic causes and 8 (20%) hepatic causes. In pre-hepatic causes of portal hypertension, out of 32 children, portal vein thrombosis was found in 20 (62.5%) cases, splenic vein thrombosis in 4 (12.5%) & 8 (25%) were idiopathic. On the other hand hepatic causes of portal hypertension, out of 8 children, cryptogenic was found in 4 (50%) cases, wilson's disease, chronic hepatitis B virus infection, biliary cirrhosis & autoimmune hepatitis each was found in 1 (12.5%) case. In pre-hepatic cases first variceal bleed was much earlier than hepatic cases (4.4±3.6 Vs 7.6±4.6 years). **Conclusion:** Extra-hepatic diseases were the most common etiology of portal hypertension in studied the children. Portal venous thrombosis in extra-hepatic cases & cryptogenic liver disease in intra-hepatic cases were the most common causes.

Keywords: Extra-hepatic portal venous obstruction (EHPVO), Intra-hepatic portal venous obstruction (IHPVO).

INTRODUCTION

Portal hypertension (PHT) is a clinical syndrome defined by a portal venous pressure gradient between the portal vein (PV) and inferior vena cava exceeding 5 mmHg. Cirrhotic portal hypertension is associated with an elevated hepatic venous pressure gradient (HVPG) predominantly due to raised sinusoidal resistance, while in the non-cirrhotic portal hypertension (NCPH), HVPG is normal or only mildly elevated & is significantly lower than Portal Venous pressure.^[1]

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Clinically significant portal hypertension is diagnosed when clinical manifestations of the disease appear or the portal pressure gradient exceeds 10 mmHg.^[2] It can present as esophageal

variceal bleeding, ascites or hypersplenism.^[3] The causes of portal hypertension are classified anatomically as pre-hepatic, hepatic & post hepatic. Hepatic causes are further subdivided into pre-sinusoidal, sinusoidal & post-sinusoidal.^[1] Portal vein thrombosis is the predominant cause of pediatric portal hypertension in India.^[3] A careful investigation for the causes of the portal hypertension is essential for choosing the best treatment.^[2] This study was conducted to document the etiology of portal hypertension in children admitted in a tertiary care centre of Lucknow, Uttar Pradesh, India.

MATERIALS AND METHODS

A cross sectional study was done in the department of Pediatric Era's Lucknow Medical College & Hospital from Jan. 2014 to Dec. 2014. A total of 40 admitted cases of portal hypertension between 2-16 years of age enrolled in this study after obtaining their consent.

In children, extra-hepatic portal venous obstruction (EHPVO) is defined clinically as history of hematemesis and/or melena, no history of jaundice, with or without history of umbilical catheterization or abdominal sepsis, absence of stigmata of chronic liver disease (CLD) with splenomegaly. Upper gastrointestinal endoscopy (UGI) showed esophageal varices of different grades. Doppler ultrasound also showed increase portal venous pressure with or without portal/splenic vein thrombosis.

In children, intra-hepatic portal venous obstruction (IHPVO) is defined clinically as history of jaundice and/or persistence of jaundice for more than 6 months, history of hematemesis and/or melena with presence of any stigmata of chronic liver disease (Jaundice, ascites, spider angioma, gynecomastia, caput medusae, testicular atrophy, thenar hypothenar wasting, palmer erythema, leukonychia & clubbing). Raised liver enzymes by liver function test (ALT, AST), increased hepatic echogenicity, irregular margins, coarse texture or nodular liver, hepato-splenomegaly with or without ascites by abdominal ultra-sonogram, increase portal venous pressure by doppler ultrasound, upper gastrointestinal endoscopy (UGI) showed esophageal varices of different grades and fibrosis or nodular regeneration in liver biopsy. To find out the etiology, history of taking any offending drugs like acetaminophen, halothane, anti-inflammatory (NSAID), anti-convulsant (phenytoin, sodium valproate, carbamazepine), anti-TB (Isoniazid), antibiotics (Penicillin, erythromycin, tetracyclines, sulfonamides) etc. were taken, HBsAg, Anti-HBc total (IgM and/or IgG), Anti-HCV antibody, HCV RNA, ANA, Anti-SMA antibody, slit lamp examination of eye (KF ring), serum ceruloplasmin, 24 hours urinary copper, penicillamine challenge test (if necessary) were done. When etiology of portal hypertension is not evident then it is called cryptogenic.^[3]

A preformed semi structured data collecting form was used as a data collection instrument. Data were collected by the researcher and analyzed by Statistical Package of Social Science (SPSS) version 11.5 programme. Data was analyzed by Z test for proportion testing. A right tailed p-value of <0.05 was considered as significant.

RESULTS

All the children were between 2-12 years of age mean age was 7.2±4.3 years. In pre-hepatic cases mean age were 4.4±3.2 years and hepatic cases it was 6.2±4.3 years. There were 30 (60%) male & 16 (40%) female cases.

The mean age at onset of the first variceal bleeding was at 5.3±4.5 years. In pre-hepatic cases it was 4.4±3.6 years & in hepatic cases it was 7.6±4.6

years. So, in pre-hepatic cases first variceal bleed much earlier than hepatic cases.

Out of 40 children, 32 (80%) developed portal hypertension due to pre-hepatic causes and 08 (20%) due to hepatic causes. No patient was found with post-hepatic cause. A one sample Z-test for proportion suggested that proportion of children with pre-hepatic causes were significantly higher (<0.001) than the proportion of children with hepatic cases.

Table 1: Etiological Pattern of portal hypertension with significant difference.

| Pre-hepatic | Hepatic | P-value for difference |
|-------------|----------|------------------------|
| N (%) | N(%) | (<0.05 significant) |
| 32 (80%) | 08 (20%) | <0.001 |

In pre-hepatic causes of portal hypertension, out of 32 children, portal vein thrombosis was found in 20 (62.5%) cases, splenic vein thrombosis in 4 (12.5%) cases & others in 08 (25%) cases. So, among studied children, portal vein thrombosis was the leading cause in extra-hepatic portal venous obstruction (EHPVO).

In hepatic causes of portal hypertension, out of 08 children, cryptogenic was found in 4 (50%) cases, Wilson's disease, chronic hepatitis B, biliary cirrhosis and autoimmune hepatitis was found in 1 (12.5%) case each. So, cryptogenic was the leading cause of intra-hepatic portal venous obstruction (IHPVO) in studied children.

Table 2: Frequency in percentage underlying causes of portal hypertension.

| Etiology of Portal Hypertension | | N (%) |
|---------------------------------|-------------------------|------------|
| Pre-hepatic | Portal vein thrombosis | 20 (62.5%) |
| | Splenic vein thrombosis | 4(12.5%) |
| | Others | 8 (25%) |
| Hepatic | Cryptogenic | 4 (50%) |
| | Wilson's disease | 1 (12.5%) |
| | Hepatitis B virus | 1(12.5%) |
| | Biliary cirrhosis | 1(12.5%) |
| | Autoimmune hepatitis | 1 (12.5%) |

DISCUSSION

Portal hypertension leads to formation of portal systemic collaterals which shunt a portion of the portal blood to the systemic circulation, bypassing the liver. Portal hypertension can arise from disorders with blood flow at any level within the portal system.^[5,6]

In the present study of children, mean age was 7.2±4.3 years. Similar mean age was also observed in a study in Iran. Their mean age was 7.6±4.7.^[2] In this study, mean age of pre-hepatic cases was 4.4±3.2 years and in hepatic cases it was 6.2±4.3

years. So, bleeding occurred in pre-hepatic cases much earlier than hepatic cases. Similar observation was also reported in others Studies on North Indian children.^[7]

Imanieh et al.^[2] reported that the mean age at onset of the first variceal bleeding was at 4.3±4.5 years of age. This study also found the near similar result. The mean age at onset of the first variceal bleeding was at 5.3±4.5 years. In pre-hepatic cases it was 4.4±3.6 years & hepatic cases 7.6±4.6 years. So, in pre-hepatic cases first variceal bleed much earlier than hepatic cases.

In the current study, among total children male were 24 (60%) & female 16 (40%). Male: female ratio was 1.5:1. So, portal hypertension more observed in male than female. But Imanieh et al.^[2] reported the different result. There ratio was 1.01:1. Several studies have reported the pattern of portal hypertension to be different in children and adults. In adults the etiology of portal hypertension is mostly intra-hepatic, whereas the pattern is extra-hepatic in children.^[8-11]

Several studies from India stated that the most common causes of pediatric portal hypertension were extra-hepatic portal venous obstruction.^[12,13] In the current study we also observed the similar result. Here, out of 40 children, 32 (80%) developed portal hypertension due to pre-hepatic causes and 08 (20%) were hepatic causes. Arora et al.^[7] also observed 76.5% cases of extra-hepatic portal hypertension in North Indian children. So, among studied children, pre-hepatic causes were significantly (<0.001) higher than hepatic causes. On the other hand, Grimaldi et al.^[14] reported that the main causes of portal hypertension in children were cirrhosis and congenital hepatic fibrosis. Bernard et al.^[15] also reported that intra-hepatic portal venous obstruction (EHPVO) or cirrhosis was responsible for 51% of portal hypertension in children and extra-hepatic portal venous obstruction was found in 34% of cases. Imanieh et al.^[2] in Iran also observed portal hypertension due to hepatic causes in 93.3% of children.

In the present study, among all children with extra-hepatic portal venous obstruction, portal vein thrombosis was the leading cause. Out of 32 children, it was observed in 20 (62.5%) cases. Podder et al.^[12] and Arora et al.^[7] also reported similar results. Other causes were splenic vein thrombosis in 4 (12.5%) cases & others in 08 (25%) cases.

Imanieh et al.^[2] reported that, main cause of intra-hepatic portal hypertension was cryptogenic. Out of 45 children, it was observed in 12 (26.7%) cases. Other causes were biliary cirrhosis 11 (24.4%) cases, Wilson's disease 8 (17.8%) cases & congenital hepatic fibrosis 3 (6.7%) cases. Similar results were observed in our study. Out of 8 children, cryptogenic were 4 (50%) cases, Wilson's disease, chronic hepatitis B virus infection, biliary

cirrhosis and auto-immune hepatitis were observed in 01 (12.5%) cases each. In adult, again cryptogenic was the predominant cause of intra-hepatic portal hypertension, followed by alcohol, hepatitis B & hepatitis C virus infection.^[16-18]

CONCLUSION

Extra-hepatic portal hypertensions were the most common among studied children. Portal vein thrombosis in extra-hepatic cases & cryptogenic in intra-hepatic cases were the most common cause. In pre-hepatic cases first variceal bleeding much earlier than hepatic cases.

Limitations of study

Study was conducted in single centre. Multicentre study will provide more accurate information.

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