Egyptian Journal of Bronchology

Vol 3, No 2, December, 2009

ORIGINAL ARTICLE

STUDY THE BLOOD COAGULOPATHY AND PULMONARY EMBOLISM IN CHRONIC LIVER CIRRHOSIS

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Background: *The liver weighs about 3 pounds and is the largest solid organ in the body. It performs many important functions. Cirrhosis is a consequence of chronic liver disease characterized by replacement of liver tissue by fibrous scar tissue as well as regenerative nodules, leading to progressive loss of liver functions..*

Aim of study: *Study the blood coagulopathy and pulmonary embolism in patients with chronic liver cirrhosis.*

Materials and Methods: *Thirty patients who had proved chronic liver cirrhosis. Patients were selected from General Medicine Department El Matarya Teaching and El-Nile (Health Insurance) Hospitals. Patients were divided into:-Group A: Fifteen patients with complicated decompensated chronic liver cirrhosis such as ascites, deep vein thrombosis and hepatopulmonary syndrome. Group B: Fifteen patients with compensated liver cirrhosis (no ascites). Ten normal healthy subjects was participated in the present study as a controls (group C). Age of patients ranged from 40 to 65 years. Laboratory tests including: CBC, ESR, liver functions including (ALT, AST, S. Albumin), renal functions (s.urea and s.createnine); Coagulation profile (PT, INR and aPTT) was done by coagulometer..Serum D'Dimer estimation; Abdominal ultrasound and echo-doppler study for veins of lower limbs when indicated, CXR. ventilatory function(FVC,FEV_1,FEV_1/FVC%,$FEF_{25-75\%}$). Pulmonary perfusion scan was performed with technetium 99 m (99 m Tc) - labeled macroaggregated albumin*

Results: *The current study revealed a highly significant restrictive ventilatory function, increased PT, aPTT, INR, serum D'Dimer level. Deep venous thrombosis/pulmonary embolism is not uncommon in liver cirrhosis*

Conclusion: Although cirrhosis of the liver can cause many complications e.g. deficient coagulation and anticoagulation factors, but deep venous thrombosis and pulmonary embolism is not uncommon in liver cirrhosis

Keywords: *Liver cirrhosis, blood coagulopathy, pulmonary embolism.*

INTRODUCTION

Liver cirrhosis is defined histologically as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules. The progression of liver injury to cirrhosis may occur over weeks to years. Indeed, patients with hepatitis C may have chronic hepatitis for as long as 40 years before progressing to cirrhosis.(1)

The diagnosis of liver cirrhosis was based on clinical, biochemical and ultrasound criteria .Often a poor correlation exists between histological findings and the clinical picture. Some patients with cirrhosis are completely asymptomatic and have a reasonably normal life expectancy. Other individuals have a multitude of the most severe symptoms of end-stage liver disease and have a limited chance for survival. Common signs and symptoms may stem from decreased hepatic synthetic function

(e.g.,coagulopathy), decreased detoxification capabilities of the liver (eg, hepatic encephalopathy), or portal hypertension (e .g, variceal bleeding).[2]

Patients also may have hepatopulmonary syndrome (HPS), in this condition, pulmonary arteriovenous anastomoses result in arteriovenous shunting. HPS is a potentially progressive and life-threatening complication of cirrhosis. Classic HPS is marked by the symptom of platypnea (i.e. dyspnea induced by the upright position and relieved on recumbence) and the finding of orthodeoxia (i.e. arterial deoxygenation induced by the upright position and relieved by recumbence), but the syndrome must be considered in any patient with cirrhosis who has evidence of oxygen desaturation. HPS is detected most readily by echocardiographic visualization of late-appearing bubbles in the left atrium following the injection of agitated saline. Patients can receive a diagnosis of HPS when their PaO_2 is less than 70 mm Hg.[3,4]

It is a commonly held notion that patients with cirrhosis do not suffer from deep vein thrombosis (DVT) or pulmonary embolism (PE) because they are naturally anticoagulated. However, to date, no studies have been carried out that objectively address this issue. We conducted a study to examine the relationship between cirrhosis and DVT/PE events.[5] Coagulation disorder is prevalent in patients with chronic liver disease which is usually detected in laboratory tests and characterized by prolonged prothrombin time (PT), decreased fibrinogen, coagulation factor 5 levels and thrombocytopenia.[6]

Patients with liver cirrhosis do not have a lower risk of deep venous thrombosis/pulmonary embolism (DVT/PE) than non-cirrhotic controls without other significant co-morbidities, such as Congestive heart failure, chronic renal disease, and solid organ cancers. Partial thromboplastin time and serum albumin were found to be independently predictive of DVT/PE in cirrhotic patients[5]

Pulmonary embolism (PE) can be life threatening as well as very difficult to diagnose. PE has a myriad of presentations, and imaging studies often are not diagnostic. Researchers studied the utility of D-dimer testing in the diagnosis of patients with suspected PE who had negative helical computed tomography results or nondiagnostic ventilation-perfusion lung scans.[7]

D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. D-dimer concentration may be determined by a blood test to help diagnose thrombosis. Since its introduction in the 1990s, it has become an important test performed in patients suspected of thrombotic disorders. While a negative result practically rules out thrombosis, a positive result can indicate thrombosis but does not rule out other potential causes. Its main use, therefore, is to exclude thromboembolic disease where the probability is low.[7]

Routine plasma d-dimer measurement has limited benefit as an exclusion test for inpatients with suspected pulmonary embolism (PE). The diagnosis of pulmonary embolism is difficult because the clinical diagnosis is non specific and all of the objective tests have limitations. The assay for plasma d-dimer may be useful as an exclusion test if results are negative.[8]

Aim of the work: Study the blood coagulopathy and pulmonary embolism in patients with chronic liver cirrhosis.

PATIENTS AND METHOD

Thirty male patients who had proved chronic liver cirrhosis in addition to ten normal male healthy subjects participated in the present study. Patients were selected from General Medicine Department El Matarya Teaching and El-Nile (Health Insurance) Hospitals. Their ages ranged from 40 to 65 years. Subjects were divided into three groups:-

Group A: Fifteen patients with complicated decompensated liver cirrhosis such as ascitis, deep vein thrombosis and hepatopulmonary syndrome.

Group B: Fifteen patients with compensated chronic liver cirrhosis.

Group C: Included ten normal healthy persons as a control group.

All subjects were submitted for:

1. Thorough clinical history including smoking habits and occupational history; and thorough clinical examination.
2. Laboratory tests including: CBC, ESR, liver functions including (ALT, AST, S. Albumin); and renal functions (s. urea and s. createnine).
3. Coagulation profile (prothrombin time "PT", international randomized ratio "INR" and activated partial thromoplastin time "aPTT) was done by coagulometer.[9]
4. Serum D'Dimer estimation was done for all subjects using quantitative enzyme immunosorbant assay(ELISA).[10]
5. Arterial blood gases analysis (ABG);
6. Abdominal ultrasound including estimation of portal vein diameter and echo-doppler study for veins of lower limbs when indicated.

7. Plain chest X ray postero-anterior view.
8. Ventilatory function was performed using electronic spirometer (Schiller AG, CH 6340). Patient was asked to expire forcefully and rapidly as he can after deep inspiration as much as possible in the mouthpiece and what appeared on the screen were printed on a tape.They were tested from standing position The data were obtained for three successive readings, and the best readings for forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), FEV/FVC % and forced expiratory flow between 25-75% of FVC maneuver were recorded.
9. Pulmonary perfusion scan was performed with technetium 99 m (99 m Tc) - labeled macroaggregated albumin.

Inclusion Criteria:

1- The patient's ages ranged from 40 to 65 years.
2- Patients were non-smokers or ex-smokers for at least 6 months.

Exclusive criteria:-

1- Patients who have cardiac or renal diseases.
2- Patients who have hepatic encephalopathy and admitted to ICU.

RESULTS

The present study was carried out in Chest department of El-Mataria Teaching Hospital in the period between 0ctober 2008 and July 2009.

Forty subjects were included in this study and were divided into 3 groups:

Group (A): Fifteen patients with proved decompensated liver cirrhosis.

Group (B): Fifteen patients with proved compensated liver cirrhosis.

Group (C): Ten normal and healthy persons studied as a control.

As regards table 1. Statistical comparison between groups C & A for age of subjects, ventilatory functions (FVC, FEV_1, FEV_1/FVC %, $FEF_{25-75\%}$), and arterial O_2 saturation on up-right and supine positions revealed the following results: There were high statistical significant differences (P< 0.05) of mean values of patient's age, ventilatory functions FVC, FEV_1 and $FEF_{25-75\%}$ but FEV_1/FVC % showed non-significant difference, these findings are highly suggestive severe restrictive ventilatory pattern. There were high statistical significant differences (P<0.001) of mean values of arterial O_2 saturation on up-right and supine positions (P< 0.001).

Table 2. Showed statistical comparison between groups C &B for mean values of age of subjects, ventilatory functions (FVC, FEV_1, FEV_1/FVC %, $FEF_{25-75\%}$) and arterial O_2 saturation on upright and supine positions revealed the following results: There were high statistical significant differences (P<0.05) of mean values of patient's age, ventilatory functions FVC, FEV_1 and $FEF_{25-75\%}$ but FEV_1/FVC % showed non-significant difference, these findings are highly suggestive severe restrictive ventilatory pattern . There were high statistical significant differences (P<0.001) of mean values of arterial O2 saturation on up-right and supine positions (P< 0.001).

Table 3. Showed statistical comparison between groups A & B for mean values of age of subjects, ventilatory functions (FVC, FEV_1, FEV_1/FVC %,$FEF_{25-75\%}$) and arterial O_2 saturation on upright and supine positions revealed the following results: There were high statistical significant differences (P<0.05) of mean values of patient's age, ventilatory functions FVC, FEV_1 and $FEF_{25-75\%}$ but FEV_1/FVC % showed non-significant difference, these findings are highly suggestive severe restrictive ventilatory pattern . Also,there were high statistical significant differences of mean values of arterial O_2 saturation on up-right & supine positions (P<0.001) and (P<0.001) respectively.

Table 4. The one way repeated measure analysis of variance (ANOVA test) of age of subjects, ventilatory functions (FVC, FEV_1, FEV_1/FVC%,$FEF_{25-75\%}$) and arterial O_2 saturation on upright and supine positions for the three groups (A,B,C) revealed the following results:
There were high statistical significant differences (P<0.05) of mean values of patient's age, ventilatory functions FVC, FEV_1 and $FEF_{25-75\%}$ but FEV_1/FVC % showed non-significant difference, these findings are highly suggestive severe restrictive ventilatory pattern . Also, there were high statistical significant differences of mean values of arterial O_2 saturation on up-right and supine positions (P<0.001) & (P< 0.001) respectively.

Table 5. The one way repeated measure analysis of variance (ANOVA test) of coagulation parameters (PT, INR , aPTT, and D' Dimer) among three groups (A,B and C) showed that there are highly statistical significant difference (P< 0.001).

Pulmonary perfusion scan (PPS) was conclusive in diagnosis of pulmonary embolism for 11 (73.3%) patients in group A, while out of 15 patients in group B 6(40%) patients were diagnosed as pulmonary embolism Table 6.

Table 7. Shows statistical comparison (Z test) between the three groups as regards D' dimer and revealed highly significant differences between each two groups, (group C & A, group C & B and group A & B), (P <0.001).

Table 1. Statistical comparison between groups A& C as regard age, ventilatory functions, and arterial O_2 saturation.

Variables	Group A $\bar{X}$ ± SD n =15	Group C $\bar{X}$ ± SD n = 10	t-value	P-value	Sig.
Age (years)	56.47 ± 4.34	39.2 ± 7.95	-6.27	0.001	HS
FVC (L)	1.77 ± 0.46	4.14 ± 0.23	16.79	0.001	HS
FEV_1(L)	1.45 ± 0.49	3.45 ± 0.29	12.81	0.991	HS
FEV_1 / FVC %	80.06 ± 12.42	83.37 ± 4.30	0.95	0.353	NS
$FEF_{25-75\%(L/Sec.)}$	1.46 ± 0.29	3.67 ± 0.32	17.75	0	HS
SaO2 Upright	83.48±4.15	97.77± 0.84	12.95	0.001	HS
SaO2 Supine	89.31± 2.38	97.46 ± 0.53	12.79	0.001	HS

$\bar{X}$ = mean, SD= standard deviation, FVC =forced vital capacity, FEV_1= forced expiratory volume in first second, FEV_1 /EFC %=forced expiratory volume in first second to forced vital capacity ratio.
$FEF_{25-75=}$ forced expiratory flow rate between 25 to 75 % of FVC maneuver, SaO_2 = arterial O_2 saturation, P= Probability.

Table 2. Statistical comparison between groups B&C as regard age, ventilatory functions, and arterial O_2 saturation.

Variables	Group B $\bar{X}$ ± SD n =15	Group C $\bar{X}$ ± SD n = 10	t-value	P-value	Sig.
Age (years)	56.87 ± 4.56	39.2 ± 7.95	-6.36	0.001	HS
FVC (L)	2.77 ± 0.54	4.135 ± 0.23	8.6	0.001	HS
FEV_1 (L)	2.35 ± 0.52	3.45 ± 0.29	6.82	0.001	HS
FEV_1 / FVC%	84.89 ± 5.67	83.37 ± 4.303	-0.76	0.46	NS
FEF25-75% (L/Sec.)	1.83 ± 0.60	3.67 ± 0.31	9.89	0.001	HS
SaO_2 % Upright	96.09 ± 1.57	97.77 ± 0.84	3.468	0.002	HS
SaO_2% Supine	96.39 ± 1.23	97.46 ± 0.52	2.964	0.008	HS

$\bar{X}$=mean, SD= standard deviation, FVC =forced vital capacity, FEV_1= forced expiratory volume in first second, FEV_1 /FVC %=forced expiratory volume in first second to forced vital capacity ratio,FEF 25-75= forced expiratory flow rate between 25 to 75 % of FVC, SaO_2 = arterial O2 saturation.

Table 3. Statistical comparison between groups A& B as regard age, ventilatory functions and arterial O_2 saturation.

Variables	Group A $\bar{X}$ ± SD n =15	Group B $\bar{X}$ ± SD n = 15	t-value	P-value	Sig.
Age (years)	56.47 ± 4.34	56.87 ± 4.56	-0.25	0.81	HS
FVC (L)	1.77 ± 0.46	2.77 ± 0.54	-5.39	0.808	HS
FEV1 (L)	1.45±0.49	2.35 ± 0.52	-4.88	0	HS
FEV1 / FVC%	80.05 ± 12.42	84.89 ± 5.67	-1.37	0.186	NS
FEF 25-75% (L/Sec.)	1.46 ± 0.28	1.83 ± 0.60	-2.19	0.041	HS
SaO2 Upright	83.47±4.15	96.08 ± 1.57	-11.008	0	HS
SaO2 Supine	89.31± 2.38	96.39 ± 1.29	-10.24	0	HS

$\bar{X}$ = mean, SD = standard deviation, FVC = forced vital capacity, FEV_1 = forced expiratory volume in first second, FEV_1 /FVC % = forced expiratory volume in first second to forced vital capacity ratio, FEF 25-75%= forced expiratory flow rate between 25 to 75 % of FVC maneuver, SaO_2 = arterial O_2 saturation.

Table 4. Comparative analysis of the mean values of age, ventilatory functions and arterial O_2 saturation among groups of the study (C,A,B).

Variable	Group C $\bar{X}$ ± SD n = 10	Group A $\bar{X}$ ± SD n =15	Group B $\bar{X}$ ± SD n = 15	F-value	P-value	Sig.
Age (years)	39.2 ± 7.96	56.47 ± 4.34	56.8 ± 4.56	-0.25	0.81	HS
FVC (L)	4.14 ± 0.24	1.77 ± 0.46	2.77 ± 0.55	-5.39	0.808	HS
FEV_1 (L)	3.45 ± 0.29	1.45±0.49	2.35 ± 0.52	-4.88	0.001	HS
FEV_1 / FVC%	83.37 ± 4.30	80.05 ± 12.42	84.89 ± 5.67	-1.37	0.186	NS
$FEF_{25-75\%}$(L/Sec.)	3.67 ± 0.32	1.46 ± 0.29	1.83 ± 0.60	-2.19	0.041	HS
SaO2 Upright	97.77 ± 0.84	83.48 ±4.15	96.09 ± 1.57	-11.01	0.001	HS
SaO2 Supine	97.46 ± 0.52	89.31± 2.38	96.4 ± 1.23	-10.24	0.001	HS

$\bar{X}$ = mean, SD = standard deviation, FVC = forced vital capacity, FEV_1 = forced expiratory volume in first second, FEV_1 / FVC%=forced expiratory volume in first second to forced vital capacity ratio, FEF 25-75= forced expiratory flow rate between 25 to 75 % of FVC maneuver, SaO_2 = arterial O_2 saturation.

Table 5. Statistical comparison between groups C, A and B as regard coagulation parameters and D ' Dimer.

Variables	Group C $\bar{X}$ ± SD n = 10	Group A $\bar{X}$ ± SD n = 15	Group B $\bar{X}$ ± SD n = 15	F-value	P-value	Sig.
PT	12 ± 1.05	±1.21 18.77	17.87 ± 2.47	1.27	0.22	HS
aPTT	24.1± 2.42	29.53 ± 3.87	28.47±3.04	0.84	0.41	HS
INR	0.9 ± 0.08	1.66 ± 0.21	1.5067 ± 0.2	2.08	0.05	HS
D' Dimer	0.11±0.03	1.01±0.76	0.44 ± 0.46	8.76	0.001	HS

PT = Prothrombin time, a PTT =activated partial thromboplastine time; INR = international normalized ratio.

Table 6. Comparative findings of pulmonary perfusion scanning for groups of study.

			Groups			Total
			C	A	B	
PPS	Negative Findings	Count % within groups	10 0 %	4 26.7%	9 60%	23 57.5%
	Positive Findings	Count % within groups	0 0%	11 73.3%	6 40%	17 42.5 %
	Total	Count % within groups	10 100%	15 100%	15 100%	40 100%

PPS = Pumonary perfusion scam.

Pulmonary perfusion scan (PPS) was conclusive in diagnosis of pulmonary embolism for 11 (73.3%) patients in group A, while out of 15 patients in group B 6(40%) patients were diagnosed as pulmonary embolism Table 6.

Table 7. Statistical comparison between the three groups (A,B,C) as regards D'dimer.

		D' dimer	
	Z	P	Sign.
HS	Groups C & A	3.64	HS
HS	Groups C & B	3.44	HS
HS	Groups A & B	1.786	HS

Table 7. Shows statistical comparison (Z test) between the three groups as regards D' dimer and revealed highly significant differences between each two groups P < 0.001) (group C & A, group C & B and group A & B).

DISCUSSION

The present study was conducted to study the blood coagulopathy and pulmonary embolism in patients with chronic liver cirrhosis. Thirty male patients who had proved chronic liver cirrhosis, they were divided to: Group A included fifteen patients with decompensated chronic liver cirrhosis associated with complications such as ascitis , deep vein thrombosis and hepato-pulmonary syndrome; group B included fifteen patients with compensated liver cirrhosis. Ten normal male healthy subjects participated in the present study as controls (group C). Patient's ages ranged from 40 to 65 years.

The liver weight about 3 pounds and is the largest solid organ in the body. It performs many important functions. Cirrhosis is a consequence of chronic liver disease characterized by replacement of liver tissue by fibrous scar tissue as well as regenerative nodules (lumps that occur as a result of a process in which damaged tissue is regenerated), leading to progressive loss of liver function. Cirrhosis is most commonly caused by alcoholism, hepatitis B and C, and fatty liver disease but has many other possible causes. Some cases are idiopathic.[11]

Cirrhosis can cause many complications e.g. immune system dysfunction, leading to infection. Fluid in the abdomen (ascites) may become infected with bacteria normally present in the intestines (spontaneous bacterial peritonitis); blood coagulopathy; hepatorenal syndrome - insufficient blood supply to the kidneys, causing acute renal failure that has a very high mortality (over 50%); hepatopulmonary syndrome; portopulmonary hypertension - increased blood pressure over the lungs as a consequence of portal hypertension.[12]

The results of our study showed that there were highly significant restrictive ventilatory functions including FVC, FEV_1, FEV_1/FVC and $FEF_{25-75\%}$) in patients with decompensated and compensated liver cirrhosis (groups A & B) when compared with control group (C).

These results were in agreement with the findings of Edison et al., (1986)[13] who found significant reduction in ventilatory functions including forced vital capacity (FVC), first second of forced expiratory volume (FEV_1), functional residual capacity , total lung capacity as measured in 21 cirrhotic patients with ascites, and compared with 50 normal controls: These results imply that in cirrhosis of the liver there are prominent restrictive ventilatory disorders as well as obstructive disorders.

The hepatopulmonary syndrome (HPS) is a reversible pulmonary insufficiency in association with liver disease, most frequently liver cirrhosis. HPS is characterized by arterial hypoxemia caused by intrapulmonary arterio-venous shunts or marked vasodilatation of the pulmonary vessels and ventilation-perfusion mismatch in the absence of intrinsic heart or lung disease.[14]

The present study showed that arterial oxygen saturation (SaO_2) on upright position in groups A and B was markedly decreased ($P<0.001$) in comparison to group C. Also SaO2 on supine position was highly significantly reduced in groups A& B when compared to group C but these findings revealed significant improvement when compared to upright position.

Liver injury and/or portal hypertension trigger the release of endothelin-1, TNF-α, cytokines and mediate vascular shear stress and release of nitric oxide and carbon monoxide, all contributing to intrapulmonary vasodilation. Severe HPS increases mortality (30%) after liver transplantation, especially if PaO_2 is below 50 mmHg.[15,16]

As regards the coagulation profile, the results of our study revealed a highly significant increased values of prothrombin time (PT), international normalized ratio (INR) and activated partial thromboplastin time (aPTT), for patients of groups A&B in comparison to controls.

Liver cirrhosis causes coagulation defects because the liver produces most of the coagulation factors and thus coagulopathy correlates with worsening liver disease Thrombocytopenia due to both congestive splenomegaly as well as decreased thrombopoietin from the liver. However, this rarely results in platelet count < 50,000/mL.[17]

Also, although patients with cirrhosis do not suffer from deep vein thrombosis (DVT) or pulmonary embolism (PE) because they are naturally anticoagulated, Gulley et al., 2008[5] conducted a study to examine the relationship between cirrhosis and deep venous thrombosis / pulmonary embolism (DVT/PE) events. This study consisted of 963 cirrhotics and 12,405 controls. They found that both the incidence of DVT/PE (1.8 vs. 0.9%, P = 0.007) were higher in cirrhotics than in the controls; Partial thromboplastin time (PTT; OR 0.88, P = 0.04) and serum albumin (OR 0.47, P = 0.03) were the independent predictors of DVT/PE. They concluded that patients with cirrhosis do not have a lower risk of DVT/PE than non-cirrhotic controls.

Pulmonary embolism (PE) can be life threatening as well as very difficult to diagnose. PE has a myriad of presentations, and imaging studies often are not diagnostic. Researchers studied the utility of D-dimer testing in the diagnosis of patients with suspected PE who had negative helical computed tomography results or non-diagnostic ventilation-perfusion lung scans.[7]

A total of 99,444 patients with venous thromboembolism and 496,872 population controls were included in the study. Patients with liver disease had a clearly increased

relative risk of venous thromboembolism, varying from 1.74 (95% CI, 1.54–1.95) for liver cirrhosis to 1.87 (95% CI, 1.73–2.03) for non-cirrhotic liver disease. The risks were higher for deep venous thrombosis compared with pulmonary embolism. Conclusion: Patients with liver disease have a substantially increased risk of venous thromboembolism.[18] Also, Northup et al., 2009[19] concluded in their study that approximately 0.5% of admissions involving cirrhosis patients resulted in a new thromboembolic event. Low serum albumin was strongly predictive of increased risk for developing VTE, independent of international normalized ratio or platelet count. Serum albumin deficiency may indicate low levels

Pulmonary perfusion scanning (PPS) is an informative procedure when performed in well selected patients. In the present study , out of the 15 patients with decompensated liver cirrhosis (group A) 11 (73.3%) cases were diagnosed as PE by PPS, while 6 (40%) patients in group B (compensated liver cirrhosis) were diagnosed as pulmonary embolism, (Table.6). These findings were confirmed by highly significant increased levels of D'dimer in serum's patients of groups A&B when compared to group C Table 7.

D' dimer is a degradation product that is released into the systemic circulation by endogenous fibrinolysis of cross-linked fibrin (i.e. a thrombus). The use of D'dimer assays is most useful as an exclusionary test; it has an excellent negative value for PE and deep venous thrombosis in outpatients.[20]

Our results were compatible with Fimognari et al 2005[21] in their study, they investigated the behavior and the diagnostic usefulness of D-dimer and factor VIII in cirrhotic patients with asymptomatic portal venous thrombosis. Factor VIII coagulant and D-dimer values were measured in 136 consecutive outpatients with stable cirrhosis. They concluded that D-dimer and factor VIII levels rise in advanced cirrhosis.

Protein C is a major physiological anticoagulant. It is a vitamin K-dependent serine protease enzyme that is activated by thrombin into activated protein C (APC). Protein C is activated in a sequence that starts with Protein C and thrombin binding to a cell surface protein thrombomodulin. Thrombomodulin binds these proteins in such a way that it activates Protein C. The activated form, along with protein S and a phospholipid as cofactors, degrades activated factor 5 and activated factor 8 (VIIIa). Quantitative or qualitative deficiency of either may lead to thrombophilia (a tendency to develop thrombosis). Impaired action of Protein C (activated Protein C resistance), for example by having the "Leiden" variant of Factor V or high levels of Factor VIII also may lead to a thrombotic tendency.[22]

Conclusion: Although cirrhosis of the liver can cause many complications e.g. deficient coagulation and anticoagulation factors, but deep venous thrombosis and pulmonary embolism are not uncommon in liver cirrhosis.

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