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Assessing the prognostic effects of hematologic indices in mortality of patients with methanol poisoning

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Abstract

Background: Methanol poisoning is an important cause of death, especially in countries where alcohol consumption is forbidden by law. Due to unspecific symptoms, diagnosis of this condition is made by a delay; however, having a prognostic tool for predicting the outcome of patients with methanol poisoning would help physicians stratify the risk imposed to each patient. We aimed to evaluate the prognostic effect of hematologic indices in patients with methanol poisoning.

Methods: In this cross-sectional study, 311 patients with methanol poisoning were evaluated. The hematologic indices of the patients including hemoglobin, mean corpuscular volume, platelets, leukocytes and lactate dehydrogenase levels were extracted from the patient files. The factors were compared in survived and expired patients. The correlation of the hematologic indices and mortality was evaluated using spearman's correlation test and the ROC curves were drawn.

Results: Among the 311 patients who entered in our study, the mean age was 32.56 ± 10.672 and 282 patients (90.7%) were male. Fifty-eight patients (18.6%) expired in our study. The expired patients were older, and had higher leukocytes, MCV, and LDH levels. An LDH higher than 381 had a sensitivity and specificity of 93.5% and 55.1%, respectively for mortality due to methanol poisoning.

Conclusions: Leukocytosis, macrocytosis, and higher serum LDH levels were associated with higher mortality in methanol poisoning, and high LDH had the highest prognostic factor for prediction of death in this condition.

Keywords: Methanol poisoning, Hematologic indices, MCV, LDH, Toxicology.

Abbreviations: ROC: Receiver Operating Characteristic; LDH: Lactate Dehydrogenase; MCV: Mean Corpuscular Volume; MP: Methanol Poisoning; WBC: White Blood Cell

Background

Methanol or wood alcohol is derived from wood distillation and can be found in illegally-made alcoholic beverages due to improper methodologies [1]. Methanol Poisoning (MP) has long been reported as sporadic causes of death around the world; however, at times epidemics of this problem have occurred in different countries, mostly developing regions [2,3]. This disease is underdiagnosed and underestimated due to the unspecific symptoms [4]. Furthermore, in countries such as Iran, since alcoholic beverages are illegal, medical care seeking is overlooked due to the fear of punishment [2].

Methanol is first metabolized by the enzyme Alcohol dehydrogenase to make formaldehyde and is then oxidized by aldehyde dehydrogenase to make formic acid [5]. Accumulation of this toxic metabolite is responsible for the detrimental effects of methanol poisoning that can initiate in 0.5-4 hours from its ingestion [6]. Methanol poisoning can manifest as nausea, vomiting, abdominal pain, vertigo, and headache. It can result in the patient becoming blind or having multiple end-organ damages or losing their lives due to severe high-anion gap metabolic acidosis caused by methanol [7]. The mortality rate for MP reaches about 40% in the six-month period following methanol contact [8].

Delay in medical care and hyperglycemia are found to be associated with poor outcomes in MP [9]. The basis for severity assessment of this condition and further decisions regarding the management plan of methanol poisoning patients is based on the level of metabolic acidosis [10]. However, blood gas measurement is not available everywhere. Consequently, we aimed to use the data from the 2020 methanol poisoning epidemic of Iran [11] in devising a new prognostic tool for prediction of death in methanol poisoning.

Methods

In this cross-sectional study, 311 patients with Methanol Poisoning who were admitted to hospitals affiliated to Shiraz University of Medical Sciences during the March 2020 outbreak were assessed. The demographic data, the lab results of the patients, and the outcome of their hospitalization were extracted and a checklist was filled for each patient.

The inclusion criteria of the study were: all of the patients regardless of age and sex, with the diagnosis of Methanol poisoning who were admitted in the hospitals of Shiraz University of Medical Sciences. The exclusion criteria of the study were: the existence of underlying hematologic disease, the positive history of anemia, positive history of cirrhosis including alcoholic cirrhotic patients, a positive history of consumption of drugs with the ability to alter hematologic indices, history of chronic obstructive pulmonary disease, and heavy smoker patients.

All of the data were then entered into IBM SPSS version 26.0. The qualitative variables were reported as frequency and percentage and the quantitative variables were reported as mean and standard deviation. The patients were divided to "survived" and "deceased" groups. The quantitative variables were compared using independent two-sample T test and the qualitative variables were compared using Chi-square test or Fischer's exact test. Finally, a binomial regression analysis was performed for the correlated variables to find a model for prediction of mortality in patients with methanol poisoning.

The study has been approved by Shiraz University of Medical Sciences Committee of Ethics in Biomedical Research by the code IR.SUMS.MED.REC.1401.553.

Results

A total of 311 patients entered the study, 282 (90.7%) of whom were male and 29 (9.3%) were female. The mean age of the patients was 32.56 ± 10.672 years old. fifty-three male patients (18.8%) and five female patients (17.2%) expired. Chi-square test was used to evaluate the association between sex and survival which showed no such relation (P = 0.838). patients who expired due to methanol poisoning were significantly older and had significantly lower blood pressure than the patients who survived. They also had higher leukocyte counts, and higher MCV and LDH. Table 1 summarizes the basic vital signs and lab data of the patients who survived and who expired in this study.

Table 1: The demographic and clinical information of the patients

Variable	Survived	Expired	P-value
Age	31.55 ± 10.324	37.24 ± 11.166	<0.001
Systolic blood pressure	130.73 ± 17982	114.52 ± 31.489	0.001
Diastolic blood pressure	81.50 ± 10.174	73.07 ± 15.476	0.001
Pulse rate	92.67 ± 16.372	86.88 ± 20.707	0.07
Respiratory rate	18.54 ± 3.412	16.57 ± 4.025	0.290
Temperature	36.51 ± 2.179	36.70 ± 0.402	0.579
Initial pH	7.21 ± 0.141	6.80 ± 0.193	<0.001
Initial pCO_2	26.18 ± 11.465	39.81 ± 19.932	<0.001
Initial HCO_3^-	11.98 ± 7.451	6.37 ± 3.589	<0.001
White Blood Cells	10.59 ± 4.171	14.75 ± 8.093	<0.001
Hemoglobin	17.12 ± 2.402	16.88 ± 2.960	0.506
Platelet	253.92 ± 101.609	263.38 ± 105.189	0.545
Mean Corpuscular Volume	87.302 ± 11.148	93.56 ± 10.044	<0.001
Blood glucose	118.83 ± 71.574	252.33 ± 162.380	<0.0001
Lactate dehydrogenase	401.31 ± 218.699	992.62 ± 1136.672	0.001

A spearman's correlation test was used to assess the correlations between the hematologic parameters of the patients and the outcome of their disease. Leukocyte count, MCV, and LDH were significantly and directly correlated with the mortality of methanol poisoning. LDH had the greatest correlation among the tested variables. The results of Spearman correlation are summarized in Table 2.

A binomial regression analysis was conducted to devise a model for prediction of survival in patients with methanol poisoning. Age, WBC, MCV, and LDH of the patients were entered into the model and the omnibus test of model coefficient was used to determine the fitness of the model. with a P-value <0.001, our model could predict the mortality of methanol poisoning based on the hematologic parameters. The Nagelkerke R2 of the model was 0.460, and our model had an 86.1% accuracy in predicting the outcome of the patients. The sensitiv-

Table 2: Correlation of the hematologic indices with mortality due to methanol poisoning.

Variable	N	Spearman's rho	P-value
Age	311	0.209	<0.001
WBC	304	0.220	<0.001
Hemoglobin	304	-0.032	0.580
MCV	304	0.036	0.535
Platelets	299	0.288	<0.001
LDH	259	0.460	<0.001

Table 3: Modelling of predicting mortality due to methanol poisoning based on hematologic indices

Variable	B	Wald	P-value	Exp(B)
Age	0.057	8.943	0.003	1.059
WBC	0.000	15.651	<0.001	1.000
MCV	0.098	13.344	<0.001	1.102
LDH	0.004	20.526	<0.001	1.004
constant	-16.342	30.513	<0.001	0.000

Table 4: The optimal cutoff values of the variables for prediction of mortality in methanol poisoning

Variable	Cutoff	Sensitivity	Specificity
Age	31.5	0.717	0.580
WBC	10250	0.630	0.507
MCV	99.70	0.783	0.610
LDH	381	0.935	0.551

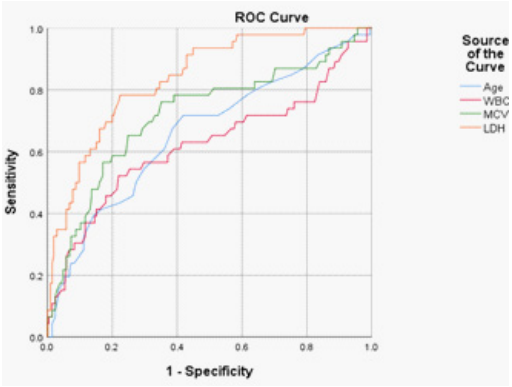

Figure 1: ROC of the variables

ity, specificity, positive predictive value, and negative predictive value of our model were 73.9%, 87.3%, 37.0%, and 97.0%, respectively. Table 3 summarizes the findings of this model.

Moreover, the Receiver Operating Characteristic (ROC) curve of the variables were drawn which are shown in Figure 1. The area under the curve for age, WBC, MCV, and LDH were 0.660, 0.621, 0.720, and 0.838, respectively. The optimal cutoff values for the defined variables and the sensitivity and specificity of mortality regarding such cutoffs are summarized in table 4.

Discussion

In this article, we evaluated 334 patients to devise a model for prognosis of the outcome in methanol poisoning using hematologic parameters. For this matter, we used the data of the 2020 methanol poisoning outbreak of Iran.

Methanol poisoning outbreaks usually occur in developing countries, especially regions in which the consumption of alcoholic beverages are legally restricted. In such countries such as Iran people who consume alcohol will use home-made drinks the quality of which is not controlled. These drinks may contain some levels of methanol. Moreover, since patients are often afraid of facing punishments by the governments, they hesitate referring to healthcare centers; consequently, the epidemics may happen. In 2020 Iranian outbreak of methanol poisoning, a contributing factor would have been the shortage of ethanol that was routinely being used for hand sanitizers in the contest of COVID-19 pandemic [12].

Routine risk stratification of patients with methanol poisoning is achieved by the results of blood gas analysis by which patients who experience more severe acidosis, will be more likely to experience morbidity or even death [10]. However, due to resource restriction, blood gas analysis is not available in all healthcare centers; therefore, devising a new prognostic scale for methanol poisoning might be of use, especially in developing regions.

Previous studies have been conducted to find other prognostic factors for lethality in methanol poisoning. In a study by Gulen et al. performed on 67 patients in Turkey, they found that lower Glascow Coma Scale score, and higher lactate were associated with higher mortality. It is reasonable that methanol poisoning patients with lower levels of consciousness have had higher concentrations of formic acid that could enter the central nervous system through the blood brain barrier [13].

We found that patients who will die of methanol poisoning were more likely to have lower blood pressures as a sign of hemodynamic instability. They also had higher levels of creatinine and aspartate aminotransferase. Higher creatinine in deceased patients indicate that acute kidney injury is a predictive factor for mortality that can indicate the need for emergency hemodialysis [14]. Higher aspartate aminotransferase in deceased patients with no significant difference in alanine aminotransferase levels might show that patients with underlying alcoholic liver disease were more likely to die due to methanol poisoning. The findings of our study in this matter are in line with the study of Gulen et al. [13].

In a meta-analysis by Sanaei-Zadeh et al., they found that hyperglycemia was a strong predictive factor for death in methanol poisoning. They speculated that increased blood glucose levels might rise from the increased risk of acute pancreatitis and the increase in the level of stress-related counterregulatory hormones as glucagon and epinephrine [15]. In our study also, the patients who died of methanol poisoning had higher blood glucose levels ($P < 0.001$). consequently, the findings of our study confirm the previous studies.

The hematologic indices of the patients were put under the spotlight to find a prognostic model for mortality in methanol poisoning. We found that leukocytosis, macrocytosis and elevated lactate dehydrogenase were in favor of more severe status of the patients. Macrocytosis might indicate a long-term alcohol consumption since this condition is associated with larger erythrocytes. Leukocytosis might rise from hemoconcentration and also the acute pancreatitis that was explained by Sanaei-Zadeh et al. [15]. Guillaume et al. also found that patients with higher MCV were more likely to die in the context of methanol poisoning [16].

Finally the correlation between the hematologic indices and the mortality of methanol poisoning was evaluated which showed that serum LDH had the highest direct relationship with mortality. However, no previous studies had been conducted on this matter.

Conclusions

In conclusion, we found that leukocytosis, macrocytosis, and higher serum LDH levels were associated with higher mortality in methanol poisoning, and high LDH had the highest prognostic factor for prediction of death in this condition.

Declarations

Ethics approval and consent to participate: All experimental protocols were approved by Committee for Ethics in Biomedical Research of Shiraz University of Medical Sciences by the code IR.SUMS.MED.REC.1401.553. All methods were carried out in accordance with relevant guidelines and regulations. The need for informed consent forms was waived by the Shiraz University of Medical Sciences Committee for Biomedical Research Ethics.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: S.S.B, A.H.H, and M.H.J were responsible for designing the study. F.K.H.S, J.R, M.P, M.H.N, V.R.O, Z.K, and P.K gathered the data, and S.S.B with the help of A.H.H analyzed the data. the draft was written by M.H.J and A.H.H. All of the authors then read and revised the manuscript. the final version of the manuscript has been accepted by all of the authors.

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References

1. Nekoukar Z, Zakariaei Z, Taghizadeh F, Musavi F, Banimostafavi ES, Sharifpour A, Ebrahim Ghuchi N, Fakhar M, Tabaripour R, Safanavaei S. Methanol poisoning as a new world challenge: A review. Ann Med Surg (Lond). 2021 Jun 2;66:102445. doi: 10.1016/j.amsu.2021.102445. PMID: 34141419; PMCID: PMC8187162.

2. Hassanian-Moghaddam H, Nikfarjam A, Mirafzal A, Saberinia A, Nasehi AA, Masoumi Asl H, Memaryan N. Methanol mass poisoning in Iran: role of case finding in outbreak management. J Public Health (Oxf). 2015 Jun;37(2):354-9. doi: 10.1093/pubmed/fdu038. Epub 2014 Jun 18. PMID: 24944254.

3. Rostrup M, Edwards JK, Abukalish M, Ezzabi M, Some D, Ritter H, Menge T, Abdelrahman A, Rootwelt R, Janssens B, Lind K, Paasma R, Hovda KE. The Methanol Poisoning Outbreaks in Libya 2013 and Kenya 2014. PLoS One. 2016 Mar 31;11(3):e0152676. doi: 10.1371/journal.pone.0152676. Erratum in: PLoS One. 2016;11(6):e0157256. PMID: 27030969; PMCID: PMC4816302.

4. Hassanian-Moghaddam H, Zamani N, Roberts DM, Brent J, McMartin K, Aaron C, Eddleston M, Dargan PI, Olson K, Nelson L, Bhalla A, Hantson P, Jacobsen D, Megarbane B, Balali-Mood M, Buckley NA, Zakharov S, Paasma R, Jarwani B, Mirafzal A, Salek T, Hovda KE. Consensus statements on the approach to patients in a methanol poisoning outbreak. Clin Toxicol (Phila). 2019 Dec;57(12):1129-1136. doi: 10.1080/15563650.2019.1636992. Epub 2019 Jul 22. PMID: 31328583.

5. Pietzke M, Meiser J, Vazquez A. Formate metabolism in health and disease. Mol Metab. 2020 Mar;33:23-37. doi: 10.1016/j.molmet.2019.05.012. Epub 2019 Jul 30. PMID: 31402327; PMCID: PMC7056922.

6. Wiener S.W. Toxic alcohols. In: Nelson L.S., editor. Goldfrank's Toxicologic Emergencies. ninth ed. McGraw-Hill; 2011. pp. 1400–1413.

7. Mousavi-Roknabadi RS, Arzhangzadeh M, Safaei-Firouzabadi H, Mousavi-Roknabadi RS, Sharifi M, Fathi N, Zarei Jelyani N, Mokdad M. Methanol poisoning during COVID-19 pandemic; A systematic scoping review. Am J Emerg Med. 2022 Feb;52:69-84. doi: 10.1016/j.ajem.2021.11.026. Epub 2021 Nov 24. PMID: 34883289; PMCID: PMC8611855.

8. Chung JY, Ho CH, Chen YC, Chen JH, Lin HJ, Wang JJ, Hsu CC, Huang CC. Association between acute methanol poisoning and subsequent mortality: a nationwide study in Taiwan. BMC Public Health. 2018 Aug 7;18(1):985. doi: 10.1186/s12889-018-5918-3. PMID: 30086726; PMCID: PMC6081913.

9. Yousefinejad V, Moradi B, Mohammadi Baneh A, Sheikhesmaeili F, Babahajian A. Prognostic Factors of Outcome in Methanol Poisoning; an 8-year Retrospective Cross-sectional Study. Arch Acad Emerg Med. 2020 Sep 5;8(1):e69. PMID: 33134965; PMCID: PMC7587997.

10. Paasma R, Hovda KE, Hassanian-Moghaddam H, Brahmi N, Afshari R, Sandvik L, Jacobsen D. Risk factors related to poor outcome after methanol poisoning and the relation between outcome and antidotes--a multicenter study. Clin Toxicol (Phila). 2012 Nov;50(9):823-31. doi: 10.3109/15563650.2012.728224. Epub 2012 Sep 20. Erratum in: Clin Toxicol (Phila). 2013 Feb;51(2):125. PMID: 22992104.

11. 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? Alcohol. 2020 Sep;87:25-27. doi: 10.1016/j.alcohol.2020.05.006. Epub 2020 Jun 4. PMID: 32505493; PMCID: PMC7272173.

12. Holzman SD, Larsen J, Kaur R, Smelski G, Dudley S, Shirazi FM. Death by hand sanitizer: syndemic methanol poisoning in the age of COVID-19. Clin Toxicol (Phila). 2021 Nov;59(11):1009-1014. doi: 10.1080/15563650.2021.1895202. Epub 2021 Mar 23. PMID: 33755514.

13. Gulen M, Satar S, Avci A, Acehan S, Orhan U, Nazik H. Methanol poisoning in Turkey: Two outbreaks, a single center experience. Alcohol. 2020 Nov;88:83-90. doi: 10.1016/j.alcohol.2020.07.002. Epub 2020 Jul 20. PMID: 32702502.

14. Kadam DB, Salvi S, Chandanwale A. Methanol Poisoning. J Assoc Physicians India. 2018 Apr;66(4):47-50. PMID: 30347953.

15. Sanaei-Zadeh H, Esfeh SK, Zamani N, Jamshidi F, Shadnia S. Hyperglycemia is a strong prognostic factor of lethality in methanol poisoning. J Med Toxicol. 2011 Sep;7(3):189-94. doi: 10.1007/s13181-011-0142-x. PMID: 21336799; PMCID: PMC3550199.

16. Guillaume C, Perrot D, Bouffard Y, Delafosse B, Motin J. Intoxication au méthanol [Methanol poisoning]. Ann Fr Anesth Reanim. 1987;6(1):17-21. French. doi: 10.1016/S0750-7658(87)80004-7. PMID: 3578941.