ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF INTERNAL MEDICINE

Research title

Sociodemographic features, risk factors, clinical characteristics and treatment outcomes of patients with Chronic portal vein thrombosis seen at TASH and Adera medical center during the period between August 2019 and August 2021, Addis Ababa, Ethiopia

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A thesis to be submitted to Addis Ababa University, College of HealthSciences, School of Medicine, Department of Internal Medicine in preparation for partial fulfillment of the requirement for a Specialty certificate in Internal Medicine.

Addis Ababa, Ethiopia, 2021

Title: Socio demographic features, risk factors, clinical characteristics and treatment outcomes of patients with Chronic portal vein thrombosis seen at TASH and Adera medical center during the period between August 2019 and August 2021, Addis Ababa, Ethiopia

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Declaration

I, Selamawit Yizelkal, declare that this thesis is my original work and has not been submitted elsewhere. I also declare that a complete list of references is provided indicating all the sources of information quoted or cited.

Signature _____ Date _____

Acknowledgment

I want to express my sincere gratitude to the Department of Internal Medicine, College of Health Sciences, Addis Ababa University, for facilitating the opportunity and providing the funding to conduct this research.

My utmost appreciation goes to my advisor Professor Abate Bane for his immense guidance and support in the design and conduction of this study.

I would like to acknowledge Adera Medical Center for letting me conductthe study and facilitating this research.

I would also want to thank patients, participating colleagues, Dr. Balew Yihonal and those who assisted in data collection and analysis.

Last of course but not least; my special thanks goes to my family and friendsfor the support and assistance they provided me with.

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List of abbreviations

ACLF	Acute-on-chronic liver failure
CKD	chronic kidney disease
DOACS	Direct oral anticoagulants
DM	Diabetes mellitus
ED	Emergency department
EHPVO	Extra hepatic portal vein obstruction
EV	Esophageal varices
EVL	Endoscopic variceal ligation
GI	Gastrointestinal
HCC	Hepatocellular carcinoma
HIV	Human immunodeficiency virus
HPS	Hepatopulmonary syndrome
HTN	Hypertension
ICU	Intensive care unit
IHD	Ischemic heart disease
LMWH	Low molecular weight heparin
MPN	Myeloproliferative neoplasms
NASH	Non-alcoholic steatohepatitis
NSBB	Nonselective beta blocker
PHG	Portal hypertensive gastropathy
PSVD	Post sinusoidal vascular disease

PV	Portal vein
PVT	Portal vein thrombosis
SPSS	Statistical package for the social sciences
TASH	Tikur Anbessa Specialized hospital
TIPS	Trans jugular intrahepatic Porto systemic shunt
UVC	Umbilical vein catheterization
VKA	Vitamin K antagonist

Abstract

Background:Portal vein thrombosis is the most common cause of extra-hepatic portal vein obstruction. Its prevalence is variable based on studied population, but is higher in developing countries than developed countries. PVT is mainly associated with cirrhosis and depends on the severity of the disease.

Objectives: This study was conducted to assess the socio-demographic features, risk factors, clinical characteristics and treatment outcomes of patients with chronic portal vein thrombosis seen at Tikur Anbessa specialized hospital (TASH) and Adera medical center during the period between August 2019 and August 2021, Addis Ababa, Ethiopia. The study also tried to assess the difference of presentation and outcome of patients between cirrhotic andnon-cirrhoticPortal vein thrombosis (PVT).

Methods and materials: The study will be conducted as a cross sectional cohort descriptive study in two centers to describe the socio-demographic features risk factors, clinical characteristics and treatment outcome of PVT in patients following at Gastrointestinal (GI) outpatient clinic, or admitted at the emergency department (ED), intensive care unit (ICU) or medical wards in TASH and Adera medical center, Addis Ababa University. Datawas gathered through review of medical records and a questionnaire regarding their demographic characteristics, and clinical information including etiology, results of laboratory and imaging tests.The data was checked for clarity and completeness. Computerized data analysis was conducted by using SPSS (statistical package for the social sciences) version 26 software.

Results: The mean age at diagnosis was 34.64 (± 11.86) years. Majority of patients in the study were male (52 (69.3%) Vs 23(30.7%)). Majority of patients (63.9%) had chronic presentation than acute presentation, which was seen in 36.1%. Majority of patients had normal liver enzymes and coagulation profile. The most common risk factors identified in this study were cirrhosis (28%), MPD (17.3%) and intra-abdominal infections (12%). The most common compilations identified were esophageal varices, portal hypertensive gastropathy, ascites and gastric varices. Endoscopic variceal band ligation was done, nonselective beta blocker, anticoagulation was given for 29, 38& 24 patients, respectively. Mortality among the 75 patients were 2.7%, 12 patients were lost to follow up and 61 patients continued follow up. Mortality was mainly as a result of the underling cirrhosis.

Conclusion: Most Portal vein thrombosis patients in this study had chronic presentations of symptoms. Mortality of patients with cirrhosis is higher than those without cirrhosis.

Introduction

Background

Portal vein thrombosis (PVT) refers to a primary obstruction by a thrombus located on the trunk or the left or right branches of the portal vein in the absence of malignant invasion or constriction. The adjective “chronic” refers to a long-standing thrombosis, and the term “portal cavernoma” (or cavernous transformation of the portal vein) defines the set of collateral veins replacing the portal vein. In adult patients, these two terms are synonymous, while in children, Portalcavernoma may be the consequence of a congenital malformation as well as the sequel of PVT. [1]

The term chronic PVT is betterreserved for cases where the initial stage of acute PVThas been well documented; otherwise portal cavernomais the more appropriate descriptive term. Acute PVT is characterized by thepresence of a thrombus, shown on imaging, in the absence of a cavernoma. Therefore, extra-hepatic portal vein obstruction (EHPVO)is the preferred term for all conditions leading toobstruction of the portal vein.[2]

PVT was first described in 1868 in a 20 year-old man, since then PVT in liver cirrhosis has been increasingly recognized due to amelioration of diagnostic imaging methods and better awareness. The relative risk of developing PVT in the presence of liver cirrhosis is increased more than 7-fold above the risk observed in the general population. [3]

Portal vein thrombosis is a rare illness with a global incidence of 0.05-0.5% in post-mortem studies. The incidence differs, depending on the group of patients included (global population vs. patients with liver cirrhosis) and on the approach used to identify PVT condition.[4]

The prevalence/incidence of PVT greatly varies according to the characteristics of study population. Based on a large-scale population-based study involving 23796 autopsies in Sweden the population prevalence of PVT was up to 1.0 %. [5]In another Swedish study basedon hospital discharge diagnoses, however, the prevalence was muchlower (3.7 per 100,000 population).The difference betweenthese 2 estimates suggests that extra hepatic portal vein obstruction (EHPVO) commonly develops at alate stage of many diseases. Chronic liver disease and abdominalmalignancy are each found in about one third of patients.[2]

The imbalance between procoagulant and anticoagulant factors induces hypercoagulability, which is responsible for venous thrombus formation. In profound venous thrombosis, the Virchow Triad of venous stasis, endothelial dysfunction, and hypercoagulability statuscan be applied.[4]

A risk factor for venous thrombosis is identified in 75% of patients with PVT and without an underlying liver disease (cirrhosis or porto-sinusoidal vascular disease (PSVD). Etiological factors are not identified in 25% of patients with PVT. There are various risk factors, which can be local or systemic. Systemic risk factors are more frequent, and they are represented especially by thrombophilic conditions (i.e. protein S or C deficiency, antiphospholipid antibodies, factor V Leiden and prothrombin mutation) and myeloproliferative neoplasm MPN). [1]Local risk factors are mainly represented by inflammatory conditions affecting intraperitoneal organs, and they can be found in only one-third of the patients.[1]

PVT is most often seen as a complication of liver cirrhosis or hepatobiliary malignancies. The occurrence of PV thrombosis correlates with the severity of liver disease with the incidence being high in patients with cirrhosis. For this reason patients awaiting liver transplantation need to be treated in selected cases. [6]In advanced hepatic cirrhosis (Child B/C) the risk of developing PVT is high; either way, it is difficult to determine whether PVT worsens hepatic cirrhosis or advanced hepatic cirrhosis leads to PVT.[4]

It is essential to establish the underlying primary disorder for the development of PVT because this guides the therapeutic approach. Clinical presentation depends on thrombus location, the degree of portal occlusion, and extension to the superior mesenteric vein, splenic vein, or both.

Presentation can be acute or chronic; in practice, it may be difficult to discern between the types only from physical examination. The usual presentation of acute PVT includes abdominal pain, nausea, and fever. Extension of mesenteric venous thrombosis associated with bowel ischemia may produce severe symptoms such as vomiting, diarrhea, rectal bleeding and splenomegaly and in some cases even sepsis. Ascites is uncommon; it may be present before the progression of collateral circulation; while majority of patients manifest splenomegaly. [4]Patients with acute PVT may develop abdominal discomfort or worsening ascites, but are most often asymptomatic.[7]

Chronic PVT can be almost asymptomatic, except the appearance of varices, cutaneous collaterals, or ascites. It may be diagnosed when an ultrasound evaluation is performed for non-related problems, or investigations of portal hypertension (thrombocytopenia, jaundice, variceal bleeding, or splenomegaly).[4]

PVT in cirrhosis is most often detected incidentally on routine ultrasound, but should be suspected in any patient with worsening hepatic decompensation. Diagnosis is based on the absence of blood flow intoportal vein and on the presence portal cavernoma.[1]Ultrasound diagnosis necessitates follow-up imaging with cross-sectional CT or MRI to confirm the diagnosis and assess for tumor thrombus.[7]In advanced cirrhosis, PVT is a frequent complication, crucial to early diagnosis due to decompensated portal hypertension that

produces variceal hemorrhages (approximately 30% of patients), affecting the pre- and post-transplant condition.There might be symptomatic cases due to spontaneous recanalizzation of thrombus or it could be the manifestation of developed collateral circulation that leads to chronic PVT. [4]

Moreover, other less specific features of the disease are the presence of a dysmorphic liver where segment 1 and segment 4 are enlarged but surface is smooth; a mosaic pattern of parenchymal enhancement in the arterial phase, with homogeneous enhancement at a later phase; an increased enhancement of the peripheral parts of the liver at the arterial phase; a dilated hepatic artery; and a mild irregular dilatation of intra- and extrahepatic bile secondary to the compression by the collateral veins constituting the cavernoma (portal biliopathy). MR imaging cholangiography is the choice imaging for the diagnosis of portal biliopathy.[1]

Laboratory findings include a mild or absent liver dysfunction with normal levels of transaminases. These findings typically contrast with the severity of signs of portal hypertension. Alkaline phosphatase and gamma-glutamyltransferase may be altered in the presence of portal biliopathy. In cases of pure portal vein thrombosis, liver biopsy shows anessentially normal liver, and it is actually not indicated unless in the presence of persistently abnormal liver tests, of a dysmorphic liver or of abnormal results of liver elastometry in the suspicion of an underlying liver disease (cirrhosis and porto-sinusoidal vascular disease (PSVD)). Non-invasive tests like elastometry would be most useful in recognizing underlying liver disease.[1]

Frequent complications during follow-up were oesophageal- and gastric varices, portal hypertensive gastropathy, bleeding from varices and ascites. A larger part of patients with chronic PVT developed oesophageal varices in comparison with patients with acute PVT. Thus, the development of varices is a time dependent phenomenon, and it is advisable to screen all PVT patients endoscopically.[8]

Treatment options for PVT includes anticoagulation therapy, thrombolysis, thrombectomy, transjugular intrahepatic portosystemic shunt (TIPS). Current data suggest that anticoagulation is necessary, being the best therapeutic option in restoring vascular flow, aiming to prevent thrombus enlargement, prevent its recurrence and also decrease the rate of complications (esophageal varices, mesenteric ischemia, or secondary peritonitis). Anticoagulation depends on the location of the obstruction, the extent of thrombosis, the degree of occlusion, the severity of the underlying disease and may also depend on the duration of the thrombotic episode.[4]

In patients with portal cavernoma, the aim of anticoagulant treatment is not to achieve the recanalization of the portal vein axis as in acute portal vein thrombosis, but it is forthe prevention of the thrombotic extension and recurrence in the splanchnic area. However, the indications for permanent anticoagulation are still unclear.[1]

Early initiation of anticoagulation is associated with completeand partial recanalization of the portal vein in about 40% and15% of patients with acute PVT, respectively. It also prevents extension of thrombosis in the portal venous system, intestinalischemia and necrosis.Complications of anticoagulationtherapy appear to be uncommon.Even at a later stageof intestinal ischemia, anticoagulation may increase survival.[2]The outcome in patients with PVT is mostly determined by age and the course of the underlying disease. Therefore, the first step for the management of these patients is the early detection and treatment of the diseases known to be associated to PSVD and PVT. [1]

In individuals with acute PVT, anticoagulant therapy is given for 6 months. However, long-term treatment is sometimes given, depending upon the underlying disorder. The duration of anticoagulant therapy is strongly dependent upon the risk of recurrent thrombosis.The underlying prothrombotic state was an independent predictor of recurrent thrombosis. On the other hand, the risk of bleeding in these patients, who frequently present with variceal bleeding, should be taken into account. Therefore recent guidelines have suggested long-term anticoagulant therapy only to those individuals with major underlying thrombophilic risk factors.[9]

Statement of the problem

Occurrence and natural history of PVT is still unpredictable. Despite the advanced knowledge in PVT treatment options, factors leading to disease progression or recurrence after spontaneous recanalization, variables for prognostic significance and treatment are still not clear.Although PVT in livercirrhosis was widely studied since it was first described almost 150 years ago, many issues regarding pathogenesis, natural history, prevention and treatment are not yet clarified. Impact of anticoagulation and TIPS on mortality needs further extensive study.[3]

There is limited information on socio-demographic, clinical characteristics, risk factors and treatment outcome of patients with PVT in Africa in general and specifically Ethiopia. So this study will help in understanding the disease burden, diagnosis and treatment.

Significance of the study

Portal vein thrombosis is increasingly frequently being diagnosed, butsystematic descriptions of the natural history and clinical handling of the condition are sparse.[8]

There are several unresolved issues regarding PVT that due to the rarity of the condition cannot be clarified by large trials. In Africa there are very limited studiesand there is no study done in our country on portal vein thrombosis.

Therefore, the aim of this study is to describe risk factors, clinical presentation, complications and treatment outcome of patients with PVT in a tertiary hospital. The information provided by this study will help in developing effective health care strategies.

Literature review

Epidemiology

In a concise review on PVT, the incidence of liver cirrhotic patients with associated PVT, the incidence oscillates from 5 to 18% involving cases listed for liver transplant with an advanced degree of liver disease. Extra-hepatic PVT is valued to be around 5-10% of all cases of portal hypertension.[4]

One of the largest study performed in 1234 patients with compensated cirrhosis reported a cumulative incidence of PVT of 4.6%, 8.2% and 10.7% at 1, 3 and 5 years, respectively Prevalence of PVT is heterogenic based on different methods used which range from 0.6% to 16% in angiography or surgery studies to 10%-25% in ultrasound (US) studies.PVT prevalence increases with the degree of liver failure and in the setting of HCC, being as low as 1% in patients with compensated disease and rising to 8%-25% in candidates for liver transplant and 40% in the presence of HCC. Cirrhosis etiology may also play a role in PVT development.[3]

Recently, the multicenter prospective study including 753 cirrhotic patients (50% outpatient, 50% with mild severity disease), reported a prevalence of US-documented PVT of 17% (43% asymptomatic cases) and an annual incidence rate of 6.05%. Such incidence resulted much higher in patients with a history of PVT (18.9 per 100 patient-years *vs* 4.1 per 100 patient-years in those without prior PVT at admission).[3]Host and environmental factors may play a causal role in the initiation and development of PVT in various ethnicities and geographic locations.[10]

Socio demographic features

In an observational cross sectional study of 56 patients with PVT in a hospital in India, 43 (76.8%) were males and 13 (23.2%) were females[6]. In a case-series of 67 patients with PVT, mean age at time of admission was 44 ± 17 SD (range 15–74) for patients without cancer and cirrhosis. Twenty three were women and 25 men. Seventeen had acute PVT and 31 chronic PVT. There was no difference in age between genders, but higher age in patients with acute (51 ± 16) compared to chronic (40 ± 16) PVT at time of diagnosis. Mean time elapsed from time of admission was 39 ± 41 months (range 0–158). For patients with cancer and cirrhosis, mean age at time of admission was 57 ± 12 SD (range 34–78). Six were women and 13 men. Ten had acute PVT and 9 chronic PVT. There was no difference in age between genders, or between acute and chronic PVT at time of diagnosis. Mean time elapsed from time of admission was 26 ± 27 months (range 0–92).[8]

Risk factors

A large-scale population-based study involving 23796 autopsies in Sweden, the underlying etiology for PVT included liver cirrhosis (28 %), primary and secondary hepatobiliary malignancy (67%), major abdominal infectious or inflammatory disease (10%), and myeloproliferative disorders (3 %).[5]

A prospective series of neonates who had undergone umbilical vein catheterization (UVC) showed that, despite development of PVT in 45%, there is spontaneous recanalization of portal vein (PV) within 3 months. The study inferred that prolonged or traumatic cannulation or presence of omphalitis or sepsis are risk factors and need careful surveillance for PVT.[11]

In a case series of 67 patients risk factors were established in 58 cases (87%). Twentynine cases (43%) had two risk factors, and 14 (21%) had three risk factors. When including all risk factors, 43 cases (64%) had a local risk factor, and 28 cases (42%) had a systemic risk factor. In patients without cancer or cirrhosis, 27 cases (56%) had a local risk factor, and 24 cases (50%) a systemic risk factor. [8]

In a large multicenter study on patients with BCS (n = 163) and PVT (n = 105), prothrombotic factors were present in up to 84% and 42%, respectively. The etiology were often multifactorial. A combination of two or more genetic or acquired prothrombotic factors occurred in 10% of PVT patients and a prothrombotic factor was found in 36% of patients with a local risk factor.The prevalence of antithrombin deficiency ranges between 0–5% in PVT, of protein C deficiency between 0–7% in PVT, and of protein S deficiency between 0–30% in PVT, which is strikingly higher than in the general population.[9]

In a study including 100 adult patients with cirrhosis, even though plasma levels of antithrombin, protein C and protein S were significantly lower in PVT group, the only variable independently associated with PVT development was reduced portal vein flow velocity. So reduced portal flow velocity seems to be the most important predictive variable for PVT development in patients with cirrhosis.[12]

The prevalence of non-neoplastic PVT in cirrhotic patients ranges from 0.6% to 16%, while its incidence is unknown. PVT can be an important factor for morbidity and mortality, early detection and treatment for de novo thrombosis is an important issue, especially in patients on the waiting list for liver transplantation. Male sex, previous abdominal surgery including splenectomy and portocaval shunts, encephalopathy, ascites, past history of bleeding varices, low platelet count, and Child–Pugh class C have been considered predisposing factors to PVT in liver cirrhosis.[12]

In one of the hospitals in Italy, out of a total of 701 cirrhotic patients admitted and routinely screened with Doppler ultrasound, 79 (11.2%) were found to have PVT. Most patients were in class Child-Pugh B and C. Among thrombophilic risk factors studied only the mutation 20210 of the prothrombin gene resulted independently associated to PVT. And it`s presence increases the risk of PVT more than fivefold.[13]

In a study on extrahepatic portal vein obstruction (EHPVO) in Egypt, the main identified causes of PVT In children and adolescents are direct injury of the vein (omphalitis and umbilical vein catheterization) and sepsis with abdominal focus. Other possible causes are abdominal trauma, surgical trauma, cysts and tumors in the portahepatis, neonatal sepsis, dehydration, cardiovascular malformations, and exchange transfusion. Most of the cases remain idiopathic.[14]

Ina single center Egyptian Study, which enrolled 73 patients with JAK2-positive MPN, seventeen (23%) had superior mesenteric and portal vein thrombosis. Six (8%) had iliofemoral (8%) and 4 (5%) had combined lower limbs and portal thrombosis. Eight (10.8%) had active thrombosis at screening. Only 3 patients (4%) were symptomatic with abdominal pain during screening. So routine screening for venous thrombosis in any case of MPN when diagnosed and screening for MPN in any patient with venous thrombosis especially of the portal vein or atypical sites is recommended. [15]

In a retrospective study in Ethiopia, at TASH on patients with HCC including 51 patients, 35% were found to have portal vein thrombosis, almost a third of patients have portal vein thrombosis.[16]

Clinical profile

In a study in Italy out of a total of 701 cirrhotic patients admitted to one of the hospitals in Italy and routinely screened with Doppler ultrasound, 79 (11.2%) were found to have PVT. Of these, 34 (43%) were asymptomatic and 45 (57%) were symptomatic (31 presented with portal hypertensive bleed and 14 with abdominal pain, 10 of whom had intestinal infarction). Mesenteric vein involvement was never asymptomatic and lead to intestinal ischemia or infarction. Most patients were in class Child-Pugh B and C.[13]

Patients with acute PVT usually have no sufficient time for the development of adequate collaterals. Ascites, which develops after acute PVT, is mild and transient because of intestinal congestion and is associated with decreased long-term survival rate.[17]

In a retrospective study including 67 patients with PVT, symptoms were abdominal pain, splenomegaly, fever, ascites, hematemesis, and weight loss. The typical presentation of acute PVT was abdominal pain, splenomegaly, fever and ascites, while the presentation of chronic PVT was abdominal pain and splenomegaly together with gastrointestinal hemorrhages and ascites. Abdominal pain and fever were more frequent in in patients with acute PVT than in those with chronic PVT. The higher presenting occurrence of ascites in acute PVT than other studies may be due to inclusion of ascites both detected by physical examination and by ultra sound. The ascites was in no case tense, most likely caused by intestinal venous congestion.[8]

In an observational cross sectional study of 56 patients with PVT in a hospital in India, 43 (76.8%) were males and 13 (23.2%) were females. Six had acute or recent presentation. Cirrhosis (*n*=46) and HCC (*n*=4) were major liver related causes. Acute severe pancreatitis (*n*=6) was major non-liver causes. Among patients with cirrhosis major causes were alcohol (*n*=35), Hepatitis B(*n*=8), Hepatitis C (*n*=3). Mean MELD score was 17. One patient presented as acute on chronic liver failure (ACLF). Majority of cirrhotic patients were in Child Pugh Score (CPS) B (82.6%) and CPS A (10.9%). The occurrence of PV thrombosis correlates with the severity of liver disease with the incidence being high in patients with cirrhosis. Majority of PVT were in portal vein main trunk (Type 1) and were non occlusive.[6]

In a concise review on PVT, acute variceal bleeding was the most frequent clinical manifestation with well-tolerated bleeding and mortality is lower than in cirrhotic patients, perhaps as a result of liver preservation. Notably, 30-40% of patients present with gastric varices. In patients with cirrhosis it is more common to identify ectopic varices that appear in the duodenum, gallbladder bed, and the anorectal region; in these cases, portal hypertensive gastropathy is a rare condition.[4]

Diagnosis

In a retrospective study on risk factors, clinical presentation and treatment of PVT, in 51 (76%) patients, diagnosis was established by means of Doppler ultrasound. Among 12 patients with a negative ultrasound, 11 were diagnosed by CT angiography andone by MRI-scanning. In four patients, the diagnosis was initially established with CT or MRI. In all patients diagnosedby means of Doppler ultrasound, CT angiography was later performed. MRI-scanning was only performed in five of the patients with a positive Doppler ultrasound, and supported the diagnosis in all five cases. Sensitivity was calculated to be 81% (51/63) for Doppler ultrasound and 94% (51/54) for CT.[8]

Treatment

In a retrospective study including 67 patients with PVT, it was observed that partial or complete recanalization was more frequent in patients treated with anticoagulation therapy, and that regression of varices was more pronounced in patients who were treated with endoscopic management combined with pharmacological treatment.[8]

In a concise review on PVT anticoagulation is the best therapeutic option, although there is no ideal anticoagulant, use of low molecular weight heparin (LMWH) was preferred. Vitamin K antagonists (VKA) such as Warfarin with oral administration, INR should be carefully controlled; direct oral anticoagulants (DOACs) have to be avoided in renal dysfunction.[4]

In a Randomized controlled trial of rivaroxaban versus warfarin in the management of acute HCV related non-neoplastic PVT was done. In the rivaroxaban group, the resolution of PVT was achieved in 34 patients (85%) within 2.6 ± 0.4 months and delayed, partial recanalization after 6.7 ± 1.2 months (n=6.15%). Complications such as major bleeding, abnormal liver functions, death, or recurrence did not occur during treatment, and patients in this group showed improved short-term survival rate (20.4 ± 2.2 months) compared to the survival rate in the control group (10.6 ± 1.8 months) in which warfarin achieved complete resolution in 45% of patients. Complications such as severe upper GI bleeding (43.3%), hepatic decompensation (22.5%), progression to mesenteric ischemia (12.5%), recurrence (10%), and death (20%) were observed in the control group. The duration until complete resolution of thrombus correlated with age, the extent of the thrombus, creatinine level, and MELD score. The recurrence after complete resolution of thrombus correlated with age, the extent of the thrombus, thrombogenic gene polymorphism, and the use of warfarin. They concluded that rivaroxaban was effective and safe in acute HCV-related non-neoplastic PVT with improved shortterm survival rate.[17]

A systematic review and meta-analysis of observational studies reported that anticoagulation could achieve a relatively high rate of portal vein recanalization in cirrhotic patients with PVT. There were a small number of non-randomized comparative studies; randomized controlled trials are warranted to confirm the risk-to-benefit of anticoagulation in such patients.[18]

Based on a systematic review and meta-analysis, patients with cirrhosis and PVT who receive anticoagulant therapy have increased recanalization and reduced progression ofthrombosis, compared to patients who do not receive anticoagulants, with no excess of major and minor bleedings and less incidence of variceal bleeding.[19]

Objectives

General objective

To describe the socio-demographic features, risk factors, clinical characteristics and treatment out comes of chronic portal vein thrombosis(PVT) patients seen at TASH and Adera medical center during the period between August 2019 and August 2021, Addis Ababa, Ethiopia.

Specific objective

- To describe the socio-demographic features and clinical characteristics of chronic portal vein thrombosis in our patients
- To determine the major associated factors for chronic PVT development
- To identify the complications and treatment outcome of complications of chronic PVT
- To review treatment out comes of chronic PVT
- To compare between cirrhotic and non-cirrhotic PVT

Methods

Study area

The study was conducted in TASH and Adera Medical center, Addis Ababa. TASH is the largest governmental referral hospital in Ethiopia. TASH gives service for 50,000 patients per year. The hospital has comprehensive health care service through different specialty clinics and inpatient service departments. The hospital is also a teaching hospital for the Addis Ababa University, College of Medicine and Health sciences and is involved in undergraduate, postgraduate and fellowship trainings in different fields of clinical medicine.

Adera medical center, located in Bole road close to Addis Ababa Museum, is a private health care organization established by Professor Abate Bane (Consultant internist and gastroenterologist/hepatologist). It provides service in gastroenterology/hepatology, general surgery, ENT, neurology, orthopedics and oncology along with general laboratory.

Study period

The study was conducted on chronic PVT patients having follow-up in GI outpatient clinicor admitted at the emergency department (ED), intensive care unit (ICU) or medical wards with chronic PVT at TASH, Addis Ababa University and Adera medical center, from August 2019 to August 2021.

Study design

A cross sectional descriptive study to describe the socio-demographic features, risk factors, clinical characteristics and treatment outcomes of chronic PVT in patients following at GI outpatient clinicor admitted at the emergency department (ED), intensive care unit (ICU) or medical wards, Tikur Anbessa Specialized hospital (TASH), Addis Ababa University and Adera medical center.

Source and Study population

Source population – all patients seen at GI clinic or admitted at the emergency department (ED), intensive care unit (ICU) or medical wards with in TASH and Adera medical center.

The study population of this study are all chronic PVT patients seen at GI outpatient clinicor admitted at the emergency department (ED), intensive care unit (ICU) or medical wards in TASH and Adera medical center with diagnosis of chronic PVT.

Sample size and Sampling technique

Sample size is calculated using a single proportion formula and correction done as depictedbelow

$$\mathrm{n} = \frac{Z^2 x\ (p)(1-\mathrm{p})}{d^2}$$

$$n_{new} = \frac{n_o}{\left(1 + \frac{n_0}{N}\right)}$$

While n_o is the estimated sample size, N is the total number of PVT patients on follow up.d is margin of error, P is population proportion, Z is z-score

A sample size of 67 patients is calculated assuming a population proportion of 0.5 (because there have been no similar published studies done in TASH before; and given the estimated number of PVT patients seen at GI clinic over 2 year period 80). Confidence interval of 95% and degree of freedom of 0.05. Given the total population is less than 10,000 the final corrected sample size after 10% was added for possible dropout is determined to be 74.

All patients who fulfilled the inclusion criteria of the study were included in the study. Convenient sampling method was used. Total of 75 patients were included.

Inclusion and Exclusion criteria

Inclusion criteria

- ✓ Age 18 years and above during the study period
- ✓ Any patient with confirmed chronic PVT(both new and follow up patients)
- ✓ Only PVT patients diagnosed with imaging(can be ultrasound, CT scan of the abdomen)

Exclusion criteria

- ✓ Individuals whose data is lost/incomplete
- ✓ Patients whose diagnosis of chronic PVT was not confirmed with imaging
- ✓ Patients with acute PVT
- ✓ Diagnosis was doubtful after full investigations

Study Variables

Dependent variables

- ✓ Treatment outcome of patients with chronic PVT (death, regression on varices)

Independent variables

- ✓ Sociodemographic profiles: age, gender, address/region, educational and marital status; history of intra-abdominal surgery or procedure; family history of thrombosis

- ✓ Variables for clinical profile included:

    - Patients' symptoms
    - Duration of symptoms
    - Diagnostic findings
    - Location of thrombosis and extension to superior mesenteric vein or splenic vein
    - Presence of underlying cirrhosis
    - Presence of underlying malignancy
    - Complications of PVT
    - ICU admission

- ✓ Therapeutic characteristics/intervention

    - Pharmacologic therapy used
    - Endoscopic intervention
    - Surgical intervention

Operational definitions

Portal vein thrombosis: Obstruction of the portal vein by a clot evidenced with imaging and thrombus, may be complete or partial.

Acute portal vein thrombosis: A recent formation of a thrombus within the portal vein and/or right or left branches with no cavernous transformation.

Chronic portal vein thrombosis: There will be cavernous transformation.

Data collection procedures

Data collection instruments

All patients with PVT was reviewed. Data was collected from the medical records (charts and electronic medical records) and recorded on a questionnaires. The questionnaire was designed with the aim to capture all the relevant information related to PVT patients who are treated in TASH and Adera medical center during the study period which includes items on sociodemographic details, risk factors, clinical characteristics and treatment out comes. The collected data was stored in electronic spreadsheet and managed by the investigator.A database of medical chart records was searched from August 2019 to August 2021.

Data quality management

All patients with PVT seen at the GI clinic in TASH and Adera medical centerwas identified from the outpatient and inpatient registers. Questionnaire was prepared and was used to collect data from patients' charts and iCare registry. To ensure quality of data the collected information was checked out for the completeness, accuracy and clarity by the principal Investigator before execution of any data entry process.

Data analysis and presentation

Collected data was verified, validated and recorded before the analysis. The IBM SPSS Statistics software package version 26 was used for entry of statistical data analysis. Descriptive statistics was used as a statistical data analysis method and was expressed as frequencies and numbers (percentages %) with their corresponding confidence intervals. The results was summarized by using tables, and figures.Continuous variables was represented as means, standard deviations and minimum and maximum values, and categorical variables as frequencies. A 95% CI was used for most variables.A P-value < 0.05 was considered to indicate statistical significance.

Ethical consideration

The collected data was anonymous. The study protocol was submitted to the department of internal medicine and ethical review committees of the department and the college of health sciences.

Dissemination of the results

The results of the study will be presented to the department of Internal Medicine, college of health sciences. It will also be submitted to Ministry of Health of Federal Democratic Republic of Ethiopia. Finally, it will be published on peer reviewed journals.

Results

Socio demographic features of study participants

In this study, 75 patients with PVT with or without cirrhosis were included. The mean age at diagnosis in years was 34.64 (± 11.9). The sex distribution of the study showed majority 52 (69.3%) of patients in the study were male and 23(30.7%) were female. Most patients were from an urban area (73.3%) and majority (57.3%) were from Addis Ababa.

Table 1. Socio demographic data of patients with chronic Portal vein thrombosis at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Variables		Frequency	Percentage
Age groups	<40	55	73.3
	40-60	16	21.3
	>60	4	5.3
Gender	Male	52	69.3
	Female	23	30.7
Residence	Urban	55	73.3
	Rural	20	26.7
Address	Addis Ababa	43	57.3
	Oromia	12	16.0
	SNNP	7	9.3
	Amhara	3	4.0
	Others	10	13.3

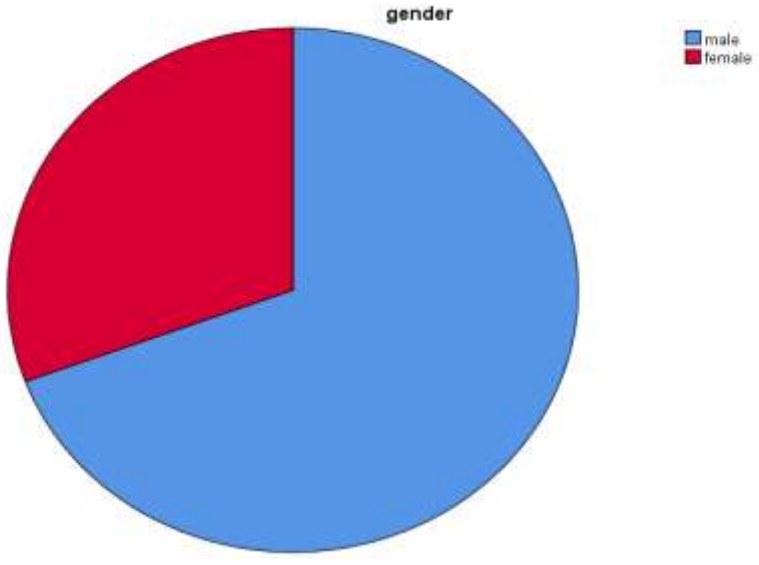

Figure 1. Sex distribution of patients with chronic Portal vein thrombosis seen at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

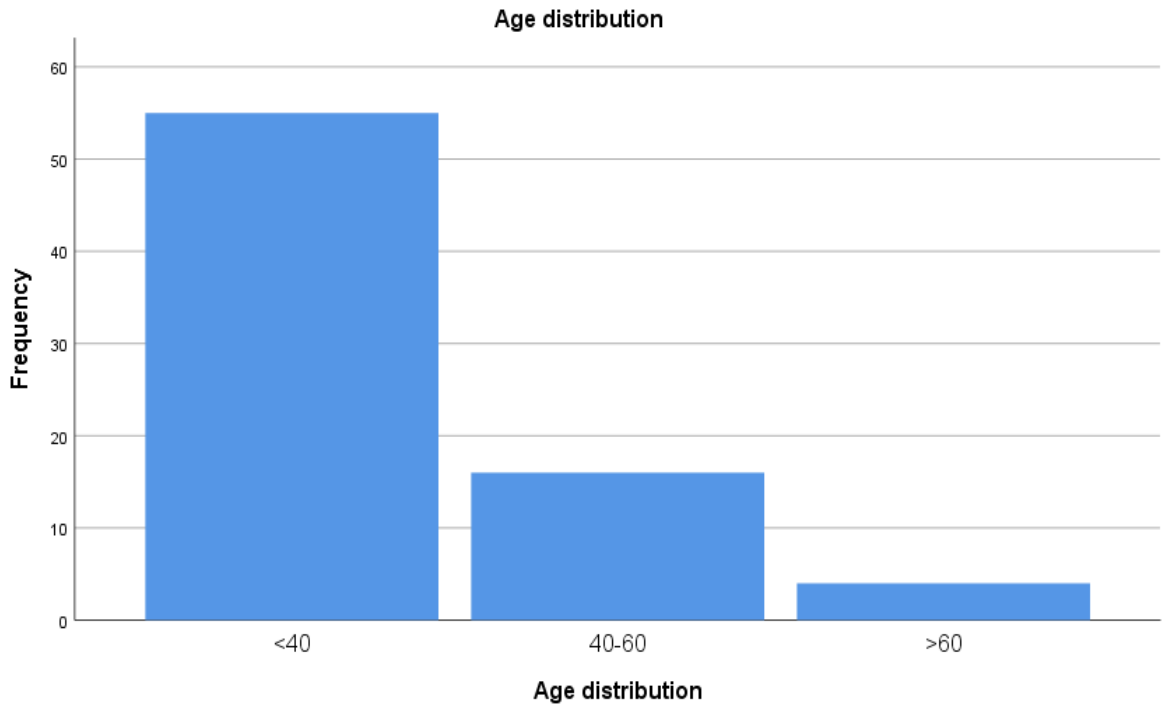

Figure 2. Age distributionof patients with Chronic Portal vein thrombosis seen at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Clinical presentation of study participants

Among the 75 patients included in this study 54(72%) were patients with PVT without cirrhosis and 21(28%) were patients with cirrhosis. The mean age at diagnosis in patients with cirrhosis was 37.14(± 13.43) and in patients without cirrhosis 33.63(± 11.17) years (p=0.413). Majority of patients (63.93%) had chronic presentation (> 60 days) than acute presentation(< 60 days) which was seen in 36.07% of patients and the rest was not documented. There was no significant difference in the mean duration of presenting symptoms for patients with or without cirrhosis. (6.25(±8.11) Vs 8.26(±12.9) months) p=0.299. There was more males (52(69.3%) than females (23(30.7)). There was no significant difference in sex distribution among the two groups (p=0.174).

The most common symptoms at presentation for PVT patients without cirrhosis were abdominal pain, splenomegaly, hematemesis or melena,and abdominal distension, respectively. For those patients with cirrhosis, the most common symptoms at presentation were hematemesis or melena, abdominal pain, splenomegaly, and abdominal distension, respectively. Fever was not a frequent symptom with no significant difference between the groups with or without underlying cirrhosis. Presentation with hematemesis or melena was

seen more in patients with cirrhosis with significant difference between the two groups. (27 (50%) Vs 17(80.95%), p=0.018). The details on clinical presentations of these patients are described on table 2.1 & table 2.2.

In patients without cirrhosis, extension of splenic vein thrombosis was observed in 12 patients and 5 patients with cirrhosis. (p=0.883). There were extension to superior mesenteric vein in 7 patients without cirrhosis and 5 patients in patients with cirrhosis (p=0.25).

Table 2.1. Socio-demographic and clinical presentation of patients with Chronic Portal vein thrombosis at TASH and Adera medical center between August 2019 to August 2021 (N=75)

Variables		PVT without cirrhosis N(54)	PVT with cirrhosis N(21)	P value
Age	<40	41(75.93)	14(66.66)	0.543
	40-60	11(20.37)	5(23.81)	
	>60	2(3.70)	2(9.52)	
Mean age at diagnosis in years		33.63(±11.17)	37.14(± 13.43)	0.413
Duration of symptoms	<2 months	18(39.13)	4(26.66)	0.274
	>2 months	28(60.86)	11(73.33)	
	Not documented	8	6	
Mean duration of symptoms in months		8.26(±12.9)	6.25(± 8.11)	0.299
Gender	Male	35(64.81)	17(80.95)	0.174
	Female	19(35.19)	4(19.04)	

Table 2.2. Specific symptoms at presentation of patients with Chronic Portal vein thrombosis at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Characteristics	PVT without cirrhosis N(54)	PVT with cirrhosis N(21)	P value*
Abdominal pain	42(77.77)	15(71.42)	0.563
Abdominal distension	13(24.07)	6(28.57)	0.68
Hematemesis or melena	27(50.00)	17(80.95)	**0.018**
Vomiting of ingested matter	10(18.51)	2(9.52)	0.34
Fever	1(1.85)	0(0.00)	0.58
Splenomegaly	29(53.73)	9(42.85)	0.39
Ascites	6(11.11)	4(19.04)	0.36
Nausea	1(1.85)	0(0.00)	0.53
Fatigue	7(12.96)	2(9.52)	0.681
Loss of appetite	7(12.96)	2(9.52)	0.681
Weight loss	2(3.70)	1(4.76)	0.834
Jaundice	3(5.56)	1(4.76)	0.891

*Chi-square

In this study including 75 patients, different laboratory investigations and imaging studies were done for both PVT patients with or without cirrhosis. Majority of patients had a normal complete blood count with no significant difference between the two groups (29(54.7%) and 10(47.61%), P= 0.712). Majority of patients in both chronic PVT with or without cirrhosis had normal liver enzymes and coagulation profile and there was no significant difference between the twogroups. The details on laboratory investigations of these patients are included on the table 2.3.

Table 2.3. Laboratory investigations of patients with Chronic Portal vein thrombosis at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Laboratory investigation		PVT without cirrhosis N(54)	PVT with cirrhosis N(21)	P value*
WBC	<4,000	20(37.73)	10(47.61)	0.712
	4000-11000	29(54.71)	10(47.61)	
	>11000	4(7.54)	1(4.76)	
	Not documented	1	0	
Hemoglobin	<7	1(1.86)	1(4.76)	0.426
	7-13.5	31(58.49)	942.85()	
	>13.5	21(39.62)	11(52.38)	
	Not documented	1	0	
Platelet	<150,000	23(43.39)	15(71.42)	0.069
	150,000-450,000	26(49.05)	6(28.57)	
	>450,000	4(7.54)	0	
	Not documented	1	0	
AST	<40	35(68.62)	14(66.66)	0.873
	40-60	10(19.61)	4(19.04)	
	60-80	5(9.80)	3(14.28)	
	Not documented	3	0	
ALT	<40	40(74.07)	19(90.47)	0.386
	40-60	8(14.81)	2(9.53)	
	60-80	3(55.55)	0	
ALP	<270	41(75.92)	17(80.95)	0.073
	270-405	2(3.70)	3(14.28)	
	>405	7(12.96)	0	

Bilirubin direct	<0.25	26(48.15)	10(47.61)	0.998
	0.25-0.5	10(18.52)	4(19.04)	
	>0.5	10(18.52)	4(19.04)	
Bilirubin total	<1.1	32(59.25)	13(61.90)	0.991
	1.1-2.2	9(16.66)	4(19.04)	
	>2.2	5(9.25)	2(9.52)	
PT	<16	22(40.74)	5(23.80)	0.148
	16.1-18	4(7.40)	2(9.52)	
	>18	10(18.51)	2(9.52)	
PTT	<44	26(48.14)	7(33.33)	0.64
	44-50	4(7.40)	1(4.76)	
	>50	3(55.55)	2(9.52)	
HBsAg	Positive	5(9.25)	5(23.80)	0.098
HCV Ab	Positive	0	1(4.76)	0.108

* Chi-square

Among the studied 75 patient with chronic PVT, most patients (29 patient (38.6%)) were diagnosed with ultrasound of the abdomen. Extension to splenic vein was seen in 17 patients (22.6%) and extension to superior mesenteric vein was seen in 12 patients (16%). The details on the diagnostic imaging studies used for the two different groups is shown on Table2.4.

Table 2.4. Imaging studies in patients with Chronic Portal vein thrombosisat TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Variable		PVT without cirrhosis N(54)	PVT with cirrhosis N(21)	P value*
Imaging studies	Ultrasound	24(44.44)	5(23.80)	0.423
	CT scan	14(25.92)	8(38.09)	
	MRI	1(1.85)	0	
	Ultrasound & CT scan	15(27.77)	6(28.57)	
	Ultrasound & MRI	0	0	

*Chi-square test

Risk factors identified in the study participants

In this study both local and systemic risk factors were identified. Risk factors were identified in 46(61.3%) patients. Some patients had more than one risk factors, 41(54.7%) had only one risk factor, 2(5.3%) patients had two three risk factors, 1(1.3%) patienthad three risk factors.As shown on table 3 the most common risk factors identified in this study were cirrhosis (28%), MPD (17.3%) and intra-abdominal infections (12%). In our study screening for

prothromboticdisorders was done for 28 patients, withno significant difference between the two groups, 40.74% patients with PVT without cirrhosis or malignancy and 28.57% patients with cirrhosis. P=0.328. JAK 2 mutation was detected in 11 patients, protein C deficiency in 1 patient and Protein S deficiency in 2 patients.

Table 3. Risk factors in patients with Chronic Portal vein thrombosis at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Variables		Frequency	Percentage
MPD		13	17.3
	ET	1	1.3
	PV	8	10.7
	Unclassified	4	5.3
Cirrhosis		21	28
Intra-abdominal infection		9	12.0
	HSS	4	5.3
	Cholecystitis	3	4.0
	Pancreatitis	2	2.7
History of surgery		6	8.0
	Splenectomy	3	4.0
	Cholecystectomy	1	1.3
	Umbilical catheterization	1	1.3

Comorbidities identified in the study participants

Among the 75 patients, 16 patients (21.3%) had one or more comorbidities and the most frequent medical comorbidities identified were hypertension (6.7%), and diabetes (5.4%). As shown on table 4 other less commonly observed comorbidities were HIV(2.7%)and Ischemic heart disease in (2.7%).

Table 4. Comorbidities in patients with Chronic Portal vein thrombosis at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Comorbidities	Frequency	Percentage
HTN	5	6.7
DM	4	5.4
HIV	2	2.7
IHD	2	2.7

Complications identified in the study participants

In our study complications were documented in 66 patients (88%), the most common compilations identified were esophageal varices, portal hypertensive gastropathy, ascites and gastric varices. The details on identified complications in this study are shown on table 5. When we compare between the two groups, complications occurred in 46 patients without cirrhosis and 20 patients in those with cirrhosis. p=0.28

Table 5. Complications in patients with Chronic Portal vein thrombosis at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

Variables	Frequency	Percentage
EV	51	68.0
PHG	29	38.7
Ascites	15	20.0
Gastric varies	9	12.0
Mesenteric ischemia	2	2.7

Treatment of the study participants

Treatment of all chronic PVT patients in the study was variable. Among the 51 patients with esophageal varices 29 patients were treated endoscopically with band ligation. There was no significant difference between the two groups. P=0.949. Forty eight patients received Non selective beta blocker and there was no significant difference between the groups. P=0.225. Anticoagulation was provided for 24 patients, the anticoagulants used were Vitamin K antagonist in 19 patients or direct acting oral anticoagulants (DAOC) in 5 patients.

Table 6. Treatments given to patients with Chronic Portal vein thrombosis seen at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

	PVT without cirrhosis N(54)	PVT with cirrhosis N(21)	p value*
EVL	21(38.88)	8(38.09)	0.949
NSBB	25(46.29)	13(61.90)	0.225
Anticoagulation	17(31.48)	7(33.33)	0.877
warfarin	13(24.07)	6(28.57)	0.688
DOAC	4(7.40)	1(4.76)	0.680

* Chi-square test

Outcome of the study participants

In our study including 75 patients with chronic PVT, 2 (2.67%) patients died, 12(16%) patients were lost from follow up and 61(81.3%) patients continued their follow-up. As shown on table 7 all the deaths occurred in patients with cirrhosis.The causes of death was not known. There was no significant association between death and use of NSBB, EVL or anticoagulation. P=0.985, p=0.741, p=2.174

Table 7. Outcome in patients with Chronic Portal vein thrombosis at TASH and Adera Medical Center between August 2019 to August 2021 (N=75)

		PVT without cirrhosis N(54)	PVT with cirrhosis N(21)	P value*
Out come	Death	0(0.00)	2(9.52)	0.071
	On follow up	45(83.33)	16(76.19)	
	Lost to follow up	9(16.66)	3(14.28)	

* Chi-square

Table 8. Binary logistic regression on the association between the independent variable death and other variables in patients with Chronic PVT at TASH and Adera Medical Center between August 2019 and August 2021(N=75)

Variables		Death		P value	COR(95%CI)	AOR(95%CI)
		Yes (%)	No (%)			
Gender	Male	1(1.9)	51(98.1)	0.558	1	
	Female	1(4.3)	22(95.7)		2.318(0.14,38.76)	
Age	<40	1(1.8)	54(98.2)		1	
	40-60	0(0.0)	16(100)	0.999	0.00(0.00)	
	>60	1(25)	3(75)	0.998	18.00(0.891,363.6)	
Anticoagulants	Yes	1(4.2)	23(95.8)	0.589	2.174(0.13,36.3)	
	No	1(2.0)	50(98.0)		1	
NSBB	Yes	1(2.6)	37(97.4)	0.985	0.973(0.59,16.15)	
	No	1(2.7)	36(97.3)		1	
EVL	Yes	1(3.4)	28(96.6)	0.741	1.607(0.097,26.739)	
	No	1(2.2)	45(97.8)		1	

Discussion

In 75 patients included in this study, 54 were patients without cirrhosis and 21 were patients with cirrhosis. In this study there were more male patients than female with male to female ratio of 2.3:1. The mean age at diagnosis in patients with cirrhosis was 37.14(± 13.43) and in patients without cirrhosis 33.63(± 11.17) years (p=0.413) which are comparable with similar retrospective study on risk factors, clinical presentation & treatment of PVT patients in Denmark. Duration of symptoms for most patients in previous similar studies,retrospective study on risk factors, clinical presentation & treatment of PVT patients and retrospective single institution study on demographics, clinical characteristics, cirrhosis, presence of malignancy on PVT patients were acute than chronic but in this study most patients presented with chronic course which may be due to delayed presentation of patients.[8][20]

The most common presenting symptoms for both groups were abdominal pain, splenomegaly, hematemesis, abdominal distension, ascites and melena, which are similar with symptoms as other studies, a retrospective study on incidence of Hepatitis B virus infection-associated cirrhosis & HCC in South East Asian patients and retrospective study on risk factors, clinical presentation & treatment of PVT patients in Denmark. In the above studies the common clinical presentations included fever but in our study fever was not a frequent symptom with no significant difference between the two groups with or without underlying cirrhosis or malignancy. [8], [21].

The most common risk factors identified are cirrhosis (28%), MPD (17.3%) and intra-abdominal infections (12%), which are similar as other studies, a retrospective study on incidence of Hepatitis B virus infection-associated cirrhosis & HCC in South East Asian patients and retrospective study on risk factors, clinical presentation & treatment of PVT patients in Denmark. In these studies intra-abdominal infections were identified in 9.3% patients than MPD which was 4.6%. [8],[21]. In these studies HCC was identified as one of the most common risk factor for PVT but in our study patients with HCC were not included in this study.

Screening for prothrombotic disorders was done for 28 patients, with no significant difference noted between the two groups, (40.74% in patients without cirrhosis and 28.5% in patients with cirrhosis. P=0.328).Risk factors were identified in 61.3% patients, which is lower when compared to a retrospective study on incidence of Hepatitis B virus infection-associated cirrhosis & HCC in South East Asian patients and retrospective study on risk factors, clinical presentation & treatment of PVT.[8],[21] Some patients had more than one risk factors, 54.7% had only one risk factor, 5.3% patients had two three risk factors, 1.3% patients had three risk factors.

Complications of PVT were seen in 66 patients (88%), the most common compilations identified were esophageal varices, portal hypertensive gastropathy, ascites and gastric varices with no significant difference between the two groups. There was no significant association with duration of presentation in our study. P=0.332

In our study 61 (81.3%) patients continued follow up, the overall mortality was 2.66% and mortality was 9.52 % in patients with cirrhosis and no death was noted in patients without cirrhosis. The mortality noted in this study is relatively lower than mortality in one year seen in a retrospective study on risk factors, clinical presentation & treatment of PVTdone in Denmark and retrospective single institution study on demographics, clinical characteristics, cirrhosis, presence of malignancy on PVT patients. [8],[20]

Regarding effect of treatment on outcome of patients, there was no significant association between death and endoscopic variceal band ligation, use of anticoagulation or non-selective beta blockers. (p=0.741, p=2.174, p=0.985, respectively). This may be as a result of delayed presentation in our patients, limited number of patients involved in the study or the seriousness of underlying cirrhosis and death was noted only in patients with cirrhosis. Variceal hemorrhage is not the main cause of mortality in PVT patients. The main aim of treating patients with chronic PVT with anticoagulants is to prevent recurrence.

In a retrospective observational study, including 27 patients with extra hepatic portal vein thrombosis (EPVT) with variceal bleeding, seven patients died and none was caused by variceal haemorrhage. The overall survival was 100% at 5 years and 62% (95% CI, 38%-96%) at 10 years. There was no rebreeding in patients who were started on b-blockers as secondary prophylaxis. [22]

In a systemic review including 8 studies, comprising 353 patients, majority 71 % of patientswho were treated with anticoagulants had PVT recanalization than 42% of patients who did not. (P<0.0001). Among 217 patients included in 6 studies, complete recanalization was reported in 53% ofpatients treated with anticoagulants and 33% of patients who did not.(p=0.002).[19]

In a retrospective study on PVT, 45% of thepatients without cancer or cirrhosis and 67 % of patients with cancer or cirrhosis who received anticoagulation therapy had partial or complete recanalization during follow up. Among patients who did not receive anticoagulation therapy, only 15% improved their portal flow and had anydegree of spontaneous resolution of the thrombosis.[8]

Limitations

Limitation of a retrospective study, small number of patients and some incomplete data.

Conclusion

Liver cirrhosis and MPN are the most common risk factors for chronic PVT complicated by portal hypertension manifested as ascites, splenomegaly, varices, and portal HTN gastropathy. Mortality related to chronic PVT is higher among those with cirrhosis than those without.

Recommendations

We recommend further prospective studies to get more representative multicenter studies on PVT.

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Annex

Questionnaires

Questionnaire number_____

MRN _____

NO.	**Part I**Demographic data	
1.	Age	_____years
2.	Gender	1) Male 2) Female
3.	Residence	1) Urban 2) Rural
4.	Address	1) Addis Ababa 2) Oromia 3) Amhara 4) SNNPR 5) Others (specify) _____
5.	Level of education	1) Cannot read and write 2) Can read and write 3) Primary (1-8) 4) Secondary and above
6.	Occupation	1) Employed 2) Merchant 3) Farmer 4) Daily laborer 5) Student 6) House wife 7) Others (specify)_____
7.	Marital status	1) Single 2) Married 3) Separated (divorced, widowed)
8.	Religion	1) Orthodox 2) Muslim 3) Protestant 4) Catholic 5) Others (specify)
9.	Risk factor identified	1) Yes 2) No
10.	Family history of thrombosis	1) Yes 2) No
11.	History of surgery	1) Yes, Specify_____ 2) No
12.	History of trauma	1) Yes 2) No

13.	Intra-abdominal infection	1) Yes, specify _____ 2) No
14.	History of malignancy	1) Yes, specify _____ 2) No
15.	HCC	1) Yes 2) No
16.	MPN	1) ET 2) PV 3) Unclassified
17.	Other malignancies	1) Yes, Specify____ 2) No
18.	Pregnancy	1) Yes 2) No
19.	Comorbidities	1) T1 DM 2) T2 DM 3) HTN 4) CKD 5) IHD/CRVHD/DCMP 6) RVI 7) others
	Part II Disease characteristics	
20.	Presenting symptoms	1) Abdominal pain 2) Abdominal distension 3) vomiting 4) Fever 5) Splenomegaly 6) Ascites 7) Hematemesis 8) Melena 9) Nausea 10) Fatigue 11) Loss of appetite 12) Weight loss 13) Jaundice 14) Leg swelling 15) Asymptomatic 16) Others _____
21.	Duration of symptoms	_____
22.	CBC	1) WBC 2) Hgb 3) MCV 4) PLT

23.	Coagulation profile	1) PT 2) PTT 3) INR
24.	PICT	1) Reactive 2) Non-reactive
25.	Liver function tests	1) AST 2) ALT 3) ALP 4) GGT 5) Albumin 6) Bilirubin D 7) Bilirubin T
26.	HepBsAg	1) Negative 2) Positive
27.	HCV Ab	1) Negative 2) Positive
28.	Screening	1) Yes 2) No
29.	Specific tests	1) JAK 2 mutations 2) Calreticulin mutations 3) MPL 4) ANA 5) EPO 6) Protein C 7) Protein S 8) APA 9) Others _____
30.	RFT	1) Creatinine BUN/Urea
31.	Electrolyte	1) Na K Cl
32.	Diagnosis finding	1) Ultrasound 2) CT scan 3) MRI 4) US and CT scan 5) US and MRI
33.	Cavernous transformation (imaging)	1) Yes 2) No
34.	Extension to splenic vein	1) Yes 2) No
35.	Extension to superior mesenteric vein	1) Yes 2) No
36.	Other site of thrombosis	1) Yes 2) No

37.	Presence of cirrhosis	1) Yes 2) No
38.	History of bleeding	1) Yes 2) No
39.	Complications	1) Esophageal varices 2) Gastric varices 3) Portal hypertensive gastropathy 4) Portal bilopathy 5) Ascites 6) Mesenteric ischemia 7) Others _____
	Part III Treatment	
40.	Anticoagulation	1) Vit k antagonist 2) LMWH (low molecular weight heparin) 3) DOAC (direct oral anticoagulants) 4) No anticoagulation
41.	Others	1) NSBB 2) EVL 3) Surgical intervention 4) ASA 5) Others
	Part IV Out come	
42.	ICU admission	1) Yes 2) No
43.	ICU stay	1) 1-7 days 2) 8-14 days 3) > 14 days
44.	Outcome	1) Recanalization documented 2) Regression of varices 3) Death 4) Continued follow up 5) Lost to follow up