ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 68 . 16
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 5, Issue – 1, February - 2020, Page No. : 241 - 249

Profile of Extrahepatic Portal Vein Obstruction in Coastal Eastern Region of Odisha, A Single Center Experience

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Citation this Article: Girish Kumar Pati, Haribhakti Seba Das, Prasant Kumar Parida, Preetam Nath, Chitta Ranjan Panda, "Profile of Extrahepatic Portal Vein Obstruction in Coastal Eastern Region of Odisha, A Single Center Experience", IJMSIR- February - 2020, Vol – 5, Issue -1, P. No. 241 – 249.

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background: Extrahepatic portal venous obstruction (EHPVO) is an important cause of Portal hypertension. There is paucity of data regarding EHPVO cases in Odisha.

Aim of the study: The aim of the study was to assess demographic features, etiology, clinical presentations, and outcome in cases with EHPVO

Materials and Methods: Consecutive EHPVO cases attending the department of Gastroenterology, S.C.B. Medical College, Cuttack in-between October 2013 to September 2015 were included in the study and evaluated ambriceptively.

Result: Out of total 118 EHPVO patients, most of the cases were males (Male: Female ratio–1.56:1). Median age at the time of diagnosis was 9.5 years (0.6-55 years). 20.33% cases were children. 88.13% patients presented with UGI bleed; whereas 72.88% cases required blood transfusion. 34% cases developed ascites following UGI bleed. Mean frequency of UGI bleed and blood transfusion requirement were 2±1 times and 1.64±1.2 units annually respectively. 50% and 75% children had history of umbilical sepsis and growth retardation respectively. 8.47% and 3.5% cases had associated cholelithiasis and chronic pancreatitis respectively. 17.39% cases had successful pregnancy. 3% cases had portal biliopathy. 84.74% patients had splenomegaly; whereas 10.16% and 3.33% cases had undergone splenectomy and shunt surgery respectively. 96.6% patients had esophageal varices; where as 28.8% patients had also gastric varices. 67.79% cases received endotherapy [80% (sclerotherapy), 20% (band ligation)]; whereas complete sclerosis of varices occurred only in 13.55% cases. 10.56% cases had gastric variceal bleed and undergone glue injection. 2.5% cases incidentally diagnosed to be hepatitis B

antigen positive during follow up evaluation. 12% cases found to have chronic liver disease (CLD) after a median duration of 4 (1-28) years. 2.4% cases expired due to massive UGI bleed.

Conclusion: EHPVO is an important cause of portal hypertension in Odisha. Most cases could be managed with endoscopic therapy in a tertiary care hospital.

Keyword: Extrahepatic Portal Vein Obstruction, Portal Hypertension, Upper Gastrointestinal Bleed

Introduction:

Extrahepatic portal veins obstruction (EHPVO) is a vascular disorder of the liver which is defined as obstruction in the extra hepatic portal vein with or without involvement of the intrahepatic portal veins or splenic or superior mesenteric veins. Isolated splenic vein or superior mesenteric veinocclusion does not constitute EHPVO.[1] Extrahepatic portal venous obstruction (EHPVO), described earlier as portal vein thrombosis,[2] is a distinct disease entity that may present with symptomatic portal hypertension, portal biliopathy, growth retardation, hepatic dysfunction, and bleeding from varices.[1,3–6] Portal vein obstruction associated with chronic liver disease or neoplasia is a separate entity and does not constitute EHPVO.[3] EHPVO cases is usually suspected whenever presence of recent thrombosis or portal hypertension with characteristically formation of portal cavernoma were detected due to long term portal vein obstruction in the cases.[1, 3] It is a heterogeneous disease with regard to demography, etiology, pathogenesis, and outcome and it's classification based on site of portal vein thrombosis, acute or chronic presentation, complete or incomplete portal vein occlusion, and extent of involvement of the extrahepatic portal venous system.[1,3] EHPVO cases usually amount to >20 % of all cases of portal hypertension (PHT) in India, whereas in the west, it was fairly less common (usually <than 5% of total cases of PHT were due to EHPVO).[7] In India, usually most of the EHPVO cases are children with poor socioeconomic status, and good number of them also have history of umbilical sepsis, umbilical vein catheterization, or intra-abdominal sepsis. The difference in prevalence has been attributed to differences in the standard of living and availability of medical care.[8–12] Limited studies from Asia reported the presence of hypercoagulable states in children.[8–12] EHPVO cases during childhood period usually present with variceal bleeding and left sided abdominal lump due to marked splenomegaly. Radiological imaging is the mainstay for the diagnosis of EHPVO. Ultrasound is a reliable non-invasive technique with a high degree of accuracy for the detection of portal cavernoma and usually is the investigation of choice.

Aim of the study

As there is scarcity of robust data on EHPVO cases in this part of Coastal Eastern India the aim of the present study was to assess demographic features, etiology, clinical presentation, and outcome in cases with EHPVO in this region.

Methods

The study was conducted in the gastroenterology department of S.C.B. Medical College and Hospital, Cuttack, Odisha. This was a single centered open labeled cohort study. Cosequetive cases of EHPVO attending the Gastroenterology department of S.C.B. Medical College and Hospital during October 2013 to September 2015 were included in the study and ambriceptively evaluated. In our study EHPVO was diagnosed on the basis of clinical and endoscopic features of portal hypertension, ultrasonographic evidence of portal cavernoma without evidence of chronic liver disease at the time of inclusion. The

weight of the cases was measured in light clothing without shoes by standing on a calibrated weight machine. The height of the cases was measured in standing position by help of calibrated meter scale. Wasting was calculated basing on weight for height. Less than 80% of expected weight for height taken as wasted. Stunting was calculated as height for age. Less than 90% of expected height for age taken as stunted. Routine investigations like complete blood count, liver and renal function tests along with viral marker evaluation were carried out in all patients. Endoscopy was performed using video endoscope (Olympus GIF-V-150, Olympus Corporation, Tokyo, Japan) in all cases to look for esophageal varices, gastric varices and portal hypertensive gastropathy (PHG). Endotherapy was carried out by doing either endoscopic intra/paravariceal sclerotherapy (EST) with diluted 95% ethyl alcohol or by doing endoscopic varieceal ligation (EVL) with multiband ligator in cases with esophageal variceal bleed and by endoscopic variceal glue injection in fundic variceal bleed. Repeated endoscopic procedure like EST, EVL were usually carried out in every 7-21 days for complete eradication of varices. Response to nonselective betablocker therapy as a prophylactic measure against variceal or, PHG related bleed was assessed during follow up evaluation. This study was approved by the Institutional Ethical committee. Written informed consent was obtained from the patients or their parent/guardian as appropriate before inclusion in to the study.

Statistical analysis

The results were expressed as mean ± standard deviation (SD) or frequency (in percentage). Normally distributed quantitative and categorical variables were compared using student's t test and Chi square test respectively. All the analysis was done with SPSS 22 software. A 'p-value of < 0.05 was considered statistically significant.

Results

A total of 118 patients (Male: Female ratio–1.56:1) with median age at the time of diagnosis 9.5 years (range 0.6-55 years) included in this study. Out of total 118 cases, 20.33% cases were children (age $\leq$ 14 years). Age wise distribution of all (Adult+ Children) EHPVO cases were described in the figure 1. The mean weight and height of the patients were 36.9±12.9 Kg and 146.9±20.62 cm respectively. Baseline demographics of all EHPVO cases were narrated in table 1. Baseline biochemical parameters of all cases were described in the table 2. Clinical Presentations of all cases were described in table 3. The total average disease duration was 5.87 ± 5.83 years at the time of evaluation. 16.66% children had history of delayed mile-stone development whereas 75% children had growth retardation. 50% children had past history of neonatal umbilical sepsis. Variants of important past history in all cases were narrated in table 4. Upper GI bleeding (variceal bleed) was present in 88.13% patients followed by anemia and lump abdomen in left upper quadrant in 83% and 74.57%cases respectively. At the time of diagnosis 84.74% patients were found to have splenomegaly, other physical findings included: shrunken liver (30.5%), jaundice (20.33%) and ascites (6.77%). 10.16% cases had history of splenectemy whereas 5% cases had history of biliary operation in the past at the time of evaluation. 3.33% cases had history of shunt surgery. 72.88% cases received blood transfusion for survival whereas 54.23% cases received beta blocker as a secondary prophylactic measure for prevention of variceal bleed out of which 40% cases had some response to betablocker as they did not have any variceal bleed during period of betablocker use.

67.79% cases were treated with variceal band ligation and endoscopic sclerotherapy when variceal banding was not feasible. Average duration between 2 sittings of endotherapy was 19.35 ± 12 days. During follow up study it was found that esophageal varix was completely obliterated in 13.55% cases and 12% cases had chronic liver disease (CLD) after a median duration of 4 (1-28) years during follow up evaluation. Only 17.39% females had successful pregnancy outcome. 18.64% cases developed ascites mostly following massive variceal bleed. 2.4% cases expired due to massive UGI bleed. Radiological investigations revealed splenic vein collateral in 33.89% cases; features of portal biliopathy in 5% cases. All the cases had portal cavernoma. 25.42% cases had portal vein thrombosis. 69.49% cases had normal liver size whereas 30.5% cases had shrunken liver. Radiological Findings in all cases were described in table 5. 22% cases had portal hypertensive gastropathy (PHG); whereas 61.53% cases had severe PHG. 96.6% cases had esophageal varix whereas 28.8% cases had associated fundic varix. 3.4% cases had isolated fundic varix, whereas 25.4% cases had both esophageal and gastric varix. Endoscopy Findings of all cases were described in table 6. 5% cases had associated chronic pancreatitis whereas 8.47% cases had associated gall bladder stone. Normal liver function parameters were seen in most of our patients. However increased serum bilirubin, raised ALT, and AST were present in 27.1%, 16.94% and 27.1%cases respectively mostly in cases following massive bleed and in cases who developed chronic liver disease. 4% cases found to be affected by hepatitis B virus infection despite of no family history of Australian antigen positivity.

Discussion

EHPVO is the most common cause of noncirrhotic portal hypertension in India[7] and accounts for 40% cases of portal hypertension in children.[13] In our study 75% of children had growth retardation which was relatively higher compared to the previous observations by Sarin et al[7] and Mehrotra et al[14] who, reported that 51% and 54.5% EHPVO cases had growth retardation respectively. Study by Jena S.K. et al from this part of Coastal Eastern region reported that 25.8% cases had stunted growth; where as 9.8% cases had both stunting and wasting.[15] The causes of growth retardation in children with EHPVO was not completely understood. The possible hypotheses were: portal venous congestion of the gut, concurrent mal-absorption, and anorexia from splenomegaly may lead to nutritional deficiency and growth retardation in extrahepatic portal venous hypertensioncases. Mehrotra et alsuggested that EHPVO cases may have relatively higher level of growth hormone (GH) along with decreased insulin like growth factor 1 (IGF‑1) levels which suggests a state of GH resistance.[14] 50% of children in our study had history of neonatal umbilical sepsis which was relatively higher compared to the findings of previous study,[15] which showed that neonatal umbilical sepsis and umbilical vein catheterization ware found in 16.1% and 9.6% patients respectively in his study.[15] Umbilical sepsis is the frequently postulated predisposing condition for the development of EHPVO in children. History of home delivery was observed in 40% of our cases which was in consistent with the recently published study[15] and study by Bhandarkar et al.[16] In our study 40% pregnant females with EHPVO were lost to follow up, 20% cases had preterm delivery and low birth weight babies, 10% cases had still birth, 12.61% cases had postdatism and 17.39% females had

successful pregnancy outcome. Women with EHPVO have normal fertility, unlike women with cirrhosis who have reduced fertility and up to 40% fetal-loss rate.[17] However, data regarding the pregnancy outcome and complications in patients with EHPVO were sparse. In our study none of pregnant female with EHPVO developed variceal bleed as all of them undergone prophylactic variceal ligation during pregnancy, which was similarly reported by Aggarwal et al[18] although the incidence of variceal bleeding in pregnancy in patients with EHPVO has been reported to range from 20% to 34%.[19,20] Subbaiah et al. also reported similar type of finding as found in our study as none of their pregnant EHPVO cases had developed variceal bleed during pregnancy.[21] It has been postulated that pregnancy may aggravate portal hypertension in EHPVO cases because of the increased blood volume, increased cardiac output, and mesenteric vasodilatation during pregnancy period.[22] Increasing intra-abdominal pressure in the second and third trimesters may also lead to portal hypertension by increasing the inferior vena cava pressure[23] resulting in rerouting of blood via gastroesophageal collaterals, which increases the risk of variceal bleeding. Pregnancy outcome in our study was in consistent with the findings of study by Mandal et al; who reported a higher incidence of preterm delivery, low birth weight, and stillbirth among pregnant women who were diagnosed for the first time in pregnancy and presented with variceal bleed.[24] All of our pregnant cases with high grade esophageal varices had received EVL as a prophylactic measures against variceal bleed without concurrent use of betablocker as an additional prophylactic measure. Usually cases with EHPVO initially present with gastrointestinal bleeding or rarely with left sided abdominal lump. In our study most (88.13%) of the cases initially presented with variceal bleed which was similarly reported in a prior study which showed that 85.48% cases had variceal bleed.[15] In our study 74.14% cases had left sided lump suggestive of enlarged spleen which was relatively lesser compared to finding of a previous study which showed that 91.9 % cases had splenomegaly.[15] 18.64% cases developed ascites mostly following massive variceal bleed in our study which was similarly found in a previous study [11.2% patients had ascites following gastrointestinal (GI) bleed].[15] Portal biliopathy was present in 5% of our cases; which was similarly reported in previous study, which showed that 3.2% of EHPVO cases had portal biliopathy. Most (83%) of our cases had anemia as similarly found in a prior study (90.3% cases had hemoglobin < 10 gm%).[15] Normal liver function parameters were seen in most of our patients. 27.1% of cases had deranged LFT. Rangari et al postulated that the liver dysfunction in EHPVO could be due to a prolonged reduction in portal blood flow and /or development of portal biliopathy.[25]All the cases had portal cavernoma (distinctive tangle of tortuous vessels in the porta hepatis) in our study; which was relatively higher compared to previous study (87.2% cases had portal cavernoma).[15] In our study 96.6% and 28.8% cases had esophageal and gastroesophageal varices respectively where as Sarin et al found that esophageal and gastric varices were present in 90-95% and 35-40% patients with EHPVO respectively.[7] Similarly El-Hamid et al reported that esophageal varices were present in 85.3% patients.[26] Study by Amarapurkara D et al[27] has reported a high prevalence of myeloproliferative disorder in patients with EHPVO as a contributory factor which was not assessed in our study.

Limitations

We have some limitations in our study. We could not assayed different etiology of EHPVO in our region. We could not look for long term natural outcome in EHPVO cases. We could not look for the predictive factors responsible for morbidity and mortality both on short term and long term basis. We could not do a comparative analysis on response to combined therapy with non selective beta blocker along with endotherapy with only endotherapy or use of betablocker as a prophylactic measure against occurrence of variceal bleed in future.

Conclusion

In our region majority of EHPVO cases present with UGI bleed as the most common and initial mode of presentation along with left sided swelling in the abdomen. Most of our cases had esophageal varix and responded well to the endotherapy. In our region most of pregnant ladies with EHPVO did not have a good fetal outcome despite of absence of any UGI bleed. Our study is possibly the largest study on EHPVO from this region of Coastal Eastern India. Further long term prospective studies in future may validate our findings.

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Tables and Figures

Figure 1: Age distribution of all case of EHPVO

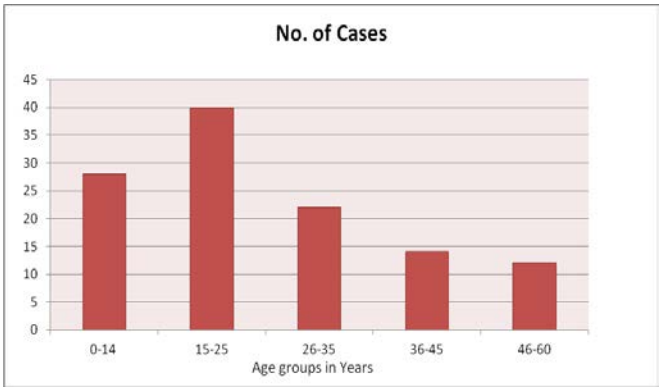

Table 1: Baseline Demographics of all (Adult+ Children) EHPVO cases

Demographic variables	Findings
Mean age of presentation	19.61±15.38 years
Male: Female	72:46
Height	146.9±20.62 cm
Weight	36.97±12.97 Kg
Age of first bleed	20.41±14.33 years

Table 2: Baseline Biochemical Parameters of all (Adult+ Children) EHPVO cases

Biochemical parameters	Values
Hemoglobin	9±2.27 Gm/ dl
Total Platelet Count	1.99±1.22 lakhs/ cmm
Total Bilirubin	1.84±2.81mg/ dl
Aspartate Transaminase	46.67±30.7 IU/ dl
Alanine Transaminase	38.3±26.23 IU/ dl
Alkaline Phosphatase	304±173.51 IU/ dl
Albumin	3.3±0.74 Gm/ dl

Table 3: Clinical Presentations of all (Adult+ Children) EHPVO cases

Clinical Presentations	Percentage of cases
Blood Vomiting	88.13%
Melaena	88.13%
Left Sided Lump	74.57%
Anemia	83%
Growth Retardation	15.25%
Pedal Edema	1.69%
Ascites	18.64%
Jaundice	20.33%

Table 4: Variants of Important Past History in all (Adult+ Children) EHPVO Cases

Past History Variants	Percentage of Cases
Umbilical Sepsis	23.72%
Delayed Milestone	5.08%
History of (H/O) Biliary	5.08%
History of Splenectomy	10.16%
History of Shunt Surgery	3.33%
History of Repeated Blood	72.88%
H/O Regular Endoscopic variceal lligation	67.79%
H/O Uninterrupted	54.23%
History of Chronic	5.08%
History of Cholelithiasis	8.47%

Table 5: Radiological Findings in all (Adult+ Children) EHPVO cases

Ultrasonography findings	Percentage of cases
Splenomegally	84.74%
Pregnancy	17.39%
Splenic Vein Collaterals	33.89%
Portal Cavernoma	100%
Portal Vein Thrombosis	25.42%
Portal Biliopathy	5.08%
Dilated Portal Vein	18.64%
Normal Sized Liver	69.49%
Shrunken Liver	30.5%
Chronic liver disease	12.03%

Table 6: Endoscopy Findings of all (Adult+ Children) EHPVO cases

Endoscopy Findings	Percentage of Cases
Esophageal Varix	96.61%
Fundic Varix	28.81%
Severe Portal Hypertensive Gastropathy (PHG)	61.53%
Mild Portal Hypertensive Gastropathy (PHG)	22.03%
Sclerosed Varix	13.55%
Gastroesophageal Varix	28.81%