

# Epidemiological Attern of Extracorporeal Methods in Acute Poisoning: A-Five-Year Study

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## Abstract

**Background:** The use of hemodialysis is a prevalent extracorporeal technique for managing the poisoning of certain patients.

**Objectives:** In this study, we examined the frequency of extracorporeal methods and the prognosis of using these methods in various poisonings.

**Methods:** This retrospective study was conducted at Loghman Hakim hospital in Tehran between 2016 and 2020. The study investigated all patients who were hospitalized and underwent hemodialysis at the poisoning center. The study analyzed demographic data, clinical information, and certain laboratory findings from a sample size of 980 cases. The data obtained from the study were analyzed using SPSS 22.

**Results:** 793 (80.9%) males and 187 (19.1%) females were investigated. The mean age of the subjects was 36.5±14 years. Methanol consumption was the highest cause of poisoning (858 cases, 87.6%). Hemodialysis was the most widely used extracorporeal method (971 cases, 99.1%). The median number of hemodialysis was 1 times and the maximum was 18. The mortality rate was 13.3%. Metabolic acidosis was observed in 823 cases (84%). Acute kidney injury (AKI) was present in 536 cases (54.7%).

**Conclusions:** Although there have been some published studies and conferences on extracorporeal methods for treating poisonings, the lack of cases treated with these methods has resulted in weak evidence. To address this issue and provide more widely applicable data, studies like this can help to improve the treatment of poisoned patients.

**Keywords:** Extracorporeal, hemodialysis, methanol, poisoning

## Introduction

Poisoning is usually caused by swallowing poisons but can be caused by injections, inhalations, or exposure to body surfaces (skin, eyes, and mucous membranes). The general approach to the poisoned patient is divided into five stages; 1) stabilizing the patient's condition; 2) laboratory tests; 3) gastrointestinal, skin, or eye decontamination; 4) prescribing an antidote and 5) enhancing the removal of toxins from the body. Among the methods to enhance the removal of toxins from the body, the use of extracorporeal treatments (ECTR) such as hemodialysis and hemoperfusion play a significant function in saving the patient's life<sup>1,2</sup>.

Hemodialysis is the best treatment for water-soluble drugs, especially low molecular weight drugs, which have a low volume of distribution and low protein binding that can be rapidly distributed through the filter membrane. Some examples of these drugs are salicylates, ethanol, methanol and lithium<sup>3,4</sup>. In hemoperfusion, blood passes through a cartridge containing activated charcoal. Compared to hemodialysis, hemoperfusion is more effective in clearing

the blood from most protein-bound drugs because the charcoal in the cartridge competes with the plasma proteins to bind to the drug, absorb the drug, and remove it from the bloodstream<sup>1,5</sup>.

Abel et al. reported the initial application of extracorporeal techniques in 1913, wherein they eliminated salicylates from a dog's body<sup>6,7</sup>. Kyle et al. were first successfully using hemodialysis to treat barbiturates poisoning<sup>6,8</sup>. The initial extensive examination of employing hemodialysis in cases of sudden poisoning was presented by George Schreiner in 1958<sup>6,9</sup>. Physicians and researchers have since conducted several studies on these methods, which have led to the identification of drugs and toxins that can be removed through these methods<sup>10-13</sup>.

Despite the existence of studies and conferences on extracorporeal therapies, the lack of poisonings treated with these methods has resulted in weak evidence for their effectiveness. Considering that Loghman Hakim Hospital is one of the most reference places for the treatment of poisoned people, in this study we examined the frequency

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of extracorporeal methods and the prognosis of using these methods in various poisonings.

## Methods

This study was performed as a retrospective study. By referring to the dialysis ward of Loghman Hakim Hospital in Tehran, all cases of poisoning from 2016-2020 were investigated and the desired variables were extracted. The sampling method was census (All relevant files were reviewed). From 68181 patients admitted to the poisoning wards, 980 underwent hemodialysis and hemoperfusion that were our sample size and 67201 patients were excluded.

The studied variables included age, sex, type of poisoning, history of underlying disease, medication use and habits, number of times the extracorporeal method was used, type of extracorporeal method, patient's outcome (death, healing, sequela or discharge by personal consent), laboratory tests result and vital signs.

This study has been approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences under the code IR.SBMU.RETECH.REC.1400.444.

The data obtained from the study were analyzed by IBM SPSS STATISTICS 22 (IBM Corp, Armonk, New York, USA). Initially, the statistical population's normal distribution was established through the Kolmogorov-Smirnov test. Subsequently, the central and descriptive indices were computed and articulated. All samples were subjected to a significance level of  $P < 0.05$ .

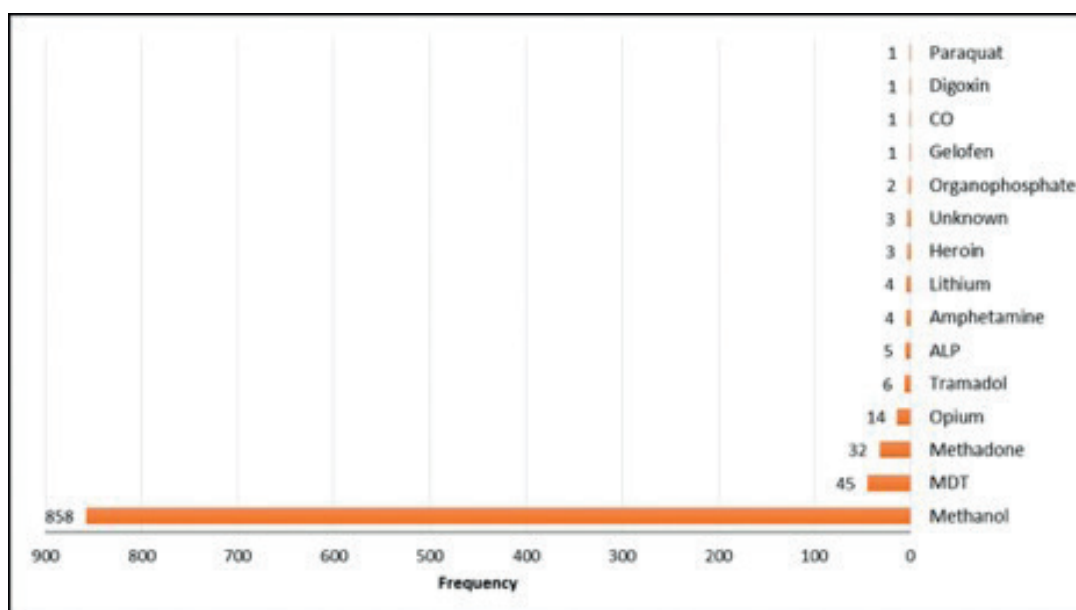
## Results

From 68181 patients admitted to the poisoning wards, 980 underwent hemodialysis and hemoperfusion that covered

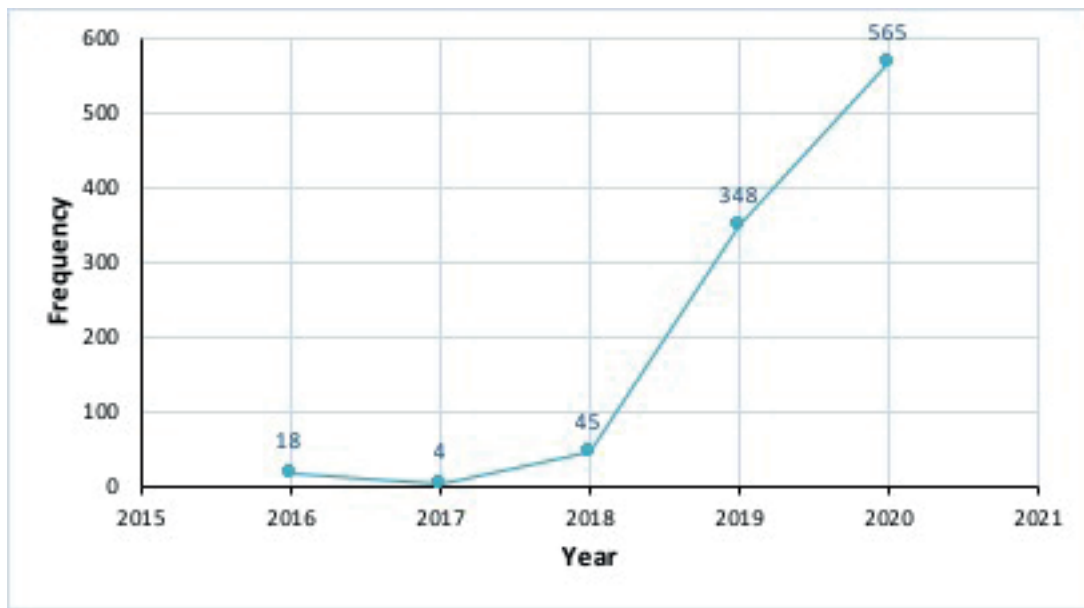
**Table 1:** Demographic information of the studied patients.

Variables	Frequency (%)
Gender (Male)	793 (80.9%)
Under 20 years old	100 (10.2%)
21-40 years	604 (61.6%)
41-60 years	211 (21.5%)
61-80 years	60 (6.1%)
Above 81 years	5 (0.5%)
Co-ingestion	62 (6.3%)
Smoking	46 (4.7%)
Alcohol consumption	627 (64%)
Opium abuse	75 (7.7%)
Stimulants abuse	13 (1.3%)
History of pervious disease	150 (15.3%)
History of taking medication	77 (7.9%)
Hemoperfusion	9 (0/9%)
Intubation	203 (20.7%)
ICU admission	187 (19.1%)
Antidote therapy	904 (92.2%)
Duration of hospitalization (day). median (min-max)	2 (1-116)
Death	130 (13.3%)

1.4% of the cases. 793 (80.9%) males and 187 (19.1%) females were investigated. Some demographic information is shown in Table 1. The mean age of the subjects was  $36.5 \pm 14$  years. The age distribution was significantly different ( $p < 0.001$ ). 604 cases (61.6%) were in the age range of 21-40 years. 117 cases (11.9%) had intentional poisoning. As shown in Figure 1, the highest cause of poisoning was due to methanol consumption (858 cases, 87.6%). 830 cases (84.7%) had no previous history of the disease. Two cases had a history of kidney disease. 903



**Figure 1:** Cause of intoxication in the studied patients. MDT= Multiple Drug Toxicity.



**Figure 2:** Frequency of extracorporeal methods during 2016-2020 years.

cases (92.1%) had no history of taking drugs and 627 (64%) cases had a history of alcohol consumption.

Hemodialysis was the most widely used extracorporeal method (971 cases, 99.1%). The median number of hemodialysis was 1 and the maximum was 18 times. Hemoperfusion was performed for 5 cases of methanol, 3 cases of multidrug and 1 case of methadone poisoning. As shown in Figure 2, there is a significant ( $p < 0.05$ ) increase in hemodialysis and hemoperfusion cases (during 2019 and 2020). 36.25% and 59.8% of methanol poisoning cases were in 2019 and 2020, respectively.

The most used antidotes were ethanol and folic acid, which were 38.1% (373 cases) and 32.8% (321 cases), respectively. The median duration of hospitalization was 2 days. 792 cases (80.8%) recovered. In 15 cases (1.5%), injury caused by poisoning remained and the mortality rate was 13.3% (130 cases). 2 out of 9 individuals who underwent hemoperfusion did not survive, while the remaining 7 individuals successfully recovered. The mortality rate for the hemodialysis method was 13.18%, while the hemoperfusion method had a mortality rate of 22.22%.

Clinical and laboratory tests results are shown in Table 2. Metabolic acidosis was observed in 823 cases (84%). Acute kidney injury (AKI) was present in 536 cases (54.7%). Hyponatremia, hyperkalemia, increased BUN (Blood Urea Nitrogen) and hyperglycemia were observed in 3.3% (32 cases), 14% (137), 16.8% (165) and 24.1% (236) of patients, respectively. 84.3% of acute kidney injury (452) and 63.1% of deaths (82) were among patients with methanol poisoning.

## Discussion

There are four categories of extracorporeal therapies based on their mechanism: hemodialysis and peritoneal

dialysis fall under diffusion, hemofiltration is categorized under convection, hemoperfusion falls under adsorption, and therapeutic plasma exchange is classified under centrifugation<sup>14, 15</sup>. Hemodialysis offers several benefits compared to other extracorporeal treatments. It effectively and quickly removes toxins from the blood and dialysate due to its high flow rates. Additionally, it can simultaneously address other medical conditions like uremia, acid-base imbalances, and electrolyte abnormalities. Furthermore, hemodialysis is the most accessible, cost-effective, and time-efficient method available<sup>14</sup>.

**Table 2:** Laboratory and clinical tests results.

	Frequency (%)
$13 \leq \text{GCS} < 15$	659 (67.2%)
$8 \leq \text{GCS} < 13$	62 (6.3%)
Coma (GCS < 8)	108 (11%)
Bradypnea	46 (4.7%)
Temperature (Mean±SD)	36.9±0.56
Bradycardia	14 (1.4%)
Tachycardia	145 (14.8%)
Hypotension	38 (3.9%)
Hypertension	293 (29.9%)
Metabolic Acidosis	823 (84%)
Acute Kidney Injury (AKI)	536 (54.7%)
Serum HCO <sub>3</sub> (Mean±SD)	14.4±23.8
BUN (meq/l) (Mean±SD)	36.7±27.2
Creatinine (meq/l) (Mean±SD)	1.7±4.1
Blood Glucose (mg/dl) (Mean±SD)	132.5±66.6
Blood PH (Mean±SD)	7.2±0.4
Sodium (meq/l) (Mean±SD)	137.8±10.8
Potassium (meq/l) (Mean±SD)	4.7±3.4

In this study, the most used method was hemodialysis. The most common cause of hemodialysis was methanol poisoning (858 cases, 87.6%). 793 males and 187 females were investigated. 61.6% of cases were in the age range of 21-40 years. The total mortality rate was 13.3%. The mortality rate of hemodialysis method was 13.18% and hemoperfusion method was 22.22%.

A study has been conducted in Urmia in the same period of time in the poisoning center of Taleghani Hospital. This research involved the evaluation of 200 patients. The overall mortality rate was 31.5%. The main causes of poisoning among patients treated with hemodialysis were toxic alcohol (methanol, ethylene glycol) 43% and paraquat 29%. The most common signs and symptoms among patients were loss of consciousness 41% and gastrointestinal discomforts such as nausea, vomiting, and epigastric pain 34%<sup>16</sup>. In our study, methanol was the primary cause of poisoning, while paraquat was observed in only 1 case. The shift in the pattern of poisoning in 2 cities has resulted in a death rate of 13.18% among our hemodialysis patients, which is much lower than that reported in the aforementioned study.

According to methanol is the most common cause of poisoning, it can be assumed that these cases have increased due to the prevalence of coronavirus. Other studies confirm that methanol poisoning increased during the COVID-19 pandemic<sup>17-21</sup>.

Methanol poisoning can happen through various means, such as ingestion, inhalation or skin contact. The symptoms of methanol poisoning can include digestive issues, suppression of the central nervous system, metabolic acidosis, and vision problems including blurred vision and even blindness<sup>22,23</sup>. Data that was gathered by Hassanian Moghadam and colleagues in 2019 on individuals suffering from methanol poisoning across the globe revealed that the use of hemodialysis and antidotes could be a safe and effective treatment for patients affected by poisoning<sup>24</sup>. In our study, the most common toxin treated with hemodialysis was methanol. Also, most of the antidotes were related to the treatment of methanol poisoning.

A study has been done in Urmia on patients undergoing hemodialysis. In that study, 200 patients (158 males, 42 females) were studied. The reported mortality rates were 31.5%, with 79% of the deaths being male and 21% being female. The main reasons for poisoning in patients were toxic alcohols such as methanol and ethylene glycol, accounting for 43%, and paraquat, accounting for 29%<sup>16</sup>. Our research also found that methanol, a toxic alcohol, had the highest number of cases requiring hemodialysis, while paraquat was only associated with 1% of the substances.

Vivek et al. conducted a study on methyl alcohol poisoning and hemodialysis. They reported that 91 males with mean age  $40 \pm 8.5$  years underwent hemodialysis, and 13 patients required a second session. Before hemodialysis, the mean pH was  $7.11 \pm 0.04$  (range 6.70–7.33) and mean bicarbonate levels were  $8.5 \pm 4.9$  mmol/L (range 2–18). Three patients died due to methanol intoxication 25. In

our study, 147 people (17.13%) of people poisoned with methanol needed hemodialysis more than once. 85 people (9.56%) of people poisoned with methanol died, which is higher than the above study (nearly 9 times).

A study on extracorporeal treatments for child and adolescent poisoning was conducted in California in 2013. 90 patients were examined. Hemodialysis was the main method of using extracorporeal treatments<sup>26</sup>. Our study also showed that hemodialysis is the main extracorporeal method for the treatment of poisoned people.

A study was conducted on the methanol outbreak in Rafsanjan in 2013. A total of 694 subjects were observed. Resistant metabolic acidosis was the primary reason for hemodialysis in 175 patients, out of which eight patients passed away. The serum methanol levels were only accessible for the deceased cases and not for the rest<sup>27</sup>. Our research also revealed that 84.2% of the patients (825 individuals) exhibited acidosis, indicating that one of the primary purposes of hemodialysis and hemoperfusion was to address acidosis.

In the case of opioid poisoning, extracorporeal treatment is not the best treatment. Typically, antidote and supportive treatments are enough to address the issue. Nevertheless, individuals who have reached end-stage kidney disease (ESKD) may experience an accumulation of specific opioids and their byproducts. To prevent toxicity in such cases, hemodialysis could be the solution. One of the primary active byproducts of morphine, morphine 6-glucuronide, may lead to lasting effects in ESKD patients, but it can be removed through dialysis<sup>6</sup>. Patients with renal impairment may experience accumulation of hydromorphone-3-glucuronide, which can be removed through hemodialysis<sup>28</sup>. In our study, after methanol, methadone (32 cases, 3.2%) and opium (14 cases, 1.4%) were the most hemodialysis toxins.

A man, aged 34, who had suicidal thoughts and took methadone, was studied. The patient's condition showed metabolic acidosis, acute renal failure, and rhabdomyolysis, which indicated the need for hemodialysis. After 11 days of hemodialysis, his metabolic disorders resolved but his hearing loss remained<sup>29</sup>. In our study, there were 32 cases (3.2%) with methadone poisoning. 81.25% of these cases had AKI and 68.75% had metabolic acidosis.

Although hemodialysis and other extracorporeal removal methods are performed for a limited number of toxins, they are very important and can save patients' lives and eliminate the effects of poisoning. Our study at the Loghman Hakim Center showed that methanol, multidrug and opioid (methadone & opium) poisoning are the most common causes of hemodialysis. Further studies (even case reports) on other toxins are recommended to increase the scope of knowledge about these methods and their effectiveness.

## Limitation

One major constraint of this study was the inadequate documentation of certain laboratory information.



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**Conflict of interest:** None to be declared.

## References

- Shannon MW, Borron SW, Burns MJ, Haddad LM, Winchester JF. Haddad and Winchester's clinical management of poisoning and drug overdose: Saunders/Elsevier; 2007.
- Al-Jelaify M, AlHomidah S. The individualized management approach for acute poisoning. *Advances in pharmacological and pharmaceutical sciences.* 2021;2021:1-5.
- Otten EJ. *Goldfrank's Toxicologic Emergencies*, by Lewis S. Nelson, Mary Ann Howland, Neal A. Lewin, Silas W. Smith, Lewis R. Goldfrank, and Robert S. Hoffman. New York, McGraw-Hill Education 2019, 2070 pages, \$245.79. Elsevier; 2020.
- Arasu R, Jegatheesan D, Sivakumaran Y. Overview of hemodialysis access and assessment. *Canadian Family Physician.* 2022;68(8):577-82.
- Ronco C, Bellomo R. Hemoperfusion: technical aspects and state of the art. *Critical care.* 2022;26(1):1-12.
- King JD, Kern MH, Jaar BG. Extracorporeal removal of poisons and toxins. *Clinical journal of the American Society of Nephrology.* 2019;14(9):1408-15.
- Abel JJ. On the removal of diffusible substances from the circulating blood by means of dialysis. *Trans Ass Am Physicians.* 1913;28:51.
- Kyle LH, Jeghers H, Walsh WP, Doolan PD, Wishinsky H, Pallotta A. The application of hemodialysis to the treatment of barbiturate poisoning. *The Journal of Clinical Investigation.* 1953;32(4):364-71.
- Schreiner GE. The role of hemodialysis (artificial kidney) in acute poisoning. *AMA Archives of Internal Medicine.* 1958;102(6):896-913.
- Palmer BF. Effectiveness of hemodialysis in the extracorporeal therapy of phenobarbital overdose. *American journal of kidney diseases.* 2000;36(3):640-3.
- Quintero Parra N, Wurgaft Kirberg A, Orellana Araya YV, Arellano Lorca J, Rojas Wettig L, Pefaur Penna J. Haemodialysis management for salicylate intoxication. *Nefrología (English Edition).* 2009;29(2):182-3.
- Lavergne V, Nolin TD, Hoffman RS, Roberts D, Gosselin S, Goldfarb DS, et al. The EXTRIP (EXtracorporeal TReatments in poisoning) workgroup: guideline methodology. *Clinical Toxicology.* 2012;50(5):403-13.
- Arelin V, Schmidt JJ, Kayser N, Kühn-Velten WN, Suhling H, Eden G, et al. Removal of methadone by extended dialysis using a high cut-off dialyzer: implications for the treatment of overdose and for pain management in patients undergoing light chain removal. *Clinical nephrology.* 2016;85(6):353-7.
- Ghannoum M, Hoffman RS, Gosselin S, Nolin TD, Lavergne V, Roberts DM. Use of extracorporeal treatments in the management of poisonings. *Kidney International.* 2018;94(4):682-8.
- Yaxley J, Scott T. Dialysis and extracorporeal therapies for enhanced elimination of toxic ingestions and poisoning. *Therapeutic apheresis and dialysis.* 2022;26(5):865-78.
- Majidi M, Delirrad M, Yousefpour A, Mehrno M. An Investigation of Intoxicated Patients who Underwent Hemodialysis: A-five Year Cross-sectional study. *Asia Pacific Journal of Medical Toxicology.* 2021;10(4):128-33.
- Delirrad M, Mohammadi AB. New methanol poisoning outbreaks in Iran following COVID-19 pandemic. *Alcohol and Alcoholism (Oxford, Oxfordshire).* 2020:0-.
- Mehrpour O, Sadeghi M. Toll of acute methanol poisoning for preventing COVID-19. *Archives of toxicology.* 2020;94(6):2259-60.
- Iranpour P, Firoozi H, Haseli S. Methanol poisoning emerging as the result of COVID-19 outbreak; radiologic perspective. *Academic radiology.* 2020;27(5):755-6.
- Shokoohi M, Nasiri N, Sharifi H, Baral S, Stranges S. A syndemic of COVID-19 and methanol poisoning in Iran: Time for Iran to consider alcohol use as a public health challenge? : Elsevier; 2020. p. 25-7.
- Mousavi-Roknabadi RS, Arzhangzadeh M, Safaei-Firouzabadi H, Mousavi-Roknabadi RS, Sharifi M, Fathi N, et al. Methanol poisoning during COVID-19 pandemic; A systematic scoping review. *The American journal of emergency medicine.* 2022;52:69-84.
- Najari F, Baradaran I, Najari D. Methanol poisoning and its treatment. *Int J Med Toxicol Forensic Med.* 2020;10(1):26639.
- Nekoukar Z, Zakariaei Z, Taghizadeh F, Musavi F, Banimostafavi ES, Sharifpour A, et al. Methanol poisoning as a new world challenge: A review. *Annals of medicine and surgery.* 2021;66:102445.
- Hassanian-Moghaddam H, Zamani N, Roberts DM, Brent J, McMartin K, Aaron C, et al. Consensus statements on the approach to patients in a methanol poisoning outbreak. *Clinical toxicology.* 2019;57(12):1129-36.
- Kute VB, Godara SM, Shah PR, Gumber MR, Goplani KR, Vanikar AV, et al. Hemodialysis for methyl alcohol poisoning: A single-center experience. *Saudi Journal of Kidney Diseases and Transplantation.* 2012;23(1):37.
- Darracq MA, Cantrell FL. Hemodialysis and extracorporeal removal after pediatric and adolescent poisoning reported to a state poison center. *The Journal of Emergency Medicine.* 2013;44(6):1101-7.
- Hassanian-Moghaddam H, Nikfarjam A, Mirafzal A, Saberinia A, Nasehi AA, Masoumi Asl H, et al. Methanol mass poisoning in Iran: role of case finding in outbreak management. *Journal of public health.* 2015;37(2):354-9.
- Gagnon DJ, Jwo K. Tremors and agitation following low-dose intravenous hydromorphone administration in a patient with kidney dysfunction. *Annals of Pharmacotherapy.* 2013;47(7-8):e34-e.
- Ghasemi S, Izadpanahi S, Yaghoubi MA, Brent J, Mehrpour O. Methadone associated long term hearing loss and nephrotoxicity; a case report and literature review. *Substance Abuse Treatment, Prevention, and Policy.* 2019;14(1):1-5.