Available online at www.medicinescience.org

ORIGINAL RESEARCH

Medicine Science 2017;6(2):338-46

Medicine Science International Medical Journal

Correlation between diabetes mellitus and the clinical outcome of acute variceal bleeding in cirrhotic patients in Suez Canal University Hospital, Ismailia, Egypt

Adel Hamed Elbaih[1], Mohammed Mahmoud Abdo[2], Khalil Ali Khalil[2], Mayada Mahmmoud Mohammed[2]

[1]Assistant professor of emergency medicine, Faculty of Medicine, Suez Canal University, Ismailia, Egypt
[2]Department of Internal Medicine, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

Received 17 September 2016; Accepted 30 November 2016
Available online 22.12.2016 with doi: 10.5455/medscience.2016.05.8570

Abstract
Variceal bleeding is one of the major complications of portal hypertension. Gastro-esophageal varices are present 40-60% of patients with cirrhosis; bleeding occurs in 25-35% of patients and account for 80-90% of bleeding episodes in these patients. Hepatic venous pressure gradient (HVPG) > 20 mmHg is associated with early re-bleed and failure to control bleeding (83%) with high mortality (64%) In the last two decades variceal re-bleeding has decreased from 47% to 13% with the use of pharmacological, endoscopic, and radiological intervention.DM co-existing with cirrhosis is considered to be one of the factors in the genesis of variceal bleeding. This may be due to an increase in portal blood flow. is to determine the correlation between DM as a risk factor and failure to control variceal bleeding and re-bleeding in cirrhotic patients. This study is a case-control study, sixty cirrhotic patients with variceal bleeding with or without DM were included in the study. The patients were divided into two groups: Group 1 (diabetic group): this group included 30 cirrhotic patients with variceal bleeding and had a history of DM. Group 2 (control group): this group included 30 cirrhotic patients with variceal bleeding and had no history of DM. All Patients were subjected to the following:-Complete clinical evaluation (history and physical examination) with Laboratory and imaging investigations. Tthere were significantly higher frequency of unstable course and mean times of previous admission in diabetic patients than control patients (73.3% and 1.6 times versus 36.6% and 1.3 times, respectively). Other variables showed insignificant differences between both groups (p>0.05). There were significantly higher mean numbers of attacks of hematemesis and melena and times of previous admission with these attacks in diabetic patients than control patients.

Keywords: Diabetes mellitus, acute variceal bleeding, cirrhosis

Introduction

Variceal bleeding is one of the major complications of portal hypertension. Gastro-esophageal varices are present 40-60% of patients with cirrhosis; bleeding occurs in 25-35% of patients and account for 80-90% of bleeding episodes in these patients. Hepatic venous pressure gradient (HVPG) > 20 mmHg is associated with early re-bleed and failure to control bleeding (83%) with high mortality (64%) [1].

In the last two decades variceal re-bleeding has decreased from 47% to 13% with the use of pharmacological, endoscopic, and radiological intervention [2, 20].

Various factors have been proposed as predictors of outcome of variceal bleed such as age of the patient, gender, stage of cirrhosis, etiology of the disease, associated conditions like renal failure, hepatocellular carcinoma, and diabetes mellitus [3].

***Coresponding Author:** Adel Hamed Elbaih, Assistant professor of emergency medicine, Faculty of Medicine, Suez Canal University, Ismailia, Egypt
E-mail: elbaihzico@yahoo.com

DM co-existing with cirrhosis is considered to be one of the factors in the genesis of variceal bleeding. This may be due to an increase in portal blood flow secondary to fluctuating blood sugar levels leading to an increase in portal pressure. In previous studies the over-all in-patient re-bleeding rate among cirrhotic patients was between 12%-13% [4].

In most of the cases, DM seems to follow cirrhosis and is called hepatogenous diabetes. Early cirrhosis with DM is characterized by marked postprandial hyperglycemia and insulin resistance [3].

The higher mortality rate in patients with diabetes is not only due to the complications of DM but also to increased risk of hepatocellular failure in long-term follow up [5].

Hyperglycemia induces splanchnic hyperemia, increases portal pressure and may increase the risk of variceal bleeding [6].

The diagnosis of cirrhosis depends on demonstrating widespread nodules in the liver combined with fibrosis. This may be done by direct visualization, for instance at laparotomy or laparoscopy. Laparoscopy visualizes the

nodular liver and allows directed liver biopsy. Radio-isotope scanning may show decreased hepatic uptake, an irregular pattern and uptake by spleen and bone marrow. Nodules are not identified. Using ultrasound, cirrhosis is suggested by liver surface nodularity and portal vein mean flow velocity. The caudate lobe is enlarged relative to the right lobe. However, ultrasound is not reliable for the diagnosis of cirrhosis. Regenerating nodules may be shown as focal lesions [7].

CT scan is cost-effective for the diagnosis of cirrhosis and its complications. Benign regenerative nodules are not visualized by CT. After intravenous contrast, the portal vein and hepatic veins can be identified in the liver, and a collateral circulation with splenomegaly may give confirmation to the diagnosis of portal hypertension. Large collateral vessels, usually peri-splenic or para-esophageal, may add confirmation to a clinical diagnosis of chronic Porto-systemic encephalopathy. Ascites can be seen. Biopsy diagnosis of cirrhosis may be difficult. Since neither liver biopsy nor scanning have a diagnostic sensitivity greater than 90% (ultrasound, 87%; liver biopsy, 62%), it has been proposed that ultrasound be done before liver biopsy is performed. Liver failure is assessed by such features as jaundice, ascites encephalopathy low serum albumin, and a prothrombin deficiency not corrected by vitamin K. Portal hypertension is shown by splenomegaly, esophageal varices and by the newer methods of measuring portal pressure [8].

Diabetes mellitus:-While up to 80% of cirrhotic are glucose intolerant, only 10-20% are truly diabetic.

Hemodynamic alterations in portal hypertension: The pathogenesis of portal hypertension involves the relationship between portal venous blood flow and the resistance offered to this blood flow within the liver (the Porto-hepatic resistance) and within Porto-systemic collateral blood vessels (the Porto-collateral resistance) that form during the evolution of portal hypertension. The movement of blood within the portal vascular system is driven by a pressure difference or gradient that exists along the length of the system. The portal pressure gradient (P), that is, the difference in pressure between the portal and systemic venous systems, is the resultant product of portal venous blood flow (Q) and «the vascular resistance to this flow (R), as expressed by Ohm's law P = Q X R [8].
DEVELOPMENT OF VARICES: - Esophageal varices, Gastric varices, Duodenal varices, Colorectal varices, others.

Diagnosis and grading of esophageal varices
Upper gastrointestinal endoscopy provides the most sensitive and specific method available for demonstration of varices. Endoscopy used for diagnosing the presence of varices, assessment and definition of risk factors for bleeding, for treatment of varices and for measurement of intra variceal pressure [9].

Paquet (1979) presented the following grading:

Grade I: Small varices are those protruding by less than half their diameter into the lumen.

Grade II: Medium sized are those protruding by approximately hall their diameter.

Grade III: Large varices are those protruding by more than half their diameter [9].

Red color sign
The "cherry red spots" or "red wale markings" correspond to dilated blood-filled channels laying within and beneath the squamous epithelium which communicate with submucosal deep intrinsic veins [10].

Endoscopic risk factor for variceal hemorrhage
During the last decade, efforts have been made to define endoscopic criteria for the prediction of variceal hemorrhage. Within a follow up time of 2 to 3 years, patients with large varices had a double risk for bleeding than patients with small varices. However, another study suggested that variceal size is a less potent bleeding risk which indicates a combined endoscopic evaluation of the size and pressure of the varices (i.e. estimation of variceal wall tension) may represent a better index for the risk of variceal bleeding. In addition, to variceal size, Japanese Research Society for Portal Hypertension describes the previously mentioned red color sign. Patients with positive red color sign bleed 2 to 3 times more often than patients without that sign [10].

Red color sign strongly correlates with variceal size; both signs reflect an increased variceal pressure found that concomitant finding of gastric varices may be a further predictive for esophageal variceal bleeding which is 3 times more frequent than in absence of fundal varices [10].

The aim of our study is to determine the correlation between DM as a risk factor and failure to control variceal bleeding and re-bleeding in cirrhotic patients also the prevalence of DM in cirrhotic patients

Material and Methods

Study Design and Site
Study Type

This study is a case-control study to determine the correlation between DM and the clinical outcome of acute variceal bleeding in cirrhotic patients.

Study Site

This study was undertaken at the emergency medicine, Internal Medicine Department and Gastroenterology Endoscopic Unit of Suez Canal University Hospital.

Patients

Sixty cirrhotic patients with variceal bleeding with or without DM were included in the study. The patients were divided into two groups:

Group 1 (diabetic group): this group included 30 cirrhotic patients with variceal bleeding and had a history of DM.

Group 2 (control group): this group included 30 cirrhotic patients with variceal bleeding and had no history of DM.

Inclusion Criteria

Adult patients aged ≥18years.

Both sexes.

Cirrhotic patients with variceal bleeding with or without DM.

Patients gave informed consent and able to adhere to visit schedules.

Diabetic patients diagnosis using FBS more than 126 mg\dl or RBS more than 180 mg\dl

Exclusion Criteria

HCC with bleeding.

Patient in hepatic encephalopathy.

Hematemesis of other causes, which was excluded by history, laboratory & radiologically investigation (ex NSAIDS, peptic ulcer disease "PUD")

Patients′ refusal.

Sampel Size

The study included 30 patients within study group (diabetic group) and a same number of control group (30 patients without DM) matching age and sex of the study group was added.

Study Procedure

Cirrhosis and portal hypertension were diagnosed on the basis of clinical, biochemical, virological data and imaging scanning including age, gender, Child-Pugh class, site of varices and etiology of cirrhosis was recorded.

Source of upper gastrointestinal bleed will be confirmed by upper GI endoscopy. Esophageal varices were graded from I-IV [9]. Gastric varices were classified as described by Sarin and Kumar [11] .The source of bleeding was identified as variceal if there is active bleeding from a varix or there are signs of recent bleeding from a varix, or there is a single varix without any other potential source of bleeding.

All endoscopic interventions were performed by a gastroenterologist who had good experience in therapeutic endoscopy. The preferred therapeutic modality used was endoscopic variceal ligation (EVL) with Six Shooter Saeed multiband ligator. In some patients with massive bleeding, variceal sclerotherapy with ethanolamine oleate was performed. Gastric varices were injected with n-butyl cyanoacrylate. No therapeutic intervention was done for patients with portal gastropathy.

Somatostatin is given as 2amp+ 500cc glucose 5% /8h (if the pt is not diabetic) and 2amp+500cc glucose 5%+4 I.U regular insulin /8h (if the patient diabetic) then when the patient is vitally stable (no tachycardia or hypotension and not shocked) he is ready for UGI endoscopy of endoscopy unit .the patient is prepared by Midazolam (10 mg I V or diazepam 5 mg Iv bolus tell patient is sedated. Then mouth piece put and upper GI endoscopy is introduced under complete visualization, the esophagus is assessed for presence of O.V bleeding and if he has evidence of recent bleeding cord is injected by E.O (ethanolamine oleate) and if there is evidence of recent bleeding on fundal (gastric) area it is injected by Histocryl amp (Enbucrilat 0.5gm) mixed with dextrose 5%, the number of ampules is determined by the endoscopist according to the size of varix. Then pt is given antibiotic in the form of ciprofloxacin 500mg/12 h for 5 days and PPI (omeprazole 20 mg /12 h for 7 days). B.Blocker "propranolol" is given 20-240 mg/d guided by heart rate.

Other causes of variceal re-bleeding as Thrombocytopenia and coagulopathy were corrected by platelet or Fresh Frozen Plasma (FFP) transfusion if needed. Then the patient is followed up in inpatient for 1-2 days tell melena stopped (enema is clear) and vitally stable then discharged to be followed up in outpatient sessions of UGI endoscopy

Material and Methods

All Patients were subjected to the following:

o Complete clinical evaluation (history and physical examination).

o Laboratory and imaging investigations.

A) Complete History Taking:

- Personal history: name, age, sex and residence.
- Complaint: onset, course and duration.
- Present history.
- Past history.
- Family history.

B) Complete Physical Examination:

- General, pulmonary and cardiac examinations.
- Complete abdominal examination.

C) Laboratory investigations:

- Complete blood count.
- Liver function tests (ALT, AST, S. Albumin, S. Bilirubin and Alkaline phosphates)
- Renal function tests (S. creatinine, B. urea)
- Fasting, postprandial sugar and Glycated hemoglobin.

D) Imaging investigation:

- Pelvic-abdominal ultrasonography.

Failure to control bleed is defined according to the Baveno III consensus report as the occurrence of hematemesis and reduction in blood pressure of more than 20 mmHg and/or transfusion of 2 units of blood or more (over and above previous transfusions) required to keep the hemoglobin above 9 g/dL, or a drop in hemoglobin of 2 g/dL within first 24 hours of control of bleed [11].

Re-bleeding is defined as recurrent hematemesis or melena after an interval of 24 hours and a drop in hemoglobin of 2 g/dL or transfusion of 2 units of blood or more within an interval of 24 hours to maintain hemoglobin to above 9 g/dL.

Data Management and Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigation, and imaging results were coded, entered and analyzed using Microsoft Excel software. Data were then imported into (SPSS 13.0) software for analysis. According to the type of data the following tests were used to test differences for significance; chi square and Fisher exact test, for categorical data and Student's t-test for continuous data. Multivariate logistic regression analysis was used to analyze the different studied variables. Continuous data were presented as the mean ± SD unless otherwise specified. Categorical data were presented as numbers and percentages. P value was set at <0.05 for significant results.

Etical Considerations

An informed consent was taken from all the participants before taking any data or doing any procedures.
The consent contains:

- o Explanation of the study aim in a simple manner to be understood by the common people.
- o Every Patient was interviewed in privacy.
- o All data were considered confidential and weren't going to be used outside this study without patient's approval.
- o Researcher phone number and all possible communicating methods were identified to the participants to return at any time for any explanation.
- o All participants were announced by the result of the study.
- o Participants have the right to withdraw from the study at any time without giving any reason.
- o The procedure was discussed with the patients.
- o Written informed consent for the benefits of the procedure and its risks was obtained and agreed.

Results

Table 1. Demographic data of both studied groups

		Diabetic (n=30)		Control (n=30)		Used test	p-value
Age (years)	**Mean ± SD**	53.8	10.5	52.1	11.9	t=0.59	0.56
	Range	36	76	25	75		
Gender (%)	**Male**	18	60.0	24	80.0	X^2=2.86	0.09
	Female	12	40.0	6	20.0		
Residence (%)	**Urban**	11	36.7	7	23.3	X^2=1.27	0.26
	Rural	19	63.3	23	76.7		
Marital status (%)	**Single**	1	3.3	1	3.3	Fisher exact	1.00
	Married	29	96.7	29	96.7		

*Significant p-value <0.05, **highly significant p-value <0.01

Table 2. Risk factors of HCV infection and co-morbidities of both studied groups

		Diabetic (n=30)		Control (n=30)		Used test	p-value
		No.	**%**	**No.**	**%**		
Previous surgery	**Yes**	8	26.7	6	20.0	X^2=0.37	0.54
	No	22	73.3	24	80.0		
Bilharzial injection therapy	**Yes**	1	3.3	2	6.7	Fisher exact	0.99
	No	29	96.7	28	93.3		
Dental procedures	**Yes**	6	20.0	10	33.3	X^2=1.36	0.24
	No	24	80.0	20	66.7		
Blood transfusion	**Yes**	10	33.3	13	43.3	X^2=0.63	0.43
	No	20	66.7	17	56.7		
Smoking	**Yes**	2	6.7	0	0.0	Fisher exact	0.49
	No	28	93.3	30	100.0		
Hypertension	**Yes**	4	13.3	3	10.0	Fisher exact	1.00
	No	26	86.7	27	90.0		
Pulmonary disease	**Yes**	0	0.0	1	3.3	Fisher exact	0.50
	No	30	100.0	29	96.7		

*Significant p-value <0.05

Table 3. Status of hepatic disease of both studied groups.

		Diabetic (n=30)		Control (n=30)		Used test	p-value
Pathology (%)	Cirrhosis	29	96.7	30	100.0	Fisher exact	0.50
	Cirrhosis & HCC	1	3.3	0	0.0		
Etiology (%)	HCV	26	86.7	28	93.3	Fisher exact	0.67
	HCV& HBV	4	13.3	2	6.7		
Functional (%)	Compensated	25	83.3	24	80.0	X2=0.11	0.74
	Decompensated	5	16.7	6	20.0		
Course (%)	Unstable	22	73.3	11	36.6	X2=8.2	0.004**
	Stable	8	26.7	19	63.3		
Duration of CLD (years)	Mean ± SD	25.5	14.4	24.5	13.7	0.28	0.78
Admission before (times)	Mean ± SD	1.60	0.4	1.3	0.7	2.2	0.046*

*Significant p-value <0.05

Table 4. Vital signs and anthropometric measures of both studied groups

	Diabetic (n=30)	Mean (SD)	Control (n=30)	Mean (SD)	t-test	p-value
Heart rate / minutes	69.6	9.7	68.4	8.6	0.417	0.680
Systolic BP (mmHg)	102.5	11.7	107.3	8.3	1.829	0.078
Diastolic BP (mmHg)	60.8	10.0	63.3	8.8	1.009	0.321
Temperature (^{o}C)	37.1	0.27	37.0	0.0	1.000	0.326
Weight (kg)	67.3	10.0	70.3	9.4	1.539	0.135
Height (cm)	167.2	6.1	167.9	7.03	0.398	0.694
BMI (kg/m2)	25.02	3.7	24.98	3.3	1.175	0.250

Insignificant p-value >0.05

Table 5. Clinical manifestations of the studied patients of both studied groups

		Diabetic (n=30)		Control (n=30)		Used test	p-value
Jaundice (%)	**Yes**	3	10.0	4	13.3	Fisher exact	1.00
	No	27	90.0	26	86.7		
Melena (%)	**Yes**	29	96.7	26	86.7	Fisher exact	0.35
	No	1	3.3	4	13.3		
No. of attacks	**Mean ± SD**	2.2	1.03	1.7	0.88	2.01	0.041*
Fresh bleeding per rectum (%)	**Yes**	1	3.3	0	0.0	Fisher exact	0.50
	No	29	96.7	30	100.0		
Spider nevi (%)	**Yes**	7	23.3	4	13.3	X^2=1.0	0.32
	No	23	76.7	26	86.7		
Tremors (coarse) (%)	**Yes**	4	13.3	1	3.3	Fisher exact	0.35
	No	26	86.7	29	96.7		
Palmer Erythema (%)	**Yes**	7	23.3	8	26.7	X^2=0.09	0.76
	No	23	76.7	22	73.3		
Lower limb edema (%)	**Yes**	1	3.3	0	0.0	Fisher exact	0.50
	No	29	96.7	30	100.0		
Consciousness level (%)	**Conscious**	19	63.3	27	90.0	X^2=5.96	0.015*
	Disturbed	11	36.7	3	10.0		
Suprapubic hair (%)	**Normal**	17	56.7	16	53.3	X^2=0.07	0.79
	Abnormal	13	43.3	14	46.7		
Gynecomastia (male n=42) (%)	**Yes**	14	77.8	16	66.7	X^2=0.27	0.60
	No	4	22.2	8	33.3		
Nutritional status (%)	**Good**	5	16.7	10	33.3	X^2=2.22	0.14
	Fair	22	73.3	18	60.0		
	Poor	3	10.0	2	6.7		

*Significant p-value <0.05, **highly significant p-value <0.01

Table 6. Abdominal examinations of both studied groups

		Diabetic (n=30)		Control (n=30)		Used test	p-value
		No.	**%**	**No.**	**%**		
Liver size	**Impalpable**	1	3.3	7	23.3	X^2=15.6	<0.0001**
	Enlarged	28	93.3	14	46.7		
	Shrunken	1	3.3	9	30.0		
Liver consistency	**Soft**	28	93.3	25	83.3	Fisher exact	0.42
	Firm	2	6.7	5	16.7		
Liver surface	**Smooth**	28	93.3	28	93.3	Fisher exact	1.00
	Irregular	2	6.6	2	6.7		
Spleen	**Impalpable**	9	30.0	14	46.7	X^2=1.67	0.18
	Enlarged	21	70.0	16	53.3		
Ascites	**Absent**	27	90.0	26	86.7	Fisher exact	0.99
	Present	3	10.0	4	13.3		
Dilated veins	**Yes**	16	53.3	10	33.3	X^2=2.44	0.12
	No	14	46.7	20	66.7		
Piles	**Yes**	2	6.7	1	3.3	Fisher exact	0.99
	No	28	93.3	29	96.7		

Insignificant p-value >0.05

Table 7. Laboratory investigations of both studied groups

	Diabetic (n=30) Mean (SD)		Control (n=30) Mean (SD)		t-test	p-value
Hb	9.02	2.2	8.7	2.5	0.417	0.680
Platelet count	144.8	89.7	133.3	56.8	0.540	0.593
Total serum bilirubin	1.47	0.96	1.6	0.9	0.337	0.738
ALT	52.5	37.8	55.9	65.02	0.233	0.817
AST	71.3	85.2	69.8	101.2	0.058	0.954
Albumin	3.057	0.43	2.96	0.57	0.767	0.449
Alkaline Phosphatase	33.7	9.59	31.1	7.9	1.445	0.159
S. creatinine	1.18	0.59	0.9	0.25	1.057	0.299
B. urea	63.5	45.6	51.8	26.9	1.130	0.268
PT	16.34	3.42	16.3	3.01	0.004	0.997
INR	1.399	0.48	1.3	0.43	1.064	0.296
FBS	150.9	66.7	80.9	13.7	5.350	<0.0001**
PPS	238.4	108.6	115.8	9.01	6.078	<0.0001**

*Significant p-value <0.05, **highly significant p-value <0.01

Table 8. Abdominal ultrasound evaluation of the studied patients

		Diabetic (n=30)		Control (n=30)		X^2 test	p-value
		No.	%	No.	%		
Right lobe	**Normal**	8	26.7	18	60.0	X^2=9.5	0.002**
	Enlarged	21	70.0	8	26.7		
	Shrunken	1	3.3	4	13.3		
Left lobe	**Normal**	10	33.3	18	60.0	X^2=4.3	0.038*
	Enlarged	20	66.7	12	40.0		
Echogenicity	**Echogenic**	9	30.0	20	66.7	X^2=8.1	0.004**
	Bright (fatty) liver	21	70.0	10	33.3		
Portal vein	**Normal**	8	26.7	25	83.3	X^2=19.5	<0.0001**
	Dilated	22	73.3	5	16.7		
Collaterals	**Yes**	15	50.0	7	23.3	X^2=15.6	<0.0001*
	No	15	50.0	23	76.7		
Spleen size	**Normal**	12	40.0	18	60.0	X^2=4.6	0.032*
	Enlarged	18	60.0	12	40.0		
Splenic vein diameter	**Normal**	20	66.7	28	93.3	X^2=6.7	0.0098**
	Dilated	10	33.3	2	6.7		
Ascites	**Absent**	27	90.0	26	86.7	Fisher exact	0.99
	Mild /moderate	3	10.0	4	13.3		

*Significant p-value <0.05, **highly significant p-value <0.01

Discussion

This Chronic liver disease (CLD) constitutes a major health problem among Egyptians. Viral hepatitis competes with schistosomiasis as a leading cause of chronic liver disease in Egypt [11].

Diabetes mellitus (DM) and insulin resistance is commonly associated with hepatitis C virus (HCV) infection, and development of DM can occur early in the course of HCV infection [12].

Up to 96% of patients with cirrhosis may be glucose intolerant and 30% may be clinically diabetic. McCormick stated that 80% of patients with chronic diffuse liver disease may have glucose intolerance and 10-20% is truly diabetics and the prevalence of diabetics is greater among those with hepatitis C liver disease [2].

The exact pathogenic mechanisms responsible for this association are still unknown; however, they may be related to both HCV itself and to liver injury. Hence, insulin resistance is a major independent determinant of fibrosis in chronic HCV infection, regardless of the genotype and the severity of liver damage [13].

Both insulin resistance and beta-cell dysfunction contribute to glucose intolerance in patients with chronic HCV. In addition, insulin resistance may be the earliest abnormality in this process, which in the following years may progress to glucose intolerance and also DM [2].

Thus, impaired glucose tolerance (IGT) has been reported in HCV-infected patients before the onset of cirrhosis. HCV infection also is associated with an increased prevalence of DM [7].

These data indicate the specific role of HCV in the evolution of impaired insulin action and IGT, independent from the development of cirrhosis [14-].

There are many potential diabetogenic factors operative in cirrhosis which may induce diabetes. The appropriate disorders could result in diabetes of hepatogenous,

pancreatitis, hemosiderotic, kaliopenic, portal-systemic anastomotic, insulin-resistant, somatotropin, or genetic origin. The data suggest that these factors, acting individually or perhaps in various combinations, may precipitate diabetes in genetically susceptible patients or may even induce diabetes de novo in some cirrhotic patients [13].

Several studies suggest that DM may have an etiological role in CLD and hepatocellular carcinoma (HCC) [15].

In a recent issue of hepatology, the article of Cammà et al. (2009) investigated the role of liver stiffness and insulin resistance in the noninvasive prediction of portal hypertension. In conclusion, they reported [16].

The presence of diabetes, significantly predicts the presence of esophageal varices, in subjects with HCV-related cirrhosis.

It has been observed that the fatty liver, obesity and insulin resistance act as co-factors to cause liver damage. Fatty liver is the result of an intracellular accumulation of triglycerides because of increased uptake of free fatty acids and de novo liponeogenesis in the hepatocytes. At the same time, there is a reduction in the hepatic secretion of very low density lipoproteins. The liver damage consists of cellular necrosis and inflammation, and these disorders result from an increase in mitochondrial oxidative stress on triglycerides with the consequential generation of free radicals and peroxisomes.

This case-control study was performed to determine the correlation between DM and the clinical outcome of acute variceal bleeding in cirrhotic patients. It was undertaken at the emergency medicine, Internal Medicine Department and Gastroenterology Endoscopic Unit of Suez Canal University Hospital. Sixty cirrhotic patients were divided into two groups; group 1 (diabetic group) that included 30 cirrhotic patients with variceal bleeding and had a history of DM and group 2 (control group) that included 30 cirrhotic patients with variceal bleeding and had no history of DM.

The mean age of the patients was 52.95±11.1 years. The frequency of male patients was higher than female patients (70% versus 30%, respectively). The majority of patients resided in rural areas (70%) and almost all patients were married (96.7%).

Male sex and hyperglycemia are factors leading to liver disease [17].The prevalence of liver disease and type 2 DM in the Taiwanese population is 13.4% [6]. In addition, old age and diabetes predict liver fibrosis [7].

The most frequent risk factors are blood transfusion (38.3%), dental procedures (26.7%), previous surgery (23.3%), and injection therapy for bilharziasis (5%). The minority of patients had smoking history (11.7%) and history of hypertension (11.7%).

The majority of patients had HCV infection only (90%) and 10% of them had HCV and HBV co-infections. The frequency of decompensated patients was 18.3%. All patients (100%) had Child class A. The mean duration of liver disease in the studied patients was 24.96±13.9 months. The mean times of previous admission before were 1.5±0.79 times.

The mean heart rate was 69.02±9.09 beat/minutes, the mean systolic BP/diastolic BP was 104.92/62.08 mmHg, the mean weight was 68.8±9.76 kg and the mean BMI was 24.5±3.4 kg/m2.

The most frequent clinical manifestations of the patients were hematemesis (100%), melena (55%), abnormal suprapubic hair (45%), abdominal pain (23.3%), and disturbed consciousness (23.3%).

The majority of the examined patients had enlarged liver (70%), soft in consistency (88.3%) and has smooth surface (93.3%). The frequency of splenomegaly was 56.7%, ascites was 11.7%, dilated veins were 43.3% and piles were 5%.

The mean value of Hb was low (anemic level) this indicates that the severity of esophageal varices bleeding in diabetic patients is more than non-diabetic cirrhotic patients. The mean AST and ALT enzymes, serum urea, FBS and PPS were high.

The frequency of enlarged right lobe was 48.4, enlarged left lobe was 51.7%, enlarged spleen was 50%, and mild to moderate ascites was 11.7%.

There was no significant difference between the mean age of diabetic and control patients (53.8 versus 52.1 years, respectively). Other demographic data showed insignificant differences between both groups ($p>0.05$). Risk factors of HCV infection and co-morbidities showed insignificant differences between both groups ($p>0.05$).

There were significantly higher frequency of unstable course and mean times of previous admission in diabetic patients than control patients (73.3% and 1.6 times versus 36.6% and 1.3 times, respectively). Other variables showed insignificant differences between both groups ($p>0.05$).

There was significantly higher mean number of attacks of hematemesis and melena in diabetic patients than control patients (2.2 versus 1.7 times, respectively). The frequency of disturbed level of consciousness in diabetic patients was higher than control patients (36.7% versus 10%, respectively). Other clinical manifestations showed insignificant differences between both groups ($p>0.05$).

The frequency of hepatomegaly in diabetic patients was higher than control patients (93.3% versus 46.7%, respectively). There was no statistically significant differences between both groups regarding other abdominal examinations ($p>0.05$). There were significantly higher mean values of FBS and PPS in diabetic patients than control patients ($p<0.0001$). Other laboratory investigations showed insignificant differences between both groups ($p>0.05$).

The frequency of enlarged right and left lobe of liver, bright liver, dilated portal vein, presence of collaterals, splenomegaly and dilated splenic vein diameter in diabetic patients were significantly higher than control patients ($p<0.05$).This occurred with diabetes and steroid administration [18] .

Liver biochemical tests and abdominal sonography should be considered in CLD patients with overt obesity and diabetes [19].

With the increasing prevalence of DM in Egypt, numbers of patients with liver disease are expected to grow. Mild liver disease can evolve into severe liver disease, such as liver cirrhosis by the action of diabetes on liver. The mortality rate in CLD patients with the clinical manifestations of DM and esophageal varices bleeding is high. Therefore, proper liver function tests, blood cell counts, and abdominal sonography surveillance are suggested in patients with morbid obesity and long-term poorly controlled DM. Once the AST/ALT ratio exceeds 1 or thrombocytopenia or leucopenia is noted, pan-endoscopy examination is recommended. If a large varix with red-color sign is found, prophylactic esophageal varices ligation or administration of beta-blockers may be considered to prevent esophageal varices bleeding [20].

Conclusions

At the end of the study there were significantly higher mean numbers of attacks of hematemesis and melena and times of previous admission with these attacks in diabetic patients than control patients. Also, the frequency of bleeding per rectum in diabetic patients was higher than control patients. The frequency of disturbed level of consciousness in diabetic patients was higher than control patients. There were significantly lower mean values of HB in diabetic patients than control patients. The frequency of enlarged left lobe of liver, hyperechoic echogenicity, dilated portal vein, presence of collaterals, splenomegaly, and dilated splenic vein diameter in diabetic patients were significantly higher than control patients. Diabetes mellitus worsen the clinical outcome of variceal bleeding in cirrhotic patients regarding recurrence of bleeding, hospital admission times and severity of bleeding.

References

1. Monescillo A, Martinez-Lagares F, Ruiz-del-Arbol L, Sierra A, Guevara C, Jiménez E, Marrero JM, Buceta E, Sánchez J, Castellot A, Peñate M, Cruz A, Peña E. Influence of portal hypertension and its early decompression by TIPS Placement on the outcome of variceal bleeding. Hepatology. 2004;40(4):793-801.
2. McCormick PA, O'Keefe C. Improving prognosis following a first variceal haemorrhage over four decades. Gut. 2001;49(5):682-5.
3. Imano E, Kanda T, Nakatani Y, Motomura M, Arai K, Matsuhisa M, Yamasaki Y, Hori M. Impaired splanchnic and Peripheral glucose uptake in liver cirrhosis. J Hepatol. 1999;31(3):469-73.
4. Carbonell N, Pauwels A, Serfaty. L, Fourdan O, Lévy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. Hepatology. 2004;40(3):652-9.
5. Moreau R, Chagneau C, Heller J, Chevenne D, Langlet P, Deltenre P, Hillaire S, Lefilliatre P, Pateron D, Sogni P, Valla D, Lebrec D. Hemodynamic, metabolic and hormonal responses to oral glibenclamide in patients with cirrhosis receiving glucose. Scand J Gastroenterol. 2001;36(3):303-8.
6. Bianchi G, Marchesini G, Zoli M, Bugianesi E, Fabbri A, pisi E. Prognostic significance of diabetes in patients with cirrhosis Hepatology. 1994;20(1Pt1):119-25.
7. Kondo F, Ebara M, Sugiura N, Wada K, Kita K, Hirooka N, Nagato Y, Kondo Y, Ohto M, Okuda K. Histological features and clinical course of large regenerative nodules: evaluation of their precancerous potential. Hepatology. 1990;12(3Pt1:592-8.
8. Schalm SW. The diagnosis of cirrhosis: clinical relevance and methodology. J. Hepatol. 1997;27(6):1118-9.
9. Paquet KJ. Causes and pathomechanisms of oesophageal varices development. Med Sci Monit. 2000;6(5):915-28.
10. Kitada T, Seki S, Ikeda K, Nakatani K, Sakaguchi H, Kawada N, Kadoya H, Kaneda K. Clinicopathological characterization of prion: a novel marker of activated human hepatic stellate cells. J. Hepatol. 2000;33(5):751.
11. Sarin SK, Kumar A. Gastric varices: profil, classification, and management. Am J Gastroenterol. 1989;84(10):1244-9.
12. Puri P, Sanyal AJ. Role of obesity, insulin resistance, and steatosis in hepatitis C virus infection. Clin Liver Dis. 2006;10(4):793–819
13. Maeno T, Okumura A, Ishikawa T, Kato K, Sakakibara F, Sato K, Ayada M, Hotta N, Tagaya T, Fukuzawa Y, Kakumu S. Mechanisms of increased insulin resistance in non-cirrhotic patients with chronic hepatitis C virus infection. J Gastroenterol Hepatol. 2003;18(12):1358–63.
14. Weinman SA, Belalcazar LM. Hepatitis C: a metabolic liver disease. Gastroenterology. 2004;126(3):917–9.
15. El-Serag HB, Everhart JE. Diabetes increases the risk of acute hepatic failure. Gastroenterology. 2002;122(7):1822-8.
16. Cammà C, Petta S, Di Marco V, Bronte F, Ciminnisi S, Licata G, Peralta S, Simone F, Marchesini G, Craxì A. Insulin resistance is a risk factor for esophageal varices in hepatitis C virus cirrhosis. Hepatology. 2009;49(1):195–203.
17. Neuschwander-Tetri BA, Caldwell SH. Nonalcoholic steatohepatitis: summary of an AASLD single topic conference. Hepatology. 2003;37(5):1202–19.

18. Wisner E, Zwingenberger A. What do hyperechoic and hypoechoic mean: Atlas of Small Animal CT and MRI. 1st edition. Wiley Blackwell & Son, Inc, 2007.

19. Tang CP, Huang YS, Tsay SH, Chang FY, Lee SD. Nonalcoholic Fatty Liver Disease Manifesting Esophageal Variceal Bleeding. J Chin Med Assoc. 2006; 69(4):175–8.

20. Elbaih AH, Ismail MT, Elgwad EEA, Hassan F, Helmy A. Detection of medical errors in management of traumatic hypovolemic shocked adult patients presented to emergency department in Suez Canal University Hospital, Ismailia, Egypt. Int Surg J. 2016; 3(2): 882-6.