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RESEARCH ARTICLE

Predictors of poor outcomes among patients of acute methanol intoxication with particular reference to Sequential Organ Failure Assessment (SOFA) score

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Abstract

Methanol intoxication is a global problem with serious morbidities and mortalities. Apart from the lifelong disabilities experienced by methanol intoxication survivors, mortality rates of up to 44% of exposed patients have been reported. The aim of the current study was to outline the early findings that could be utilized as effective in-hospital outcome predictors among cases of methanol exposure. Furthermore, the role of the Sequential Organ Failure Assessment (SOFA) score was evaluated as an early in-hospital outcome indicator among patients presented with acute methanol intoxication. A multicenter study including 37 patients diagnosed with acute methanol intoxication and referred to three major poison control centers in Saudi Arabia during the past 3 years (January 1, 2018–January 1, 2021) was conducted. Data including demographics, exposure history, presenting complaints, clinical findings, and laboratory investigation were collected. The patients were scored on Glasgow Coma Scale (GCS), Poison Severity Score (PSS), and SOFA score on admission. Out of the presented patients, 83.8% were alcoholic men. No deaths have been reported, and 51.4% were discharged with unfavorable outcomes, including 29.7% suffered optic neuropathy and blindness, 18.9% showed acute renal impairment, and 10.8% were complicated with respiratory failure. The diastolic blood pressure, anion gap, visual acuity, number of hemodialysis sessions, PSS, duration of Intensive Care Unit (ICU) stay, and SOFA score were all significant organ failure predictors ($P < 0.05$). However, only the SOFA score showed the best significant prediction on multivariate analysis, with an odds ratio (95% confidence interval) of 0.10 (0.04–0.17) and $P = 0.003$. At a cutoff of greater than 4.5, the SOFA score could significantly predict unfavorable outcomes with area under curve (AUC) = 0.955, accuracy 89.2%, specificity 94.4%, and sensitivity 84.2%. Early identification of methanol exposed patients at risk is critical and lifesaving. The SOFA score is a substantially useful and early inclusive unfavorable outcome predictor.

Keywords Methanol · Glasgow Coma Scale · Sequential Organ Failure Assessment Score · Blindness · Renal injury · Respiratory insufficiency

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Introduction

Methanol is an organic compound called methyl alcohol or weed alcohol, which is used as raw material in various chemical industries, mainly as a solvent or feedstock (Dalena et al. 2018). Illegal alcoholic beverages might be altered with methanol, exposing humans to the substance's extreme toxicity (Kaewput et al. 2021). Methanol intoxication is a global problem related to severe morbidities and mortalities (Kurtas et al. 2017). Apart from the lifelong disabilities suffered by survivors of methanol intoxication, mortality rates of up to 44% of exposed patients have been reported (Md Noor et al. 2020).

Indeed, the multiorgan system affection caused by methanol is not mediated by the methanol itself. The formation of the toxic metabolites formic acid and formaldehyde, which inhibit cytochrome oxidase enzyme and cellular respiration, is the leading cause of multiorgan system failure (Kaewput et al. 2021). Formic acid damages the optic nerve and permanent blindness by damaging the optic nerve. Furthermore, methanol exposure results in severe metabolic, renal, and neurological impairments. Also, cardiovascular arrhythmia and respiratory failure are commonly encountered (Paasma et al. 2012).

Management of intoxicated patients starts with decontamination and supportive measurements besides the corrective metabolic therapy. Antidotal therapy with fomepizole or ethanol is a cornerstone, as it helps to inhibit toxic metabolites formation. Hemodialysis is an essential treatment for enhancing toxic metabolite removal (Rietjens et al. 2014). The time interval between methanol exposure and receiving treatment is closely related to the outcomes (Md Noor et al. 2020). The identification of at-risk patients requiring admission to the intensive care unit (ICU) and prompt treatment may prevent complications and long-term deaths (Lee et al. 2014).

Because alcohol in Saudi Arabia is illegal and religiously prohibited, patients with methanol poisoning are rarely brought to the emergency department unless severe, which further complicates the outcome. Moreover, reports of methanol poisoning are underreported because exposed patients attempt to avoid responsibility and prosecution by seeking treatment at poison control centers (Ginawi 2013).

The literature on early detection of exposed patients at risk is scarce and primarily based on single-organ complications. Subsequently, the current study aims to outline the early findings that could be utilized as reliable predictors of multiorgan failure in cases of methanol exposure, and furthermore, to evaluate the role of Sequential Organ Failure Assessment (SOFA) score as an early in-hospital outcome predictor among patients presented with acute methanol intoxication.

Subjects and methods

Study design and setting

The current study is a multicenter study, including all patients diagnosed with acute methanol poisoning referred to three poison control centers in Riyadh, the capital city of Saudi Arabia, during the past three years (January 1, 2018–January 1, 2021).

Inclusion and exclusion criteria

All patients aged 18 years and older diagnosed with acute methanol intoxication during the study period were included. The diagnosis of methanol intoxication is based on the history of exposure, clinical examination, and confirmed by gas chromatography-mass spectrophotometry (GCMS). However, patients aged less than 18 years old and those with incomplete medical records and suffering from co-ingestions, chronic renal illness, or chronic visual impairments were excluded.

Sampling and sample size

Non-probable convenience sampling was adopted to approach the highest number of patients. Fifty-five patients were presented to the three poison control centers over the past 3 years (January 1, 2018–January 1, 2021). Thirty-seven patients met the inclusion criteria and were included in the current study.

Compliance with ethical standards

The current study was carried out following the Declaration of Helsinki. Ethical approval was obtained from the institutional review boards from King Saud Medical City (IRB Number: H1R1-30-Dec20-01), King Fahad Medical City (IRB Log Number: 21-024), and College of Medicine, Dar Al-Uloom University (IRB Number: Pro20110001). Data were retrieved from the medical records without personal identity declaration to maintain the confidentiality of the patients.

Data collection

Demographics and history

The demographics regarding the age, sex, and residence of the patients were extracted from the database. Furthermore, the history of chronic illnesses such as diabetes mellitus, hypertension, and psychiatric problems was mentioned. The exposure history was reported, including chronic alcohol consumption (more than two years or less), smoking, the relative ingested amount in milliliters, the manner of exposure

(accidental or suicidal), and the source of the methanol, which could be industrial, homemade, or well-known brand.

Clinical data and scoring

Vital data were recorded upon admission, involving the pulse (beat/minute), the blood pressure (mmHg), the respiratory rate (cycle/minute), and the axillary temperature in Celsius. The primary complaints presented were documented. The patients were scored on three scoring systems: Glasgow Coma Scale (GCS), Poison Severity Score (PSS), and (SOFA) score. Based on total GCS, the patients were categorized into mild (13–15), moderate (9–12), and severe (3–8) (Matsushima and Nagami 2002). Regarding PSS, the patients were classified into none (no symptoms), minor (transient symptoms), moderate (pronounced symptoms), severe (life-threatening symptoms), and fatal poisoning (death) (Sam et al. 2009). The total SOFA score was considered, ranging from 0–24 (Ferreira and Sakr 2011). A detailed clinical examination was carried out, including evaluations of the cardiovascular, respiratory, and neurological systems. Moreover, the patients were referred to an ophthalmologist to evaluate the visual acuity and check for optic neuropathy (Önder et al. 1998).

Laboratory investigations

Upon admission, an initial methanol screening in the blood by immunoassay was performed utilizing the ARCHITECT ci4100 system (Abbott Laboratories, Chicago, IL, USA). Methanol exposure was then confirmed by the GCMS-QP2010 Ultra system (Shimadzu, Kyoto, Japan). An extensive laboratory workout was conducted, starting with arterial blood gas analysis, which included anion gap calculation (Fujita et al. 2004). Moreover, random blood sugar, complete blood count (CBC), blood electrolyte levels (Na, K, Cl), prothrombin time (P.T.), partial thromboplastin time (PTT), and international normalization ratio (INR) were reported. Liver and kidney functions were assessed, including liver transaminases, total bilirubin level, serum urea, and creatinine (Ran et al. 2019).

Management and in-hospital outcome

After the patients were stabilized, they received supportive therapy in the form of sodium bicarbonate infusion to restore the base deficit, fluid therapy, folic acid administration, thiamine, and proton pump inhibitors. Benzodiazepines and phenytoin were given for patients with seizures. Gastric lavage was not included in the treatment guidelines (Lee et al. 2014). According to antidote availability, some patients received fomepizole injection, and a few received ethanol as an antidote (Alzahrani et al. 2017). Hemodialysis was performed for patients with severe metabolic acidosis not responding to the corrective therapy and patients with visual issues and renal impairments (Chang et al. 2019). Referral for ICU was mandatory for patients who needed renal replacement therapy, mechanical ventilation, or cardiopulmonary resuscitation, and those requiring vasopressor therapy and a high concentration of oxygen > 4 L/min.

The patients were classified into favorable and unfavorable outcomes based on their in-hospital outcomes. Patients complicated by one or more organ failures were deemed to have a poor prognosis. The unfavorable outcome group included patients who suffered from significant optic neuropathy or blindness, and those who underwent significant acute renal impairment (elevated serum urea or creatinine and oliguria or anuria), and those who underwent mechanical ventilation due to respiratory failure. The delay time between the exposure and reaching the emergency service and total length of hospital stay (LOS) between admission and discharge were calculated in hours.

Statistical analysis

The collected data were analyzed using Statistical Package for the Social Sciences SPSS software version 26 (IBM Corporation, Armonk, NY, USA). The mean ± standard deviation (SD) and median (range; minimum-maximum) were used to present the quantitative data. Based on the data distribution using the Shapiro–Wilk test, Student's t-test and Mann–Whitney *U* test were utilized to determine significance for parametric data and non-parametric data, respectively. Categorical data were analyzed using the chi-square test, Fisher's exact test, or Monte Carlo test based on their number and percentage values. Univariate binary logistic regression had been carried out to ascertain the effect of different variables as outcome predictors. Significant predictors were inputted in multivariate analysis. The receiver operating characteristic curve (ROC) was adopted to outline the best cutoff, sensitivity, and specificity of different predictors. The area under the curve (AUC) was considered excellent, good, fair, poor, and fail if it was 0.9–1, 0.8–0.9, 0.7–0.8, 0.6–0.7, and 0.5–0.6, respectively (Jessen and Menard 1996). For all conducted tests, $P < 0.05$ was considered significant.

Results

Thirty-seven patients with acute methanol poisoning were enrolled, where all patients were exposed accidentally with no suicidal intention. Out of them, 48.6% wholly recovered (18 patients) compared to 51.4% (19 patients) who had unfavorable outcomes. Patients with unfavorable outcomes were classified as follows: 29.7% (n = 11) had optic neuropathy and blindness, 18.9% (n = 7) had acute renal impairment, and 10.8% (n = 4) had respiratory failure requiring mechanical

ventilation. Three patients showed more than one unfavorable outcome. Most of the exposed patients were males (83.8%) with a mean age of 33.9 ± 11.5 years. Table 1 shows that the median age of studied patients was 29 years. Around 35.2% presented patients were divorced or widowed, while 21.6% of patients were married, and only seven patients (18.9%) reported a history of psychiatric illness. More than half of the studied patients (54.1%) were smokers, and 83.8% had consumed alcohol for more than 2 years. All demographic data and medical illnesses revealed no statistically significant variations among patients with different outcomes.

According to Table 2, the median value of delay time was 24 h, with no statistically relevant differences between both groups. Many patients could not judge the ingested amount (59.5%) and claimed consuming industrial alcohol (48.6%), and 10.8% were discharged against medical advice. The duration of hospitalization varies from 12 h to 72 days, where the patients with unfavorable outcomes were admitted for significantly more time (median value of 48 h, $P = 0.002$).

When the vital signs of both groups were compared, patients with unfavorable outcomes showed slightly lower pulse, systolic and diastolic blood pressures, mean arterial pressure, and respiratory rate. However, only the diastolic blood pressure showed significant differences between the studied groups. As shown in Table 3, the patients with unfavorable outcomes showed significantly lower diastolic blood pressures (mean 74.2 ± 9.2 mmHg) than those with favorable outcomes (mean 83.6 ± 14.5 mmHg) ($P = 0.024$).

Table 4 summarizes the different presentations and clinical findings observed in the studied patients. The most frequently reported symptoms were nausea and vomiting (51.4%), dizziness (45.9%), blurred vision (29.7%), and headache (24.3%). The assessment of visual acuity showed that in 73% of presented patients, visual acuity was unaffected. However, patients with unfavorable outcomes demonstrated significantly more visual affection than another group (36.8% of patients with unfavorable outcomes suffered from decreased visual acuity, and 15.8% showed no light perception). Although seizures occurred at a lower rate of 18.9% (n = 7 patients), they were significantly associated with unfavorable outcomes ($P = 0.008$), as 63.2% of patients with unfavorable outcomes presented with repeated seizures.

Table 1 Comparison of sociodemographic characteristics and medical history between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

Demographic data and medical history	Total (n = 37)		Outcomes				Test of Sig.	*p*
			Favorable (n = 18)		Unfavorable (n = 19)			
Sex	**N.**	**%**	**N.**	**%**	**N.**	**%**	FE	0.660
Female	6	16.2	2	11.1	4	21.1	0.672	
Male	31	83.8	16	88.9	15	78.9		
Age (year)							Z	0.807
Median	29.0		28.5		33.0		0.244	
Min.–Max.	18.0–60.0		18.0–59.0		19.0–60.0			
Marital status							MC	0.641
Single	16	43.2	9	50.0	7	36.8	0.916	
Married	8	21.6	4	22.2	4	21.1		
Others (divorced and widowed)	13	35.2	5	27.8	8	42.1		
Psychiatric illness							FE	1.000
None	30	81.1	15	83.3	15	78.9	0.116	
Yes	7	18.9	3	16.7	4	21.1		
Diabetes mellitus							FE	0.693
No	30	81.1	14	77.8	16	84.2	0.249	
Yes	7	18.9	4	22.2	3	15.8		
Hypertension							FE	0.447
No	31	88.6	15	83.3	13	68.4	1.117	
Yes	4	11.4	3	16.7	6	31.6		
Smoking							χ^2	0.254
Not smoker	17	45.9	10	55.6	7	36.8	1.303	
Smoker	20	54.1	8	44.4	12	63.2		
Chronic alcoholic consumption (> 2 years)							FE	0.180
No	6	16.2	1	5.6	5	26.3	2.932	
Yes	31	83.8	17	94.4	14	73.7		

N number, χ^2 chi-square test, *FE* Fischer's exact test, *MC* Monte Carlo exact test, *Z* Mann–Whitney test

Table 2 Comparison of exposure history, length of hospital stay, and discharge type between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

Exposure history	Total (n = 37)		Outcome				Test of Sig.	*p*
			Favorable (n = 18)		Unfavorable (n = 19)			
	N.	%	N.	%	N.	%		
Delay (h)							Z	0.836
Median	24.0		24.0		24.0		0.207	
Min.–Max.	3.0–96.0		3.0–96.0		3.0–72.0			
Amount							MC	0.714
Unknown	22	59.5	11	61.1	11	57.9	1.056	
< 100 mL	4	10.8	1	5.6	3	15.8		
> 100 mL	11	29.7	6	33.3	5	26.3		
Source of the ingested substance							MC	0.686
Industrial	18	48.6	10	55.6	8	42.1	0.939	
Homemade	13	35.2	6	33.3	7	36.8		
Known brand	6	16.2	2	11.1	4	21.1		
Length of hospital stay (h)							Z	0.002*
Median	48.0		24.0		48.0		3.080	
Min.–Max.	12.0–1728.0		12.0–96.0		24.0–1728.0			
Length of hospital stay (days)							Z	0.001*
Median	2.0		1.0		2.0		3.176	
Min.–Max.	0.5–72.0		0.5–4.0		1.0–72.0			
Discharge type							FE	0.604
Regular for follow-up	33	89.2	17	94.4	16	84.2	1.004	
Discharge against medical advice	4	10.8	1	5.6	3	15.8		

N number, *FE* Fischer exact test, *MC* Monte Carlo exact test, *Z* Mann–Whitney test

*$P < 0.05$ (statistically significant)

Table 3 Comparison of vital signs on admission between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

Vital signs	Total (n = 37)		Outcome				Test of Sig.	*p*
			Favorable (n = 18)		Unfavorable (n = 19)			
Pulse (beat/min)							Z	0.784
Median	92.0		93.5		92.0		0.274	
Min.–Max.	61.0–145.0		61.0–142.0		63.0–145.0			
Systolic blood pressure (mmHg)							t	0.446
Mean ± SD	124.4 ± 19.5		126.8 ± 22.0		121.8 ± 16.6		0.770	
Min.–Max.	79.0–185.0		79.0–185.0		96.0–150.0			
Diastolic blood pressure (mmHg)							t	0.024*
Mean ± SD	79.0 ± 13.0		83.6 ± 14.5		74.2 ± 9.2		2.353	
Min.–Max.	51.0–109.0		51.0–109.0		55.0–94.0			
Temperature (°C)							Z	0.550
Median	36.8		36.9		36.8		0.598	
Min.–Max.	36.0–37.6		36.0–37.2		36.0–37.6			
Respiratory rate (cycle/minute)							Z	0.442
Median	20.0		20.0		19.0		0.768	
Min.–Max.	15.0–24.0		18.0–22.0		15.0–24.0			
Tachypnea	**N.**	**%**	**N.**	**%**	**N.**	**%**	χ^2	0.642
No	13	35.1	7	38.9	6	31.6	0.217	
Yes	24	64.9	11	61.1	13	68.4		

N number, χ^2 chi-square test, *t* Student's t-test, *Z* Mann–Whitney test

*$P < 0.05$ (statistically significant)

Table 4 Comparison of presenting complaints and clinical examination on admission between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

Presenting complaints and clinical examination	Total (n=37)		Outcome				Test of Sig.	*p*
			Favorable (n = 18)		Unfavorable (n = 19)			
Headache	**N.**	**%**	**N.**	**%**	**N.**	**%**	FE	0.269
No	28	75.7	12	66.7	16	84.2	1.546	
Yes	9	24.3	6	33.3	3	15.8		
Blurred vision							χ^2	0.091
No	26	70.3	15	83.3	11	57.9	2.863	
Yes	11	29.7	3	16.7	8	42.1		
Nausea and vomiting							χ^2	0.618
No	18	48.6	8	44.4	10	52.6	0.248	
Yes	19	51.4	10	55.6	9	47.4		
Dizziness, slurred speech, and confusion							χ^2	0.402
No	20	54.1	11	61.1	9	47.4	0.703	
Yes	17	45.9	7	38.9	10	52.6		
Seizures							FE	0.008*
No	30	81.1	18	100.0	12	63.2	8.179	
Yes	7	18.9	0	0.0	7	36.8		
Chest auscultation							MC	0.359
Normal	34	91.9	18	100.0	16	84.2	3.093	
Crepitation	2	5.4	0	0.0	2	10.5		
Wheezes	1	2.7	0	0.0	1	5.3		
Visual acuity							MC	0.001*
No affection	27	73.0	18	100.0	9	47.4	12.982	
Decreased visual acuity	7	18.9	0	0.0	7	36.8		
No perception of light	3	8.1	0	0.0	3	15.8		

N number, χ^2 chi-square test, *FE* Fischer's exact test, *MC* Monte Carlo exact test

*$P < 0.05$ (statistically significant)

The laboratory workout carried out in both groups is detailed in Tables 5, 6, and 7. Regarding arterial blood gas analysis, 73% of presented patients suffered from metabolic acidosis where pH was comparable in both groups (mean 7.2 ± 0.1). Patients with unfavorable outcomes showed lower HCO_3 and PO_2 levels, as well as a higher PCO_2 level compared to another group. Among all parameters, only the anion gap exhibited substantial variations among the studied groups ($P = 0.022$), where high anion gap metabolic acidosis was a significant finding among patients with unfavorable outcomes (84.2%).

Electrolyte analysis found that patients with unfavorable outcomes showed higher K and lower Na, Cl, and Ca levels than patients with favorable outcomes. Moreover, higher serum urea, creatinine, total bilirubin, liver transaminases, and random blood glucose were more pronounced among patients with unfavorable outcomes. The mean value of random blood glucose levels was 6.6 ± 4.7 mmol/L in patients with unfavorable outcomes compared to 5.9 ± 3.7 in patients with favorable outcomes. CBC and coagulation profile revealed insignificant differences between both groups. However, patients with unfavorable outcomes showed fewer red blood cells (RBCs), white blood cells (WBCs), platelets, and hemoglobin. Median values of 13.5 and 34.7 s, and 1.1 were reported for P.T., PTT, and INR. Except for the anion gap, all lab investigations revealed insignificant differences among the studied groups.

The evaluation of enrolled patients using different scorings revealed that 72.2% of the patients with favorable outcomes were within the mild category based on GCS. Similarly, 66.7% of the patients with favorable outcomes were minorly intoxicated based on PSS. Patients with unfavorable outcomes were more likely to experience moderate and severe intoxication than those with favorable outcomes. This distribution was significant in PSS but not in GCS. Table 8 depicts the variations in SOFA score and GCS among the patients of different outcomes. Patients with unfavorable outcomes showed significantly higher SOFA scores (mean 7.0 ± 2.5) than patients with unfavorable outcomes (mean 2.9 ± 1.4). Although the patients with unfavorable outcomes showed lower GCS scores (median 12) than those with favorable outcomes (median 14), this difference is statistically insignificant.

Table 5 Comparison of arterial blood gas analysis on admission between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

Arterial blood gases analysis	Total (n = 37)		Outcome				Test of Sig.	*p*
			Favorable (n = 18)		Unfavorable (n = 19)			
pH							t	0.803
Mean ± SD	7.2 ± 0.1		7.2 ± 0.1		7.2 ± 0.1		0.251	
Min.–Max.	6.9–7.45		6.95–7.45		6.9–7.45			
HCO_3 (mEq/L)							t	0.271
Mean ± SD	17.4 ± 5.0		18.4 ± 4.9		16.5 ± 5.0		1.119	
Min.–Max.	7.5–28.6		7.5–24.3		10.3–28.6			
PCO_2 (mmHg)							t	0.487
Mean ± SD	37.6 ± 11.6		36.2 ± 10.0		38.9 ± 13.0		0.703	
Min.–Max.	18.0–65.0		18.0–59.5		21.4–65.0			
PO_2 (mmHg)							Z	0.375
Median	95.0		96.5		95.0		0.888	
Min.–Max.	52.0–100.0		89.0–100.0		52.0–100.0			
Anion gap							Z	0.022*
Median	19.0		15.8		22.3		2.282	
Min.–Max.	3.0–38.0		3.0–38.0		4.1–30.7			
Anion gap	**N.**	**%**	**N.**	**%**	**N.**	**%**	MC	0.046*
Normal	9	24.3	7	38.9	2	10.5	6.422	
Low	4	10.8	3	16.7	1	5.3		
High	24	64.9	8	44.4	16	84.2		
Metabolic acidosis							χ^2	0.141
No	10	27.0	7	38.9	3	15.8	2.501	
Yes	27	73.0	11	61.1	16	84.2		

N number, χ^2 chi-square test, *MC* Monte Carlo exact test, *t* Student's t-test, *Z* Mann–Whitney test

*$P < 0.05$ (statistically significant)

The current study revealed that admission to ICU was significantly more frequent among patients with unfavorable outcomes than another group ($P = 0.019$). Ultimately, 51.4% of the included patients treated with supportive measures without requiring hemodialysis or antidotal therapy, 21.6% received fomepizole, 13.5% underwent hemodialysis, 10.8% underwent hemodialysis, and received fomepizole, while 2.7% only received ethanol. There were significant differences between the two studied groups ($P = 0.028$). The significant variations are attributed to the predominance of supportive therapy in patients with favorable outcomes (z = 2.5) and hemodialysis in patients with unfavorable outcomes (z = 2.3).

As shown in Table 9, an initial univariate analysis was carried out to ascertain the effect of different variables as unfavorable outcomes' predictors. Among the studied parameters, the diastolic blood pressure, anion gap, visual acuity, number of hemodialysis sessions, duration of ICU admission (days), PSS, and SOFA scores were significant predictors ($P < 0.05$). However, only SOFA score illustrated meaningful predictive ability in multivariate analysis (odds ratio: 0.10 95% confidence interval (0.04–0.17), $P = 0.003$). Figure 1 shows the receiver operating characteristic (ROC) curve for SOFA score as an unfavorable outcomes predictor in patients diagnosed with methanol ingestion who presented to the three centers examined. At a cutoff of greater than 4.5, the SOFA score could significantly predict unfavorable outcomes ($P < 0.001$), with an excellent AUC of 0.955, 89.2% accuracy, 94.4% specificity, 84.2% sensitivity, 94.1% positive predicted value, and 85% negative predicted value. Table 10 shows that the SOFA score demonstrated the best accuracy and AUC compared to the other outcome predictors.

Discussion

Acute methanol intoxication is a significant health problem affecting populations worldwide and resulting in severe lifelong complications (Rulisek et al. 2020). The current study focused on the early prediction of methanol-induced multisystem organ failure. Thirty-seven patients were evaluated for unfavorable outcomes throughout the study period, accounting for a significant proportion of presented patients (51.4%). As seen in Table 11, ocular, renal, and respiratory complications have been extensively reported elsewhere in variable proportions in different studies. Apart from seizures, the

Table 6 Comparison of electrolytes and some laboratory investigations between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

Lab investigations	Total (n = 37)	Outcome		Test of Sig.	*p*
		Favorable (n = 18)	Unfavorable (n = 19)		
Na (mmol/L)				t	0.217
Mean ± SD	139.3 ± 4.5	140.2 ± 4.1	138.4 ± 4.8	1.256	
Min.–Max.	130.0–149.0	134.0–149.0	130.0–148.0		
K (mmol/L)				t	0.161
Mean ± SD	4.0 ± 0.7	3.8 ± 0.4	4.1 ± 0.8	1.439	
Min.–Max.	2.8–5.3	2.98–4.7	2.8–5.3		
Cl (mmol/L)				t	0.116
Mean ± SD	104.9 ± 6.4	106.7 ± 5.9	103.4 ± 6.6	1.605	
Min.–Max.	90.0–122.0	98.0–122.0	90.0–112.0		
Ca (mmol/L)				Z	0.107
Median	2.1	2.2	2.1	1.612	
Min.–Max.	0.5–3.0	2.0–3.0	0.5–2.5		
Urea (mmol/L)				Z	0.132
Median	4.7	4.2	5.2	1.505	
Min.–Max.	1.4–24.5	1.4–6.2	2.3–24.5		
Creatinine (μmol/L)				Z	0.078
Median	78.9	67.5	81.0	1.763	
Min.–Max.	40.0–195.0	40.0–102.0	51.0–195.0		
Total bilirubin (μmol/L)				Z	0.059
Median	10.0	6.4	12.0	1.885	
Min.–Max.	3.0–56.3	3.8–25.1	3.0–56.3		
ALT (U/L)				Z	0.403
Median	33.0	29.5	33.0	0.836	
Min.–Max.	8.0–153.0	8.0–60.0	15.0–153.0		
AST (U/L)				Z	0.287
Median	32.0	30.0	33.0	1.065	
Min.–Max.	14.0–317.0	17.0–72.0	14.0–317.0		
RBS (mmol/L)				Z	0.975
Median	5.0	5.0	5.0	0.032	
Min.–Max.	3.0–24.0	3.3–20.0	3.0–24.0		

N number, *t* Student's t-test, *Z* Mann–Whitney test, *AST* aspartate transaminase, *ALT* alanine transaminase, *RBS* random blood sugar

absence of neurological complications in the current study might be attributed to the absence of fatalities in the current cohort.

The mean age of patients involved in the current study was 33.9 ± 11.5 years, which is consistent with multiple case reports in various settings (Kraut 2016; Diagne et al. 2019). On the other hand, Ahmed et al. reported slightly higher age (mean 36.2 ± 8.6 years) (Ahmed et al. 2017). Furthermore, Kurtas et al. indicated that individuals aged 41–50 years are more exposed (Kurtas et al. 2017). Rulisek et al. reported an increased incidence of methanol intoxication in the elderly aged 50.9 ± 2.6 years (Rulisek et al. 2020). The noticed age variation indicates the prevalence of methanol exposure in all age groups, especially during outbreaks. The current study established male predominance over females, which was thoroughly reported (Ahmed et al. 2017; Kurtas et al. 2017; Dalena et al. 2018). A substantial proportion of the intoxicated patients was reported utilizing alcohol and tobacco for more than 2 years, which is consistent with another study in Saudi Arabia where 72% of alcohol users were also smokers (Ginawi 2013).

The current study revealed the predominance of accidental exposure without suicidal intentions, partially agreeing with other studies (Aisa and Ballut 2016; Chang et al. 2019). Although accidental exposure was the most frequent, suicidal exposure was not uncommon elsewhere (Chang et al. 2019). Regarding the type of ingested methanol, 48.6% consumed industrial alcohol, and 35.2% consumed homemade alcohol. The diverse types were reported in other studies. A similar study reported that 74.5% of patients consumed industrial alcohol versus 25.5% consumed homemade (Massoumi et al. 2012). Illegal homemade alcohol (80%) outnumbered

Table 7 Comparison of CBC and coagulation profile between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

CBC and coagulation profile	Total (n = 37)	Outcome		Test of Sig.	*p*
		Favorable (n = 18)	Unfavorable (n = 19)		
RBCs (10^6/microliter)				Z	0.236
Median	4.9	4.9	4.7	1.186	
Min.–Max.	3.4–7.7	4.5–6.2	3.4–7.7		
WBCs/microliter				Z	0.162
Median	7800.0	8315.0	7200.0	1.398	
Min.–Max.	3880.0–18190.0	5590.0–18190.0	3800.0–13650.0		
Platelets/microliter				t	0.903
Mean ± SD	274648.7 ± 93198.2	276611.1 ± 81245.6	272789.5 ± 105499.7	0.123	
Min.–Max.	59000.0–534000.0	180000–480000	59000.0–534000.0		
HB (g/dL)				Z	0.080
Median	13.9	14.0	13.3	1.750	
Min.–Max.	6.0–17.7	9.9–17.0	6.0–17.7		
P.T. s				Z	0.392
Median	13.5	13.6	13.3	0.857	
Min.–Max.	10.5–21.7	10.7–15.3	10.5–21.7		
PTT s				Z	0.185
Median	34.7	36.0	33.8	1.325	
Min.–Max.	21.0–78.5	22.7–78.5	21.0–45.0		
INR				Z	0.436
Median	1.1	1.1	1.1	0.779	
Min.–Max.	0.7–1.9	0.7–1.2	0.9–1.9		

N number, *t* Student's t-test, *Z* Mann–Whitney test, *CBC* complete blood count, *RBCs* red blood cells, *WBCs* white blood cells, *HB* hemoglobin, *P.T.* prothrombin time, *PTT* partial thromboplastin time, *INR* international normalization ratio

the industrial preparations (10%) in another study (Shadnia et al. 2013).

The current study reported a potential delay in presentation to the hospital (median 24 h), which agrees with another study that reported a typical presentation between 24 and 96 h following ingestion (Md Noor et al. 2020). The noticed negligible relationship between delay time and the unfavorable outcome contradicts the findings from another study carried out in Taiwan, in which considerable delay was associated with poor outcomes (Lee et al. 2014). Another study was carried out in Saudi Arabia, in which five cases of methanol died due to 72-h delay (Saddique 2001). The noticed delay until seeking the emergency services is attributed to the initial symptomless period and the latent manifestations following methanol ingestion. During this period, methanol is metabolized into formic acid (Azeemuddin and Naqi 2012), and rapid deterioration occurs (Desai et al. 2013). The current study reported a median hospital stay of 2 days, with a statistically significant association between a prolonged hospital stay and unfavorable outcomes. These results are in line with a previous study conducted in the USA, in which patients intoxicated with methanol spent approximately 4.0 ± 6.1 days. Prolonged hospitalization places a noticeable burden on health care providing services (Kaewput et al. 2021).

The current study revealed that patients with unfavorable outcomes showed a lower pulse, blood pressure, temperature, and respiratory rate than those with favorable outcomes. Considerably significant lower diastolic blood pressure was reported in patients with unfavorable outcomes. Correspondingly, hypotension, hypothermia, and bradycardia were common findings in patients with poor outcomes following methanol intoxication in patients complicated by acute kidney injury (Chang et al. 2019). Methanol-induced hypotension might be explained by dehydration due to vomiting and the vasomotor center depression induced by methanol. The noticed substantial reduction in diastolic blood pressure and unfavorable outcomes bolster this explanation (Barceloux et al. 2002).

The current research revealed that nausea and vomiting, dizziness, blurred vision, and headache were the most common presentations, while seizure was the least frequent manifestation (18.9%) and the only substantially present presenting symptom in patients with unfavorable outcomes. Similarly, Ahmed et al. reported that about half of the presented patients suffered from blurred vision and (28%) had complete blindness (Ahmed et al. 2017). The current study's findings corroborate those of Md Noor et al. They reported that approximately one-third of studied patients presented with

Table 8 Comparison of different scorings and ICU admission between patients with favorable and unfavorable outcomes diagnosed with acute methanol ingestion presenting to the three studied centers

Scoring and ICU admission	Total (n = 37)		Outcome				Test of Sig.	*p*
			Favorable (n = 18)		Unfavorable (n = 19)			
SOFA score							t	< 0.001*
Mean ± SD	5.0 ± 2.9		2.9 ± 1.4		7.0 ± 2.5		6.131	
Min.–Max.	1.0–13.0		1.0–6.0		4.0–13.0			
GCS							Z	0.079
Median	13.0		14.0		12.0		1.754	
Min.–Max.	3.0–15.0		5.0–15.0		3.0–15.0			
GCS	**N.**	**%**	**N.**	**%**	**N.**	**%**	MC	0.248
Mild (13–15)	22	59.5	13	72.2	9	47.4	3.481	
Moderate (9–12)	9	24.3	4	22.2	5	26.3		
Severe (3–8)	6	16.2	1	5.6	5	26.3		
PSS grade							χ^2	< 0.001*
Minor	13	35.1	12	66.7	1	5.2	16.836	
Moderate	14	37.9	5	27.7	9	47.4		
Severe	10	27.0	1	5.6	9	47.4		
ICU admission							FE	0.019*
No	28	75.7	17	94.4	11	57.9	6.708	
Yes	9	24.3	1	5.6	8	42.1		

N number, *FE* Fischer's exact test, χ^2 chi-square test, *MC* Monte Carlo exact test, *t* Student's t-test, *Z* Mann–Whitney test, *SOFA* Sequential Organ Failure Assessment, *GCS* Glasgow Coma Scale, *PSS* Poison Severity Score, *ICU* intensive care unit

*$P < 0.05$ (statistically significant)

vomiting, blurred vision, and altered consciousness level; however, only 6.5% had seizures (Md Noor et al. 2020). Methanol-induced visual impairment results from the accumulation of formic acid, which inhibits cytochrome oxidase and induces histotoxic hypoxia. Subsequently, ATP depletion and mitochondrial dysfunctions occur, halting the action potential conduction and inducing visual loss and ocular toxicity (Barceloux et al. 2002). Multiple previous studies have confirmed the correlation between seizures and unfavorable outcomes, including death (Sanaei-Zadeh et al. 2011; Lee et al. 2014). The neurological complications arise from different brain areas, including the cerebral cortex, hypothalamus, basal ganglion, and pons (Diagne et al. 2019). Moreover, cerebral ischemia, hemorrhage, and cerebral edema have been documented in the autopsy of methanol intoxication fatalities (Paasma et al. 2012).

The analyses of arterial blood gases illustrated that metabolic acidosis was commonly observed in the patients presented with acute methanol exposure (73%). Lower HCO_3, PO_2, and significantly higher anion gap were observed in patients

Table 9 Univariate and multivariate binary logistic regression analysis for the significant parameters affecting outcome among patients diagnosed with acute methanol ingestion presenting to the three studied centers

Outcome predictors	Univariate		Multivariate	
	p	OR (95%CI)	*p*	OR (95%CI)
Diastolic blood pressure	0.024*	0.01 (0.01–0.03)	0.177	0.01 (− 0.01–0.02)
Anion gap	0.014*	0.23 (0.05–0.42)	0.817	− 0.02 (− 0.16–0.13)
Visual acuity	< 0.001*	0.44 (0.21–0.67)	0.918	− 0.01 (− 0.26–0.24)
Number of hemodialysis sessions	0.005*	0.16 (0.05–0.27)	0.052	0.12 (− 0.00–0.24)
PSS	< 0.001*	0.42 (0.26–0.58)	0.358	0.13 (− 0.16–0.43)
SOFA score	< 0.001*	0.12 (0.08–0.17)	0.003*	0.10 (0.04–0.17)
Duration of ICU admission (days)	0.009*	0.49 (0.13–0.86)	0.619	− 0.10 (− 0.52–0.31)

OR odds ratio, *CI* confidence interval, *PSS* Poison Severity Score, *SOFA* Sequential Organ Failure Assessment, *ICU* intensive care unit

*$P < 0.05$ (statistically significant)

Table 10 Sensitivity, specificity, and accuracy of the significant parameters affecting outcome among patients diagnosed with acute methanol ingestion presenting to the three studied centers

Outcome predictors	Cutoff value	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC	*P* value
Diastolic blood pressure	78.5	73.7%	77.8%	77.8%	73.7%	75.7%	0.731	0.016*
Anion gap	19.5	63.2%	66.7%	66.7%	63.2%	64.9%	0.719	0.023*
Visual acuity	0.5	52.6%	100.0%	100.0%	66.7%	75.7%	0.763	0.006*
Number of hemodialysis sessions	0.5	68.4%	72.2%	72.2%	68.4%	70.3%	0.741	0.012*
PSS	1.5	94.7%	66.7%	75.0%	92.3%	81.1%	0.860	< 0.001*
SOFA score	4.5	84.2%	94.4%	94.1%	85.0%	89.2%	0.955	< 0.001*
Duration of ICU admission (days)	0.5	42.1	94.4	88.9%	60.7%	67.6%	0.683	0.049*

AUC area under curve, *PPV* positive predicted value, *NPV* negative predicted value, *PSS* Poison Severity Score, *SOFA* Sequential Organ Failure Assessment, *ICU* intensive care unit

*$P < 0.05$ (statistically significant)

with unfavorable outcomes. Comparable results following methanol exposure were published elsewhere (Md Noor et al. 2020). Moreover, when completely recovered patients without complications were compared to recovered patients with complications and non-survivors, it was found that non-survivors showed the lowest pH, HCO_3, PO_2, and highest anion gap, followed by complicated patients (Paasma et al. 2012). The current study reported the significant function for the anion gap as an unfavorable outcome predictor, which agrees with other studies. The association between methanol toxicity and high anion gap metabolic acidosis is due to formic acid formation. The parallel decrease in HCO_3 and elevated serum formic acid in patients with unfavorable outcomes supports the crucial role of formic acid in methanol-induced acidosis. Acidosis accelerates the toxicity by enhancing more formic acid diffusion into the cells (Barceloux et al. 2002).

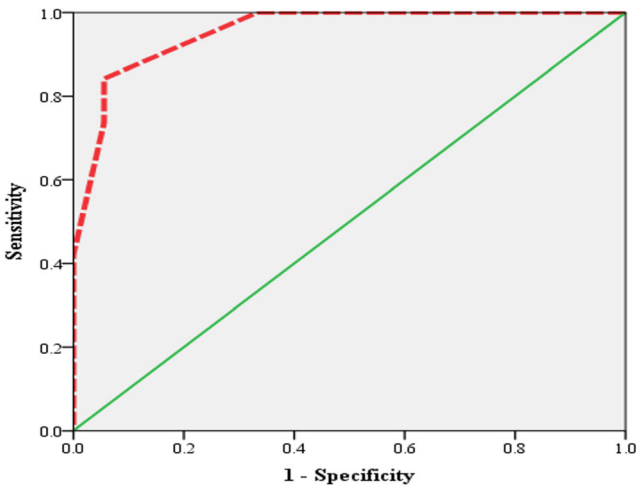

Fig. 1 Receiver operating characteristic ROC curve for SOFA score as unfavorable outcome predictor among patients diagnosed with acute methanol ingestion presenting to the three studied centers. At a cutoff of greater than 4.5, the SOFA score could significantly predict unfavorable outcomes ($P < 0.001$), with an excellent AUC of 0.955, 89.2% accuracy, 94.4% specificity, 84.2% sensitivity, 94.1% positive predicted value, and 85% negative predicted value

The current study reported higher potassium and blood glucose levels in patients with unfavorable outcomes, consistent with previous research indicating that hyperkalemia and hyperglycemia were significant signs in non-survivors compared to survivors following methanol intoxication (Ran et al. 2019; Md Noor et al. 2020). Besides hyperglycemia, hyperkalemia had been reported earlier and believed to be due to severe vomiting (Desai et al. 2013). Compared to these findings, hypokalemia following methanol intoxication had been widely documented and was due to respiratory compensation or bicarbonate therapy (Shah et al. 2012). In contrast to the current study, hyperglycemia was considered a poor prognostic factor and a mortality predictor (Sanaei-Zadeh et al. 2011).

Urea and creatinine elevation was noticed in patients with unfavorable outcomes compared to patients with favorable outcomes. Although this variation was insignificant, it matches multiple studies (Paasma et al. 2012; Lee et al. 2014; Chang et al. 2019). Postmortem examination of methanol-induced fatalities revealed various renal injuries, including hyperemia and parenchymal degeneration, in addition to tubular injury and necrosis (Kurtas et al. 2017). However, renal dysfunction peaks 1 week after exposure and lasts for 1 month (Barceloux et al. 2002).

The current study showed that the hematological parameters, including hemoglobin, red blood cells, leukocytic count, and platelets were slightly decreased in patients with unfavorable outcomes. However, these parameters were within the standard reference, with insignificant differences among the studied groups; these findings corroborate those of other studies (Barceloux et al. 2002; Chang et al. 2019). The acute accidental nature of the intoxication is a reasonable justification. Moreover, median values of 13.5 and 34.7 s, and 1.1 were reported for P.T., PTT, and INR, which are less than the obtained mean values of 16.22 ± 5.9, 36.64 ± 13.05, and 1.40 ± 0.85 in another study, respectively (Massoumi et al. 2012).

Table 11 Comparison of poor outcomes following acute methanol intoxication between current and published studies (sample size ≥ 10)

Study	Year	Area	Sample size	Duration of the study	Optic neuropathy and/or blindness	Renal impairment	Respiratory failure	Mortalities
Current study	2021	Saudi Arabia	37	3 years	29.7%	18.9%	10.8%	0%
Kaewput et al.	2020	USA	603	11 years	8%	22%	21%	6.5%
Md Noor et al.	2020	Malaysia	31	Outbreak	6.4%	---	64.5%	61.3%
Chang et al.	2019	Taiwan	50	13 years	5%	66%	52%	28%
Ran et al.	2019	China	52	---	1.9%	---	---	3.9%
Ahmed et al.	2017	Pakistan	35	27 years	28%	---	---	54.2%
Lee et al.	2014	Taiwan	32	8 years	---	59.4%	50%	34.4%
Salek et al.	2014	Czech	13	Outbreak	7.14%	15.4%	---	0%
Shadnia et al.	2013	Iran	30	24 months	7%	---	---	30%
Massoumi et al.	2012	Iran	51	9 years	3.9%	---	---	7.8%
Hassanian-Moghaddam et al.	2007	Iran	25	9 months	32%	---	16%	48%
Verhelst et al.	2004	Belgium	25	14 years	8%	60%	---	24%
Mégarbane et al.	2001	France	14	12 years	28.6%	---	14.3%	0%

The current study showed that 21.6% of presented patients received fomepizole, 13.5% underwent hemodialysis, 10.8% underwent hemodialysis and received fomepizole, and just 2.7% received ethanol. Various therapeutic regimens had been reported in different studies based on the availability of antidotes and the followed guidelines. In all reports, hemodialysis is a commonly used reliable management procedure. The preference for fomepizole over ethanol agrees with Rietjens et al. It can be attributed to the minimal adverse effects, longer duration of action, and the easy monitoring, which does not necessitate ICU admission compared to the ethanol (Rietjens et al. 2014). However, the preference for fomepizole over ethanol contradicts other studies, prioritizing ethanol as an antidote (Paasma et al. 2012; Chang et al. 2019). It could be explained by the availability of ethanol in some poison control centers and its economical price compared to fomepizole. Moreover, in agreement with the current study, hemodialysis might be combined with fomepizole, as the latter prolongs the half-life of methanol (Rietjens et al. 2014). Underutilization of ethanol in the current study could be referred to its unavailability, uncertainty of most physicians in Arabic countries regarding its religious and cultural prohibition.

The current study showed that 24.3% of presented patients were admitted to ICU. Significantly more patients with unfavorable outcomes required ICU admission, and the need for ICU admission was considered a significant outcome predictor. A median length of 5 days of ICU stay was reported in a similar study (Mégarbane et al. 2001). The primary goals of extended ICU admission were to determine the need for artificial ventilation, renal replacement therapy, and antidotal therapy. The present paper revealed that the median GCS was about 13, where 83.8% of studied patients were within the mild and moderate grade and insignificant differences among the studied groups. Unreliability of the GCS as an outcome predictor agrees with postmortem analysis of 383 deaths due to methanol exposure, where most of them were conscious with a relatively high GCS (Kurtas et al. 2017). However, most patients deteriorated rapidly soon after admission. The median GCS reported in the current study is above the scores reported in another study in Pakistan (10.4 ± 4.4) (Ahmed et al. 2017). These findings support the results of Fayed and Sharif, who mentioned that GCS is not linked to toxic ingestion but instead to head trauma (Fayed and Sharif 2021). The evaluation of patients based on PSS yielded similar results; however, more moderate and severe cases showed unfavorable outcomes, and PSS showed significant outcome prediction. Utilizing PSS for evaluating methanol intoxication severity had been reported earlier (Lepik et al. 2009); however, its utility in its current form is limited, and it needs further modifications to be applicable in multiple poisoning contexts (Schwarz et al. 2017).

In the current study, univariate analysis verifies that the diastolic blood pressure, anion gap, visual acuity, number of hemodialysis sessions, PSS, number of days in ICU, and SOFA score are significant outcome predictors. However, among the studied parameters, multivariate analysis proves that only SOFA score above 4.5 could significantly predict unfavorable outcomes with high accuracy of 89.2% and an excellent AUC (0.955). In patients with unfavorable outcomes, the mean SOFA score was 7.0 ± 2.5 compared to 2.9 ± 1.4 in completely recovered patients. The SOFA score was selected as it includes a graded evaluation of six body systems, including respiratory, renal, hepatic, cardiovascular, hematological, and neurological systems (Bota et al. 2002).

Even though the SOFA score was initially invented to judge the patients with sepsis, its role in evaluating the poisoned patients has been reported. Patients with high SOFA scores are at more risk for developing organ failure and mortality (Masson et al. 2012). Most previous works evaluated a single outcome following methanol intoxication (Verhelst et al. 2004; Hassanian-Moghaddam et al. 2007; Salek et al. 2014). To the best of our knowledge, the SOFA score was introduced as a multiple outcomes predictor among patients suffering from methanol intoxication in the current study for the first time. The prognostic role of SOFA score has been reported with few toxins but not with methanol. The SOFA score was found to be predictive of outcomes in patients exposed to aluminum phosphide (Sheta et al. 2019), hydrogen cyanamide (Sharif and Fayed 2021), cholinergic (Schwarz et al. 2017), and paraquat (Weng et al. 2013). However, similar cutoffs have been reported for unfavorable outcomes (3, 4.5) (Sheta et al. 2019; Sharif and Fayed 2021).

Conclusion

Methanol intoxication is a serious life-threatening problem that occurs unintentionally. Visual impairment, renal injury, and respiratory failure are the most common complications. Early identification of patients at risk is critical and lifesaving. The diastolic blood pressure, anion gap, visual acuity, number of hemodialysis sessions, PSS, number of days in ICU, and SOFA score are significant organ failure predictors. However, the SOFA score is the most accurate and early inclusive unfavorable outcome predictor.

Recommendations

- Establishing an effective triage system (including SOFA score) for evaluation of toxic alcohol-exposed patients.
- Providing antidotes stocks in Poison control centers and implementing clear management guidelines.
- Ensuring high quality-controlled production and distribution of alcoholic beverages.
- Establishing a tracking system to limit illegal alcohol production.
- Increasing orientation of populations about hazards of industrial alcohol and illegal alcoholic beverages.

Limitation

Few studied patients might influence the reliability of the results. However, given the underreporting of methanol exposure, we tried to increase the credibility of the study by collecting the data from three large poison control centers. Moreover, 6 months of follow-up will confirm the unfavorable visual outcomes in the presented patients. However, predicting multiple outcomes based on clinical and laboratory investigations strengthens the current study and narrows the knowledge gap.

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Author contributions A. Sharif conceptualized the study, analyzed, and interpreted the data; the corresponding author wrote the manuscript draft, proofread it, and approved the final manuscript.

M. AlAmeer conceptualized the study, collected the data, obtained ethical approval, and approved the final manuscript.

D. AlSubaie conceptualized the study, collected the data, obtained ethical approval, and approved the final manuscript.

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M. BuSaleh conceptualized the study, collected the data, and approved the final manuscript.

AlSabr conceptualized the study, collected the data, and approved the final manuscript.

K. Al-Mulhim supervised the data collection, obtained ethical approval, interpreted the data, proofread the manuscript, and approved the final manuscript.

Data Availability The dataset used and/or analyzed during the current study is available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate The current study was carried out following the Declaration of Helsinki. Ethical approvals were obtained from the institutional review boards from King Saud Medical City (IRB Number: H1R1-30-Dec20-01), King Fahad Medical City (IRB Log Number:21-024), and College of Medicine, Dar Al-Uloom University (IRB Number: Pro 20110001).

Consent for publication Not applicable as the current study was conducted retrospectively and informed consents were waived by IRB committees. Data were retrieved from the medical records without personal identity declaration to maintain the confidentiality of the patients

Competing interests The authors declare no competing interests.

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