ORIGINAL ARTICLE

A Retrospective Analysis of a Methanol Poisoning Outbreak in an Indian Tertiary Care Hospital during the COVID-19 Era: A Pandemic within a Pandemic

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Abstract

Background: Methanol poisoning is associated with high morbidity and mortality, due to its toxic metabolites namely formaldehyde and formic acid. Though explicit treatment guidelines exist but management becomes an arduous task when a cluster of cases present in resource limited settings. We describe here an outbreak of methanol poisoning during COVID 19 pandemic, the challenges faced and the outcome.
Objectives: To review the clinical manifestations, biochemical parameters, management and outcome of patients of methanol poisoning
Methodology: A retrospective analysis of methanol poisoning patients presenting to our hospital during an outbreak.
Results: A total of 108 patients presented to our center over a span of 13 days. All had allegedly consumed adulterated alcohol 12 to 96 hours prior to admission. 41had expired en-route to hospital, 20 expired within 6 hours of presentation and 8 were intubated. Among survivors, the most common complaint was visual blurring (n=31) followed by neurological symptoms (n=27). The mean pH and anion gap were 7.06 and 27.2 respectively at presentation and 7.38 and 8.0 respectively on discharge. 30 patients underwent hemodialysis to remove the toxic alcohol and its metabolites. All patients with ocular involvement received injection methylprednisolone 500 mg for 3 days. The overall mortality was 67.5%.
Conclusion: Methanol poisoning needs to be recognized early and managed emergently. Delay in seeking medical care substantially increases mortality. In case of inaccessibility to fomepizole and ethanol, dialysis has a pivotal role in management. Methylprednisolone therapy should be considered in all patients with visual complaints to reduce complications.

Keywords: Methanol; Outbreak; Acidosis; Hemodialysis

How to cite this article: Amir SH, Zafar L, Nasreen F, Khalid A, Siddiqu SM, Abdullahi DR. A Retrospective Analysis of a Methanol Poisoning Outbreak in an Indian Tertiary Care Hospital during the COVID-19 Era: A Pandemic within a Pandemic. ***Asia Pac J Med Toxicol*** **2022; 11(3):80-84.**

INTRODUCTION

Amidst the rising crisis of COVID 19 globally in 2021, our hospital witnessed another outbreak in the form of methanol poisoning. Almost, every family in India has been affected by the COVID-19 pandemic, which is predicted to have long-term consequences for public health and well-being. Alcohol consumption is already a public health issue, and it has the potential to worsen the COVID-19 pandemic in several ways. At a time when COVID 19 had taken a heavy toll on public health and all hospital resources were being diverted to the management of COVID patients, a sudden surge in the number of patients with methanol poisoning created a pandemic within pandemic situation for us.

Methanol, or methyl alcohol, is a colourless liquid. Industrial methylated spirit consists of 95% ethyl alcohol and 5% methyl alcohol. Mineralized methylated spirit contains 90% ethyl alcohol and 10% methyl alcohol. [1]. It is used in paints, varnishes, solvents, antifreeze, photographic materials, and household cleaning products. It smells a little sweeter than ethanol. Methyl alcohol poisoning can happen by cutaneous contact, inhalation, or ingestion [2, 3]. It is more common in the lower socioeconomic strata of society since it is inexpensive and readily available, making it a convenient alternative to ethanol for alcoholics.

Methanol is readily absorbed from the gastrointestinal tract, achieving peak plasma concentrations in 30-90 minutes. After 12-24 hours of exposure, patients develop signs and symptoms of poisoning [4, 5]. Although methanol is not harmful in its pure form, it oxidizes and produces harmful metabolites such as formaldehyde and formic acid. Formic acid interferes with anaerobic metabolism leading to lactate production [6, 7]. Hence, the levels of formic acid and lactic acid rise, producing metabolic acidosis and an increase in the anion gap [8, 9]. There is a clear link between the accumulation of formic acid and the toxicity of methanol. As the serum level of formic acid rises above 10–12 mmol/L, optic nerve dysfunction and damage to the basal ganglia occur

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[10, 11].

Permanent visual loss may result from intake of even 10 ml of methanol [12]. The mortality ranges from 18% to 44% [13]. The most common causes of death in patients are dyspnea and respiratory failure [14]. Survivors have reported adverse consequences such lifelong vision impairment and severe neurological sequelae [15].

Because ethanol is primarily metabolized by alcohol dehydrogenase (ADH) and Fomepizole is proven to be a powerful inhibitor of the enzyme, the treatment consists of ethanol or Fomepizole.

In May 2021, as Covid-19 cases escalated in India, stay-at-home orders were issued. Many workers were furloughed, laid off, or told to work from home. Alcoholics found it difficult to procure alcohol as their freedom of movement is restricted and they are confined to their residences. On the 28th of May 2021, the first few patients arrived at our hospital with abdominal pain, vomiting, and shortness of breath. Initially, food poisoning was suspected, but as more patients arrived, one common thread in their histories emerged. All the patients were factory workers and they all claimed to have consumed liquor from a crate found near the river. The suspicion was switched to methanol intoxication and the Arterial blood gas (ABG) levels matched the diagnosis. Massive epidemics of methyl alcohol poisoning are uncommon. However, our hospital saw over 100 patients with a history of ingestion of country-made liquor and accompanying symptoms from May 28 to June 10, 2021. We confronted another pandemic at our hospital while another pandemic was already underway. This study explored current understanding and the strategies indicated in the treatment of methanol intoxication.

METHODS

This is a retrospective cohort study of 108 patients, who presented to a tertiary hospital in Northern India with a history of illicit liquor consumption. Relevant data including demographic, clinical, and biochemical parameters of the patients were retrospectively retrieved from the hospital record section. After data analysis, an attempt was made to review the clinical manifestations, biochemical parameters, management, and outcome of patients of methanol poisoning. Exploration of the retrieved data revealed that 41 out of the 108 patients died on the way to the hospital, and 20 perished in the emergency room within 6 hours of presentation. A total of 47 patients were admitted, 39 in ward and 8 were intubated and transferred to the intensive care unit (ICU).

The patients were admitted after undergoing a detailed medical history and physical examination. For those who arrived early, gastric lavage was performed. Since the exact history of intake of alcohol could not be elicited in many patients, therefore gastric lavage was done to exclude other poisonings. All the patients underwent routine biochemical analysis like Complete blood count, ABG, serum electrolytes, Liver function test (LFT) , Random blood sugar (RBS) and urine examination. A detailed ophthalmological examination was performed by an expert ophthalmologist.

Because the estimation of serum levels of methanol or its metabolites could not be done, the treatment was initiated based on the history and investigation data. All patients were stabilized, started crystalloids, and airway was wherever needed. Injection sodium bicarbonate was given to patients with a pH of less than 7.30. Intravenous thiamine (100mg), pyridoxine (50mg), dextrose, folic acid and antiemetics were administered. The patients with visual complaints were given injectable methylprednisolone 500 mg for 3 days followed by oral therapy. All patients with pH less than 7.30 and hemodynamically stable underwent two to three sessions of hemodialysis. Despite the fact that ethanol and fomepizole are the preferred therapies, they were unavailable. However, in this study, most of the clinical and biochemical parameters of patients improved gradually.

RESULTS

A total of 108 patients presented to our center over a period of 13 days. The median age of the patients was 35 (range: 18-65) years, majority of them were males (88 out of 108). Since all the patients had consumed country made liquor, which is common in this part of the world, the constituents are highly unspecified.

Mortality

All patients presented between 12 to 96 hours after ingestion. 38% (41/108) patients were brought dead. 29.8% (20/67), who reported to hospital died within 6 hours of presentation, 11.9% (8/67) died between 6 to 12 hours of admission, and 5.9% (4/67) patients died within 12 to 48 hours of admission. The overall mortality rate was 67.5% (73/108).

There were 47 patients admitted. 12 of the 47 patients died, while the rest were discharged between 2 and 12 days following their first presentation.

Presentation

The age of the patients ranged from 18 to 65 years, mostly males (88 out of 108). Perhaps the lack of involvement of women in methanol poisoning is due to religion and social ties.

Of the 67 patients, who came alive, 27 presented with confusion, headache, altered sensorium, or abnormal movements, 23 had vomiting and abdominal pain, and 17 patients presented with shortness of breath, and 31 patients among them had blurring of vision (Table1).

14 patients presented with pH <6.95, Serum K^+ > 6.0mEq/L and serum Bicarbonate <10 mEq/L, of these 11 died within 6 hours and 3 were intubated and shifted to ICU, 6 patients presented with pH < 7.15, serum K^+> 5.0mEq/L and serum Bicarbonate > 10.0 mEq/L and less than 22.0, 1 of

Table 1. Clinical symptoms at presentation:

Clinical symptoms	Number of patients (n=67)
confusion, headache, altered sensorium or abnormal movements	27
vomiting and abdominal pain	13
shortness of breath	17
Blurring of vision	31

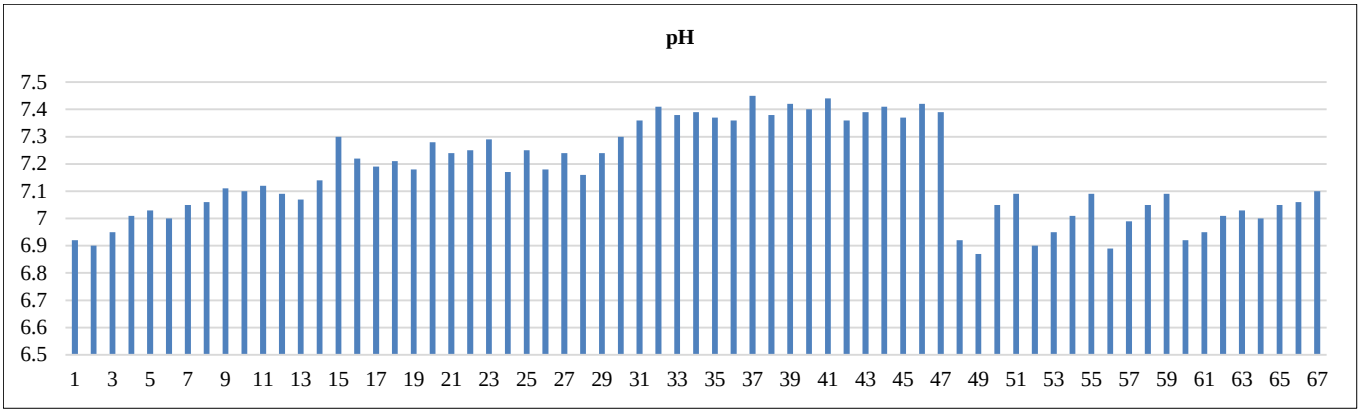

Figure 1. pH of the alive reported patients (n=67)

them died in the emergency, 2 were shifted to the ward and later intubated, and 3 were intubated in the emergency. Moreover, 30 patients came with pH > 7.16 and <7.35 and bicarbonate >10.1 and <22.0, and 17 patients came with pH in the normal range (Figure1 and 2).

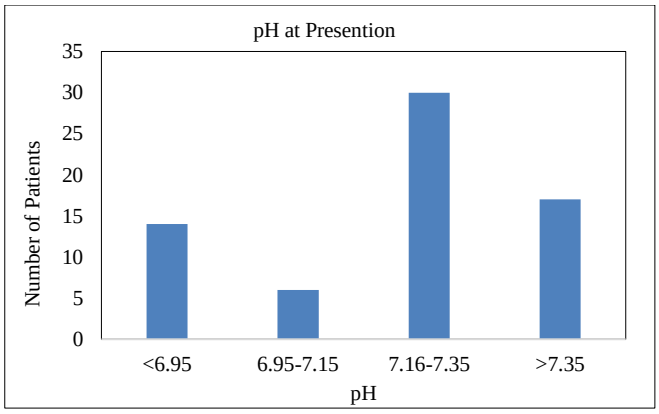

Figure 2. pH at presentation (n=67)

Dialysis

Out of the 8 patients in the ICU, 7 were dialyzed after intubation. Of these, 5 patients passed away and 3 survived. 39 patients were admitted in ward, out of which 23 were dialysed. 12 patients died and the rest were discharged between 2 to 12 days after presenting.

Patients with a pH of less than 7.30 underwent dialysis, and the majority of them improved after two to three cycles. The median pH upon admission was 7.06, and after one dialysis session and three days of intensive treatment, the median pH was 7.24. After two days, the median lactate had decreased from 3.9 at presentation to 1.6 (Table 2)

Ophthalmological manifestations:

Visual abnormalities ranging from diplopia to blurred vision and complete blindness were reported by individuals presenting 24 hours after ingestion (n=31). Each patient underwent a thorough ophthalmologic examination. Fundoscopic findings revealed optic atrophy (n=7), Retinal nerve fiber layer (RNFL) edema (n=19), and hyperemic disc with blurred margin (n=14) (see Figure 3). All of them were started on pulse steroid therapy – Injection Methyl Prednisolone 500 mg OD for 3 days followed by oral Methyl Prednisolone 0.5 mg/kg for 6 weeks. Most patients, who arrived early responded favorably to treatment, with restoration of vision. Nine of the 35 patients, who survived developed long-term ophthalmic complications such as uveitis, optic nerve atrophy, loss of visual acuity, and concentric visual field decrease. Most of them turned up 48 to 96 hours after consumption.

Table 2. Serial ABGs of the dialysed patients (n=7)

	On presentation	Day 3	At discharge
pH	7.06	7.24	7.38
Lactate	3.9	1.6	0.9
Serum K+	5.3	3.6	3.2
Serum Bicarb	12.3	18.8	24.5
Anion gap	27.2	13.7	8.0

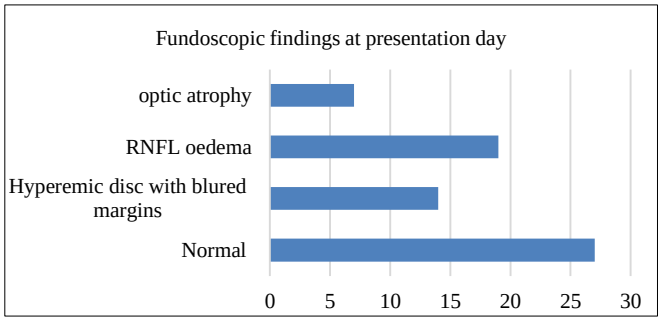

Figure 3. Fundoscopic findings at presentation (n=67)

Neurological manifestations:

27 patients had neurological manifestations at presentation. Six individuals had one or more seizures, nine had sensorium changes, and the rest had headaches and confusion. Patients with low GCS were intubated, while others were monitored for signs of progression. Most patients responded satisfactorily to treatment, regaining sensorium after dialysis. Two patients, however, were discharged with polyneuropathy, while one was discharged with ataxic gait.

DISCUSSION

There have been a few documented reports of such a large-scale methanol poisoning in literature. At the time of COVID-19 pandemic crisis, an outbreak of methanol poisoning rapidly overwhelmed our medical facilities. We discuss here the clinical presentations, biochemical parameters, management, and outcome of 108 patients, who presented to our emergency department after consumption of methanol adulterated liquor.

In the absence of definite history of methanol intake, most isolated poisonings remain undiagnosed. But with the background of common source of alcohol consumption, homogenous clinical presentation and high anion gap metabolic acidosis, a presumptive diagnosis of methanol poisoning was made, thereby leading to early and effective management.

Methanol is absorbed and metabolized early after ingestion. The initial clinical presentation occurs in 30 min to 4 hours and is mainly gastrointestinal (nausea, vomiting, abdominal pain) and neurological (inebriation, confusion). This phase is often ignored by the patient and his family, attributing it to the effect of ethanol. But after 6 to 24 hours, with the accumulation of products of methanol metabolism and subsequent acidosis, visual symptoms, respiratory distress and coma ensues. The patient usually presents to hospital in a critical state. Our patients came 12 to 96 hours after alleged ingestion of contaminated liquor. 38 % were already passed away at presentation and the total mortality was 67.5%, substantially higher than the average range of 28 to 48 percent [7, 16]. A case fatality rate of 80% was observed in an outbreak of methanol poisoning in Uganda [17]. The delay in seeking medical care contributes to morbidity as well as mortality. Gulen M et al observed that 76.2% patients admitted within 24 hours of methanol ingestion had no complications, in contrast to 70% mortality in patients admitted after 48 hours [18].

The other factors contributing to poor outcome in methanol poisoning are high anion gap metabolic acidosis (pH <7.07, AG > 26.7), low Glasgow Coma Scale (GCS <8) and raised lactate (> 2.55 mmol/L) [18]. The high mortality in our study is well explained by the ABG findings at presentation with a mean pH 7.06 ± 1.71 and anion gap 27.2 ± 6.39.(Table 3 and Figure 4)

The level of methanol in serum is not associated with the outcome [19]. Since the laboratory estimation of serum levels of methanol or its metabolites are not readily available, the management needs to be initiated emergently on clinical suspicion. This is in compliance with WHO guidelines (2014) on methanol poisoning outbreak. Our center also lacks the facility for estimation of serum methanol levels, so we started aggressive management based on suggestive history and ABG levels. This is consistent with previous studies wherein high level of clinical suspicion along with supporting lab investigations led to effective treatment in resource limited settings [20, 21].

Table 3. ABG of the admitted patients (n=47)

	Mean ± Standard Deviation
pH	7.06 ± 1.71
Serum K+	5.3 ± 1.2
Serum Bicarbonate	12.3 ± 5.18
Lactate	3.9 ± 4.75
Anion gap	27.2 ± 6.39

After stabilizing the airway, breathing and circulation, the cornerstone of management is blockage of Alcohol dehydrogenase (ADH) by ethanol or fomepizole, but accessibility is an issue. Due to non-availability of ethanol or fomepizole, our patients underwent hemodialysis in view of persistent acidosis (pH<7.25), anion gap >30 meq/L and signs of end organ damage. After two to three cycles of hemodialysis patients improved clinically and acidosis resolved. (Table 3) Continuous Renal Replacement Therapy (CRRT) is also an alternative if hemodialysis is contraindicated due to hypotension. But, it is less effective in removing the toxic metabolites and correcting acidosis [19].

The optic nerve and the pigmented retinal epithelial cells are affected by methanol [22, 23]. The reason for this selective involvement has not been clearly elucidated. However, optic nerve demyelination caused by the destruction of myelin by formic acid has been suggested as the underlying pathogenesis. In our study, 31 patients had ocular complaints ranging from visual blurring to blindness. They were administered injectable methylprednisolone 500 mg for 3 days followed by oral therapy. Nine patients failed to improve with therapy. The beneficial effect of pulse steroid therapy in methanol poisoning has not been systematically evaluated but is documented in uncontrolled case series [24].

Neurological manifestations are one of the most common findings in methanol poisoning. Cluster of symptoms ranging from altered consciousness to deep stupor may occur. The CNS effects of methanol poisoning are mediated by increased gamma-aminobutyric acid (GABA) tone directly and inhibition of presynaptic GABA (GABA-A receptors) and N-Methyl-D-aspartic acid (NMDA) glutamate receptors subsequent to accumulation of formic acid and formaldehyde [19].

In the present study, 27 patients had neurological manifestations at presentation spanning from headache, confusion to altered sensorium. Most patients responded satisfactorily to treatment, regaining sensorium after dialysis. However, neurological sequelae in the form of polyneuropathy was seen in two patients, while one was discharged with ataxic gait. Severe poisoning leads to necrosis of the basal ganglion, particularly the putamen and this has been attributed as the possible mechanism for ataxia [25].

Patients with methanol poisoning can present as an outbreak to the emergency department with neurological, gastrointestinal, and visual symptoms. In resource limited settings, such cases can be a diagnostic challenge for the emergency physicians. Hence, a high level of clinical suspicion together with supporting ABG findings of high anion gap metabolic acidosis should alert the attending physician about methanol poisoning as the possible cause. The initiation of treatment including intensive alkali therapy, antidote if available, steroid, and hemodialysis at incipient level can reduce large scale morbidity and mortality.

LIMITATIONS

The serum levels of methanol or its metabolites were not estimated. The diagnosis of methanol poisoning was assumed on the basis of history, clinical, and laboratory parameters. Moreover, the study reviews the acute manifestations of methanol intoxication, but fails to explore the long-term complications and outcomes in the survivors.

CONCLUSION

Methanol poisoning is a global public health problem, which can specially affect the poor and under-privileged parts of the society. Early recognition and intervention are of paramount significance to reach favorable outcomes. The population as well as the health personnel at the periphery needs to be aware of early manifestations of methanol poisoning. The tertiary care canters should be well equipped with diagnostic and treatment facilities. Although this methanol poisoning outbreak during the COVID19 pandemic challenged the limits of our health care, still adequate management was imparted and lives salvaged.

Conflict of Interest: None to be declared.

Ethical Clearance: This study was initiated after obtaining ethical clearance from Institutional ethics committee (Regd) JNMCH AMU Aligarh under National Ethics Committee Registry for Biomedical and Health Research- NECRBHR DHR-ICMR. All ethical principles related to participants were considered in this article.

Funding and Support: None

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