PREDICTORS OF POOR OUTCOMES IN ACUTE METHANOL POISONING

Samah M. Elbastawesy[1], Mohamed A. Shama[2], Ahmed E. Elsharkawy [2] and Nadia E. Helal[1]

[1]Forensic Medicine and Clinical Toxicology Department, [2]Emergency Medicine and Traumatology Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding author: Samah M. Elbastawesy, Mobile No.: 01032636965**, Email:** doctor_samahmaher@yahoo.com, Samah.elbastawesy@med.tanta.edu.eg

Submit Date 2021-05-31
Revise Date 2021-09-04
Accept Date 2021-09-06

ABSTRACT

Background: Methanol is a highly toxic compound. Severe metabolic acidosis, intense neurological and visual affection are the hallmark of toxicity. Despite maximal supportive care, the mortality rate is yet high. **Objectives:** This study aimed to determine the predictors of poor outcomes in acute methanol poisoning. **Methods:** In this retrospective study, forty acute methanol poisoned patients were recruited. Data of four years (2017 to 2020) was obtained from Tanta university Poison Control Center (TUPCC) archive. Data of patients' outcomes were recorded in addition to demographic data, clinical examination, and laboratory investigations results. **Results:** Out of the 40 enrolled patients, 17 patients had poor outcomes, either death or visual affection, and the remaining 23 patients had completely recovered. A significantly prolonged time elapsed between methanol ingestion and admission in the poor outcome group compared to good outcome one. Likely, the mean GCS, arterial ph, and HCO3 levels were significantly lower in the poor outcome group. Additionally, the poor outcome group noticed a significant increase in total leucocytic count, RBS, ALT, AST, serum creatinine, blood urea, PT, and anion gap. **Conclusions:** Our study shows that delayed hospital admission and on admission GCS were identified as potential predictive factors of poor outcome in acute methanol poisoning.

Keywords: Acute poisoning, Methanol, Outcome, Ophthalmologic affection, predictors.

INTRODUCTION

Methanol, the wood alcohol or Columbian spirit, is a colorless liquid with an alcoholic taste and smell. It serves as an industrial solvent and is commonly used as counterfeit ethanol owing to its low price **(Kruse,2012)**. Methanol is a highly toxic chemical, where 15 ml of 40% methanol solution can cause toxicity **(Boyaci et al.,2012)**. Methanol is catalyzed in the liver via zero-order kinetics by alcohol and aldehyde dehydrogenase to formaldehyde and formic acid, respectively **(Barceloux et al.,2002)**. Clinical findings usually evolve over 6 to 24 hours but can be delayed as long as 72-96 hours if ethanol is co-ingested. Patients with acute methanol poisoning may present with ataxia, drowsiness, nausea, vomiting, and epigastric pain. Drowsiness may progress to seizure and coma in later stages, which mandates intubation **(Hantson,2005; Kraut & Kurtz,2008)**. Ophthalmological findings, including retinal toxicity, optic disc edema, and hyperemia even complete visual loss, are distinctive features of methanol poisoning **(Sharpe et al.,1982)**. High anion gap metabolic acidosis is the trait of acute methanol intoxication, especially in early toxicity **(Zakharov et al.,2015)**. However, acidosis, together with histotoxic effects, is responsible for the late stage of toxicity owing to formic acid-induced mitochondrial paralysis and tissue hypoxia **(Jacobsen & McMartin,1986)**. Methanol-related mortality may reach up to 40% even if the patients survive; poisoning may lead to permanent visual affection and

long-term effects on the central nervous system **(Barceloux et al.,2002; Bezdicek et al.,2014; Vaneckova et al.,2014)**. This mandates prompt intensive interventions, including adequate supportive care, correction of acidosis, administration of ethanol and fomepizole to decrease methanol conversion to its toxic metabolites **(Hovda et al.,2005).** Early hemodialysis is a marvelous way for early and rapid removal of both methanol and its toxic metabolites. Elimination of methanol and its toxic metabolites by hemodialysis is recommended when there is coma, seizures, new visual deficit, and metabolic acidosis (blood pH $\leq$ 7.15), especially when acidosis persists despite adequate supportive therapy. Calculated serum anion gap more than 24 mmol/L, measured serum methanol level greater than 50 mg/dL particularly in the absence of antidotes and renal failure mandate also hemodialysis **(Roberts et al.,2015; Nizhu et al.,2018)**. Gastric decontamination and activated charcoal have no value due to the rapid absorbance of methanol within 30 minutes of ingestion **(Williams & Erickson,1998)**. Using ethanol as an antidote in our country is limited by religious issues in addition to its adverse effects. Additionally, fomepizole therapy is highly costly and not available in developing countries like Egypt **(Zakharov et al.,2016)**. Access to hemodialysis in our center is difficult and takes a long time to start the session owing to the availability of the limited number of dialysis machines, also, increasing need for dialysis for other medical indications that forces the patient to wait long. With this noticeable lack of available resources in the management of methanol intoxication, hemodialysis remains a standalone available and effective way of management. Because methanol levels cannot be detected in our center, indications of hemodialysis were principally settled on the basis of clinical and non-specific laboratory criteria. For the prementioned reasons, the clinician should be aware of outcome predictors that will eventually guide early diagnosis of methanol poisoning, rapid prompt therapy, and early planning for hemodialysis sessions, thereby step up towards better outcomes in such patients. Accordingly, this study aimed to evaluate the predictors of poor outcomes in acute methanol poisoned patients.

PATIENTS & METHODS:

This retrospective comparative observational study was performed in Tanta university Poison Control Center (TUPCC) using the data of four years' interval (2017-2020). Data was retrieved from the patients' clinical files of the TUPCC archive. The privacy of patients' data was preserved through using coding numbers. The study was carried out in accordance to the World Medical Association Declaration of Helsinki, following agreement of the research ethical committee, Faculty of Medicine, Tanta University, Egypt (approval number: 34389/1/21), after authorization of managers of TUPCC and Tanta university Emergency hospital.

The current research included all patients with acute methanol poisoning of both sexes. Diagnosis of methanol poisoning based mainly on a positive history of methanol consumption (either from patient himself or the relatives), presence of characteristic symptoms and signs including (elevated anion gap metabolic acidosis, visual manifestations ranging from blurring of vision up to blindness and neurological manifestations) **(Hovda et al.,2005; Zakharov et al.,2016)**. Patients reported with metabolic acidosis due to other etiologies like diabetes mellitus, starvation and chronic kidney disease were excluded and patients with previous optic neuritis or diminution of vision due to any ophthalmologic cause. Additionally, missed patients' records were excluded.

Acute methanol poisoned Patients were classified according to primary outcome into two major groups, good outcome group (patients discharged free with no residual ophthalmologic sequelae) and poor outcome group (patients either died or survivors with residual sequelae). In each

group, demographic data including (age, sex, residence), medical history, and habits as smoking or addiction were recorded. Toxicological history included mode of poisoning (intentional, accidental, or substance abuse), place of exposure, and delay time since admission were also noted. Initial clinical data were noted, including pulse rate, systolic and diastolic blood pressure, and consciousness level assessment by Glasgow Coma Scale (GCS), pupil size, and reaction. Assessment of vital signs in adults was based on reference ranges **(Hoffman et al.,2011)**. Clinical manifestations including gastrointestinal, neurological, ophthalmologic, and fundoscopic examination were reported. Laboratory investigations consisted of arterial blood gases from arterial blood samples obtained on admission and serum electrolytes as serum sodium, potassium, random blood sugar level (RBS), complete blood count, creatinine, urea, prothrombin time (PT), International Normalized Ratio (INR), and liver enzymes measurements from venous blood samples. Records of twelve-leads Electrocardiogram (ECG) at admission were included. Methanol level wasn't included in diagnostic steps as it is not available in Egypt. The severity of intoxication was determined and was given a score from 0 to 3 using poison severity score (PSS) according to **Persson et al. (1998)**. All patients were treated according to the protocol of treatment of acute methanol poisoned patients used in TUPCC. Hemodialysis was recorded whether indicated or not, performed or not. Secondary outcomes were also recorded in all participants, including the requirement of intensive care admission and/or mechanical ventilation, hemodialysis whether performed or indicated, and duration of hospital stay.

Statistical analysis

The SPSS program, version 22, was used to statistically analyze the tabulated data. The Shapiro Wilk test checked the normality of all continuous variables. Normally distributed data usually presented as mean + SD; meanwhile, differences between the studied groups were proved using the Independent T-test. Instead, data showing abnormal distribution were presented by the median and interquartile range (25th–75th percentile) and compared by using the Mann-Whitney U test. Categorical variables were précised as frequencies and percentages. Association between variables was tested using X2 tests (Pearson's Chi-Square for independence or Fisher's Exact Tests as appropriate). A p-value of < 0.05 was considered statistically insignificant. In order to identify factors that probably be used to search for variables associated with poor outcomes (in statistical terms, a decision tree), a multivariate logistic regression analysis was used. Odds ratio (OR) and 95% confidence intervals (CI) are presented. The choice of risk factors entered the regression model was based on clinical relevance, and the p-value in univariate analysis (variables were p-value less than 0.2 were considered, according to **Bursac et al. (2008)**.

RESULTS

All patients in the current study (n=40) were categorized into good outcome group (23 representing 57.5%) and poor outcome group (n=17 representing 42.5%). The poor outcome group gathered those with residual visual sequelae after their discharge (30% (n=11) and those who died (15% (n=6) fig. (1).

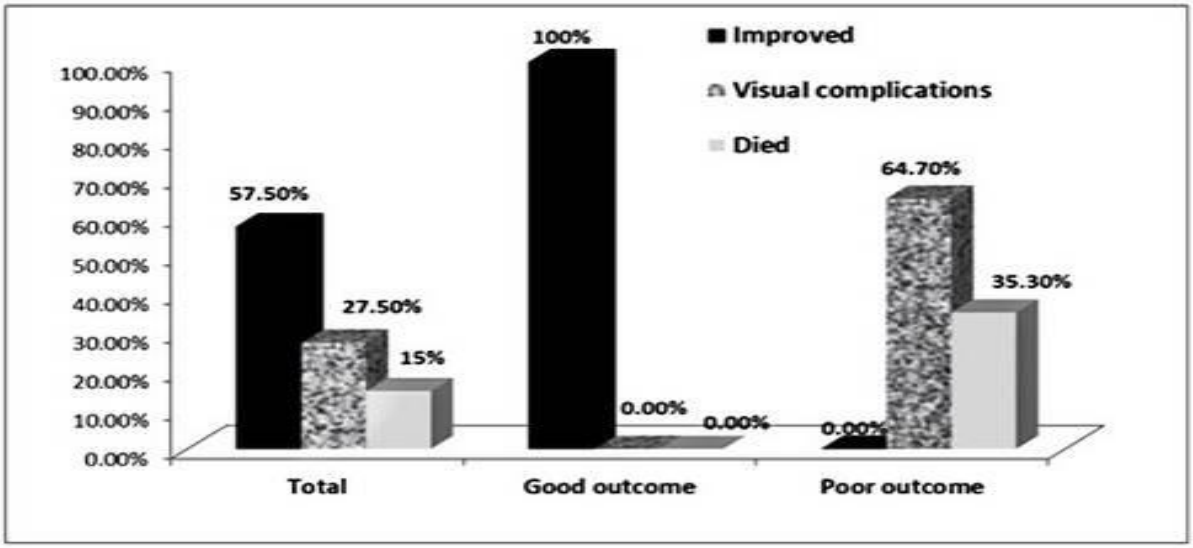

Figure (1): Primary outcome of the studied patients (n= 40).

Table (1) shows that there were insignificant statistical differences between the studied groups as regards their sociodemographic data, including (age, sex, and residence), co-morbidities, and manner of intoxication (p>0,05, each). The majority (62.5%) of exposures occurred accidentally due to consumption of tempted ethanol, while the least exposures were suicidal (7.5%).

Eight patients had co-morbidities; 3 patients (7.5%) had a psychiatric illness, one patient is asthmatic (2.5%), two patients (5%) were cardiac, and two patients (5%) were hypertensive. The median time elapsed between methanol ingestion and hospitalization was significantly prolonged in the poor outcome group compared with good outcome one (36 and 3.5 hours respectively) (p<0,05).

Table (2) demonstrates the baseline clinical, severity, and ECG characteristics of the studied patients. Vomiting was the most predominant complaint (67.5%); meanwhile, the minority of cases had an asymptomatic initial presentation on admission (7.5%). Disturbed consciousness level was more significantly reported among poor outcomes compared to good outcome group (p<0,05). Likewise, the mean GCS was significantly lower in the poor outcome group than good outcome one (10±5.8 and 14.3±2.2 respectively (p<0,05). An insignificant difference could be noticed between the studied groups as regards their vital baseline measurements, including (systolic, diastolic blood pressure, temperature, pulse, and respiratory rates) and ECG (p>0,05).

Table (1): Sociodemographic and toxicological characteristics of the studied patients (n = 40)

Characteristics		**Total (n = 40)**		**Good outcome (n = 23)**		**Poor outcome (n = 17)**		Test statistic	P value
Age (years)	Median [IQR] (Range)	24 [20.0 - 35.0] (3.0 - 80.0)		22 [18.0 - 35.0] (3.0 - 80.0)		26[21.0 - 34.0] (17.0 - 42.0)		1.192 a	0.242
Gender	Female	1	2.5%	1	4.3%	0	0.0%	FE	1.000
	Male	39	97.5%	22	95.7%	17	100.0%		
Residence	Rural	24	60.0%	14	60.9%	10	58.8%	0.017 b	0.896
	Urban	16	40.0%	9	39.1%	7	41.2%		
Medical history	Positive	8	20.0%	5	21.7%	3	17.6%	FE	1.000
	Negative	32	80.0%	18	78.3%	14	82.4%		
Alcoholic	Yes	25	62.5%	13	56.5%	12	70.6%	0.825 b	0.364
	No	15	37.5%	10	43.5%	5	29.4%		
Manner of intoxication	Homemade alcohol	25	62.5%	13	56.5%	12	70.6%	0.825 b	0.364
	Occupational	8	20.0%	7	30.4%	1	5.9%		

	Accidental ingestion in non-labeled container	4	10.0%	3	13%	1	5.9%		
	Suicidal	3	7.5%	0	0.0%	3	17.6%		
Delay time (hours)	Median [IQR] (Range)	17.0 [3.0 - 36.0] (0.5 - 120.0)		3.5 [1.0 - 13.0] (0.5 - 48.0)		36.0 [24.0 - 48.0] (4.0 - 120.0)		4.284 a	<0.001*

a: Mann-Whitney test; b: Pearson's Chi square test; FE: Fisher's exact test; IQR: interquartile range; * significant at p<0.05

Most of the studied patients had normal ECG (87.5%) on admission. Five patients had abnormal findings (sinus tachycardia in two patients (5%), ST segment elevation in two patients (5%), and ST-segment depression in one patient (2.5%). Dilated nonreactive pupil and optic neuritis were more significantly seen among those who had poor outcomes compared with good outcome ones (p<0,05). Application of PSS on admission revealed that the majority of good outcome patients were minor (91.3%). Meanwhile, moderate scores were more frequently traced among poor outcomes than good outcome patients (29.4% and 8.7%, respectively). Severe cases were exclusively found among poor outcome patients (p<0,05).

Table (2): Clinical and severity characteristics of the studied patients (n = 40)

Clinical characteristics		**Total (n = 40)**		**Good outcome (n = 23)**		**Poor outcome (n = 17)**		**Test statistic**	P
Symptoms	Asymptomatic	4	7.5%	4	13.0%	0	0.0%	FE	0.624
	Disturbed consciousness level	15	37.5%	5	21.7%	10	58.8%	5.736 a	0.017*
	Seizure	3	7.5%	0	0.0%	3	17.6%	FE	0.069
	Vomiting	27	67.5%	17	73.9%	10	58.8%	1.015 a	0.314
	Abdominal pain	8	20.0%	5	21.7%	3	17.6%	FE	1.000
	Blurred vision	9	22.5%	2	8.7%	7	41.2%	FE	0.023*
GCS	Mean±SD (Range)	12.5 ± 4.6 (3.0 - 15.0)		14.3 ± 2.2 (7.0 - 15.0)		10.0 ± 5.8 (3.0 - 15.0)		2.869c	0.010*
Pulse	Mean±SD (Range)	93.3 ± 15.8 (68.0 - 130.0)		92.4 ± 14.3 (70.0 - 130.0)		94.5 ± 18.1 (68.0 - 127.0)		0.406 c	0.687
Systolic	Mean±SD (Range)	113.5 ± 21.2 (70.0 - 170.0)		113.9 ± 19.7 (90.0 - 170.0)		112.9 ± 23.7 (70.0 - 160.0)		0.142 c	0.888
Diastolic	Mean±SD (Range)	67.8 ± 14.6 (30.0 - 100.0)		68.3 ± 13.7 (50.0 - 100.0)		67.1 ± 16.1 (30.0 - 80.0)		0.255 c	0.800
Respiratory Rate	Mean±SD (Range)	22.7 ± 5.3 (12.0 - 40.0)		22.2 ± 4.0 (15.0 - 30.0)		23.4 ± 6.8 (12.0 - 40.0)		0.616 c	0.544
Temperature	Mean±SD (Range)	36.9 ± 0.4 (35.8 - 37.5)		36.9 ± 0.2 (36.3 - 37.3)		36.8 ± 0.5 (35.8 - 37.5)		0.998 c	0.329
Pupil	Normal	24	60.0%	20	87.0%	4	23.5%	17.509 d	<0.001*
	sluggish reaction	3	7.5%	0	0.0%	3	17.6%		
	constricted	2	5.0%	1	4.3%	1	5.9%		
	dilated sluggish	11	27.5%	2	8.7%	9	52.9%		
Ophthalmic examination	Normal	21	52.5%	21	91.3%	0	0.0%	32.677 a	<0.001*
	Optic neuritis	19	47.5%	2	8.7%	17	100.0%		
ECG	Normal	35	87.5%	22	95.7%	13	76.5%	FE	0.144
	Abnormal	5	12.5%	1	4.3%	4	23.5%		
Poison Severity Score	normal	35	87.5%	22	95.7%	13	76.5%	17.822 a	<0.001*
	Moderate=2	7	17.5%	2	8.7%	5	29.4%		
	Severe=3	7	17.5%	0	0.0%	7	41.2%		

a: Pearson's Chi square test; b: Mann-Whitney test; c: Independent samples T-test; d: Fisher-Freeman-Halton exact test; FE: Fisher's exact test; SD: standard deviation; IQR: interquartile range; * significant at p<0.05.

A significant increase in the on admission white blood cells count, random blood glucose, Alanine transaminase (ALT), Aspartate aminotransferase (AST), serum creatinine, blood urea, PT and, INR was observed among poor outcomes compared with good outcome group ($p<0.05$, each). On the other hand, a significant decrease was recorded in the mean arterial pH (7.23± 0.19 and 7.39± 0.05 respectively) and HCO3 levels (13.3±7.1 and 22.8±3.5 respectively) in the poor outcome than good outcome group ($p< 0.05$, each). Calculation of anion gap (AG) revealed a significant increase in the mean AG among poor outcome group than good outcome one (26.5±10.8 and 16.0±5.9 respectively). However, no significant difference could be detected between the two studied groups regarding baseline arterial PCO2, SO2, K, and Na levels ($p> 0.05$, each) (Table 3).

Table (4) illustrates that hemodialysis was indicated in 18 patients in the current study; however, only 14 of them actually underwent hemodialysis as the remaining four patients died before the start of dialysis sessions. Out of the fourteen patients who underwent hemodialysis and intensive care unit (ICU) admission, 13 belonged to the poor outcome group of patients (76.5%), and only one patient had a good outcome (4.3%). Poor outcome patients stayed in the hospital for a significantly longer median time (72 hours) than good outcome ones (17 hours) ($p<0.05$).

Table (5) illustrates the results of binomial logistic regression analysis that was conducted to evaluate potential factors that may affect the likelihood of a poor outcome in acute methanol poisoned patients. Only GCS measured on admission and delay time in hours till hospitalization were significant independent predictors of poor outcome in acute methanol intoxication. The highest odds ratio for poor outcome was increased delay time since admission in hours till hospitalization (an increased delay time by 1 hour was significantly associated with the poor outcome's probability. Odds values 1.106, 95% CI: 1.109 to 1.200, and P values 0.016. Moreover, a decrease in GCS by one was significantly associated with poor outcomes. Odds values 0.609, 95% CI: 0.418to 0.889, and P values 0.010.

DISCUSSION

Methanol poisoning is a medical emergency with significant mortalities and morbidities **(Hovda et al.,2005)**. Out of 40 patients in this study, 23 patients (57.5%) had a good outcome, and 17 patients (42.5%) had a poor outcome group (6 patients died (15%), and 11 patients (27.5%) had residual visual affection). This is in agreement with **Nizhu et al. (2018)** and **Yousefinejad et al.** (**2020),** who reported mortality rates of 18% and 15.4%, respectively. Meanwhile, **Desai et al. (2013)** reported lower mortality rates (8.2%) and visual affection (13.9%). This outcome variability could be attributed to the discrepancy in patients' characteristics, poisoning severity, and the standardized treatment guidelines.

Table (3): laboratory data of the studied patients (n = 40)

		Total (n = 40)	Good outcome (n = 23)	Poor outcome (n = 17)	Test statistic	P value
SO2	Mean±SD (Range)	97.3±2.4 (90.0 - 100.0)	97.4±2.6 (90.0 - 100.0)	97.2±2.2 (92.0 - 100.0)	0.336 a	0.739
PH	Mean±SD (Range)	7.32± 0.15 (6.86 - 7.49)	7.39± 0.05 (7.31 - 7.48)	7.23± 0.19 (7.1 - 7.49)	3.378 a	0.003*
PCO2 mmHg	Median [IQR] (Range)	36.0 [32.0 - 44.0] (16.0 - 62.0)	36.5 [34.0 - 44.0] (18.0 - 51.0)	34.0 [28.0 - 44.0] (16.0 - 62.0)	0.808 b	0.424
HCO3 (mEq/L)	Mean±SD (Range)	18.7±7.1 (2.8 - 30.0)	22.8±3.5 (13.8 - 30.0)	13.3±7.1 (7.2 - 28.9)	5.096 a	<0.001*
Anion gap	Mean±SD (Range)	20.5±9.7 (3.4 - 41.0)	16.0±5.9 (4.0 - 26.5)	26.5±10.8 (3.4 - 41.0)	3.638 a	0.001*

Na (mEq/L)	Mean±SD (Range)	141.8±7.6 (125.0 - 169.0)	141.4±6.0 (134.0 - 155.0)	142.3±9.5 (125.0 - 169.0)	0.362 a	0.720
K (mEq/L)	Mean±SD (Range)	3.7 ± 0.8 (2.4 - 6.5)	3.6± 0.4 (3.1 - 4.5)	3.7 ± 1.2 (2.4 - 6.5)	0.146 a	0.885
RBS (mg/dl)	Mean±SD (Range)	127.9±46.1 (70.0 - 298.0)	113.4±19.3 (70.0 - 153.0)	147.5±63.0 (76.0 - 298.0)	2.155 a	0.045*
AST (IU/L)	Median [IQR] (Range)	22.0 [16.0 - 30.5] (11.0 - 84.0)	18.0 [16.0 - 24.0] (11.0 - 48.0)	31.0 [20.0 - 46.0] (12.0 - 84.0)	2.385 b	0.016*
ALT (IU/L)	Median [IQR] (Range)	25.0 [19.0 - 33.5] (14.0 - 131.0)	22.0 [18.0 - 28.0] (14.0 - 64.0)	32.0 [26.0 - 44.0] (18.0 - 131.0)	2.567 b	0.010*
Serum Creatinine (mg/dl)	Mean±SD (Range)	1.08± 0.49 (0.60 - 2.80)	0.84± 0.16 (0.60 - 1.30)	1.40± 0.59 (0.60 - 2.80)	3.770 a	0.001*
Blood Urea (mg/dl)	Mean±SD (Range)	33.1±12.4 (18.0 - 75.0)	27.1±6.7 (18.0 - 39.0)	41.2±13.8 (20.0 - 75.0)	3.884 a	0.001*
WBC s Cells/mm^3	Median [IQR] (Range)	10.0 [6.9 - 15.5] (4.2 - 28.6)	7.6 [6.4 - 10.5] (4.2 - 28.0)	15.5 [12.6 - 16.4] (6.6 - 28.6)	3.353 b	0.001*
PT (seconds)	Mean±SD (Range)	14.2±1.8 (11.9 - 22.0)	13.6 ± 0.8 (13.0 - 16.6)	15.1±2.4 (11.9 - 22.0)	2.597 a	0.018*
INR	Mean±SD (Range)	1.2 ± 0.2 (1.0 - 2.2)	1.1 ± 0.1 (1.0 - 1.5)	1.3± 0.3 (1.0 - 2.2)	2.965 a	0.008*

a: Independent samples T-test; b: Mann-Whitney test; SD: standard deviation; IQR: interquartile range; *significant at p<0.05.

Table (4): Outcomes and hospitalization period of the studied patients (n= 40)

		Total (n = 40)		**Good outcome (n = 23)**		**Poor outcome (n = 17)**		**Test statistic**	**P value**
Hemodialysis performed	No	26	65.0%	22	95.7%	4	23.5%	22.350 b	<0.001*
	Yes	14	35.0%	1	4.3%	13	76.5%		
Hemodialysis Indicated	No	22	55.0%	22	95.7%	0	0.0%	36.135 b	<0.001*
	Yes	18	45.0%	1	4.3%	17	100.0%		
Need for ICU admission/MV	No	26	65.0%	22	95.7%	4	23.5%	22.350 b	<0.001*
	Yes	14	35.0%	1	4.3%	13	76.5%		
Hospital stay (hours)	Median [IQR] (Range)	29.0 [11.0 - 72.0] (4.0 - 216.0)		17.0 [9.0 - 48.0] (6.0 - 96.0)		72.0 [42.0 - 96.0] (4.0 - 216.0)		3.595 c	<0.001*

MV: mechanical ventilation; a: Fisher-Freeman-Halton exact test; b: Pearson's Chi square test; c: Mann-Whitney test; IQR: interquartile range; * significant at p<0.05.MV: mechanical ventilation

Table (5): Result of multivariate logistic regression analysis on the factors related to poor outcome in patients with methanol poisoning

Variable	**OR**	**95% CI**	**P value**
On admission GCS	0.609	0.418-0.889	0.010*
Delay time (hours)	1.106	1.019-1.200	0.016*

OR: odds ratio; CI: confidence interval; * significant at p<0.05.

Young males predominate in the current study with a median age of 24 years. This partially agreed with previous studies (**Desai et al.,2013**; **Galvez-Ruiz et al.,2015; Nizhu et al.,2018)**. Unlikely, **Chang et al. (2019)** reported a mean age of 47.8 ± 14.9 years. Males commonly consume counterfeit alcohol, therefore more susceptible to methanol intoxication and fatalities **(Kurtas et al., 2017)**.

The significantly observed longer delay time in poor outcome patients in the present study was in accordance with **Yousefinejad et al. (2020)**. The reverse was reported by **Sanaei-Zadeh et al. (2011)**; survivors had more elapsed time to treatment than non-survivors (41±18 and 32±17, respectively). However, other studies performed by **Masoud et al. (2016)** in Alexandria Main University Hospital,

Egypt, reported insignificant differences between survivors and non-survivors.

In the present study, lower mean GCS was more significantly observed in the poor outcome group. This was agreeable with other studies (**Chang et al.,2019; Yousefinejad et al.,2020)**. Delayed presentations allowed sufficient time for methanol metabolism and production of formic acid that is considered to be responsible for toxicity in late stages.

In the current study, 47.5% of cases had optic neuritis. Poor outcome patients had mainly mydriasis with sluggish pupillary reaction. **Hassanian-Moghaddam et al. (2007)** reported blindness in 23% of the studied patients, and 56% of them had fixed and/or dilated pupils. Previous studies reported pupillary reaction as an important predictor of visual function and mortality in methanol poisoning **(Unnikrishnan &Raju,2014; Masoud et al.,2016)**. Dilated pupils may be explained in the light of the fact that the optic nerve is the afferent nerve for pupil light reflex **(Bremner,2004)**. Visual impairment occurs secondary to anoxia which mainly affects high adenosine triphosphate (ATP) requirements tissues as the optic nerve and retina **(Hovda et al.,2005)**. Moreover, **Eells et al. (1981)** reported much more accumulation and slower oxidation of formic acid in the eyes than in the brain.

Poor outcome patients were reported with significantly lower arterial pH and HCO3 levels and an increase in AG. This coincided with other past studies **(Masoud et al.,2016; Kurtas et al., 2017; Chang et al.,2019)**. In contrast, **Yousefinejad et al. (2020)** reported an insignificant difference in pH and HCO3 between good and poor patient outcomes. High AG metabolic acidosis is the result of accumulated lactic and formic acid; the latter inhibits cytochrome C oxidase activity, thus produces histotoxic hypoxia **(Soghoian et al.,2009)**.

The total white blood cells (WBCs) count, RBS, ALT, AST, serum creatinine, blood urea, PT and, INR at admission were significantly elevated among the poor outcome group. **Kurtas et al. (2017)** and **Yousefinejad et al. (2020)** also noticed an increase in RBS and creatinine in poor outcome patients. The increased WBCs count in the present study may be related to formaldehyde and formic acid-induced inflammatory changes. Thus, leucocytosis may be used as a marker of the severity of toxicity **(Eells et al.,1981)**. Hyperglycemia is due to methanol-induced acute pancreatitis **(Hantson &Mahieu,2000)**. **Morteza Bagi et al. (2015)** demonstrated that elevated creatinine level was an independent risk factor for alcohol-related death, which mandates prompt hemodialysis.

Regarding the significantly elevated liver enzymes in those with poor outcomes can be related to oxygen free radicals and lipid peroxidation induced by methanol metabolism **(Skrzydlewska&Fabriszewski,1998; Chrostek et al.,2001).** This was proved by **Akhgari et al. (2015)** in their study that revealed that liver injury is accompanied by histopathological changes as steatosis and hepatocyte degeneration. In addition, chronic alcoholics, especially to adultered ethanol, may have hepatotoxicity and affection of liver functions. Reports from **Ran et al. (2019)** revealed that the severity of methanol poisoning was positively correlated with levels of creatinine, AST, and PT.

Unfortunately, those who were admitted to ICU and underwent hemodialysis (35%) in the present study had a poor outcome. Unlikely **Masoud et al. (2016)** reported that those who underwent dialysis had better outcomes. This could be attributed to the delayed presentation, severity of intoxication, multi-organ involvement in poor outcome patients, and delay in hemodialysis start point.

The current study concluded that delayed hospitalization and the grade of coma as assessed by GCS at admission were significant independent predictors of poor

outcome in acute methanol intoxication, as shown by regression analysis. These findings are in harmony with other similar studies (**Hassanian-Moghaddam et al.,2007; Galvez-Ruiz et al.,2015 and Yousefinejad et al.,2020)**. However, this was contrasted by **Desai et al. (2013),** who found that early presentation did not seem to significantly alter the course of visual recovery or final visual outcome, but the degree of acidosis at admission played this role. Delayed onset manifestations of methanol poisoning, which ranged from (30 minutes-72 hours) led to delayed hospitalization. Furthermore, Fear of legal punishment together and social embarrassment force may add factors **(Shadnia et al.,2013)**. Moreover, some hospitals in rural areas in our country do not equipped enough with facilities for aids methanol diagnosis and management, which delays the onset of treatment.

LIMITATIONS

This study was limited by its retrospective nature which only reviews the patients' files; the patients were not followed up after discharge for more detection of irreversible visual affection—additionally, absence of methanol and format levels measurement in the patients.

CONCLUSION

Based on the findings of this study, delayed hospital admission was significantly prolonged, and coma on admission as assessed by GCS was significantly lowered in patients with poor outcome methanol poisoned group compared to good outcome one in acute methanol poisoning. Therefore, they might be useful as new prognostic factors of poor outcomes in methanol poisoning.

RECOMMENDATIONS

Finally, the authors recommend future planned prospective studies on a large scale of patients and a long follow-up period for further evaluation and detection of irreversible visual and/or neurological affection.

REFERENCES

Akhgari, M., Panahianpour, M., Bazmi, E., Etemadi-Aleagha, A., Mahdavi, A., and Nazari, S. H. (2013): Fatal methanol poisoning: features of liver histopathology. Toxicology and industrial health, 29(2):136–141.

Barceloux, D. G., Randall Bond, G., Krenzelok, E. P., Cooper, H. and Allister Vale, J. (2002): American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. Journal of toxicology: Clinical toxicology, 40(4):416–446.

Bezdicek, O., Klempir, J., Liskova, I., Michalec, J., Vaneckova, M., Seidl, Z., et al. (2014): Sequelae of methanol poisoning for cognition. Ceska a Slovenska Neurologie a Neurochirurgie, 77(3):320–325.

Boyaci, I. H., Genis, H. E., Guven, B., Tamer, U., and Alper, N. (2012): A novel method for quantification of ethanol and methanol in distilled alcoholic beverages using Raman spectroscopy. Journal of Raman Spectroscopy, 43(8):1171–1176.

Bremner, F. D. (2004): Pupil assessment in optic nerve disorders. Eye, 18(11):1175–1211.

Bursac, Z., Gauss, C. H., Williams, D. K. and Hosmer, D. W. (2008): Purposeful selection of variables in logistic regression. Source code for biology and medicine, 3:17.

Chang, S., Wang, Y., Hou, Y., Wang, I. K., Hong, H. H., Weng, C. H., et al. (2019): Acute kidney injury and the risk of mortality in patients with methanol intoxication. BMC Nephrology, 20(1):205.

Chrostek, L., Szmitkowski, M., and Jelski, W. (2001): Alcohol and aldehyde dehydrogenase activity measured with fluorogenic substrates in the liver of rats poisoned with methanol. Experimental and Toxicologic Pathology, 53(1):77–80.

Desai, T., Sudhalkar, A., Vyas, U. and Khamar, B. (2013): Methanol Poisoning. Predictors of Visual Outcomes. JAMA Ophthalmology, 131(3):358–364.

Eells, J. T., McMartin, K. E., Black, K., Virayotha, V., Tisdell, R. H., and Tephly, T. R. (1981): Formaldehyde Poisoning. Rapid Metabolism to Formic Acid. Journal of the American Medical Association, 246(11):1237–1238.

Galvez-Ruiz, A., Elkhamary, S. M., Asghar, N. and Bosley, T. M. (2015): Visual and neurologic sequelae of methanol poisoning in Saudi Arabia. Saudi medical journal, 36(5):568–574.

Hantson, P. and Mahieu, P. (2000): Pancreatic injury following acute methanol poisoning. Journal of toxicology: Clinical toxicology, 38(3):297–303.

Hantson, P. E. (2005): Acute methanol intoxication: pathophysiology, prognosis and treatment. Bulletin et memoires de l'Academie royale de medecine de Belgique, 160(5-6):294–300.

Hassanian-Moghaddam, H., Pajoumand, A., Dadgar, S. and Shadnia, S. H. (2007): Prognostic factors in methanol poisoning. Human & experimental toxicology, 26(7):583–586.

Hoffman, R., Nelson, L., Goldfrank, L., Howland M. A. and Lewin N. A. (2011): Initial evaluation of the patient: vital signs and toxic syndromes. In: Flomenbaum N (eds) Gold frank's toxicologic emergencies. 9th edition. New York, NY: McGraw-Hill Professional;36–41.

Hovda, K. E., Urdal, P. and Jacobsen, D. (2005): Increased serum formate in the diagnosis of methanol poisoning. Journal of analytical toxicology, 29(6):586–840.

Jacobsen, D. and McMartin, K. E. (1986): Methanol and ethylene glycol poisonings. Mechanism of toxicity, clinical course, diagnosis and treatment. Medical toxicology, 1(5):309–334.

Kraut, J. and Kurtz, I. (2008): Toxic alcohol ingestions: clinical features, diagnosis, and management. Clinical Journal of the American Society of Nephrology, 3(1):208–225.

Kruse, J. A. (2012): Methanol and ethylene glycol intoxication. Critical care clinics, 28(4):661–711.

Kurtas, O., Imre, K.Y., Ozer, E., Can, M., Birincioğlu, İ., Bütün, C., et al. (2017): The evaluation of deaths due to methyl alcohol intoxication. Biomedical Research, 28(8):3680–3687.

Masoud, R. A., Khalifa, E. A. and Kabeel, M. A. (2016): The role of pulse steroid therapy in cases of methanol induced ocular toxicity. Egyptian Journal of Forensic Sciences and Applied Toxicology, 16(2):37–54.

Morteza Bagi, H. R., Tagizadieh, M., Moharamzadeh, P., Pouraghaei, M., Kahvareh Barhagi, A. and Shahsavari Nia, K. (2015): Epidemiology of alcohol poisoning and its outcome in the North-West of Iran. Emergency (Tehran, Iran), 3(1):27–32.

Nizhu, L. N., Barua, D., Anam, A. M., Polash, M. M. I., Tun, S. S., Nessa, R. R., et al. (2018): Haemodialysis in Methanol Poisoning. Bangladesh Critical Care Journal, 6(1):23–25.

Persson, H. E., Sjöberg, G. K., Haines, J. A. and de Garbino, J. P. (1998): Poisoning severity score. Grading of acute poisoning. Journal of Toxicology: Clinical Toxicology, 36(3):205–213.

Ran, M., Li, Y., Zhang, L., Wu, W., Lin, J., Liu, Q., et al. (2019): Clinical features, treatment, and prognosis of acute methanol poisoning: experiences in an outbreak. International Journal of Clinical and Experimental Medicine, 12(5):5938–5950.

Roberts, D. M., Yates, C., Megarbane, B., Winchester, J. F., Maclaren, R., Gosselin, S., et al. (2015): Recommendations for the role of extracorporeal treatments in the management of acute methanol poisoning: a systematic review and

consensus statement. Critical care medicine, 43(2):461–472.

Sanaei-Zadeh, H., Esfeh, S. K., Zamani, N., Jamshidi, F. and Shadnia, S. (2011): Hyperglycemia is a strong prognostic factor of lethality in methanol poisoning. Journal of Medical Toxicology, 7:189–194.

Shadnia, S., Rahimi, M., Soltaninejad, K. and Nilli, A. (2013): Role of clinical and paraclinical manifestations of methanol poisoning in outcome prediction. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences, 18(10):865–869.

Sharpe, J. A., Hostovsky, M., Bilbao, J. M. and Rewcastle, N. B. (1982): Methanol optic neuropathy: a histopathological study. Neurology, 32(10):1093–1100.

Skrzydlewska, E. and Fabriszewski, R. (1998): Lipid peroxidation and antioxidant status in the liver, erythrocytes and serum of rats after methanol intoxication. Journal of Toxicology and Environmental Health Part A, 53(8):637–649.

Soghoian, S., Sinert, R., Wiener, S. W. and Hoffman, R. S. (2009): Ethylene glycol toxicity presenting with non-anion gap metabolic acidosis. Basic & clinical pharmacology & toxicology, 104(1):22–26.

Unnikrishnan, S. and Raju, K.V. (2014): Clinico-biochemical correlation of ocular manifestations and visual prognosis in victims of hooch tragedy. Journal of Clinical Ophthalmology and Research, 2(2):87–92.

Vaneckova, M., Zakharov, S., Klempir, J., Ruzicka, E., Bezdicek, O., Liskova, I., et al. (2014): Methanol intoxication on magnetic resonance imaging-case reports. Ceska a Slovenska Neurologie a Neurochirurgie, 77(2):235–239.

Williams, R. and Erickson, T. (1998): Evaluating toxic alcohol poisoning in the emergency setting. Laboratory Medicine, 29(2):102–108.

Yousefinejad, V., Moradi, B., Mohammadibaneh, A., Sheikhesmaeili, F., and Babahajian, A. (2020): Prognostic Factors of Outcome in Methanol Poisoning; an 8-year Retrospective Cross-sectional Study. Archives of academic emergency medicine, 8(1):69.

Zakharov, S., Kotikova, K., Vaneckova, M., Seidl, Z., Nurieva, O., Navratil, T., et al., (2016): Acute methanol poisoning: prevalence and predisposing factors of haemorrhagic and non-haemorrhagic brain lesions. Basic & clinical pharmacology & toxicology, 119(2): 228–238.

Zakharov, S., Kurcova, I., Navratil, T., Salek, T., Komarc, M. and Pelclova, D. (2015): Is the measurement of serum formate concentration useful in the diagnostics of acute methanol poisoning? A prospective study of 38 patients. Basic & clinical pharmacology & toxicology, 116(5):445–551.

الملخص العربى

العوامل المتنبئة بالنواتج السيئة للتسمم الحاد بالميثانول

مقدمة

يعد الكحول الميثيلى (الميثانول) من المواد شديدة السمية. وقد يؤدى التسمم الحاد بالميثانول الى حدوث تغيير فى حمضية الدم والى التأثير على أعضاء الجسم المختلفة خاصة الجهاز العصبى بالأضافة على تأثيره السلبى على الإبصار والذى قد يصل إلى العمى وانعدام الرؤية.

الهدف من البحث:

تهدف الدراسة الحالية الى دراسة العوامل التى قد يمكنها التنبؤ بالنواتج السيئة للتسمم الحاد بالميثانول.

طريقة البحث:

تم إجراء الدراسة بأثر رجعي على أربعين مريضا بالتسمم الحاد بالميثانول. تم الحصول على بيانات أربعة سنوات (2017 إلى 2020) من أرشيف وحدة علاج التسمم بمستشفى طنطا الجامعى حيث تم تسجيل بيانات نواتج التسمم الحاد بالميثانول بالإضافة إلى البيانات الشخصية الخاصة بالمرضى وكذلك بيانات الفحوصات السريرية والمخبرية.

النتائج :

من بين 40 مريضا بالتسمم الحاد بالميثانول، كان لدى 17 مريضا نواتج سيئة إما الوفاة أو مضاعفات تمثلت فى التأثير على قوة الابصار والعمى بينما تعافى 23 مريضا تماما. وقد لوحظ العلاقة بين طول الفترة ما بين تناول الميثانول ودخول المرضى الى المستشفى لتلقى العلاج وحدوث النواتج السيئة للميثانول مقارنة بالنواتج الجيدة فى المجموعة الثانية. بينما كان متوسط الوعى بمقياس جلاسجو ، ودرجة الحموضة الشريانية ومستويات البيكربونات أقل بشكل ملحوظ في مجموعة النواتج السيئة. بالإضافة إلى ذلك ، لوحظ زيادة كبيرة في إجمالي عدد كريات الدم البيضاء ، سكر الدم العشوائى ، إنزيمات الكبد ،والكرياتينين ، و بولينا الدم ، وزمن البروثرومبين والفجوة الأيونية في مجموعة النواتج السيئة.

الاستنتاج :

تظهر دراستنا أنه تم تحديد تأخر توقيت دخول المستشفى وسوء مستوى الوعى بمقياس جلاسجو للمريض على أنهما من العوامل التنبؤية المحتملة للنواتج السيئة في التسمم الحاد بالميثانول.

المقترحات:

يقترح الباحثون اجراء دراسات مستقبلية مخططة على مرضى التسمم الحاد بالميثانول مع متابعة المرضى لفترة طويلة للمزيد من التقييم والكشف عن المضاعفات البصرية و العصبية اللاحقة للتسمم بالميثانول .