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RESEARCH ARTICLE

EARLY PREDICTORS OF OUTCOME IN BLEEDING OESOPHAGEAL AND/OR GASTRIC VARICES IN THE EMERGENCY DEPARTMENT

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Abstract

Background and Objective: Acute upper GIT bleeding is a life threatening emergency. Many scoring systems have been developed to evaluate patients with acute UGIB. The purpose of this study was to confirm value of Modified Blatchford scoring system, Full rockall score, AIM65 score & lactate level as a predictor of outcome as regard patient's mortality, their need for ICU, duration of hospitalization and need for endoscopic intervention in the emergency department.

Patients and Methods: This study was performed on 100 patients who presented to the emergency department with acute UGIB in Alexandria main university hospital. All the study scores (GBS, AIMS65, PRS, and FRS) were able to predict the clinical outcomes in the UGIB patients.

Results: GBS was the best performing risk score among the four scores for predicting all the clinical outcomes except the prediction of endoscopic intervention. Lactate was a sensitive predictor for ICU admission, hospital stay, rebleeding and mortality during first 48 hrs of admission in patients presenting with UGIB.

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Introduction:-

Gastrointestinal bleeding is a common medical emergency in ED and the primary care setting with high morbidity and mortality. The admissions of gastrointestinal bleeding patients in United Kingdom and United States have been estimated annually at up to 150 patients per 100000 populations with a mortality rate of 5%-10%.

Common causes of acute UGIB include peptic ulcer disease, variceal hemorrhage, neoplasms, and Mallory-Weiss tear. Other causes include esophagitis, gastritis and duodenitis, erosions, vascular ectasias and Dieulafoy's lesions.(1)

There are several risk scores that can be applied prior and without endoscopy, and particularly useful in the ED. The commonly used risk scores include the Glasgow-Blatchford Score (GBS), the Rockall score and the recent AIMS65 score. These scores use only pre-endoscopic criteria except the full Rockall score which included endoscopic data.(2)

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Lactate levels are commonly evaluated in acutely ill patients. Although most commonly used in the context of shock evaluation, lactate can be elevated for many reasons.

Elevated lactate is not clearly and universally defined but most studies use cut-offs between 2.0 and 2.5 mmol/L whereas “high” lactate has been defined as a lactate level > 4mmol/L in a number of studies.(3) Furthermore, the “normal value” may vary depending on the assay. The exact pathophysiology of elevated lactate in various conditions is likely multifactorial, patient-specific, and disease-specific. In general, lactate elevation may be caused by increased production, decreased clearance, or a combination of both.

Recent studies demonstrated that Lactate is a sensitive predictor of outcome for patients with UGIB(4,5&6).

Aim Of The Study:

The present study aimed primarily to confirm value of Modified Blatchford scoring system, Full Rockall score, AIM65 score & lactate level as a predictor of outcome as regard patient’s mortality, their need for ICU, duration of hospitalization and need for endoscopic intervention in the emergency department. While the secondary aim was to evaluate lactate for predicting outcomes of patients with UGIB in correlation to the modified Blatchford scoring system, Full rockall score & AIM65 score.

Patients and Methods:-

All 100 patients with acute upper gastrointestinal bleeding have presented to the emergency department in Alexandria Main University Hospital with acute variceal bleeding. Risk stratification was done using the AIMS65, Glasgow-Blatchford score (GBS), pre-endoscopy Rockall, and full Rockall scores. **The following data was assessed according to the above mentioned scores:**

1. Inpatient mortality,
2. Blood transfusion,
3. Endoscopic, radiologic, or surgical intervention,
4. Intensive care unit (ICU) admission,
5. Incidence of rebleeding
6. Duration of hospitalization.

The sensitivity and specificity of the scoring systems were calculated for each score and also for lactate clearance at presentation and after resuscitation.

Consequently Receiver Operating Curve was plotted and the area under curve (AUROC) was calculated for each score and compared.

Study design:

Prospective study

For each patient, the following data was collected through structured form:

1. Age and gender.
2. History of previous and current medical illness such as :
 - A)History of liver disease whether cirrhotic or not ,
Chronic liver disease is classified into Child–Pugh class A to C⁽⁷⁾.
 - B)History of previous endoscopy or any intervention used before.
3. History of medication used as a primary or a secondary prophylaxis (Beta blockers, proton pump inhibitors ,ACE inhibitors , NSAIDS) .
4. Symptoms on admission: hematemesis (coffee-ground or bloody vomitus), melena, Hematochezia, fresh bleeding per rectum (including duration and amount of bleeding), and syncope
5. Vital signs and mental status by Glasgow Coma Scale score.
6. Laboratory results including: complete ***blood picture, blood urea nitrogen (BUN), international normalized ratio of prothrombin time (INR) ,albumin, Sodium and Potassium and serum lactate level at presentation and after resuscitation by 24 hours .
7. ICU admission and the length of hospital stay⁽⁸⁾.
8. The clinical interventions including: blood transfusion(whether whole blood , packed RBC's and or fresh frozen plasma with the number of units),and the endoscopic ED treatments.
9. The clinical outcomes including: duration and place of hospital stay , morbidity ,mortality, endoscopic or surgical interventions and rebleeding.

Results:-

65% of the study cases were male patients and 35% were female patients.

Ages of patients included in the study ranged between 20-89 years old with mean 54.87 ± 19.56 ,

63% of patients were taking prescribed drugs before onset of presentation, and only 37% were not taking any medications at time of presentation.

Table 1 shows the Child Pugh Class of the studied cases. While table 2 shows descriptive analysis of the different risk scores used.

Table 3 compared the serum lactate level at presentation and after proper resuscitation. And finally table 4 describes the different outcomes of the patients included in the study.

Table (1):- Distribution of the studied cases according to child-Pugh (n = 100).

Child-Pugh	No.	%
A	19	19.0
B	40	40.0
C	41	41.0
Min. – Max.	5.0 – 15.0	
Mean \pm SD.	9.31\pm2.85	
Median (IQR)	9.0 (7.0 – 12.0)	

Table (2):- Descriptive analysis of the studied cases according to different Risk Scores (n = 100).

	Min. – Max.	Mean \pm SD.	Median (IQR)
Full Rockal	2.0 – 7.0	4.0 \pm1.54	4.0 (3.0 – 5.0)
Aims65	0.0 – 5.0	1.62\pm1.88	1.0 (0.0 – 3.0)
Modified Blatchford score	1.0 – 16.0	8.17\pm4.85	8.0 (3.0 – 13.0)

Table (3):- Comparison between serum lactate level at presentation and after resuscitation (n = 100).

Lactate level (mmol/L)	At presentation	After resuscitation
Min. – Max.	1.0 – 5.0	1.0 – 4.0
Mean \pm SD.	3.0 \pm 1.40	1.71 \pm 0.93
Median (IQR)	3.0 (2.0 – 4.0)	1.0 (1.0 – 2.0)

Table (4):- Distribution of the studied cases according to Follow up after 48 hours (n = 100).

	No.	%
Follow up after 48 hours		
Discharged from hospital	26	26.0
Discharged from ED	5	5.0
Internal medicine ward admission	34	34.0
ICU stay	13	13.0
Died	22	22.0

Discussion:-

Recent guidelines recommended risk assessment for early management of UGIB patients, and accurate stratification can help physicians to decide hospital admission or discharge, the level of care, appropriate interventions (medical, endoscopic, or surgical), and predicting possible adverse events, such as rebleeding or death. Many risk scores that combine clinical and endoscopic parameters have been emerged to serve as a decision guide for emergency physicians. This study aimed to evaluate and compare the performances of AIMS65, GBS, and CPS, FRS in predicting clinical outcomes in acute UGIB patients in the ED.

In addition the present study tried to formulate the use of lactate as a predictor for outcome of UGIB comparing its levels at time of presentation and after resuscitation.

In this study the overall mortality rate was (22%) within the duration of hospital stay starting from admission up to 48 hours.

Other studies such as Mokhtare et al (2016)⁽⁹⁾, Tang et al (2018),⁽¹⁰⁾ and Martinez-Cara et al (2016)⁽¹¹⁾ reported a mortality rate of (11.5%), (10.4%), and (9.4%), respectively during the same period.

The higher in – hospital mortality rate may be attributed to the severity of liver disease in the studied patients(41% Child Pugh Class C).

All the used scores in this study were statistically significant with P value < 0.05, the predictive accuracy and performance of the scores was assessed by the AUC value.

Comparing the power of the used scores to predict mortality, GBS then AIMS65 had the higher predictive value and the better performance with AUC of 0.80, and 0.76, while PRS and FRS demonstrated lower predictive accuracy with AUC= 0.69.

Similarly, Zhong et al (2016)⁽¹²⁾ reported in a prospective Chinese study prediction of mortality using GBS and AIMS65 showed AUC of 0.79 and 0.78 respectively with no significant difference. and Tang et al (2018)⁽¹⁰⁾ reported the AIMS65 and GBS outperformed both the PRS and PBS.

Current study also demonstrated the optimal cutoff value that maximized the ability to predict the mortality was 1 for AIMS65, 12 for GBS, 2.5 for PRS, and 6 for FRS.

The cutoff value of 1 or more in AIMS65 had high sensitivity 72% and specificity 64% and negative predictive value of 95% for high risk patients , while a value less than 1 can identify low risk patients for mortality consequently can be safely discharged from ED.

In GBS a value of 12 or more can identify high risk of mortality with a higher sensitivity 81% and specificity 71% and negative predictive value of 97% compared to AIMS65.

Regarding the need for blood transfusion the present study, GBS/ Modified Blatchford outperformed AIMS65 and RS (whether Pre –endoscopic or Full Rockall) with the highest predictive power (AUC=0.92) and the best performance, with the best cutoff value of 8 or more.

This finding is in consistence with almost all other studies: Martinez-Cara et al (2016),⁽¹¹⁾ Venkat et al (2017),⁽¹³⁾ Choe et al (2017),⁽¹⁴⁾ Alexandrino et al (2018)⁽¹⁵⁾ a study from Portugal reported superiority of GBS in predicting blood transfusion but in non-variceal bleeding patients only.

The GBS superiority to predict the need of blood transfusion could be explained by the fact, that it is the only score which included hemoglobin in its calculation where Hb is one of the most weighted variables within this score.

The current research demonstrated that GBS got the best performance for predicting rebleeding, with (AUC=0.81), then AIM65 with (AUC=0.77) and the lowest performance to PRS and FRS with (AUC of 0.70, 0.69 respectively). The optimal cutoff value for GBS is 11 and AIMS65 is 1.

In agreement with this research results, Yaka et al (2015)⁽¹⁶⁾ and Hyett et al (2013)⁽¹⁷⁾ reported both GBS and AIMS65 had similar accuracy for predicting rebleeding with no difference in performance. According to multiple retrospective and prospective studies.

The present study reported nearly same accuracy of the used scores in predicting the need for ICU admission with best performance to GBS with (AUC=0.86), then AIMS65 with (AUC=0.83), then PRS and FRS of (AUC=0.81) for both.

The best cutoff value was 11 for GBS and 1 for AIMS65. This result is consistent with a previous study; Hyett et al (2013)⁽¹⁸⁾ who reported both GBS and AIMS65 had similar accuracy for predicting ICU admission.

A cut-off value is important for every scoring system for predicting clinical outcomes and helping emergency physicians to identify the high and low risk patients, therefore, the optimal cutoff value in each score should be specified to increase the power of identifying the high risk patients.

Detection of serum Lactate level got a very important role in resuscitation patients in the ED especially those who are bleeding as in the case of our research- patients suffering from variceal bleeding.

Lactate is an available, rapid and cheap tool which helps the emergency physician predicting the adequacy of resuscitation and in- hospital mortality together with other parameters.

The etiology of elevated lactate is perhaps best studied in shock states. Contributing factors appear to include: hypoperfusion due to macro- and/or microcirculatory dysfunction, mitochondrial dysfunction (including potential lack of key enzymatic co-factors) and the presence of a hypermetabolic state, among others. Liver dysfunction may contribute to both increased production and decreased clearance, which becomes even more important in states of hypoperfusion.⁽²⁰⁾

In the present study Lactate level at time of presentation was compared to that after resuscitation in the ED. Lactate level was used as a predictor of outcome and in-hospital mortality for UGIB patients participating in the study. It was found that the higher the lactate level whether at presentation or after resuscitation the more the in-hospital mortality during first 48 hours after admission with AUC of 0.855 & 0.728 respectively; probability value for both is ≤ 0.001 & 95% C.I 0.929 & 0.857 respectively.

Figure (1):- ROC curve for different parameters to predict mortality:

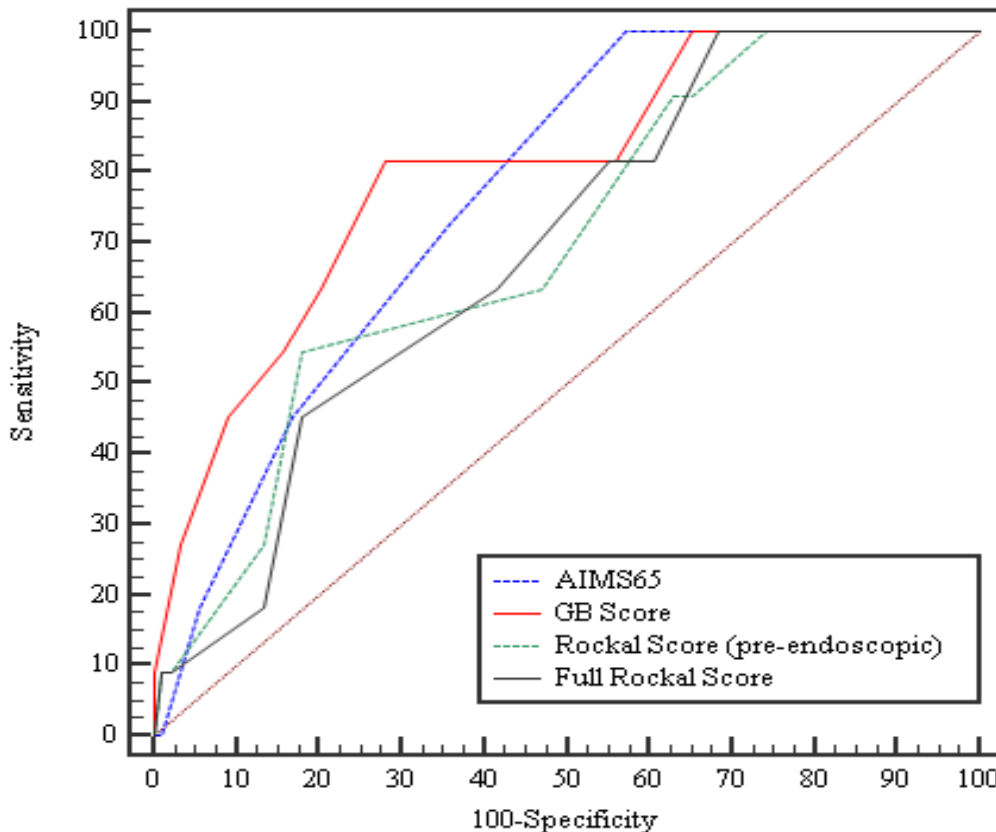


Figure (2):- ROC curve for Lactate to predict mortality:

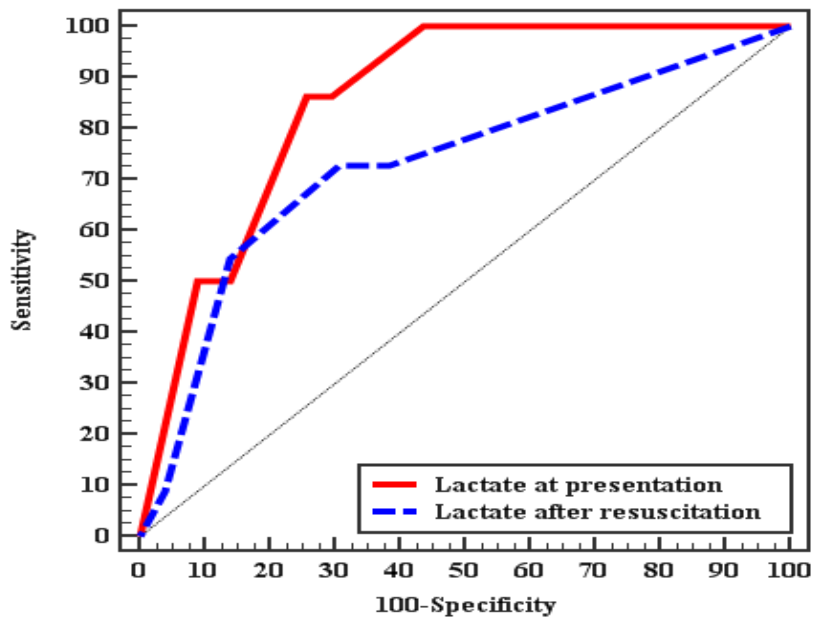
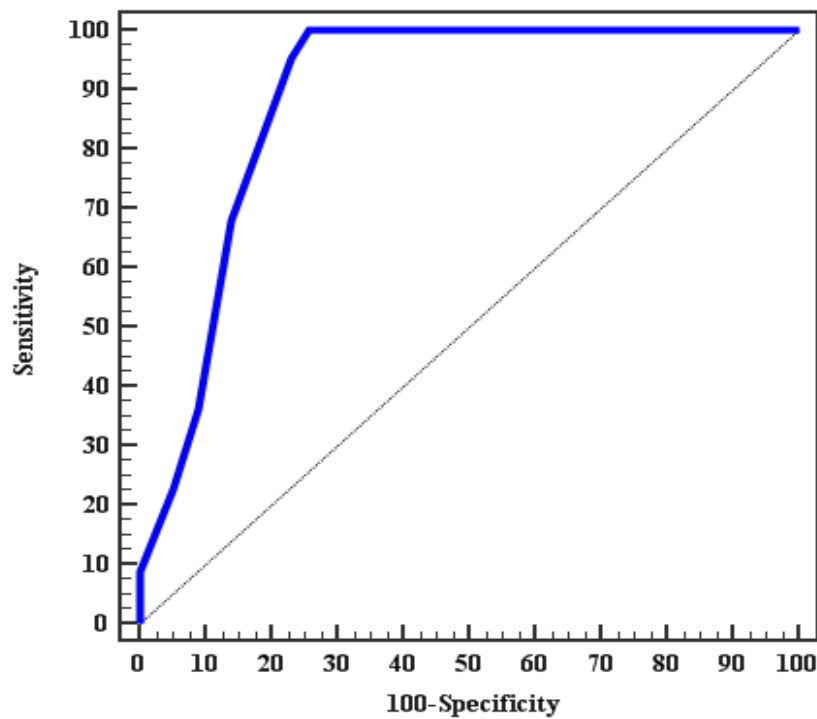


Figure (3):- ROC curve for Child-Pugh to predict mortality:



Conclusion:-

GBS is the best score to risk stratify patients with UGIB of variceal origin in the ED.

GBS outperformed other risk scores (AIMS65, PRS and FRS) in predicting the risk for in hospital mortality, rebleeding in addition to the duration of hospital stay.

Serum Lactate level before and after resuscitation is an important available cheap tool for monitoring resuscitation in patients with UGIB .

Lactate is a sensitive predictor hemodynamic instability , ICU admission and mortality during first 48 hrs of admission .

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Appendix1:

Abbreviations :

AIMS65: Albumin, INR, Mental status, Systolic blood pressure, Age

AUC : Area Under a Curve

CPS: Child- Pugh Score

ED : Emergency Department

FRS : Full Rockall score

GBS : Glasgow Blatchford score/**Modified Blatchford**

GCS : Glasgow Coma Scale

GERD : Gastro-esophageal reflux disease

Hb : Hemoglobin

HCC : Hepatocellular carcinoma

ICU : Intensive care unit

INR : International normalized ratio

NPV : Negative predictive value

NSAIDs: Non-steroidal anti-inflammatory drugs

P value : Probability value

PPV : Positive predictive value
RS/ PRS : Rockall score/ Pre-endoscopic Rockall Score
U/S: Ultrasonography
UGIB: Upper gastrointestinal bleeding
WBCs: White blood cells count

Appendix2:**RISK SCORES****Ø Child- Pugh**

- Encephalopathy: None = 1 point, Grade 1 and 2 = 2 points, Grade 3 and 4 = 3 points
- Ascites: None = 1 point, slight = 2 points, moderate = 3 points
- Bilirubin: under 2 mg/ml = 1 point, 2 to 3 mg/ml = 2 points, over 3 mg/ml = 3 points
- Albumin: greater than 3.5mg/ml = 1 point, 2.8 to 3.5mg/ml = 2 points, less than 2.8mg/ml = 3 points
- Prothrombin Time* (sec prolonged): less than 4 sec = 1 point, 4 to 6 sec = 2 points, over 6 sec = 3 points

*Frequently INR will be used as a substitute for PT, with INR under 1.7 = 1 point, INR 1.7 to 2.2 = 2 points, INR above 2.2 = 3 points

The severity of cirrhosis:

- Child-Pugh A: 5 to 6 points
- Child-Pugh B: 7 to 9 points
- Child-Pugh C: 10 to 15 points

Ø Full Rockall Score:

The FRS range is from 0 to 11, classifies the patients into three groups: (i) low-risk (score: 0–2); (ii) moderate risk(score: 3–7); and (iii) high risk (score: 8–11).

The PRS (range, 0–7) uses only clinical data available immediately at presentation, which are related to hemodynamics (pulse rate and systolic blood pressure) and to the patient (age and comorbidities)

The Full Rockall score.

Variable		Score			
		0	1	2	3
Age (years)		<60	60-79	≥ 80	
Shock	Pulse rate	<100	≥100	-	-
	Systolic BP	≥100	≥100	<100	-
Comorbidity		None	-	Cardiac failure, ischemic heart disease	Renal failure, liver failure, disseminated malignancy
Diagnosis		Mallory-Weiss tear, no lesion identified	All other diagnosis	Malignancy of upper GI tract	-
Endoscopic stigmata		No stigmata	-	Blood, adherent clot, spurting vessel	-
Range of score= 0-11.					

Ø The Glasgow Blatchford score classifies patients into two groups: (i) low risk (score: 0) which identifies low-risk patients who might be suitable for outpatient management, and (ii) high risk(score: >6) patients requiring interventions with high risk of rebleeding and mortality.

The Glasgow Blatchford score:

Variable	Score
Blood urea nitrogen level (mg /dl) ≥18.2 to <22.4 ≥22.4 to <28.0 ≥28.0 to < 70.0 ≥70.0	2 3 4 6
Hemoglobin level for men (g /dl) ≥12.0 to < 13.0 ≥10.0 to < 12.0 <10.0	1 3 6
Hemoglobin level for women (g /dl) ≥10.0 to < 12.0 <10.0	1 6
Systolic blood pressure (mmHg) ≥100to < 109 ≥90 to < 99 <90	1 2 3
Other markers Pulse rate ≥100 beats/min Presentation with melena Presentation with syncope Hepatic disease Heart failure	1 1 2 2 2
Range of score = 0-23	

Ø **The AIMS65 score** is a new risk stratification score introduced by Saltzman JR et al. for evaluating the prognosis of UGIB patients. It is based on only laboratory investigations commonly available in the ED and mental status of the patient. It does not require endoscopic data, and not relying on medical history

Each variable is given one point, and the score ranged from 0 to a maximum of 5. It classifies patients into two groups: (i) low-risk (score: 0–1); and (ii) high-risk (score: >1).

The AIM65 score.

Variable	Score
Albumin < 3.0(g/dL)	1
INR > 1.5	1
Altered mental status (Glasgow Coma score less than 14, disorientation, lethargy, stupor, or coma)	1
Systolic blood pressure ≤ 90 (mmHg)	1
Age ≥ 65 (yrs)	1
Range of score = 0–5	