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Prevalence of non-cirrhotic portal hypertension among GIT bleeding patients at single center Alexandria governorate, Egypt

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Abstract

Background: Estimates the different etiological varieties of non cirrhotic portal hypertension (NCPH) among GIT bleeding patients, helps to set priorities when deciding policies of investigations and management.

Objective: To assess the diversity of non-cirrhotic portal hypertension patients and causes among GIT bleeding patients in our hospital Alexandria Fever Hospital (AFH).

Methods: A hospital-based cross sectional study was conducted at AFH, a tertiary hospital in Alexandria governorate. The GIT unit, was responsible for setting the protocol of investigations and management.

Results: The most common causes were Schistosomal periportal fibrosis (48%) followed by portal vein thrombosis (28%), then Myeloproliferative diseases (12%), then Budd-Chiari syndrome (8%), then Sarcoidosis (4%).

Conclusion: In our city, Schistosomal periportal fibrosis (PPF) was the most common cause for non-cirrhotic portal hypertension patients presenting by GIT bleeding followed by portal vein thrombosis (PVT). There was less common causes; Myeloproliferative diseases (MPN), Budd-Chiari syndrome and Sarcoidosis.

Key words: Non-cirrhotic portal hypertension, extra-hepatic portal venous obstruction, portal hypertension, periportal fibrosis

Abbreviations:

NCPH: Non-cirrohtic portal hypertension

EHPVO: Extra-hepatic portal venous obstruction

HVPG: Hepatic venous pressure gradient

PVT : Portal vein thrombosis

PHT : portal hypertension

AFH: Alexandria Fever Hospital

GAVE: Gastric antral vascular ectesia

PHG: portal hypertensive gastropathy

MPNs or MPD: Myeloproliferative neoplasms or disorders

Schistosomiasis PPF: Schistosomiasis periportal fibrosis

Introduction

Non-cirrhotic portal hypertension (NCPH) is a group of disorders, which present only with features of portal hypertension (PHT) without any evidence of significant parenchymal liver dysfunction. (1)

Diseases leading to NCPH are primarily vascular in nature and classified anatomically on the basis of site of resistance to blood flow as prehepatic, hepatic and post-hepatic. Hepatic causes are subdivided to pre-sinusoidal, sinusoidal and Post-sinusoidal. (2)

Diagnosis of NCPH is by radiological (CT, MR, Doppler) and liver biopsy. (3)

Table 1: APASL criteria for non-cirrhotic portal hypertension / idiopathic portal hypertension (NCPH/IPH)

APASL criteria for NCPH/IPH
<ul style="list-style-type: none"> • Presence of moderate to massive splenomegaly • Evidence of portal hypertension, varices and/or collaterals • Patent spleno-portal axis on ultrasound Doppler • Test results indicating normal or near-normal liver functions • Normal or Near normal HVPG • Liver histology no evidence of cirrhosis or parenchymal injury <p>Other features:</p> <ul style="list-style-type: none"> • Absence of signa of chronic liver disease • No decompensation after variceal bleed except occasional transient ascites • Absence of serum markers of hepatitis B & C infection • No known etiology of liver disease • Imaging with ultrasound or other imaging technique showing dilated and thickened portal vein with peripheral pruning and periportal hyperechoic areas

Patients with acute GIT bleeding are commonly admitted to our GIT Center in Alexandria Fever Hospital (AFH) for management, and follow up. After resuscitation, endoscopic management would be tried.

We found a group of patients of GIT bleeding due to portal hypertension whether esophageal, gastric or duodenal varices without any previous history of liver cirrhosis or liver disease. These patients were the target of our study.

The present study was aimed to assess the diversity of non-cirrhotic portal hypertension patients and causes among GIT bleeding patients in our hospital.

Subjects and Methods

A hospital-based cross-sectional study was conducted at Alexandria Fever Hospital (AFH), a tertiary hospital in Alexandria governorate, Egypt after approval of local ethical committee approval. The GIT center in AFH was responsible for setting the protocol of investigations and management. The study took place over a period of three years from July

2018 to July 2021.

A total of 25 patients were prospectively enrolled in the study, with the following inclusion criteria: acute GIT bleeding due portal hypertension collateral including esophageal, gastric or duodenal varices without any history of liver cirrhosis or liver disease.

Exclusion criteria were: Patients who are known as previous liver cirrhosis or liver disease or proved later by investigation to be liver cirrhosis.

Data collection: Demographic characteristics (age, gender, race, address), history taken included (previous liver disease, drug and alcohol consumption, previous pregnancy and operations). The state of patients upon admission (primary diagnosis, associated co-morbidities), results of laboratory, radiological and endoscopic workup and clinical data details were recorded.

Laboratory data were obtained for all patients at the selected time points. They included liver enzymes and liver function tests, complete blood picture and coagulation profile. If coagulation profile is disturbed, we refer patient to hematologist for evaluation and may need bone marrow sampling.

Doppler USG is the first line radiological investigation followed by Contrast-enhanced computed tomography (CT), which help in differentiating NCPH from Extra-hepatic portal venous obstruction (EHPVO). Magnetic resonance (MR) angiography and portography may be needed.

Upper and lower GIT endoscopic examination was performed. Careful endoscopic examination management of esophageal, gastric, duodenal or even colonic varices is the role.

Liver biopsy is not essential for the diagnosis of EHPVO unless the underlying chronic liver disease is suspected, but it is indicated in NCPH to exclude cirrhosis and other etiologies of PHT.

Results

In our GIT center of AFH, we reported 25 patients of NCPH presented endoscopically by esophageal varices, gastric varices, gastropathy, duodenal varix or colonic varix:

After doing investigations including laboratory, imaging and sometimes biopsies the diagnosis of the cause of non-cirrhotic portal hypertension was made as illustrated in table 2

We did liver biopsy in 4 patients of the 25 patients of NCPH; one patient diagnosed with sarcoidosis (fig 1), one patient with myeloproliferative disease and two patients were Schistosomiasis periportal fibrosis.

Table 2: Etiological diagnosis in patients with NCPH

Findings	Number (%)
Schistosomal periportal fibrosis	12 patients (48%)
Myeloproliferative diseases	3 patients (12%)
Sarcoidosis	One patient (4%)
Budd-Chiari syndrome	2 patients (8%)
Portal vein thrombosis	7 patients (28%)

Table 3: Age distribution of NCPH patients

	Age (years)	Number of patients
PVT (children)	4,10	2
PVT (adults)	21-35	5
Schistosomal PPF	40-55	12
MPNs	55-65	3
Budd Chiari syndrome	32,35	2
Sarcoidosis	67	1

Table 4: Gender distribution of NCPH patients

	Number of patients	Number of male patients	Number of female patients
Schistosomal PPF	12	11	1
PVT	7	2	5
MPNs	3	1	2
Budd Chiari syndrome	2	1	1
Sarcoidosis	1	1	-
Total number	25	16	9

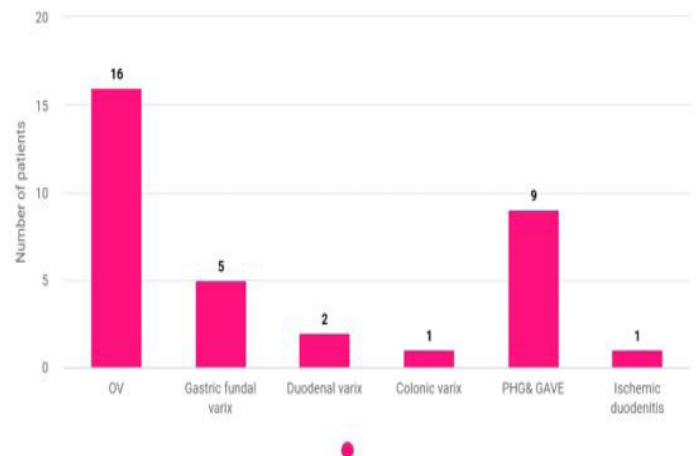


Figure 2: Endoscopic finding in patients of NCPH

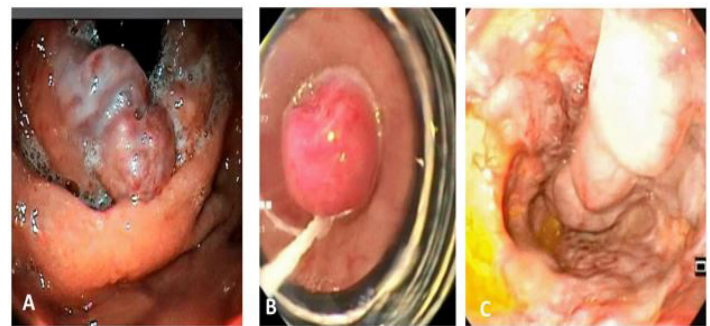


Figure 3: A) Bleeding fundal varix B) Ligated esophageal varix C) Bleeding esophageal varices

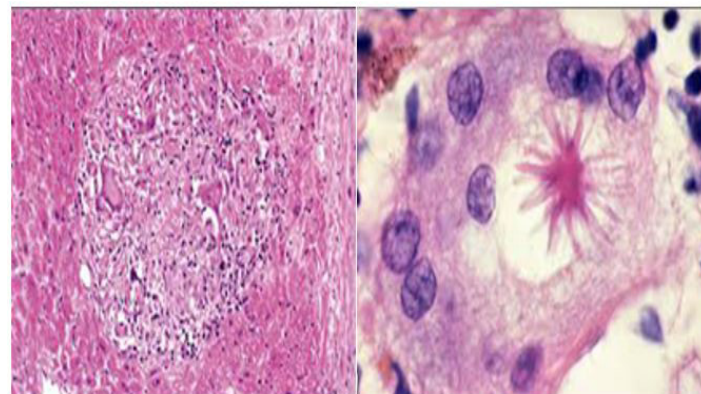


Figure 1: Liver biopsy of Sarcoid liver: Infiltrative non-caseating granulomatous lesions with mild fibrosis of portal venous walls

21 patients of the 25 patients of NCPH were diagnosed by Doppler ultrasound and Contrast-enhanced computed tomography (CT); 7 patients were portal vein thrombosis; 2 patients were Budd-Chiari syndrome and 10 patients were diagnosed as Schistosomiasis periportal fibrosis.

Hematologic workup was done for 8 of the 25 patients of NCPH. The 3 patients' myeloproliferative disease were diagnosed by bone marrow sampling. Four patients of portal vein thrombosis needed hematologic evaluation; 2 children patients (4 & 10 years) were diagnosed as Sickle cell anemia and Factor V Leiden mutation, 2 adult patients



Figure 4: PHG and GAVE

(20 & 23 years) were diagnosed as protein C deficiency and Factor V Leiden mutation. One Budd Chiari patient (Male, 32 years) was diagnosed as polycythemia vera. The other Budd Chiari patient (Female, 35 years) was predisposed by contraceptive pills.

The remaining 3 adult patients of portal vein thrombosis (35, 43 & 48 years) were diagnosed by ultrasound and Contrast-enhanced computed tomography (CT) after abdominal surgery or infection; one post splenectomy, one post infected cholecystectomy and one patient of walled off necrosis pancreatic cyst underwent cysto-gastrostomy.

The endoscopic findings were: 16 patients of bleeding esophageal varices, 5 patients of bleeding fundal varices, 2 patient of ectopic duodenal varix, 1 patient of ectopic colonic varix, one patient of ischemic duodenitis, and 9 patients of portal hypertensive gastropathy (PHG).

Discussion

Noncirrhotic portal hypertension (NCPH) is a heterogeneous group of liver disorders of vascular origin, leading to PHT with near normal HVPG (4 & 5).

IN Western countries cirrhosis is the most common cause > 90%, otherwise non-cirrhotic causes are < 10% worldwide (6). NCPH commonest causes are Schistosomiasis, portal vein thrombosis and idiopathic (7).

NCPH is often asymptomatic until complications of portal hypertension develop which include: variceal hemorrhage, portal hypertensive gastropathy, ascites, hepatorenal syndrome, hepatopulmonary syndrome and cardiomyopathy (8).

The current study demonstrated the diversity of non-cirrhotic portal hypertension (NCPH) patients and their causes among GIT bleeding patients in our city. In addition, it demonstrated its novel aspect in exploring age and gender distribution among Alexandria fever hospital (AFH) patients. Among our 25 patients of NCPH, the study revealed that the most common cause is Schistosomal periportal fibrosis (PPF) 12 patients (48%) most of them were males between 40 – 55 years old, followed by Portal vein thrombosis (PVT) 7 patients (28%) most of them were adults between 21 – 35 years and 2 patients were children (4, 10 years), followed by Myeloproliferative diseases 3 patients (12%), then Budd-Chiari syndrome 2 patients (8%) and lastly Sarcoidosis 1 patient (4%).

Schistosomiasis PPF was the most common cause of NCPH in our study as other studies throughout the worldwide. Chronic hepatic schistosomiasis is characterized by features of portal hypertension: esophageal varices, gastric varices, gastropathy, splenomegaly with hypersplenism. In Indian and Uganda studies, Schistosomiasis was the most common cause of NCPH (8-9). Studies showed that 20% to 50% of adult patients diagnosed with hepatic schistosomiasis from an endemic area also have portal hypertension, varices, variceal upper gastrointestinal bleeding at the time of first diagnosis (10).

In our study we found 7 patients (28% of all NCPH patients) were diagnosed as portal vein thrombosis (PVT), 2 children patients (4 & 10 years) were diagnosed as Sickle cell anemia and Factor V Leiden mutation, 2 adult patients (20 & 23 years) were diagnosed as protein C deficiency and Factor V Leiden mutation, the remaining 3 adult

patients of portal vein thrombosis (35, 43 & 48 years) were diagnosed by ultrasound and Contrast-enhanced computed tomography (CT) after abdominal surgery or infection; one post splenectomy, one post infected cholecystectomy and one patient of walled off necrosis pancreatic cyst underwent cysto-gastrostomy..

Patients with acute PVT have sudden onset of portal hypertension leading to GIT collaterals and bleeding. PVT may be complete or partial and clot may extend to the mesenteric veins or the splenic vein (11).

Extra-hepatic portal venous obstruction (EHPVO) is characterized by a chronic blockage of PV blood supply leading to PHT and its sequelae in the setting of a well-preserved liver function. EHPVO is a major cause of PHT (54%) and upper gastrointestinal bleeding in children (68–84%) from the developing world. In the West, non-cirrhotic non-tumoral PVT is the second most frequent cause of PHT in adults, whereas in children it constitutes a small proportion (11%) (12).

Like other studies of venous thrombosis, the factors leading to EHPVO can be grouped as those within the vessel lumen, within the wall and outside the vessel; and also, as prothrombotic states (inherited or acquired) and local factors (trauma, injury, inflammatory conditions). The most common prothrombotic states seen in children are methylene tetrahydrofolate reductase (MTHFR) deficiency and prothrombin gene mutations, whereas in adults, primary myeloproliferative disorders (MPN) (with or without janus kinase 2, JAK2 mutation are the commonest (13).

A previous Egyptian study performed to assess the prevalence of factor V Leiden mutation and other thrombophilic factors as risk factors in the development of PVT in the pediatric age group had detectable hereditary thrombophilia (62.5%), 12 had factor V Leiden mutation (30%), 11 had protein C deficiency (27.5%), 6 had factor II mutation (15%) (14).

In our study, we found 3 patients (12%) of Myeloproliferative disorders or neoplasms (MPN) after hematologic and bone marrow evaluation.

Myeloproliferative disorders or neoplasms (MPN) diagnosis is based on the morphology of peripheral blood and bone marrow aspirate. Clinically, splenomegaly and hepatomegaly due to extramedullary hemopoiesis are common. The clinical symptoms and complications are primarily due thrombocytosis and polycythemia causing circulatory problems or thrombotic events as PVT (15). In a recent meta-analysis, the prevalence of MPD and JAK2 mutations in PVT was found to be 31.5% and 27.7%, respectively (16). On the other hand, in a patient with non-

malignant non-cirrhotic PVT, the odds ratios of usage of oral contraceptives, or presence of prothrombin gene mutation, factor-V Leiden, or deficiencies of protein-C, protein-S and antithrombin-III are 50, 7, 1.5, 5, 3, and 1, respectively (16).

In our study, we found 2 patients (8%) of Budd Chiari syndrome, one patient (Male, 32 years) was diagnosed as polycythemia vera, the other patient (Female, 35 years) was predisposed by contraceptive pills.

In our study, we found 1 patient (4%) of Sarcoidosis diagnosed by liver biopsy.

Sarcoidosis is a multisystemic disease characterized by the presence of non-caseating granulomas in affected organs. Hepatic and pulmonary involvement is common (17). Long-standing sarcoid liver has been reported to result in portal hypertension in 3–18% of patients. This may be due initially to compression of portal venules by granulomas, and can result in variceal bleeding. Liver biopsy is usually required to confirm diagnosis (18). Similar to our case, Hitoshi Yoshiji and coworkers documented a histologically proven case of progressive liver sarcoidosis with variceal rupture (19).

Conclusion

In our study, we investigated the etiology amongst inpatients of our GIT center in AFH to try to capture the diversity of noncirrhotic portal hypertension (NCPH) causes responsible for GIT bleeding.

In our study, we record 25 inpatients of NCPH presenting by GIT bleeding through the three years duration of our study. The commonest etiological diagnosis was schistosomal periportal fibrosis (12 patients) followed by portal vein thrombosis (7 patients), Myeloproliferative disease (3 patients), Budd Chiari syndrome (2 patients) and sarcoidosis (1 patient).

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