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Prevalence and Trends of Tricyclic Antidepressant Poisoning in Ilam: A Comparative Analysis

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ABSTRACT

Introduction: Tricyclic antidepressants (TCAs) are widely prescribed for treating depression, but they are also associated with a significant global mortality rate due to their overuse by healthcare providers. Given the severe side effects and high mortality associated with TCA poisoning, as well as the frequent occurrence of poisoning cases involving various drugs, including TCAs, this study aims to examine the prevalence of TCA poisoning in symptomatic patients referred to the poisoning department of Shahid Mostafa Khomeini Hospital in Ilam City from Iran during 2021 and 2022.

Methods: This study reviewed poisoning cases from 2021 and 2022 at the poisoning department of Shahid Mostafa Khomeini Hospital in Ilam City. Data collected included patient age, gender, and TCA levels in blood samples. Statistical analysis was performed using SPSS software, with the Mann-Whitney test employed for data comparison.

Results: The analysis of 2,217 poisoning cases in 2021 and 1,120 cases in 2022 revealed a TCA poisoning rate of 6.4% in 2021 and 2.6% in 2022. Nortriptyline was identified as the most commonly involved drug in poisoning incidents, with the highest frequency observed in individuals aged 20-35, across both genders.

Conclusion: TCA poisoning remains prevalent, especially among individuals aged 20-35 years, with nortriptyline being the most frequently implicated drug. The observed decline in poisoning cases in 2022 compared to 2021 may reflect changes in prescribing practices or the implementation of preventive measures. These findings underscore the importance of careful TCA prescription management and increased monitoring to minimize associated risks.

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Introduction

Mental health serves as a crucial gauge of a society's overall well-being. Among the prevalent mental disorders, depression stands out as a widespread neurological and psychological ailment affecting individuals from all walks of life (Huang et al, 2024). Depression, a pervasive and potentially life-threatening condition, impedes personal growth and performance of responsibilities. The World Health Organization identifies depression as the fourth leading cause of disability globally (Jalali et al., 2024; Reddy, 2010). This condition can impact physical health, emotions, behavior, and mental well-being, leading to various negative consequences such as diminished self-esteem, addiction, academic underachievement, and disruptions in familial, occupational, and social dynamics (Chaudhury et al., 2006). Furthermore, depression poses a significant economic burden on society, with potential outcomes including suicide (Beck et al, 2024). The likelihood of experiencing depression at some point in life is 10% for men and 20% for women, yet only a small percentage of affected individuals receive treatment (Kaplan and Sadock, 2003). In Iran, the reported prevalence of depression ranges from 20-24% (Hosseinizadeh-Shanjani et al., 2024; Schonwald, 2003). Poisonings represent critical medical emergencies typically resulting from accidental or intentional ingestion of substances like drugs or chemicals. Drug poisoning ranks among the leading causes of hospital admissions (Ahmad et al., 2024; Sobhani et al., 2000; Sakinofsky, 2000).

Tricyclic antidepressants (TCA), such as amitriptyline, nortriptyline, imipramine, etc., are among the most widely used categories of drugs that are used in the treatment of severe depression. The use of these drugs has other therapeutic uses as well. Unfortunately, the incidence of poisoning with these drugs is very high for various reasons, and according to the statistics available in Iran, the death rate caused by poisoning with these drugs is significant (Sobhani et al., 2000; Sakinofsky, 2000; Hawton et al., 2003). TCAs are one of the important causes of death due to therapeutic overdose (overdose) of prescription drugs in America and other parts of the world (López-Muñoz and Alamo, 2009). In Iran and other countries, the most common cause of death in recent years has been drug poisoning with these drugs (Ahmad et al., 2024). Studies have shown that in case of lack of access to

medical aid and before the arrival of medical services, the death rate in patients who attempted suicide by using TCA drugs was around 70% (Alexopoulos et al., 2005). The main reason for the risk of complications and death caused by the use of TCA drugs is the limitation of the therapeutic and toxic dose of TCA, and cardiovascular complications occur after TCA poisoning, which in the absence of proper treatment leads to the death of the patient (Jackson et al., 2010). Cardiovascular symptoms of TCA poisoning are conduction defects, dysrhythmias, and hypotension, and the most common cause of death in these patients is treatment-resistant hypotension (Jackson et al., 2010). The correlation between TCA overdose and the severity of coma is apparent in certain studies (Karami et al., 2004; Amro et al., 2013; Buckley et al., 1964).

Investigations have shown that the highest number of poisonings with TCAs are related to the age group of 11-30 years (76.6%), women (64.2%), and men (35.8%). Amitriptyline (2.36%) and nortriptyline (3.32%) are the most commonly used drugs among tricyclic antidepressants. Also, the rate of complications in poisoning with nortriptyline is higher compared to other TCAs (Karami et al., 2004). Meanwhile, 79.4% of the poisoned people go to the doctor within the first six hours after taking the drug. Among the cardiovascular side effects caused by the use of these drugs, hypotension at 6.9%, tachycardia at 6.31%, QRS wave prolongation at 4.4%, and among non-cardiac side effects decreased Acidosis at 1.52%, level of consciousness with 2.65%. Mepodiasis with 5.5% was the most common side effect of poisoning with these drugs, respectively. There is a direct relationship between the amount of side effects and the amount of medication used, while there is an inverse relationship between age and side effects. No relationship has been observed between the rate of side effects and the time interval between the drug and the start of treatment (Karami et al., 2004).

Considering the significant adverse reactions and the elevated mortality rate associated with tricyclic antidepressant (TCA) poisoning, coupled with an analysis of the existing data on TCA poisoning cases at the Poisoning Department of Martyr Mustafa Khomeini (RA) Hospital in Ilam City, this investigation sought to determine the prevalence of TCA poisoning among individuals presenting to the Poisoning Department of Martyr Mostafa Khomeini (RA) Hospital in Ilam City, West of Iran between the years 2021 and 2022.

Materials and Methods

For the measurement of TCA levels in serum of blood samples of patients with poisoning using High-Performance Liquid Chromatography (HPLC), the following steps were carried out:

Sample Collection

Blood samples were collected from patients with poisoning at Shahid Mostafa Khomeini Hospital in Ilam city. The serum was separated from whole blood by centrifugation, and the samples were stored at -20°C until further analysis.

Sample Preparation

For serum samples, proteins were precipitated using solvents like acetonitrile or methanol to remove interfering substances. The samples were then centrifuged to separate the supernatant, which was subsequently transferred for HPLC analysis.

HPLC Analysis

The samples were analyzed using an HPLC system equipped with a UV/Vis detector and a reverse-phase C18 column. Chromatographic conditions, such as the flow rate and column temperature, were optimized for TCA detection. A calibration curve was prepared using standard solutions of known TCA concentrations. The TCA concentrations in the patient samples were quantified by comparing their peak areas to the calibration curve.

Statistical Analysis

Data were analyzed using SPSS 22 software, with the Mann-Whitney U test applied to compare TCA levels across different groups (e.g., age, gender).

Results

The study covered a total of 2,217 poisoning cases that occurred between 2021 and 2022, along with 1,120 poisoning incidents reported in 2021. The results indicated that in 2021, poisoning caused by TCA drugs accounted for 142 cases, which represented approximately 6.4% of the total

poisoning cases. In contrast, the number of TCA-related poisonings decreased to 30 cases in 2022, making up around 2.6% of the total. Gender distribution of TCA poisoning cases between 2021 and 2022 showed that 122 cases (about 85.91%) involved women, while 20 cases (roughly 14.08%) were men. In 2022, the gender distribution shifted, with women accounting for approximately 70% of cases and men 30%. It was also noted that the majority of individuals affected by TCA poisoning, regardless of gender, were predominantly in the 20-35 years age range, as depicted in figure 1.

The analysis also revealed that nortriptyline was the most frequently utilized drug within this category. Furthermore, the levels of these drugs detected in serum samples did not exhibit any significant variance between men and women, as depicted in figures 2 and 3. This consistency suggests that the distribution and concentration of TCA drugs in the body were relatively uniform across genders, regardless of the sample type analyzed. The comprehensive examination of the data collected from these cases provided valuable insights into the prevalence and characteristics of TCA drug poisoning, elucidating the patterns observed among affected individuals.

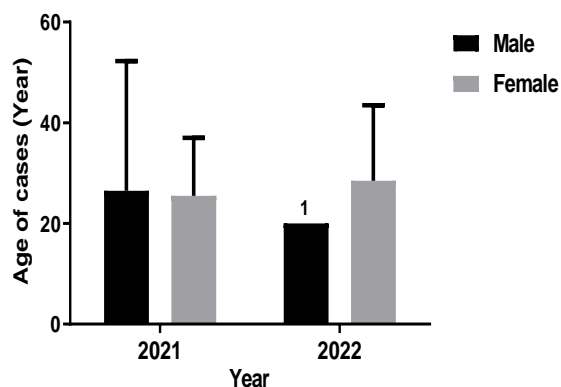


Figure 1. Comparison of the mean age of individuals with tricyclic antidepressant poisoning between 2021 and 2022

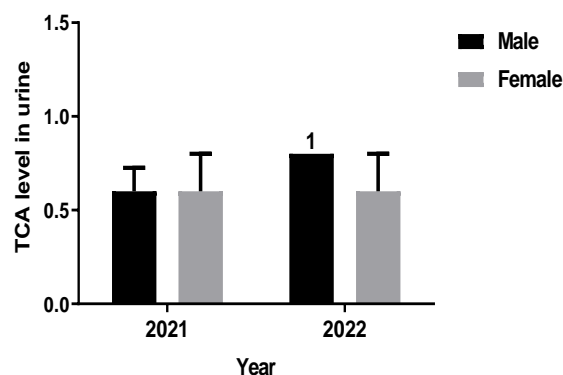


Figure 2. Comparison of the mean of TCA levels in blood samples in the groups.

No significant difference was observed between men and women.

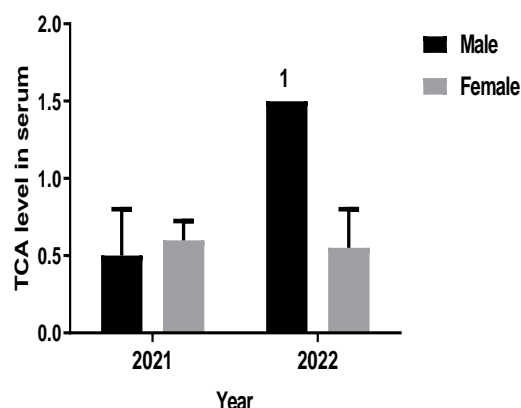


Figure 3. Comparison of the mean of TCA levels in blood samples in the groups.

No significant difference was observed between men and women.

Discussion

Depression is the fourth leading cause of disability in human societies, affecting individuals' physical, mental, emotional, and behavioral health (Huang et al, 2024). Among those suffering from depression, only 20-25% of individuals who meet the diagnostic criteria receive treatment (Sharifi et al., 1987). The prevalence of poisoning with tricyclic antidepressants is concerning, as TCAs represent one of the oldest classes of antidepressants, utilized since the 1960s and still offering significant benefits (Rahmani et al., 2015). The rapid progression from asymptomatic or mild symptoms to severe outcomes such as dangerous cardiac arrhythmias, coma, convulsions, low blood pressure, and cardiac arrest highlights the critical

need for prompt treatment and severity assessment in cases of TCA poisoning. Research findings from Ilam corroborate that individuals affected by TCA poisoning predominantly fall within the 20 to 35 age range, consistent with prior studies by Rahmani et al. Earlier studies conducted in Isfahan (Sharafi, 2001) indicated that the highest rates of TCA poisoning were observed in age groups of 15-22 (3.47) and 15-40 (5.62 years).

Additionally, the study results highlighted a significant gender disparity in TCA poisoning cases, with rates of poisoning in women (85.91% in 2021 and 70% in 2022) compared to men (14.08% and approximately 30%, respectively). These findings align with Barzegar et al.'s study in 2013, which reported a prevalence of TCA poisoning of 54.9% in women and 45.1% in men. Future research endeavors could focus on identifying factors contributing to depression, the duration of depressive episodes, the length of antidepressant usage, and concurrent drug use. Such investigations could inform the development of effective health interventions for affected individuals.

Conclusion

The data reveals a concerning prevalence of TCA (tricyclic antidepressant) poisonings, with rates of 6.4% recorded in 2021 and a decrease to 2.6% in 2022. This trend underscores the significant misuse of this class of medications, especially among younger populations. Notably, female patients have been disproportionately affected within the province, raising critical questions about the accessibility and regulation of these drugs. The findings indicate an urgent need for targeted interventions to address the factors contributing to the misuse of TCAs. Increased educational efforts focusing on the risks associated with these medications could play a vital role in preventing future poisonings. Additionally, healthcare providers should be vigilant in monitoring prescriptions, particularly for younger patients, to mitigate the risks of misuse and overdose. Overall, while there has been a decline in TCA poisonings from 2021 to 2022, the figures still highlight an ongoing issue that requires continued attention from healthcare professionals, policymakers, and educators alike. Addressing this challenge will be crucial in safeguarding the health of vulnerable populations, particularly young women, within the province.

Declarations

Conflict of Interest

The authors declare no conflict of interests. All authors read and approved final version of the paper.

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Consent to participate

All participants agreed to consent to participate anonymously.

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NA.

Authors Contribution

HGH: Conceptualization, original draft writing, investigation, writing (including reviewing and editing), investigation, and formal analysis.
HH: Conceptualization, supervision, and project administration.

GZ: Conceptualization, original draft writing, investigation, writing (including reviewing and editing).

NA: Investigation, writing.

KS: Original draft writing.

MS: Original draft writing.

Availability of data and material

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

References

Ahmad FB, Cisewski JA, Anderson RN. Leading causes of death in the US, 2019-2023. *JAMA*. 2024;332(12):957-958. doi: 10.1001/jama.2024.15563.

Alexopoulos GS, Lerner DM, Salzman C. Treatment of depression with tricyclic antidepressants, monoamine oxidase inhibitors, and psychostimulants. In: Salzman C, editor. *Clinical*

Geriatric Psychopharmacology. 4th ed. Baltimore: Lippincott Williams & Wilkins; 2005; 233-303.

Amro S, Ghada EG, Mohy EM, Aba AER, Mervat AES. Morbidity and mortality predictors in patients with acute tricyclic antidepressant toxicity. *Shams Journal of Forensic Medicine & Clinical Toxicology*. 2013;20(1):1-9.doi: 10.21608/ajfm.2013.19381

Beck AT, Rush AJ, Shaw BF, Emery G. *Cognitive Therapy of Depression*. Guilford Publications; 2024.

Buckley NA, Dawson AH, Whyte IM, et al. Greater toxicity of dothiepin in overdose than of other tricyclic antidepressants. *Lancet*. 2006;343(8894):159-62. doi: 10.1016/s0140-6736(94)90940-7.

Chaudhury PK, Deka K, Chetia D. Disability associated with mental disorders. *Indian Journal of Psychiatry*. 2006;48(2):95-101. doi: 10.4103/0019-5545.31597.

Eric NK, Gabor KD. *Manual of Toxicologic Emergencies*. Chicago: Year Book Medical; 1989. p. 3-5.

Hawton K, Zahl D, Weatherall R. Suicide following deliberate self-harm: long-term follow-up of patients who presented to a general hospital. *British Journal of Psychiatry*. 2003; 182: 537-42. doi: 10.1192/bjp.182.6.537.

Hosseinzadeh-Shanjani Z, Khodayari-Zarnaq R, Khosravi MF, Arab-Zozani M, Alizadeh G. Factors affecting major depression in Iran: a mixed-method study. *J Health Population Nutrition*. 2024;43(1):73.

Huang YY , Gan YH , Yang L , Cheng W , Yu JT. Depression in Alzheimer's disease: epidemiology, mechanisms, and treatment. *Biological Psychiatry*. 2024;95(11):992-1005. doi: 10.1016/j.biopsych.2023.10.008. doi: 10.1016/j.biopsych.2023.10.008.

Izadi MN, Gheshlaghi F, Jargouei M. Evaluation of ECG and APACHE II score in tricyclic antidepressant poisoning. *Journal of Anesthesiology & Special Care*. 1998;28(56):1-11.

Jackson JL, Shimeall W, Sessums L, et al. Tricyclic antidepressants and headaches: systematic review and meta-analysis. *BMJ*. 2010;341. doi: 10.1136/bmj.c5222.

Jalali A, Ziapour A, Karimi Z, Rezaei M, Emami B,

Kalhor RP, et al. Global prevalence of depression, anxiety, and stress in the elderly population: a systematic review and meta-analysis. *BMC Geriatrics*. 2024;24(1):809. doi: 10.1186/s12877-024-05311-8.

Kaplan HI, Sadock BJ. *Synopsis of Psychiatry: Behavioral Science, Clinical Psychiatry*. 5th ed. Baltimore: Williams & Wilkins; 2003; 20.

Karami M, Ebrahimzadeh MA, Yousefi P, Khani K. Investigation of drug poisoning effects in Boo-Ali and Nimeh-Shaban hospitals during 2000-2002. *Razi Journal of Medical Sciences*. 2004;10(42):629-35.

Lance JW, Curran DA. Treatment of chronic tension headache. *Lancet*. 1964; 1: 1236-39.

López-Muñoz F, Alamo C. Monoaminergic neurotransmission: the history of the discovery of antidepressants from the 1950s until today. *Current Pharmaceutical Design*. 2009;15(14):1563-86. doi: 10.2174/138161209788168001.

Punay NC, Couch JR. Antidepressants in the treatment of migraine headache. *Current Pain & Headache Reports*. 2003;7:51-54. doi: 10.1007/s11916-003-0010-8.

Rahmani AH, Jafari M, Farnam M, Zafari J. Evaluation of epidemiology of drug poisoning in Ahvaz Razi Hospital during 2004-2008. *Iranian Journal of Forensic Medicine*. 2015;10(1):43-46.

Reddy MS. Depression: the disorder and the burden. *Indian Journal of Psychological Medicine*. 2010;32(1):1-2. doi: 10.4103/0253-7176.70510.

Sakinofsky I. Repetition of suicidal behaviour. In: Hawton K, Van Heeringen K, editors. *The International Handbook of Suicide and Attempted Suicide*. Chichester: Wiley; 2000; 385-404.

Schonwald S. *Medical Toxicology*. Philadelphia: Lippincott-Williams & Wilkins; 2003; 2-3.

Sharifi K, Souki Z, Khademi Z, Hoseynian M, Tagharrobi Z. Depression level and related factors amongst students in Kashan Medical University. *Kashan Research Science Journal*. 1987;16(4):54-58.

Sobhani AR, Shojaii-Tehrani H, Nikpour E, Noroozi-Rad N. Drug and chemical poisoning in Northern Iran. *Archives of Iranian Medicine*. 2000;3(2):32-36.

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