An Audit of Extrahepatic Portal Vein Obstruction: Experience from Tertiary Referral Center

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Abstract

Background: Extra hepatic portal vein obstruction (EHPVO) is a common cause of portal hypertension in India.

Aims: (1) To evaluate the clinical presentation and the natural history of EHPVO; (2) to describe the risk factors, rebleeding rates and development of portal biliopathy on follow-up; and requirement of surgery in EHPVO at a tertiary care center.

Methods: Data from 318 consecutive patients with EHPVO from June 2012 to October 2020 were analyzed. All patients underwent liver biochemistry, ultrasonography (USG) abdomen, upper gastrointestinal (GI) endoscopy, and viral serology. Color Doppler, computed tomography (CT) abdomen and magnetic resonance cholangiopancreatography (MRCP) were done as indicated.

Results: Mean age of presentation was 15.08 years (standard deviation (SD) 12.74; 6 months–60 years; 210 males). The presenting features were upper GI bleed (n = 227) (age at first bleed 11 years; 4 months–56 years), left hypochondrium pain or lump (n = 67), and only lower GI bleed (n = 1). Incidentally detected EHPVO on USG was seen in 10.69% (n = 34) patients. Postbleed ascites were seen in 10.69% (n = 34) patients. Six patients had symptomatic portal biliopathy and 14 had hypersplenism. Around 14.77% (n = 47) of patients had a history of being delivered at home, while 3.45% (n = 11) had a history of umbilical sepsis. During follow-up, 35.3% (n = 82) of patients had rebled. On imaging, associated splenic vein (SV) collaterals and superior mesenteric vein (SMV) collaterals were seen in 35.84% (n = 114) and 11.01% (n = 35) patients, respectively. Gallbladder varices were seen in 44.3% (n = 106), while gallstones in 5.66% (n = 18). On endoscopy, 87.42% (n = 278) patients had esophageal varices, 18.86% (n = 60) had isolated fundic varices, and three had ectopic varices. Only two patients had rectal varices and colopathy. Emergency devascularization was required in 3.45% (n = 14) patients for the failure of variceal bleed control, 1.88% (n = 7) underwent splenectomy, and four patients had proximal splenorenal shunt (PSRS) surgery.

Conclusion: Extrahepatic portal hypertension (EHPVO) is an important cause of portal hypertension (PHT) in our country. The majority of them present with GI bleed; postbleed ascites were seen only in ~10%. Rebleed occurs in one-third of cases. Gallbladder varices were common; portal biliopathy occurred in 10% and were usually asymptomatic.

Introduction

Portal hypertension (PHT) as a result of portal vein occlusion in the absence of cirrhosis of the liver is termed Extra Hepatic Portal Vein Obstruction (EHPVO). The entity was first described by Balfour and Stewart, later termed “cavernomatous transformation of the portal vein”1 in 1869 as thrombosis and varicose dilatation of the portal vein leading to splenomegaly and ascites.

In India, EHPVO accounts for 20–46% of patients presenting with variceal bleeding.2–4 Unlike the West, where the proportion of such patients is ~5%,5,6,8 Among children, EHPVO is the most common cause of PHT in India.9,10 EHPVO in children manifests with gastro-intestinal (GI) bleeding, massive splenomegaly, and portal biliopathy.

Patients and Methods

A retrospective analysis of consecutive newly diagnosed patients with EHPVO from June 2012 to October 2020, and those with prior diagnosis following up in the liver clinic, Department of Gastroenterology, BYL Nair Hospital, Mumbai, Maharashtra, India, was performed. Patients with evidence of chronic liver disease, portal vein thrombosis secondary to malignancy, chronic pancreatitis, splenectomy, myeloproliferative disorders, and abdominal inflammatory conditions were excluded from the study.

The diagnosis of EHPVO was based on the demonstration of portal cavernoma (portal vein occlusion with the presence of collateral vessels) with or without splenic vein (SV) blockage by abdominal sonography with Doppler study, in the presence of a normal biochemical test of liver function. A detailed history was obtained, including details of the age of onset of GI bleeding, noticing a lump in the left hypochondrium, or abdominal distension and growth retardation. The time elapsed since GI bleeding or splenomegaly, and the diagnosis was noted. Clinical examination included the size of splenomegaly and the stigmata of chronic liver disease and congenital anomalies in children.

Doppler sonography evaluated the entire spleno-portal axis, the presence of gallbladder varices, and gallstones. CT scan of the abdomen and MRCP were done to rule out secondary causes of EHPVO and preoperatively in those with suspected portal biliopathy, respectively, whenever possible. All patients underwent upper GI endoscopy (GIF V series, Olympus, Japan) for the presence of esophageal and gastric varices, portal hypertensive gastropathy, and the presence of ectopic varices. All had complete hemograms, liver biochemistry, and viral serology done. A liver biopsy was done where there was a doubt of cirrhosis on clinical or biochemical investigations. The records were assessed for symptomatic hypersplenism and the development of portal biliopathy.

Statistical Analysis

All the categorical variables were presented as frequency (n) and percentage (%), and the continuous parameters were presented as mean ± SD. All the statistical analyses were carried out by using Statistical Package for the Social Sciences version 23.0 (United States of America). A p-value of <0.05 was considered statistically significant.

Results

A total of 318 patients (210 males) were seen during the study period. The mean age at presentation was 15.08 years (SD 12.74 years; range 6 months–60 years). The diagnosis of EHPVO was based on Doppler sonography. The presenting features were upper GI bleeding in 227 (71.38%) and left hypochondrium pain and/or lump in 67 patients (20.6%). Around 34 patients (10.69%)

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were detected incidentally on USG. Around 14 patients had GI bleeding 6 months–4 years after the detection of splenomegaly. History of home delivery was obtained in 141 patients, only 11(7.8%) of whom had a history of umbilical or neonatal sepsis. Demographic and biochemical details are described in Table 1.

Table 1: Clinical, biochemical, sonographic, and etiological profile of patients with EHPVO

<table>
<thead>
<tr>
<th>Clinical profile</th>
<th>N = 318</th>
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<tbody>
<tr>
<td>Mean age (in years, SD)</td>
<td>22.58 (11.82)</td>
</tr>
<tr>
<td>Males (n)</td>
<td>210</td>
</tr>
<tr>
<td>Age at presentation (in years, SD)</td>
<td>15.08 (12.74)</td>
</tr>
<tr>
<td>Age at first GI bleed (in years, SD)</td>
<td>10.88 (12.07)</td>
</tr>
<tr>
<td>Hematemesis at presentation (n)</td>
<td>227</td>
</tr>
<tr>
<td>Splenomegaly (n)</td>
<td>296</td>
</tr>
<tr>
<td>Hepatomegaly (n)</td>
<td>40</td>
</tr>
<tr>
<td>Jaundice (n)</td>
<td>14</td>
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</tbody>
</table>

Biochemical profile
- Hemoglobin (in gm/dL, SD) 9.33 (2.39)
- Total leucocyte count 5559.12 (8218.94)
- Platelet count 121643.4 (83622.1)
- Total protein 6.56 (0.96) gm%
- Albumin 3.51 (0.60) gm%
- Aspartate aminotransferase 40.98 (30.68) IU/mL
- Alanine transaminase 28.90 (23.56) IU/mL
- Alkaline phosphatase 129.41 (103.11) IU/mL
- Potential transformer difference 2.26 (1.79)
- Total bilirubin 0.61 (1.13) mg/dL
- Direct bilirubin 0.94 (0.70) mg/dL

USG Doppler findings in EHPVO
- SV collaterals (n) 114
- SMV 35
- Lienorenal collaterals (n) 79
- Gallbladder varices (n) 106
- Gallbladder calculi (n) 18

Etiological factors in EHPVO
- Umbilical sepsis (home delivery) 11 (141)
- Factor V Leiden mutation 1 heterozygous (120)

A total of 14 had jaundice at presentation, two had only menorrhagia as the presentation, one had easy bruisability for the last 7 years, and another had only lower GI bleed (due to rectal varices and portal colopathy). Clinically detected postbleed ascites were seen in 34 patients (10.69%). Congenital malformations were observed in seven children (Tables 2 and 3). Portal biliopathy was identified in 27 biochemical tests and was supported by USG; six were symptomatic and required therapy. Patients testing positive for hepatitis B surface antigen and Hepatitis C antibody were 12 and five patients, respectively.

In addition to the portal vein, other vascular obstructions, and collaterals were also seen (Table 1). SV collaterals were seen in 114 (35.84%) patients, while superior mesenteric vein (SMV) collaterals were seen in 35 (10.01%) patients. Gallstones were noted in 18 (5.66%). Gallbladder varices were seen in 44.3% (n = 106).

Upper GI endoscopy revealed esophageal varices in 278 (87.42%) and fundic varices in 60 (18.86%), with a mean number of sessions required for variceal eradication as 4.31 (SD 4.21); range 1–12, 113 (49.77%) had ≥three episodes of bleeding after the presentation. Surgery was required in 25 (7.86%) patients (14 devascularization, seven splenectomies, and four proximal splenorenal shunt (PSRS) surgery).

**Discussion**

This is a large, single-center experience of EHPVO, a condition unique for patients presented with repeated episodes of well-tolerated variceal bleeding and splenomegaly. The mean age at GI bleed was 10.88 (SD 12.07) years, compared to the series quoted by Webb and Sherlock, where almost 50% were adults. The mean age at presentation was 15.08 (12.74) years, signifying a delay in reporting the illness. The clinical presentation was similar to other reported series from India. Majority [227/318 (71.38%)] of the patients had upper GI bleeding at some time during the course of the disease and 63 (75%) of patients had it before 18 years of age.

The etiological factors in EHPVO were not clear; those implicated included umbilical sepsis, congenital etiology, abdominal sepsis, hypercoagulability, and latent myeloproliferative disorders from the West. History of umbilical or neonatal sepsis has been reported in 4.8–40% of patients with EHPVO. However, Thompson and Sherlock failed to find progression to EHPVO in any of the 80 infants with umbilical vein catheterization and sepsis. We found umbilical or neonatal sepsis in 11 (3.45%).

In our series, 34 patients (10.69%) incidentally diagnosed as EHPVO were...
An Audit of Extrahepatic Portal Vein Obstruction

Table 4: EHPVO as a cause of portal hypertension (modified from national collaborative study on Non-cirrhotic portal fibrosis, 1991)

<table>
<thead>
<tr>
<th>Center</th>
<th>EHPVO</th>
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<tbody>
<tr>
<td>Sanjay Gandhi Postgraduate Institute of Medical Sciences (Lucknow, Uttar Pradesh, India)</td>
<td>20%</td>
</tr>
<tr>
<td>Postgraduate Institute of Medical Education and Research (Chandigarh, India)</td>
<td>36%</td>
</tr>
<tr>
<td>Govind Ballabh Pant Hospital (Delhi, India)</td>
<td>20%</td>
</tr>
<tr>
<td>All-India Institute of Medical Sciences (Delhi, India)</td>
<td>55%</td>
</tr>
<tr>
<td>Sawai Man Singh Medical College (Jaipur, Rajasthan, India)</td>
<td>27%</td>
</tr>
<tr>
<td>Institute of Post Graduate Medical Education &amp; Research (Kolkata, West Bengal, India)</td>
<td>13%</td>
</tr>
</tbody>
</table>

adults without any clinical evidence of portal hypertension (Table 4). Sugiuara et al.17 observed signs of portal hypertension in 67% of adult patients, and they remained free of its signs for >3 years of follow-up. Symptomatic hypersplenism was noted in 11 patients, and all needed surgery. Shah and Mathur,12 reported hypersplenism (in 22%), which was symptomatic in only 6%.

One patient with EHPVO presented with recurrent shunt encephalopathy due to a large gastrolenal shunt (28 mm). In 1987, Dilawari and Chawla18 reported large spontaneous (natural) splenoadrenorenal shunt in 9.4% (20 of the 213 patients with EHPVO) on splenoportovenography. Splenomegaly and hepatomegaly (mild) were similar to prior series from the country. Hepatomegaly is seen in 10–39% of children with EHPVO.19,20

In 1977, Odievre et al.21 found a greater frequency of congenital malformations (of the heart, kidneys, intestine, and skeleton) in 40% of children with “idiopathic” EHPVO, than in children who had portal vein thrombosis after umbilical catheterization and concluded that some cavernomas were congenital. In another series, seven of the 29 (24%) patients had associated nonbiliary congenital abnormalities.22 Congenital malformations were observed in seven (of 135 cases ≤years of age) children.

Postbleed ascites have been reported in 3–16% of those with EHPVO.2–22 Ascites were usually transient following hemorrhage or surgery. Webb and Sherlock,3 in their series of 97 patients, observed ascites as a presenting symptom in 13 patients; in seven, it was transient, but six required treatment with a low sodium diet and diuretics. Ascites were more frequent in adult patients than in children.5,27 Shah and Mathur observed ascites in 16% in an earlier study from western India.12

Portal biliopathy was identified in 27 patients on imaging, six of whom were symptomatic (mean 33.83 years, range 28–40 years; duration of disease (EHPVO) prior to diagnosis was 2–30 years); and required therapy (one had repeated seven stent exchanges). Endoscopic retrograde cholangiopancreatography (ERCP) studies had shown biliopathy changes in 80–100% of patients with EHPVO.28–31 however, only a few (5–38%)28,29 were symptomatic. A recent study by Shin et al. demonstrated biliopathy changes in 12/30 asymptomatic32 patients on MRCP. Symptomatic portal biliopathy usually develops in patients with long-standing disease.

Growth retardation (stunting) was reported in 51–54.5% of children with EHPVO,33,34 diminished portal blood supply, and deprivation of hepatotropic hormones were possibly responsible for it. Growth hormone resistance and decreased insulin-like growth factor 1 (IGF-1) levels have been proposed in the causation of the decreased lean muscle mass and preserved subcutaneous fat in these patients.34 In another study in Western India, approximately one-third of children and one-fourth of adult patients with EHPVO did not achieve their target height, and low levels of IGF-1 and IGF-3 did not predict growth retardation.35

The presence of SV collateral or SMV thrombosis and/or replacement collaterals were seen in 35.84% and 11%, and the presence of GB varices in 44.3% and gallstones in 5.66% in the present study. Complete blockage of the spleno-portal axis was demonstrated in 24% and 35% of cases of EHPVO. Chawla et al. has reported GB varices in 34% and gallstones in 4.3% of patients. GB varices appear as tortuous, dilated vessels in or around the wall of the gallbladder or in the bed of the gallbladder fossa. Gallstones are more than two times more common in portal hypertension patients compared to the control population.35 Chiu and Superina reported an increased incidence (10.3%) of cholelithiasis in EHPVO.23

Upper GI endoscopy revealed the presence of esophageal varices of varying grade in 278 (87.42%) patients, fundic varices in 60 (18.86%) patients, and duodenal and antral varices in three and two patients, respectively. The mean number of sessions required for variceal eradication (either by sclerotherapy or variceal band ligation) was 4.31 ± 4.2. Eight patients were found to have fundic varices on follow-up. The endoscopic findings and the number of sessions required for variceal eradication were similar to the previously reported series.12,38–42

Mathur et al.42 reported variceal obliteration rates of 92% over a mean of 5.1 (range 2–11) sessions. Shah et al.39 found no patient with antral varix (AV) on index endoscopy. After a mean follow-up of 15 months, 4.1% of patients developed AV. Esophageal varices took a longer number of sessions to obliterate in patients with atrioventricular (AV) (11.1 vs 5.98 sessions, p < 0.0001). Two patients with mild dysphagia without stricture after sclerotherapy revealed esophageal dysmotility on manometry. Narawane et al.43 have reported altered esophageal motility after endoscopic variceal sclerotherapy or ligation in both noncirrhotic and cirrhotic patients with portal hypertension.

The rebleeding rates in our series were—63 (26.14%) of them never bled again; 40 (17.62%) had only one episode of GI bleeding, and 113 (49.77%) had ≥two episodes of bleeding after the presentation. A study from north India reported cumulative recurrent bleeding rates of 0, 6, 8, 10, and 12%, respectively, at 1–4, and 12 years after initial variceal eradication in EHPVO.44 Results of long-term (1.6–8.7 years) follow-up of endoscopic sclerotherapy in children with EHPVO showed recurrent variceal bleeding in 0–31%.39–42,44

Surgery was required in 25 patients in the present series. Most of the emergency surgeries were devascularization alone because it was done for uncontrollable bleeding or since the SV was not available for the shunt, either due to thrombosis or small-sized SV (emergency devascularization with a shunt in four).

A total of 12 patients had elective surgery; 11 for symptomatic hypersplenism, seven had splenectomy for pain and discomfort caused by a large spleen greater than 10 cm below the costal margin; four were PSRS surgery; and one had elective revascularization with splenectomy for large fundal varices with red color signs. One patient with biliopathy underwent PSRS surgery. Prasad et al.45 performed 160 PSRS surgeries in children with EHPVO. A total of 20 were emergency procedures for uncontrollable bleeding and 140 were elective procedures (102 for recurrent bleeding and 38 for hypersplenism).
Insulin-dependent diabetes mellitus was diagnosed in one patient (diagnosed at the age of 5 years). Alexander et al. have reported three cases of EHPVO who developed type 1 diabetes mellitus and have suggested a causal association. One patient developed hemiparesis at 26 years of age (thrombosis of superior sagittal sinus and vein of Galen and thalamo-striate (MOU6) vein); one patient developed flank veins after 9 years of presentation. Recurrent shunt encephalopathy developed in 1 patient due to a large gastrorenal shunt of 28 mm.

**Conclusion**

Extrahepatic portal hypertension (EHPVO) is an important cause of PHT in our country. The majority of them present with GI bleed; postbleed ascites were seen only in ~10%. Rebleed occurred in one-third of cases. Gallbladder varices were common; portal biliopathy occurred in 10% and is usually asymptomatic. Surgery was required in 7.86% of patients and the most commonly performed surgery was devascularization followed by splenectomy. Future multicentre prospective studies should look into the natural history of EHPVO and outcomes with early detection and management.

**References**