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Rayyan Saqah, Jaber Sharaheeli, and Lamman Abdulkareem

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Characteristic of Paracetamol Overdose Before and During COVID-19 Pandemic, Saudi Arabia, 2019-2020

[1*]Rayyan Saqah, [1]Jaber Sharaheeli, [2]Lamman Abdulkareem
[1]Saudi Field Epidemiology Training Program, Ministry of Health, Riyadh, Saudi Arabia
[2]East Jeddah Hospital, Ministry of Health, Jeddah, Saudi Arabia
[*]Corresponding Author's Email: dr-rayyan@hotmail.com

Abstract

Purpose: Paracetamol is the most used medication worldwide; due to its analgesic and antipyretic effect; it had been included within the recommended regimen for COVID-19 patients. This study aimed at exploring the changes in the incidence of paracetamol overdose during pandemic compared to pre-pandemic periods.

Methodology: Through a record-based study, all cases of paracetamol overdose who had been reported to the ministry of health in Saudi Arabia in the period between January 2019 and December 2020 were included in the study. Data stored in electronic form were retrieved and analyzed using SPSS version 26. Frequency distribution was used to describe categorical variables.

Findings: Two hundred and forty four paracetamol overdose cases were reported in 2020 (during the pandemic) compared to 449 in 2019 (pre-pandemic) with dominance of females (62.6%) and Saudis (86.7%). Most cases ingested paracetamol orally mainly in solid forms (76.5%), and they were mostly diagnosed as confirmed cases on admission (84.6%). The great majority recovered and discharged (87.8%). The overall annual incidence of paracetamol in (pre-pandemic) was 1.32/100,000 which dropped markedly during pandemic to 0.71/100,000.

Conclusion: There was a general decline in the incidence of paracetamol overdose during COVID-19 pandemic, with relative increase in incidence in home incidents and in children.

Recommendation: Health education to the public to increase their awareness about proper and safe use of paracetamol is highly recommended, as well as introducing instructions and guidelines for practitioners about prescribing it.

Keywords: *Paracetamol overdose, COVID-19, epidemiological trend.*

1. Introduction

Paracetamol is the most commonly used medication worldwide as it is available as an over-the-counter (OTC). In addition to ease of access, its common use has come from the popular perception that it is a safe medication(1). Paracetamol overdose is the most common form of drug overdose in developed as well as developing countries(2). In United Kingdom, paracetamol overdose represented one half of all reported drug overdose;(3) and in Australia, it came as a first cause for frequent calls to the poison center; and as a significant cause of hospital admissions in many countries. Previous researches showed that although there is no significant difference between males and females regarding paracetamol overdose, (4) however, males tend to seek medical services later than females(5). In a large scale study in Australia, it was found that the median age for paracetamol overdose was 18 years (IQR; 16-28 years)(6). Since declaration of the world health organization (WHO) COVID-19 as a pandemic started in China in 2019, recommendations for management of the disease has been developed(7). As fever and pain are common symptoms in COVID-19 cases; there was a growing concern about using acetaminophen rather than ibuprofen to relief pain and fever; which resulted in its widely use during the pandemic(8). In Saudi Arabia the treatment protocols for COVID-19 have changed dramatically since the onset of the pandemic, however, analgesics including paracetamol consistently existed in all protocols; therefore, a recent research reported that paracetamol is the most prescribed medication for COVID-19 cases in Saudi Arabia(9).

The witnessed increase in the paracetamol use in Saudi Arabia during the pandemic is expected to have its impact on the pattern of paracetamol overdose; this pattern is not well studied. Therefore, the current study aimed at exploring the changes in the epidemiological pattern of paracetamol overdose during the pandemic. The results are expected to highlight unrevealed side for the consequences of the pandemic and could draw attention towards reforming the rules and guidelines for prescribing paracetamol.

2. Material and Methods

A cross section was conducted through a retrospective record-based review. Where all paracetamol overdose cases who had been reported to the environmental health department, MOH, Saudi Arabia in the period between January 2019 and December 2020 were included. Paracetamol overdose cases are reported in electronic form as a part of the national program of food, drug and chemical safety.(10) The overall number of cases reported in 2019 was 449 and 244 were reported in 2020. Data included the demographic characteristics of the cases (age, gender and nationality), incident characteristics (place of the incident, form of the drug, date of exposure, date of signs and symptoms), general condition on arrival at the hospital, patient medical history (signs and symptoms), management details and prognosis. Data entry and statistical analysis was done using Statistical Package for Social Science (SPSS) version 26. Categorical variables are presented as frequency distribution and percentages. Approval was collected from King Fahad Medical City Institutional Research Board (KFMC-IRB) in Saudi Arabia.

3. Result

Table 1 demonstrates that females represented 62.6% of the cases, while males formed 37.4% with marked dominance of Saudis (86.7%). The pre-school children represented (36.3%) and (37.3%) during pre and pandemic periods respectively, followed by those in the age group (20-39 years) (33.3%).

Table 1: Distribution of paracetamol poisoning cases by years according to their demographic characteristics before and during COVID-19 Pandemic in Saudi Arabia.

	Time				Total	
	Pre-Pandemic (2019) N=449		During Pandemic (2020) N=244		N=693	
	Freq	%	Freq	%	Freq	%
Gender						
Male	167	37.20%	92	37.70%	259	37.37%
Female	282	62.80%	152	62.30%	434	62.63%
Nationality						
Saudi	388	86.80%	210	86.40%	598	86.67%
Non-Saudi	59	13.20%	33	13.60%	92	13.33%
Age groups						
<1 Year	11	2.40%	4	1.60%	15	2.16%
1-5 Years	163	36.30%	91	37.30%	254	36.65%
6-12 Years	11	2.40%	6	2.50%	17	2.45%
13-19 Years	104	23.20%	56	23.00%	160	23.09%
20-39 Years	149	33.20%	82	33.60%	231	33.33%
>39 Years	11	2.40%	5	2.00%	16	2.31%

Regarding clinical characteristics of the cases, table 2 shows that there was an increase in the proportion of cases who had the incident at home from 94.2% in pre to 95.5% during the pandemic. Most of the cases ingested paracetamol orally mainly in solid forms (76.5%), and more than one third of them (38.8%) expressed that they took it intentionally, and one half (51.1%) consumed it unintentionally. Most of the cases were diagnosed as confirmed cases on arrival to the hospitals (84.6%), with a slightly higher proportion during the pandemic (85.7%) than pre-pandemic (84%). However, it was observed that there was a decline in the percentage of cases who reached the hospital in critical condition, it decreased from 6.5% to 3.3% during pre and pandemic respectively. Nausea was the commonest symptom recorded in pre-pandemic (24.9%), it decreased to (17.6%) during the pandemic. More than one half of cases (59.8%) were treated with activated charcoal, in addition to one third (32.7%) received N-acetylcysteine, and the great majority recovered and discharged (87.8%), while 12.2% were discharged against medical advice. The overall incidence of paracetamol overdose/100,000 in pre-pandemic was 1.32, which dropped markedly during

pandemic to 0.71/100,000. The highest incidence was observed in Hail (6.93/100,000) and Northern borders in pre-pandemic (4.92/100,000), while the highest incidence during the pandemic was recorded in Al-Jawf (3.51/100,000), Hail (3.13/100,000) and Northern borders (3.11/100,000) as shown in table 3.

Table 2a: Clinical characteristics of paracetamol poisoning cases before and during COVID-19 Pandemic in Saudi Arabia.

	Pre-Pandemic (2019) N=449		During Pandemic (2020) N=244		Total N=693	
	No.	%	No.	%	No.	%
Place of incidence						
Home	423	94.20%	233	95.50%	656	94.66%
Others	26	5.80%	11	4.50%	37	5.34%
Circumstances of exposure						
Intentional	146	39.00%	82	38.50%	228	38.84%
Unintentional	188	50.30%	112	52.60%	300	51.11%
Unknown	40	10.70%	19	8.90%	59	10.05%
Form of paracetamol						
Solid	300	76.50%	160	76.60%	460	76.54%
Liquid	92	23.50%	49	23.40%	141	23.46%
Provisional assessment						
Confirmed	377	84.00%	209	85.70%	586	84.56%
Suspected	72	16.00%	35	14.30%	107	15.44%
Condition on arrival to hospital						
Stable	420	93.50%	236	96.70%	656	94.66%
Critical	29	6.50%	8	3.30%	37	5.34%
Symptoms						
Nausea	112	24.90%	43	17.60%	155	29.30%
Vomiting	99	22.00%	61	25.00%	160	30.25%
Abdominal colic	82	18.30%	37	15.20%	119	22.50%
Dizziness	36	8.00%	22	9.00%	58	10.96%
Headache	14	3.10%	9	3.70%	23	4.35%
Others	10	2.20%	4	1.60%	14	2.65%

Source of data: MOH, Saudi Arabia

Table 2b: Clinical characteristics of paracetamol poisoning cases before and during COVID-19 Pandemic in Saudi Arabia.

	Pre-Pandemic (2019) N=449		During Pandemic (2020) N=244		Total N=693	
	No.	%	No.	%	No.	%
Antidote						
Activated charcoal	153	60.70%	72	58.10%	225	59.84%
N-acetylcysteine	80	31.70%	43	34.70%	123	32.71%
Others	19	7.50%	9	7.30%	28	7.45%
Outcome						
Recovered	215	87.40%	109	88.60%	324	87.80%
DAMA	31	12.60%	14	11.40%	45	12.20%

Source of data: MOH, Saudi Arabia

Table 3: Distribution of paracetamol poisoning cases and rates per 100,000 population before and During COVID-19 Pandemic in Saudi Arabia, according to Admin Region.

Admin Region	Pre-Pandemic (2019) N=449			During Pandemic (2020) N=244		
	Freq	%	Rate per 100,000 population	Freq	%	Rate per 100,000 population
Riyadh	81	18.04%	0.92	70	28.81%	0.80
Al-Bahah	2	0.45%	0.40	5	2.06%	0.99
Al-Jawf	4	0.89%	0.74	19	7.82%	3.51
Al-Qassim	8	1.78%	0.53	3	1.23%	0.20
Asir	17	3.79%	0.73	3	1.23%	0.13
Eastern Region	118	26.28%	2.28	38	15.64%	0.73
Hail	51	11.36%	6.93	23	9.47%	3.13
Jazan	13	2.90%	0.79	5	2.06%	0.30
Makkah	91	20.27%	1.00	28	11.52%	0.31
Medina	16	3.56%	0.71	10	4.12%	0.44
Najran	15	3.34%	2.44	13	5.35%	2.12
Northern Borders	19	4.23%	4.92	12	4.94%	3.11
Tabouk	14	3.12%	1.46	14	5.76%	1.46
Total	449	100.00%	1.32	243	100.00%	0.71

Source of data: MOH and General Authority of Statistics, Saudi Arabia

4. Discussion

Since its discovery in Germany at the end of 19th century, paracetamol has been widely used as a safe analgesic when used in normal dose; however, the abuse of Over-the-counter (OTC) drugs in general, and paracetamol in specific was accompanied with clinical toxicity noticed and first reported in 1960th (11). Recently, since declaration of the world health organization (WHO) COVID-19 as a pandemic after it had started in China in 2019,(9) recommendations for management of the disease has been developed (7). As fever and pain are common symptoms in COVID-19 cases; there has been a growing concern about using acetaminophen rather than ibuprofen to relief pain and fever; which resulted in its widely use during the pandemic (8).

Accordingly, it has been suggested that adherence to this guideline could be reflected on the rate of paracetamol utilization and consequent possible changes in the epidemiological pattern of paracetamol overdose. Therefore, the current study aimed at comparing pre and during pandemic incidence of paracetamol overdose in Saudi Arabia. One of the strengths of the current study, is that the results are based on official data for all the cases reported to the ministry of health in Saudi Arabia. Therefore, the described epidemiological pattern of paracetamol overdose during the pandemic presents succinct reference for further comparative epidemiological studies.

The incidence of paracetamol overdose varies significantly between countries worldwide (12). The wide variation of the reported incidence of paracetamol overdose could be attributed to many reasons, first is that only cases who needed hospitalization are recorded,(11) and mandatory official reporting is essentially dependent on the rules and guidelines governing health systems in each country. The decline in the reported paracetamol overdose during the pandemic if compared to pre-pandemic observed in the current study could partly be attributed to the lockdown measures adopted during the pandemic, with difficult access to health facilities except for vulnerable and serious cases (13). Also, the lockdown measures, which necessarily include long stay at homes, could explain the observed significant increase in the home incidents.

Moreover, closure of schools in response to the lockdown measures could explain the relative increase in incidence of paracetamol overdose in school age children and kindergarten during the pandemic. The overall relative high incidence of paracetamol overdose among children observed in the current study had been discussed in previous studies (14) where it was claimed that there is an age-bimodality pattern across paediatric population, the first occurs in the age group (2-5 years), where it usually occurs accidentally at the time when child is out of the caregiver's attention. The second mode occurs in children aged 12 years or older, which is mainly due to medication error, when parents unintentionally exceed recommended dose (15,16).

Paracetamol is the most used drug for intentional overdose, as it is easily accessible and inexpensive (17) the current study showed that more than one third of the cases expressed that they intentionally used paracetamol; without clarifying the purpose of intentional use. The intentional use for suicide had been criticized in early 1990s where the researchers found that most patients

who conceive that paracetamol could cause death, they unaware of the delay in onset of severe symptoms and many thought that overdose would cause unconsciousness (18).

Patients who are taking massive dose of paracetamol are at high risk of developing acute hepatotoxicity,(19) the most common symptoms are nausea, vomiting and abdominal pain (20). That has been observed in the current study; therefor, the recent guideline for management of paracetamol overdose recommended that patients who are suffering from these symptoms in the course of paracetamol treatment, should consult their treating physician (20).

The current study showed that the great majority of the cases recovered safely, with no recorded serious consequences or mortalities; that could assert appropriateness of the treatment provided to cases; where the overwhelming majority received activated charcoal (59.8%) or N-acetylcysteine (32.7%) which accords the updated guideline for treatment of paracetamol overdose; where the researchers stated that "Paracetamol concentrations were markedly reduced in those receiving activated charcoal within 4 h. In those with high paracetamol concentrations, treatment with increased acetylcysteine dose within 21 h was associated with a significant reduction in hepatotoxicity (20).

5. Conclusion and Recommendations

Paracetamol overdose is a frequent health problem in Saudi Arabia, with relatively higher incidence in home incidents and in children. Despite of the decline in incidence during COVID-19 pandemic, still there is a need for planned health education campaign to the public to increase their awareness about proper and safe use of paracetamol, as well as introducing official guidelines and instructions to the practitioners about prescribing it.

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