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Unwanted Clinical Complications Following the Consumption of *Death Coffee*: A Case Series

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ABSTRACT

"*Death Coffee*" is an incredibly potent brew with caffeine content three times higher than conventional coffees, making it the strongest coffee in the world. Caffeine, a relatively safe psychostimulant substance consumed as dietary products or daily drinks, enhances physical and mental performance. According to long-lasting safe experiences of daily coffee consumption, caffeine intoxication with a cup of coffee is hardly believable in Iran. This paper reports five cases of coffee toxicity with a single cup of coffee within the last weeks. Presentation of toxicity varied among patients and ranged from lethargy to hallucination, tremors, agitation, shortness of breath, and decreased level of consciousness. Surprisingly, all five patients consumed an unknown caffeinated beverage called *Death Coffee* within 12 weeks, demonstrating that a new and unknown beverage prevails in our region.

1 | Introduction

"*Death Coffee*" is an incredibly potent brew with caffeine content three times higher than conventional coffees, making it the strongest coffee in the world. Despite its high demand, the cost of this potent brew remains relatively expensive in Iran. Drinking coffee, which is currently popular worldwide, became prevalent in Arab and Istanbul societies in the 15th and 16th centuries [1]. Caffeine (1, 3, 7-trimethylxanthine) is the primary active ingredient in coffee, with psychoactive effects [2]. A cup of brewed coffee contains about 95–200 mg, while a shot of espresso contains 47–64 mg of caffeine [3, 4]. Caffeine is found in coffee, tea, chocolate, cola, cocoa, energy drinks, some over-the-counter drugs, and appetite suppressants [2, 5, 6]. It is likely the most commonly consumed stimulant in the world, enhancing physical and mental performance and providing energy [5, 7]. Caffeine consumption is increasing globally, particularly in more concentrated forms, with the greatest concern surrounding anhydrous caffeine [6, 8]. The bother augments more concerns in conditions when no regulatory structure analyzes caffeine-containing products to protect consumers [9].

Caffeine's effects are attributed to its multi-modal mechanism of action, functioning as an adenosine antagonist, phosphodiesterase inhibitor, and sympathomimetic agent. By influencing adenosine α1 receptors and the adrenal medulla, caffeine triggers the release of catecholamines, boosting sympathetic activity, which leads to increased alertness, smooth muscle contractions, and heart rate [2–5]. Caffeine, at high concentrations of 25 μg/mL, has been found to inhibit monoamine oxidase, leading to an elevation in the levels of epinephrine, dopamine, and glutamate, which may contribute to its toxic effects in cases of excessive consumption [3, 10]. This elevation induces general vasoconstriction, tachycardia, hypokalemia, hypernatremia, and increased water excretion [3, 10, 11]. In closer view, caffeine affects intracellular calcium through different pathways like inhibition of inositol triphosphate (IP3) and activation of the ryanodine receptor [12]. Previous studies have not demonstrated any

correlation between coffee consumption and an increased risk of coronary artery disease or mortality. Studies have indicated that the slightly elevated risk of coronary artery disease mortality observed in male heavy coffee drinkers is largely associated with other risk factors, such as smoking and elevated serum cholesterol levels [13].

Caffeine intoxication can occur if caffeinated beverages are consumed in excess [7]. There is a wide range of different complaints and disease severity among emergency department visits related to caffeine [5]. Intentional overdose is the most common cause of caffeine intoxication in adults [2]. The safe consumption limit is considered to be less than 400 mg per day for adults and 2.5–3 mg/kg per day for children, with significant individual variation [4]. This case series highlights the adverse effects of a new and previously unreported caffeinated beverage, named *Death Coffee*, on five patients who exhibited varying symptoms of caffeine toxicity, ranging from lethargy to decreased consciousness, after consuming a single cup of the beverage within the preceding weeks.

2 | Case Presentation

2.1 | Case 1

In February 2024, a 34-year-old male was admitted to the emergency room (ER) 2 h after consuming an unknown quantity of caffeine known locally as *Death Coffee* and reported symptoms of palpitations, dizziness, lethargy, weakness, and dry mouth. The patient had no known history of pre-existing medical conditions, mental health issues, or substance abuse. On arrival, his vitals were HR 150 beats per minute, RR 22 breaths per minute, BP 140/90 mmHg, and temperature 38°C, with no electrocardiography (ECG) findings except sinus tachycardia. Upon thorough evaluation of the patient's symptoms, brain imaging was deemed unnecessary given the absence of neurological symptoms. A rapid urine toxicology screen was negative for opioids and amphetamines. Subsequently, the patient was administered 10 mg of midazolam intravenously for 6 h, in addition to fluid management. After 12 h of observation, the patient's clinical symptoms were fully stabilized, leading to his discharge from the hospital in good general condition.

2.2 | Case 2

On March 8, 2024, a 24-year-old man with no pre-existing medical conditions or history of drug or stimulant abuse was brought to the ER 3 h after consuming a cup of *Death Coffee*, with unknown caffeine content. The patient exhibited symptoms of nausea, vomiting, blurred vision, visual hallucinations, and delusions, indicative of severe caffeine toxicity. At the time of admission, his vital signs were HR, 119 beats per minute; RR, 20 breaths per minute; BP, 130/85 mmHg; and body temperature, 37.4°C. The patient was admitted to the poisoning ward for treatment. To manage the hallucinations, he was administered a 5-mg IV dose of haloperidol and a 10-mg intramuscular dose of diazepam to prevent potential seizures. After 6 h of treatment, the patient's symptoms improved significantly. Finally, he was discharged with stable hemodynamic conditions.

2.3 | Case 3

On March 28, 2024, a 37-year-old man with a 5-year history of psychiatric disorders and no history of drug, tobacco, or alcohol addiction was being treated with a combination of 250 mg sodium valproate tablets twice daily, 2 mg biperiden tablets twice daily, 2 mg perphenazine daily, and 25 mg quetiapine at night. The patient was brought to the ER 1 h after consuming half a cup of *Death Coffee*, a highly caffeinated beverage with unknown caffeine content. The patient reported palpitations, shortness of breath, flushing, and agitation as primary symptoms. This was not his first experience with *Death Coffee*, as he had previously consumed it, leading to similar symptoms.

Upon arrival, his vitals were recorded as HR, 120 beats per minute; RR, 24 breaths per minute; and body temperature, 37.5°C. Except for a potassium level of 3.3, other laboratory results were within normal limits. To address the patient's shortness of breath, the following treatments were administered: 200 mg of hydrocortisone, 250 mL of normal saline, and budesonide via a nebulizer. Upon admission to the poisoning ward, due to the patient's agitation, 2.5 mg of IV midazolam was prescribed as a sedative. After 24 h of observation and treatment in the hospital, the patient's condition improved, and he was discharged with a favorable prognosis.

2.4 | Case 4

On April 2, 2024, a 49-year-old man was referred to the hospital 45 min after drinking a cup of *Death Coffee* with symptoms of tachycardia, restlessness, and tremors. He had no prior history of caffeine use disorder, substance use disorder, or other mental or neurological disorders. Notably, he was undergoing methadone maintenance therapy, taking 40 mg of methadone tablets daily. The patient reported that this was his first experience with *Death Coffee*. His vital signs at presentation were HR, 103 beats per minute; RR, 18 breaths per minute; and body temperature, 37°C, with normal laboratory results and only sinus tachycardia on ECG. Based on the patient's history and clinical presentation, a diagnosis was made without the need for any imaging tests. To control his symptoms, 3 mg of IV midazolam was administered, which successfully mitigated his symptoms.

2.5 | Case 5

On April 14, 2024, a 55-year-old male patient with no known medical history was admitted to the hospital 30–60 min after consuming a cup of *Death Coffee* with symptoms of restlessness, sleepiness, and decreased level of consciousness. The patient was also taking low-dose aspirin (80 mg) daily for an unspecified reason. The patient reported that this was his first time-consuming *Death Coffee* and that he smoked daily. An ECG on arrival showed premature ventricular contractions (PVC), but his laboratory data were within normal limits. His vital signs were recorded as HR, 101 beats per minute; RR, 18 breaths per minute; and body temperature, 37°C. Following admission to the intensive care unit (ICU), the patient was administered 10 mg of intramuscular diazepam to alleviate his symptoms,

which proved successful in reducing restlessness, and a subsequent ECG showed no abnormal findings.

3 | Discussion

Caffeine is well absorbed after oral consumption, and clinical effects can be observed within 15 min of ingestion. Peak plasma levels are reached 50–60 min after consumption [4, 6]. Typically, its half-life is 3–6 h, but in cases of overdose, the half-life can extend to about 15 h [4, 10]. Symptoms of caffeine intoxication are generally dose-dependent [1]. The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) defines caffeine intoxication as "recent consumption of caffeine (typically a high dose well over 250 mg)", but recognizes that 200 mg can cause intoxication in children, the elderly, and individuals who have not previously exposed to caffeine [14].

Consuming large amounts of caffeine can lead to caffeine intoxication, which can present with a range of symptoms, including restlessness, tremors, anxiety, mood changes, irritability, vomiting, hypokalemia, ventricular dysrhythmias, hypotension, rhabdomyolysis, and death. Caffeine intoxication can be life-threatening, and the lethal dose is estimated to be 150 mg/kg of body weight. This is equivalent to approximately 50 caffeine tablets or 1 tablespoon of powdered caffeine. Mortality resulting from excessive caffeine consumption can be due to dysrhythmias or secondary complications such as acute kidney injury (AKI) associated with rhabdomyolysis [3, 4, 7, 10, 14].

Hypokalemia in caffeine intoxication is primarily secondary to intracellular potassium shift, driven by increased catecholamine release [4]. Low potassium levels are particularly important due to the risk of cardiac dysrhythmias [3]. Elbokl et al. [4] reported a case of a patient who consumed 60,000 mg of caffeine and required dialysis, with a potassium level of 2.6 mmol/L on admission. In this patient, potassium was utilized as a marker of adrenergic activity, and the need for large doses of IV potassium replacement persisted even after dialysis, likely indicating ongoing caffeine activity or one of its metabolites post-dialysis.

Sometimes caffeine consumption results in psychosis or psychosis-like experiences, such as hallucinations [15]. In 2023, Adeleye et al. reported caffeine psychosis with a coffee sachet containing 51 mg of caffeine [2]. In this report, like our second case, a young adolescent boy experienced hallucinations in addition to nausea and vomiting. Previous studies claim that caffeine-psychoactive chattels are linked to dopaminergic effects. Solinace et al. demonstrated that 10 and 30 mg/kg caffeine administration among rats leads to enhanced release of dopamine and glutamate in the shell of the nucleus accumbens (NAc), the same region where other psychostimulants and addictive drugs, such as amphetamine, increase dopamine level [16].

Despite NAc, caffeine does not increase dopamine levels in the striatum, but it has been reported that 300 mg oral caffeine can increase the availability of dopamine (D2/D3) receptors in putamen and ventral striatum [17]. It is precious to remember not only that caffeine may induce new-onset psychosis but also that it can interfere with medical response in psychotic patients receiving medical treatments [18]. Moreover, it should be highlighted that caffeine may aggravate pre-existing psychotic or mood disorders; therefore, caffeine should be used cautiously in this population.

While no direct association between caffeine ingestion and dopamine concentration in the chemoreceptor trigger zone has been established, the simultaneous occurrence of hallucinations, nausea, and vomiting in young adults consuming caffeine warrants further investigation into the potential relationship between caffeine and dopamine. This warrants additional research to better understand the effects of caffeine on dopamine levels and the implications for health and safety [19].

Treatment of caffeine intoxication is individualized based on the patient's symptoms and clinical status, with close monitoring being vital throughout the treatment period. As no specific antidote or reversal agent exists for caffeine, treatment is primarily supportive [2, 3]. Activated charcoal may be useful in cases of recent ingestion, as it binds to methylxanthines, preventing caffeine absorption [2]. For hospitalized patients, various tests are recommended, including a complete blood count, serum electrolytes, creatine kinase, urine analysis, and toxicology screening [3]. The mainstay of caffeine intoxication treatment involves the administration of IV fluids and benzodiazepines, such as diazepam, with beta-blockers being considered as an alternative option [2, 3, 5]. Caffeine can be removed from the bloodstream via dialysis or hemodialysis, though some symptoms may persist beyond the treatment period [2, 4, 10]. Notably, none of the patients in our study required dialysis.

4 | Conclusion

To effectively mitigate the health risks associated with high-caffeine products, a multifactorial approach must be adopted, encompassing regulation to ensure proper labeling and informative warnings; education of the public regarding the potential dangers of caffeine intoxication; training of healthcare professionals to accurately identify and effectively manage cases of caffeine intoxication; and the provision of sufficient laboratory facilities in poison control centers to enable prompt diagnosis and management of suspected cases.

Author Contributions

Amir-Hassan Bordbari, Yousef Ashoori, and Fatemeh Moslemi Najarcolaii are involved in the interpretation and collection of data, writing and editing of the manuscript. Zakaria Zakariaei and Mahkameh Soltani were involved in editing and preparing the final version of the manuscript. Zakaria Zakariaei submitted the manuscript. All authors reviewed the paper and approved the final version of the manuscript.

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The authors have nothing to report.

Ethics Statement

The study was approved by our local ethics committee.

Consent

Written informed consent was obtained from the patients to publish this report in accordance with the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The raw data are provided as Supporting Information.

References

1. C. Willson, "The Clinical Toxicology of Caffeine: A Review and Case Study," *Toxicology Reports* 5 (2018): 1140–1152.

2. Q. A. Adeleye, C. M. Attama, O. Egbeobauwaye, and O. Angela, "Psychosis Following Caffeine Consumption in a Young Adolescent: Review of Case and Literature," *Annals of African Medicine* 22, no. 3 (2023): 392.

3. C. C. Carreon and B. Parsh, "How to Recognize Caffeine Overdose," *Nursing* 49, no. 4 (2019): 52–55.

4. M. Elbokl, I. Randall, and C. Lok, "Severe Caffeine Intoxication Treated With Hemodialysis: A Case Report," *Kidney Medicine* 3, no. 2 (2021): 299–302.

5. S. F. Li, L. Edwards, and V. Nguyen, "Treatment of Caffeine Toxicity With Metoprolol," *American Journal of Emergency Medicine* 37, no. 3 (2019): 562.e5–e10.

6. S. B. Jabbar and M. G. Hanly, "Fatal Caffeine Overdose: A Case Report and Review of Literature," *American Journal of Forensic Medicine and Pathology* 34, no. 4 (2013): 321–324.

7. G. A. Beauchamp, A. R. Johnson, B. I. Crouch, M. Valento, B. Z. Horowitz, and R. G. Hendrickson, "A Retrospective Study of Clinical Effects of Powdered Caffeine Exposures Reported to Three US Poison Control Centers," *Journal of Medical Toxicology* 12, no. 3 (2016): 295–300.

8. G. R. Quadra, J. R. Paranaíba, J. Vilas-Boas, et al., "A Global Trend of Caffeine Consumption Over Time and Related-Environmental Impacts," *Environmental Pollution* 256 (2020): 113343.

9. J. L. Pomeranz, C. R. Munsell, and J. L. Harris, "Energy Drinks: An Emerging Public Health Hazard for Youth," *Journal of Public Health Policy* 34 (2013): 254–271.

10. T. Omi, "Protracted Effects of Caffeine After Hemodialysis for Severe Caffeine Intoxication," *Toxicology Communications* 5, no. 1 (2021): 73–75.

11. B. J. Gurley, S. C. Steelman, and S. L. Thomas, "Multi-Ingredient, Caffeine-Containing Dietary Supplements: History, Safety, and Efficacy," *Clinical Therapeutics* 37, no. 2 (2015): 275–301.

12. H. Kong, P. P. Jones, A. Koop, L. Zhang, H. J. Duff, and S. W. Chen, "Caffeine Induces Ca2+ Release by Reducing the Threshold for Luminal Ca2+ Activation of the Ryanodine Receptor," *Biochemical Journal* 414, no. 3 (2008): 441–452.

13. P. Kleemola, P. Jousilahti, P. Pietinen, E. Vartiainen, and J. Tuomilehto, "Coffee Consumption and the Risk of Coronary Heart Disease and Death," *Archives of Internal Medicine* 160, no. 22 (2000): 3393–3400.

14. American Psychiatric Association, DSM-5 Task Force, *Diagnostic and Statistical Manual of Mental Disorders: DSM-5* (American Psychiatric Association, 2013).

15. C. Ágoston, L. Bernáth, P. J. Rogers, and Z. Demetrovics, "Stress, Caffeine and Psychosis-Like Experiences—A Double-Blind, Placebo-Controlled Experiment," *Human Psychopharmacology: Clinical and Experimental* 37, no. 3 (2022): e2828.

16. M. Solinas, S. Ferre, Z. B. You, M. Karcz-Kubicha, P. Popoli, and S. R. Goldberg, "Caffeine Induces Dopamine and Glutamate Release in the Shell of the Nucleus Accumbens," *Journal of Neuroscience* 22, no. 15 (2002): 6321–6324.

17. N. D. Volkow, G. J. Wang, J. Logan, et al., "Caffeine Increases Striatal Dopamine D2/D3 Receptor Availability in the Human Brain," *Translational Psychiatry* 5, no. 4 (2015): e549.

18. L. Dratcu, A. Grandison, G. McKay, A. Bamidele, and V. Vasudevan, "Clozapine-Resistant Psychosis, Smoking, and Caffeine: Managing the Neglected Effects of Substances That Our Patients Consume Every Day," *American Journal of Therapeutics* 14, no. 3 (2007): 314–318.

19. G. Jenkins, "Review of Dopamine Antagonists for Nausea and Vomiting in Palliative Care Patients," *Journal of Pain & Palliative Care Pharmacotherapy* 38, no. 1 (2024): 38–44.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.