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Predictors of mortality in patients with acute upper gastrointestinal hemorrhage who underwent endoscopy and confirmed to have variceal hemorrhage

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Abstract *Background:* Variceal hemorrhage (VH) is a major complication of chronic liver disease. Several factors have been validated for the prediction of the outcome of an acute VH. The clinical risk characteristics reported in developed countries may be different from developing countries.
Aim: The aim of this study was to determine the predictors of mortality in patients admitted to our hospital with acute upper gastrointestinal (UGI) hemorrhage who underwent endoscopy and confirmed to have VH.
Patients and methods: This was a cross sectional hospital based study performed over a seven-year period between January 2006 and January 2013.
Results: A total of 224 patients were analyzed. Nineteen patients (8%) died within the first two weeks of their hospital admission. Eighteen variables were studied and included in a multivariate analysis using a logistic regression model. Five variables were predictors of death. Hemodynamic instability at admission (AOR = 5.5, 95% CI = 22.3 + 1.4, $P = 0.017$), Child class C (AOR = 5.9, 95% CI = 24 + 1.5, $P = 0.013$), blood in upper gastrointestinal (UGI) tract at the

Abbreviations: UGI, upper gastrointestinal; VH, variceal hemorrhage; OR, odds ratio; AOR, adjusted odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; EV, esophageal varices; GV, gastric varices; GEV, gastroesophageal varices; IGV, isolated gastric varices.

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index endoscopy (AOR = 12.8, 95% CI = 126.5 + 1.3, $P = 0.03$), rebleeding within five days of endoscopy (AOR = 25.4, 95% CI = 109.2 + 5.9, $P = 0.000$), and in-hospital complications (AOR = 23.4, 95% CI = 122.5 + 4.5, $P = 0.000$) were independent predictors of mortality after the acute VH episode.

Conclusion: Patients with acute VH and hemodynamic instability at admission, Child class C, blood in UGI tract at the index endoscopy, rebleeding within five days of endoscopy and in-hospital complications are at an increased risk of mortality after the acute VH episode. Rebleeding within five days of endoscopy and in-hospital complications are the most significant independent predictors of mortality.

1. Introduction

Variceal hemorrhage (VH) is a major complication of chronic liver disease and is associated with significant morbidity and mortality.[1,2] Although overall survival may be improving over the past 40 years, mortality is still closely related to failure to control bleeding or early rebleeding and this is not uncommon during the first days to 6 weeks after admission.[2–5]

A variety of clinical risk characteristics have been adopted to assist with patient assessment and a number of them have been applied for use in prognostic scoring algorithms (e.g. Rockall score). These are used to evaluate risk of death and/or re-bleeding in upper gastrointestinal (UGI) hemorrhage patients, and also to screen for and to select high risk patients for intervention within an appropriate time. Several factors have been specifically validated for the prediction of the outcome of acute VH.[5,6]

Prognostic factors of mortality in acute VH included presentation with hematemesis, failure to control bleeding within five days, raised bilirubin, presence of ascites, encephalopathy, shorter interval to admission to hospital, plasma urea, bleeding starting in hospital, prothrombin time $<40\%$, recent use of steroid drugs within seven days of bleeding, age $>$ 60 years, hepatic venous pressure gradient, concomitant hepatocellular cancer and transfusion need.[6]

The clinical risk characteristics reported in developed countries may be different from those in developing countries.

Egypt has a large burden of chronic liver disease. Schistosomiasis and hepatitis C virus are common diseases in Egypt. The overall prevalence positive for antibody to hepatitis C virus was 14.7%.[7] Despite the advent of endoscopy and endoscopic therapy, access to medical centers with experienced medical staff and adequate equipment in Egypt is still limited. Most government hospitals refer patients with acute UGI hemorrhage to teaching hospitals, academic institutes, insurance hospitals and private hospitals. Many patients never reach hospital. A plan for management of UGI hemorrhage was designed in a governmental hospital to be within the available resources and was formulated in two stages. Stage one, 2000–2004, was the training of staff and preparation. During this time we assessed the capability of the hospital for dealing with these cases. Following the assessment we went to stage two. Stage two started in 2004 and all patients presenting with acute UGI hemorrhage have been assessed and managed in house.[8–10]

The aim of this study was to determine the predictors of mortality in patients admitted to our hospital with acute UGI hemorrhage who underwent endoscopy and confirmed to have VH.

2. Patients and methods

This was a cross sectional hospital based study. The study was performed in a secondary-care governmental hospital (Bolak Eldakror Hospital, Giza, Egypt) on cirrhotic patients presenting with acute UGI hemorrhage who underwent endoscopy and confirmed to have VH over a seven-year period between January 2006 and January 2013.

A management plan for acute UGI hemorrhage composed of five steps (assessment, resuscitation, diagnosis, stoppage of bleeding and prevention of rebleeding) was designed. A management protocol, based on international standards, was established with the intention of improving the quality and efficiency of our health care delivery (Table 1).[11,12] Clinical guidelines and a clinical care pathway were developed within the availability of local therapeutic options in order to provide a stand-alone practical guide for the team (Table 1). The care pathway was developed to improve patient management and resource utilization. The guidelines and care pathway were disseminated to house officers, residents, physicians, and nursing staff. This was accomplished via medical rounds and conferences for the medical staff. Printed sheets were posted in the emergency room, intensive care and medical department that outlined the care pathway. A consultant gastroenterologist was on-call 24/7 days a week to attend resuscitation when bleeding was detected. The gastroenterologist served as a facilitator for the medical staff caring for the patients, often monitoring intravenous hydration and delivering blood/blood products.

Stratification of patients in low and high-risk categories for rebleeding and mortality was performed using the Rockall score. Patients with a low risk were discharged home and subsequently underwent diagnostic endoscopy on the next available list. Those at high risk were admitted to hospital for intensive monitoring and early, energetic resuscitation. Endoscopy was performed on the morning of the second day to establish diagnosis, to control bleeding and to prevent rebleeding if considered appropriate. All patients presenting with acute UGI hemorrhage and a confirmed diagnosis of liver cirrhosis were admitted, assessed and resuscitated in a three-bed intensive-care unit. Liver cirrhosis was diagnosed on the basis of clinical and laboratory data and ultrasonography. Child classification was used to assess hepato-cellular function in

Table 1 Upper gastrointestinal hemorrhage care pathway.

Definition

Acute UGI hemorrhage is bleeding started within 3–7 days from presentation

Admission day

- Admit any patient with bleeding or suspicious of bleeding
- History, physical examination and initial hemoglobin level
- Hemodynamic stability: normal pulse and blood pressure in both supine and erect position
- Hemodynamic instability: heart rate > 100 beats/min, hypotension with a systolic pressure < 90 mmHg and/or diastolic value < 60 mmHg

Initial management

- If young, hemodynamically stable, has minor co morbidity (hypertension or diabetes mellitus) and does not have major co morbidity: discharge the patient home and endoscopy can be done as outpatient (elective/scheduled)
- If elderly (> 60 years), hemodynamically instable or with major co morbidity: admit the patient in the intensive care unit of UGI bleeding
- Inform the on call specialist to attend and monitor until the patient is stable (systolic blood pressure > 100 mmHg in 2 readings 10 min apart)
- Secure airways
- IV access with 2 peripheral cannulae (16 gauge)
- Cross match for at least 2 units of blood
- Insert a nasogastric tube and perform aspirate and lavage procedure. Do not insert the tube if the patient could not tolerate it
- Rectal examination to assess stool color
- Insert urinary catheter and measure hourly volume
- 1–2 L of saline will correct volume losses. If the patient remains unstable add plasma expanders (hemagel) and blood
- Blood transfusion is continued until the patients is stable and hemoglobin level reaches 7–8 g/dl in patients with liver cirrhosis, 9–10 g/dl in patients without liver cirrhosis, 11–12 g/dl in patients with ischemic heart disease
- If blood is not available contact other governmental blood banks through Giza Governorate of Health direct line or National Blood Bank in Dokki. Both are in service 24/7
- IM vitamin K every 12 h if the patient has bleeding tendency
- Prophylactic antibiotic therapy (IV third generation cephalosporin or oral ciprofloxacin 1 g/d for I week) if the patient has liver cirrhosis
- Lactulose orally and enema once daily in case of encephalopathy
- Analgesic or anxiolytic if the patient has severe pain or irritable (IV pethidine 25 mg or diazepam 5 mg, Half the dose should be used in elderly and those with cardio respiratory disease)
- Insulin if the patient has diabetes mellitus
- ECG if the patient has cardiac co morbidity or in shock at presentation
- Plain X-ray chest if the patient has rales, wheeze, bronchial breathing
- Plain X-ray abdomen if the patient has peritoneal signs, severe tenderness, vomiting with distention
- Vasoactive drugs (e.g. IV sandostatin or glypressin) can be used, when available in the future, in case of suspicious of variceal bleeding
- IV proton pump inhibitors can be used, when available in the future, in case of suspicious of peptic ulcer bleeding

Monitoring

- Vital signs every one hour until stable then every 4–8 h until time of endoscopy
- Hemoglobin or hematocrit every 6–12 h
- If bleeding stops and the patient is stable, transfer to the general medical ward and allow fluid to drink
- If bleeding continues the patient should be kept in the intensive care fasting with IV fluid replacement

Morning of the next day

- Blood sample for all routine laboratory tests
- Ultrasonography of abdomen
- Endoscopy is undertaken in the morning of the next day. The patient should be alert and hemodynamically stable

Procedure

- Patients who have either endoscopically diagnosed bleeding varices or peptic ulcer with a visible vessel or active bleeding should receive endoscopic therapy in a variety of forms at the time of initial endoscopy according to the protocol

Post procedure

- If bleeding is controlled transfer the patient to the general medical ward
- Allow the patient to eat or drink after 6 h from therapeutic endoscopy
- If therapeutic endoscopy was performed for variceal hemorrhage: oral proton pump inhibitors for 2 weeks and paracetamol (for chest pain)
- If therapeutic endoscopy was performed for ulcer hemorrhage: IV proton pump inhibitors for 48 h then continue with ordinary dose
- If ulcer hemorrhage without therapeutic endoscopy: start treatment with oral H2 antagonist or proton pump inhibitors
- If bleeding is not controlled or rebleeding occurs transfer the patient to the intensive care, assess, start resuscitation and repeat endoscopy is arranged

Follow up

- Vital signs is measured every 8 h and hemoglobin every 12–24 h for the following 48 h
- Patients should be observed for five days

Discharge criteria

- No evidence of on-going bleeding
- No orthostatic signs at discharge

(*continued on next page*)

Table 1 *(continued)*

Patient discharge

Discharge information includes:

- Medical follow up in the outpatient clinic within 2 weeks
- An appointment for the second therapeutic session in cases of variceal hemorrhage

Management of variceal hemorrhage

Endoscopic diagnosis of variceal hemorrhage

- Active bleeding from a varix
- Clots overlying a varix
- A white nipple a rupture point on a varix
- Varices in absence of another potential source of bleeding

Esophageal varices (EV) grading

- Grade 1: varices that collapse to inflation of the esophagus with air
- Grade 2: varices between grades 1 and 3
- Grade 3: varices which are large enough to occlude the lumen

Gastric varices (GV) classification

- Primary: GV that can be detected at the first endoscopy
- Secondary: GV that occur within two years of eradication of EV

Types of gastric varices

- Gastro-esophageal varices (GEV) types 1 and 2: those GV that are continuous with EV and occur along the lesser curvature or the fundus, respectively
- Isolated gastric varices types 1 and 2 (IGV): those GV that are discontinuous from the EV and occur either in the fundus of the stomach or anywhere else in the stomach, including the body, antrum, pylorus, and duodenum, respectively. GV can occur in the absence of EV or in the presence of only grade I EV

Control of acute variceal hemorrhage

– *Esophageal varices*
  - Band ligation is the method of first choice
  - If banding is difficult because of continued bleeding sclerotherapy should be performed
  - Injection sclerotherapy with ethanolamine oleate is first choice and if failure to control bleeding histoacryl can be used

– *Gastric varices*
  - Baveno IV consensus: Treat all GV with histoacryl
  - BSG guidelines 2000: Treat GEV as for EV and IGV with histoacryl

Secondary prophylaxis of variceal hemorrhage

– *Non-selective beta blockers with or without endoscopic therapy*

– *Esophageal varices*
  - Band ligation after 4–10 days, then every 2–4 weeks until eradication then every 3–6 months. Single band to each varix
  - Sclerotherapy to other small vessels and to complete eradication

– *Gastric varices*
  - A repeat session for GEV should be done after one week (unless there is diffuse ulcers) and on weekly basis. IGV usually requires one or two sessions for obliteration

Injection of sclerosant

– *Injection sclerotherapy of EV using ethanolamine oleate*
  - Use 23- gauge sclerotherapy needle
  - Intravariceal or perivariceal injection
  - 2–4 ml is injected into a single EV
  - During active bleeding start injection below the site of bleeding
  - During follow up start injection at Z line

– *Injection sclerotherapy of GV using histoacryl*
  - All attendants should use goggles during the procedure
  - Use 21-gauge sclerotherapy needle with 6–8 mm long needle tip
  - Prepare a mixture of 0.5 ml of histoacryl with 0.7 ml of lipiodol
  - Use 5 ml syringe and inject 1.2–4.6 ml in of this mixture into single GV
  - All GV must be injected at the same time and should be Intravariceal
  - For better view of the fundus especially with IGV1 or GOV2: the patient in the prone or right lateral position, head end of the patient raised to 30–45 degree and injection is performed by retroflexion the endoscope
  - To avoid injury of endoscope channel: before retroflexion push the injector outside the tip for 1 cm
  - To fix the tip of the endoscope in front of fundal varices: after retroflexion of the endoscope, lock the right-left knob
  - Precautions for preventing endoscope channel and injector blockage: apply lipiodol at the tip of the endoscopic channel, avoid suction during injection of the glue, water irrigation after injection of the glue and do not pull the injector out through the endoscopic channel until the injector is properly cleaned from any adherent material

Table 1 *(continued)*

Management of peptic ulcer hemorrhage

Stigmata of recent hemorrhage

- Clean base
- Red or dark blue "flat spot"
- Adherent clot
- Non-bleeding visible vessel
- Active bleeding

Indications for endoscopic therapy in ulcer hemorrhage

- Ulcer with clean base: no endoscopic therapy
- Ulcer with red or dark blue "flat spot": no endoscopic therapy
- Ulcer with adherent clot: Vigorous water irrigation to dislodge the clot and endoscopic therapy if visible vessel or active bleeding
- Ulcer with non-bleeding visible vessel: Endoscopic therapy
- Ulcer with active bleeding: Endoscopic therapy

Endoscopic therapy for peptic ulcer hemorrhage

- Epinephrine injection and thermal electrocoagulation
- Epinephrine is diluted (1:10,000) and administered through a 23-gauge sclerotherapy needle. 2 ml can be given in increments targeting four quadrants of the ulcer. Larger volumes (35–45 ml) were more effective in providing hemostasis as compared to standard volumes (15–25 ml) though there are no clear guidelines as to the ideal volume required
- Thermal (bipolar) electrocoagulation: The probe, of Boston Scientific Corp., is forcefully opposed directly on the major stigmata of hemorrhage and pulse treatment of 5–10 s with a power of 10–15 W are applied followed by water irrigation until target coagulation is achieved

Follow up after endoscopic therapy

- IV proton pump inhibitors for 48 h then continue with ordinary dose
- Hemostasis after first endoscpoic therapy is usually achieved in more than 94% of procedures when thermocoagulation of bleeding lesions is used
- After bleeding from ulcers is controlled endoscopically the rate of recurrent bleeding is 15 to 20%
- The minority of patients in whom hemostasis is not achieved by an initial endoscopic therapy or rebleeding occurs at least one more endoscopic therapy is preferable to surgery

Indications of surgery

- Failure of endoscopic therapy: common in posterior wall duodenal ulcers or large ulcer
- Active severe bleeding during endoscopy

Types of surgery

– According to patient's condition, competence and preference of the surgeon
– Conservative surgery (minimal surgery)
  - Underrunning of the bleeding vessel or ulcer excision
  - Followed by H2 antagonist
– Conventional surgery (ulcer-curing surgery)
  - Vagotomy and gastrectomy or vagotomy and pyloroplasty

cirrhosis. Every patient was assigned a class based on the presence of ascites, neurological disorder, nutritional status, serum bilirubin and albumin levels. Histological examination of the liver was not performed. The etiology of the liver disease was not determined in any patient. Those who were hemodynamically unstable (heart rate > 100 beats/minute, hypotension with a systolic pressure < 90 mmHg and/or diastolic value < 60 mmHg) were managed with crystalloid solutions with or without blood transfusion. Patients with hemoglobin less than 7 g/dl were transfused according to individual requirements. All patients suspected to have VH received prophylactic antibiotic therapy (IV third generation cephalosporin). Endoscopy was performed on the morning of the second day to establish the diagnosis, to control bleeding and prevent rebleeding. All patients received conscious sedation. IV midazolam (2.5 mg) was the agent used. All endoscopies were performed by two well-trained experienced endoscopists. All patients with VH received initial endoscopic therapy (sclerotherapy, band ligation or both). If hemostatic therapy was unsuccessful, either because bleeding was not controlled or rebleeding occurred, repeat endoscopy was considered. Balloon tamponade, vasoactive drugs, surgical shunts and trans-jugular intrahepatic porto-systemic shunts were not locally available. Patients were observed in the medical department for a minimum of five days before discharge.

During the study period 500 patients with concomitant acute UGI hemorrhage and liver cirrhosis were admitted. One hundred and forty-two patients (28%) did not undergo an inpatient endoscopy for various reasons and 358 patients (72%) underwent endoscopy (Tables 2 and 3). Patients who did not undergo inpatient endoscopy and those who had non variceal hemorrhage were excluded.

Two hundred and twenty-four patients with concomitant acute UGI hemorrhage and liver cirrhosis who underwent endoscopy and confirmed to have VH were included in the analysis. A standardized data collection form (sheet) was completed for each patient. Recorded data included demographic information and historical data: smoking history, drugs used (aspirin, non-steroidal anti-inflammatory drugs and anticoagulants), alcohol consumption, patient condition at the time of bleeding, presenting symptoms and co-morbid illnesses. Physical and laboratory examination findings included

Table 2 Patients with liver cirrhosis and acute UGI hemorrhage who did not undergo endoscopy.

Causes	Incidence (%)
Died rapidly on admission	45 (9%)
Unfit for endoscopy	35 (7%)
Specifically categorized as terminal care patients	32 (6.4%)
Self-discharging prior to endoscopy being undertaken	9 (1.8%)
Refused or whose family refused to consent to endoscopy	7 (1.4%)
Specific contraindication to endoscopy	7 (1.4%)
Incomplete procedure due to agitated patient	5 (1%)
Unsuccessful esophageal intubation	2 (0.4%)

Total = 142.

Table 3 Endoscopic findings among cirrhotic patients with acute UGI hemorrhage.

Endoscopic finding	Incidence (%)
Varices	224 (62.6%)
Peptic ulcer	62 (17.3%)
Multiple lesions	19 (5.3%)
Portal hypertensive gastropathy	15 (4.2%)
Variceal treatment site ulcer	12 (3.4%)
No lesion found	10 (2.8%)
Mucosal erosions	7 (2%)
Esophagitis	4 (1.1%)
Vascular ectasias	3 (0.8%)
Gastric polyps	2 (0.6%)

Total = 358.

hemodynamic data, initial hemoglobin level, resuscitative efforts (blood transfusion requirement), Child status and Rockall score. The endoscopic components of the database included identification of the time to endoscopy, bleeding lesion and endoscopic therapy. Outcome measures were rebleeding within five days of endoscopy, complications (organ failure), the need for intervention (re-endoscopy, endoscopic therapy) and mortality. The cause of death and the time interval (in hours) between endoscopy and death was determined. In patients with multiple admissions for acute VH, each admission was treated separately. In case of death in the second or subsequent admission, the patient's data were analyzed as 'survivor' in the initial admission(s) and as 'deceased' in the last admission.

The relationship between various clinical parameters at admission to mortality was assessed. The parameters were: gender, age, patient condition at the time of bleeding, presence of ascites, hepatocellular carcinoma, other comorbidity, Child class, presenting symptom, hemodynamic status, hemoglobin level, transfusion need, time to endoscopy, blood in UGI tract at the index endoscopy, source of bleeding, endoscopic therapy, Rockall risk score, rebleeding within five days of endoscopy and in-hospital complications. Univariate and multivariate analyses were performed on the data. Eighteen variables were studied and included in a multivariate analysis using a logistic regression model.

2.1. Statistical analysis

The data were registered, tabulated and analyzed statistically using a program of SPSS version 15. Data on quantitative variables are presented as mean and (SD), and numbers and percentages are reported for qualitative variables. Differences between the proportion of survivors and deceased were assessed by using chi-squared. Variables with a P value of <0.05 on univariate analysis were included in step-wise multiple logistic regression analysis to identify independent risk factors for mortality. Wald statistics was used to assess the importance of each variable in the model, with P values <0.05 taken as significant.

3. Results

A total of 224 patients were analyzed. Sixty-three percent were male and 37% female. Ages ranged from 20 to 87 years, mean 53 ± 10 years. One hundred and sixty-three patients (73%) aged <60 years. Sixty-five patients (29%) had a history of smoking. Seventy-one patients (32%) were taking aspirin or non-steroidal anti-inflammatory drugs and two (1%) anticoagulants. Three patients (1%) were consuming alcohol. Two hundred and twelve patients (95%) were emergency admissions and 12 (5%) were inpatients at the time of bleeding. Cirrhosis was newly diagnosed during hospitalization for VH in 22 patients (10%) and had been previously diagnosed in 202 (90%). The presenting symptoms were hematemesis in 139 patients (62%), melena in 27 (12%) and both in 58 (26%). One hundred and eighty-five patients (83%) were hemodynamically stable at admission and 39 (17%) were hemodynamically unstable. Ninety patients (40%) had cirrhosis alone and 134 (60%) had cirrhosis and ascites. Thirty-three patients (15%) had concomitant hepatocellular carcinoma. Forty-nine patients (22%) were Child class A, 78 (35%) class B and 97 (43%) class C. Co-morbidities other than liver cirrhosis are shown in Table 4. The mean hemoglobin concentration was 8 ± 2 g/dl and 44% had initial hemoglobin less than 7 g/dl. One hundred and fifty-four patients (69%) required blood transfusion and the average number of transfused blood units was three.

All patients underwent emergency endoscopy during admission. The mean time from presentation to endoscopy was 23 ± 22 h (30 min–168 h). Endoscopy was conducted within 24 h of presentation in 170 patients (76%). Endoscopy was delayed more than 24 h in 54 patients (24%). The most

Table 4 Co-morbidities other than liver cirrhosis in patients with acute variceal hemorrhage.

Co-morbidity	Incidence (%)
Diabetes mellitus	95 (42.4%)
COPD* ± respiratory failure	26 (11.6%)
Hypertension	16 (7.1%)
Ischemic heart disease	9 (4%)
Arrhythmia	5 (2.2%)
Prosthetic valve replacement	2 (0.9%)
Asthma	2 (0.9%)
Pneumonia	1 (0.4%)
Tuberculosis (under treatment)	1 (0.4%)

* Chronic obstructive pulmonary disease.

Table 5 Factors related to mortality among patients with acute VH.

Factors	Deceased (n = 19) n (%)	Survival (n = 205) n (%)	P value
Gender			
Male	13 (9%)	129 (91%)	0.635
Female	6 (7%)	76 (93%)	
Age			
<60 years	14 (9%)	149 (91%)	0.924
$\geqslant 60$ years	5 (8%)	56 (92%)	
Patient condition at the time of hemorrhage			
Inpatients	2 (17%)	10 (83%)	0.296
Emergency admissions	17 (8%)	195 (92%)	
Ascites			
Liver cirrhosis alone	4 (4%)	86 (96%)	0.076
Liver cirrhosis and ascites	15 (11%)	119 (89%)	
Hepatocellular carcinoma			
Liver cirrhosis alone	14 (7%)	176 (93%)	0.157
Liver cirrhosis and hepatocellular carcinoma	5 (15%)	29 (85%)	
Child class			
Class A	1 (2%)	48 (98%)	0.004
Class B	3 (4%)	75 (96%)	
Class C	15 (15%)	82 (85%)	
Other comorbidity			
Liver cirrhosis alone	5 (6%)	83 (94%)	0.226
Liver cirrhosis and other comorbidity	14 (10%)	122 (90%)	
Presenting symptoms			
Hematemesis	14 (10%)	125 (90%)	0.488
Melena	1 (4%)	26 (96%)	
Hematemesis and melena	4 (7%)	54 (93%)	
Hemodynamic status			
Stable	11 (6%)	174 (94%)	0.003
Unstable	8 (21%)	31 (79%)	
Hemoglobin levels			
<7 gm/dl	7 (7%)	91 (93%)	0.526
$\geqslant 7$ gm/dl	12 (10%)	114 (90%)	
Transfusion needed			
Transfusion needed	15 (10%)	139 (90%)	0.316
No blood transfusion	4 (6%)	66 (94%)	
Time to endoscopy			
Within 24 h	16 (9%)	154 (91%)	0.376
More than 24 h	3 (6%)	51 (94%)	
Blood in UGI tract at the index endoscopy			
Blood in UGI tract	17 (13%)	115 (87%)	0.005
No blood in UGI tract	2 (2%)	90 (98%)	
Source of bleeding			
Esophageal varices	13 (7%)	164 (93%)	0.236
Gastric varices	6 (13%)	41 (87%)	
Endoscopic therapy applied			
Injection sclerotherapy	15 (12%)	108 (88%)	0.006
Band ligation	2 (2%)	92 (98%)	0.001
Both	2 (29%)	5 (71%)	
Rockall risk score			
Score 3–5	5 (4%)	118 (96%)	0.009
Score 6–8	14 (14%)	87 (86%)	

(*continued on next page*)

Table 5 *(continued)*

Factors	Deceased (n = 19) n (%)	Survival (n = 205) n (%)	P value
Rebleeding within 5 days of endoscopy			
Rebleeding	11 (48%)	12 (52%)	0.000
No rebleeding	8 (4%)	193 (96%)	
In-hospital complications			
Complications	8 (32%)	17 (68%)	0.000
No complications	11 (6%)	188 (94%)	

Total = 224.

Table 6 Significant predictor variables for mortality.

Significant factors	OR*	95% CI**	AOR†	95% CI	P value
Hemodynamic status					
Stable	4.1	10.9 + 1.5	5.5	22.3 + 1.4	0.017
Unstable					
Child class					
Class A	5.6	17.5 + 1.8	5.9	24 + 1.5	0.013
Class B					
Class C					
Blood in UGI tract					
Blood in UGI tract	0.15	0.7–0.03	12.8	126.5 + 1.3	0.03
No blood in UGI tract					
Rockall risk score					
Score 3–5	3.8	10.9–1.3	1.4	6.9 + 0.2	0.7
Score 6–8					
Endoscopic therapy					
Injection sclerotherapy	6.4	28.7 + 1.4	0.15	2.5 + 0.01	0.155
Band ligation					
Both					
Rebleeding within 5 days					
Rebleeding	0.45	0.1–0.01	25.4	109.2 + 5.9	0.000
No rebleeding					
In-hospital complications					
Complications	0.12	0.3–0.04	23.4	122.5 + 4.5	0.000
No complications					

Total = 224.
* OR = odds ratio.
** CI = confidence interval.
† AOR = adjusted odds ratio.

common reasons for delay were unavailable staff or equipment in 28 patients, admission during weekends or holidays in 17, hemodynamic instability in five and medical condition (chronic obstructive pulmonary disease with respiratory distress and asthma) in four. One hundred and seventy-seven patients (79%) bled from esophageal varices and 47 (21%) from gastric varices. Blood in UGI tract was detected at the index endoscopy in 132 patients (59%). The mean full Rockall score was five and 101 patients (45%) had Rockall score six to eight.

All patients received endoscopic therapy at the time of initial endoscopy. Injection sclerotherapy was performed in 123 patients (55%), band ligation in 94 (42%) and both in seven (3%). Injection sclerotherapy with ethanolamine oleate solution was used to treat 82 patients (37%), tissue adhesive (histoacryl) in 32 (14%) and both in 16 (7%). Initial hemostasis was achieved in 201 patients (90%) and 23 (10%) had rebleeding during the same admission. Seventeen patients (8%) had therapy at a subsequent endoscopy for further bleeding. Complications were reported in 25 patients (11%) during the same hospitalization. The most frequent complications were encephalopathy (5%), ascites (5%) and acute myocardial infarction (1%). Two hundred and five patients (92%) were discharged improved and 19 (8%) died within the first two weeks of their hospital admission. The time interval from endoscopy to death ranged from 15 min to 288 h, mean 42 ± 70 h. Death was caused by continuing bleeding in 11 patients (5%), associated complications (mainly organ failure)

in four (2%), co-morbid disease (cardiac arrest) in two (1%) and endoscopy was considered a possible cause (sedation related complications in patients with major co-morbidity) in two (1%). Univariate and multivariate analyses of variables in relation to mortality are shown in Tables 5 and 6.

4. Discussion

VH is a major complication of cirrhosis and portal hypertension, and is responsible for considerable morbidity and mortality. In recent years, improvements in patient management, including the use of terlipressin, prophylactic antibiotics, variceal band ligation and trans-jugular intrahepatic portosystemic shunts, have resulted in a decline in in-hospital mortality.[13–17] Though the mortality rate has decreased with advances in the management of VH, it continues to be unacceptably high.[17] Mortality in acute VH has decreased to current levels by only approximately 20%.[18]

One of the most challenging topics for physicians in their approach to the management of cirrhosis is the evaluation of their patients' prognosis. Those with cirrhosis who have VH are at a substantially higher risk of mortality so the identification of factors that influence prognosis should be helpful in planning their management. The factors that predict prognosis however vary between studies.[17] One of the difficulties with predicting prognosis is that outcome is influenced not only by the severity of the bleeding episode itself, but also by the severity of the underlying liver disease.[18] Currently, there is no well-established model for the accurate prediction of survival in patients with cirrhosis following an episode of acute VH.[18] The aim of this study was to determine the predictors of mortality in patients admitted to our hospital with acute UGI hemorrhage who underwent endoscopy and confirmed to have VH.

Our in-hospital mortality rate of 8% is consistent with the experience of other centers. Studies reported that in-hospital mortality in cirrhotic patients admitted with acute VH ranged from 7.4% to 14.2%.[17,19,20] However, in other studies, the rate of mortality was at least 20% at 6 week in patients with acute VH.[3,21] During the study period, 9% of cirrhotic patients admitted to our hospital with acute UGI hemorrhage died rapidly after admission without having undergone an endoscopy due to continued bleeding or rebleeding. Endoscopy was performed on the morning of the second day and not on admission, so patients who died before performing the endoscopy were not included in the analysis. The mean time from admission to death was six hours (range 25 min–18 h). The future plan is to perform endoscopy as soon as the patients have been resuscitated.

Univariate and multivariate analyses of variables in relation to mortality were performed. Eighteen variables were studied and included in the analysis. Five variables were independent predictors of death: the hemodynamic instability at admission, Child class C, blood in UGI tract at the index endoscopy, rebleeding within five days of endoscopy, and in-hospital complications. Rebleeding within five days of endoscopy and in-hospital complications were the most significant.

Mortality was related to the severity of bleeding episode as expressed by hemodynamic instability at admission and presence of blood in UGI tract at the index endoscopy. Our results are in line with previously published data.[17,22,23] Energetic resuscitation and early endoscopy might improve the prognosis of these patients.

Mortality was related to the severity of liver dysfunction as expressed by Child classification. The effectiveness of Child classification as a predictor of in-hospital death in cirrhotic patients with acute VH proved to be similar to that reported in other studies.[22–25] The different statuses of liver cirrhosis had different prognosis in terms of progression toward death. This might help inform patients of the risks of potential outcomes.

Mortality was related to the occurrence of rebleeding within five days of endoscopy and in-hospital complication. Our results are in line with previously published data.[17,22,24] In hospital rebleeding and complications played a highly significant role for stratification of patients with high mortality. Both occurred after admission which indicates that prognosis may change from day to day. This necessitates intensive monitoring of cirrhotic patients with acute VH during hospitalization and further improvement to control bleeding might still improve the prognosis of these patients.

Mortality was high in patients with a high risk Rockall score. Surprisingly, patients with a high Rockall score had a higher risk of mortality in univariate analysis while the risk of mortality was not significant in multivariate analysis. A high Rockall score was not an independent risk of mortality in our patients. The Rockall risk assessment score was devised to allow prediction of the risk of rebleeding and death in patients with UGI hemorrhage.[26] Only 4.4% of patients included in the initial study had esophageal varices, and analysis was not performed according to the etiology of bleeding.[27] The objective of the Rockall score was to predict patient poor clinical outcomes. It was also validated in many other settings, but with diverse conclusions.[26] Some authors reported good prediction for re-bleeding, but poor prediction for death while the others reported the opposite directions.[26]

Endoscopic therapy applied was effective in controlling VH in 90% of patients. It was reported that endoscopic therapy was effective in controlling VH in 84% and 90% of patients in two studies.[18,25] Mortality was high when endoscopic therapy applied was injection sclerotherapy. Injection sclerotherapy was commonly performed in patients with severe hemorrhage. Hemodynamic instability at admission and blood in UGI tract at the index endoscopy were significantly associated with the injection sclerotherapy. The risk of mortality with injection sclerotherapy was significant in univariate analysis and not significant in multivariate analysis. Endoscopic therapy applied was not an independent risk of mortality.

Eleven variables were not predictive of mortality: gender, age > 60 years, inpatients at the time of bleeding, presence of ascites, concomitant hepatocellular carcinoma, other comorbidity, presentation with hematemesis, initial hemoglobin less than 7 g/dl, transfusion need, delay to endoscopy more than 24 h and source of bleeding. Most of these risk factors were identified as predictors of mortality from acute VH in published studies.[5,6,21]

The clinically and statistically important factors detected from this study allow for early identification of patients with acute VH who are at a substantially increased risk of death over the short term in Egypt. These patients may require care in more specialized units during the bleeding episode, intensive monitoring, energetic resuscitation, early endoscopy, various options to control bleeding and aggressive follow-up in the

immediate post-variceal bleed setting. Our hospital, like most governmental hospitals in Egypt, has limited resources so our findings can be generalized to the broader community. Limitations of this study: etiology of the underlying liver disease, laboratory parameters and variceal size were not assessed. Additionally, the initial version of Child classification, which includes a subjective criterion (nutritional status), was used. Some patients whose individual values fall into different groups could not be properly categorized in this version. The study was not designed to collect the parameters necessary for the accurate calculation of the Child–Pugh score.

5. Conclusion

This study demonstrates that the hemodynamic instability at admission, Child class C, blood in UGI tract at the index endoscopy, rebleeding within five days of endoscopy and in-hospital complications were independent predictors of mortality after the acute VH episode with rebleeding within five days of endoscopy and in-hospital complications being the most significant. This study may guide clinicians to pay particular attention to patients with these risks. For future implications, these risk characteristics may be used in the process of VH risk stratification.

Conflict of interest

None declare.

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