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Methanol Intoxication as a Public Health Issue: A Three-Year Retrospective Analysis

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Abstract

Aim: In recent years, methanol intoxication has become an increasingly important public health problem, particularly in developing countries affected by economic crises. This study aimed to contribute to the existing literature by providing a comprehensive analysis of methanol intoxication cases, identifying prognostic factors associated with mortality, and describing treatment strategies and clinical outcomes.

Study Design: This retrospective study included 54 critically ill adult patients admitted to the intensive care unit (ICU) with methanol intoxication between 2022 and 2025. Patients were stratified into survivor and non-survivor groups. Demographic, clinical, and laboratory data were analyzed.

Results: The mean age of the patients was 52 ± 10 years, and 79.6% were male. The overall mortality rate was 61.1%. More than 15 demographic, clinical, and laboratory variables were significantly associated with mortality. Among patients with severe metabolic acidosis, the Simplified Acute Physiology Score II (SAPS-II) and serum lactate level demonstrated the strongest prognostic performance. Among the analyzed parameters, the strongest predictors of mortality were a serum lactate level >4.1 mmol/L, Glasgow Coma Scale (GCS) score <13 , and SAPS-II >31 . Delayed initiation of antidotal therapy and hemodialysis was significantly associated with increased mortality ($p=0.004$ and $p=0.005$, respectively).

Conclusions: Methanol intoxication was associated with a high mortality rate in this cohort. Elevated serum lactate levels, lower GCS scores, and higher SAPS-II scores were the most powerful predictors of mortality. Delayed hospital presentation and delays in diagnosis and treatment were associated with poorer clinical outcomes. These findings underscore the critical importance of rapid diagnosis, early initiation of antidotal therapy, timely extracorporeal treatment, and increased awareness of methanol intoxication among healthcare professionals and the general public.

Keywords: Intoxication; methanol; outcomes; treatment.

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Introduction

Methanol (methyl alcohol) is a leading cause of mass poisoning worldwide. Owing to its lower cost and widespread availability compared with ethanol, exposure most commonly occurs through the consumption of adulterated or illicitly produced alcoholic beverages. In recent years, the World Health Organization has reported numerous outbreaks of methanol intoxication across many developing countries, including Türkiye, with outbreak sizes ranging from 20 to more than 800 affected individuals.^[1] In severe cases, reported mortality rates reach up to 75%.^[2] A nationwide analysis covering the period from 2000 to 2018 estimated the inpatient prevalence of methanol intoxication at 6.4 cases per 1,000,000 hospital admissions.^[3] Cases have been documented globally, and the steadily increasing incidence represents a growing public health concern.^[4] Notably, more than 5,000 cases of methanol intoxication attributed to adulterated alcohol were reported in Iran during the coronavirus disease 2019 (COVID-19) pandemic.^[5]

Methanol, the simplest aliphatic alcohol (CH_3OH), is widely used as an industrial solvent, in antifreeze production, and as a fuel additive. Because methanol is a colorless, volatile liquid with an odor similar to that of ethanol, it may be consumed in place of ethanol, either accidentally or intentionally. The lethal dose of orally ingested methanol in adults has been reported to range from 30 to 240 mL (20–150 g).^[6] Ethanol, on the other hand, is generally considered relatively safe; however, excessive intake can lead to respiratory depression and death. The lethal dose of ethanol in adults is reported to be approximately 5–8 g/kg body weight (6–10 mL/kg of pure ethanol), and a blood ethanol concentration exceeding 300–400 mg/dL may result in death due to respiratory depression.^[7]

The clinical presentation of methanol intoxication varies according to the route of exposure, ingested dose, and time elapsed since ingestion. Early manifestations often resemble mild ethanol intoxication; however, patients may rapidly progress to profound metabolic acidosis, end-organ dysfunction, and multi-organ failure. The latent period between methanol ingestion and the onset of symptoms is one of the most important determinants of poisoning severity. Because toxic manifestations develop after methanol is metabolized to formic acid, delayed presentation is frequently associated with more severe metabolic acidosis, neurological injury, and increased mortality.

Current treatment approaches include inhibition of alcohol dehydrogenase using fomepizole or ethanol, correction of metabolic acidosis, extracorporeal elimination of the toxin via dialysis, and comprehensive supportive care. The key advantages of fomepizole over ethanol are its 500- to 1000-fold higher affinity for alcohol dehydrogenase and the absence of central nervous system depressant effects.^[8] Owing to these properties, fomepizole offers clinical advantages, including easier maintenance of therapeutic blood levels and avoidance of ethanol-related adverse effects such as hypoglycemia and sedation. Prompt recognition, early therapeutic intervention, and a coordinated multidisciplinary approach are critical determinants of clinical outcome.^[7] Despite advances in management, methanol intoxication remains a major public health challenge.

Although numerous studies have evaluated clinical and biochemical markers predictive of mortality in methanol intoxication and assessed treatment approaches, evidence from comprehensive evaluations of critically ill patients using established intensive care unit (ICU) severity scoring systems remains limited. Therefore, further studies are needed to identify the most valuable parameters for early risk stratification and prognostic assessment in the ICU.

This study aimed to identify early prognostic markers that should be closely monitored in critically ill patients admitted to the ICU with methanol intoxication by evaluating demographic, clinical, laboratory, and treatment-related variables together with established ICU severity scoring systems. We also aimed to contribute to the body of knowledge in this field by comprehensively evaluating treatment strategies and clinical outcomes in the context of the current literature.

Materials and Methods

Study Design and Setting

This population-based, retrospective, single-center cohort study was conducted at Kartal Dr. Lütfi Kırdar City Hospital. The study was approved by Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital (Approval Number: 2025/010.99/13/10, Date: 26.02.2025), and was registered in the ClinicalTrials.gov Protocol Registration System (registration number: NCT06931587). The study adhered to the principles of the 2013 Declaration of Helsinki and followed Good Clinical Practice guidelines.

Patient Population

Patients admitted to the intensive care unit between 2022 and 2025 with suspected or laboratory-confirmed methanol intoxication were included in the study. Patients with other intoxications, those younger than 18 years of age, and pregnant women were excluded from the analysis (Fig. 1).

Data Collection

Data were collected in three sequential steps. First, the hospital's electronic medical database was queried using International Classification of Diseases (ICD) code T51.1 to identify eligible cases. Subsequently, detailed patient medical records were reviewed to assess clinical progression and therapeutic interventions. Finally, laboratory data were retrieved from the hospital's patient information system.

For each patient, we recorded demographic characteristics, Charlson Comorbidity Index (CCI), serial Glasgow Coma Scale (GCS) scores, illness severity scores, Sequential Organ Failure Assessment (SOFA), Acute Physiology and Chronic Health Evaluation II (APACHE-II), Simplified Acute Physiology Score II (SAPS-II), Simplified Acute Physiology Score III (SAPS-III), hemodynamic parameters, arterial blood gas variables (pH, bicarbonate, base deficit, partial pressure of carbon dioxide, an-

ion gap, and calculated serum osmolality), laboratory parameters (serum lactate, glucose, urea, creatinine, aspartate aminotransferase [AST], alanine aminotransferase [ALT], sodium, potassium, chloride, and C-reactive protein), treatment characteristics (antidotal therapy, renal replacement therapy [RRT] modality, mechanical ventilation [MV], and vasopressor use), and clinical outcomes (ICU length of stay, hospital length of stay, and in-hospital mortality).

GCS scores were recorded on ICU admission and daily thereafter as part of routine neurological examinations. GCS assessments were performed during sedation interruption or sedation-free periods.

Visual symptoms were defined as any patient-reported visual disturbance at presentation, including blurred vision, decreased visual acuity, visual field defects, photophobia, or complete vision loss, as documented in the medical records.

Ethanol Therapy

Ethanol therapy was initiated in patients with suspected methanol intoxication based on a history of methanol exposure and compatible clinical findings, including high-anion-gap metabolic acidosis (pH <7.25), visual symptoms, or neurological impairment. Treatment was not delayed while awaiting confirmation of serum methanol levels when clinical suspicion was high. Intravenous 10% ethanol was administered at a loading dose of 0.8 mL/kg, followed by a maintenance dose of 0.83 mL/kg/h in patients without a history of chronic alcohol use and 1.96 mL/kg/h in those with chronic alcohol use. The dose was adjusted to maintain a target serum ethanol concentration of approximately 100 mg/dL. During hemodialysis, the ethanol maintenance dose was doubled.^[9,10]

Supportive Therapies

Sodium bicarbonate and calcium folinate were administered as supportive and adjunctive treatments, respectively, in addition to antidotal therapy and renal replacement therapy. Sodium bicarbonate therapy was initiated in patients with severe metabolic acidosis, defined in our treatment protocol as an arterial pH <7.25 and/or serum bicarbonate (HCO_3^-) level <15 mmol/L. Sodium bicarbonate was administered intravenously at a dose of 1–2 mEq/kg and continued while the arterial pH remained below 7.25. Calcium folinate was administered intravenously at a dose of 50 mg every 6 hours for 24–48 hours.^[7,8]

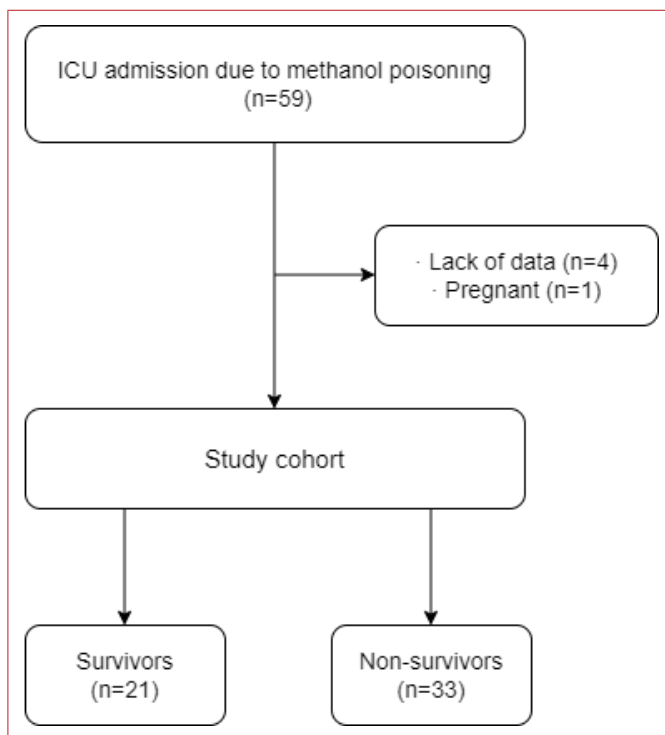


Figure 1. Flow diagram of the patient selection process.

Continuous Renal Replacement Therapy and Intermittent Hemodialysis

Treatment decisions were based primarily on clinical and laboratory findings. RRT was initiated according to the Extracorporeal Treatments in Poisoning (EXTRIP) Workgroup recommendations in patients with severe metabolic acidosis, impaired consciousness, or hemodynamic instability.

The choice between continuous renal replacement therapy (CRRT) and intermittent hemodialysis (IHD) was at the discretion of the attending ICU physician, based on clinical care standards and patient hemodynamics. CRRT was selected for hemodynamically unstable patients.

Because IHD was not available in our ICU, patients requiring IHD were transferred to the dialysis unit for treatment. IHD was performed using low-molecular-weight heparin (LMWH) anticoagulation when clinically appropriate, according to the patient's clinical condition.

CRRT was performed according to the standard institutional protocol using the Multifiltrate CRRT system (Vantive, Germany) with regional citrate anticoagulation. Blood and dialysate flow rates were adjusted according to the patient's body weight and the clinical judgment of the attending intensivist to achieve a target dialysis dose of 25 mL/kg/h.

Statistical Analysis

Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD), and categorical variables as frequencies and percentages. Normality was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Comparisons were made using Student's t-test or the Mann–Whitney U test. Categorical data were analyzed using the chi-square test or Fisher's exact test. Mortality predictors were evaluated using receiver operating characteristic (ROC) analysis, with odds ratios (OR) and 95% confidence intervals (CI) reported. A p value ≤ 0.05 was considered statistically significant.

Results

Study Population

The mean age of the 54 patients included in the study was 52 ± 10 years, and 79.6% were male. The number of hospital admissions due to methanol intoxication increased progressively each year. Notably, 44.4% of patients (n=24) were hospitalized for methanol intoxication during the final year of the study period (Fig. 2). Methanol exposure resulted from the consumption of adulter-

ated alcohol in 87% of cases and chemical products in 13%. Serum methanol concentrations were available for only 22 patients. The mean serum methanol concentration was 103 mg/dL. Serum ethanol was detectable (≥ 10 mg/dL) in all 54 patients, with a mean concentration of 29.1 mg/dL (0.29‰). Visual symptoms were observed in a substantial proportion of patients (83.3%) upon presentation to the emergency department (Table 1).

Comparison Between Survivors and Non-Survivors

Patients were stratified into survivors (n=21) and non-survivors (n=33), yielding an overall mortality rate of 61.1%. Mortality was significantly higher among patients with anuria and those presenting with visual impairment ($p < 0.001$ and $p = 0.020$, respectively). Compared with survivors, non-survivors were older, had higher Charlson Comorbidity Index scores, and exhibited significantly greater illness severity, as reflected by higher SOFA, APACHE-II, SAPS-II, and SAPS-III scores (all $p < 0.001$). Serial GCS scores were consistently lower in non-survivors, with the greatest between-group difference observed on Day 3. Non-survivors also demonstrated more profound hemodynamic instability, metabolic acidosis, and biochemical derangements (Table 2).

Predictors of Mortality

ROC analysis demonstrated excellent discriminative ability for several clinical variables. Among all evaluated parameters, Day 3 GCS had the highest discriminative ability for predicting mortality (area under the curve [AUC]=0.976), followed by SAPS-II (AUC=0.934), APACHE-II (AUC=0.930), serum lactate (AUC=0.889), SOFA (AUC=0.882), arterial pH (AUC=0.879), and serum creatinine (AUC=0.864) (Table 3).

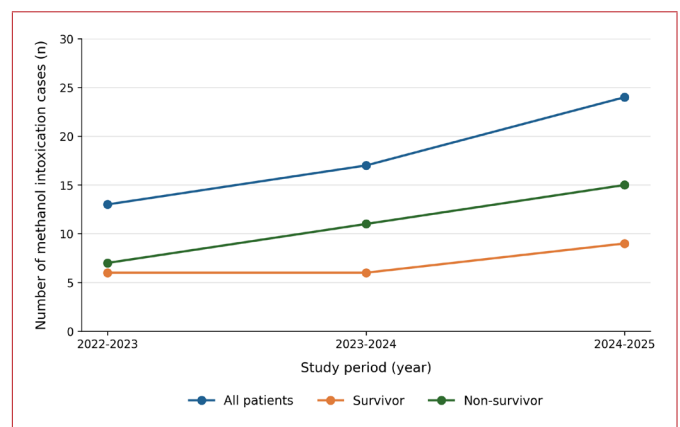


Figure 2. Annual distribution of methanol intoxication cases during the study period.

Table 1. Baseline demographic and clinical characteristics of the study population

Variable	Overall (n=54)	Survivors (n=21)	Non-survivors (n=33)	p
Male sex, n (%)	43 (79.6)	17 (81.0)	26 (78.8)	1.000
Age, years	52±10.42	43±9.42	55±7.59	<0.001*
Immigrant status, n (%)	5 (9.3)	1 (4.8)	4 (12.1)	0.638
Source of methanol exposure, n (%)				
Adulterated alcohol	47 (87.0)	18 (85.7)	29 (87.9)	1.000
Chemical products	7 (13.0)	3 (14.3)	4 (12.1)	
Visual symptoms, n (%)	45 (83.3)	14 (66.7)	31 (93.9)	0.020*
Anuria, n (%)	15 (27.8)	0 (0.0)	15 (45.5)	<0.001*

*Statistically significant at p<0.05. Chemical products included cologne, disinfectant, and spirits.

Univariable logistic regression analysis was performed to identify variables associated with mortality. Age, visual symptoms, MV requirement, SOFA, APACHE-II, SAPS-II, SAPS-III, arterial pH, bicarbonate, base deficit, serum lactate, anion gap, serum osmolality, creatinine, urea, AST, ALT, and serial GCS measurements were significantly associated with mortality (all p<0.05). Variables that were significant in the univariate analysis were subsequently considered for inclusion in the multivariable logistic regression model.

Day 3 GCS, APACHE-II, SOFA, SAPS-II scores, serum lactate concentration, and age remained independent predic-

tors of mortality. Specifically, higher SAPS-II, APACHE-II, and SOFA scores, higher serum lactate concentrations, and older age were independently associated with a higher risk of mortality, whereas higher Day 3 GCS scores were associated with improved survival (Table 4).

Treatment Characteristics

The median ICU length of stay was six days, with no significant difference between survivors and non-survivors. MV and vasoactive support were required significantly more frequently in non-survivors than in survivors (p<0.001 and p=0.004, respectively). The most frequently

Table 2. Baseline clinical and laboratory findings in survivors and non-survivors

Variable (mean±SD)	Overall	Survivors	Non-survivors	p
CCI	0.63±1.20	0±0.44	1±0.45	0.016*
SOFA score	4.70±3.78	2±1.47	6±3.85	<0.001*
APACHE-II score	14.07±7.83	7±3.70	19±6.85	<0.001*
SAPS-II	39.28±21.85	19±7.37	50±19.13	<0.001*
SAPS-III	51.54±15.61	38±5.85	60±13.82	<0.001*
GCS score, Day 1	10.70±5.24	13±0.51	8±5.22	<0.001*
GCS score, Day 2	9.15±5.63	14±2.08	6±3.72	<0.001*
GCS score, Day 3	8.31±5.66	15±0.40	5±4.24	<0.001*
MAP (mmHg)	68.48±16.81	72±14.08	63±17.01	<0.001*
pH	6.94±0.19	7.0±0.11	6.7±0.17	<0.001*
Anion gap (mEq/L)	28.99±7.62	25±6.60	31±7.43	0.005*
Osmolality (mOsm/L)	290.74±8.98	285±8.631	296±8.059	<0.001*
Base deficit (mmol/L)	-22.13±6.47	-19±7.18	-26±5.11	0.002*
HCO ₃ ⁻ (mmol/L)	8.27±4.61	9.8±4.56	5.1±4.01	<0.001*
Lactate (mmol/L)	7.13±5.57	2.2±5.93	9±4.27	<0.001*
Creatinine (mg/dL)	1.12±0.29	0.9±0.23	1.2±0.24	<0.001*

*Statistically significant at p<0.05. CCI: Charlson Comorbidity Index; GCS: Glasgow Coma Scale; SOFA: Sequential Organ Failure Assessment; APACHE-II: Acute Physiology and Chronic Health Evaluation II; SAPS-II: Simplified Acute Physiology Score II; MAP: Mean arterial pressure.

Table 3. Receiver operating characteristic (ROC) analysis of predictors of mortality

	AUC (95% CI)	Standard error	Cutoff value	p	Sensitivity (%)	Specificity (%)
GCS score, Day 3	0.976 (0.936–1.000)	0.020	13.000	0.000	90.9	100
SAPS-II	0.934 (0.873–0.996)	0.031	31.000	0.000	84.8	90.5
APACHE-II	0.930 (0.864–0.996)	0.034	9.000	0.000	87.9	76.2
Lactate	0.889 (0.781–0.996)	0.055	4.100	0.000	90.9	90.5
SOFA	0.882 (0.795–0.970)	0.045	3.500	0.000	75.8	85.7
pH	0.879 (0.786–0.972)	0.047	7.000	0.000	84.8	90.5
Creatinine	0.864 (0.761–0.967)	0.053	1.030	0.000	93.9	71.4

GCS: Glasgow Coma Scale; APACHE-II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; SAPS-II: Simplified Acute Physiology Score II; pH: Potential of hydrogen; AUC: Area under the receiver operating characteristic curve.

observed organ failures were neurological (20%), renal (27%), and respiratory (68%).

RRT was administered to all patients. The median duration of CRRT was 32 hours. Continuous venovenous hemodialysis (CVVHD) alone was used in 61.1% of cases, whereas IHD alone was used in 29.6%; some patients received both treatment modalities. Mortality was significantly higher among patients treated with CVVHD ($p=0.014$).

Delayed initiation of hemodialysis after ICU admission was significantly associated with mortality ($p=0.005$). Ethanol therapy was administered to 79.6% of patients, and delayed initiation of antidotal therapy was significantly more frequent among non-survivors than among survivors ($p=0.004$). Sodium bicarbonate therapy was administered to patients meeting the predefined criteria for severe metabolic acidosis and was significantly more frequent among non-survivors ($p=0.028$). Calcium folinate therapy was administered to 81.5% of patients and was not significantly associated with mortality ($p=0.162$) (Table 5).

Discussion

In this retrospective study of critically ill patients with methanol intoxication, we identified several demographic, clinical, and laboratory variables associated with mortality. Among these, higher SAPS-II scores, elevated serum lactate levels, lower GCS scores, older age, and severe metabolic acidosis demonstrated the strongest associations with poor clinical outcomes. In addition, delayed hospital presentation, delayed diagnosis, and delayed initiation of antidotal therapy and RRT were associated with increased mortality.

Severe metabolic acidosis and elevated serum lactate levels were among the strongest laboratory predictors of mortality in our cohort. Non-survivors presented with significantly lower arterial pH and bicarbonate levels, together with markedly higher lactate concentrations, and serum lactate remained an independent predictor of mortality in the multivariable analysis. These findings are biologically plausible because methanol toxicity re-

Table 4. Multivariable logistic regression analysis of independent predictors of mortality

	B	SE	Wald	p	Exp(B)	95% CI	
						Lower	Upper
GCS score, Day 3	-0.476	0.111	18.334	<0.001	0.621*	0.500	0.773
APACHE-II	0.404	0.130	9.706	0.002	1.498*	1.162	1.933
SOFA	0.832	0.244	11.639	0.001	2.297*	1.425	3.705
SAPS-II	0.163	0.046	12.654	<0.001	1.177*	1.076	1.288
Lactate	0.314	0.100	9.975	0.002	1.369*	1.127	1.664
Age	0.186	0.051	13.118	0.001	1.205*	1.089	1.332

GCS: Glasgow Coma Scale; APACHE-II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; SAPS-II: Simplified Acute Physiology Score II.

Table 5. Treatment characteristics and intensive care interventions

Variable	Overall	Survivors	Non-survivors	p
Advanced life support requirements				
MV	37 (68.5%)	8 (21.6%)	29 (78.4%)	<0.001*
Vasoactive agent infusion	11 (20.4%)	0 (0.0%)	11 (100.0%)	
Hemodialysis modality				
IHD	16 (29.6%)	9 (56.3%)	7 (43.8%)	0.014*
CVVHD	33 (61.1%)	8 (24.2%)	25 (75.8%)	
IHD + CVVHD	5 (9.3%)	4 (80.0%)	1 (20.0%)	
Time to initiation of dialysis				
Within 3 h of ICU admission	40 (74.1%)	17 (42.5%)	23 (57.5%)	0.005*
3–6 h after ICU admission	9 (16.6%)	0 (0.0%)	9 (100%)	
Initiated in the ED	5 (9.3%)	4 (80.0%)	1 (20.0%)	
Ethanol therapy				
Received	43 (79.6%)	13 (30.2%)	30 (69.8%)	0.015*
Not received	11 (20.4%)	8 (72.7%)	3 (27.3%)	
Timing of ethanol therapy				
Initiated in the ICU	41 (75.9%)	11 (26.8%)	30 (73.2%)	0.004*
Initiated in the ED	2 (3.7%)	2 (100.0%)	0 (0.0%)	
Not administered	11 (20.4%)	8 (72.7%)	3 (27.3%)	

*Statistically significant at $p < 0.05$. MV: Mechanical ventilation; IHD: Intermittent hemodialysis; CVVHD: Continuous venovenous hemodialysis; ICU: Intensive care unit; IV: Intravenous; ED: Emergency department.

sults from the accumulation of formic acid, which inhibits mitochondrial cytochrome oxidase, impairs oxidative phosphorylation, and ultimately leads to profound metabolic acidosis and systemic tissue hypoxia. Consequently, elevated lactate reflects not only tissue hypoperfusion but also the severity of mitochondrial dysfunction and the overall metabolic burden of poisoning.

Our findings are consistent with the current literature. A systematic review and meta-analysis identified severe metabolic acidosis, elevated serum lactate, impaired consciousness, renal dysfunction, and delayed treatment as the most consistent predictors of mortality in methanol intoxication.^[11] Several studies have demonstrated that profound acid–base disturbances and delayed hospital presentation are associated with poor outcomes.^[12,13] Likewise, Kayalı et al.^[14] demonstrated that serum lactate remained an independent predictor of mortality after multivariable adjustment.

Although APACHE-II and SOFA have been extensively evaluated in previous studies of methanol intoxication, evidence regarding the prognostic utility of SAPS-II remains limited. Our findings are partially consistent with those reported by Kuusela et al.^[15] In their cohort, as in ours, lower GCS scores, severe metabolic acidosis, a higher anion gap, lower bicarbonate levels, and the need for MV were associated with 90-day mortality.

Although SAPS-II was reported as a baseline severity measure (median score: 38), its prognostic performance was not specifically evaluated. By contrast, our study demonstrated that SAPS-II not only differed significantly between survivors and non-survivors but also showed strong discriminative performance for mortality prediction (cutoff value: 31) and remained an independent predictor after adjustment for other clinical variables (AUC=0.934). These findings suggest that SAPS-II may represent a practical and readily available tool for early risk stratification in critically ill patients with methanol intoxication. The strong performance of SAPS-II may be explained by its incorporation of multiple physiological variables together with age and underlying comorbidities, allowing a more comprehensive assessment of overall disease severity.

Although composite severity scores provide an overall assessment of disease severity, serial neurological evaluation offers complementary prognostic information by reflecting the dynamic progression of central nervous system injury during methanol intoxication. In our cohort, deterioration in GCS scores, particularly a Day 3 score below 13, emerged as one of the strongest predictors of mortality. This observation is biologically plausible because impaired consciousness reflects both the direct neurotoxic effects of formate accumulation and secondary cerebral hypoperfusion resulting from

profound metabolic acidosis. Moreover, the excellent discriminative performance of Day 3 GCS (AUC=0.976) highlights the value of repeated neurological assessment beyond the initial clinical examination.

Our findings are consistent with recent reports.^[16-18] Extending these observations, our study demonstrates that assessment of serial GCS scores, rather than a single baseline measurement, provides excellent prognostic discrimination. Given its simplicity, low cost, and universal availability, repeated GCS evaluation should be considered an integral component of routine ICU monitoring in patients with methanol intoxication.

Although prognostic markers are essential for early risk stratification, patient outcomes ultimately depend on timely therapeutic interventions. The cornerstones of methanol intoxication management include correction of metabolic acidosis, inhibition of alcohol dehydrogenase (ADH), and extracorporeal elimination of toxic metabolites through hemodialysis. According to the international consensus statement published by the EXTRIP Workgroup, extracorporeal treatment should be initiated without delay in patients presenting with severe metabolic acidosis, visual disturbances, coma, or markedly elevated serum methanol concentrations. Furthermore, IHD is recommended over CRRT whenever feasible because of its superior clearance of methanol and formate.^[19] In our center, however, IHD was not available in the intensive care unit; therefore, CVVHD was predominantly used in unstable or intubated patients because of infrastructural limitations, whereas stable patients underwent IHD. This institutional limitation may have influenced our treatment strategy and, consequently, clinical outcomes. The greater use of CVVHD among non-survivors likely reflects greater disease severity rather than treatment efficacy. Consistent with previous reports, Zakharov et al.^[20] demonstrated the superiority of intermittent hemodialysis over continuous modalities in methanol intoxication. In the present study, intermittent hemodialysis was performed more frequently among survivors, whereas CRRT predominated among non-survivors. This finding should not be interpreted as evidence that continuous therapies are less effective. Rather, it most likely reflects the greater severity of illness and hemodynamic instability among patients requiring continuous modalities.

Current evidence supports prompt recognition of methanol intoxication and early initiation of antidotal therapy

and extracorporeal treatment without waiting for laboratory confirmation when clinical suspicion is high.^[21,22]

Although Kuusela et al.^[15] reported a 90-day mortality rate of 46% among patients with severe methanol intoxication requiring dialysis, mortality in our cohort reached 61.1%. This difference may be attributable to the inclusion of exclusively critically ill ICU patients in our study, the presence of more advanced metabolic derangements at presentation suggestive of delayed hospital admission, and differences in the availability of antidotal therapy, particularly fomepizole. Moreover, initiation of RRT was frequently delayed in our cohort, with a median interval of approximately six hours after ICU admission, potentially reducing the opportunity to prevent irreversible neurological injury.

This concept is well illustrated by the case reported by Kraut and Mullins, in which antidotal therapy and extracorporeal treatment were initiated immediately on the basis of a history of methanol exposure, severe metabolic acidosis, and a high anion gap, without waiting for serum methanol confirmation.^[22] Although the serum methanol concentration was obtained two days later, confirming the diagnosis, the severely intoxicated patient survived after treatment had been initiated immediately on the basis of strong clinical suspicion. Interestingly, in our cohort of 54 patients, 11 (20.4%) did not receive ethanol therapy because of access limitations and clinician-related factors, and the majority of these patients (n=8) survived with supportive care. This finding may indicate that patients presenting with milder toxicity have more favorable outcomes. The remaining three patients in this subgroup died, which was more likely associated with greater toxicity and later presentation. In our cohort, serum ethanol was detectable in all patients (≥ 10 mg/dL), with a relatively low mean concentration of 29.1 mg/dL (0.29‰). This value was substantially below the target therapeutic concentration of 100 mg/dL during ethanol antidote infusion and continued to decrease over time in patients who did not receive infusion therapy. Therefore, we concluded that the ethanol concentrations were insufficient to provide a clinically meaningful antidotal effect in our cohort.

Reported mortality rates following methanol intoxication vary considerably across the literature, ranging from approximately 20% to 60%, depending on poisoning severity, healthcare accessibility, timing of treatment, and patient selection.^[12,13,23] Importantly, most published studies have in-

cluded all hospitalized patients with methanol intoxication, regardless of disease severity, and have not reported mortality specifically among ICU patients.^[24-26] In this respect, our study provides valuable data by focusing exclusively on critically ill patients requiring ICU admission.

Recent studies from Türkiye have reported similarly unfavorable outcomes while emphasizing the impact of delayed hospital presentation and limited access to optimal treatment. Güler et al.^[24] evaluated 43 patients who presented to the emergency department with methanol intoxication during the COVID-19 pandemic and identified delayed hospital admission, severe metabolic acidosis, and limited availability of fomepizole as major challenges. Similarly, Kaçer et al.^[25] reported that impaired consciousness and delayed presentation were strongly associated with mortality. Unlike these studies, our cohort consisted exclusively of critically ill patients admitted to the ICU, the majority of whom required RRT. Therefore, differences in patient selection should be carefully considered when comparing mortality rates across studies.

An additional factor influencing prognosis is the latent period between methanol ingestion and hospital presentation. Because methanol itself is relatively nontoxic, clinical deterioration occurs after its metabolism to formic acid. Although the latent period could not be evaluated in the present study, delayed presentation was clinically suspected in many patients because of the severity of metabolic derangements at admission. Visual symptoms typically develop after a latent period and may progress from blurred vision and visual field disturbances to severe visual impairment or blindness, primarily as a consequence of formate-induced optic nerve and retinal toxicity.^[27] In our study, the high prevalence of visual symptoms, together with low GCS scores and profound metabolic acidosis at presentation, suggests that many patients sought medical attention relatively late. A retrospective study conducted in Türkiye between 2002 and 2010 found that 64.7% of deaths from methanol intoxication occurred at home and 7.5% outdoors, suggesting that many patients died before recognizing that they had been poisoned.^[28]

This observation further highlights the critical importance of public awareness of the early symptoms of methanol intoxication and the implementation of effective public health strategies to reduce mortality. Improving recognition of the early manifestations of methanol intoxication and encouraging prompt presentation to

emergency departments may reduce delays in diagnosis and treatment.

Finally, in many centers, including ours, serum methanol concentrations cannot be consistently measured, requiring diagnosis to be based on clinical suspicion, patient history, neurological findings, and high-anion-gap metabolic acidosis. Under these circumstances, clinicians should adopt a syndromic approach and initiate appropriate treatment promptly whenever methanol intoxication is strongly suspected.

Limitations and Strengths

This study has several limitations that should be acknowledged. First, serum methanol levels were not measured in all patients, which may have reduced the accuracy of severity stratification. In addition, the exclusive use of ethanol rather than fomepizole as an antidote, along with the limited feasibility of IHD, may have influenced clinical outcomes. Furthermore, because serum ethanol concentrations at hospital admission remained below the therapeutic target in all patients, the potential effect of therapeutic ethanol levels at admission on prognosis could not be investigated in detail. Finally, the absence of long-term follow-up, particularly among patients with visual and neurological sequelae, limits our ability to comprehensively assess functional recovery and long-term prognosis.

Despite these limitations, the present study has several important strengths. To our knowledge, it represents one of the largest cohorts focusing exclusively on critically ill patients with methanol intoxication requiring ICU management. Unlike many previous studies that included all hospitalized patients regardless of disease severity, our cohort consisted entirely of ICU patients, allowing a more detailed evaluation of prognostic factors in this high-risk population. Furthermore, we comprehensively assessed demographic characteristics, clinical findings, laboratory parameters, treatment modalities, and established ICU severity scoring systems, enabling an integrated analysis of mortality predictors. Finally, given the unavailability of fomepizole, reliance on ethanol as the primary antidote provides valuable real-world insights applicable to resource-limited healthcare settings.

Conclusion

In critically ill patients with methanol intoxication, established ICU severity scores, particularly SAPS-II, together

with serial neurological assessment using the Glasgow Coma Scale and serum lactate measurements, provide valuable prognostic information and may facilitate early risk stratification. Our findings suggest that integrating clinical and laboratory parameters with severity scores may improve prognostic assessment and support timely therapeutic decision-making in the intensive care setting.

Given the high mortality observed in this critically ill patient population, increasing awareness of methanol intoxication, promoting early diagnosis, and ensuring appropriate clinical management are essential for improving patient outcomes.

Ethics Committee Approval: Ethics committee approval was obtained from Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital (Approval Number: 2025/010.99/13/10, Date: 26.02.2025).

Informed Consent: Routine written informed consent is obtained from the patient's relatives upon the initial admission to the ICU. The need for obtaining informed consent was waived because of the retrospective nature of the study.

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