The Egyptian Journal of Internal Medicine

RESEARCH

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Role of lactate level in predicting admission need to intensive care unit and short term outcomes in patients with acute gastrointestinal bleeding

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Abstract

Background One of the most common emergencies seen in emergency departments is acute gastrointestinal bleeding (GIB). It's associated with more disease burden and mortality.

Increased venous lactate levels are common in critically ill patients, and it has been used as a possible predictor of patients' outcomes in many critical cases, but not much is known about its predictive role in patients with acute GIB.

With increasingly limited health care resources, there has been such an interest in coast saving measures and measuring lactic acid through venous blood gases is such a simple bedside test which can be easily done to patients with acute GIB at emergency department.

Objective This study assessed the predictable value of lactate level on hospital admission on resource use, including length of hospital stay and admission to the intensive care unit (ICU), as well as other patient-oriented outcomes, including the need for blood transfusions and endoscopy.

Patients and methods A prospective cohort hospital based study that included 300 patients with acute GIB who presented to emergency department (ED) of Assiut University Hospital between September 2019 and June 2022 were subjected to venous blood lactate through venous blood gases.

Results The current study enrolled 300 patients with acute GIB. Two hundred of those patients had elevated blood lactate and 100 patients had normal blood lactate. It was found that patients with elevated blood lactate had significantly prolonged hospital stay (7.38 days ± 2.05 days vs. 3.96 days ± 1.74 days; ($P < 0.001$). Also they had higher frequency of blood transfusion (98% vs. 72%), ICU admission (95% vs. 67%) and mortality (9% vs. 3%) in comparison to those with normal lactate level.

Conclusion It was found that venous lactate level is an effective predictor for patient's outcomes among patients with acute GIB.

Keywords Acute gastrointestinal bleeding, Venous, Lactate, Outcomes

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Introduction

Acute gastrointestinal bleeding (GIB) is one of the most frequent conditions seen in emergency department (ED); and is considered a life-threatening condition [1]. It could be divided into two broad categories; upper and lower sources of bleeding. Upper gastrointestinal bleeding (UGIB) is extra common place than lower gastrointestinal bleeding (LGIB) [2]. With a prevalence of 67/100,000 population and accounts for 75% of all patients with GIT bleeding while that of LGIB is roughly 36/100,000 population and accounts for 20–30% [3]. Peptic ulcer disease account for 40–50% of the potential causes of UGIB, erosive esophagitis 11%, duodenitis 10%, varices 5–30%, Mallory Weiss tears 5–15%, and vascular malformation 5% [4]. The most common causes of lower GIB in patients younger than 50 years are anorectal diseases specifically hemorrhoids, inflammatory bowel disorders and non-steroidal anti-inflammatory drugs (NSAIDs) use should be evaluated also in lower GIB. Post-polypectomy is more common among patients aged more than 65 years [5].

Identifying high and low risk individuals is frequently the basis of the initial clinical care decision for patients with acute GIB who are presenting to the ED. Low-risk patients may be considered for early hospital discharge or even outpatient management, whereas high-risk patients with negative outcomes like recurrent bleeding or death are more likely to benefit from early aggressive management [6], such as intensive care unit admission for monitoring hemodynamically instable patients, interventions (upper and lower endoscopy, surgical interventions or angioembolization) and blood transfusion.

Lactic acid is an organic molecule whose conjugate base, lactate, is vital in many metabolic processes [7]. Araki and Zillessen noticed that when they interrupted oxygen supply to mammals' muscles, lactic acid was formed and increased. In current practice, normal lactate levels are < 2mmol/L; lactate is evaluated to indicate tissue hypoxia. Increased lactate levels, however, can reflect more than just tissue hypoxia, given its metabolism and the influence of acute sickness on glucose metabolism [8]. Measurements of lactate levels were considered a vital predictor of mortality in cases of sepsis, trauma and cancer [9].

In individuals with acute GIB, a reduction in circulating blood volume and consequent tissue hypoxia may also contribute to elevated blood lactate [10]. Additionally, it may appear even before other common clinical symptoms as hypotension [9].

Therefore, lactate appears to be beneficial for those with acute GIB. Early detection of high-risk patients may aid in identifying those who need quicker measures such as urgent endoscopic care. Rapid identification of critically ill individuals with acute GIB can help to avoid negative clinical consequences.

Aim of the study

This study was designed to assess whether blood lactate on hospital admission is predictive for need of interventions and short term outcomes among patients with acute GIB.

Patients and methods

This prospective cohort study included patients who presented to emergency department of Assiut University Hospital with acute GIB between September 2019 and end of June 2022, after obtaining approval from the Medical Ethics Committee, Faculty of Medicine, Assiut University, (approval code: 17/00999).

Inclusion criteria

All adult patients (aged ≥ 18 years old, from both sex) who presented with acute GIB, inclusive of both upper and lower GIB were included in the current study.

Exclusion criteria

Patients who were known to have tumors which may cause bleeding, patients with post-procedure or post-surgical site bleeding, patients who presented with an active systemic infection or who had just undergone cardiopulmonary resuscitation, patients with chronic seizures and convulsions were excluded from the current study.

Patients presenting with acute GIB to ED of Assiut University Hospital were subjected to the following

Data collection

Patient's characteristics including patient's age, sex, and associated comorbidities. Detailed clinical history including history of prior GIB bleeding, use of NSAID, use of anticoagulants, use of aspirin, bright blood per rectum, melena, and hematemesis.

Methods

Patients presenting with acute gastrointestinal bleeding to emergency department of Assiut University hospital were subjected to blood lactate level through venous blood gases by collecting peripheral blood samples by venipuncture using Cobas 6000 fully automated analyzer (roche diagnostics).

Normal lactate levels are less than 2 mmol/L, with hyperlactatemia defined as lactate levels between 2 and 4 mmol/L, severe levels of lactate are 4mmol/L or higher.

Laboratory investigations

And laboratory data as initial hemoglobin level, complete blood count, international randomized ratio (INR), liver function tests and kidney function tests were also done.

Intensive care unit admission, in-patient procedures (upper endoscopy, colonoscopy, angioembolization and surgical interventions) and needed amount of packed red blood cell transfusion were assessed as outcomes. The length of hospital stay was compared between both studied groups.

Sample size

Our study included 200 patients with acute GIB and elevated blood lactate and 100 patients with acute GIB and normal blood lactate by using sample size equation which is =

$$\frac{\frac{z^2 \times p\,(1-p)}{e^2}}{1 + \left(\frac{z^2 \times p\,(1-p)}{e^2 N}\right)}$$

N = population size
Z = z-score, which is 95% = 1.96
e = margin of errors (5%)
p = standard of deviation

According to the equation 300 patients with acute GIB were included in the study and were evaluated for lactate level through blood gases.

Statistical analysis

SPSS (statistical package for the social sciences, version 20, IBM, Armonk, New York) was used to analyze the data. Normal distributed quantitative data were expressed as mean ± standard deviation (SD) and compared using the student t-test. Nominal data were given as a number (n) and percentage (%). Chi2 test was implemented on such data. The level of confidence was kept at 95% and hence, the *P*-value was considered significant if < 0.05.The multivariate regression analysis was used to identify various risk factors for mortality among patients with upper GI hemorrhage.

Results

The present study enrolled 300 patients with acute gastrointestinal bleeding (GIB). Out of those patients; 200 patients had elevated blood lactate and 100 patients had normal blood lactate.

The mean age of the studied patients with elevated lactate was significantly higher in comparison to those with normal lactate (61.30 years ± 10.72 years vs. 46.14 years ± 15.91 years, ($P < 0.001$).

Table 1 Baseline data of the studied patients

	Blood lactate level		*P* value
	Normal (*n* = 100)	Elevated (*n* = 200)	
Age (years)	46.14 ± 15.91	61.30 ± 10.72	**< 0.001**
Sex			0.34
Male	71 (71%)	136 (68%)	
Female	29 (29%)	64 (32%)	
Diabetes mellitus	28 (28%)	42 (21%)	0.11
Hypertension	32 (32%)	51 (25.5%)	0.14
Liver cirrhosis	62 (62%)	120 (60%)	0.41
ESRD	34 (34%)	60 (30%)	0.28
IHD	4 (4%)	16 (8%)	0.58
No comorbidities	28 (28%)	4 (2%)	**< 0.001**

Data expressed as number (percentage) or mean ± SD. *P*-value considered significant if < 0.05; *ESRD* end stage renal disease, *IHD* ischemic heart disease

Table 2 Risk factors for gastrointestinal bleeding among enrolled patients

	Blood lactate level		*P* value
	Normal (*n* = 100)	Elevated (*n* = 200)	
Smoking	15 (15%)	25 (12.5%)	0.33
Use of NSAIDs	26 (26%)	8 (4%)	**< 0.001**
Use of anticoagulant	3 (3%)	5 (2.5%)	0.53
Use of aspirin	12 (12%)	20 (10%)	0.36
History of UGIB	32 (32%)	140 (70%)	**< 0.001**

Data expressed as number (percentage). *P* value considered significant if < 0.05. *NSAIDs* non-steroidal anti-inflammatory drugs, *UGIB* upper gastrointestinal bleeding

Liver cirrhosis and end stage renal disease (ESRD) presented in 62 patients (62%) and 34 patients (34%) with normal lactate and presented in 120 patients (60%) and 60 patients (30%) with elevated lactate, respectively (Table 1).

No significant differences were observed between both groups regarding risk factors for bleeding as smoking (15 cases (15%) vs. 25 cases (12.5%)) ($P = 0.33$), use of anticoagulants (26 cases (26%) vs. 8 cases (4%);) ($P = 0.53$) and use of aspirin (12 cases (12%) vs. 20 cases (10%)) ($P = 0.36$). Use of NSAIDs was significantly higher among patients with normal lactate (26 cases (26%) vs. 8 cases (4%); ($P < 0.001$), while history of UGIB was significantly higher among patients with elevated lactate (140 cases (70%) vs. 32 cases (32%)) ($P < 0.001$) (Table 2).

Both studied groups had no significant differences regarding to different endoscopic findings and intervention. The most frequent endoscopic findings in both groups were esophageal varices, portal hypertensive gastropathy and bleeding ulcer either at the stomach or duodenum.

Angioembolization was performed in 6 patients (6%) with normal lactate and 9 patients (4.5%) with elevated lactate, respectively. While surgical intervention was performed in two patients with normal lactate and three patients with elevated lactate level (Table 3).

Patients with elevated lactate had significantly prolonged hospital stay (7.38 days ± 2.05 days vs. 3.96 days ± 1.74 days) ($P < 0.001$). Also, patients with elevated lactate had significantly higher frequency of blood transfusion (196 cases (98%) vs. 72 cases (72%); ($P < 0.001$), ICU admission was among (67 cases (67%) vs. 190 cases (95%); ($P < 0.001$) and also mortality (3 cases (3%) vs. 18 cases (9%); ($P = 0.04$) in comparison to those with normal lactate level (Table 4, Fig. 1).

It was found that lactate had significant positive correlation with leucocytes ($r = 0.35$, $p = 0.01$) and CRP ($r = 0.40$, $p < 0.001$) and significant negative correlation was found with hemoglobin level ($r = -0.65$, $P < 0.001$). All other correlations were non-significant ($p > 0.05$) (Table 5, Fig. 2).

It was found that lactate level was significantly higher among dead patients in comparison to those who were alive (12.83 mmol/l ± 3.98 mmol/l vs. 4.20 mmol/l ± 2.23 mmol/l);($p < 0.001$) (Table 6).

Table 4 Length of hospital stay and outcome among both studied groups

	Blood lactate level		*P* value
	Normal ($n = 100$)	Elevated ($n = 200$)	
Hospital stay (days)	3.96 ± 1.74	7.38 ± 2.05	**< 0.001**
Blood transfusion	72 (72%)	196 (98%)	**< 0.001**
ICU admission	67 (67%)	190 (95%)	**< 0.001**
Mortality	3 (3%)	18 (9%)	**0.04**

Data expressed as number (percentage), or mean ± SD. *P*-value considered significant if < 0.05. *ICU* intensive care unit

Discussion

Acute gastrointestinal bleeding (GIB) is a common place critical condition that is seen in emergency department. The annual incidence of upper GIB in Egypt is nearly 100 patients per 100,000 and it's about 4 times as common as lower GIB [11]. Numerous scoring systems, including Glascow Blatchford score (GBS), Rockall score, and AIM65 score, have been established to predict the results of UGIB, these scoring systems used endoscopic results which are not always available at the time of initial assessment [12]. So the need for risk scoring systems that uses clinical and laboratory data maybe more helpful at the time of initial assessment [13]. Lactate level has been used in the prediction of severity of the disease and risk estimation in many different illnesses [7], such as lactate area score which is the sum of the area under the curve of serial lactate levels from repeated measurements using the trapezoidal rule, divided by the time interval, which is used to predict mortality among septic shock patients in the ED [14]. But not much is known about its role in patients with acute GIB [15]. With increasingly limited health care resources, there has been such an interest in coast saving measures and measuring lactic acid through venous blood gases is such a simple bedside test which can be easily done to patients with acute GIB at crowded

Table 3 Endoscopic findings and interventions among the studied groups

	Blood lactate level		*P*
	Normal ($n = 100$)	Elevated ($n = 200$)	
Endoscopic findings			
Gastroesophageal varices	62 (62%)	120 (60%)	0.41
PHG	47 (47%)	107 (53.5%)	0.17
Gastric ulcer	27 (27%)	53 (26.5%)	0.51
Duodenal ulcer	14 (14%)	23 (11.5%)	0.32
Angiodysplasia	12 (12%)	34 (17%)	0.16
Mallory Weiss syndrome	5 (5%)	3 (1.5%)	0.08
Dieulafoy lesion	2 (2%)	0	0.11
Endoscopic hemostasis			0.54
Band ligation/histoacryl injection	62 (62%)	120 (60%)	
Endoscopic clips	8 (8%)	10 (5%)	
Adrenaline injection	25 (25%)	67 (33.5%)	
APC	5 (5%)	3 (1.5%)	
Angioembolization	6 (6%)	9 (4.5%)	0.19
Surgical intervention	2 (2%)	3 (1.5%)	0.07

Data expressed as number (percentage). *P* value considered significant if < 0.05. *PHG* Portal hypertensive gastropathy, *APC* argon plasma coagulation

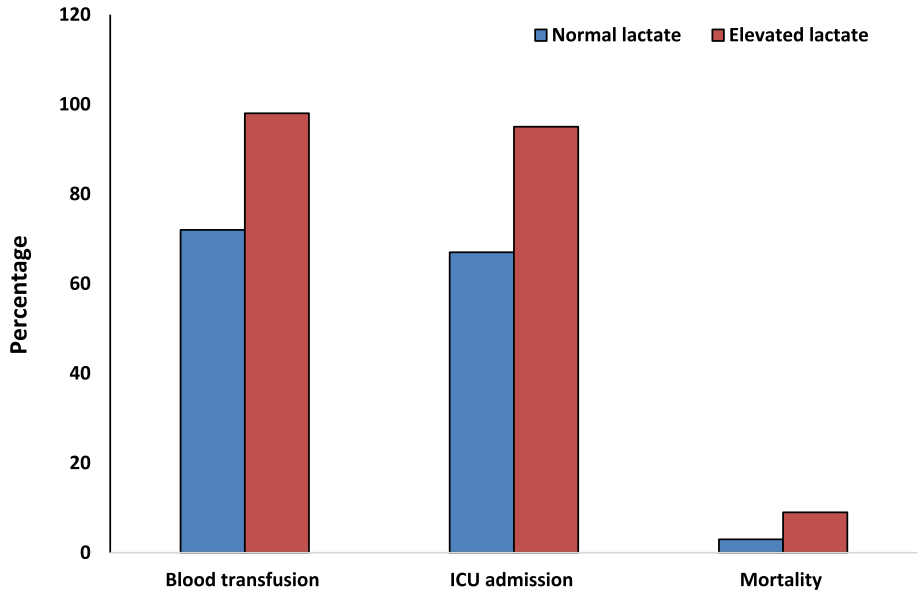

Fig. 1 Outcome among enrolled patients

Table 5 Correlation of blood lactate with other variables in the current study

	r value	*P* value
Age (years)	0.09	0.54
Hemoglobin (g/dl)	**-0.65**	**< 0.001**
Platelets count (10^3/ul)	0.13	0.32
Leucocytes (10^3/ul)	**0.35**	**0.01**
Bilirubin (mg/dl)	0.08	0.21
Albumin (g/dl)	0.21	0.30
Aspartate transaminase (u/L)	0.22	0.06
Alanine transmarine (u/L)	0.01	0.31
INR	-0.21	0.34
Urea (mg/dl)	0.21	0.22
Creatinine (mg/dl)	0.22	0.41
C-reactive protein (mg/dl)	**0.40**	**< 0.001**
ESR (ml/hr)	0.12	0.97

Data expressed as *r* value (strength of correlation) and *p* value (significance of correlation). *P* value considered significant if < 0.05. *INR* international randomized ratio, *ESR* erythrocyte sedimentation rate

ED. This study examined whether blood lactate at hospital admission is predictable of the need for interventions and the short-term outcome among patients with acute GIB.

The current study enrolled 200 patients with acute GIB and elevated serum lactate level and 100 patients with acute GIB and normal serum lactate level. It was found that mean age was higher among those with elevated lactate (61.30 years ± 10.72 years vs. 46.14 years ± 15.91 years); ($P < 0.001$). Also, the frequency of no comorbidities was higher among those with normal lactate (28% vs. 2%). The use of NSAID was found to be more prevalent among patients with normal lactate (26% vs. 4%), while the history of prior GIB was higher among patients with elevated lactate (70% vs. 32% %; $P < 0.001$). It was found that the most frequent endoscopic findings in both groups were esophageal varices and portal hypertensive gastropathy. This was consistent with the most common cause of bleeding in our society that is secondary of gastroesophageal varices. This was in contrast to Gulen et al., who stated that the frequent endoscopic finding in their patients was duodenal ulcer 40.3% [16].

It was found that patients with elevated lactate had significantly prolonged hospital stay (7.38 days ± 2.05 days vs. 3.96 days ± 1.74 days), ($P < 0.001$), higher frequency of blood transfusion (98% vs. 72%; ($P < 0.001$), ICU admission was among (95% vs. 67%; ($P < 0.001$) and higher mortality rate (9% vs. 3%) in comparison to those with normal lactate level. Also, it was found that lactate level was significantly higher among patients who could not survive in comparison to those who survived (12.8 ± 3.98 vs. 4.20 ± 2.23; ($P < 0.001$).

According to Gulen et al., the mean venous lactate in patients who survived was 2.37 mmol/L and 4.80 mmol/L in dead patients [16]. Another study found that as serum lactate levels increased, death also increased. When evaluating mortality, lactate was shown to have a high sensitivity and low specificity [17]. Additionally, Shrestha et al. discovered that in patients with acute GIB, a high lactate level at presentation was an independent predictor of ICU admission, inpatient endoscopy, and

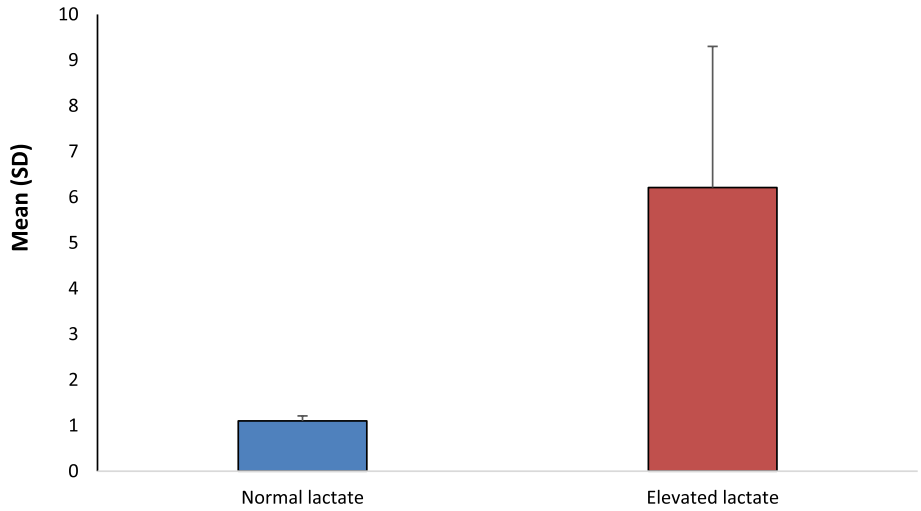

Fig. 2 Mean lactate level of studied patients in different groups

Table 6 Blood lactate based on mortality of the enrolled patients

	Mean (SD)
Outcome	
Alive	4.20 ± 2.23
Died	12.83 ± 3.98
***P* value**	**< 0.001**

Data expressed as mean (SD). *P* value was significant if < 0.05

RBC transfusion [15]. Based on this study, predictors of mortality among patients with acute GIB were old age (odd' ratio (OR) = 2.22), liver cirrhosis (OR = 1.34), elevated lactate level (OR = 3.02) and variceal bleeding (OR = 2.98).

The limitation of the study

However, the main limitation of the current study was that, it was a single-center based study. Thus, it is recommended that further larger multi-center studies to be done to provide reliable accurate results.

Conclusion

Findings of this study suggested that venous lactate level is an effective predictor for ICU admission, length of hospital stay, blood transfusion, interventions and mortality in patients with acute GIB.

Abbreviations

APC	Argon plasma coagulation
CI	Confidence interval
ED	Emergency department
ESR	Erythrocyte sedimentation ratio
ESRD	End stage renal disease
GBS	Glascow Blatchford score
GI	Gastrointestinal
GIB	Gastrointestinal bleeding
ICU	Intensive care unit
IHD	Ischemic heart disease
INR	International randomized ratio
LGIB	Lower gastrointestinal bleeding
NSAIDS	Non-steroidal anti-inflammatory drugs
OR	Odd ratio
PHG	Portal hypertensive gastropathy
RBC	Red blood cell
SD	Standard deviation
SPSS	Statistical package for social science
UGIB	Upper gastrointestinal bleeding

Acknowledgements
Not applicable.

Authors' contributions
Hekmat Nashat Shawky collected the data and prepared the manuscript. Zain Elabdeen Ahmed Sayed, Hossam Mahmoud Abdelwahab and Hala Mostafa Kamel revised the manuscript. All the authors approved the final manuscript.

Funding
None.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The Medical Ethics Committee, Faculty of Medicine, Assiut University approved the study protocol and waived the requirement for informed consent, since de-identified data were used, (Approval code: 17/00999). De-identifed data did not require patient informed consent to access.

Competing interests
The authors declare that they have no competing interests.

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Received: 5 September 2023 Accepted: 1 January 2024
Published online: 22 January 2024

Publisher's Note

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