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Analyzing the Trends of Paracetamol Overdose Toxicity in Mecca, Saudi Arabia: Implications for forensic analysis

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ABSTRACT
Background: Acetaminophen poisoning is the commonest cause of poisoning worldwide and contributes to 30% of cases in Saudi Arabia. Pilgrimage seasons make it difficult for the city of Mecca to manage the specific issues related to medication abuse such as paracetamol overdose. This paper aims to analyse the rising incidence of Paracetamol poisoning in Mecca in comparison with other regions of KSA including during COVID-19 pandemic**.**
Methodology: Cross-sectional retrospective record analysis was done using data obtained from the Ministry of Health (MOH) website on paracetamol overdose cases between years 2019 to 2020. Sociodemographic data, antidote use and outcomes data were obtained from the patient files on case record form and entered into Microsoft Excel spreadsheets. The analysis was based on the Paracetamol overdose incident in Mecca in relation to other areas.
Results: Mecca's overdose cases were 91 in 2019, but the numbers dropped to 28 in 2020. The spread per capita in people decreased from 1.00 per cent to 0.31 per cent in this period. This trend parallels a national decline, which appears to result from the COVID-19 pandemic and related limitations.
Conclusion: The study's results imply that measures attributable to the COVID 19 disease outbreak such as mobility restrictions and improved awareness of health concerns helped decrease cases of paracetamol overdose. Future studies should aim to investigate antecedent psychological, social, cultural factors and characteristics of overdose among users in Saudi Arabia.

Keywords: Paracetamol poisoning, paracetamol overdose, toxicology, N-acetylcysteine (NAC), medication misuse, overdose trends.

1. INTRODUCTION

Paracetamol poisoning is one of the leading causes of toxicity in the world and accounts for 30% of the poisoning cases in Saudi Arabia [1]. Prior literature suggested that about 53% of paracetamol overdose patients who received admission were females with a median age of 34 years [2]. Out of these patients, 45% had a history of alcohol abuse, and 42% had a clinical history of psychiatric disorders [2]. While paracetamol poisoning has higher mortality as compared to other poisoning cases, it is generally safe when used within the therapeutic levels. The early features of paracetamol intoxication are frequently vague and identical to symptoms observed at other stages of the disease, which makes risk assessment of hepatotoxicity ambiguous [3]. Paracetamol, which comes as an analgesic as well as an antipyretic, is readily available and is probably prescribed more often than not on the Saudi Arabian territory.

The incidents of paracetamol overdose are on the rise globally, and this demonstrates a significant concern in public health [4]. In Saudi Arabia, this has been compounded by cultural beliefs and a lack of knowledge about the possible adverse effects of overdosing on drugs. With the visitor population increasing during the pilgrimage season in Mecca, stress and unfamiliarity with the medication may lead to an increase in medication abuse, including paracetamol overdose [5]. Paracetamol overdose also affects others since it is a healthcare burden and exhausts the emergency response system [6]. If the trends of paracetamol overdose toxicity are discovered, then this public health problem can be tackled, and educational interventions can be made to prevent patient overdose cases.

The increased incidence of paracetamol overdose toxicity in Saudi Arabia is a public health concern due to the country's demographical characteristics and cultural interactions [1]. In major cities like Mecca, which are easily accessible and characterized by increased consumption of drugs, including paracetamol, the latter has become the most commonly ingested overdose substance that tends to overload the local health care facilities [7]. This is compounded by the fact that the toxicity of the drug, especially when consumed at high levels or with no regard to its over-the-counter accessibility, is poorly understood among the public [7]. Mecca city witnesses a high

spirit of population during the pilgrimage season, and the pilgrims may be new to the health care systems and correct use of drugs, resulting in high chances of overdosing [5]. Self-medication during the pilgrimage seasons significantly contributes to paracetamol overdose. However, Mecca's social, economic, and cultural situation raises different concerns while dealing with this problem. Awareness of the population characteristics and the causes of these overdoses is essential due to the pressure on the healthcare system and the developing liver failure [1]. Against this backdrop, this study established the trends in paracetamol overdose toxicity in Mecca, Saudi Arabia. It also examined how forensic toxicology could be used to explain cases of overdose, aid in early identification of the conditions, and contribute to overall health interventions.

Research Question

What are the general trends in paracetamol overdose toxicity in Mecca and its implications for forensic analysis?

Justification and Rationale

The increasing cases of paracetamol overdose toxicity in Saudi Arabia warrants comprehensive research considering the significant implications that it has on public health. Paracetamol is the most frequently used drug, and its availability, combined with high consumption, elevates the probability of toxicity and overdosage, particularly during pilgrimage when many people who are unaware of the Saudi medical services flood the Mecca region. There is no insight into the drug's toxicity, and this is made worse by cultural practices as well as taking drugs due to stress. This has resulted in a high incidence of toxicity from paracetamol, which has overloaded the healthcare system response teams. Considering these issues, forensic toxicology is valuable when it comes to the precise identification of overdose cases as well as the explanation of such incidents for facilitating an early diagnosis and intervention. It is in this context that this study established the trends in paracetamol overdose toxicity to issue best practice guidelines to practitioners and officials serving the Mecca region. Knowledge of these patterns will aid clinical future risk predictions and serve an educational purpose in steering clear of such instances. The results of this study will help to improve the management and prevention of overdose and the subsequent burden on the healthcare system due to paracetamol toxicity.

2. LITERATURE REVIEW

Over-the-counter analgesics and antipyretics such as paracetamol (acetaminophen) overdose is one of the leading causes of poisoning in the world, especially in countries where the drug is readily accessible [8]. Studies have shown that the abuse of paracetamol has the potential to cause unfavorable consequences like hepatic as well as renal failure, which are a result of NAPQI toxicity [9]. This metabolite reduces extra glutathione reserves in the body, which affects the damaged hepatic and renal tissues, which is the healing process, and boosts the risk of organ dysfunction. The research established that only 30% of caregivers stated that they had given paracetamol to their sick children in a dosage more than the therapeutic dosage among the caretakers [1]. The increased danger of intentional or accidental paracetamol overdose is likely where doses are not timed appropriately; children are given adult paracetamol formulations, or multiple preparations containing paracetamol are administered concomitantly [10,26]. They concluded that practices like this increase the possibility of developing toxicity as well as liver harm.

It has been established that paracetamol poisoning is one of the leading health concerns in the world. Poisoning by paracetamol in Spain and Norway is in the range of 4.5 to 12% of all cases of toxicological acute deterioration. In Saudi Arabia alone, about thirty percent of poisoning incidents are attributed to paracetamol overconsumption [1, 11]. The findings have revealed that even developed countries like the United Kingdom have high incidence rates – ranging from 40% to 44% of poisoning cases are associated with paracetamol [12]. In another study, [13] asserted that case numbers are worrying as the poison control center in the United States reported 80,000 cases of paracetamol poisoning in 2021 alone. One acute ingestion of supratherapeutic dose of paracetamol can cause acute toxicity, whereas multiple ingestion can produce chronic toxicity. Doses of aspirin are, therefore, hazardous in pediatric cases, and doses as low as 150 mg/kg or 100 mg/kg, especially in the presence of other precipitating factors, can cause acute poisoning [14]. These results highlight the importance of health literacy regarding the non-toxic dose of paracetamol to avoid such toxicity as well as its consequences.

Studies have established the specific trends concerning unintentional overdose owing to the drug’s reputation for safe use and intentional self-harming instances [15,16]. Other works highlight the same concerning hepatotoxicity, which arises when the liver conjugates and metabolizes an overdose of paracetamol into dangerous products such as N-acetyl-p-benzoquinone imine (NAPBQI) [9, 17]. This hepatic injury often presents a need for acetylcysteine, which, if not provided, may lead to acute liver failure and can be fatal. Paracetamol poisoning is, hence, a significant cause of mortality that must be recognized in any suspicious death, especially with notable groups such as adolescents and mentally ill persons [18,19,20]. Therefore, this calls for high-performance liquid chromatography (HPLC) and mass spectrometry to establish toxic levels of paracetamol in the post-mortem blood samples [21,24].

The literature also points out that forensic experts aid in determining whether the incident is accidental or intentional based on medical evidence, the patient's history, psychological records, and any letters left behind (emotional state) [22,23,25]. However, there are missing links in the overload studies experimenting with Saudi Arabia because culture and religion may be influential in overdose purposes and in getting medical assistance.

3. METHODOLOGY

The study adopted a cross-sectional study design, and specifically, a retrospective record-based review was used to collect data on all the reported cases of paracetamol overdose. The data was retrieved from the Ministry of Health (MOH) website for a period ranging from 2019 to 2020. The cases were reported under the national food, drug, and chemical analytical results program. Participant data included sociodemographic data (such as age, gender, and nationality); the antidotes (such as N-acetylcysteine (NAC), Activated charcoal, etc.) and outcomes (like Discharge Against Medical Advice (DAMA) and recovered); and distribution of paracetamol overdose toxicity cases in Mecca, which were eventually compared with the other selected regions in Saudi Arabia. In data analysis, categorical variables were expressed in the number of frequency distributions and percentages by Microsoft Excel. The findings aided the comparisons of recent trends in paracetamol toxicity in Mecca and the related clinical characteristics, focusing on NAC's effectiveness and factors that contribute to patient survival and hospitalization stay. Besides, the research aimed to give an overall picture of the nature of paracetamol overdose cases to contribute to better health interventions and the development of accurate practices in overdose cases in Saudi Arabia.

4. RESULTS

A total of 449 and 244 paracetamol overdose toxicity cases in Saudi Arabia were reported in 2019 and 2020, respectively. Table 1 below gives a summary of the findings. From the table, deductions were made about the distribution of paracetamol overdose toxicity cases for gender, nationality, and age group, as explained in Figures 1, 2, and 3 below. The data revealed the demographics most affected by paracetamol toxicity in Saudi Arabia.

Table 1: Distribution of Paracetamol Overdose Toxicity Cases between 2019 and 2020 in Saudi Arabia

		2019		**2020**	
		Number (N=449)	**Percent (%)**	**Number (N=244)**	**Percent (%)**
Gender	Male	167	37.20%	92	37.70%
	Female	282	62.80%	152	62.30%
Nationality	Saudi	388	86.80%	210	86.40%
	Non-Saudi	59	13.20%	33	13.60%
Age Group	Less than 1 Year	11	2.40%	4	1.60%
	1-5 years	163	36.30%	91	37.30%
	6-12 years	11	2.40%	6	2.50%
	13-19 years	104	23.20%	56	23.00%
	20-39 years	149	33.20%	82	33.60%
	40 years and above	11	2.40%	5	2.00%

Gender

Female gender dominated overdosage cases for paracetamol both in 2019 and 2020. In 2019, there 62.8% of the paracetamol overdose cases were attributed to females as opposed to males (37.2%). In 2020, 62.3% of the cases were females, while 37.7% of the overdose cases were males. This steady pattern revealed that females may, in reality, be more susceptible to paracetamol poisoning in Saudi Arabia as opposed to males.

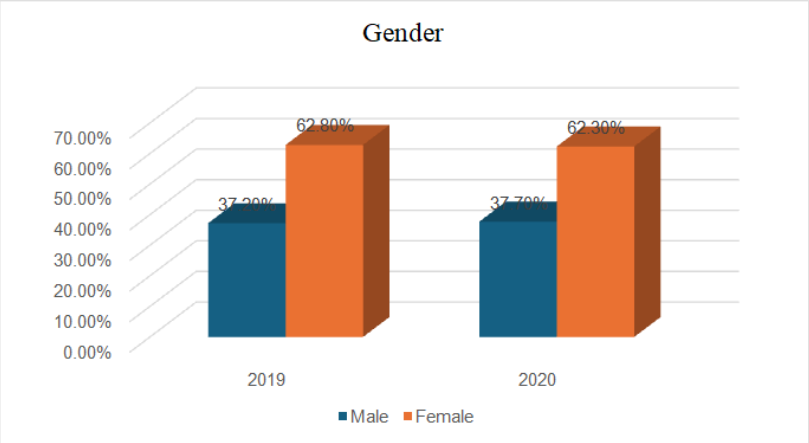

Figure 1: Gender

Nationality

As shown in Figure 2 below, most recorded cases were Saudis (86.8% in 2019 and 86.4% in 2020), while non-Saudis accounted for 13.2% and 13.6% of the total cases in 2019 and 2020, respectively. This indicates that cases of paracetamol overdose are even higher in Saudi Arabian citizens than non-citizens.

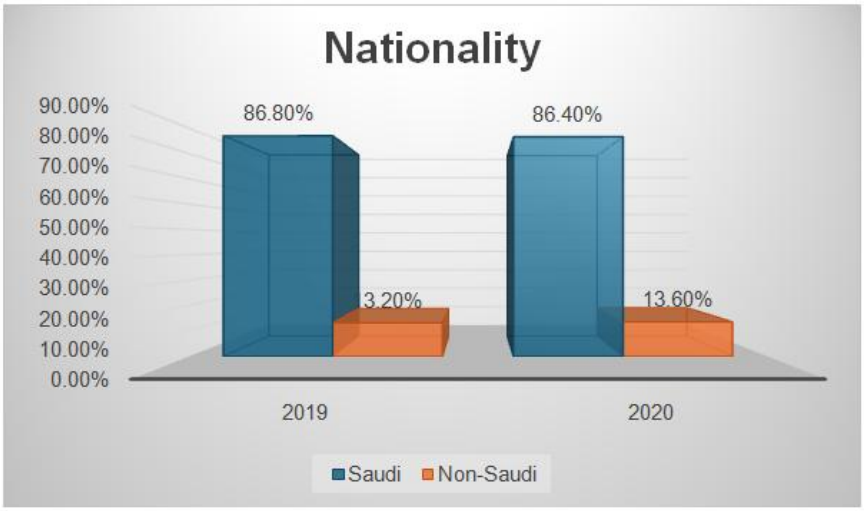

Figure 2: Nationality

Age Group

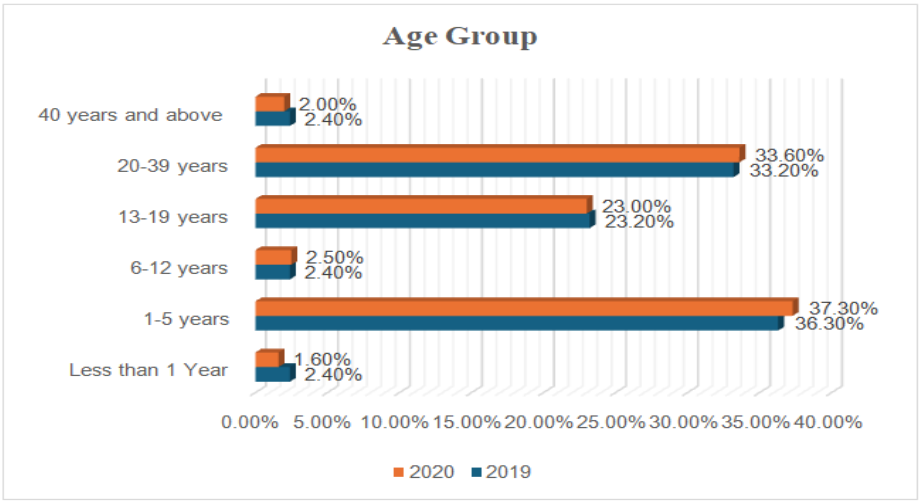

Figure 3: Age group

The highest proportion of the affected age group was children aged 1-5, contributing to 36.3% in 2019 and 37.3% in 2020, respectively. This may be attributed to poor prescription through wrong storage of the medications or no supervision. Adults in the age range of 20-39 years of age also contributed significantly, with 33.2% in 2019 and 33.6% in 2020, while other age groups had low incidence rates. They can have intentional overdoses or misuse due to stress or other mental illness compounds in this age of their lives. Another group that contributed a good number of cases was those between 13 and 19 years old, who accounted for 23.2% in 2019 and slightly dropped to 23% in 2020. This points to the need to bridge this group's psychological and emotional health needs.

In conclusion, the findings revealed that paracetamol overdose is a prevalent problem among people of all ages, from childhood to adulthood, including females and Saudi citizens. There is an indication that adequate public health promotion activities that expressly point to the various age centers need to be employed to map out the correct usage of medications with particular reference to storage and utilization practices.

Table 2: Clinical Characteristics of Paracetamol Overdose Toxicity Cases in Saudi Arabia between 2019 and 2020

	2019		**2020**	
Antidote	**Number (N=252)**	**Percent (%)**	**Number (N=124)**	**Percent (%)**
N-acetylcysteine (NAC)	80	31.7%	43	34.7%
Activated charcoal	153	60.7%	72	58.1%
Others	19	7.6%	9	7.2%
Outcomes	**Number (N=246)**	**Percent (%)**	**Number (N=123)**	**Percent (%)**
Discharge Against Medical Advice (DAMA)	31	12.6%	14	11.4%
Recovered	215	87.4%	109	88.6%

As shown in Table 2 above, NAC and activated charcoal were the widely used remedies for paracetamol overdose in Saudi Arabia and the Mecca region by extension. As an antidote, the use of NAC was higher in 2020 (34.7%) than in 2019 (31.7%) (See Table 2). This rise may show better handling of cases of paracetamol overdose, where it has been widely recognized that NAC is an effective antidote, especially if given early. However, the treatment with activated charcoal prevailed, and its use slightly diminished in 2020 compared to 2019 – from 60.7% to 58.1%. The relatively high use of activated charcoal suggests it helps to block paracetamol absorption in cases where the drug is ingested in excessive amounts as long as it is provided within a definite period after drug intake.

Furthermore, positive trends are revealed from the data collected. Patient survival was 87.4% in 2019 and 88.6% in 2020. Such a high recovery rate constantly observed indicates that regardless of fluctuations in antidote use, the general trend in treatment was quite favorable. On the other hand, there was a slightly reduced tendency in the number of patients who left against medical advice (DAMA), and the proportion reduced from 12.6% in 2019 to 11.4% in 2020. If this continues, DAMA cases are of particular concern as these patients may not receive complete treatments and are at a higher risk of developing complications. The data has clearly shown the high number of patients treated and recovered from paracetamol overdose in Mecca and Saudi Arabia at large, and slight changes in using NAC as an antidote. Nonetheless, the reported cases of DAMA imply that there is a future need to develop measures for preventing early discharges, so all patients should get proper treatment.

Table 3: Distribution of paracetamol overdose toxicity cases in Mecca, compared with other regi**ons**

	2019			**2020**		
City	**Number (N=360)**	**Percent (%)**	**Rate per 100,000 people**	**Number (N=171)**	**Percent (%)**	**Rate per 100,000 people**
Mecca	91	25.30%	1.00	28	16.40%	0.31
Riyadh	81	22.50%	0.92	70	40.90%	0.8
Eastern Region	118	32.80%	2.28	38	22.20%	0.73
Northern Borders	19	5.30%	4.92	23	13.50%	3.11
Hail	51	14.20%	6.93	12	7.00%	3.13

As demonstrated in the table above, there is a fluctuation in the incidence of paracetamol overdose across regions in Saudi Arabia during the observed period of 2019 to 2020. Out of the 449 reported cases of paracetamol overdose in 2019, 25.30% (91 cases) were from the Mecca region. Accordingly, the number of paracetamol overdose cases in Mecca dropped significantly from ninety-one (91) in 2019 to twenty-eight (28) or 16.4% in 2020. This is well illustrated by the rate per 100,000 people, which was 1.00 in 2019 and was reduced to 0.31 in 2020. The decline in the incidence and the rate of paracetamol overdose in Mecca during the COVID-19 pandemic may be due to changes in access and communal behaviors during the pandemic or public health measures during that period. Compared to other regions, Mecca trailed Riyadh with 22.5% in 2010 and 40.9% of overdose cases in 2020. Although these numbers only saw a slight upturn, the proportion of cases to the national figure has risen noticeably. It also dropped from 0.92 to 0.80 per 100000 people, meaning Riyadh had more people affected than Mecca during the pandemic. The Eastern Region recorded 118 cases, a rate of 2.28 per 100,000 persons in 2019. However, in 2020, Mecca recorded 38 cases (or 22.20%) with a rate of 0.73 per 100,000 persons. This may lead to lowering poisoning cases to that of Mecca.

Analyzing the data for the Northern Borders, the number of cases grew slightly – 19 in 2019 and 23 in 2020, but the rate per 100,000 population was consistently higher in the Northern Borders, 4.92 in 2019 and 3.11 in 2020. This region is still in the high-incidence category even after this fall in the rate. They recorded fewer cases in 2019 at 51 but a higher rate per 100,000 people at 6.93. While it indicates a considerable decline in poisoning cases during the pandemic, the results make it possible to conclude that there was a similar trend regarding paracetamol poisoning overall when it comes to most of the analyzed regions during the COVID-19 outbreak, except Riyadh, where the cases remained more or less concentrated. Such trends are in these rates per 100,000 people, where Northern Borders and Hail rates are consistently high compared to other regions.

5. DISCUSSION

The preliminary observations established a possible decrease in paracetamol overdose cases in the Mecca region from 2019 to the COVID-19 pandemic year of 2020. A reduction from 91 cases in 2019 to 28 in 2020, with a corresponding drop in the rate per 100,000 persons lowered from 1.00 to 0.31, could indicate the effects of the various pandemic influences, including restricted movement to seek medical attention, disease control measures like the lockdowns, and increased community.

The above results are consistent with the current empirical analysis of paracetamol poisoning, a worldwide concern since it is still among the top causes of toxic syndrome due to overdose [8]. The public considers paracetamol to be a safe and readily available over-the-counter drug. However, its reckless use, whether as a result of negligence or with malice, is dangerous to health as it can cause hepatic and renal failure due to the toxicity level of NAPQI. This metabolite invokes glutathione oxidant depletion, causing tissue injury [9]. It was found that more than one-third of cases of poisoning in Saudi Arabia are due to an overdose of paracetamol [1,11], which supports the fact that such cases are pretty standard worldwide. For instance, in the case of Spain and Norway, it covers 4.5% – 12% of poisoning cases, while in the UK, it takes 40% – 44% of poisoning cases [12]. The above statistics substantiate the fact that paracetamol toxicity is still an essential problem in the developed as well as the developing world.

The reduced cases of overdose in Mecca during the pandemic may be explained by limited access to medication, new regulations that sought to close and minimize the operations of pharmacies, or people's reduced interaction, which prevented them from stocking up on substances. It is also possible that the health campaigns embarked on during the pandemic to ensure that people practiced high hygiene standards, had enhanced health literacy, and used medicines cautiously have also contributed to the decrease. Still, according to the studies, the fact is that, despite being considered safe, paracetamol overdose is not intentional but depends on the wrong time of intake, misuse of adult formulations for children, and taking several medicines containing paracetamol [15,16].

Further, cultural and religious factors could play a vital role in increased paracetamol overdose in Mecca. For example, the influx of visitors in Mecca during the pilgrimage season could amount to higher incidents of paracetamol overdose [5]. Besides, psychological records and emotional states are used to determine if overdoses are intentional or accidental [22,23]. Nevertheless, the influence of religion and religion-related concerns in Saudi Arabia about seeking help in the case of an overdose has not been discussed in sufficient detail yet. This scarcity of regional studies emphasizes a call for culturally relevant widespread studies of the precise psychological reasons that precipitate overdose behavior there.

6. CONCLUSION

To conclude, the recognizable decrease in the number of cases of paracetamol overdose in the Mecca region from the year 2019 to 2020, which has gone down from 91 to 28, is crucial, especially in lessening the burden on households and healthcare facilities. The decrease could be associated with COVID-19 pandemic containment measures, including mobility reduction, quarantines, and raising population awareness in the context of the pandemic. Despite the closure of medication access and pharmacies during the pandemic, the pandemic probably encouraged more health literacy and careful use of medicines that may have helped in

decreasing the number of overdose cases. These findings are in tandem with the previous findings on paracetamol toxicity worldwide, showing that it remains a significant problem or concern. Paracetamol is generally regarded as a safe over-the-counter medication if not taken inappropriately. Otherwise, it can lead to hepatic and renal failure. Even overdose behavior may be affected by cultural or religious practices specific to the area, such as Mecca. These influences have been discussed in the literature. However, a lack of forensic analysis focuses on Saudi Arabian cities, especially Mecca. For this reason, there is a need for psychological, social, and religious exploration of overdose in Saudi Arabia.

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