PORTAL VEIN THROMBOSIS IN PATIENTS WITH LIVER CIRRHOSIS ;RISK FACTORS,CLINICAL PRESENTATION AND OUTCOME

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ABSTRACT

Introduction: The liver has many haemostatic functions, including the synthesis of most coagulation factors and inhibitors as well as fibrinolytic factors **.**The balance between procoagulant and anticoagulant factors is essential to avoid excessive thrombin generation under physiological conditions. Therefore, advanced liver disease results in a complex pattern of defects in haemostatic functions in the form of reduced synthesis of coagulation factors, inhibitors, and abnormal clotting factors, abnormalities of fibrinolytic activity, disseminated intravascular coagulation and platelet function defects.

Development of portal vein thrombosis (PVT) is asignificant milestone in the natural history of cirrhosis. It is associated with worsening liver function, ascites, and the occurrence of gastroesophageal variceal bleeding. It is clear that PVT increases morbidity and mortality associated with liver transplant and may even contraindicate it and. Thus, taken together, these data suggest that PVT is a major index of poor prognosis in patients with cirrhosis.

Although spontaneous resolution of PVT has been reported in the literature specific therapeutic management is mandatory to resolve portal vein obstruction and avoid serious complications. The goal of treatment is similar correction of causal factors, prevention of thrombosis extension, and achievement of portal vein patency

Objective: the aim of the work was to clarify the risk factors , clinical presentation and complications of portal vein thrombosis in patients with liver cirrhosis and to study the out come after short term follow up.

Subject and methods :- A total number of 80 patients with cirrhosis were included and were classified into two main groups. Group I (50) cirrhotic patients with portal vein thrombosis. Group II (30) cirrhotic patients without portal vein thrombosis. Each group was divided in two sub groups A and B a ccording to prescence or absence of HCC respectively.The 2 groups were compared as regard risk factors and clinical presentation and out come.

Result:

PVT developed as result of combination of both local and systemic risk factors. HCC and abdominal infection specially spontaneous bacterial peritonitis and intervention to the portal system ,were the most important local risk factors . Protein C and S defficincy were amog systemic risk factors. Most of cases were asymptomatic and accidentally discovered , other patients presented with upper GIT bleeding or other complications of liver cell failure .Anticoagulant administration was associated with increased incidence of partial or complete recanalization without increased risk of bleeding.

Conclusion and Recommendations:- Portal vein thrombosis occurs mostly in a cirrhotic patient with advanced liver disease. Patients with advanced liver cirrhosis and not so prolonged coagulation parameters might be at particular risk of developing PVT. So regular monitoring using Doppler-ultrasound should be carried out in these patients. Development of varices is a time dependent phenomenon, so it is advisable to screen all PVT patients endoscopically.Early administration of anticoagulation was associated with increased incidence of partial or complete recanalization.

Keywords :Portal vein ,Thrombosis, risk factors, cirrhosis

INTRODUCTION

The term "Portal vein thrombosis" refers to the development of thrombosis within the extrahepatic portal venous system with possible extension downstream to the intrahepatic portal vein branches or upstream to the superior mesenteric and splenic veins **(1).**

PVT is an important complication of liver cirrhosis. Its reported incidence in compensated disease is between 0.6% and 5%, but becomes much higher (up to 25%) in advanced disease **(2).** Hepatocellular carcinoma is the most frequent cause of PVT in cirrhosis, being present in up to 44% of cases, and always it has to be searched or when a new diagnosis of PVT is made **(3).**PVT in patients with HCC is associated with worsened survival **(4).**

Clinical presentation always depends on the onset and the extent of the thrombosis and the development of collateral circulation. In acute PVT Intestinal congestion and ischemia are typical manifestations ; acute abdominal pain , rectal bleeding, fever, splenomegaly and sepsis might be variably present (**5**). If the obstruction is not resolved quickly, intestinal perforation, peritonitis, shock, and death from multiorgan failure might occur (**6**).

On the other hand, chronic PVT can be nearly asymptomatic and incidentally detected following aroutine imaging procedure. Patients with chronic PVT present with portal hypertension related complications like oesphageal varices, splenomegaly, anaemia and thrombocytopenia (**7**).

Although spontaneous resolution of PVT has been reported in the literature (**8**), a specific therapeutic management is mandatory to resolve portal vein obstruction and avoid serious complications. The

goal of treatment is similar correction of causal factors, prevention of thrombosis extension, and achievement of portal vein patency (**9).**

Therefore, the aim of our study was to clarify the risk factors , clinical presentation and complications of portal vein thrombosis in patients with liver cirrhosis and to study the out come after short term follow up.

SUBJECTS AND METHODS

This work has been carried out in collaboration between the Internal Medicine , radiology and Clinical pathology Departments, Faculty of Medicine, Zagazig University, during the period from January 2011 to June 2013.

*** Subjects:**

A total number of 80 patients with cirrhosis were included and were classified into two main groups:

1) Group I:

includes 50 cirrhotic patients with portal vein thrombosis (31males and 19 females), with age ranged from 40 years to 70 years with a mean values + SD 56. 4±7.8 years. Then divided into two sub groups A and B according to presence or abscence HCC. Group IA (30 patients) and group IB (20 patients).

2) Group II:

Includes 30 cirrhotic patients without portal vein thrombosis patients (17males and 13 females) with age ranged from 39 years to 69 years with a mean values + SD 55.7±6.1years as acontrol group. Then divided into two sub groups A and B according to presence or abscence HCC. Group IIA (10 patients) and group IIB (20 patients)

Inclusion critieria :

- Patients with evidence of liver cirrhosis.
- Partial or complete thrombosis of the portal vein or one of its branches or tributaries .

Exclusion critieria :

- patient with portal vein thrombosis without evidence of liver cirrhosis.

Written consents were taken from all patients included in the study . Results and possible adverse effects of the anticoagulation therapy were explored to all patients received anticoagulation therapy

*** Methods:**

All subjects of the study were subjected to the following:-

A) Thorough history and full clinical examination.

B)* Routine investigations*:

They were all done according to the methods applied in the laboratories of zagazig university hospitals and included:

1- Complete blood picture (by automated blood counter).

2- Liver function tests: serum bilirubin (total and direct), serum albumin, serum ALT and AST by kinetic method

3- Renal function tests: serum creatinine , urea .

4- coagulation profile : PT,PTT and INR.

5- Diagnosis of viral hepatitis by viral markers :- HCV by HCV antibodies and HBV by HBsAg.

➢ ***Diagnosis of liver cirrhosis :-*** is done by physical signs, laboratory, and ultrasound findings and severity of the liver disease was scored according to Child's–Pugh score .

C- Special Investigations : include

1-Meaurment of protein C and by ELISA:-

2-Meaurment of protein S and by ELISA:-

Specimen collection and preparation :-

Plasma collected with either 3.2% or 3.8% sodium citrate as an anticoagulant should be used as the sample matrix. Blood should be collected by venipuncture, and the sample centrifuged immediately. Remove the plasma and store at 2 - 8°C until testing can be performed. If not tested within 8 hours of collection, the sample should be stored at - 70°C and tested within 1 month.

3- Diagnosis of portal vein thrombosis :- is done by doppler ultrasound and contrast enhanced triphasic CT in some cases(patients with HCC and in cases with acute onset especially when SMV affection was suspected).

➢ PVT was classified as complete or partial if thrombus determined absence or reduction of blood flow in the main portal trunk, left and right lobar branches, superior mesenteric vein and splenic vein; the presence of a portal cavernoma was evaluated.

➢ PVT was defined asymptomatic if thrombosis was occasionally revealed during a routine ultrasound examination and symptomatic when the patient was admitted because of one or more of pvt complications either acute or chronic.

4- Diagnosis of hepatocellularr cacinoma :- is done by abdominal ultrasound, contrast enhanced triphasic CT and alpha feto protein .

Staging of HCC is according to The Barcelona-Clinic Liver Cancer (BCLC) staging system.

5-Diagnosis of portal hypertensive gastropathy and grading of oesophageal- and gastric varices :- was made by means of upper GIT endoscopy.

Follow up.

- Follow-up started from the time of diagnosis and lasted for 6 months latter.
- During the follow up period patients were followed as regard:-

✓ Mortality
✓ Morbidity (new onset or recurrence of upper gi bleeding or encephalopathy)
✓ Extension of pvt thrombosis by Doppler ultrasound
✓ Grading of varices and gastropathy by upper gi endoscopy

❖ ***Treatment.***

Six (12%) patients without HCC had been selected according to the following criteria :-

1- Acute onset (less than 1 months).
2- Absence of OV by upper GI endoscope.
3- Absence of portal cavernoma by Doppler ultrasound.
4- Platelet count >50×109/L.
5- Accepted coagulation profile INR less than 1.7.
6- Stage A or early B according to CTP classification.

(**Xingshun et al.,2010**).

They received anticoagulation therapy (low molecular wt heparin and oral anticoagulant (warfarin) with INR adjustment 2-2.5 ..

- ***Statistical analysis:-***

Data were analyzed with SPSS for version 15.0 (statistical package for the Social Science, Chicago, IL). Quantitative data were expressed as mean±standard deviation (SD) or standard error (SE). SE=SD/square root of patients number which was used in case of big SD, data were analyzed by independent sample, paired t test and one way analysis of variance (ANOVA). While qualitative data were expressed as number and percentage and were analyzed by Chi square (X2) test. Correlation was done using Pearson correlation test. The receiver operating characteristic (ROC) curve and 95% confidence interval (CI) was performed to determine cutoff values for the studied biomarkers. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were determined. P-value was considered significant if <0.05 and highly significant if <0.001.

RESULTS

Table (1): Etiology of liver diseases

	Group I (N=50)		Group II (N=30)		χ2	P-value
	No	%	No	%		
1ry billiary cirrhosis	1	2.0	0	0.0		
Autoimmune Hepatitis	1	2.0	0	0.0		
					8.0	
HBV	6	12.0	3	10.0		0.1
HCV	40	80.0	26	86.66		
HCV&HBV	2	4.0	1	3.33		

Table (1) describes Etiology of liver diseases among both groups , there are no statistical significance differences between both groups as regard etiology of liver diseases as (P>0.05).

Table (2) Distribution of cases according to Child score

	Group I (N=50)	Group II (N=30
Child score A	7	5
Child score B	10	5
Child score C	33	20

Table (3):Prevalence of local risk factors in both groups

Local risk factors (%)	PVT group (50)	Control group (30)	Pvalue
Cancer (HCC)	30	10	0.02
Abdominal inflammation	9	4	0.7
Abdominal infection	21	3	.010
Abdominal intervention	20	4	0.01
Previous sclerotherapy	13	5	0.3

Table (1) describes the local risk factors it shows that **HCC ,abdominal intervention** (11 cases with splenctomy ,2cases with chemoemboliezation for HCC,2casses with radiofrequency ablation for HCC ,2 cases with cholycystectomy,one case with appendctomy and one case shows drainage for complicated liver abcess) **and abdominal infection** (20 cases with sbp and one case with liver abcesses) were statistically significant in pvt group than in control group as (P<0.05).Although prevelance of **abdominal inflammation** 9 cases(5 cases of cholycystitis and 4 cases of appendicitis) and **previous sclerotherapy** is higher in pvt group than in control group it is statistically in significant .

Table (4) protein C level between both groups according to Child score:-

	Group I	Group II	t-test	P-value
Child score A	3.3±.2	3.6±0.1	-1.2	0.2
Child score B	2.5±0.7	2.9±0.1	-2.0	0.03
Child score C	1.9±0.2	2.5±0.3	-9.7	0.000

Table (5) protein S level between both groups according to Child score:

	Group I	Group II	t-test	P-value
Child score A	19.4±1.8	20.5±0.6	-1.4	0.2
Child score B	17.1±1.5	19.5±0.4	-3.5	0.004
Child score C	15.2±1.3	18.2±1.0	-8.9	0.001

Table (4),Table (5) shows protein C and S level between both groups.there are no significant difference in both groups as regard Child A. but there were significant reduction of protein C and S level in PVT group than control group as regard Child B and C .

Table (6) Coagulation profile level between both groups according to Child score:

	Group I	Group II	t-test	P-value
PTT				
Child score A	28.6±0.9	29.1±1.2	0.8	0.4
Child score B	43.0±6.0	48.9±0.9	-2.1	0.05
Child score C	46.5±6.1	58.1±2.9	-7.9	0.000
INR				
Child score A	1.1±0.04	1.1±0.1	-0.4	0.7
Child score B	1.5±0.2	1.8±0.1	-4.1	0.001
Child score C	1.7±0.3	2.0±0.3	-2.1	0..04

Table (6) shows changes in coagulation profile in both groups,there are increase in PTT and INR level with increase severity of liver disease in both groups . In Child B and C thre is significant decease in PTTand INR in PVT group in comparison with control group. But in chils A no significant difference between both groups

Table (7) Platelet level between both groups according to Child score:

	Group I	Group II	t-test	P-value
Child score A	148.7±23.7	146.2±27.0	1.3	0.2
Child score B	132.2±25.3	102.8±12.9	0.9	0.4
Child score C	97.1±45.5	80.7±18.6	4.8	0.000

Table (7) shows changes in platelet count in both groups,there is decease in platelet count with increase severity of liver disease in both groups . In patients with child C there were significant increase in platelet count in PVT group in comparison with control group. But in patients with child A and B ,there were no significant difference between both groups

Table (8): Clinical presentation of the PVT group:

Clinical presentation	Number of cases	%
Asymptomatic	15	30.0
Upper GIT bleeding	14	28.0
Other manifestations of liver cellfailure	15	30.0
Lower GIT bleeding	1	2
Acute Abdominal pain	5	10

Table (8) describes the Clinical presentation of the PVT group About (30%)of cases are asymptomatic and discovered during routine ultrasound ,(30%) presented with complications of liver cell failure,(28%) presented with upper gi bleeding and (12%) presented withabdominal pain and lower gi bleeding.

Table (9): Endoscopic grading among groups.

	Group I (N=50)		Group II (N=30)		$\chi 2$	P-value
Gastropathy	**No**	%	**No**	%		
Gastropathy grade 1	9	18.0	10	26.7	23.6	0.001
Gastropathy grade 2	20	40.0	5	16.7		
Gastropathy grade 3	14	28.0	1	3.3		
Oesph. Varieces						
OV1	3	6.0	3	10.0		
OV2	5	10.0	4	13.3	20.6	0.002
OV3	16	32.0	5	16.7		
OV4	20	40.0	1	3.3		

Table (9): describes the comparison between the 2 groups as regard Endoscopic grading , it shows that grading of Gastropathy and oesphygeal varices as endoscopic findings are highly statistically significant among pvt group than control group .

Table (10): Distribution of thrombotic involvement of branches of portal system in our patients :-

Site of thrombosis	Complete	Partial
Main stem	**9**	**12**
Main stem and right branch	**7**	**4**
Main stem and left branch	**6**	**2**
Right branch	**2**	**1**
Left branch	**3**	**1**
Extension to SMV	**3**	**0**

Table (11): Correlation between the extension of PVT and clinical presentation

PVT presentation Site of thhrombosis	Asymptomatic	Ischemic	Haemorrhagic	P value
Main stem	11	1	9	0.51
Main stem and right branch	6	1	4	0.51
Main stem and left branch	4	1	3	0.87
Right branch	2	0	1	0.14
Left branch	2	0	2	0.25
Extension to SMV	0	3	0	0.04

There is no correlation between extension of pvt and clinical presentation except when SMV is involved was never asymptomatic

Table (12): 6months follow up between both groups as regard recurrent upper GIT bleeding.

Parameters	Group I (N=50)		Group II (N=30)		$\chi 2$	P-value
	No	%	**No**	%		
Recurrent upper GIT bleeding	23	46.0	5	16.6	2.4	0.005

Recurrent upper gi bleeding is highly statistically significant in pvt group than control group as regard follow up

Table (13):): 6months follow up between both groups as regard recurrent hepatic encephalopathy.

Parameters	Group I (N=21)		Group II (N=26)		$\chi 2$	P-value
	No	%	**No**	%		
Recurrent encephalopathy	7	33.3	6	23	2.4	0.08

There is no stastical difference as reguard recurrence of hepatic encephalopathy during the follow up period

Table (14): Follow up doppler ultrasound after 6 months in live patients only

Site of thrombosis	Complete	Partial	anticoagulant	complete	partial	cavernoma	Complete resolution
Main stem	5	7	3	8	3	4	1
Main stem and rt branch	1	1	N0	2	0	2	0
Main stem and lt branch	2	1	N0	1	0	1	2
Right branch	0	1	N0	1	0	0	0
Left branch	1	0	N0	1	0	0	0
Extension to SMV	2	0	2	0	1	0	1

Table (14) demonstrates the Follow up doppler ultrasound after 6 months in live patients only in pvt group it shows. that as regard thrombosis of **the main stem** ,anticoagulant was administrated in 3 patients 2 complete , one partial .The partial thrombosis shows complete resolution and the 2 complete thrombosis one shows partial resolution and the next shows no change in thrombus extension . 9 patients received anticoagulants (3 complete and 2 partial) . the 3 complete patients still had complete pvt and 2 devolop portal cavernoma . 4 patients from the 6 patients with partial pvt developed complete pvt and 2 of them develop cavernoma.

2 cases had Thrombosis of the **main stem and extend to right branch** (1 partial and 1 complete thrombosis) the partial one extended to became complete . 2 cases had Thrombosis of the **main stem and extend to left branch** (1 partial and 2 complete thrombosis) the partial one shows spontaneous resolution , one patient with complete thrombosis with acute onset shows complete recanalization .one case with partial tthrombosis in **rt branch only** extended to became complete thrombosis. AS regard **thrombosis extend to smv** anti coagulant was administrated in the 2patients one patient shows complete reolution and 1 patients show partial resolution .one case of partial thrombosis in the main stem and left branch sows complete resolution without anticoagulant.one case of partial rt branch canged to complete thrombosis without anticoagulant

Table (15): Comparison between PVT patients with anticoagulation and patients with PVT without anticoagulation therapy

	PVT patients with anticoagulation	PVT patient without anticoagulation
Number	**6 (12 %)**	**44 (88 %)**
Recurrent upper GIT bleeding	**0**	**23**
Resolution	**5**	**1**
progression	**0**	**6**
Mortality	**0**	**29**

Table (15) shows comparison between patients with and without anticoagulant administration in the PVT group . 6 patients had been given anticoagulation therapy 5 of them shows resolution opposite to 44 patients without anticoagulation shows only case with spontaneous resolution. No risk of upper GIT bleeding nor mortality in patients with treatment ,opposite to 23 patient with risk of upper GIT bleeding and 29 cases of death in the patients without treatment.

Table (16): Mortality among both groups.

Mortality	Group I (N=50)		Group II (N=30)		χ2	P-value
	With HCC	Without HCC	With HCC	Without HCC		
	30	20	10	20	17.5	0.001
Living	5(16.6%)	16(80%)	7(70%)	19(85%)		
Dead	25(83.3%)	4(20%)	3(30%)	1(5%)		

Table (16): describes mortality among both groups,mortality was 20% in PVT patients without HCC incomparison to 5% in other group without HCC. Mortality was 83.3 % in PVT patients with HCC incomparison to 30% in other group with HCC.So Mortality was highly statistically significant among PVT group than Contrpl group (P<0.05).

Table (17): Cause of death among both groups.

Cause of death	Group I (N=29)		Group II (N=4)		χ2	P-value
	N	%	N	%		
Unknown	2	6.9	0	0.0	Fisher exact	1.0
Chest infection	1	3.4	0	0.0	Fisher exact	1.0
DIC	2	6.9	0	0.0	Fisher exact	1.0
LCF	3	10.3	1	25.0	Fisher exact	0.4
RF	6	20.7	1	25.0	Fisher exact	1.0
RF and LF	1	3.4	0	0.0	Fisher exact	1.0
Sepsis	3	10.3	1	25.0	Fisher exact	1.0
UG bleeding	11	37.9	1	25.0	Fisher exact	1.0

There are no statistical significant differences between both groups as regard cause of death.

DISCUSSION

The liver has many haemostatic functions, including the synthesis of most coagulation factors and inhibitors as well as fibrinolytic factors .The balance between procoagulant and anticoagulant factors is essential to to prevent excessive blood loss from injured vessels and to prevent spontaneous thrombosis **(10).** Thus, the global effect of liver disease with regard to hemostasis is complex, so that patients with advanced liver disease can experience severe bleeding or even thrombotic complications **(11).**

PVT is common in patients affected by liver cirrhosis, with a risk related to the severity of the disease; the prevalence ranges from 1%, at the earlier stages, to 30% in candidates for liver transplantation, **(12).** Moreover, in patients with a hepatocellular carcinoma, the incidence of PVT rises to 10%-40%. Figures vary widely depending on how long ago the study was conducted, the diagnostic tool used and the inclusion or exclusion of patients with hepatocellular carcinoma (HCC). **(7).**

As already mentioned, PVT in patients with liver disease is the result of concomitant local and systemic thrombophilic factors **(13)** .Our study demonstrated that malignancy (HCC) was the most common local risk factor for pvt (60%) followed by abdominal infection esp sbp (42%) then abdominal intervention especially splenectomy(40

%) .These results also were reported by other studies with different distribution as the study done by **Sogaard et al., (6)** in which abdominal inflamation esp. pancreatitis is the most common(19 %) followed by cancer (13 %) then abdominal intervention (8 %) .This is due to high prevelance of HCC in our country and high prevelance of pancreatitis abroad.

As regard HCC, 22 patients had multiple focal lesions 8 had single lesion , most of them were large . 15 patients were classified as category D and 8 as category C and 5 as category A and B according to BCLC staging for HCC .21 patients were stage C and 5 were stage B and 2 were stage A according to CTP classifications, these results come with agreement with the result reported by **Gregory etal.,(4)** which demostrated that advanced tumor stage, higher CTP classification,multifocal tumor and were associated with incresed risk of PVT .

Previous endoscopic sclerotherapy, even if more frequent in patients with PVT than in those without PVT, did not show statiscal significance which goes in agreement with **Mangia et al .,(14) and Francoz et al.,(15)** this is opposite to study was done by **Amitrano et al.,(16)** which demonstrated that endoscopic sclerotherapy of esophageal varices may represent a trigger factor for portal vein thrombosis in cirrhotic patients.

liver cirrhosis is generally associated with profound alterations of the coagulation and anticoagulation systems.For example, INR and PTT, both important parameters indicating coagulation functions, were significantly prolonged in severe liver cirrhosis, which was cleared by our data in the present study. Our study showed that patients with advanced liver cirrhosis and PVT show a significantly lower PTT and INR compared with those without PVT. In patients with early stages of liver cirrhosis, there were no differences in PTT and INR between the PVT and control group. The PLT level was decreased also with advanced stages of liver disease, **Zarbock et al.,(17).** .In patients with Child A and B ,there were no significant diffierences between the two groups,while in patients with Child C the platelet count was relatively higher in PVT group than controls.Similar reults were in agreement with studies **by Francoz et al. (15)** and **Donglei et al., (9)** who reported that cirrhotic patients with PVT had higher platelet level in comparison with cirrhotics without PVT with advanced stages of liver disease**.** Therefore, patients with advanced liver cirrhosis and not so prolonged coagulation parameters appear to carry a higher risk of PVT compared with patients advanced liver cirrhosis and markedly prolonged coagulation parameters. These findings were also reported by **Weber et al.,(20)**

As regard protein C and S ,our study showed that in early stage of liver cirrhosis,there were no differences betweeen both groups.But with increasing severity of liver disease protein Cand S level were significantly decreased in pvt group in comparison with control group,the same results were also reported by **Tacke et al.,(21) and Donglei et al., (19).** One of the underlying mechanisms may be due to the fact that hepatocytes fail to synthesize adequate amounts of PC and PS under ischemic and hypoxic conditions. Also, the decrease in PC and PS may be attributed to the endothelial cells damage caused by portal hypertension, which leads to the activation and subsequent consumption of PC and PS in fibrolytic processes .

Clinical presentation always depends on the onset and the extent of the thrombosis and the development of collateral circulation(**Northup et al .,2008)** 15 (30 %) patients were asymptomatic and accedientally discovered during routine ultrasound examination, 15(30%) patients presented with complications of liver cell failure as aggrevation of ascites and hepatic encephalopathy,14(28 %)patients presented with upper git bleeding ,5 (10 %) patients presented with acute abdominal pain and only one patient(2%) presented with lower git bleeding .similar results reported by **Amitrano et al., (13)** in their study on 79 cirrhotic patients with PVT(43%)were asymptomatic and (39%) presented with upper git bleeding ,(17%) presented with abdominal pain (7.9 %) presented with intestinal infarction.

The presence of complete occlusion of superior mesentericvein was never asymptomatic and presented with the clinical features of intestinal ischemia or infarction. It depends mostly on the absence of an efficient collateral circulation in the mesenteric bed. Conversely a complete thrombosis of main portal trunk or in right or left branche swas symptomless in many patients and we could not find a relationship between the extension of portal thrombosis and the risk of gastrointestinal bleeding .Similar findings were supported by **Amitrano etal., (13)**.

Follow up :-

Strict 6 months follow up had occurred for all patients ,revealed that Spontaneous resolution of

the thrombosis had occurred in one case without treatment, but the frequency of partial or complete recanalization appeared to be higher in patients treated with anticoagulation therapy . Six patients were selected according to criteria reported by **Xingshun et al.,(22)** and anticoagulation in the form of (low molecular weight heparin and oral warfarin) were adminstered to the patients with INR adjustment (from 2 to 2.5). The critera of patients were as follow ,three patients had main stem thrombosis (1 partial and 2 complete) and one patient with complete main stem thrombosis and exted to left branch the remainning two patients had complete thrombosis and extended to SMV. The results were , complete recanaliztion had occurred in two cases (33.3%) , partial recanalization had occurred in three patients (50 %) and no change had occurred in one case (16.6 %). similar results also were reported by **Senzolo et al.,(23)** who made study on 39 cirrhotic pvt patients with anticoagulant admistration showed recanalization of 16 patients (41 %)in comparison with no recanalization in patients not given anticoagulant.

Inspite of anticoagulation therapy to cirrhotic patients ,there were no bleeding episodes during the follow up period , which came in agreement with study was made by **Buteral et al .,(24)** , who gave anticoagulant therapy to sixteen cirrhotic patients with PVT with oesphageal varcices, threre were no evidence of bleeding.

Frequent complications during follow-up, in non treated patients , were detected as new onset of varices,recurrent upper git bleeding and aggrevation of liver decompenastion . A larger part of patients with chronic PVT developed oesophageal varices in comparison with patients with acute PVT. These results come with agreement with the result reported by **Janssen et al.,(25)**. Thus, the development of varices is a time dependent phenomenon, and it is advisable to screen all PVT patients endoscopically.

The recurrence of upper git bleeding was higher in PVT group (46 %) than in control group (16.6%)and ,these results were similar to results of study done by **sogaard et al.,(6)** in which the recurrence rate was (43%) and higher than recurrence rate in the study done by **Zargar et al.,(26)** in which the recurrence rate in PVT group was (19.4). The results were higher in our study may be due to inclusion of patitents with HCC in our study and not present in study of **Zargar et al.,(26) .The** grade of oesphageal varices and gastropathy were also higher in pvt group than in control group(19.04%) grade II,(28.5%) grade III and (33.3%) grade IV, similar results reported by **sogaard et al.,(6)** in which (11%) were grade II and (26%) were grade III and (33%) grade IV**.** There were no stastical difference as reguard recurrence of hepatic encephalopathy during the follow up period.

As regard mortality , mortality was 20% in PVT patients without HCC incomparison to 5% in other group without HCC which were near to results reported by **soggard et al.,(6)** in which mortality rate were (26 %) and **Ferreira et al.,(27)** in which mortality rate was (24%) and mortality was 83.3 % in PVT patients with HCC incomparison to 30% in other group with HCC which was near to results of a study by **Gregory et al.,(4)** which demonstrated that the median survival in patients with PVT and HCC was 2.3 months compared to 17.4 months in HCC patients without PVT. Causes of death are recurrent upper GIT bleeding(37.9 %), sepsis (10.3 %),renal failure(20.7%) and DIC (6.9 %). In comparison with other group in which 4 patients only (13.3%)died .

On conclusion, Portal vein thrombosis occurs mostly in a cirrhotic patient with advanced liver disease; it is completely asymptomatic in half of cases but when symptomatic, it presents with life-threatening complications as gastrointestinal bleeding or intestinal infarction. Partial/complete recanalization was more frequent in patients treated with anticoagulation therapy than without treatment .Anticoagulation therapy in cirrhotic patients with pvt were not associated with increased risk of recurrent upper GIT bleeding.

REFERENCES

1- Senzolo M, Burra P, Patch D .,(2011):Tips for portal vein thrombosis (pvt) in cirrhosis: not only unblocking a pipe. J Hepatol;55:945–946, author reply 947–948.

2- Garcia JC, Hernandez M, Bosch J et al.,(2008): Extrahepatic portal vein thrombosis. Semin Liver Dis;28:282–92 .

3- Huseyin A, Selime A, Nurgul Set al .,(2011): Hemostatic Abnormalities in Cirrhosis and Tumor-Related Portal Vein Thrombosis. CLIN APPL THROMB HEMOST . DOI: 10.1177/1076029611427900.

4- Gregory C. Connolly MD, Rui Chen et al .,(2008): Incidence, risk factors and consequences of portal vein and systemic thromboses in hepatocellular carcinoma.*hromb Res*. ; 122(3): 299–30.

5- Northup PG, Sundaram V, Fallon MB et al .,(2008): Hypercoagulation and thrombophilia in liver disease. *J Thromb Haemost* 2008; 6: 2-9
6- Sogaard KK, Astrup LB, Vilstrup H et al., (2007): Portal vein thrombosis; risk factors, clinical presentation and treatment. *BMC Gastroenterol*; 7: 34.
7- Hoekstra J and Janssen H (2009): Vascular liver disorders (II): portal vein thrombosis. Neth J Med 2009; 67: 46-53.
8- Condat B, Pessione F, Helene Denninger Met al.,(2000): Recent portal or mesenteric venous thrombosis: increased recognition and frequent recanalization on anticoagulant therapy. *Hepatology*; 32: 466-470.
9- DeLeve LD, Valla DC and Garcia-T et al., (2009):Vascular disorders of the liver. *Hepatology* 2009; 49: 1729-1764 .
10- Tripodi A, Salerno F, Chantarangkul V, et al.,(2005): Evidence of normal thrombin generation in cirrhosis despite abnormal conventional coagulation tests. Hepatology.;41(3):553-558.
11- Lisman T, Leebeek FW and de Groot PG et al., (2002): Haemostatic abnormalities in patients with liver disease. J Hepatol;37(2):280-287.
12- Condat B and Valla D (2006):Nonmalignant portal vein thrombosis in adults. *Nat Clin Pract Gastroenterol Hepatol* ; 3: 505-515.
13- Amitrano L, Guardascione MA, Brancaccio V et al.(2004): Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. J Hepatol ; 40: 736-741.
14- Mangia A, Villani MR, Cappucci G, et al.,(2005): Causes of portal venous thrombosis in cirrhotic patients: the role of genetic and acquired factors. Eur J Gastroenterol Hepatol;17:745e51.
15- Francoz C, Durand F, Sommacale D et al.,(2002): Incidence of splanchnic vein thrombosis in candidates for liver transplantation and usefulness of anticoagulant therapy while awaiting for liver transplantation. Hepatology;36:191A.
16- Amitrano L, Brancaccio V, Guardascione M et al.,(2002):Portal vein thrombosis after variceal endoscopic sclerotherapy in cirrhotic patients: role of genetic thrombophilia. Endoscopy;34:535–537
17- Zarbock A, Polanowska Grabowska RK and Ley K(2007). Platelet–neutrophil-interactions: linking hemostasis and inflammation. Blood Rev;21(2):99–111.
18- Francoz C, Belghiti J, Vilgrain V et al.,(2005):Splanchnic vein thrombosis in candidates for liver transplantation: usefulness of screening and anticoagulation.*Gut* ; 54: 691-697.
19- Donglei Z, Jianyu H , Nin Y et al ., (2010): Protein C and D-dimer are related to portal vein thrombosis in patients with liver cirrhosis. Journal of Gastroenterology and Hepatology (25) 116–121.
20- Weber A, Krebs S, Lenhardt L et al.,(2009): Correlation of routinely used coagulation parameters and presence of portal vein thrombosis in patients with liver cirrhosis. *Hepatology Research* ; 39: 882–887.
21- Tacke F, Schöffski P, Trautwein C et al.,(2001): Tissue factor and thrombomodulin levels are correlated with stage of cirrhosis in patients with liver disease. *Blood Coagul. Fibrinolysis* ; 12: 539–45.
22- Xingshun Q, Guohong H, Kaichun W et al., (2010): Anticoagulation for Portal Vein Thrombosis in Cirrhosis The American Journal of Medicine, Vol 123, No 9, September 2010.
23- Senzolo M , Sartori MT , Gasparini D et al.,(2010): Algorhithm for the treatment of PVT and splanchnic vein thrombosis in patients with liver cirrhosis. *Digestive and Liver Disease 42 Suppl. ;1 :S1–S51*
24- Buteral G, Simone1 F, Iaco A et al .,(2010): Anticoagulant treatment for non neoplastic portal vein thrombosis in patients with liver cirrhosis and oeashageal varices . Digestive and Liver Disease 42 Suppl. (1) S1–S51 S37
25- Janssen HL, Wijnhoud A, Haagsma EB et al.,(2001):Extrahepatic portal vein thrombosis: aetiology and determinants of survival. *Gut*; 49: 720-724.
26- Zargar S , Javid G , Khan B et al.,(2005): Endoscopic ligation vs. sclerotherapy in adults with extrahepatic portal venous obstruction: a prospective randomized study.J of gastrointestinal endoscopy (61);1:58-67.
27- Ferreira C, Alexandrino P, Ramalho Fet al.,(2010): Portal vein thrombosis in cirrhotic patients is associated with advanced liver disease and predicts poor long term prognosis. *Hepatology*; 52: 1072A
28- Englesbe MJ, Kubus J, Muhammad W et al.,(2010): Portal vein thrombosis and survival in patients with cirrhosis. Liver Transpl ;16:83–90.
29-

عوامل الخطوره والاعراض الاكلينيكيه ونتائج تجلط الوريد البابي في مرضي تليف الكبد

مقدمه-:

*يلعب الكبد دورا اساسيا في تجلط الدم و ذلك من خلال تكوين معاملات و مضادات التجلط و لذلك فان ا*عتلال الحاله الصحيه للكبد تؤثر بالسلب علي تكوين تلك المواد ولذلك ايضا ليس من الغريب ان تجد مريض الكبد يعانى من زيادة فى سيولة الدم واخر يعانى من حدوث جلطات .

هناك عوامل كثيره قد تؤدي الي تجلط الوريد البابي منها ما هو موضعي مثل الاورام الكبدية وجراحات سابقه بالبطن (استئصال الطحال وجراحات علاج ارتفاع ضغط الوريد البابي.....) وايضا التهابات القناه الهضميه مثل (التهاب الزائده الدوديه والحوصله المراريه والتهاب البنكرياس و خراج الكبد) .ومنها ما هو عام مثل نقص مضادات التجلط مثل بروتين (c) وبروتين (s) ومعامل (V) بالاضافه الي اضرابات الجهاز المناعى و امراض الدم.

يعتبر تجلط الوريد البابى من المضاغفات المهمة لتليف الكبد و تتراوح نسبة حدوثه من 1% فى المراحل البسيطة الى حوالى 25 % فى المراحل المتقدمة وذلك عن طريق بطء معدل سريان الدم فى الوريد البابى و كذلك التاثير السلبى على معاملات و مضادات التجلط كما ذكر سابقا .

تتوقف اعراض تجلط الوريد البابي علي نسبه انسداد الوريد اما انسداد جزئي او كلي وكذلك مكان التجلط اما بالوريد البابي نفسه او في احد فروعه او روافده وكذلك سرعه التجلط هل هي حاده او مزمنه .

الهدف من الرسالة :

دراسة الاعراض الاكلينيكية و معاملات الخطورة لتجلط الوريد البابي في مرضي تليف الكبد و كذلك النتائج المترتبة عليه من خلال متابعة المرضى

وقد شملت الدراسة 80 مريض تم تقسيمهم الى مجوعتان .المجموعة الاولى و تشمل 50 مريض يعانون من تجلط الوريد البابى بالاضافة الى تليف الكبد. المجموعة الثانية و تشمل 30مريض يعانون من تليف الكبد فقط و ذلك للمقارنة مع المجموعة الاولى.

و تم اجراء فحوصات معملية روتينية تشتمل علي صورة دم كاملة ووظائف كبد وكلي بالاضافة الى قياس مضادات التجلط بروتين(C و (S) و اشعة دوبلر لتشخيص تجلط الوريد البابى و كذلك عمل اشعة مقطعية ثلاثية المراحل لتشخيص اورام الكبد بالاضافة الى منظار على المرئ و المعدة لتشخيص و علاج دوالى المرئ و المعدة

النتائج :

لوحظ ان اورام الكبد بالاضافة الى التهابات البطن ووكذلك نقص مضادات التجلط من اهم العوامل المسببة لحدوث تجلط الوريد البابى

اغلب الحالات قد لا تعاني من اي اعراض و يتم اكتشافها بالصدفة اثناء عمل الاشعة التلفزيونية الروتينية لمريض الكبد .وبعض الحالات تعانى من نتائج ارتفاع ضغط الوريد مثل نزيف دوالى المرئ والمعده وكذلك استسقاء بالبطن و البعض الاخر يعانى من زيادة فى مضاعفات فشل الكبد مثل الغيبوبة الكبدية.

ارتفاع معدل نزيف الدوالى و كذلك معدل الوفيات فى مرضى تليف الكبد

التوصيات :

- الاكتشاف و العلاج المبكر لتجلط الوريد البابى يقى حدوث المضاعفات المحتملة .
- استخدام ادوية السيولة يؤدى الى زيادة معدل انحلال تجلط الوريد البابى
- استخدام ادوية السيولة فى مرضى تليف الكبد لا يؤدى الى زيادة نسبة النزف طالما استخدمت طبقا للتوصيات المذكورة فى الرسالة