Clinico-epidemiological Profile of Extra Hepatic Portal Vein Obstruction: A Tertiary Care Hospital Based Retrospective Study

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ABSTRACT

Background

Extra hepatic portal vein obstruction (EHPVO) is a common cause of portal hypertension in the developing countries (up to 30% of all variceal bleeders) and is second to cirrhosis in the West (up to 5-10%). Our understanding of the disease is poor compared with other illnesses.

Objective

To undertake a retrospective study of the clinicoepidemiological profile of Extra hepatic portal vein obstruction in a tertiary care hospital in eastern Nepal.

Method

All consecutive adult patients whose features were consistent with the diagnosis of extra hepatic portal vein obstruction from June 2014 to June 2016 were retrospectively analyzed to explore the various clinico-epidemiological parameters.

Result

A total of 58 patients were enrolled in the study with a median age of 24 years (20.5-40). Portal vein thrombosis was the most common cause of extrahepatic portal vein obstruction. Hematemesis followed by melena were the most common presenting symptoms. All patients had splenomegaly on examination. None of the patients had clinical, biochemical or radiological evidence of chronic liver disease.

Conclusion

The diagnosis of extra hepatic portal venous obstruction and differentiation from cirrhosis can be easily made by characteristic clinical features, normal liver function tests and doppler ultrasound. Portal vein thrombosis (PVT) is the predominant cause of extra hepatic portal vein obstruction in Nepali patients, as seen at this tertiary care hospital in Nepal.

KEY WORDS

Cirrhosis, Extra hepatic portal vein obstruction, Thrombosis

INTRODUCTION

Extra hepatic portal vein obstruction (EHPVO) is a vascular disorder of the liver defined by obstruction of the extra-hepatic portal vein with or without involvement of the intra-hepatic portal veins or splenic or superior mesenteric veins. EHPVO is a common cause of portal hypertension in the developing countries (up to 30% of all variceal bleeders) and is second to cirrhosis in the West (up to 5-10%).[1] Its etiology is still not clear but has been attributed to umbilical sepsis after birth with thrombosis extending to the portal system via the patent umbilical vein. Underlying hypercoagulable and prothrombotic states are commonly reported from the West.[2]

There are only a few studies on the clinical profile of subjects with EHPVO in Nepal.

In this study, we sought to ascertain the clinical profile of subjects with EHPVO in eastern Nepal, especially with regard to risk factors, clinical features and therapeutic modalities.

METHODS

This was a retrospective observational study conducted in the department of Internal medicine from June 2014 to June 2016. Ethical approval was taken from the Institute Research Committee. Consecutive patients > 18 years age admitted in ward of the department with various symptoms of EHPVO were considered. Patients with EHPVO of varied etiologies were considered for the study.

Adult subjects (≥ 18 years of age) with characteristic clinical features, normal LFTs and ultrasound Doppler findings of EHPVO admitted in Medicine wards in the Department of Internal Medicine from June 2014 to June 2016 were included in the study. The diagnosis of EHPVO was based on characteristic clinical features, laboratory test, imaging diagnostics, and whenever possible, on liver histology. EHPVO is a vascular disorder of the liver characterized by obstruction of the extra-hepatic portal vein with or without involvement of the intra-hepatic portal veins or splenic or superior mesenteric veins.[2] It was reevaluated according to the following criteria: (i) clinical history of hematemesis or upper pain abdomen of varying severity or ascites/jaundice. (ii) Ultrasonic Doppler (USG Doppler) examination of the upper abdomen (replacement of portal vein by multiple tortuous vessels, also known as cavernous transformation, with hepatopetal blood flow in the collaterals, normal liver echotexture) or (iii) Contrast-enhanced CT and MRI (MRA) (cavernomatous transformation with splenomegaly and/or no opacification of the hepatic portal vein).[2,3]

Since this was a retrospective study we enrolled all consecutive patients who met the case definition and inclusion criteria for EHPVO within the study period of two years. Data were collected from the medical record section after approval from the department. A detailed socio-demographic data for every patient was collected and information was recorded in a structured proforma. The demography included age, sex, race, occupation, BMI and socioeconomic status. Socioeconomic status was assessed according to the Kupuswammy index modified for nepali rupees.

After extensive survey of the medical records, the following parameters were collected: liver function test, complete blood count, renal function test, prothrombin time, HbsAg and anti HCV. The patients work up for hypercoagulable state was analysed whenever feasible with protein c and protein s deficiency. Records of other specialized procedures including Endoscopy and ultra sound abdomen were collected in all patients.

Data was entered in MS Excel 2007 and converted to SPSS 11.5 version for statistical analysis. Descriptive and inferential statistics was used to describe the data in number, frequency, mean and standard deviation. Quantitative data was described in mean and standard deviation considering the normality of data. Median and interquartile range was calculated in the case of skewed distribution. Unpaired 't' test was applied to compare two independent means and their significance level was estimated using 95% confidence interval and p-value at 5%.

RESULTS

Fifty-eight patients were enrolled in the study. There were 33 males (56.9%) and 25 females (43.1%). The average age of the study subjects was 24 years (20.5-40). The socioeconomic distribution of the subjects (according to Modified Kuppuswamy Index) was: upper class 0(0%), upper middle class 12(20.7%), middle/lower middle class 21(36.2%), lower/upper lower class 25(43.1%) and lower class 0(0%).

Factors related to the disease

The most common presentations with which the patients were admitted were: hematemesis and melena. The distribution of presenting complaints is listed in (Table 1).

Table 1. Distribution of presenting complaints observed in patients with EHPVO

Presenting Complaints	Frequency (n=58)
Hematemesis	34(58.6%)
Melena	30(51.7%)
Pain abdomen	12(20.7%)
Ascites	7(12.1%)
Jaundice	7(12.1%)

Risk factor assessment of EHPVO

Of the 58 subjects, 54(93.1%) did not have any of the risk factors generally described in the literature. Four patients (6.9 %) were a diagnosed case of Chronic Myeloid Leukemia (proven by bone marrow examination and presence of

Philadelphia chromosome). It was possible to conduct protein c and protein s deficiency level measurement in only five patients (8.6%) which came out to be in the normal range. Similarly none of the patients had any evidence of Intra-abdominal sepsis and a thrombotic stimulus like pregnancy, abdominal surgery and oral contraceptives.

Forty seven subjects (81%) were non alcoholic while 19% (11 patients) were social drinkers. None of the study subjects were smokers.

Parameters on examination

The most common findings on examination of the 58 subjects were: splenomegaly 58(100%), pallor 41(71.7%), icterus 7(12.1%), ascites 7(12.1%) and hepatomegaly 5(8.6%).

Laboratory parameters

The average hemoglobin and platelets were 8.20 g/dl (6.3-9) and 64,000 per microliter (46,000-110000) respectively. Fifty one patients (87.9%) had evidence of microcytic hypochromic anemia.

Liver function test was abnormal in seven patients (12.1%). The only derangement in liver function was conjugated hyperbilirubinemia. The average Prothrombin time of study subjects was 12 secs (11-13 secs).

Imaging modalities

Ultrasound data was available in all of the 58 patients (100%) and the most common findings were: splenomegaly, cavernous transformation of the portal vein and portal vein thrombosis.

Similarly CT findings were available in all patients and the most common findings were: splenomegaly, cavernous transformation of the portal vein and portal vein thrombosis. Common findings noted on imaging are listed in (Table 2) and demonstrated in (fig. 1)

Table 2. Common findings noted on imaging.

Variable	Ultrasound (n=58)	CT(n=58)
Splenomegaly	58 (100%)	58 (100%)
Cavernous transformation Of portal vein	58 (100%)	58 (100%)
Portal vein thrombosis	46 (79.3%)	37 (63.8%)
Hepatopetal portal flow	44 (75.9%)	NA
IHBRD	0 (0%)	7 (12.1%)

Upper G I Endoscopy

All the 58 subjects had undergone upper gastro intestinal endoscopy. Eighteen patients (31%) had grade 1 esophageal varices while 35 patients (60.3%) had grade 3 esophageal varices. Upper GI endoscopy was normal in 5 patients (8.6%). Thirteen patients (22.4%) had gastroesophageal varices type-2 (GOV-2) (Sarin classification). None of the patients had GOV-1 (gastroesophageal varices type 1), IGV-1 (isolated gastric varices- 1) or IGV-2 (isolated gastric varices-2). Of the 34 patients who presented with hematemesis, 30(85.7%) had Grade III esophageal varices and 4(22.2%) had Grade I esophageal varices which was statistically significant ($p<0.001$). Endoscopic finding of Grade 3 esophageal varices noted in EHPVO patients is depicted in (fig. 2)

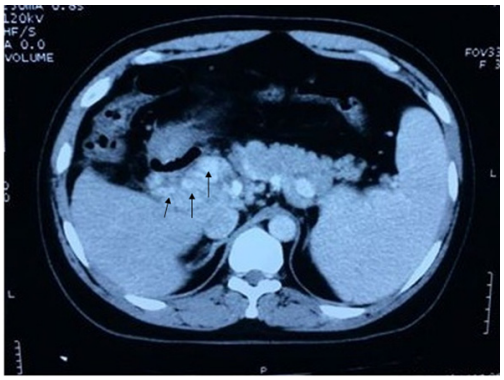

Figure 1. Contrast enhanced axial CT scan shows non visualization of the main portal vein and splenomegaly. Multiple dilated tortuous vessels (arrows) seen in the region of portal vein and porta hepatis s/o Cavernous transformation.

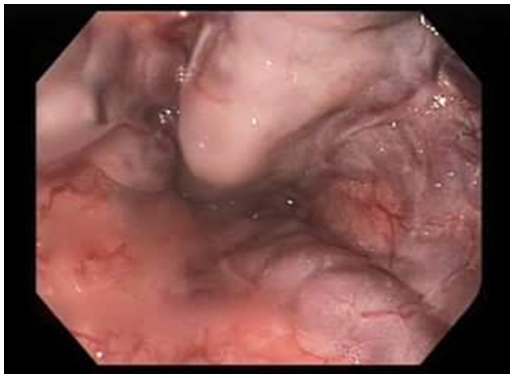

Figure 2. Endoscopy image shows grade 3 esophageal varices in a patient with Extra hepatic portal vein obstruction.

Treatment modalities for EHPVO

Of the 58 subjects enrolled in the study four patients (6.9%) received i.v. somatostatin analogue (IV Octreotide), 12 patients (20.7%) received beta blockers (Propranolol), 20 patients (34.5%) received combination of somatostatin analogue and beta blockers, 17 patients (29.3%) received a combination of somatostatin analogue and endoscopic variceal band ligation and five patients (8.6%) received a combination of somatostatin analogue, endoscopic variceal band ligation and beta blockers. None of the patients received anticoagulation.

DISCUSSION

We report the results of a Tertiary Care Hospital based retrospective study of subjects with EHPVO in Eastern Nepal. The results of our study, conducted on 58 patients, clearly show that the most common cause of EHPVO in Nepal is idiopathic. Only four patients had an underlying myeloproliferative neoplasm (Chronic myeloid leukaemia). In adults and older age group extra hepatic portal

vein obstruction is relatively rare and the causes are myeloprolifrative disorders, deficiencies of protein C and S and anti thrombin III leading to hypercoagulable state and portal vein thrombosis. Other rare causes in older age groups are tumours in liver, bile ducts, and pancreas.[4] Tests for venous thromboembolism such as the presence of factor V Leiden, protein C, S and antithrombin III levels, and prothrombin gene mutation may also be positive in certain adult patients but have not had a high yield in the Indian scenario.[5-7] Stuart et al. concluded in his study that etiology of EHPVO in most cases is unknown.[8]

Median age of of the subjects in our study was 24 years (20.5-40). The most common presentations were hematemesis (n=34, 58.6%) and melena (n=30,51.7%). Variceal bleeding in EHPVO usually occurs in the first or second decade of life.[9] Variceal bleeding and hypersplenism are the common manifestations of chronic EHPVO.[2] Hypersplenism was common as evident by splenomegaly (n=58,100%) and the average platelet count of 64,000 per microliter (46,000-110000). Seven patients had icterus, abnormal LFT in the form of conjugated hyperbilirubinemia and intrahepatic biliary radical dilatation on CT abdomen. These are features consistent with portal biliopathy which needed further confirmation with ERCP or MRCP. The term 'Portal biliopathy', introduced in 1992, refers to abnormalities of the extrahepatic and intrahepatic bile ducts in patients with portal hypertension. These include indentations by paracholedochal collaterals on bile ducts, localized strictures, angulation of ducts, displacement of ducts, focal narrowing, dilatations and irregular walls. While bile duct changes have been reported in 80-100% of patients with EHPVO on endoscopic retrograde cholangiopancreatography (ERCP), these are rarely symptomatic and seen in adulthood.[10]

In our study the most common findings on imaging (ultrasound and CT abdomen) were splenomegaly, cavernous transformation of portal vein and portal vein thrombosis. Hepatopetal portal flow was observed in 44 patients (75.9%) on Doppler ultrasound. The diagnosis of extra hepatic portal venous obstruction (EHPVO) is easily made by characteristic clinical features, normal liver function tests and ultra sonography or spleno porto venography. Ultrasound Doppler of the upper abdomen is the most accurate diagnostic modality. Characteristic findings are replacement of portal vein by multiple tortuous vessels, also known as cavernous transformation, with hepatopetal blood flow in the collaterals.[3]

Of the 58 subjects who had undergone upper GI endoscopy 35 patients had grade 3 esophageal varices and 18 had grade 1 esophageal varices. Similarly gastroesophageal varices type-2 (gov-2) was observed in thirteen patients. Study conducted by Shah et al. revealed that 90% patients had Grade III varices on endoscopy while proctoscopy revealed 24% patients had rectal varices.[11] Gastric varices are seen in 30-40% patients with EHPVO. Furthermore a past history of bleeding and moderate to large esophageal varices are independent risk factors for GI bleeding, and an underlying prothrombotic condition is an independent risk factor for recurrent thrombosis.[12] In our study hematemesis was noted more in grade III esophageal varices (85.7%) than grade I esophageal varices which was statistically significant.

All our study subjects received medical and/or endotherapy. All patients who presented with acute variceal bleeding were managed with somatostatin analogue. Twenty two patients underwent endoscopic variceal band ligation for large varices and were asked to follow up for subsequent sessions as per the requirement. Patients with gastroesophageal varices were advised for cyanoacrylate glue therapy (for the gastric varices) followed by endoscopic variceal band ligation. Endotherapy is the predominant treatment modality for the control of acute bleeding and also an important method for the prevention of a repeated bleeding episode. The main disadvantages of endotherapy are that it requires multiple sessions and a long-term followup with a recurrence rate of up to 40% in some studies.[11] Because the prevalence of EHPVO is the highest in developing countries and the condition affects mainly the poor, most of whom do not have access to blood transfusion facilities and are not treatment compliant, the benefits of using a less invasive procedure like endoscopic therapy must be weighed against surgery which, in the best centres carries an operative mortality of 1%, is a onetime treatment, is not associated with encephalopathy and followed by rebleeding rates of less than 10%.[13,14] Similarly Sarin et al. stated in his consensus on EHPVO that surgery should be reserved for patients who fail endoscopic therapy, have significant growth retardation in prepubertal age, symptomatic portal biliopathy and symptomatic hypersplenism.[2]

This study had several limitations. Obviously the sample size was not adequate given the study period. Furthermore the design of the study being a retrospective analysis, there were occasionally missing data.

CONCLUSION

EHPVO is one of the major causes of upper G I bleeding in the developing countries. The diagnosis of EHPVO is almost certain in young patient with splenomegaly and upper GI bleeding in the absence of stigmatas of chronic liver disease. Portal vein thrombosis (PVT) is the predominant cause of EHPVO in Nepali patients, as seen at this tertiary care hospital in Nepal. There are limited published studies conducted on EHPVO in Nepal. This can be attributed to the limited healthcare resource and proper diagnostic modalities available for the patient. So there is a need for properly conducted larger studies highlighting the various clinicoepidemiological aspect of this common but relatively underdiagnosed clinical entity.

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