PREDICTIVE RISK FACTORS FOR UPPER GASTROINTESTINAL BLEEDING WITH SIMULTANEOUS MYOCARDIAL INJURY

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ABSTRACT

Background and Rationale: Myocardial injury after UGIB is frequently ignored because the signs and symptoms may be overshadowed by severe UGIB. The aims of this study were to investigate the predictive risk factors of simultaneous upper gastrointestinal bleeding (UGIB) and myocardial injury using parameters including troponin I (TnI); and evaluate the epidemiology of this syndrome.

Subject and methods: This study was a case-control study carried out at the gastrointestinal subunit of medical intensive care unit of Internal Medicine department, Faculty of Medicine, Zagazig University.One hundred and five patients were included in this work presenting with UGIB. All participants were subjected to thorough history taking, clinical examination. Routine investigations , abdominal ultrasonography ,upper GIT endoscopy and studies of myocardial injury including ECG, echocardiography and cadiac enzymes includingCK, CK-MB and TnI.

Results:UGIB patients with a history of liver cirrhosis and more than three cardiac risk factors including systemic hypertension, smoking , BMI and hypertriglyceridaemia had a high risk of simultaneously developing myocardial injury. Longer hospital stay was found in those patients.. Other factors including age, gender, the color of nasogastric tube irrigation fluid, history of nonsteroidal anti-inflammatory drug use, octeriotide or terlipressin administration, vital signs, and creatinine recorded at the ED were not significant predictors.

Conclusions: UGIB patients with a history of liver cirrhosis and more than three cardiac risk factors had a high risk of simultaneously developing myocardial injury. Monitoring ECG and cardiac enzymes, including TnI, are recommended in highrisk patients, even if no chest complaints are present.

Key words: myocardial injury, troponin I, upper gastrointestinal bleeding

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) and myocardial ischemia/infarction may occur simultaneously because massive UGIB compromises myocardial perfusion and reflex tachycardia increases myocardial oxygen consumption. Many studies were conducted to evaluate the causes and consequences of UGIB after acute myocardial infarction (AMI) and have found that decreased gastrointestinal blood flow and anti platelet or anticoagulation therapy during AMI are two of the major causes of bleeding [1].

Myocardial injury after UGIB is frequently ignored because the signs and symptoms may be overshadowed by severe UGIB [2]. Several studies showed that this process is common, especially in critically ill patients [3].Except for those with more cardiac risk factors and more severe anemia, there is no mutual agreement about other risk factors in this group. High-output heart failure has been noticed in cirrhotic patients and this syndrome is termed cirrhotic cardiomyopathy. Ventricular hyporesponsiveness is revealed when cirrhotic patients are challenged by pharmacologic or physiologic stress [4]. In addition, hemodynamic instability is often noticed in patients with liver cirrhosis and variceal bleeding [5]. This could potentiate (subclinical) heart failure and myocardial injury. Some medications used to treat bleeding varices, including terlipressin and vasopressin, have the potential for aggravating myocardial ischemia because of their coronary artery vasoconstricting effect [6]. However, their impact on myocardial injury during UGIB is generally not recognized.

Troponin I (TnI), which is more frequently used in recent years, is a more rapidly-rising and specific marker and outcome predictor during AMI [7]. It was shown to be a better biologic marker to detect occult myocardial injury during UGIB [8]. Pateron et al showed a frequent elevated TnI (32%) above the lower detection limit in patients with cirrhosis and indicated that it was associated with subclinical left ventricular myocardial injury [9].

PATIENTS AND METHODS

Patients:-

A total number of One hundred and fivepatients were included in this work presenting with the chief complaint of tarry stool passage or blood vomitus were diagnosed with UGIB.

This number was selected from a total number of 835 patients admitted to the ICU with a preliminary diagnosis of acute upper GIT bleeding .we exclude twenty cases because of previouse history of IHD (2.3%) from total number of upper GIT bleeding cases .

Patients who included in this study (105) were underwent standardized treatment according to current guidelines [5].Most of them Underwent

emergent gastroendoscopy within 24 hours, except for those who refused or were contraindicated (irritable patients or with arrhythmia and severe shock). During gastroendoscopic examination, hemostatic strategies were employed.

Electrocardiography (ECG) was done on admission and 4 hours later. Cardiac enzymes, including creatine kinase (CK), CK-MB, and TnI were checked every 12 hours for three times after admission. The presence of liver cirrhosis was diagnosed when a typical change in abdominal ultrasound in addition to a long-standing hepatitis history or evidence of hepatic decompensation (elevated bilirubin level, prolonged prothrombin time, presence of varices in gastroendoscopic examination, encephalopathy) were identified. Previous UGIB history and drug use including aspirin, warfarin, non steroidal anti-inflammatory drug (NSAID) and steroid, and history of smoking and alcoholic beverage drinking were evaluated. Recurrent bleeding was diagnosed and recorded if patients had an increased amount of tarry stool with hemodynamic instability (tachycardia or hypotension) and decreased Hb measurement within three days of initial therapy. Such patients underwent gastroendoscopy for diagnosis and hemostasis. Intravenous medication used to control bleeding (omeprazole , Octreotide , terlipressin, or somatostatin), total amount of packed erythrocyte transfusion, length of hospital stay, and complications including severe infection, respiratory failure, acute renal failure, were also recorded and analyzed

Inclusion criteria:-

All UGIBsubjects admitted to gastrointestinal subunit of the Medical ICU of Zagazig University Hospital older than 35 years were included.

Because we consider that myocardial injury is less common in younger and previously healthy patients with minor bleeding, we put exclusion criteria.

Exclusion criteria :-

(1) patients younger than 35 years

because myocardial injury is less common in younger

(2) patients with initial systolic blood pressure(BP) >100mmHg.

(3) initial hemoglobin (Hb)>12g/dL.

(4) patients with history of actual ischaemic heart disease or rheumatic heart disease.

The patients are classified into two groups as following :-

Group (A):-

Patients with upper GIT bleeding without myocardial injury (control group). It included 66 patients, 41 males and 25 femles with average age 52.8±9.2.

Group (B):-

Patients with upper GIT bleeding with myocardial injury . It included 39 patients, 26 males and 13 femles with average age 52.9±8.2.

myocardial injury was defined as the presence of any of the following:-

- serial ST-T deviation in two consecutive leads on ECG
- elevated CK-MB> 4.9ng/ml (normal,up to 4.9)
- TnI > 0.01 ng/dL (normal, <0.01ng/ml)

METHODS OF THE STUDY

(A) CLINICAL STUDY:-

1-Thorough history taking:-

thorough history of present illness and past history of previous hospital admission and any medical disorder with particular attention to history of Liver diseases , previous attacks UGIB , previous endoscopy , smoking, alcoholic beverage drinking , hypertension ,anticoagulant, and NSAIDs use .

2 -complete physical examination**:-**

including assessing the patients for haemodynamic instability and clinical signs of poor perfusion

(B) LABORATORY INVESTIGATIONS

They were all done according to the methods applied in the clinical pathology and laboratories of Zagazig University Hospitals and included:

1- Complete blood picture

2- Liver function tests:

3- Renal function tests:

4- Bleeding profile: INR, Prothrombin time (PT) and Partial Thromboplastin Time (PTT)

5- SERUM NA^+ AND K+

6- Arterial blood gases

7- Lipid profile

8 -Fasting and post prandial blood glucose level

9- C-Reactive protein

(C) ABDOMENAL ULTRA SOUND

(D) UPPER GIT ENDOSCOPY

(E) STUDIES OF MYOCARDIAL INJURY:

1-ELECTROCARDIOGRAPHY:-

2- CARDIAC ENZYMES **:-**

creatine kinase (CK), creatine kinase-MB (CK-MB), and Troponin I (TnI) **)**

3- ECHOCARDIOGRAPHY

(F)STATISTICAL ANALYSIS:-

The $\chi 2$ test or Fisher's exact test was used to examine the presence of myocardial injury by the distribution of general characteristics. Logistic regression was used to investigate the relationship between mild or moderate myocardial injury and other potential predictors that were significant in the univariate analysis. Data were analyzed using the SAS statistical package,and the significant two-sided p value was 0.05.

RESULTS

(Table1): General characteristics among 105 upper gastrointestinal bleeding cases classified to cases with myocardial injury and control

	Control N= (66)	Cases N= (39)	t	P
Age	**52.8±9.2**	**52.9±8.2**	**0.02**	**0.97**
			X^2	P
Age				
≤55	**37 (56.1%)**	**12 (30.8%)**		
>55	**29 (43.9%)**	**27 (69.2%)**	**1.7**	**0.1**
Sex m	**41 (62.1%)**	**26 (66.7%)**		
f	**25 (37.9%)**	**13 (33.3%)**	**0.2**	**0.6**

(TABLE2): Comparison of characteristics, risk factors, history and laboratory results between myocardial injury cases and control among 105 upper gastrointestinal bleeding

	Control N= (66)	Cases N= (39)	t	P
Hb	**7.7±2.1**	**8.1±1.8**	**0.027**	**0.97**
TLC	**7.9±2.2**	**7.9±2.3**	**0.796**	**0.42**
PLT	**221±104.8**	**210.1±79**	**-0.061**	**0.95**
Urea	**47.7±31.1**	**49.1±27.5**	**-0.560**	**0.57**
Creatinine	**1.12±0.62**	**1.2±0.71**	**0.221**	**0.82**
total bilirubin	**1.6±1.5**	**2.2±2**	**1.263**	**0.2**
Direct bilirubin	**0.72±0.5**	**1.01±1**	**1.487**	**0.1**
total protein	**6.9±0.6**	**6.8±0.6**	**1.191**	**0.2**
serum albumin	**3.2±0.82**	**3±0.83**	**-0.629**	**0.53**
ALT(SGPT)	**39.7±43.5**	**37.7±41.2**	**-1.654**	**0.1**
AST(SGOT)	**49.5±34.5 39.3 (7-212)**	**44.2±34.3 38.8 (7-160)**	**Mann-whitney 1147**	**0.3**
Pulse	**92.6±19.9**	**88.5±20.2**	**-0.755**	**0.4**
MAP	**64.3±8.4**	**65.2±8.8**	**-0.992**	**0.3**

SYS BP	**88.3±10.6**		**90±10.2**		**0.471**	**0.63**
DIA B.P	**52.5±10.6**		**52.6±10.2**		**0.787**	**0.4**
RR	**17.8±3.5**		**18.7±2.8**		**0.055**	**0.9**
Temp	**37.2±0.4**		**37.3±0.4**		**1.407**	**0.16**
					X^2	P
Lowest HCT						
≤25						
>25	**33**	**(50%)**	**14**	**(35.9%)**	**1.9**	**0.16**
	33	**(50%)**	**25**	**(64.1%)**		
Endoscopy						
Variceal					**1.6**	**0.19**
Non- Variceal	**39**	**(59.1%)**	**28**	**(71.8%)**		
	27	**(40.9%)**	**11**	**(28.2%)**		
+VE Liver cirrhosis	**37**	**(56.1%)**	**30**	**(76.9%)**	**4.6**	**0.03***
NG color						
Fresh	**18**	**(27.3%)**	**13**	**(33.3%)**	**0.6**	**0.7**
Not-fresh	**41**	**(62.1%)**	**21**	**(53.8%)**		
+VE History of NSAID use	**20**	**(30.3%)**	**9**	**(23.1%)**	**0.6**	**0.4**
+VE Octereotide or Terlipressin use	**16**	**(24.2%)**	**16**	**(41.0%)**	**3.2**	**0.07**
+VE History of HPN	**14**	**(21.2%)**	**26**	**(66.7%)**	**21.4**	**<0.001****
+VE Smoking	**20**	**(30.3%)**	**27**	**(69.2%)**	**15**	**<0.001****

(TABLE 3):Comparison of lipid profile and cardiac enzymes and labs between myocardial injury cases and control among 105 upper gastrointestinal bleeding

	Control N= (66)	**Cases N= (39)**	**t**	**P**
LDL	**115.9±25.4**	**121.7±24.8**	**1.139**	**0.2**
HDL	**43.5±7.6**	**44.4±8.2**	**0.571**	**0.5**
CRP	**2.1±3.7**	**6.4±3.9**	**5.588**	**<0.000****
BMI	**22.9±4.2**	**28.8±4.5**	**6.700**	**<0.000****
TRG	**145.1±31.9**	**158±35.4**	**2.026**	**0.05***
CPK(U/L)	**217.1±223**	**427.4±346.6**	**3.784**	**<0.000****
CK(MB) (ng/ml)	**1.97±0.8**	**4.7±5.4**	**4.050**	**<0.000****
TnI(ng/ml)	**0.01±0.001**	**0.4±0.8**	**3.896**	**<0.000****

TABLE 4): Comparison of ECG & ECHO and labs between myocardial injury cases and control among 105 upper gastrointestinal bleeding.

	Control N= (66)	Cases N= (39)	X^2	P
ECG(ST-T wave changes)	0 (0%)	15 (38.5%)	15	<0.001**
ECHO			X^2	P
Tricuspid Regurge	15 (22.8%)	7 (18%)	1.2	0.5
			t	P
LA	28.7±10.5	31.2±7.3	1.32	0.190
RVD	14.6±6.7	16.7±5.8	1.59	0.115
LVD	44.9±15.1	46.3±9	0.54	0.586
LVS	29.4±10	30.8±6.5	0.8	0.425
EF	51.9±18.2	58.5±11.6	2.03	0.04*
FS	28.4±10.3	32±7.7	1.75	0.082

(Table 5): Comparison of the outcome between case & control of myocardial injury among the 105 upper gastrointestinal bleeding cases

	Control N= (66)	Cases N= (39)	t	P
Hospital stay	4.3±1.5	11.5±3.5	14.2	<0.001**
blood transfusion (units)	2.1±2.3	1.8±2.4	Mann-whitney 1187	0.4
			X^2	P
Rebleeding	1 (2.6%)	5 (7.6%)	1	0.2

(Table 6): logistic regression for potential confounders among the cases

	OR	P	95% Confidence Interval	
			Lower Bound	Upper Bound
Age	1.448	0.229	-0.690	2.884
SEX	2.029	0.154	-0.466	2.944
HCT	0.687	0.407	-4.591	1.863
Variceal	0.401	0.526	-2.634	5.150
+VE Liver cirrhosis	4.872	0.03*	-5.740	2.035
NG color	1.475	0.224	-0.792	3.373
+VE History of NSAID use	0.979	0.323	-1.107	3.365
+VE Octereotide or Terlipressin use	0.448	0.503	-2.692	1.321
+VE History of HPN	7.057	0.008*	-4.335	-0.654
+VE Smoking	5.425	0.020*	-3.728	-0.321

(TABLE 7): Score for potential confounders

	SCORE	P
Age	1.787	0.181
SEX	.219	0.640
HCT	1.972	0.160
Variceal	1.713	0.191
+VE Liver cirrhosis	4.620	0.032*
NG color	.564	0.453
+VE History of NSAID use	.640	0.424
+VE Octereotide or Terlipressin use	3.259	0.071
+VE History of HPN	21.477	<0.001**
+VE Smoking	4.425	<0.001**

DISCUSSION

Myocardial injury after UGIB is frequently ignored because the signs and symptoms may be over shadowed by severe UGIB [2]. Several studies showed that this process is common, especially in critically ill patients [8].

In our study, the mean age of group with myocardial injury was 52.9±8.2 while the other group without myocardial injury was 52.8±9.2 **,** and as regard the sex of the patients, it shows that 66.7% of patients with myocardial injury were male and 33.3% were female and 62.1% of patients without myocardial injury were male while 37.9% were female. So this study show no significant difference between both groups.

Also in our study we found that there were significant difference between patients with myocardial injury and those without myocardial injury as regard CAD risk factors including systemic hypertension, smoking , BMI and hypertriglyceridaemia so these factors considered to be predictive risk factors of simultaneous UGIB and myocardial injury, these results are closely similar to previous study**,** who showed that presence ofTwo or more risk factors for CAD or a previous clinical history of CAD are among the factors that may help to stratify patients who are at increased risk of morbidity and mortality with GI hemorrhage [10].

Our study revealed that liver cirrhosis show significant difference between both groups, Univariate analysis revealed that liver cirrhosis,is a risk factor in UGIB patients for developing myocardial injury . These results are similar to a study investigating 32 patients with liver cirrhosis showed that 10 (32%) had slightly elevated TnI (range, 0.06–0.25 ng/dL) and developed myocardial injury [9] .

Our study revealed that there are no significant difference between both groups as regard NSAD use, nasogastric lavage color ,lowest HCT, initial Hb , number of blood transfusion units, vital signs and creatinine level. Although initial and minimum Hct levels (≤ 25% vs. > 25%) were not significant predictors for UGIB patients to develop myocardial injury, it is still important to consider the necessity of adequate blood transfusion before performing gastroendoscopy, which further increases heart load. However in another study**,** it is found that UGIB patients with MI had significantly lower presenting hematocrits (26.0 ±1.3 vs 30.5 ± 0.8; p = 0.007), and lower lowest hematocrits in the first 48 h (22.3 ± 0.9 vs 25.1 ± 0.5; p = 0.01) than those without MI [4].

Our study showed that there is a significant difference between UGIB patients with myocardial injury and those without as regard hospital stay (mean duration, 4.3±1.5 vs. 11.5±3.5 days; p<0.001) . These results are in agreement with a previous study which showed that UGIB patients with MI had significantly tended to have longer lengths of stay in the ICU(7.9 ± 2.2 vs 4.0 ± 0.4 days; p = 0.09) than those without MI.

In conclusion,UGIB patients with a history of liver cirrhosis and more than three cardiac risk factors including systemic hypertension, smoking , BMI and hypertriglyceridaemia had a high risk of simultaneously developing myocardial injury and longer hospital stay was found in those patients.

We recommend that Monitoring ECG and cardiac enzymes, including TnI, are recommended in high risk patients, even if no chest complaints are present. And further studies are necessary to investigate the exact mechanisms by which liver cirrhosis precipitates myocardial injury during UGIB.

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