IDENTIFICATION OF RISK FACTORS FOR EARLY REBLEEDING FROM OESOPHAGO- GASTRIC VARICES: A PROSPECTIVE STUDY.

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ABSTRACT

Background: Variceal bleeding is a severe complication of patients with portal hypertension. Early rebleeding occurs frequently in the first days after admission and mortality associated with each bleeding episode ranges from 30-50%. Aim: To identify risk factors for early rebleeding from esophageal varices in a prospective study. Patients and Methods: A consecuative series of 469 patients with variceal bleeding was evaluated. They were 406 males (86.5%) and 63 females (13.5%). Their mean age was 50.61±11.2 years. Etiology of portal hypertension was schistosomal hepatic fibrosis in 13%, post- hepatitic in 23.6% and mixed schistosomal and post hepatitis cirrhosis in 63.4%. Child- Pugh's class showed 44.1% grade A; 42.9% grade B; 13% grade C. Endoscopic treatment was carried out in less than 24hr, EIS in 60.7% , EVL in 29.9%, Histoacryl for gastric varices in 8.4% and combined EIS and EVL in 1% of cases. Results: Active bleeding at time of endoscopy was found in 57.8% and gastric varices in 17.3% of patients. Early rebleeding (within 7 days) was reported in 73 patients (15.6%) and was significantly associated with high WBC count ($p<0.001$), Child class C ($p<0.001$), presence of active bleeding during endoscopy ($p<0.001$) , gastric varices ($p<0.001$), Positive HCV-Ab ($p<0.001$), high serum creatinine ($p<0.005$) and diabetes mellitus. Conclusion: several clinical, laboratory and endoscopic factors were strongly associated with early rebleeding from oesophago-gastric varices. Diabetes mellitus and HCV positive cases

could be considered as new risk factors for early variceal rebleeding.

INTRODUCTION

Variceal bleeding is a frequent and severe complication of patients with portal hypertension for 2 main reasons; the high mortality of each episode of bleeding which ranges from 30% to 50% (D' Amico et al., 1995), and early rebleeding which is a distinct characteristic of portal hypertensive bleeding and occurs in as many as 50% of patients in the first days after admission (Burroughs et al., 1989 & Goulis et al., 1998).

Early rebleeding was recorded as a prognostic factor for death and bad prognosis (Burroughs et al., 1989) and identification of the factors associated with early rebleeding is important to identify high risk patients.

Factors that influence early rebleeding in portal hypertensive patients have been rarely studied (Heresbach et al., 1991, Ben- Ari et al., 1996 and Madwar et al., 1998). Moreover, in these studies, analysis and comparison of results are difficult because of difference in the criteria used for the definition of failure to control haemorrhage, in the source of gastrointestinal bleeding (rupture oesophageal varices or upper gastrointestinal bleeding in general), in study duration (ranging from 5 days to 6 weeks) and in the prognostic factors analysed (Goulis et al., 1998).

The aim of the present prospective clinical study was to identify risk factors for early variceal rebleeding (within 7 days) after endoscopic therapy of gastro- oesophageal varices.

PATIENTS AND METHODS

Patient population: This study was conducted in Mansoura Emergency Hospital, Mansoura University, on a consecuative series of 469 patients with acute attacks of upper gastrointestinal bleeding, endoscopically confirmed to originate from gastro-esophageal varices.

Exclusion criteria: Upper gastrointestinal bleeding from any site other than gastro-esophageal varices, bleeding tendency due to haematological diseases, associated hepatic malignancy, history of surgical treatment for portal hypertension, terminal hepatic disease (as hepato-renal syndrome or severe encephalopathy) and advanced cardiopulmonary or any other terminal disease.

Aetiology of liver disease was diagnosed by combination of clinical and biochemical findings, and by imaging data (e.g. ultrasound finding of bilharzial hepatic affection)(Abdel-Wahab et al., 1992).

Severity of liver disease was graded on the basis of Pugh-Child classification (Pugh et al., 1973).

Definition of End points related to Bleeding: Esophageal variceal bleeding was defined with clinical signs of hematemesis, coffee ground vomitus, hematochezia or tarry stool, and with endoscopic signs of active bleeding from varices, or large varices with coffee ground material fresh blood clots, or red color signs without other bleeding site. Emergent treatment was defined as therapy performed only when there was endoscopic evidence of active bleeding or fresh blood. If only coffee ground material or red color signs were found, even if endoscopic therapy was performed on an emergent basis, it was regarded as elective treatment. Success in arresting variceal bleeding was defined as stable vital signs with no sign of rebleeding within 24 hours of treatment. Rebleeding was defined as new onset of hematemesis, coffee ground vomits, or melena with increasing pulse rate over 110 beats per minute and decreasing blood pressure below 90 mm Hg. Complications were defined as any untoward event that required active treatment or prolonged hospitalization. Treatment failure was defined as failure to control active bleeding after two attempts with the same method, rebleeding more than twice, death related to bleeding or complication, or physician decision to change modality of treatment (De Franchis, 1996).

Management of patients: Thorough history taking, full clinical examination, laboratory- based evaluation, and abdominal ultrasonography were performed at entry into the hospital. Standared resuscitation management for bleeding consisted of initial colloid, fluid administration and blood transfusion (for adequate intra- vascular volume replacement), vitamin k and lactulose & colonic evacuation by enema. Emergency endoscopy was performed as soon as possible after initial resuscitation (within 12 hours after admission), injection sclerotherapy or band ligation was used to arrest bleeding. Balloon tamponade and/ or vasoactive drugs (octreotide or terlepressin)

were used to control massive bleeding or if bleeding persisted after endoscopic therapy.

Sclerotherapy (EIS) was performed by the free hand method with a flexible fiberoptic or videoscope type Olympus XQ20 or Vidioscope Pentax EPM 3300 with patients under diazipam sedation using intra- variceal injection. Each varix was injected with 2-5 ml of the sclerosant ethanolamine oleate 5% with a total less than 25ml/ session using a flexible needle (LDV1- 23G- Disposable variceal injector, Wilson-Cook Medical Inc., Winston- Salem, NJ).

Endoscopic variceal ligation (EVL) was performed by using Saeed- six shooter device. The endoscopic ligation device was attached at the tip of the endoscope (Pentax Videoscope EPM 3300), the elastic O- ring ensnaring the neck of the suctioned portion of varix.

Gastric varices were treated either by Histoacryl injection or by band ligation.

Follow up: during 7 days hospitalization, all patients were closely monitored for rebleeding & mortality.

Statistical Analysis: Statistical analysis was performed by using standared statistical analysis software (SPSS- PC + for Windows Version 6). Data were found to be normally distributed, analysis of difference was done using Chi-Square. Univariate and Multivariate analysis was done using Cox's Model regression analysis.

RESULTS

Patient characteristics: during the study period, a total of 469 patients with bleeding gastroesophageal varices were included into this study. They were 406 male (86.5%) & 63 female (13.5%) with age ranged from 17-80 years, with mean age of 50.6 _ 11.2 years. According to Child- Pugh classification, they were 207 patients (44.1%) class A, 201 patients (42.9%) class B and 61 patients (13%) class C.Aetiology of portal hypertension was schistosomal hepatic fibrosis in 13%, post- hepatitic cirrhosis in 23.6% and mixed schistosomal and post- hepatitic cirrhosis in 63.4% (table 1, Fig. 1,2 and 3).

Endoscopic treatment : active bleeding (spurting or oozing) was recorded in 271 patients (57.8%). Injection sclerotherapy (EIS) was used for

control of bleeding in 285 patients (60.7%), whereas variceal band ligation (EVL) for 140 patients (29.9%), combined EIS and EVL in 5 cases (1%) and 39 patients (8.4%) with gastric varices were treated by Histoacryl injection. (table 1).

Early rebleeding : within one week, early rebleeding recorded in 73 patients (15.6%). Source of rebleeding, as diagnosed by re-endoscopy, were: oesophageal varices in 44/73 (60.3%), gastric varices in 18 patients (24.6%), both gastric and esophagea1 varices in 4 patients (5.5%), post sclerotherapy ulcer in 6 patients (8.2%), postband ulcer in 1 patient (1.4%). About 62% of early rebleeding (45 patients) were recorded in first 48 hours after admission (Fig 4). Mortality within the first 7 days was 44 patients (9.4%), of them, 35 due to rebleeding (79.5%), 6 due to hepatic coma (13.7%) and 3 due to nonspecific hepatic cause (6.8%).

Comparing early rebleeders and non- rebleeders groups:

When comparing demographic data of patients of early rebleeding (73) to that of non - rebleeding (406), there was no significant statistical difference as regard age, sex, number of previous attacks, interval between attack & admission or admission and endoscopy (table 2) .

As regard diabetes mellitus, 55 of non diabetic patients (402) showed early rebleeding (13.7%), while 18 of diabetic patients (67) showed early rebleeding (26.9%) ($p<0.005$) (table 3).

As regard severity of liver disease, 17 of class A patients (207) showed early rebleeding (8.2%), while 35 of class B patients (201) showed early rebleeding (17.4%) and 21 of class C patients (61) showed early rebleeding (34%) ($p<0.001$) (table 3).

As regard hepatitis markers, 3 of seronegative patients for hepatitis (61) developed early rebleeding (4.9%), while 70 of anti HCV positive patients (325) showed early rebleeding (21.5%) ($p<0.001$) (table 3).

As regard endoscopic data, there was significant statistical difference, when comparing early rebleeding (73 patients) and non- rebleeding patients (396), as regard active bleeding at first endoscope (22.9% versus 5.5%) and presence of gastric varices (35.8% versus 11.3%)

(p<0.001) (table 4).

As regard laboratory data, there was significant statistical difference when comparing early rebleeders and non- rebleeders groups as regard total leucocytic count, creatinine, albumin and AST. Other laboratory results (RBCs, Hb, platelet count, total bilirubin, ALT, Prothrombin time) showed no statistical difference between early rebleeders and non- rebleeders (table 5).

Univariate analysis of clinical, laboratory and endoscopic parameters for early rebleeding using Cox's Model showed that early rebleeding was significantly associated with Child-Pugh class C (p< 0.001), diabetes mellitus (p<0.007), leucocytosis (p<0.001), high creatinine level (p<0.005), hypoalbuminaemia (P<0.0003), elevated AST (p<0.02), presence of hepatitis C (p< 0.0005), associated gastric varices (p<0.009) and active bleeding during endoscope (p<0.001). On the other hand, no significant association of early rebleeding with age , sex , RBCs, Hb, Hct, platelet, bilirubin, ALT, and prothrombin time (table 6)

Multivariate analysis of clinical, laboratory and endoscopic parameters for early rebleeding using Cox's Model of regression analysis showed that 4 parameters remained as independent risk factors for early rebleeding: active bleeding during endoscopy (P< 0.0001), associated gastric varices (p<0.04), hepatitis C (p<0.01) and leucocytosis (p<0.03) (table 7).

Table (1): Base- line characteristics of 469 patients at entry into the study:

Character	**Clinical**		
* Age (year)	Rang: 17-80, Median: 50, mean 50.6± 11.2		
* Sex	Male: 406 (86.6%)&female: 63(13.4)		
* Smoking (%)	132 (28.1%)		
* Diabetic (%)	67 (14.3%)		
* Past history of variceal bleeding (%)	148 (31.5%)		
Laboratory data.	**Range**	**Median**	**Mean ±S.D.**
* Hb (gm/dl)	2.8-16	9.1	9.05± 2.52
* Hct	10-46	28	27.2±6.96
RBCs (million/dl)	1.2-5.5	3.3	3.3±0.81
*WBCs ($x10^3$/dl)	1.1-19	8	8.9±5.17
*Platelet ($x10^3$/dl)	18-409	120	129±68.7
*Creatinine (mg/dl)	0.4-3.3	1	1.13±0.53
*Albumin (gm/dl)	1.4-5	3	3.11±0.72
*Bilirubin (mg/dl)	0.4-5.2	1	1.54±1.03
*AST (Iu/dl)	5.8-447	48	64.93±57.85
*ALT (Iu/dl)	13-540	37	47.59±39.7
*Prothrombin time (sec.)	12.5-30	15	17.6±9.6
Hepatitis markers:			
HBs Ag.	53 patients (11.3%)		
Anti HCV (ELISA).	295 patients (62.9%)		
Both HBV & HCV	30 patients (6.4%)		
Data of first endoscope:			
Patient with active bleeding	271 (57.8%)		
Patient with gastric varices	81 (17.3%)		
Endoscopic treatment:			
Sclerotherapy (EIS)	285 patients (60.7%)		
Band ligation (BL)	140 patients (29.2%)		
Both (EIS+ BL)	5 patients (1%)		
Histoacryl injection	39 patients (8.4%)		

Table (2): History and demographic results of early rebleeders and non- rebleeders .

Total number (469)	Early rebleeders (n=73)	Non bleeders (n=396)	P
Age (y) (mean ± S.D)	51.14 ± 9.18	50.43 ±11.44	NS
Sex(M/F)	59/14	347/49	NS*
Number of previous attack (mean ± SEM)	1.9 ± 0.9	1.6 ± 0.9	NS
Interval between attacks and admission (hr) (mean ± SEM)	9.76 ± 1.48	11.34 ±0.83	NS
Interval between admission and endoscopy (hr) (mean ± SEM)	2.72 ± 0.31	2.67 ± 0.12	NS

M/F= male / female ratio SEM= standard error of mean

NS= non significant * Chi- square test

Table (3): DM, Child- Pugh`grading and hepatitis serological markers results of early rebleeders.

Total number (469)	Early rebleeding	P*
DM (No &%):		
- Non diabetics (n= 402)	55 (13.7%)	<0.005
- Diabetics (n= 67)	18 (26.9%)	
Child- Pugh`s classification (No&%)		
- A =207 (44.1%)	17 (8.2%)	
- B= 201 (42.9%)	35 (17.4%)	<0.001
- C= 61 (13%)	21 (34%)	
Hepatitis serological markers		
- Seronegative(n= 61)	3(4.9%)	<0.001
- Positive anti - HCV(n=325)	70(21.5%)	

* Chi- Square test.

Table (4) : Endoscopic results of early rebleeders

Total number (469)	Early rebleeding (n= 73)	P*
Previous endoscopic therapy		
- No (n=321)	46 (14.3%)	NS
- Yes (n=148)	27 (18.2%)	
Gastric varices		
- Absent (n= 388)	44 (11.3%)	<0.001
- Present (n= 81)	29(35.8%)	
Active bleeding during endoscopy		
- Absent (n= 198)	11 (5.5%)	<0.001
- Present (n= 271)	62 (22.9%)	

*Chi - Square test.

Table (5) : Laboratory results of early and non- rebleeders

Total number (469)	Early rebleeders (n= 73)	non= rebleders (n=396)	P*
WBCs / Cmm ($x10^3$)	11.280± 5.960	8.570 ± 5.020	<0.001
RBCs/ Cmm ($x10^6$)	3.240 ± 0.840	3.350 ± 0.810	NS
Hb (gm /dl)	8.83 ± 2.25	9.12± 2.60	NS
Hct value (%)	26.46± 6.18	27.45± 7.17	NS
Platelet count /cmm	128.6± 76.29	139.0 ±68.29	NS
Serum creatinine (mg/dl)	1.27 ± 0.57	1.08 ± 0.50	<0.005
Serum albumin (gm/dl)	2.86 ± 0.76	3.17 ± 0.70	<0.001
Total bilirubin (mg/dl)	1.49 ± 1.47	1.53± 1.85	NS
AST (U/L)	79.04± 80.3	63.05± 53.84	<0.035
ALT (U/L)	50.41±38.5	47.63±41.17	NS
Prothrombin time (sec.)	18.96± 12.47	17.42±9.33	NS

Table (6): Univariate analysis of clinical, laboratory and endoscopic parameters for early rebleeding

Parameters	Coefficient	SE	P
Child-Pugh's	0.7197	0.1642	<0.001
Sex	0.4062	0.2973	N.S
Age	0.0052	0.0105	N.S
Diabetes mellitus	0.7144	0.2668	<0.0074
WBCs	0.066[illegible]	0.0157	<0.001
RBCs	-0.1611	0.1[illegible]	NS
Haemoglobin	-0.0427	0.0457	NS
Haematocrite	-0.191	0.0167	NS
Platelet	0.0021	0.0015	NS
Creatinine	0.3721	0.1335	0.0053
Albumin	-0.6241	0.1741	0.0003
Bilirubin	-0.0137	0.0678	NS
AST	0.0034	0.0015	0.0207
ALT	0.0013	0.0024	NS
Prothrombin time	0.0125	0.0087	NS
Hepatitis C	0.7169	0.2053	0.0005
Gastric varices	0.1455	0.0563	0.0098
Active bleeding	1.5524	0.3272	<0.001

P value (<0.05) indicates that the parameter is significantly related to the occurrence of early rebleeding.

Table (7): Multivariate analysis of clinical, laboratory and endoscopic parameters for early rebleeding

Parameters	Coefficient	SE	P
Child-Pugh's	0.3660	0.3721	NS
Sex	0.3823	0.3745	NS
Age	-0.0077	0.0138	NS
Diabetes mellitus	0.2859	0.4578	NS
Encephalopathy	0.2737	0.6501	NS
WBCs	0.0440	0.0206	0.0326
RBCs	0.2608	0.3538	NS
Haemoglobin	-0.0595	0.1826	NS
Haematocrite	-0.0296	0.0787	NS
Platelet	0.0022	0.0021	NS
Creatinine	0.0555	0.2334	NS
Albumin	0.0857	0.2871	NS
Bilirubin	-0.2149	0.1207	NS
AST	0.0018	0.0026	NS
ALT	-0.0022	0.0042	NS
Prothrombin time	0.0037	0.0125	NS
Hepatitis C	0.6223	0.2434	0.0106
Gastric varices	0.1288	0.0636	0.0428
Active bleeding	1.4095	0.3618	0.0001

P value (<0.05) indicates that the parameter is independent risk factor for early rebleeding.

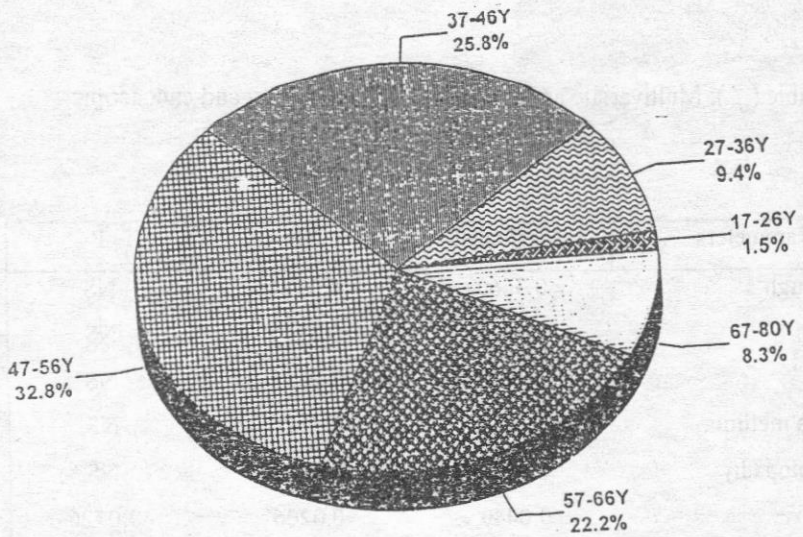

Fig. (1) : Age distribution of patients included in the study

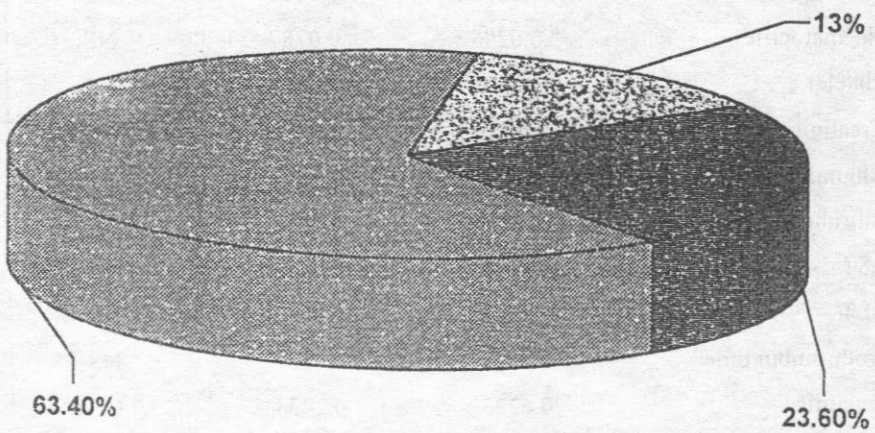

Fig. (2) : Aetiology of portal hypertension in treated patients

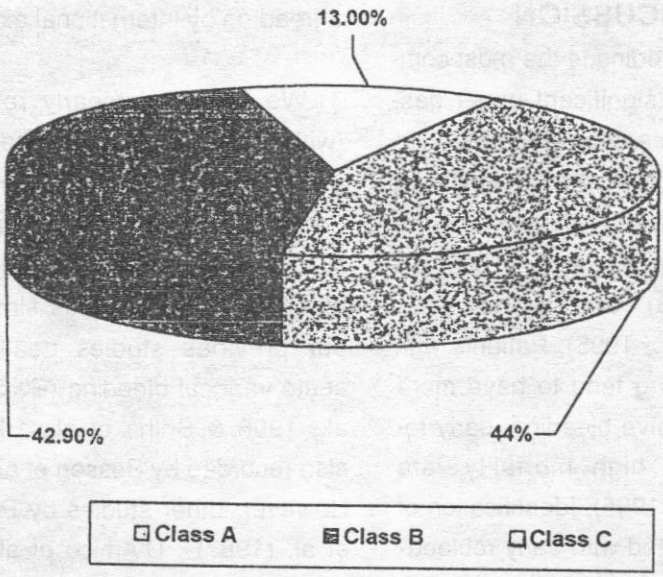

Fig. (3) : Severity of liver disease in treated patients

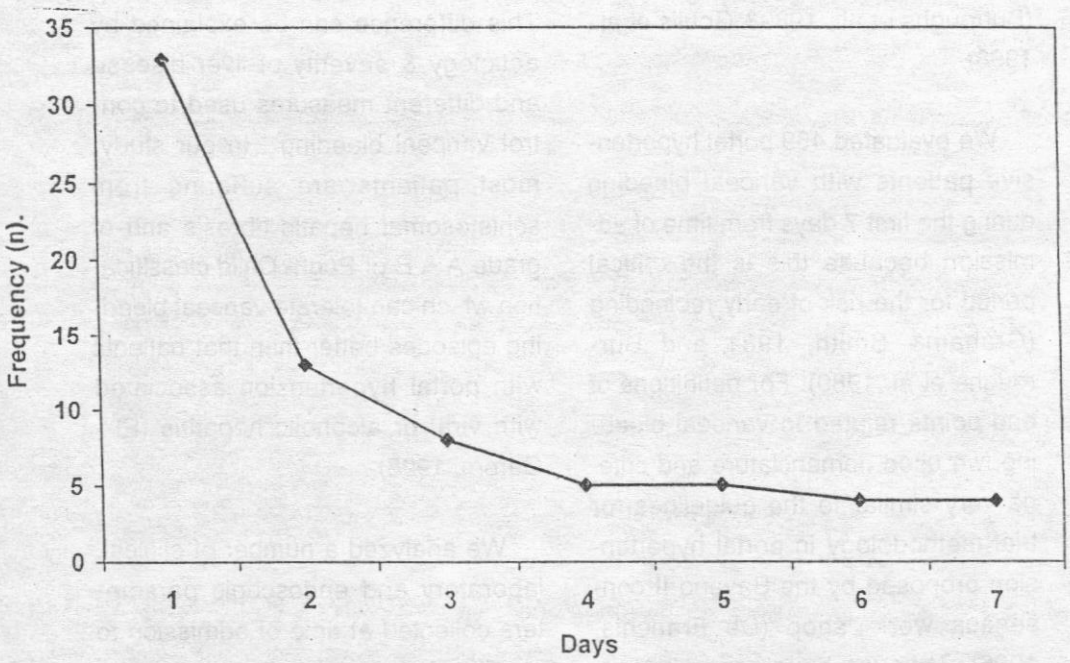

Fig. (4) : Time of early rebleeding (after index endoscopy)

DISCUSSION

Variceal bleeding is the most common cause of significant upper gastro-intestinal bleeding secondary to portal hypertension with a significant health care problem in Egypt (sheir et al. , 1980 ; Madwar et al., 1998; El-Garem, 1998) and world wide (D'Amico et al ., 1995). Patients with variceal bleeding tend to have more rapid and massive bleeding, early rebleeding with high mortality rate (Nevens et al., 1995). Identification of factors associated with early rebleeding is important to identify high risk patients with bad prognostic outcome (Burroughs et al., 1989& Goulis et al., 1998).

We evaluated 469 portal hypertensive patients with variceal bleeding during the first 7 days from time of admission because this is the critical period for the risk of early rebleeding (Graham& Smith, 1981 and Burroughs et al.,1989). For definitions of end points related to variceal bleeding, we used nomenclature and criteria very similar to the guidelines for trial methodology in portal hypertension proposed by the Baveno II consensus work- shop (De Franchis, 1996). Thus we have used clinically meaningful end points commonly agreed on by international experts.

We found that early rebleeding (within the first 7 days after admission) occured in 15.6% of our patients , emphasizing the significant role of this factor in portal hypertensive bleeding . This result is similar to 2 our previous studies dealing with acute variceal bleeding (El- Sayed et al., 1996 & Shiha et al., 1996) and also recorded by Besson et al. (1995). However, other studies by Prindiville et al. (1987) , D'Amico et al. (1995) and Goulis et al.(1998) reported higher early rebleeding rate (30% - 50%). This difference can be explained by aetiology & severity of liver disease and different measures used to control variceal bleeding . In our study, most patients are suffering from schistosomal hepatic fibrosis and of grade A & B of Pugh- Child classification which can tolerate variceal bleeding episodes better than that patients with portal hypertension associated with viral or alcoholic hepatitis (El - Garem, 1998).

We analyzed a number of clinical, laboratory and endoscopic parameters collected at time of admission to identify their prognostic role on the outcome of variceal bleeding. Our re-

sults showed that the following parameters are prognostic factors associated with early rebleeding by univariate analysis : Pugh-Child class C, diabetes millitus, leucocytosis, increased creatinine level, hypoalbuminaemia, increased AST , hepatitis C, gastric varices and active bleeding during endoscope . Multivariate analysis of data showed that active bleeding during endoscope, leucocytosis, hepatitis C and gastric varices are independent risk factors for early rebleeding.

Active bleeding during emergency endoscope was reported in 57% of our patients which was similar to that reported by Goulis et al. (1998) (53%) , but higher than that reported by Terblanche (1984) and Gimson et al. (1993) (33% & 43% respectively). This high rate of active bleeding at endoscopy in our series can be explained by relatively short interval between attack and hospitalization (9 hours) and time between admission and endoscopy (2 hours). Multivariate and univariate analysis of our study showed that active variceal bleeding at endoscopy was an independent prognostic factor for early rebleeding, this is in accordance with previous studies of Planas et al. (1994) , Ben- Ari et al. (1996) and Goulis et al. (1998). This highlight the importance of control and stoppage of variceal bleeding by vasoactive drugs (e. g. octreotide) before endoscopy and first 48 hours after endoscopy which associated with 62 % of cases with early rebleeding (Planas et al., 1994 and Shiha et al., 1996).

Gastric varices is less common and less likely to bleed when compared to oesophageal varices, however , when gastric varices bleed, it usually massive with high risk of early rebleeding (Sarin et al., 1992) . In our study , multi- and univariate analysis showed that associated gastric varices was an independent risk factor for early rebleeding , this highlight the importance of training for proper management of gastric varices in emergency situations (Shiha & El- Sayed, 1999).

Advanced liver disease was previously reported as the most important risk factor for early rebleeding (Graham & Smith , 1981). Parameters reflecting the severity of liver disease (e. g. Pugh - Child grade C, hypoalbuminaemia and elevated AST) was proved , by multi - and / or univariate analysis, to be associated with early

rebleeding in our study. This is in agreement with previously reported studies of Garcia - Pagan et al. (1989), Heresback et al. (1991) , Ben-Ari et al.(1996) , Goulis et al. (1998) and Madwar et al. (1998).

Leucocytosis was proved by multi - and univariate analysis to be an independent risk factor for early rebleeding. Presence of fever, any clinical data of infection and leucocytosis suggested bacterial infection which is a predictive factor for early rebleeding (Bernard et al., 1995) . Bacterial infection are diagnosed in 35- 66 % of cirrhotic patients with gastrointestinal bleeding (Bleichner et al. , 1986 ; Bernard et al. , 1995 and Goulis et al., 1998).This may be due to invasive diagnostic or therapeutic procedures, increase intestinal bacterial translocation, transient depression of reticuloendothelial system function caused by hypovolaemia and deficiency of complement (Rimola et al. , 1984 and Akrividis , 1994). On the other hand, there are data that may support a role of infection in the initiation of variceal bleeding or occurrence of rebleeding. During bacterial infection, there is a release of endotoxin in the systemic circulation which stimulate release of inflammatory mediators, such as cytokines, nitric oxide, platelet- activating factor, and leukotrienes (Hewett and Roth , 1993). These mediators induce structural and functional damage of the gastro- intestinal tract and severe haematologic abnormalities (Beal & Cerra, 1994) . As a result, variceal bleeding is not an uncommon event in severe bacterial infection and some studies documents the use of immediate prophylactic antibiotics during acute bleeding episode as it reduces early rebleeding (Bernard et al., 1995 & Goulis et al. , 1998).

A feature characteristic of hepatosplenic schistosomiasis is that liver perfusion is maintained by an increase of hepatic arterial flow, which allows for the preservation of hepatocyte function in the absence of hepatotropic viral co- infection (EL- Garem, 1998). This explain high percentage of our patients insss Child class A & B than in Child- C.On the other hand , patients with schistosomiasis have higher rate of hepatitis B (HBV) and hepatitis C (HCV) seropositively than do non-infected controls (Madwar et al., 1989 , Kamel et al ., 1994, Shiha et al., 1996 b and Halim et al.,1999). In our series, HBs Ag is positive in 11% and anti HCV is positive in 63% of patients . This rate is slightly higher

than that of study of Shiha et al. (1996 b) (8% & 55% respectively); This higher rate of hepatitis C seropositivity in Egyptian patients is believed to be due, at least in part , to transmission of hepatitis viruses during blood transfusion and parentral therapy for schistosomiasis with contaminated needles (Madwar et al., 1989 & Darwish et al., 1993). Shistosomiasis potentiates hepatitis B and C virus infections by prolonging hepatic inflammation after an episode of acute viral hepatitis and by increasing the risk of chronic infection (Ghaffar et al., 1991& Darwish et al., 1993). Co-infected patients (with shistosomiasis and viral) appear more likely to experience earlier deterioration of liver function with the development of severe, irreversible periportal fibrosis and a more rapid progression toward end stage liver disease (Bassily et al., 1992 and Helal et al., 1998).This explain why high percentage of patients with HCV seropositive are of grade C and that HCV is an independent risk factor for early rebleeding in the present study and in study of Shiha et al. (1996 b) .

For the first time, diabetes mellitus (DM) was found , in the present study, to be an independent risk factor for early rebleeding. Presence of diabetes mellitus doubles the risk of rebleeding. (26.9 % in diabetic versus 13.7 % in non diabetics). The exact explaination is unknown, but it may be mediated through other factors because it was significant in the univariate analysis but not significant in the multivariate COX's Model. The effect may be mediated through the recent relationship between HCV and DM . There is a strong association between HCV infection and DM, because diabetics have an increased frequency of HCV infection particularly with genotype 2 a . Also HCV infection may be serve as an additional risk factor for the development of DM (Andrew et al., 1999 and Mason et al., 1999). In the present study , all diabetics were HCV seropositive, however, furtherwork is needed to clarify this point.

Based on this study, we concluded that leucocytosis , hepatitis C infection, Pugh-Child grade C of hepatic affection, diabetes mellitus, presence of gastric varices and active bleeding during endoscopy are independent risk factors for early variceal rebleeding and should be looked for and dealt with in each patient presented with variceal bleeding.

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التعرف على العوامل الخطرة للتكرار المبكر لنزيف دوالى المرئ والمعدة - دراسة مستقبلية

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الملخص العربى

إرتفاع ضغط الدم بالوريد البابى مازال يمثل أحد أهم التحديات والمشكلات فى أمراض الجهاز الهضمى والكبد ويعد أخطر مضاعفات التليف الكبدى حيث يؤدى الى حدوث دوالى المرئ والمعدة والتى يمكن أن تؤدى الى النزف ويعتبر نزيف الدوالى من أهم المشكلات التى تهدد حياة مرضى الكبد المزمن وهو سبب شائع لدخول المستشفى، ويعتبر الأن منظار القناه الهضمية العلوى جزء متمم لعلاج هذه الحالات وعلى الرغم من ذلك فإن تكرار حدوث النزيف المبكر من دوالى المرئ والمعدة يمكن حدوثه لهؤلاء المرضى بعد العلاج بالمنظار .

الهدف من البحث :-

تهدف الدراسة الى التعرف على العوامل الخطره بتكرار النزيف المبكر من دوالى المرئ والمعده بعد علاج هذه الدوالى بالمنظار.

طريقة البحث :-

شملت هذه الدراسة ٤٦٩ مريضاً مصابون حديثاً بنزيف دوالى المرئ والمعدة أدخلوا إلى مستشفى الطوارئ بجامعة المنصورة وقد تم إستبعاد المرضى الذين يعانون من الأمراض التاليه :- التهابات أو قرح هضمية بالمعدة أو الأثنى عشر - أورام خبيثة بالكبد أو بأية أعضاء أخرى بالجسم - قابلية النزف نتيجة لأمراض بالدم - هبوط شديد ومتأخر بالقلب والرئتين وفشل كلوى أو كلوى كبدى شديد .

خضع هؤلاء المرضى الى أخذ التاريخ المرضى الدقيق - فحص إكلينيكى شامل - تحاليل معمليه وتشمل صورة دم كاملة - تحليل سكر بالدم - تحليل بول - وظائف كبد كاملة - وظائف كلى - دلالات

الالتهاب الكبدى الفيروسى C&B - أشعة فوق صوتية على البطن - ثم تقسيم هؤلاء المرضى الى ٣ مجموعات (A.B.C) حسب تقسم بيوتشايلد .

تم علاج هؤلاء المرضى عند دخولهم المستشفى بالوسائل التقليدية لعلاج النزيف (المحاليل - نقل الدم - فيتامين ك - حقنة شرجية بالاكبتيلوز) ثم عمل منظار طبى لهؤلاء المرضى لتشخيص وعلاج الدوالى النازفه إما بالحقن التصلبى أو بالربط الحلقى أو بالإثنين معا أو بحقن دوالى المعدة بالهستوأكريل أو بالربط الحلقى ثم متابعة هؤلاء المرضى متابعة دقيقة خلال الأسبوع الأول من دخولهم المستشفى من حيث تكرار النزيف (عدد المرات - شدة النزيف - توقيت حدوثة - عدد وحدات الدم المنقول للمرضى - وسيلة علاج هذا النزيف - عدد وأسباب حالات الوفاة)

نتائج البحث :-

شملت هذه الدراسة ٤٦٩ مريضاً : ٤٠٦ من الذكور (٨٦ر٥٪) و ٦٣ من الاناث (١٣ر٥٪) بمتوسط عمر ٥٠ر٦±١١ر٢ عاما ومدى العمر يتراوح بين ١٧ و ٨٠ عاما منهم ٦٧ مريضاً يعانون من مرض الداء السكرى و ٣٢٥ مريضاً مصابون بالالتهاب الكبدى الفيروسىC .

حسب تقسم بيوتشايلد وجد أن ٢٠٧ مريضاً (١ر٤٤٪) مجموعة A و ٢٠١ مريضاً (٩٨ر٤٢٪) مجموعة B و ٦١ مريضاً (١٣٪) مجموعة C.

كانت النتائج الأولية لعمل المنظار الطبى كالتالى :-

١- ٣٨٨ مريضاً لديهم دوالى مرئ و ٨١ مريضاً (٣ر١٧٪) لديهم دوالى بالمعدة، وجد نزيف من الدوالى أثناء دخول المنظار فى ٣٧١ مريضاً (٨ر٥٧٪).

٢- بعد علاج هؤلاء المرضى ومتابعتهم كما سبق وجد حدوث نزيف مبكر فى ٧٣ مريضاً (٧ر١٥٪). وببحث النتائج الأكلينيكيه والمعملية ونتائج المنظار الطبى لهؤلاء المرضى ومقارنة المرضى ذو النزيف المبكر (٧٣) مريضا مع هؤلاء بدون ذلك النزيف وجد أن هناك علاقة ذو دلالة إحصائية بين حدوث النزيف المبكر من الدوالى ومرض داء السكرى والالتهاب الفيروسى الكبدى C وجود دوالى بالمعدة ووجود نزيف من الدوالى أثناء دخول المنظار وهبوط مستوى الألبيومين بالدم وزيادة مستوى أنزيم AST وزيادة نسبه الكرياتنين وزياده عدد خلايا الدم البيضاء والمجموعة C من تقسيم بيوتشايلد لشدة مرض الكبد .

٣- وباستخدام التحليل وحيد الانحراف وجد هناك علاقة ذو دلالة إحصائية بين النزيف المبكر

للدوالى والعوامل الآتية: داء السكرى - زيادة كرات الدم البيضاء - زيادة الكرياتنين - نقص الألبيومين - زيادة أنزيم AST - وجود الفيروس الكبدى C - وجود نزيف من الدوالى أثناء دخول المنظار - وجود دوالى بالمعدة - المجموعة C من تقسيم بيوتشايلد لشدة مرض الكبد .

٤- وباستخدام التحليل المتعدد الانحراف وجد هناك علاقة ذو دلالة أحصائية بين النزيف المبكر من الدوالى والعوامل الآتية: زيادة خلايا الدم البيضاء - وجود التهاب الكبدى الفيروسى C - وجود دوالى بالمعدة - وجود نزيف من الدوالى أثناء دخول المنظار.

٥- وقد تم تسجيل عدد ٤٤ حالة وفاة مبكرة (٩ر٤٪) من بينهم ٣٥ حالة يسبب النزيف المبكر (٧٩ر٥٪) .

مما سبق يمكن استنتاج الآتى :-

- وجود أحد العوامل التالية ينذر بحدوث تكرار مبكر للنزيف من الدوالى بعد علاجها بالمنظار الطبى : داء السكرى - زيادة شدة مرض الكبد - زيادة خلايا الدم البيضآء - زيادة الكرياتنين - نقص الألبيومين - التهاب الكبدى الفيروسى C - زيادة أنزيم AST - وجود دوالى بالمعدة - وأخيراً وجود نزيف من الدوالى أثناء دخول المنظار. وعند وجود أحد هذه العوامل بأحد المرضى يجب وضع هذا المريض تحت العناية الدقيقة تحسبا لتكرار مبكر للنزيف من الدوالى .