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Diagnostic and Prognostic Value of Blood Lactate Level in Adult Acute Gastrointestinal Bleeding Patients Admitted to the Emergency Department

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Abstract

Objective: In our study, it was aimed to determine the diagnostic and prognostic value of lactate level in patients with gastrointestinal bleeding.

Methods: This study was performed by retrospective screening of the information of patients who applied to the tertiary education and research hospital with acute gastrointestinal bleeding. Data such as lactate level, age, gender, application complaint, known diseases, medications used, physical examination symptoms and findings, laboratory results, endoscopy and/or colonoscopy reports, treatment were collected and their effects on prognosis and mortality were evaluated.

Results: The median age of 506 patients included in the study was 67 (IQR: 53-80) and 61.3% of the patients were male. 87.5% of the patients were upper and 12.5% lower gastrointestinal bleeding. No relation was found between bleeding region and lactate level ($p=0.759$). The lactate level of patients who needed erythrocyte suspension, who underwent intensive care and died, was found to be high ($p<0.001$, $p=0.009$, $p<0.001$, respectively). When the test performance of lactate in predicting mortality was evaluated, the AUC value was calculated as 0.714 cm^2 according to the ROC curve ($p<0.001$). When the cut-off value was taken as 4 mmol/L, the sensitivity of lactate in predicting mortality was 29%, specificity was 91%, positive predictive value was 31%, negative predictive value was 90%, positive likelihood ratio was 3.22 and negative likelihood ratio was 0.78.

Conclusion: Lactate level is a test that can be used as a follow-up parameter in both upper and lower gastrointestinal system hemorrhage cases to confirm diagnosis and predict prognosis. In the cases with high lactate value, more hospitalization time, more erythrocyte suspension supplement requirement, increased risk of hospitalization and death were determined.

Keywords: Gastrointestinal bleeding, lactate, prognosis, mortality

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INTRODUCTION

Gastrointestinal system (GIS) bleeding has an important place among patients who applied to the emergency department (1,2). Its frequency is between 36 and 172 per 100,000 people (3). GIS hemorrhages are pathologies that develop suddenly and result in death if proper intervention is not performed. The mortality rate can go up to 30-40% (4).

Bleeding that originates above the ligament of Treitz is defined as upper GIS bleeding, and 80% of bleeding occurs in this area. In 80% of GIS bleeding cases, bleeding stops spontaneously and 20% require intervention. 20% of all GIS bleeding patients, apply to the hospital with recurrent attacks and surgical intervention is planned in 15-30% of these recurrent bleeding (4-7).

Lactate is a biomarker of hypoperfusion that can be measured from arterial blood as well as from venous blood. It has focused on the relationship of morbidity as well as mortality in emergency and intensive care patients and has been a useful biomarker in predicting the risk of death (8,9).

Foreseeing the prognosis in these patients will contribute to clinicians in terms of treatment efficacy. In our study, we determined the diagnostic and prognostic value of lactate level in patients with GIS bleeding.

METHODS

The study was conducted by retrospectively scanning the information of patients in the tertiary education and research hospital emergency department for 2 years, after the approval of the local ethics committee (B.10.1.TKH.4.34.H.GP.0.01/66). Patient data were obtained from the hospital automation system.

Patients' sex, age, application complaint, known heart and liver diseases, known malignancy, antiaggregant, anticoagulant, and nonsteroidal anti-inflammatory drugs used, arrival arterial blood pressure and pulse rate per minute, pre-existing GIS bleeding presence, blood gas lactate value, the amount of hemoglobin (Hgb) and hematocrit (Hct) in the first hemogram taken, urea and creatinine values, endoscopy and colonoscopy findings, the amount of erythrocyte suspension (ES) need during the patient's stay in hospital, and mortality were evaluated.

According to the results of the screening of the hospital data processing system, patients who were over 18 years of age who had melena, hematemesis, or hematoquesia on physical examination were determined to have no bleeding other than GI bleeding or were diagnosed with gastrointestinal bleeding by endoscopy and colonoscopy. Patients under the age of 18 years, pregnant patients, and patients with missing physical examination, history, and laboratory data were excluded from the study.

Statistical Analysis

After all the data was collected, the program called SPSS for Windows® 16.0 was used. The conformity of the data to normal distribution was tested with the Kolmogorov-Smirnov test. Continuous data that did not conform to the normal distribution were expressed as median and percentile slices, and those that did not conform were expressed as mean and standard deviation. Student's t-test was used to compare the data that fit the normal distribution, and the Mann-Whitney U test was used to compare those that did not. The chi-square test was used to compare categorical data, and Fisher's Exact test was performed where appropriate. The diagnostic value of lactate level for predicting mortality was evaluated by ROC analysis. In the analyses, $p<0.05$ value was accepted as statistically significant.

RESULTS

In the study 866 patients were evaluated as all GIS bleeding cases without discriminating between upper and lower GIS bleeding. Of these, 294 were excluded because of the lack of blood lactate level at the time of application, and 66 were excluded because of insufficiency in various other data, especially endoscopy and colonoscopy. As a result, 506 patients were included in the study.

In our study, the median age of the patients was 67 (IQR: 53-80) years and 310 (61.3%) were male. Of the patients, 443 (87.5%) had upper GIS bleeding and 63 (12.5%) had lower GIS bleeding. Other demographic data of the patients are shown in Table 1.

The median lactate level in our study was 1.8 mmol/L (IQR: 1.3-2.7); the lactate level of 311 (61.5%) of the cases was above the reference (minimum: 0.5-maximum: 1.6) values. The median lactate level in upper GIS bleeding was 1.8 mmol/L (1.3-2.7), and the median lactate level in lower GIS bleeding was 1.8 mmol/L (1.3-2.4). There was no statistical difference between the groups ($p=0.759$) (Figure 1).

Three hundred eighty six (76.3%) of the patients needed ES. The median lactate level in patients who required ES was 1.9 mmol/L (IQR: 1.3-2.88), and the median lactate level in patients without ES requirement was 1.6 mmol/L (IQR: 1.1-2.2). The lactate level of patients who were given ES was found to be significantly higher ($p<0.001$).

Nine of the patients (1.8%) were discharged from the emergency service, while 475 (93.8%) were hospitalized. Twenty-two

patients (4.4%) were admitted to the intensive care unit or died in the emergency service. The lactate median level of patients discharged was 1.3 mmol/L (IQR: 1.1-1.7), the lactate median level of patients hospitalized in the service was 1.8 mmol/L (IQR: 1.3-2.7), and the lactate median level of patients hospitalized in intensive care was 2.55 mmol/L (1.7-4.77). There was a statistically significant difference between these 3 groups in terms of lactate levels (Kruskal-Wallis, p=0.008), and in the post hoc evaluation,

Table 1. Basic descriptive data of patients

			Upper GIS bleeding (n=443) median (IQR)/n (%)	Lower GIS bleeding median (IQR)/n (%)
Age			66 (50-80)	72 (63-80.5)
Sex	Male		277 (62.5)	33 (52.4)
	Female		166 (37.5)	30 (47.6)
Symptoms	Melena		258 (58.2)	2 (3.2)
	Hemathemesis		236 (53.3)	0
	Hematoquesia		28 (6.3)	59 (93.7)
	Dizziness		54 (12.2)	1 (1.6)
	Shortness of breath		15 (3.4)	1 (1.6)
	Syncope		54 (12.2)	5 (7.9)
	Chest pain		3 (0.7)	0
Additional disease and drug use	Liver disease		68(15.3)	6 (9.5)
	Heart disease		125(28.2)	25 (39.7)
	A history of malignancy		72(16.3)	13(20.6)
	Previous GI bleeding		122(27.5)	10(15.9)
	Antiagregan use		108 (24.4)	15 (23.8)
	Anticoagulant use		52 (11.7)	12 (19)
	NSAID use		(24.4)	4 (6.3)
Endoscopy (n=473)	Ulcer		246 (52.0)	
	Forrest classification	1a	22 (9)	
		1b	21 (8.5)	
		2a	22 (9)	
		2b	20 (8.1)	
		2c	25 (10.1)	
		3	136 (55.3)	
	Gastritis		281 (59.4)	
	Varicosis		66 (14.0)	
	Mallory weiss		10 (2.1)	
	Mass in the upper GIS		54 (11.4)	
	Erosion		75 (15.9)	
	Esophagitis		60 (12.7)	
Colonoscopy (n=87)	Normal			6 (9.5)
	Mass			12 (19)
	Hemoroid			15 (23.8)
	Diverticulum			17 (27)
	Polyp			7 (11.1)
	Ulcer			14 (22.2)
	Angiodysplasia			2 (3.2)

GIS: Gastrointestinal system

the number of patients who were admitted to intensive care were significantly higher than that in the other groups.

There was no correlation between lactate level and creatinine, platelet count and forrest classification (p=0.094, p=0.243, p=0.148, respectively). Lactate level was found to have a weak negative correlation with systolic blood pressure, diastolic blood pressure, Hgb, and Htc value (r=-0.174, r=-0.114, r=-0.123, r=-0.124, respectively) ; and a weak positive correlation with pulse rate, urea, amount of ES given, and duration of hospitalization (r=0.185, r=0.172, r=0.201, r=0.093, respectively) (Table 2).

It was determined that 62 (0.3) of the patients died. The lactate median value of patients who died was 2.7 mmol/L (IQR: 1.7-4.2), and the lactate median value of those living was 1.7 mmol/L (IQR: 1.2-2.5). The lactate level of the patients who died was found to be significantly high (p<0.001).

In our study, the area under the curve was found to be 0.714 cm^2 (Figure 2). When the cut-off value of lactate is taken as 4 mmol /L, the test performance results in predicting mortality are as follows: sensitivity, 29%; specificity, 91%; positive predictive value, 31%; negative predictive value, 90%; positive likelihood ratio, 3.22; and negative likelihood ratio, 0.78. The sensitivity and specificity values of lactate for different cut-off values are given in Table 3.

Table 2. Relationship of lactate level with vital signs, laboratory parameters, ES requirement, forrest stage and number of days of hospitalization in all GIS bleeding

Groups	R	p
Systolic blood pressure	-0.174	<0.001
Diastolic blood pressure	-0.114	<0.001
Pulse (beats/min)	0.185	<0.001
Creatinine	0.074	0.094
Urea	0.172	<0.001
Hemoglobin	-0.123	0.006
Hematocrit	-0.124	0.005
Platelet	-0.052	0.243
Erythrocyte need	0.201	<0.001
Forrest stage	-0.069	0.148
Duration of hospitalization	0.093	0.037

Min: Minimum, GIS: Gastrointestinal system

DISCUSSION

In our study, the median value of the lactate level was 1.8 mmol/L in accordance with the literature, and in 61.5% of the cases, the lactate level exceeded the reference level. In studies in the literature, similar to our study, it was stated that lactate level increased in patients with GIS bleeding, and this situation developed due to hypoperfusion and hypoxia (10-12). Shrestha et al. (13) stated that a single venous lactate level provides clinically useful information in patients with acute

Table 3. Sensitivity and specificity of lactate in predicting mortality at different cut-off values

Cut-off values for lactate	Sensitivity (%)	Specificity (%)
2 mmol/L	71	64
4 mmol/L	29	91
6 mmol/L	19	97

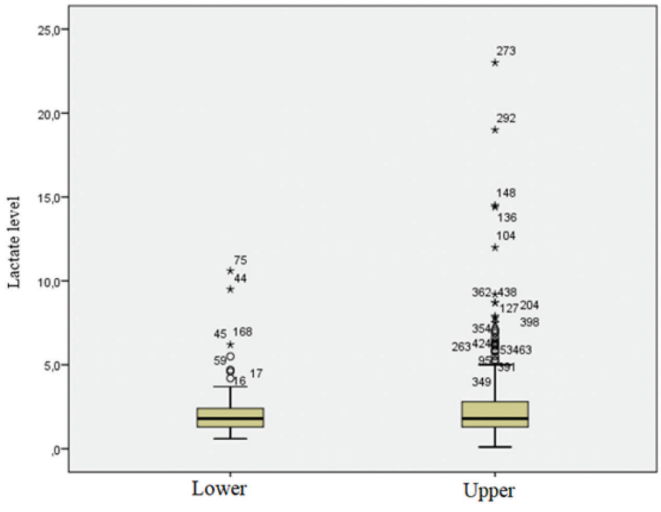

Figure 1. Comparison of lactate levels in upper and lower GIS bleeding
GIS: Gastrointestinal system

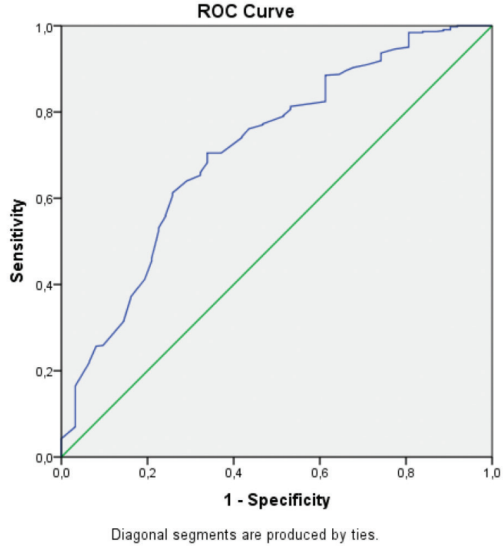

Figure 2. ROC curve of lactate for mortality in all GIS bleeding patients
GIS: Gastrointestinal system

GIS bleeding and is an important parameter in the planning of treatment.

In our study, the mortality rate was found to be 12.3% in line with the literature, and it was shown that this rate increased to 23% according to some study results (14,15). The lactate levels of patients who died were found to be higher, and when the lactate threshold value of 4 mmol/L for mortality was taken, it was observed that they had similar specificity and sensitivity with other studies (15-18). In other studies, they concluded that serum lactate levels are better than prognostic indicators, such as the Rockall or Glasgow-Blatchford systems, physiological triage criteria, such as heart rate, blood pressure, Glasgow coma scale, and respiratory rate (19,20). Although it was determined in our study that high lactate levels contributed significantly to predicting mortality, we believe that it is not reliable to estimate prognosis with lactate level alone because the test performance results are not strong enough. However, when used with other prognosis indicators, we believe that lactate levels is a very useful marker in the follow-up of patients with GI bleeding.

In our study, no difference was found between the upper and lower GIS bleeding lactate levels. Similarly, Kollef et al. (10) also stated that lactate levels increased in all GIS bleeding cases,and lactate levels were similar in upper and lower GIS bleeding. We believe that the lactate level in GIS bleeding is related to hypoxia caused by the amount of bleeding rather than the bleeding focus.

Some studies in the literature have stated that the lactate level is correlated with the severity of the lesion and may indicate rebleeding (11,12). However, in our study, no significant relationship was found between Forrest classification and lactate level. The data to explain the reason of this condition have not been determined in our study, and we believe that factors such as mild and chronic losses in the cases do not give symptoms unless they reach serious rates, and rapid intervention to serious lesions may have led to this result.

Shah et al. (16) reported that there was no relationship between lactate, pulse rate, and Htc in their study in patients with GIS bleeding. Ko et al. (21) stated that high serum lactate level can predict hypotension in patients with GIS bleeding. In their study in GIS bleeding cases, Shrestha et al. (13) stated that patients with high and normal lactate levels had similar heart rate and blood pressures, and patients with high lactate levels had low Hgb. In our study, it was determined that lactate level had negative and weak correlations with blood pressure, Hgb, and Hct, and positive and weak correlations with pulse rate and urea.

Previous studies have shown a relationship between blood transfusion and mortality and length of hospital stay (13,19,22,23). Although Kollef et al. (10) reported in their study that there is a similarity between the lactate level and the need for ES, Ayık et al. (10,24) reported that they did not find a significant relationship between the two in their studies. In our study, it was determined that 76.3% of the patients needed ES, the median value of ES requirement was 3 units, the lactate level of patients with ES requirement was high, and there was a positive correlation between the amount of ES delivered and the lactate level. This may be related to the amount of blood lost from the body, leading to a decrease in the amount of blood flowing to the tissues and thus to hypoxia.

Study Limitations

The main limitation of this study is that it was designed retrospectively. The second important limitation is the deficiencies in patient anamnesis and the fact that the lactate intake time of the patients is unknown. Again, we believe that the fact that the study was single-centered reduces the generalizability, while the relatively high number of patients increases the reliability of the study results.

CONCLUSION

As a result, lactate level is a parameter that can be used in conjunction with other clinical and laboratory markers and is effective in determining prognosis in patients with GIS bleeding. In the cases with high lactate value, more hospitalization time, more ES supplement requirement, and increased risk of hospitalization and death were determined.

Ethics

Ethics Committee Approval: The study was conducted by retrospectively scanning the information of patients in the tertiary education and research hospital emergency department for 2 years, after the approval of the local ethics committee (B.10.1.TKH.4.34.H.GP.0.01/66). Patient data were obtained from the hospital automation system.

Informed Consent: A retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.A.K., G.A., Ö.B., S.E.E., Concept: H.A.K., G.A., S.E.E., Design: H.A.K., G.A., S.E.E., Data Collection or Processing: H.A.K., Ö.B., Analysis or Interpretation: G.A., Literature Search: H.A.K., Ö.B., Writing: H.A.K., G.A., Ö.B., S.E.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol 1997;92:419-24.
2. Keçeci M, Sevinç C, Kayataş K, Koçhan K, Şahin A, Demirtaş Z et al. The correlation between leukocytosis and the severity of bleeding in patients with acute nonvariceal upper gastrointestinal system bleeding. Turk J Acad Gastroenterol 2014;13:7-12.
3. Hreinsson JP, Kalaitzakis E, Gudmundsson S, Björnsson ES. Upper gastrointestinal bleeding: incidence, etiology and outcomes in a population-based setting. Scand J Gastroenterol 2013;48:439-47.
4. Jaka H, Koy M, Liwa A, Kabangila R, Mirambo M, Scheppach W, et al. A fibreoptic endoscopic study of upper gastrointestinal bleeding at Bugando Medical Centre in northwestern Tanzania: a retrospective review of 240 cases. BMC Res Notes 2012;5:200.
5. Åhsberg K, Höglund P, Staël von Holstein C. Mortality from peptic ulcer bleeding: the impact of comorbidity and the use of drugs that promote bleeding. Aliment Pharmacol Ther 2010;32:801-10.
6. Paspatis GA, Konstantinidis K, Chalkiadakis I, Tribonias G, Chlouverakis G, Roussomoustakaki M. Changing trends in acute upper gastrointestinal bleeding in Crete, Greece: a population-based study. Eur J Gastroenterol Hepatol 2012;24:102-3.
7. Adler DG, Leighton JA, Davila RE, Hirota WK, Jacobson BC, Qureshi WA, et al. ASGE guideline: The role of endoscopy in acute non-variceal upper-GI hemorrhage. Gastrointest Endosc 2004;60:497-504.
8. Vincent JL, Quintairos E Silva A, Couto L Jr, Taccone FS. The value of blood lactate kinetics in critically ill patients: a systematic review. Crit Care 2016;20:257.
9. Revelly JP, Tappy L, Martinez A, Bollmann M, Cayeux MC, Berger MM, et al. Lactate and glucose metabolism in severe sepsis and cardiogenic shock. Crit Care Med 2005;33:2235-40.
10. Kollef MH, Canfield DA, Zuckerman GR. Triage considerations for patients with acute gastrointestinal hemorrhage admitted to a medical intensive care unit. Crit Care Med 1995;23:1048-54.
11. Wada T, Hagiwara A, Uemura T, Yahagi N, Kimura A. Early lactate clearance for predicting active bleeding in critically ill patients with acute upper gastrointestinal bleeding: a retrospective study. Intern Emerg Med 2016;11:737-43.
12. Lee SH, Min YW, Bae J, Lee H, Min BH, Lee JH, et al. Lactate Parameters Predict Clinical Outcomes in Patients with Nonvariceal Upper Gastrointestinal Bleeding. J Korean Med Sci 2017;32:1820-7.
13. Shrestha MP, Borgstrom M, Trowers EA. Elevated lactate level predicts intensive care unit admissions, endoscopies and transfusions in patients with acute gastrointestinal bleeding. Clin Exp Gastroenterol 2018;11:185-92.
14. Czernichow P, Hochain P, Nousbaum JB, Raymond JM, Rudelli A, Dupas JL, et al. Epidemiology and course of acute upper gastro-intestinal haemorrhage in four French geographical areas. Eur J Gastroenterol Hepatol 2000;12:175-81.
15. El-Kersh K, Chaddha U, Sinha RS, Saad M, Guardiola J, Cavallazzi R. Predictive Role of Admission Lactate Level in Critically Ill Patients with Acute Upper Gastrointestinal Bleeding. J Emerg Med 2015;49:318-25.
16. Shah A, Chisolm-Straker M, Alexander A, Rattu M, Dikdan S, Manini AF. Prognostic use of lactate to predict inpatient mortality in acute gastrointestinal hemorrhage. Am J Emerg Med 2014;32:752-5.
17. Lavery RF, Livingston DH, Tortella BJ, Sambol JT, Slomovitz BM, Siegel JH. The utility of venous lactate to triage injured patients in the trauma center. J Am Coll Surg 2000;190:656-64.
18. Shapiro NI, Howell MD, Talmor D, Nathanson LA, Lisbon A, Wolfe RE, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med 2005;45:524-8.
19. Koch A, Buendgens L, Dückers H, Bruensing J, Matthes M, Kunze J, et al. Ursachen, patientenspezifische Risikofaktoren und prognostische Indikatoren bei akuter gastrointestinaler Blutung und intensivmedizinischer Therapieindikation. Eine retrospektive Untersuchung der Jahre 1999-2010 [Bleeding origin, patient-related risk factors, and prognostic indicators in patients with acute gastrointestinal hemorrhages requiring intensive care treatment. A retrospective analysis from 1999 to 2010]. Med Klin Intensivmed Notfmed 2013;108:214-22.
20. Lavery RF, Livingston DH, Tortella BJ, Sambol JT, Slomovitz BM, Siegel JH. The utility of venous lactate to triage injured patients in the trauma center. J Am Coll Surg 2000;190:656-64.
21. Ko BS, Kim WY, Ryoo SM, Ahn S, Sohn CH, Seo DW, et al. Predicting the Occurrence of Hypotension in Stable Patients With Nonvariceal Upper Gastrointestinal Bleeding: Point-of-Care Lactate Testing. Crit Care Med 2015;43:2409-15.
22. Soncini M, Triossi O, Leo P, Magni G, Bertelè AM, Grasso T, Ferraris L, Caruso S, Spadaccini A, Brambilla G, Verta M, Muratori R, Attinà A, Grasso G. Management of patients with nonvariceal upper gastrointestinal hemorrhage before and after the adoption of the Rockall score, in the Italian Gastroenterology Units. Eur J Gastroenterol Hepatol 2007;19:543-7.
23. Odutayo A, Desborough MJ, Trivella M, Stanley AJ, Dorée C, Collins GS, et al. Restrictive versus liberal blood transfusion for gastrointestinal bleeding: a systematic review and meta-analysis of randomised controlled trials. Lancet Gastroenterol Hepatol 2017;2:354-60.
24. Ayık İC, Değerli V, Yılmaz G, Sevim E. Laktat Seviyesinin Üst Gastrointestinal Sistem Kanamalı Hastalarda Prognostik Amaçlı Kullanımı. Kafkas J Med Sci 2018;8:115–20.