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Tertiary referral hospital experience of methanol poisoning in the COVID-19 era: a cross-sectional study in Northwestern Iran

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Abstract

Background Methanol poisoning is a worldwide phenomenon that has resulted in deaths and irreversible complications. However, studies show it is more prevalent in developing countries and areas with lower socioeconomic status. So, accurately recognizing socio-economic risk factors, increasing people's awareness about methanol poisoning, and proper hospital management will reduce its dangerous complications and mortality.

Methods This cross-sectional study was conducted retrospectively at Sina Hospital, a poisoning center and tertiary referral center in northwestern Iran, and investigated demographic findings and hospital management indicators through systematic random sampling between February 20, 2020, and September 22, 2022 (or the COVID-19 era). We assessed variable correlations using Spearman's correlation coefficient, Mann–Whitney U, and Kruskal–Wallis.

Results Out of 131 patients, 126 (96.2%) were males, and 5 (3.8%) were females. 45.5% and 30.3% of poisoning incidents occurred between the winter and spring, respectively. 67 patients (50.8%) were referred to this hospital due to vision complaints. Unfortunately, 10 patients (7.6%) passed away despite receiving care. Employed individuals were referred to the treatment facility more quickly than unemployed individuals (P-value = 0.01). Patients with medical insurance coverage were referred faster after consuming alcohol (P-value = 0.039). Older patients referred to the hospital later. (P-value = 0.006).

Conclusions Mortality and morbidity following methanol poisoning are likely to be affected by factors including access to medical care, financial stability, and employment status. Consequently, reducing mortality and morbidity requires attention to these concerns.

Keywords Methanol, Poisoning, Methanol toxicity, Tertiary care centers, COVID-19

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Background

Methanol is a clear, colorless, and flammable liquid that is the simplest aliphatic alcohol combination. This alcohol, which results from the fermentation of wood (Pressman et al. 2020), is absorbed by the body through the digestive system, the respiratory system, and the skin (Moon 2017), where it produces tissue-damaging metabolites in the liver like formic acid and formaldehyde. Headache, vomiting, abdominal pain, dizziness, and hypersomnia are some of the clinical symptoms of methanol poisoning. Methanol poisoning can also result in coma, convulsions, and respiratory arrest (Pressman et al. 2020). Methanol poisoning can also cause damage to the visual system, leading to symptoms like blurred vision, photophobia, visual field defect, visual illusions, decreased visual acuity, and even total blindness (Liberiski et al. 2022). Formate-induced acidosis can hasten and amplify optic nerve damage (Grzybowski et al. 2015). It is possible to go blind from consuming as little as 4 ml (3.16 g) or as much as 15 g (11.85 g) of the pure substance orally (Moon 2017). Ten to thirty percent of patients who suffer from methanol poisoning have reported experiencing long-term visual complications, which can vary from blurred vision to some permanent complications, such as complete blindness in 25–33% of patients (Jafarizadeh et al. 2023; Zakharov et al. 2015).

Methanol poisoning has been linked to a fatality rate of 18–44% (Md Noor et al. 2020). However, about 5,000 cases of methanol poisoning are detected annually in the United States, with a rate of 6.4 in one million hospitalized people (Kaewput et al. 2021). From 2013 to 2019, 244 deaths were reported in Iran, Malaysia, Costa Rica, and India due to methanol poisoning (Pressman et al. 2020). Of this amount, 44 cases were declared dead in Iran in 2013 (Akhgari et al. 2013). Therefore, methanol poisoning is a global phenomenon that has caused deaths and irreparable complications all over the world, but according to studies, its prevalence is higher in developing countries and areas with lower socio-economic status (Abrishami et al. 2011). Findings suggest that the prevalence of methanol poisoning has increased significantly during the COVID-19 pandemic, which could be the result of the fact that the hospitals were forced to change their management conditions to control the COVID-19 crisis. At the very beginning of the COVID-19 pandemic, about 264 deaths were reported from 2187 reported cases of methanol poisoning in Iran (Soltaninejad 2020a).

In the case of hospital management of methanol toxicity, early diagnosis and treatment play an essential role in preventing the occurrence of blindness and death. On the other hand, immediate hospital intervention is necessary to prevent irreparable complications for the patient. Considering the half-life of methanol and the golden time of

therapeutic intervention to prevent irreversible complications; Naturally, examining the time between the onset of symptoms and the first therapeutic intervention will be a good indicator to evaluate the management of this disease (Goldfrank and Hoffman 2006; Daugirdas et al. 2012). Considering the urgency of methanol poisoning, faster medical team actions decrease the complications of the disease, such as blindness, kidney and liver damage, and the possibility of mortality (Najari et al. 2020). Therefore, the period between poisoning and the onset of symptoms until the start of treatment is crucial.

Sharing experiences is one of the ways to improve the quality of health system decisions and health policies. Therefore, this study aimed to characterize and investigate the experiences of hospital management of methanol poisoning at Sina Hospital, a tertiary referral hospital in northwest Iran, during the COVID-19 pandemic.

Methods

Data from 131 patients, aged 15–80, admitted for methanol poisoning at Sina Hospital in Tabriz, poisoning center in northwestern Iran, between February 20, 2020, and September 22, 2022, was investigated for this cross-sectional study. Based on the date of admission, we created a list of the patients, assigned them numbers, carried out a systematic sampling, and determined a sample size of at least 128 patient. Patients with a history of methanol poisoning within the past 10 days, between the ages of 15 and 80, and with no other ophthalmological issues besides refractive defects are included. Exclusion criteria included records lacking necessary demographic information, patients reporting concomitant poisoning with other substances, and patients reporting a history of significant eye problems before the poisoning.

Data analysis

IBM SPSS version 22 statistical software was used for the descriptive statistical analysis of the study data (prevalence or percentage), the Chi-square test, and Fisher's exact test. The Kolmogorov–Smirnov test was used in this study to ensure that the data followed a normal distribution. Numerical information was reported using either the mean, standard deviation, and interquartile range or the median and range. Percentages were used to report qualitative information. We used the Spearman correlation coefficients, Mann–Whitney U, and Kruskal–Wallis tests to examine the closeness of the associations between the variables; P values of less than 0.05 were considered statistically significant.

Ethical considerations

We strictly adhered to the Declaration of Helsinki's ethical principles in every aspect of this research. There were

no material or moral costs incurred by anyone taking part in this study. Informed consent was obtained from all hospitalized participants before collecting any data. This study has been approved by the Ethics Committee of Tabriz University of Medical Sciences, and its code of ethics is IR.TBZMED.REC.1401.483.

Results

From February 20, 2020, through September 22, 2022, the medical records of 131 patients admitted to Sina Hospital with methanol poisoning were reviewed. The results showed that 126 (96.2%) of the patients were male and 5 (3.8%) were female, with a non-normal distribution of patient ages (p -value = 0.12). The youngest patient was 16 years old, and the oldest was 65, with a mean age of 34.47 ± 11.85 .

Winter and spring showed the most poisoning cases, with 45.5% and 30.3% of patients, respectively. Eighty-five patients (64.4%) were literate but did not have a university education, and 80 (60.6%) held full-time jobs. In addition, 98 patients (74.2%) had health insurance. In this study, 67 patients (50.8% of the total) were referred because they were experiencing vision problems, while 109 patients (82.6%) were first-time patients (not referred from another center). Disturbances of consciousness were the second most common cause, affecting 37 patients (28%). There were 104 cases (79.5%) where the condition of the pupils was not reported. However, mydriasis was reported in 22 cases (16.7%), and miosis was reported in 5 cases (3.8%). In terms of vision,

85 cases (64.4%) had blurred vision, 2 cases (1.5%) had diplopia, and 1 case (0.8%) was blind. Only two patients (1.5%) were referred to an ophthalmologist, and a further eight (6.1%) were given written instructions to follow up with an ophthalmologist after discharge. In one case, the time from writing the ophthalmology consultation to the visit was reported to be 110 min.

Primary Venous Blood Gas (VBG) was performed on 130 (99.2%) patients, with mean $pH = 7.21 \pm 0.16$, initial $PCO_2 = 32.06 \pm 15.04$, and initial $HCO_3 = 14 \pm 8.2$. Finally, 92 (70.2%) patients required hemodialysis at least once. The poisoning way in all reported cases was oral consumption. At the same time, 84 patients (63.6%) had used cigarettes, 14 patients (10.6%) had used opiates, and 6 patients (4.5%) had used psychiatric drugs. After completing the necessary treatment with medical recommendations, 92 patients (69.7%) were discharged. Twenty-nine patients (22%) were discharged from the hospital with personal consent, and 10 patients (7.6%) died despite receiving treatment and vital care.

The results of statistical analysis performed for quantitative data were summarized in Table 1. According to Spearman’s correlation coefficient analysis of the time that passed between admission to the internal sections of the hospital and the first visit to the emergency room (shown in Table 2), there was no statistically significant relationship between the time between admission and the first visit and the other variables listed. There was no correlation between the first visit to the emergency room after admission to the internal sections and

Table 1 Statistical analysis performed for quantitative data

Variable	Mean (standard deviation)	Median (interquartile range)	P-value (Kolmogorov-Smirnov)
Age	34.47 ± 11.85	33 (18)	0.012
Consumption-to-reference time (min)	1436.65 ± 1200.9	1231 (1993)	0.001 >
Admission-to-first visit time (min)	225.64 ± 153.29	192.5 (241.25)	0.001 >
Duration of hospitalization in the ward (days)	2.24 ± 2.28	2 (2)	0.001 >
Duration of hospitalization in ICU (days)	1.76 ± 7	0 (1)	0.001 >
Total days of hospitalization	3.92 ± 7.19	3 (2)	0.001 >

Table 2 Correlation assessment of the time that passed between admission to the internal sections of the hospital and the first visit to the emergency room (minutes) time with other variables

	Total hospitalization days	Hospitalization In the ward (days)	Hospitalization In ICU (days)	Consumption to referral time	Date of referral
Spearman’s correlation coefficient	- 0.052	- 0.056	- 0.007	0.179	- 0.139
P-value	0.601	0.573	0.944	0.098	0.159

patient mortality, as determined by the Mann–Whitney U test. (Fig. 1) The Kruskal–Wallis test showed no correlation between education and the time it took before a person was referred for treatment. (Fig. 2) Based on the Mann–Whitney U test results, employed patients have been referred to the treatment center significantly faster than unemployed. (P-value=0.01) Furthermore, there was a significant relationship between insurance coverage and the consumption-to-reference time, implying that patients with insurance coverage referred faster after consuming alcohol. (P-value=0.039) (Fig. 3) Also, based on Spearman’s correlation coefficient, there was a significant relationship between people’s age and the time of consumption until the patient’s visit, and older patients have referred to the medical center later. (P-value=0.006, correlation coefficient = 0.260).

Discussion

Methanol poisoning is one of the most frequent epidemics in Iran, affecting the lower and less educated sections of society. Accidental exposure to methanol-contaminated hand sanitizer, drinking as an ethanol replacement, and intentional self-harm are three scenarios in which exposure to methanol-contaminated hand sanitizers can

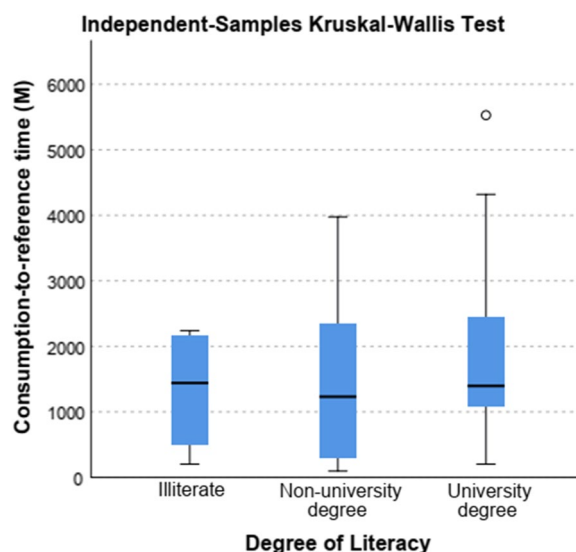


Fig. 2 Kruskal–Wallis test to evaluate the correlation between education and time elapsed between consumption to seek medical attention

occur. Due to the difficulty in making an accurate first diagnosis and the high fatality rate despite vigorous treatment, it continues to interest clinical toxicologists and

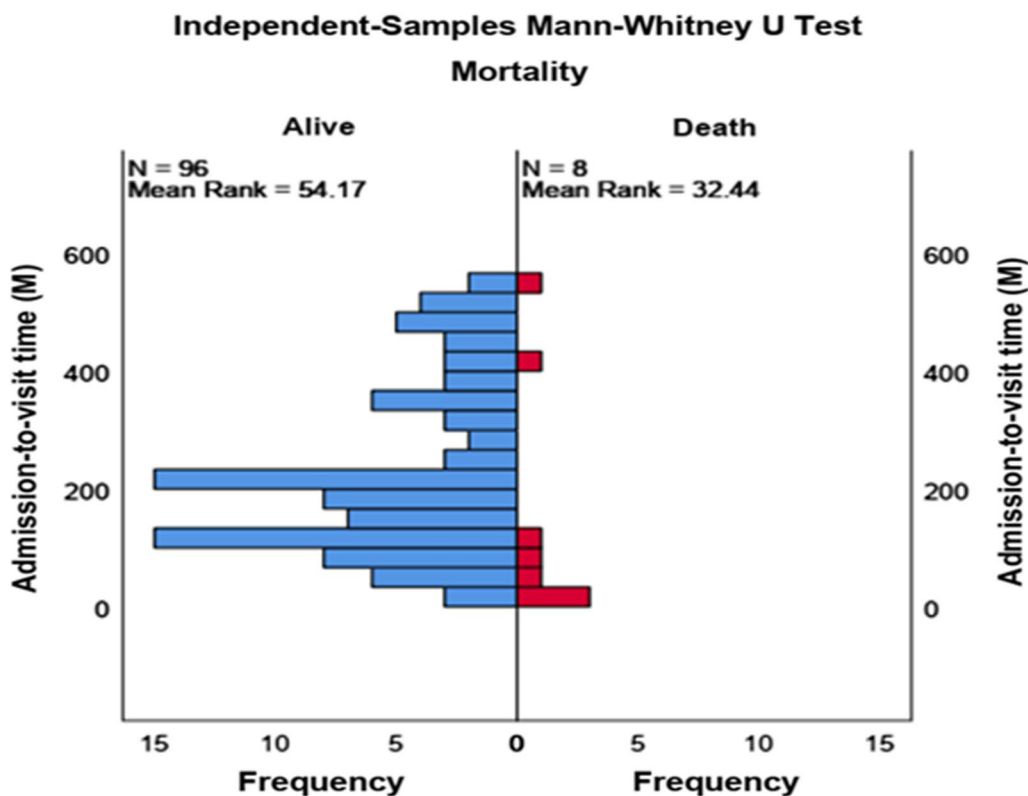


Fig. 1 The result of the Mann–Whitney U test to evaluate the relationship between mortality and the time elapsed between admission to the first visit to in the emergency room

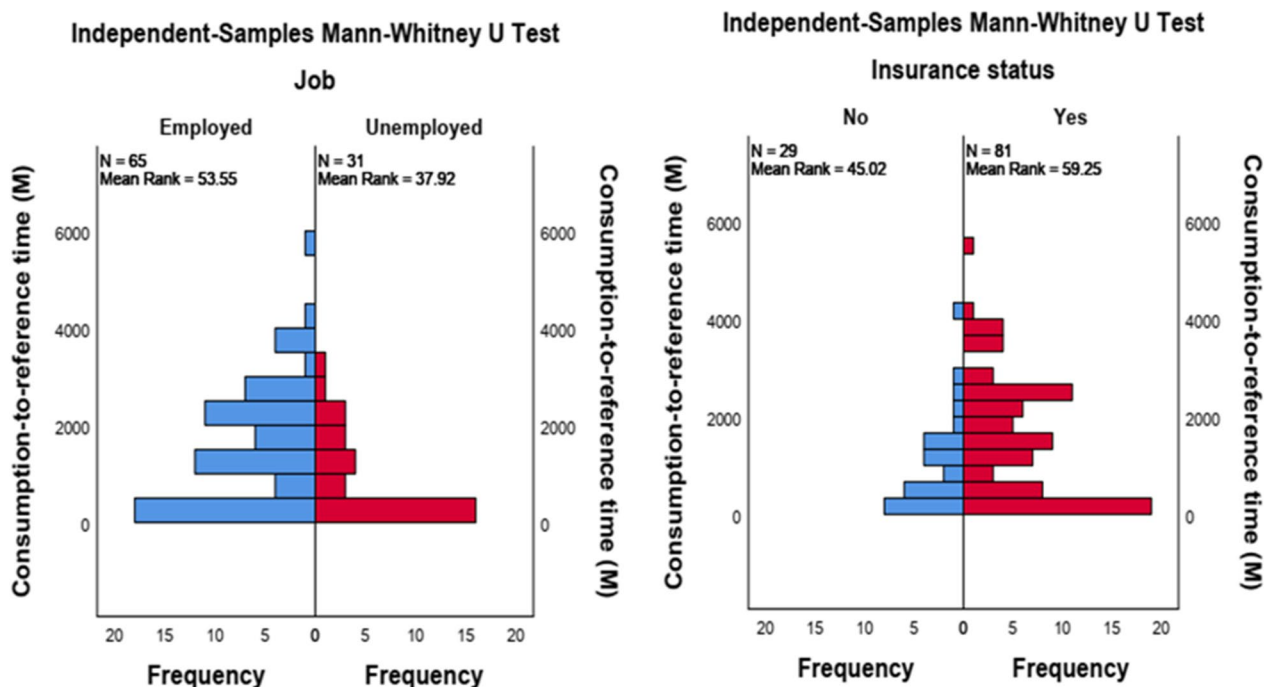


Fig. 3 The results of the Mann–Whitney U test to evaluate the relationship between employment and insurance coverage with consumption-to-reference time

emergency physicians. Extremely modest doses of methanol can cause abrupt central nervous system damage, resulting in death and severe vision impairment. In addition, neurological problems and permanent blindness may occur. Consuming even 30 ml of methanol without receiving urgent medical attention may cause lifelong blindness (Ashurst and Nappe 2023).

Patients with methyl alcohol poisoning were 34.47 ± 11.85 years old on average, which shows that such epidemics impact the working class, who, if they survive complications, may have years of disability owing to vision loss (Mahdavi et al. 2022).

Surprisingly, our study found differences in consumption-to-presentation times between insured and uninsured people as well as between employed and unemployed individuals. This difference suggests that unemployed patients and patients who did not have health insurance were referred later than employed and insured patients, possibly because they only sought medical assistance once they had a severe problem due to the lack of financial support from insurance.

Weissman et al. (Weissman et al. 1991) showed that patients’ belief that “their condition was not serious,” was the most frequent cause of delays in receiving care. According to this misconception, the likelihood of delay is associated with the patient’s socioeconomic status. This finding is a challenge for health education programmers

and healthcare systems because it supports the idea that individuals who are least integrated into the healthcare system are less able to distinguish between self-limited and care-requiring diseases. The expense of care was a significant reason for postponing care, so uninsured or lower socioeconomic status groups did not seek medical support until they had a severe problem because they lacked financial support.

The age of the population and the interval between consumption to the patient visit were also significantly correlated, such that the older the patient, the later he visited the treatment facility. Based on Leyva et al. (2020) study stated potential explanations for elderly patients’ medical avoidance; late presentations may have been caused by interpersonal issues like strained doctor-patient relationships, a lack of faith in doctors’ knowledge, anxiety about receiving bad news or experiencing pain, guilt over unhealthy behaviors, inability to take medications, denial, high cost, and patient fears of COVID-19 in a hospital environment (Mahdavi et al. 2022).

Our results also showed that 10 patients (7.6%) died despite treatment and vital measures. The mortality rate in Iran was estimated to be between 9 and 14% (Hasanian-Moghaddam et al. 2007; Sefidbakht et al. 2020; Soltaninejad 2020b). According to a study by Liu et al. (Liu et al. 1998), significant acidosis with an initial arterial pH < 7 and coma or seizures at presentation were also

linked to a higher mortality rate in methanol poisoning. According to the results of the study by Kaewput et al. (Kaewput et al. 2021), neurological failure was another significant predictor of greater mortality in methanol poisoning. This conclusion is supported by earlier research showing a relationship between altered consciousness and mortality (Paasma et al. 2012). Renal dysfunction has also been linked to more significant mortality, according to a study by Kaewput et al. (2021), in which the outcome was consistent with previous research (Chang et al. 2019).

Timely patient visits and prompt management are crucial because of the urgency of managing methanol-poisoned patients in the hospital. As a result, one of the critical elements in evaluating hospital management is investigating the relationship between the timing of the patient's initial visit and mortality and morbidity, as well as the length of hospitalization. Since prior research did not examine the correlation between the length of hospital stay and the patient's first visit, we analyzed the impact of the time between admission and the patient's first visit in minutes. Surprisingly, there was no correlation between patient mortality and the first visit following hospitalization.

Methanol poisoning is known to induce decompensated metabolic acidosis with a latent period of 6–24 h, leading to a spectrum of manifestations such as blurred vision, photophobia, diplopia, and gastrointestinal symptoms. The severity of symptoms is directly proportional to the absorbed dose of methanol. This condition can be lethal, and prompt recognition and management are critical to avoid a fatal outcome (Mousavi-Roknabadi et al. 2022; Nekoukar et al. 2021). In contrast to the findings of Kumar et al. (2019), who found that gastrointestinal symptoms were the primary presentation symptoms, in our study, the most common chief complaint was a visual disturbance, which was reported in 67 (50.8%) patients. This complaint was followed by mental status changes in 37 (28%) patients, nausea and vomiting in 22 (16%), and headache in two (1.5%).

The toxic effects of methyl alcohol remain unclear, but its metabolites, such as formaldehyde and formic acid, are known to have systemic and ocular toxic effects (Önder et al. 1998). Formic acid is the primary metabolite in methanol poisoning and can inhibit cytochrome oxidase in the retinal circulation, leading to mitochondrial dysfunction, decreased ATP production, and edema of the retinal nerve fiber layer, potentially causing interruption of axoplasmic flow and axon expansion in the optic disc (Kraut and Kurtz 2008). In this study, 85 (64.4%) patients had impaired vision, two (1.5%) had diplopia, and one (0.8%) had blindness. These ocular findings were observed during the

examination. Methanol poisoning results in moderate to severe metabolic acidosis through inhibition of the aerobic respiratory route, leading to lactic acid production. In our study, the mean arterial pH was measured in the range of 7.21 ± 0.16 , which is indicative of moderate to severe acidosis. An study by Desai et al. indicates that an initial pH above 7.2 is associated with better visual acuity outcomes, as pH has the highest correlation with final VA (Desai et al. 2013).

Although there is a strong correlation between acidosis and the development of ocular abnormalities, this correlation is not always causative. According to the Dethlefs et al. study, inflammatory retinal edema may cause retinal sheathing of arterioles, which results from perivascular fibrosis and gliosis. (Arasteh et al. 2020). Mishra et al. discovered a significant relationship between metabolic acidosis and both initial and ultimate visual acuity, including color vision outcomes. In contrast, Desai et al. identified that pH had the most robust correlation with final visual acuity (Mishra et al. 2023).

The COVID-19 pandemic has placed additional strains on healthcare systems worldwide, heightening the importance of tertiary referral hospitals in managing cases of methanol poisoning. The research on methanol poisoning in the COVID-19 era reveals significant insight on the clinical characteristics, treatment options, and outcomes of methanol poisoning during this challenging era. The research is notable because of the pandemic's effect on the increase in methanol poisoning cases brought on by the extensive consumption of alcohol-based sanitizers and disinfectants. The findings of the research ultimately have significant ramifications for clinical practice and public health policy because they can aid medical practitioners in improving patient outcomes and creating efficient plans to treat and prevent the condition.

The limitations of this study include the small sample size and the inability to perform tests, such as serum methanol levels, which could be one of the factors for the visual result. The osmolar gap is a valuable indicator for determining the need for and length of hemodialysis. Unfortunately, we could not determine the osmolar gap, a critical biochemical indicator. This study did not control for the consumption to presentation period; the period needed to collect blood for laboratory analysis, and the modes of therapy that might impact the course of methanol poisoning and ocular sequelae. Despite various limitations, we compared various demographic variables, employment, and insurance coverage with the consumption-to-reference time until the patient's first visit in emergency room, which has not been recorded in other studies.

Conclusions

In conclusion, methanol intoxication is a concerning problem among populations, with an age ratio that is skewed toward youths. The quantity of methanol consumed and the duration of time between consumption and presentation may be thought of as significant factors in the morbidity and fatality brought on by methanol poisoning. Elderly patients, unemployed people, and people without health insurance were among the reasons of late medical care visits, but surprisingly, our research discovered no correlation between patient mortality and the time elapsed between admission to the internal sections of the hospital and the first visit to the emergency room. Given this, improving public awareness about methanol poisoning, creating jobs, and encouraging people to seek treatment as soon as poisoning symptoms appear are effective ways to lower the mortality and morbidity associated with methanol poisoning.

Abbreviations

VBG Venus blood Gas
VA Visual acuity

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Author contributions

Study design and conceptualization: AJ, NS, ZK, FM, HJ. Methodology and investigation: AJ, MA, SJ. Statistical Analysis: AJ, MA, ZK, FM. Original draft preparation: All of co-authors. Approving final version: All of co-authors.

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Availability of data and materials

Upon reasonable request, the corresponding author can make available the datasets that were utilized and/or analyzed in the course of the present study.

Declarations

Ethics approval and consent to participate

The medical ethics committee at Tabriz University of Medical Sciences approved this research (IR.TBZMED.REC.1401.483). During the course of this research, the Helsinki Declaration was strictly adhered to. Participants gave informed consent according to ethical guidelines, received information on study purpose, procedures, risks, confidentiality, and right to withdraw. Participation was voluntary and all data collected were kept confidential and anonymous in compliance with the guidelines.

Consent for publication

Not applicable.

Competing interests

No author states to have any conflicts of interest.

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