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RESEARCH

Delta values as a prognostic marker in methanol poisoning: a retrospective cohort study

Metanol zehirlenmesinde prognoz belirteci olarak delta değerleri: retrospektif kohort çalışması

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Abstract

Purpose: The aim of the study was to evaluate the mortality prediction performances of delta bicarbonate, delta anion gap, and delta ratio in methanol poisoning (MP) cases.
Materials and Methods: This clinical study, which followed a cross-sectional study design, involved patients with MP who were still alive when they initially arrived at the emergency department of a tertiary care hospital. Patients were divided into two groups mortality and non-mortality. Patients who died during treatment and follow-up were assigned to the mortality group, while others were assigned to the non-mortality group. Receiver Operating Characteristic (ROC) analysis was used to determine the cut-off in the diagnostic value measurements of biomarkers predicting mortality.
Results: Nine (20%) of the 45 patients in the study died during their follow-up. The two groups showed a significant difference in the averages of pH, bicarbonate (HCO3-), lactate, anion gap, delta anion gap, delta HCO3-, and delta ratio, but not in the averages of partial carbon dioxide pressure (pCO2). In predicting mortality, pH, anion gap, and delta anion gap were found to have outstanding diagnostic power (AUC>0.9), while HCO3-, delta HCO3-, delta ratio were found to have acceptable diagnostic power (AUC: 0.7-0.8).
Conclusion: Delta anion gap, delta bicarbonate, and delta ratio can be used as prognostic factors in predicting mortality in MP cases.
Keywords:. Methanol poisoning, delta ratio, delta anion gap, delta bicarbonate, mortality

Öz

Amaç: Çalışmanın amacı metanol zehirlenmesi (MZ) vakalarında delta bikarbonat, delta anyon açığı ve delta oranının mortalite tahmin performanslarını değerlendirmektir.
Gereç ve Yöntem: Kesitsel bir çalışma tasarımına göre yapılan bu klinik çalışma, üçüncü basamak bir hastanenin acil servisine ilk geldiklerinde hala hayatta olan MZ'li hastaları içeriyordu. Hastalar ölenler ve sağ kalanlar olarak iki gruba ayrıldı. Tedavi ve takip sırasında ölen hastalar mortalite grubuna, diğerleri non-mortalite grubuna alındı. Mortaliteyi öngören biyobelirteçlerin tanısal değer ölçümlerinde eşik değeri belirlemek için Alıcı İşlem Karakteristiği (ROC) analizi kullanıldı.
Bulgular: Çalışmadaki 45 hastanın dokuzu (%20) takipleri sırasında öldü. İki grup, pH, bikarbonat (HCO3-), laktat, anyon açığı, delta anyon açığı, delta HCO3- ve delta oranı ortalamalarında önemli bir fark gösterdi, ancak kısmi karbondioksit basıncının (pCO2) ortalamalarında göstermedi. Mortaliteyi tahmin etmede pH, anyon açığı, delta anyon açığı üstün tanısal güce sahipken (AUC>0.9), HCO3-, delta HCO3-, delta oranının kabul edilebilir tanı gücüne sahip olduğu (AUC: 0.7-0.8) bulundu.
Sonuç: Delta anyon açığı, delta bikarbonat ve delta oranı MZ olgularında mortaliteyi öngörmede prognostik faktörler olarak kullanılabilir.

Anahtar kelimeler: Metanol zehirlenmesi, delta oranı, delta anyon açığı, delta bikarbonat, mortalite

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INTRODUCTION

Methyl alcohol, which is cheaper in cost than ethyl alcohol, is a toxic type of alcohol that has been used in the manufacture of illegal alcohol (smuggled alcohol, fake alcohol) recently and can cause death by causing very serious poisoning when consumed[1,2]. Methanol poisoning (MP) cases due to illicit alcohol consumption are encountered with increasing frequency in emergency services[2-4]. The "gold standard" for diagnosing methanol poisoning is the direct measurement of blood methanol by benchtop liquid (LC) or gas chromatography (GC)[5]. These tests that measure methyl alcohol levels are not available in most hospitals. This creates a serious diagnostic problem. Hence, history, clinical findings, and auxiliary tests guide emergency physicians in diagnosing. Several investigations have been carried out to find predictive indicators of methanol poisoning.

Methanol in the blood increases serum osmolality and osmolal space due to its high molar concentration. Methanol is metabolized in the human body first to formaldehyde and then to formic acid. Formic acid accumulation leads to high anion gap metabolic acidosis due to the formate's ability to inhibit mitochondrial respiration through its toxic effect on mitochondrial cytochrome c oxidase[6,7]. In MP cases, deep acidosis, increased anion gap, low HCO_3^-, high lactate, and hypercapnia are linked to a poor prognosis[1-6]. In addition, some prognostic factor research is ongoing. Delta bicarbonate is the difference between regular bicarbonate and measured bicarbonate. Delta anion gap (AG) is the difference between the calculated anion gap and the normal anion gap. The delta ratio is the ratio of the change in anion gap to the shift in bicarbonate. Delta ratio (delta AG/delta HCO_3^-) is used to detect co-existing acid-base disorders in patients with metabolic acidosis with high AG[8].

There is no clinical study to the authors' knowledge that evaluates the prognostic value of blood gas parameters delta bicarbonate, delta anion gap, and delta ratio for mortality in MP cases. Emergency physicians are constantly looking for non-invasive, reliable tools to predict life-threatening conditions in patients. The aim of this study is to evaluate the mortality prediction performances of delta bicarbonate, delta anion gap, and delta ratio in patients admitted to the emergency department due to MP.

MATERIALS AND METHODS

This study, which was conducted according to the retrospective cohort study design, included 45 patients diagnosed with MP who applied to the emergency department between February 28, 2020, and February 28, 2022. The study was approved, and the requirement for informed consent was waived by the Ethics Committee of the Istanbul Prof Dr Cemil Tascioglu City Hospital (ethics committee decision number: 2022/43 date: February 28, 2022). The study was performed in the department of emergency medicine, Istanbul Prof Dr Cemil Tascioglu City Hospital. All data collected during this study were kept confidential in terms of the reliability of the records and the confidentiality and privacy of the patients included in the study and were not shared anywhere. The present study was conducted in line with the Declaration of Helsinki.

Since methyl alcohol level measurement could not be performed in the hospital where this study was conducted, the diagnosis was generally made based on positive history, clinical findings, and blood gas values.

Sample

According to the retrospective cohort study design, the arterial pH value, which is the main outcome variable, was used to determine the reliability assessment (post-study power) of the number of patients included in the groups. While the arterial pH value was 6.87±0.15 in patients who died from methanol poisoning, it was 7.22±0.06 in patients who survived. According to the difference in the arterial pH levels between the independent group averages, the post-study power was 99%. According to the difference in the secondary outcome variables anion gap, delta anion gap, HCO3-, delta HCO3-, and delta ratio the post-study power was above 80%.

A total of 74 patients' medical records were retrieved. Inclusion criteria were 18 years of age or older, negative ethanol level, history of suspected methyl alcohol intake (unlabeled alcohol use, home-made alcohol consumption, multiple victims), suspicious symptoms (impaired vision, impaired consciousness, shortness of breath, chest pain, nausea, and vomiting), acid-base metabolism disorder suggestive of methyl alcohol poisoning in blood gas analysis (acidosis, increased osmolality, base, and anion gap: arterial pH < 7.3, serum HCO3- < 20 mEq/L, osmolal gap > 20 mOsm/L), and exclusion of other

metabolic acidosis causes that may create anion gap (metformin, uremia, diabetic ketoacidosis, paraldehyde, isoniazid, iron, lactate, ethylene glycol, salicylate)[9–11]. Forty-five patients fitted the inclusion criteria. Three of these 74 were excluded due to missing clinical exams or history data, three due to incomplete follow-up or referral to another center, four due to out-of-hospital mortality, and 19 due to positive ethyl alcohol level.

Study protocol

Data on patients diagnosed with methanol poisoning were obtained from emergency department patient registration forms and hospital information systems. Data were scanned retrospectively by emergency medicine specialists. Then, the collected data were audited by an independent emergency medicine specialist. Patients who were alive when they first arrived at the hospital were included in the study. Two independent observers reviewed the data, and patients were selected based on eligibility criteria. Patients were divided into two groups mortality and non-mortality. Patients who died during treatment and follow-up were assigned to the mortality group, while others were assigned to the non-mortality group. Patient's vital signs (blood pressure, heart rate, respiratory rate, oxygen saturation), consciousness level, blood gas parameters (ph, partial carbon dioxide pressure (pCO_2), bicarbonate (HCO_3^-), lactate, anion gap (AG), delta AG, delta HCO_3^-, delta ratio), complete blood count (white blood cell (WBC), hemoglobin (HGB), hematocrit (HTC), platelet (PLT) neutrophil/lymphocyte ratio (NLR)), biochemistry parameters (glucose (Glu), blood urea nitrogen (BUN), creatinine, sodium (Na), potassium (K), chlorine, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), lactate dehydrogenase (LDH), calcium, C-reactive protein (CRP), ethyl alcohol level, toxicological screening, cardiac marker (troponin I), coagulation parameter (international normalized ratio (INR), poisoning severity score (PSS), treatments given and mortality status were recorded. Laboratory examinations were taken within the first 60 minutes after patients presented to the emergency department. The osmolal gap (OG) in serum is the difference between measured osmolality (MO) and calculated osmolality and was calculated by the following equation[12].

Osmolality (Normal value is 285±10 mOsm/L)= (2xNa) + Glu/18 + BUN/2,8

Osmolal gap (OG) = measured osmolality – calculated osmolality

Blood gas analysis

Blood gas samples were analyzed with RAPIDPoint® 500 Blood Gas Systems (Siemens Healthineers). Blood gas parameters (pH, pCO_2, HCO_3^-, lactate, anion gap) were recorded. Serum anion gap (AG) was calculated with the suggested formulation (AG (Normal value is 8±4) = $Na^+ – (HCO_3^- + Cl^-)$[8,13]. The serum anion gap (AG) of those whose albumin level was outside the normal range was calculated as adjusted according to the recommendations[14]. Delta anion gap, delta bicarbonate, and delta ratio were calculated with the formulation suggested in the literature[8,15].

Delta AG = observed AG – upper normal value of AG (12 mEq/L)

Delta HCO_3^- = lower normal value of HCO_3^- (24 mEq/L) – observed HCO_3^-

Delta Ratio = Delta AG / Delta HCO_3^-

Mortality was considered the primary outcome. The patients were divided into two subgroups: non-mortality and mortality.

Statistical analysis

Parametric tests were used without the normality test due to the Central Limit Theorem compatibility[16]. However, since Glasgow Coma Scale Scale (GCS) is variable in ordinal structure, a non-parametric test was used. In the analysis of the data, the mean and standard deviation, minimum and maximum values of the features were used when making the statistics of the continuous data, and frequency and percentage values were used when defining the categorical variables. Student's t-test and Mann-Whitney U statistics were used to compare the means of two independent groups. Chi-square test statistics were used to evaluate the relationship between categorical variables. ROC (Receiver Operating Characteristic) analysis was used to determine cut-off measurements predicting mortality. Significance was determined by the statistics of Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV). ROC curves and 95% Confidence Interval values are given. The area under the curve (AUC) was used to decide the predictive power in the ROC analysis. An AUC of 0.5 to 0.6 was interpreted as poor, 0.6 to 0.7 as fair, 0.7 to 0.8 as acceptable, 0.8

to 0.9 as excellent, and greater than 0.9 as outstanding. The statistical significance level of the data was determined as p<0.05. The www.e-picos.com New York software and MedCalc statistical package program were used to evaluate the data.

RESULTS

After evaluating the inclusion and exclusion criteria, a total of 45 patients, 40 male (88.9%), were included in this study. While 36 (80%) of the patients were alive, 9 (20%) died. The mortality and non-mortality groups were statistically similar in sex and cranial findings (hemorrhage and edema). The two groups did not show significant differences in the mean of systolic blood pressure, heart rate, fever, sodium, albumin, calcium, BUN, ALT, CRP, INR, PLT, NLR, and pCO2 (p>0.05).

However, the two groups showed significant differences in the mean of age, PSS, intubation, diastolic blood pressure, oxygen saturation, respiratory rate, GCS score, glucose, creatinine, potassium, chloride, AST, LDH, leukocyte, hemoglobin, hematocrit, troponin I, lactate, anion gap, delta anion gap, pH, HCO3-, delta HCO3-, and delta ratio (p<0,05). The statistical evaluation of the relationship and difference of comorbidities, clinical findings, and sociodemographic characteristics according to mortality status is given in detail in table 1.

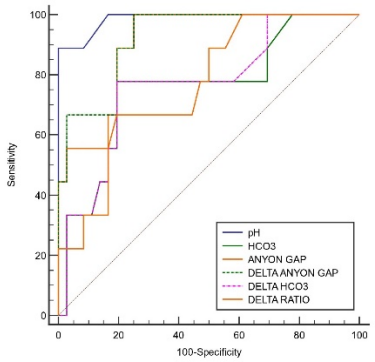

Figure 1. ROC curves of blood gas parameters in predicting mortality

pH: potential of hydrogen, **HCO_3^- :** bicarbonate

Table 1. Relationship and difference statistics of sociodemographical characteristics and biochemistry measurements with mortality

		Total (n=45)	Non-mortality (n=36)	Mortality (n=9)	
Descriptive Features		**$\bar{x}$±SD Min-Max**	**$\bar{x}$±SD Min-Max**	**$\bar{x}$±SD Min-Max**	**p-value**
Age		40.9±14.5 18-69	38.8±15 18-69	49.4±8.6 38-62	0.04
		n(%)	n(%)	n(%)	
Sex	Female	5(11.1)	4(11.1)	1(11.1)	0.99
	Male	40(88.9)	32(88.9)	8(88.9)	
PSS	1	9(20)	9(25)	-	<0.001
	2	22(48.9)	22(61.1)	-	
	3	14(31.1)	5(13.9)	9(100)	
Cranial Finding	Normal	43(95.6)	35(97.2)	8(88.9)	0.36
	Hemorrhage	1(2.2)	1(2.8)	-	
	Edema	1(2.2)	-	1(11.1)	
Intubation	none	34(75.6)	34(94.4)	-	<0.001
	there is	11(24.4)	2(5.6)	9(100)	
Vital signs					
Systolic Blood Pressure (mmHg)		119±15.71	120.14±10.95	114.44±28.33	0.34
Diastolic Blood Pressure (mmHg)		72.38±11.75	74.63±11.17	63.33±10	0.008
Heart Rate (Pulse/min)		85.1±23.4	82.1±15.3	96.7±42.4	0.1
Fever (°C)		36.67±0.17	36.65±0.19	36.73±0.05	0.23
SpO_2 (%)		90±9.9	94.1±4.1	73.4±8.9	<0.001

Respiration Rate (Respiratory/min)		18.9±5.7	20.9±4.4	10.9±1.1	<0.001
GCS		11.3±4.6	13.4±2.2	3±-	<0.001
Biochemistry					
Glucose (mg/dL)		128.27±44.41	115.25±30.22	180.33±55.11	<0.001
BUN (mg/dL)		13.86±6.66	13.72±5.86	14.45±9.64	0.77
Creatinine (mg/dL)		0.97±0.33	0.91±0.31	1.21±0.37	0.02
Sodium (mmol/L)		138.58±4.23	139.11±4.03	136.44±4.55	0.09
Potassium (mmol/L)		4.42±0.88	4.11±0.56	5.66±0.85	<0.001
Chlorine (mmol/L)		106±5.19	104.97±4.56	110.11±5.77	0.006
AST (U/L)		49.09±34.23	39.03±24.98	89.33±64.79	0.03
ALT (U/L)		28.6±16.03	26.66±17.98	36.33±14.76	0.32
LDH (U/L)		248.4±61.44	233.78±47.73	306.89±77.33	0.001
Calcium (mg/L)		8.92±0.68	8.95±0.53	8.78±1.12	0.5
CRP (mg/L)		8.13±7.13	6.38±5.37	15.01±11.32	0.1
Complete Blood Count					
WBC (10^3mcL)		11.04±3.29	10.26±3.14	14.11±1.76	0.001
Hemoglobin (g/L)		14.85±1.65	14.64±1.57	16.37±0.93	0.001
HTC (%)		44.96±4.88	43.72±4.44	49.94±3.11	<0.001
PLT (10^3mcL)		294.44±62.61	244.28±65.21	270.11±48.59	0.27
NLR		5.79±3.55	5.67±3.06	6.27±5.27	0.66
Coagulation Parameter					
INR		1.07±0.12	1.06±0.11	1.12±0.16	0.19
Cardiac Marker					
Troponin I (ng/mL)		0.02±0.01	0.01±0.001	0.04± 0.02	<0.001
Blood Gas Parameters					
pH		7.14±0.16	7.22±0.06	6.87±0.15	<0.001
pCO_2 (mmHg)		34.91±10.29	33.59±8.49	40.16±15.12	0.09
HCO_3^- (mEq/L)		8.42±2.78	8.95±2.66	6.38±2.39	0.01
Lactate (mmol/L)		5.98±1.35	5.22±1.26	6.74±1.5	0.05
Anion Gap (mEq/L)		27.13±3.76	25.95±2.99	31.83±2.71	<0.001
Delta Anion Gap (mEq/L)		15.16±3.78	13.95±2.99	20±2.55	<0.001
Delta HCO_3^- (mEq/L)		15.59±2.77	15.07±2.66	17.67±2.31	0.01
Delta Ratio		0.98±0.21	0.94±0.18	1.17±0.22	0.005

(p<0.05 significance) Student's t test. Mann-Whitney U. Chi-Square test

SD: standard deviation, Min:minimum. Max: maximum, PSS: poisoning severity score, SpO_2: oxygen saturation, GCS: Glasgow coma scale, BUN: blood urea nitrogen, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, LDH: lactate dehydrogenase, CRP: C-reactive protein, WBC: white blood cell, HGB: hemoglobin, HTC: hematocrit, PLT: platelet, NLR: neutrophil/lymphocyte ratio, INR: international normalized ratio, pH: the potential of hydrogen, pCO2: partial pressure of carbon dioxide, HCO_3^-: bicarbonate

In predicting mortality, pH, anion gap, delta anion gap were found to have outstanding diagnostic power (AUC>0.9), while HCO_3^-, delta HCO_3^-, and delta ratio were found to have acceptable diagnostic power (AUC: 0.7-0.8). Moreover, lactate had fair power to predict mortality (AUC: 0.68) (table 2, figure 1). In Table 2, the diagnostic accuracy of blood gas results used to predict mortality in methyl alcohol poisoning in ROC analysis is given in detail.

Table 2. Diagnostic accuracy of blood gas parameters in predicting mortality

Mortality:9 (%20) Non-Mortality: 36 (%80)	**AUC**	**Cut-off**	**Sensitivity%**	**Specificity%**	**AUC 95% CI**	**p value**	**PPV %**	**NPV%**
pH	0.99	≤6.99	88.89	98	0.89-0.99	<0.001	0.9	97.3
HCO_3^- (mEq/L)	0.76	≤7	77.8	80.6	0.61-0.87	0.01	60	93.5
Anion Gap (mEq/L)	0.91	>27.8	99	75	0.78-0.97	0.001	60	0.99
Delta Anion Gap (mEq/L)	0.92	>15.8	99	76	0.80-0.98	<0.001	62	99
Delta HCO_3^- (mEq/L)	0.77	>16.4	77.8	80.6	0.62-0.88	0.005	60	93.5
Delta Ratio	0.76	>1.07	70	82	0.63-0.89	0.002	62	90.6

pH: potential of hydrogen. HCO_3^- : bicarbonate

DISCUSSION

The study's significant new findings are that delta anion gap, delta bicarbonate, and delta ratio are valuable parameters in estimating mortality in adult patients diagnosed with methanol poisoning in the emergency department. This is, as far as we know, the first study in the literature in the literature to evaluate the relationship between delta values and mortality in methanol poisoning.

Despite effective treatment, methanol poisoning is associated with high morbidity and mortality[17,18]. In the study of Zakharov et al., the in-hospital mortality was 21%[19]. Mortality was 23% in the Estonian study, and 18% in the Norwegian study[7,20]. Mortality was 10.1% in the methanol poisoning epidemic that affected 768 people in Iran in September 2018[21]. Death rates of up to 30% have been reported in similar events worldwide[22]. This study was similar to the literature, with a 20% mortality rate.

Delta ratio is usually 1 in patients with uncomplicated high AG and acidosis. A value below 1 indicates a combined elevated and normal AG acidosis. A value above 2 suggests combined metabolic alkalosis and acidosis with high AG[23]. In this study, the delta ratio was 1.15±0.22 in patients who developed mortality, while it was 0.94±0.18 in patients who survived. In other words, there was a higher anion gap acidosis in patients who died. In addition, the delta ratio had acceptable diagnostic power in predicting mortality. In a study by Lipnick et al. in critically ill patients admitted to the intensive care unit, delta anion gap has the ability to predict 30-day mortality at a moderate level when compared with standard base excess and strong ion gap[24]. Xie et al. investigated the relationship between delta anion gap and mortality and 90-day survival of the patients in the 3-day follow-up of patients hospitalized in the cardiothoracic surgery intensive care unit. It was concluded that the delta anion gap was a predictor of mortality with 0.769 AUC[25]. It showed outstanding diagnostic power in our study when predicting mortality in delta anion gap MP patients (AUC: 0.92).

In the study of Gülen et al. high anion gap metabolic acidosis (pH < 7.07, AG > 26.7), low Glasgow Coma Score and elevated lactate (lactate > 2.55 mmol/L) levels were found to be associated with poor prognosis in methanol poisoning[1]. In a study examining the mass epidemic in the Czech Republic in 2012, the important parameters predicting mortality in patients poisoned with methanol were the severity of metabolic acidosis, state of consciousness, and serum ethanol at presentation[19]. Paasma et al. found that the severity of acidosis was an important prognostic factor in methanol poisoning[20]. In our study, patients who developed mortality were more acidotic, similar to the literature. On the other hand, Lactate had poor diagnostic power in predicting mortality. The cause of acidosis in the early period of methanol poisoning is the accumulation of formic acid. Since formic acid suppresses the use of oxygen in the tissues, lactic acid accumulation occurs[19]. It has been previously shown that the anion gap correlates well with formate and lactate level[7]. Thus, both formic acid and lactate contribute to increased anion gap and acidosis in methanol poisoning[12]. Zakharov et al. divided patients with methanol poisoning into three groups: those who recovered without sequelae, those who recovered with sequelae, and those who died. There was a significant difference in serum anion gap between those who recovered without sequelae and the other two groups[26]. In our study, the anion gap had outstanding diagnostic power in predicting mortality in line with the literature.

In the study of Arslan et al., the average was 12 in patients who experienced low bicarbonate levels, while it was 4 in patients who deceased[27]. Similarly, we found that bicarbonate levels were significantly lower in patients who developed mortality.

Increased pCO_2 has been associated with mortality in severely acidotic patients due to their inability to perform compensatory hyperventilation[17,20]. pCO_2 was higher in patients who developed mortality in this study, but it was insignificant.

A single-center study in Turkey reported that 95.5% of MP cases were male, and the mean age was 48.41±13.1[1]. In a retrospective study of MP cases from Norway (1979 and 2002-2005), Estonia (2001), Tunisia (2003/2004), and two different centers in Iran (Teheran 2004-2009 and Mashhad 2009), male gender more and the age group was found to be between 42-44[28]. Similarly, in this study, the male gender was higher, and the mean age was 40.9 years.

The poisoning severity score (PSS) is intended to be a general assessment of the case, considering severe clinical features. The Poisoning Severity Score grades the severity as (0) no, (1) minor, (2) moderate, (3) severe, and (4) fatal poisoning[29,30]. In prospective research by Casey et al., two of the five patients who

died had a PSS score of two, and three of them had a PSS score of three[30]. In a study by Zakharoz et al. in which methanol intoxication patients were followed up, patients with a PSS score of 3 were reported as severe intoxication[31]**.** In our study, all patients who developed mortality had a PSS score of 3, while only 13.9% of patients who survived had a PSS score of 3. That is, as expected, the PSS score was higher in patients who developed mortality significantly and in parallel with the literature.

This study has several limitations as it is a retrospective and single-center study. The laboratory results obtained at the first admission of the patients to the emergency department were analyzed, but the follow-up values were not included. The methanol levels of the patients are unknown since there is no test for measuring methanol levels in the blood. Furthermore, since the first exposure time of the cases with methanol is not known clearly, we do not know how long after the poisoning the laboratory parameters were analyzed. In addition, the small number of cases in our study is an important limitation. Therefore, the findings of our study cannot be generalized; however, it may be informative for studies with more precise results and reliable results.

We discovered that delta bicarbonate and delta ratio, basic, inexpensive, easily accessible, and quickly calculated blood gas parameters, had acceptable diagnostic power in predicting death in methanol poisoning, while the ph, anion gap, and delta anion gap have outstanding diagnostic power. This is the first study we are aware of that assesses the performance of the delta anion gap, delta bicarbonate, and delta ratio in predicting mortality in methanol poisoning cases.

Yazar Katkıları: Çalışma konsepti/Tasarımı: MD, AS; Veri toplama: MD, AS, NV; Veri analizi ve yorumlama: MD, AS, NV; Yazı taslağı: MD, NV; İçeriğin eleştirel incelenmesi: MD, AS, NV; Son onay ve sorumluluk: MD, AS, NV; Teknik ve malzeme desteği: MD, AS; Süpervizyon: MD, AS, NV; Fon sağlama (mevcut ise): yok.
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Author Contributions: Concept/Design : MD, AS; Data acquisition: MD, AS, NV; Data analysis and interpretation: MD, AS, NV; Drafting manuscript: MD, NV; Critical revision of manuscript: MD, AS, NV; Final approval and accountability: MD, AS, NV; Technical or material support: MD, AS; Supervision: MD, AS, NV; Securing funding (if available): n/a.
Ethical Approval: For this study, Istanbul Prof.Dr. Ethical approval was obtained from the Clinical Research Ethics Committee of Cemil Taşcıoğlu City Haastanesi with the decision dated 28.02.2022 and numbered 43.

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REFERENCES

1. Gulen M, Satar S, Avci A, Acehan S, Orhan U, Nazik H. Methanol poisoning in Turkey: two outbreaks, a single center experience. Alcohol. 2020;88:83-90.
2. Ashurst JV, Nappe TM. Methanol Toxicity. Treasure Island (FL), StatPearls Publishing, 2022.
3. Holt NR, Nickson CP. Severe methanol poisoning with neurological sequelae: implications for diagnosis and management. Intern Med J. 2018;48:335-9.
4. Beauchamp GA, Valento M, Kim J. Toxic alcohol ingestion: prompt recognition and management in the emergency department. Emerg Med Pract. 2016;18:1-20.
5. Kraut JA, Kurtz I. Toxic alcohol ingestions: clinical features, diagnosis, and management. Clin J Am Soc Nephrol. 2008;3:208-25.
6. Zakharov S, Kurcova I, Navratil T, Salek T, Komarc M, Pelclova D. Is the measurement of serum formate concentration useful in the diagnostics of acute methanol poisoning? a prospective study of 38 patients. Basic Clin Pharmacol Toxicol. 2015;116:445-51.
7. Hovda KE, Hunderi OH, Rudberg N, Froyshov S, Jacobsen D. Anion and osmolal gaps in the diagnosis of methanol poisoning: clinical study in 28 patients. Intensive Care Med. 2004;30:1842-6.
8. Kraut JA, Madiast NE. Serum anion gap: its uses and limitations in clinical medicine. Clin J Am Soc Nephrol. 2007;2:162-74.
9. Gallagher N, Edwards FJ. The diagnosis and management of toxic alcohol poisoning in the emergency department: a review article. Adv J Emerg Med. 2019;3:e28.
10. Kraut JA, Mullins ME. Toxic alcohols. N Engl J Med. 2018;378:270-80.
11. Kraut JA. Diagnosis of toxic alcohols: limitations of present methods. Clin Toxicol (Phila). 2015;53:589-95.
12. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol. 2002;40:415-46.
13. Farwell WR, Taylor EN. Serum anion gap, bicarbonate and biomarkers of inflammation in healthy individuals in a national survey. CMAJ. 2010;182:137-41.
14. Feldman M, Soni N, Dickson B. Influence of hypoalbuminemia or hyperalbuminemia on the serum anion gap. J Lab Clin Med. 2005;146:317-20.
15. Rudkin SE, Grogan TR, Treger RM. The Δ anion gap/Δ bicarbonate ratio in early lactic acidosis: time for another delta? Kidney360. 2021;2:20.

16. Norman G. Likert scales, levels of measurement and the "laws" of statistics. Adv Health Sci Educ Theory Pract. 2010;15:625-32.
17. Paasma R, Hovda KE, Jacobsen D. Methanol poisoning and long term sequelae – a six years follow-up after a large methanol outbreak. BMC Clin Pharmacol. 2009;9:5.
18. Hassanian-Moghaddam H, Pajoumand A, Dadgar SM, Shadnia S. Prognostic factors in methanol poisoning. Hum Exp Toxicol. 2007;26:583-6.
19. Zakharov S, Pelclova D, Urban P, Navratil T, Diblik P, Kuthan P et al. Czech mass methanol outbreak 2012: epidemiology, challenges and clinical features. Clin Toxicol (Phila). 2014;52:1013-24..
20. Paasma R, Hovda KE, Tikkerberi A, Jacobsen D. Methanol mass poisoning in Estonia: outbreak in 154 patients. Clin Toxicol (Phila). 2007;45:152-7.
21. Aghababaeian H, Ahvazi LA, Ostadtaghizadeh A. The methanol poisoning outbreaks in Iran 2018. Alcohol Alcohol. 2019;54:128-30.
22. WHO. Global Status Report on Alcohol and Health 2018. Geneva, World Health Organization, 2008.
23. Reddy P, Mooradian AD. Clinical utility of anion gap in deciphering acid–base disorders. Int J Clin Pract. 2009;63:1516-25.
24. Lipnick MS, Braun AB, Cheung JTW, Gibbons FK, Christopher KB. The difference between critical care initiation anion gap and prehospital admission anion gap is predictive of mortality in critical illness. Crit Care Med. 2013;41:49-59.
25. Xie K, Zheng C, Wang GM, Daio YF, Luo C, Wang E, et al. Association between delta anion gap and hospital mortality for patients in cardiothoracic surgery recovery unit: a retrospective cohort study. BMC Surg. 2022;22:186.
26. Zakharov S, Navrátil T, Pelclova D. Analysis of serum anion gap and osmolal gap in diagnosis and prognosis of acute methanol poisoning: clinical study in 86 patients. Monatshefte fur Chemie. 2015;146:787-94.
27. Arslan B, Akdağ D, Ünlü N, Arslan A, Açık V. The prognostic value of red cell distribution width for in-hospital mortality in patients with methanol poisoning. Hum Exp Toxicol. 2021;40:196-202.
28. Paasma R, Hovda KE, Hassanian-Moghaddam H, Brahmi N, Afshari R, Sandvik L, et al. Risk factors related to poor outcome after methanol poisoning and the relation between outcome and antidotes – a multicenter study. Clin Toxicol (Phila). 2012;50:823-31.
29. Persson HE, Sjöberg GK, Haines JA, De Garbino JP. Poisoning Severity Score: grading of acute poisoning. J Toxicol Clin Toxicol. 2009;36:205-13.
30. Casey PB, Dexter EM, Michell J, Vale JA. The prospective value of the IPCS/EC/EAPCCT poisoning severity score in cases of poisoning. J Toxicol Clin Toxicol. 1998;36:215-7.
31. Zakharov S, Navratil T, Salek T, Kurcova I, Pelclova D. Fluctuations in serum ethanol concentration in the treatment of acute methanol poisoning: a prospective study of 21 patients. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2015;159:666-76.