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Impact of COVID-19 Lockdown on the Incidence and Patterns of Toxic Exposures and Poisoning in Jordan

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Impact of COVID-19 Lockdown on the Incidence and Patterns of Toxic Exposures and Poisoning in Jordan

A retrospective descriptive study

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Abstract:

Objectives: To describe the effect of the COVID-19 lockdown in Jordan (March 21, 2020 – May 21, 2020) on the incidence and patterns of toxic exposures and poisoning as compared to the same period from the previous year (March 21, 2019 – May 21, 2019).

Design: A retrospective descriptive study.

Methods: Call data sourced from Pharmacy One[™] Poison Center was revised from the lockdown period (March 21, 2020 to May 21,2020) and the same period during 2019 (March 21, 2019 to May 21, 2019). A database was established and analyzed.

Results: We noticed that not only did calls increased, but there was also a noticeable change in call patterns. Calls increased by 91% during the lockdown period. Drugs were the most common among types of exposure, and the most prevalent route of exposure was ingestion. There was a notable increase in ocular exposure (550%). The majority of exposures were at home and there were no occupational exposures. We found that there is an increase in household cleaner's exposure among males and increase in alcohol exposure in females. Children aged below 5 are the most affected. Even though there is an increase in the total number of cases, severe cases decreased.

Conclusion: The effect of the lockdown on rates of toxic exposures was prominent, whether through the increase in calls or the change in patterns. As people spent more time at home, their exposure to toxic agents increased. Cleaning recommendations led to the misuse of cleaning and disinfectant products, increasing exposures related to abating the COVID-19 infection.

Key words: COVID-19, Lockdown, Toxic Exposures, Poisoning, Poison Control Center.

Article Summary:

This article addresses the following points:

- 1- The exposure patterns during COVID-19 lockdown.
- 2- The COVID-19 lockdown effect on the numbers and patterns of exposures.
- 3- It highlights specific exposures related to COVID-19 infection control efforts, management protocols, or self medication.
- 4- It highlights the important role poison control centers could play during crises.
- 5- Information presented in this study can be taken in consideration while planning healthcare policies. Strengths and Limitations of the study:

- 1) This study addresses different aspects of toxic exposures during the lockdown.
- 2) Our data represent the majority of calls related to toxic exposures in Jordan.
- 3) Not all exposures were reported to the poison center.
- 4) Poisoning specialists make their judgment and management recommendations based on the caller's information
- 5) It was not possible to access data from other poison centers in the country

More details on strength and limitations were written in the discussion section.

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Title: Impact of COVID-19 Lockdown on the Incidence and Patterns of Toxic Exposures and Poisoning in Jordan.

Objectives: To describe the effect of the COVID-19 lockdown in Jordan (March 21, 2020 – May 21, 2020) on the incidence and patterns of toxic exposures and poisoning as compared to the same period from the previous year (March 21, 2019 – May 21, 2019).

Design: A retrospective descriptive study.

Methods: Data source: There are three poison centers in Jordan, the first one is affiliated with Royal Medical Services, and the other is affiliated with Jordan University. The third one is the Pharmacy One[™] Poison center. Each one of these centers is working independently, and there is no central reporting system. We select to study data from Pharmacy One[™] poison center because it's the only center responsible for responding to civil defense calls the primary emergency response service in Jordan (911).

Pharmacy One[™] poison center is a large non-profit national poison center that receives unrestricted calls from the public, healthcare workers, and emergency services (911), runs for 24 hours per day, over 7 days a week, and provides free professional advice and management information regarding toxic exposures and poisoning.

Data collection: The electronic records of Pharmacy One[™] poison center were revised for the period (March 21, 2020 to May 21, 2020). All calls related to toxic exposures or poisoning were included and analyzed. In addition, all calls for the same period during 2019 (March 21, 2019 to May 21, 2019) were included and analyzed too. For each case, data about the call source (general public, healthcare worker or emergency services (911), demographic data (age, gender), data about exposure (type, site, route, and reason of exposure), and medical outcome were collected.

Medical outcomes were classified into no effect, mild, moderate, and severe effect based on Poison Severity Score, a standardized scheme for grading the severity of poisoning described by Persson and colleagues [1].

Microsoft excel was utilized for establishing a database, graphs creation, and data analysis. Percentages of change in exposure are calculated based on the following equation:

% of $\Delta = \left(\frac{\text{Percentage during Lockdown - Percentage during 2019}}{\text{Percentage during 2019}}\right) \times 100\%$

According to IRB policy at our institution, this study is exempted from review and approval. We took a consent form for data collection and records review, being that Pharmacy One[™] poison center does not record the patient or caller name or any personal data.

Patient and Public statement: Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this study.

Introduction: Coronavirus Disease 2019 (COVID-19) caused by the novel Coronavirus (SARS-CoV-2) was first reported in Wuhan, China in December of 2019 [2]. The World Health Organization (WHO) characterized the disease as a pandemic on March 11, 2020[3]. The rapid increase in the number of cases and deaths, along with the lack of vaccines and effective medical therapy; in the early course of the pandemic, has led to a global emergency response [4, 5]. Many

countries adopted classical public health measures including, isolation and quarantine, social distancing, and community containment to slow down the spread of SARS-CoV-2 virus [5-8]. In initial stages of the pandemic, lack of adequate information on the most effective prevention and treatment strategies allowed the spread of misinformation and resulted in the improper use of drugs, chemicals, and traditional remedies for their presumed protective or therapeutic roles even though many of these substances are known for their harmful and toxic effects [9-13].

Poison centers from the United States, Canada, and France reported a spike in calls related to toxic exposures during the COVID-19 lockdown [14-17]. Reported exposures included the improper use of medications, self-medication, and household chemicals [18-20]. However, the majority of the reported exposures were related to drugs supposed to be effective in COVID-19 treatment protocols, hand sanitizers, disinfectants, household cleaners, and alcohol [21-23].

The first case of COVID-19 in Jordan was confirmed on March 2, 2020. The Jordanian government announced a national lockdown that came into effect on March 21, 2020 and continued through to May 31, 2020. During this lockdown, there was a stay-at-home order with suspension of all social, religious, and work activities except for a few-hours window period each day allowing people to buy their essential goods [24]. We believe that the lockdown has led to an increase in toxic exposures and poisoning cases, especially those associated with cleaners, hand sanitizers, and alcohol. This study will analyze the patterns of toxic exposures and poisoning among the Jordanian population during the COVID-19 lockdown as compared with the exact period of the previous year.

Results:

During the Covid-19 lockdown from March 21 to May 21, 2020, Pharmacy One[™] Poison Center received a total of 544 calls related to toxic exposures, which represents a 91% increase in the number of calls during the same period in 2019 (285). Drug exposure calls ranked first with a total of 321 calls (59% of total calls), followed by household cleaners (83 calls, 15% of total calls), and alcohol exposure (37 cases, 7%). Toxic gases (8 cases, 1%) and toxic plants (1 case, < 1%) were among the least reported exposures. Notably, exposures related to toxic gases, alcohol, domestic animal bites, household cleaners, drugs, and heavy metals increased by (300%, 208%, 175%, 159%, 128%, 33%, respectively), whereas exposures related to snake bites, scorpion stings, toxic plants, and food decreased by (100%, 55%, 50%, 18% respectively). (Table, Figure 1 near here)

The most prevalent route of exposure was ingestion with 446 cases (82%), followed by dermal (56 cases, 10%), and inhalation (18 cases, 3%). Compared to 2019, there was a notable rise in ocular exposures (550% increase; 13 cases in 2020 compared to 2 cases in 2019), ingestion exposures (increased by 104%; 446 cases in 2020 compared to 219 cases in 2019) and inhalational exposures (50% increase; 18 cases in 2020 compared to 12 in 2019). (Table, figure 2 near here). Most exposures occurred at home (528 cases, 97%) followed by outdoor exposures (14 cases, 3%). While home exposures increased by 103%, outdoor, work, and school exposures decreased by 26%, 60%, 100%, respectively. (Table, figure 3 near here)

As of the reason and motive of exposure, unintentional exposures in the lockdown constitute 75% of exposures (406 cases), followed by therapeutic, suicidal, and intentional exposures (35 cases, 33 cases, 31 cases, respectively, 6% each). There was a marked increase in intentional

exposures by 933% (3 cases in 2019, 31 cases in lockdown), medical errors by 175% (8 cases in 2019, 22 cases in lockdown), unintentional by 142% (168 cases in 2019, 406 cases in lockdown), and therapeutic exposures by 119% (16 cases in 2019, 35 cases in lockdown). On the other hand, occupational exposures (9 cases in 2019, 0 cases in lockdown), bites and stings (31 cases in 2019, 3 cases in lockdown), and suicidal exposures (36 cases in 2019, 33 cases in lockdown) decreased by 100%, 90%, 8%, respectively. (Table, figure 4 near here)

57% (310 cases) of the exposures occurred in males, and 43% (243 cases) occurred in females. Males reported more drug exposures by 64% cases vs. 53% in females (198 vs. 123 cases). In contrast, females reported more alcohol exposures by 10% vs. 4% in males (24 vs. 13 cases). Males reported a drastic increase in exposures related to household cleaners by 236% vs. 100% increase for females. Females reported an increase in alcohol exposure by 243% vs. 160% for males. The exposure to toxic gases was the same when comparing genders, both increasing by 300%. (Table, figure 5 near here) Exposures were reported in all age groups, with children from 0-5years being the most affected by 61% of the cases (332 cases), followed by the age group 21-50 years by 19% (104 cases). The age group from 11-15 years reported the sharpest increase in exposures by 275%, followed by age group over 50 years by 143% increase, and age group from 0-5 years by 134%. (Table, figure 6 near here)

There were 292 (54%) calls from emergency services [911], 156 (29%) calls from the general public, and 96 (18%) calls from healthcare workers, with an increase of 170%, 68%, and 14% respectively. (Table, figure 7 near here)

Lastly, based on the Poison Severity Score (PSS), 37% (201 cases) of the cases subsided with no effects, 42% (228 cases) with minor effects, 17% (90 cases) with moderate effects, 5% (25 cases)

with severe effects, and no deaths were reported. 10% (54 cases) needed hospital admissions, and 56% (30 cases) who needed admission were children less than five years. 41% of total emergency service calls were closed only based on poison center advice, with no reported adverse outcomes. The number of cases resolved with no effects or minor effects increased by 673%, 140%, respectively, and those with moderate or severe effects decreased by 31%, 24%, respectively. The total number of admissions increased by 260% (15 cases in 2019 compared to 54 cases in lockdown), and admissions for children from 0-5 years increased by 329% (7 cases in 2019 compared to 30 cases in lockdown). The emergency service dispatch rate decreased by 33%. (Table near here, figure 8 near here)

Discussion

Our study showed that lockdown resulted in a 91% increase in calls related to toxic exposures as well as a pattern change compared to the previous year. Poison centers have also reported similar results in the United States, Canada, and France [14-16]. We didn't find apparent reason for such an increase. However, Le-Roux and colleagues suggest a possible explanation for this rise is the behavioral modifications caused by fear of coronavirus, including excessive house cleaning and misuse of cleaning products for personal hygiene or food sanitation [17]. Another additional factor is the decrease in cognitive performance and decision-making induced by isolation measures, combined with increased impulsivity contributing to such increase [17]. Chang and colleagues ascribe such increase to the cleaning recommendation and guidelines issued by many health care agencies and social media [14].

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Our study showed an increase in exposures related to toxic gases, alcohol, household cleaners, drugs, and domestic animal bites. Toxic gases exposure includes the well-described chlorine gas that results from mixing bleach and other household chemicals [17]. Notably guidelines disseminated in the early days of the pandemic as part of public infection-control campaigns have led to the misuse of alcohol-based hand sanitizers and household cleaners [14, 15]. Reportedly, disinfectants erroneously used to disinfect vegetables, and alcohol-based hand sanitizers applied to the whole body resulting in burns, or the use of highly concentrated sodium hypochlorite are examples of how people falsely interpret these campaigns[17]. Canadian poison centers have also reported similar increases in exposures to bleaches, hand sanitizers, disinfectants, chlorine and chloramine gas [15].

Exposures to drugs in our study were primarily observed in children. A possible explanation for such an observation is that families stocked drugs anticipating shortages, along with stay-athome policy, children spent more time at home, increasing their accidental exposure to such drugs [17]. This contradicts reports from France, where a fall in drug exposures was noted, which was linked to fall in suicidal attempts by drugs [17]. No reported cases of exposures due to drugs used in COVID-19 treatment. Also illicit drugs are not reported to our poison center.

We noted an increase in bites related to domestic animals. Similarly, Dixon et al. described a threefold rise in pediatric ER visits due to dog bites during the stay-at-home lockdown policy, owning such observation to decreased adult supervision over children, and increased dog stress because of confinement [25]. On the other hand, we noticed fewer snake bites, scorpion stings, toxic plant exposures, and occupational exposures, as home internment and weather conditions averted such exposures.

Our study showed increased exposure in all age groups, but a remarkable observation was the high increase in exposure in adolescents (11-15 y) group. It's possible that even though this age group understands what these chemicals are used for, they have little awareness about the potential toxicity. Other similar studies showed different age group observations. For example, the French poison center reported an increase in exposure in all age groups except 5-25 y group, and the most significant increase occurred in patients over 65 years [17]. Likewise, the Canadian poison center didn't notice an increase in exposure in those below the age of 19 years [15]. In fact, children below 5 years represented a large percentage of calls received during the study period. This might be due to closure of schools and kindergartens, with children spending more time at home, and therefore they have more chance for exposure [17]. Furthermore, Teleworking and homeschooling for older children contributed to such increase by shifting parent's attention away from younger children [17].

Among routes of exposure, the ocular route recorded the sharpest increase. This observation may be due to the fact that eyes are involved in chemical exposure, whether by accidental spraying of the eyes or touching the eyes after hand or face sanitation or via exposure to vapors. A study from the United States found that inhalational route observed the highest increase during the lockdown [14].

While intentional exposures increased during the lockdown, we suggest that the increase was due to attempts to protect from acquiring infection. Canadian poison center reported a similar observation [15]. Oppositely; we have noticed that suicidal exposures during the lockdown have decreased. This fall could be arguably due to the social and family support created by the stay-at-home order. French poison center reported a similar observation [17].

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We noted a decrease in calls from healthcare workers. This decrease was accompanied by a fall in the proportion of severe cases despite the increase in hospital admission. French poison center reported similar findings [17]. A possible explanation would be related to under-reporting cases as the volume of COVID-19 patients overwhelms the healthcare systems. Other causes of such observation are linked to the increase in awareness of toxic exposures and thereby reporting cases before progressing to a more severe presentation.

This study has its strength and limitations. Our data represent the majority of calls related to toxic exposures in Jordan, as Pharmacy One[™] poison center is the only center responsible for responding to calls from civil defense, the primary emergency response service in Jordan (911). It also receives calls unrestrictedly from the public and healthcare workers at all times. However, this study has its limitations. Not all exposures were reported to the poison center, because many were treated at home or sought direct medical help without notifying the poison center. Furthermore severely intoxicated or dead people usually arrive directly at the hospital without reporting the incidence to any poison center. In addition poisoning specialists make their judgment and management recommendations based on the caller's information. Some cases were closed by simple advice over the phone without onsite confirmation of the nature of exposure. Lastly, there were difficulties accessing data from other poison centers.

In conclusion, there is a change in both the number and pattern of toxic exposure related calls during the lockdown, mostly due to fear of coronavirus. Exposures related to toxic gases, alcohol, household cleaners, drugs, and domestic animal bites have increased, whereas exposures related to snake bites, scorpion stings, toxic plants, and occupational exposures have decreased. This observed increase in calls involved all age groups, with children below 5 years accounting for the largest percentage. Ocular exposures showed the sharpest increase among all exposure

routes. While intentional exposures showed a remarkable increase, those exposures were not of suicidal nature. In fact our study showed a decrease in suicidal exposures. In addition, calls from healthcare workers have decreased, as well as case severity, while hospital admission rate increased. This study highlights the important role of poison centers, as they help decrease the burden on healthcare facilities. Also, they can provide invaluable information about exposures that could be taken in consideration when planning healthcare policies.

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Disclosures: The authors have nothing to disclose.

IRB approval: According to IRB policy at our institution, this study is exempted from review and approval, as it is a retrospective review of records, where patient's names or personal information couldn't be identified.

Data sharing statement: Data supporting the finding of this article are available upon request.

Authors contributions:

LR, HD, KA, AF: Conceptualization, study design. LR, HD: project administration. AF: data collection. NH, HD: literature search and review. HD: draft the initial manuscript. LR, HD, MD, and SM: edit and write the final manuscript.

All authors read, edit, proof-read, and approve the final manuscript before submission.

References:

- [1]. Persson H, Sjöberg G, Haines J, Pronczuk de Garbino J. Poisoning Severity Score: Grading of acute poisoning. J Toxicology - Clinical Toxicology (1998) 36:205-13
- [2]. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727–733.
- [3]. WHO Director-General's opening remarks at the media briefing on COVID-19 -11 March 2020, Accessed on 5 march 2020, https://www.who.int/director-general/speeches/detail/whodirector-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.
- [4]. Dale Fisher, Annelies Wilder-Smith, The global community needs to swiftly ramp up the response to contain COVID-19, The Lancet, Volume 395, Issue 10230, 2020, Pages 1109-1110, ISSN 0140-6736, https://doi.org/10.1016/S0140-6736(20)30679-6.
- [5]. Neil M Ferguson, Daniel Laydon, Gemma Nedjati-Gilani et al. Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand. Imperial College London (16-03-2020), doi: https://doi.org/10.25561/77482.
- [6]. A Wilder-Smith, MD, D O Freedman, MD, Isolation, quarantine, social distancing and community containment: pivotal role for old-style public health measures in the novel coronavirus (2019-nCoV) outbreak, Journal of Travel Medicine, Volume 27, Issue 2, March 2020, taaa020, https://doi.org/10.1093/jtm/taaa020

- [7]. Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD. How will country-based mitigation measures influence the course of the COVID-19 epidemic? Lancet.
 2020;395(10228):931–4.
- [8]. Hien Lau, Veria Khosrawipour, Piotr Kocbach, Agata Mikolajczyk, Justyna Schubert, Jacek Bania, Tanja Khosrawipour, The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China, Journal of Travel Medicine, Volume 27, Issue 3, April 2020, taaa037, https://doi.org/10.1093/jtm/taaa037
- [9].Zarocostas J. How to fight an infodemic. Lancet (London, England) [Internet].2020;395(10225):676. Available from: http://dx.doi.org/10.1016/S0140-6736(20)30461-X
- [10]. Depoux A, Martin S, Karafillakis E, Preet R, Wilder-Smith A, Larson H. The pandemic of social media panic travels faster than the COVID-19 outbreak. J Travel Med. 2020;27(3):1–2.
- [11]. Michael Gottlieb, Sean Dyer, Information and Disinformation: Social Media in the COVID-19 Crisis, Acad Emerg Med 2020 Jul;27(7):640-641. doi: 10.1111/acem.14036. Epub 2020 Jun 24
- [12]. The Lancet Infectious Diseases. The COVID-19 infodemic. Lancet Infect Dis [Internet].
 2020;20(8):875. Available from: http://dx.doi.org/10.1016/S1473-3099(20)30565-X

- [13]. Galvão J. COVID-19: the deadly threat of misinformation. Lancet Infect Dis. 2020;3099(20):30721.
 - [14]. Chang A, Schnall AH, Law R, et al. Cleaning and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 — National Poison Data System, United States, January 1, 2020–March 31, 2020. MMWR Morb Mortal Wkly Rep 2020;69:496–498.
 DOI: http://dx.doi.org/10.15585/mmwr.mm6916e1
 - [15]. Yasseen III A, Weiss D, Remer S, et al. Increases in exposure calls related to selected cleaners and disinfectants at the onset of the COVID-19 pandemic: data from Canadian poison centres. Health Promotion and Chronic Disease Prevention in Canada : Research, Policy and Practice. 2021 Jan;41(1):25-29. DOI: 10.24095/hpcdp.41.1.03
 - [16]. COVID-19: home poisoning throughout the containment period.Gael Le Roux ¹; Sandra Sinno-Tellier ²; French Poison Control Centre members; Alexis Descatha³, The lancet public health DOI: 10.1016/S2468-2667(20)30095-5
 - [17]. Gaël Le Roux, Sandra Sinno-Tellier, Emmanuel Puskarczyk, Magali Labadie, Katharina von Fabeck, Fanny Pélissier, Patrick Nisse, Nathalie Paret, French PCC Research Group, Alexis Descatha & Dominique Vodovar (2021) Poisoning during the COVID-19 outbreak and lockdown: retrospective analysis of exposures reported to French poison control centres, Clinical Toxicology, DOI: 10.1080/15563650.2021.1874402

> [18]. Richards GC. Alcohol-based hand sanitisers: a warning to mitigate future poisonings and deaths BMJ Evidence-Based Medicine Published Online First: 01 December 2020. doi: 10.1136/bmjebm-2020-111568

- [19]. Wong, A. (2020), COVID-19 and toxicity from potential treatments: Panacea or poison.Emergency Medicine Australasia, 32: 697-699. https://doi.org/10.1111/1742-6723.13537
- [20]. Mohammad Delirrad, Ali Banagozar Mohammadi, New Methanol Poisoning Outbreaks in Iran Following COVID-19 Pandemic, Alcohol and Alcoholism, Volume 55, Issue 4, July 2020, Pages 347–348, https://doi.org/10.1093/alcalc/agaa036
- [21]. Chary MA, Barbuto AF, Izadmehr S, Hayes BD, Burns MM. COVID-19: Therapeutics and Their Toxicities. J Med Toxicol. 2020 Jul;16(3):284-294. doi: 10.1007/s13181-020-00777-5. Epub 2020 Apr 30. PMID: 32356252; PMCID: PMC7192319.
- [22]. Yip L, Bixler D, Brooks DE, et al. Serious Adverse Health Events, Including Death, Associated with Ingesting Alcohol-Based Hand Sanitizers Containing Methanol — Arizona and New Mexico, May–June 2020. MMWR Morb Mortal Wkly Rep 2020;69:1070–1073. DOI: http://dx.doi.org/10.15585/mmwr.mm6932e1
- [23]. Alcohol use and misuse during the COVID-19 pandemic: a potential public health crisis? James M Clay^a and Matthew O Parker^b, Lancet Public Health. 2020 May, doi: 10.1016/S2468-2667(20)30088-8

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[24]. Prime ministry of Jordan, official web site , http://www.pm.gov.jo/upload/files/Order-Defense-2.pdf, accessed on march 5, 2020

[25]. Cinnamon A. Dixon, Rakesh D. Mistry, Dog Bites in Children Surge during Coronavirus Disease-2019: A Case for Enhanced Prevention, The Journal of Pediatrics, Volume 225,2020,Pages 231-232,ISSN 0022-3476, https://doi.org/10.1016/j.jpeds.2020.06.071.

Table: Incidence and Patterns of Toxic exposures and poisoning Among Jordanian Population during COVID-19 Lockdown and 2019 (March-May).

		201		COVID-19			
		Number o		Number		% 0	
Total Number of Cases		28:		54		919	
	Drugs		141 (49%)		9%)	128%	
	Household Cleaners*	32 (1	1%)	83 (1	5%)	159	159%
	Alcohol*	12 (4	%)	37 (7	'%)	208	%
	Pesticides	20 (7	%)	20 (4		0%	0
	Hydrocarbons*	16 (6	%)	17 (3	5%)	6%	
	Food	17 (6	%)	14 (3%)		-18	%
	Insect bites	14 (5	%)	15 (3%)		7%	, 0
Class of Exposure	Domestic Animals bites*	4 (19	%)	11 (2%)		175%	
Class of Exposure	Heavy Metals	9 (39	%)	12 (2%)		33%	
	Toxic Gases (chlorine)*	2 (19	%)	8 (1%)		300	%
	Scorpion stings	11 (4	%)	5 (1%)		-55%	
	Snake bites	5 (29	%)	0 (0%)		-100	%
	Toxic Plants	2 (19		1 (0	%)	-50	%
	•	·			· ·		
	Ingestion	219 (7	7%)	446 (8	2%)	104	%
	Inhalation	12 (4		18 (2		50%	
	Dermal	46 (10		56 (1		229	
Route of Exposure	Paranteral	3 (19		3 (1			
	Ocular	2 (19		13 (2		<u>0%</u> 550%	
	Others*	3 (19		8 (1		167	
	Others	5(1	/0)	8 (1	/0)	107	/0
				a (0		<u></u>	.,
	Work	5 (2%)		2 (0%)		-60%	
Site of Exposure	Outdoor	19 (7%)		14 (3%)		-26%	
	Home	260 (91%)		528 (97%)		103%	
	School	1 (0%)		0 (0%)		-100%	
	Suicidal	36 (1	3%)	33 (0	i%)	-8%	6
	Unintentional	168 (59%)		406 (75%)		142	
	Occupational	9 (3%)		0 (0%)		-100%	
	Medical Consultation*	9 (3%)		14 (3%)		0%	
	Therapeutic*	16 (6		35 (6%)		119%	
Reason of Exposure	Intentional			31 (6%)		933%	
	Medical Error	3 (1%) 8 (3%)		22 (4%)		935 % 175%	
	Bite/Sting	31 (1		3 (1%)		-90%	
	Bite/Sting	31(1	1%)	3 (1	%)	-90	/0
	1						
	0-5 y	142 (5		332 (61%)		134%	
Distribution by Age Groups	6-10 y	18 (6%)		29 (5		61%	
	11-15 y	4 (19		15 (3%)		275%	
	16-20 y	15 (5		30 (6%)		100%	
	21-50 y	92 (32		104 (19%)		13%	
	>50 y	14 (5	%)	34 (6%)		143	%
		Male	Female	Male	Female	Male % of A	Female % o
	Drugs	84 (51%)	57 (48%)	198 (64%)	123 (53%)	136%	116%
	Pesticides	10 (6%)	10 (8%)	9 (3%)	11 (5%)	-10%	10%
	Toxic Plants	2 (1%)	0 (0%)	0 (0%)	1 (0%)	-100%	NA
	Scorpion stings	6 (4%)	5 (4%)	4 (1%)	1 (0%)	-33%	-80%
					0 (0%)	-100%	-100%
	Snake bites	4 (2%)	1 (1%)	0 (0%)	0(0%)	-100%	-100%

	Toxic Gases (chlorine)	1 (1%)	1 (1%)	4 (1%)	4 (2%)	300%	300%
	Heavy Metals	4 (2%)	5 (4%)	6 (2%)	6 (3%)	50%	20%
	Household Cleaners	14 (8%)	18 (15%)	47 (15%)	36 (15%)	236%	100%
	Hydrocarbons	10 (6%)	6 (5%)	11(4%)	6 (3%)	10%	0%
	Domestic Animals bites	4 (2%)	0 (0%)	7 (2%)	4 (2%)	75%	NA
	Food	10 (6%)	7 (6%)	5 (2%)	9 (4%)	-50%	29%
	Alcohol	5 (3%)	7 (6%)	13 (4%)	24 (10%)	160%	243%
	General public	93 (33%)		156 (29%)		68%	
Source of Calls	Emergency Services (911)	108 (38%)		292 (54%)		170%	
	Health Care Workers	84 (29%)		96 (18%)		14%	
			!		· · · · ·		
	Non (No effect)	26 (9	1%)	201 ((37%)	673	/o
	minor	95 (33%)		228 (42%)		140%	
Medical Outcome	Moderate	131 (46%)		90 (17%)		-31%	
Based on PSS*	Severe	33 (12%)		25 (5%)		-24%	
	Death	0 (0%)		0 (0%)		0%	
Hospital Admissions	Number of Admissions	15 (5%)		54 (10%)		260%	
	Children from 0-5 Years	7 (47%)		30 (56%)		329%	
Emergency Services Dispatch		80 out of 108 cases (74%)		119 out of 292 cases (41%)		-33%	

* Household cleaners: Products containing (ammonia, hydrochloric acid, sodium hypochlorite, or alkaline cleaning products - Drain and oven cleaners...etc). Alcohol: ethanol-based cleaning solutions, hand sanitizers or pure ethanol as spray (not for intake). Hydrocarbons: mainly paint thinners and kerosene. Domestic Animals Bites: from dogs, cats, and hamsters. Toxic gases: inhaled chlorine. Other routes of exposure: include rectal and unknown routes. Medical Consultation: only reported consultations without reports of toxicity. Therapeutic reasons: include incidents reported as side effects of medication and drugs. NA: not applicable (mathematical causes), PSS: Poison Severity Score. n (n%)

Figures Legend:

Figure1: Class of Exposure

This chart shows the difference in classes of exposure when comparing the period of 2019 to COVID-19 lockdown.

R.

Figure2: Route of Exposure

This chart shows changes in routes of exposure in both studied periods.

Figure3: Site of Exposure

In this chart, changes in sites of exposure are shown.

Figure4: Reason of Exposure

Reasons for exposure for both periods are set side by side, showing variance.

Figure5: Gender Variation

This chart shows the prevalence of toxic exposures across different age groups.

Figure6: Distribution Across Age Groups

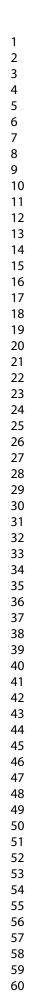
In this chart, a correlation between different exposure classes and gender is highlighted

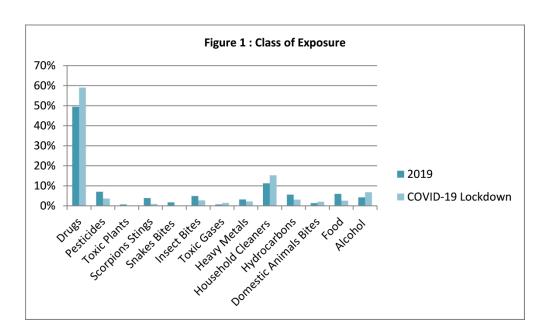
Figure7: Source of Calls

This chart shows the difference in the source of calls in both studied periods.

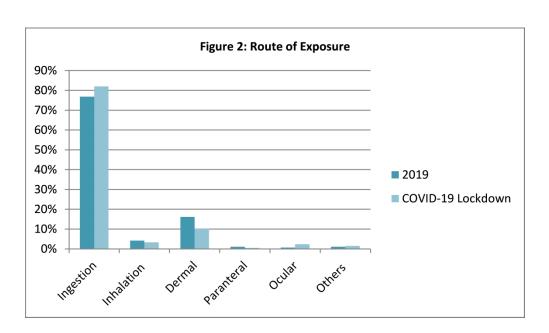
Figure8: Medical Outcome Including Admission

Changes in medical outcomes are shown in this chart. It also includes changes in the percentage of admissions and percentage of children admitted during both periods

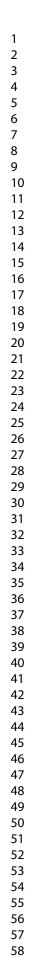




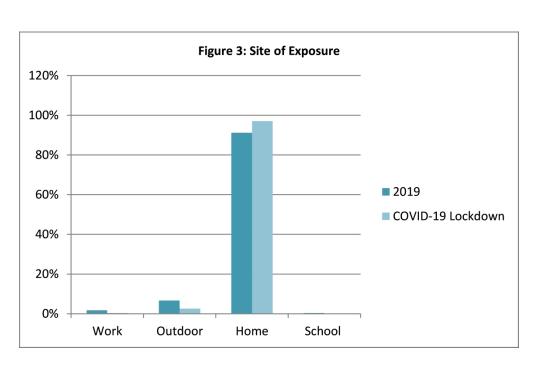
139x82mm (1200 x 1200 DPI)



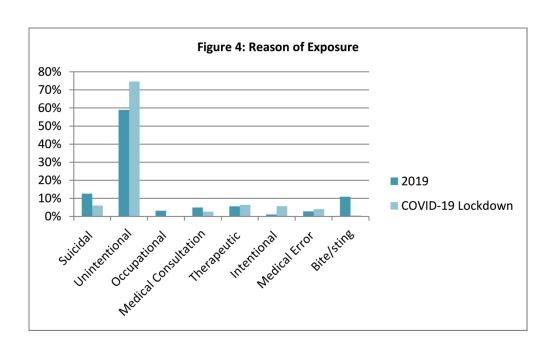
133x77mm (1200 x 1200 DPI)



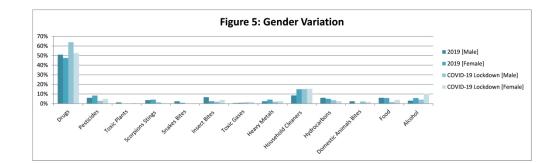
60



130x82mm (1200 x 1200 DPI)

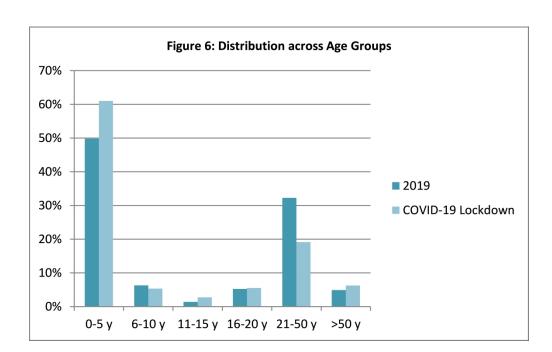


129x78mm (1200 x 1200 DPI)

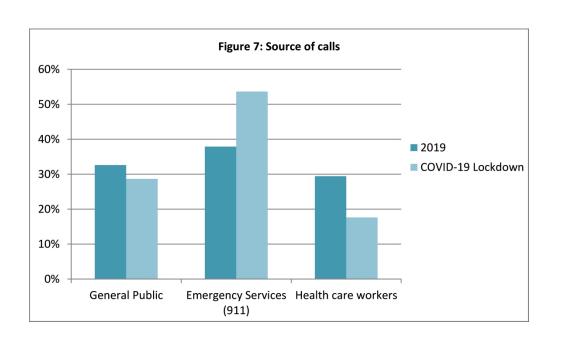


277x84mm (600 x 600 DPI)

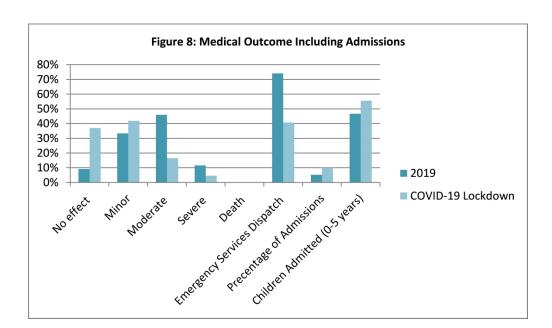




130x81mm (1200 x 1200 DPI)



140x82mm (1200 x 1200 DPI)



139x82mm (1200 x 1200 DPI)

STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Pag No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the	1,4
		abstract	
		(b) Provide in the abstract an informative and balanced summary of what	2
		was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods	-		
Study design	4	Present key elements of study design early in the paper	2,4
Setting	5	Describe the setting, locations, and relevant dates, including periods of	4-:
0		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods	-
1		of selection of participants. Describe methods of follow-up	
		Case-control study—Give the eligibility criteria, and the sources and	-
		methods of case ascertainment and control selection. Give the rationale for	
		the choice of cases and controls	
		Cross-sectional study—Give the eligibility criteria, and the sources and	4
		methods of selection of participants	
		(b)Cohort study—For matched studies, give matching criteria and number of	-
		exposed and unexposed	
		Case-control study—For matched studies, give matching criteria and the	-
		number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders,	5
		and effect modifiers. Give diagnostic criteria, if applicable	
Data	8*	For each variable of interest, give sources of data and details of methods of	4
sources/measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If	-
		applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	-
		confounding	
		(b) Describe any methods used to examine subgroups and interactions	-
		(c) Explain how missing data were addressed	-
		(d) Cohort study—If applicable, explain how loss to follow-up was	-
		addressed	
		Case-control study-If applicable, explain how matching of cases and	-
		controls was addressed	
		Cross-sectional study-If applicable, describe analytical methods taking	4
		account of sampling strategy	
		(<u>e</u>) Describe any sensitivity analyses	

Continued on next page

Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially	-
		eligible, examined for eligibility, confirmed eligible, included in the study, completing	
		follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and	7-
data		information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	Cohort study-Report numbers of outcome events or summary measures over time	-
		Case-control study—Report numbers in each exposure category, or summary	-
		measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	8,
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and	8
		their precision (eg, 95% confidence interval). Make clear which confounders were	
		adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a	-
		meaningful time period	
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and	
		sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or	1
		imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	9-
		multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	1
Other informati	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if	1
-		applicable, for the original study on which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Impact of COVID-19 Lockdown on the Incidence and Patterns of Toxic Exposures and Poisoning in Jordan; A Retrospective Descriptive Study

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Impact of COVID-19 Lockdown on the Incidence and Patterns of Toxic Exposures and Poisoning in Jordan; A Retrospective Descriptive Study

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Abstract:

Objectives: To describe the effect of the COVID-19 lockdown in Jordan (March 21, 2020 – May 21, 2020) on the incidence and patterns of toxic exposures and poisoning as compared to the same period from the previous year (March 21, 2019 – May 21, 2019).

Design: A retrospective descriptive study.

Methods: Call data sourced from Pharmacy One[™] Poison Center from the lockdown period (March 21, 2020, to May 21, 2020) and the same period during 2019 (March 21, 2019 to May 21, 2019) was revised. In addition, a database was established and analyzed.

Results: We noticed that not only did calls increased, but there was also a noticeable change in call patterns. Calls increased by 91% (544 versus 285 calls) during the lockdown period. Drugs were the most common among types of exposure, and the most prevalent route of exposure was ingestion. There was a notable increase in ocular exposure by 550% (13 versus 2 cases). The majority of exposures were at home and there were no occupational exposures. We found an increase in household cleaner's exposure among males and an increase in alcohol exposure in females. Children aged below five years are the most affected. Even though there is an increase in the total number of cases, severe cases decreased.

Conclusion: The lockdown effect on rates of toxic exposures was prominent, whether through the increase in calls or the change in patterns. As people spent more time at home, their exposure to toxic agents increased. Furthermore, cleaning recommendations led to the misuse of cleaning and disinfectant products, increasing exposures related to abating the COVID-19 infection.

Key words: COVID-19, Lockdown, Toxic Exposures, Poisoning, Poison Control Center.

Article Summary:

- 1- The exposure patterns during COVID-19 lockdown.
- 2- The COVID-19 lockdown effect on the numbers and patterns of exposures.
- 3- It highlights specific exposures related to COVID-19 infection control efforts, management protocols, or self-medication.
- 4- It highlights the important role poison control centers could play during crises.
- 5- Information presented in this study can be taken in consideration while planning healthcare policies.

Strengths and Limitations of the study:

- 1) This study addresses different aspects of toxic exposures during the lockdown.
- 2) Our data represent the majority of calls related to toxic exposures in Jordan.
- 3) Not all exposures were reported to the poison center.
- 4) Poisoning specialists base their judgment and recommendations for management on the caller's information
- 5) It was not possible to access data from other poison centers in the country

More details on strength and limitations were provided in the discussion section.

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Title: Impact of COVID-19 Lockdown on the Incidence and Patterns of Toxic Exposures and Poisoning in Jordan; A Retrospective Descriptive Study. **Objectives:** To describe the effect of the COVID-19 lockdown in Jordan (March 21, 2020 – May 21, 2020) on the incidence and patterns of toxic exposures and poisoning as compared to the same period from the previous year (March 21, 2019 – May 21, 2019). **Design:** A retrospective descriptive study. Introduction: Coronavirus Disease 2019 (COVID-19) caused by the novel Coronavirus (SARS-CoV-2) was first reported in Wuhan, China in December of 2019 [1]. The World Health Organization (WHO) characterized the disease as a pandemic on March 11, 2020 [2]. The rapid increase in the number of cases and deaths, along with the lack of vaccines and effective medical therapy; in the early course of the pandemic, has led to a global emergency response [3, 4]. Many countries adopted classical public health measures including, isolation and quarantine, social distancing, and community containment to slow down the spread of SARS-CoV-2 virus [4-7]. In the initial stages of the pandemic, lack of adequate information on the most effective prevention and treatment strategies allowed the spread of misinformation and resulted in the improper use of drugs, chemicals, and traditional remedies for their presumed protective or therapeutic roles even though many of these substances are known for their harmful and toxic effects [8-12].

Poison centers from the United States, Canada, and France reported a spike in calls related to toxic exposures during the COVID-19 lockdown [13-16]. Reported exposures included the improper use of medications, self-medication, and household chemicals [17-19]. However, the majority of the reported exposures were related to hand sanitizers, disinfectants, household cleaners, alcohol, and drugs supposed to be effective in COVID-19 treatment protocols [20-22].

The first case of COVID-19 in Jordan was confirmed on March 2, 2020. The Jordanian government announced a national lockdown that came into effect on March 21, 2020 and continued through to May 21, 2020. During this lockdown, there was a stay-at-home order with the suspension of all social, religious, and work activities except for a few-hours window period each day allowing people to buy their essential goods [23]. We conducted this study to evaluate if the lockdown has led to any change in the incidence or pattern of toxic exposures or poisoning in Jordan, especially those associated with cleaners, hand sanitizers, and alcohol. This study will analyze the patterns of toxic exposures and poisoning among the Jordanian population during the COVID-19 lockdown as compared with the exact period of the previous year.

Methods:

Data source: There are three poison centers in Jordan; Jordanian Royal Medical Services (JRMS) Poison Center, Jordan University Hospital Poison Center; and Pharmacy OneTM Poison Center. Each of these centers works independently and there is no central reporting system. All three centers receive calls directly from healthcare workers and the public; however, Pharmacy OneTM Poison Center is the only one responsible for receiving calls related to poisoning from the Civil Defense Directorate (CDD), the primary emergency response service in Jordan (911). The directorate is compelled by the law to report poisoning incidences to the poison center as soon as the command center receives the report, and reporting is near real-time. Therefore, we decided to study data from the Pharmacy OneTM Poison Center because it is the only one responsible for responding to the CDD calls.

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Pharmacy OneTM Poison Center is a large non-profit national poison center that receives unrestricted calls from the public, healthcare workers, and CDD calls (911), runs for 24 hours per day, over seven days a week, and provides free professional advice and management information regarding toxic exposures and poisoning. *Poisoning Reporting System:* Cases are reported to the poison center through the direct hotline or directed via the CDD command center. Poison center specialists will respond to the caller over the phone. Information about the patient demographics such as age, gender, residence, information about the poisoning incident (time of exposure, involved agent, single or multiple agents, dose, site, route), and the nature of symptoms, if found, were collected using open direct questions, and data directly transformed into a preformed database. Based on the American Association of Poison Control Centers (AAPCC) guidelines, Poisoning cases are categorized into drugs, hydrocarbons, pesticides, gases, household products, heavy metals, bites, and stings (insects, scorpions, snakes), and plants or foods exposures [24]. Severity is classified into five classes based on Poisoning Severity Score (PSS) described by Persson and colleagues [25]. Grade 0, 1 include patients who develop either no or mild symptoms of poisoning (nontoxic exposures, subtoxic exposures, asymptomatic exposures, or prolonged time after exposure > 24 h with no signs or symptoms) are advised for home observation or symptomatic home treatment. Grade 2, 3, 4 includes patients who develop moderate to severe symptoms or die (exposures with a known toxic agent, patients who developed moderate to severe symptoms, exposures exceeding safe doses) are directed to the hospital. Clinical information and advice about poisonous agents, safe doses, first aid actions, and home treatment protocols are obtained from the MICROMEDEX POISINDEX® toxicology information database and in-house databases

containing information about prevalent poisonous agents accounting for poisoning in our country [26].

Data collection: The electronic records of Pharmacy One[™] Poison Center were revised for the period (March 21, 2020, to May 21, 2020). All calls related to toxic exposures or poisoning were included. In addition, all calls for the same period during 2019 (March 21, 2019, to May 21, 2019) were included. For each case, data about the call source (general public, healthcare worker, or CDD calls (911)), demographic data (age, gender), data about exposure (type, site, route, and reason of exposure), and medical outcome were collected. The medical outcome was classified based on Poisoning Severity Score. PSS provides a standardized scale for grading the severity of acute poisoning based on observed signs and symptoms. We chose to use PSS because not only is it simple, based on clinical symptoms and signs, but it can also be used for both children and adults. The classification of poisoning using PSS can be made regardless of the type and number of toxic agents. It is also possible to prevent underestimation as the severity is concluded by the most severe symptoms and signs.

Data Analysis: The database was established using Microsoft Excel 2016. Descriptive analysis, statistical procedures, and graphs were done using the Data Analysis tool pack, an add-in feature on Microsoft Excel 2016. Percentages of change in exposure were calculated based on the following equation:

% of $\Delta = \left(\frac{\text{Percentage during Lockdown - Percentage during 2019}}{\text{Percentage during 2019}}\right) \times 100\%$

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According to IRB policy at our institution, this study is exempted from review and approval, as it is a retrospective review of records, and the personal information has been recorded anonymously where subjects cannot be identified directly or indirectly, and the investigators do not need to contact the subjects involved. We also took consent for data collection and records review.

Patient and Public statement: Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of this study.

Results:

During the COVID-19 lockdown from March 21 to May 21, 2020, Pharmacy OneTM Poison Center received a total of 544 calls related to toxic exposures, which represents a 91% increase in the number of calls during the same period in 2019 (n=285 calls). Drug exposure calls ranked first with a total of 321 calls (59% of total calls), followed by household cleaners (83 calls, 15% of total calls), and alcohol exposure (37 cases, 7%). Toxic gases (8 cases, 1%) and toxic plants (1 case, < 1%) were among the least reported exposures. Notably, exposures related to toxic gases, alcohol, domestic animal bites, household cleaners, and drugs increased by 300%, 208%, 175%, 159%, 128%, respectively, in contrast, exposures related to snake bites, scorpion stings, and toxic plants decreased by 100%, 55%, 50%, respectively. (Table 1, Figure 1 near here)

The most prevalent route of exposure was ingestion with 446 cases (82%), followed by dermal (56 cases, 10%). Compared to 2019, there was a notable rise in ocular exposures (550% increase; 13 cases in 2020 compared to 2 cases in 2019), ingestion exposures (increased by 104%; 446 cases in 2020 compared to 219 cases in 2019) and inhalational exposures (50% increase; 18

cases in 2020 compared to 12 in 2019). (Table 1, figure 2 near here). Most exposures occurred at home (528 cases, 97%). While home exposures increased by 103%, outdoor, work, and school exposures decreased by 26%, 60%, 100%, respectively. (Table 1, figure 3 near here)

As of the reason and motive of exposure, unintentional exposures in the lockdown constitute 75% of exposures (406 cases), followed by therapeutic, suicidal, and intentional exposures (35 cases, 33 cases, 31 cases, respectively, 6% each). There was a marked increase in intentional exposures by 933% (3 cases in 2019, 31 cases in lockdown), medical errors by 175% (8 cases in 2019, 22 cases in lockdown), and unintentional exposures by 142% (168 cases in 2019, 406 cases in lockdown). On the other hand, occupational exposures (9 cases in 2019, 0 cases in lockdown), bites and stings (31 cases in 2019, 3 cases in lockdown), and suicidal exposures (36 cases in 2019, 33 cases in lockdown) decreased by 100%, 90%, 8%, respectively. (Table 1, figure 4 near here)

57% (310 cases) of the exposures occurred in males, and 43% (243 cases) occurred in females. Males reported more drug exposures. In contrast, females reported more alcohol exposures. Males reported a drastic increase in exposures related to household cleaners by 236% vs. 100% increase for females. Females reported an increase in alcohol exposure by 243% vs. 160% for males. The exposure to toxic gases was the same when comparing genders, both increasing by 300%. (Table 1, figure 5 near here) Exposures were reported in all age groups, with children from 0-5years being the most affected by 61% of the cases (332 cases). The age group from 11-15 years reported the sharpest increase in exposures by 275%, followed by age group over 50 years by 143% increase. (Table 1, figure 6 near here)

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There were 292 (54%) calls from Civil Defenses Directorate [911], 156 (29%) calls from the general public, and 96 (18%) calls from healthcare workers, with an increase of 170%, 68%, and 14% respectively. (Table 1, figure 7 near here)

Lastly, based on the Poisoning Severity Score (PSS), 37% (201 cases) of the cases subsided with no effects, 42% (228 cases) with minor effects, 17% (90 cases) with moderate effects, 5% (25 cases) with severe effects, and no deaths were reported. 10% (54 cases) needed hospital admissions. 41% of total emergency service calls were closed only based on poison center advice, with no reported adverse outcomes. The number of cases resolved with no or minor effects increased by 673%, 140%, respectively, and those with moderate or severe effects decreased by 31%, 24%, respectively. The total number of admissions increased by 260% (15 cases in 2019 compared to 54 cases in lockdown), and admissions for children from 0-5 years increased by 329% (7 cases in 2019 compared to 30 cases in lockdown). The emergency service dispatch rate decreased by 33%. (Table 1, figure 8 near here)

Discussion

Our study showed that lockdown resulted in a 91% increase in calls related to toxic exposures as well as a pattern change compared to the previous year. Poison centers have also reported similar results in the United States, Canada, and France [13-15]. We did not find an apparent reason for such an increase. However, Roux and colleagues suggest a possible explanation for this rise is the behavioral modifications caused by fear of coronavirus, including excessive house cleaning and misuse of cleaning products for personal hygiene or food sanitation [16]. Another additional factor is the decrease in cognitive performance and decision-making induced by isolation

measures, combined with an increased impulsivity contributing to such an increase [16]. Chang and colleagues ascribe such an increase to the cleaning recommendations and guidelines issued by many health care agencies and social media [13].

Our study showed an increase in exposures related to toxic gases, alcohol, household cleaners, drugs, and domestic animal bites. Toxic gases exposure includes the well-described chlorine gas that results from mixing bleach and other household chemicals [16]. Notably, guidelines disseminated in the early days of the pandemic as a part of public infection-control campaigns have led to the misuse of alcohol-based hand sanitizers and household cleaners [13, 14]. Reportedly, disinfectants erroneously used to disinfect vegetables, and alcohol-based hand sanitizers applied to the whole body resulting in burns, or the use of highly concentrated sodium hypochlorite are examples of how people falsely interpret these campaigns [16]. Canadian poison center have also reported similar increases in exposures to bleaches, hand sanitizers, disinfectants, chlorine and chloramine gas [14].

The Jordanian society is mainly conservative, and thereby the use and consumption of drinking alcohol is limited. As a result, there were no reported cases of poisoning due to drinking alcohol (ethanol or methanol). However, in countries such as the United States and Russia stockpiling and consumption of alcohol increased as well as the misuse of alcohol-containing agents [27, 28]. In the United Kingdom, it is predicted to witness a spike in alcohol misuse with frequent relapses in addicted individuals as the increase in consumption might be related to stress and impulsivity associated with self-isolation measures [29]. In addition, ingestion of methanol-containing hand sanitizer has led to the demise of consumers in many countries such as the United States and Iran [21, 19]. In fact, the numbers of methanol poisoning-related deaths are the largest in Iran's history as it was more prevalent than COVID-19 related deaths in some Iranian

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provinces [19]. The spread of misleading messages through social media regarding alcohol use as a protective agent against COVID-19 and, in the case of Iran, sanctions on alcohol imports are one of the many reasons for such a spike in methanol consumption [21, 19]. As a result, a multitude of countries has banned alcohol sale to limit the consequences of alcohol-related health emergencies on the healthcare system [28].

Exposures to drugs in our study were primarily observed in children. A possible explanation for such an observation is that families stocked drugs anticipating shortages, along with stay-athome policy: children spent more time at home, increasing their accidental exposure to such drugs [16]. This contradicts reports from France, where a fall in drug exposures was noted, which was linked to the fall in suicidal attempts by drugs [16]. No reported cases of exposures due to drugs used in COVID-19 treatment. Also, no cases of opioid poisoning or poisoning due to recreational drugs were reported to our center. However, the global prevalence of the aforementioned poisoning incidences is conflicting in its nature. The average weekly death rate increased in Canada by 38% in the first fifteen weeks of COVID-19 compared to the fifteen weeks before [30]. In the United States, the pandemic has brought a probable surge in adverse effects related to overdosing [31, 32]. The European Monitoring Centre for Drugs and Drug Addiction reported 50% decrease in illicit drug use in European countries [33]. Roux et al reported a decrease in recreational drug use in France, and it was suggested that such a decrease is due to fewer opportunities to use such drugs, reduced availability of illicit drugs to buy, reduced ability to collect them, and loss of available income to buy it [16].

We noted an increase in bites related to domestic animals. Similarly, Dixon et al. described a threefold rise in pediatric ER visits due to dog bites during the stay-at-home lockdown policy, owning such observation to decreased adult supervision over children, and increased dog stress

because of confinement [34]. On the other hand, we noticed fewer snake bites, scorpion stings, toxic plant exposures, and occupational exposures, as home internment and weather conditions averted such exposures.

Our study showed increased exposure in all age groups, but a remarkable observation was the high increase in exposure in the adolescents (11-15 y) group. It is possible that even though this age group understands what these chemicals are used for, they have little awareness about the potential toxicity. Other similar studies showed different age group observations. For example, the French poison center reported an increase in exposure in all age groups except 5-25 y group, and the most significant increase occurred in patients over 65 years [16]. Likewise, the Canadian poison center did not notice an increase in exposure in those below the age of 19 years [14]. In fact, children below five years represented a large percentage of calls received during the study period. This might be due to the closure of schools and kindergartens, with children spending more time at home, and therefore they have more chance for exposure [16]. Furthermore, Teleworking and homeschooling for older children contributed to such an increase by shifting parent's attention away from younger children [16].

Among routes of exposure, the ocular route recorded the sharpest increase. This observation may be due to the fact that eyes are involved in chemical exposure, whether by accidental spraying of the eyes or touching the eyes after hand or face sanitation or via exposure to vapors. A study from the United States found that inhalational route observed the highest increase during the lockdown [13].

While intentional exposures increased during the lockdown, we suggest that the increase was due to attempts to protect from acquiring infection. Canadian poison center reported a similar

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observation [14]. Oppositely; we have noticed that suicidal exposures during the lockdown have decreased. This fall could be arguably due to the social and family support created by the stay-at-home order. French poison center reported a similar observation [16].

We noted an increase in calls from healthcare workers. Oppositely, this increase was accompanied by a fall in the proportion of severe cases despite the increase in hospital admission. The French poison center reported similar findings [16]. There is no palpable cause for such a decrease; however, under-reporting plays a role as it was the responsibility of the Civil Defense Directorate (CDD) during the lockdown, which might be overwhelming and could lead to under-reporting. Another possibility is related to the change in the pattern of poisoning during the lockdown resulting in fewer severe and fatal exposures. Severe cases in Jordan have been previously described as caused by animal bites and stings, toxic plants, and food [35]. Our study shows that there has been a significant decrease in the above-mentioned agents during the lockdown. It is also important to mention the decrease in the number of suicide attempts using poisonous agents and efforts to increase awareness about early reporting of toxic exposures by the healthcare authorities.

A previous retrospective study reported 1992 cases of acute poisoning in Jordan between 2014 and 2018, with an average of 498 cases per year. The most commonly reported agents were drugs, household chemicals, and animal bites and stings. The male gender was more prevalent than females, and children were the most commonly affected groups. The majority of cases were reported to occur at home, and ingestion was the most common route. Furthermore, most exposures were unintentional, and the majority of cases were mild, with no deaths reported. Therefore, when comparing the previously mentioned study with our control period of March-May 2019, we cannot describe significant changes in the pattern of poisoning incidences [35].

This study has its strength and limitations. Our data represent the majority of calls related to toxic exposures in Jordan, as Pharmacy One[™] poison center is the only center responsible for responding to calls from CDD, the primary emergency response service in Jordan (911). It also receives calls unrestrictedly from the public and healthcare workers at all times. However, this study has its limitations. Not all exposures were reported to the poison center, because many were treated at home or sought direct medical help without notifying the poison center. Furthermore, severely intoxicated or dead people usually arrive directly at the hospital without reporting the incidence to any poison center. In addition, poisoning specialists make their judgment and management recommendations based on the caller's information. Some cases were closed by simple advice over the phone without onsite confirmation of the nature of exposure. Lastly, there were difficulties accessing data from other poison centers.

In conclusion, there is a change in both the number and pattern of toxic exposure related calls during the lockdown, mostly due to fear of coronavirus. Exposures related to toxic gases, alcohol, household cleaners, drugs, and domestic animal bites have increased, whereas exposures related to snake bites, scorpion stings, toxic plants, and occupational exposures have decreased. This observed increase in calls involved all age groups, with children below five years accounting for the largest percentage. Ocular exposures showed the sharpest increase among all exposure routes. While intentional exposures showed a remarkable increase, those exposures were not of suicidal nature. In fact, our study showed a decrease in suicidal exposures. In addition, calls from healthcare workers have increased, as well as case severity, while hospital admission rate increased. This study highlights the important role of poison centers, as they help decrease the burden on healthcare facilities. At poison centers, specialists respond to calls and triage the patients based on case severity to set an appropriate treatment plan. This alleviates

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unnecessary use of ambulances and saves emergency room resources for severe cases. Furthermore, specialists at poison centers are consulted by healthcare workers, thereby saving the cost of unwarranted patient transfer, investigations, laboratory work up, and, most importantly, evading case progression and complications. Poison centers can be referenced for evidence-based protocols, and the length of stay can be curtailed. Information about routes and types of exposures provided by poison centers is also valuable when setting healthcare policies.

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IRB approval: According to IRB policy at our institution, this study is exempted from review and approval, as it is a retrospective review of records, where patient's names or personal information couldn't be identified.

Data sharing statement: Data supporting the finding of this article are available upon request.

Authors contributions:

LR, HD, KA, AF: Conceptualization, study design. LR, HD: project administration. AF: data collection. NH, HD: literature search and review. HD: draft the initial manuscript. LR, HD, MD, and SM: edit and write the final manuscript.

All authors read, edit, proof-read, and approve the final manuscript before submission.

References:

- [1]. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382(8):727–33.
- [2]. Adhanom T. WHO Director-General's opening remarks at the media briefing on COVID-19—16 March 2020; 2020. World Health Organization: https://www.who. int/dg/speeches/detail/who-director-general-s-opening-remarks-at-themedia-briefing-oncovid-19---11-march-2020.
- [3]. Fisher D, Wilder-Smith A. The global community needs to swiftly ramp up the response to contain COVID-19. Lancet. 2020;395(10230):1109–10.
- [4]. Neil M F, Daniel L, Gemma N-G, Natsuko I, Ainslie K, Marc B, et al. Impact of nonpharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand. Imp Coll COVID-19 Response Team. 2020;(March).
- [5]. Wilder-Smith A, Freedman DO. Isolation, quarantine, social distancing and community containment: Pivotal role for old-style public health measures in the novel coronavirus (2019-nCoV) outbreak. J Travel Med. 2020;27(2):1–4.
- [6]. Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD. How will country-based mitigation measures influence the course of the COVID-19 epidemic? Lancet (London, England). 2020 Mar;395(10228):931–4.
- [7]. Lau H, Khosrawipour V, Kocbach P, Mikolajczyk A, Schubert J, Bania J, et al. The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China. J Travel Med. 2021;27(3):1–7.
- [8]. Zarocostas J. How to fight an infodemic. Lancet (London, England). 2020 Feb;395(10225):676.
- [9]. Depoux A, Martin S, Karafillakis E, Preet R, Wilder-Smith A, Larson H. The pandemic of social media panic travels faster than the COVID-19 outbreak. Vol. 27, Journal of travel medicine. 2020.
- [10]. Gottlieb M, Dyer S. Information and Disinformation: Social Media in the COVID-19 Crisis. Acad Emerg Med Off J Soc Acad Emerg Med. 2020 Jul;27(7):640–1.

BMJ Open

- [11]. The Lancet Infectious Diseases. The COVID-19 infodemic. Lancet Infect Dis. 2020;20(8):875.
- [12]. Galvão J. COVID-19: the deadly threat of misinformation. Vol. 21, The Lancet. Infectious diseases. 2021. p. e114.
- [13]. Chang A, Schnall AH, Law R, Bronstein AC, Marraffa JM, Spiller HA, et al. Cleaning and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 — National Poison Data System, United States, January 1, 2020–March 31, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(16):496–8.
- [14]. Yasseen A, Weiss D, Remer S, Dobbin N, Macneill M, Bogeljic B, et al. Increases in exposure calls related to selected cleaners and disinfectants at the onset of the covid-19 pandemic: Data from canadian poison centres. Heal Promot Chronic Dis Prev Canada. 2021;41(1):25–9.
- [15]. Le Roux G, Sinno-Tellier S, Descatha A. COVID-19: home poisoning throughout the containment period. Lancet Public Heal. 2020;5(6):e314.
- [16]. Roux G Le, Sinno-Tellier S, Puskarczyk E, Labadie M, von Fabeck K, Pélissier F, et al. Poisoning during the COVID-19 outbreak and lockdown: retrospective analysis of exposures reported to French poison control centres. Clin Toxicol [Internet]. 2021;59(9):832–9. Available from: https://doi.org/10.1080/15563650.2021.1874402
- [17]. Richards GC. Alcohol-based hand sanitisers: a warning to mitigate future poisonings and deaths. BMJ Evidence-Based Med [Internet]. 2021;26(2):65–8. Available from: https://ebm.bmj.com/content/26/2/65
- [18]. Wong A. COVID-19 and toxicity from potential treatments: Panacea or poison. EMA Emerg Med Australas. 2020;32(4):697–9.
- [19]. Delirrad M, Mohammadi AB. New Methanol Poisoning Outbreaks in Iran Following COVID-19 Pandemic. Vol. 55, Alcohol and alcoholism (Oxford, Oxfordshire). 2020. p. 347– 8.
- [20]. Yip L, Bixler D, Brooks DE, Clarke KR, Datta SD, Dudley S, et al. Serious Adverse Health Events, Including Death, Associated with Ingesting Alcohol-Based Hand Sanitizers Containing Methanol — Arizona and New Mexico, May–June 2020. MMWR Morb Mortal Wkly Rep. 2020;69(32):1070–3.

- [21]. Clay JM, Parker MO. Alcohol use and misuse during the COVID-19 pandemic: a potential public health crisis? Vol. 5, The Lancet. Public health. 2020. p. e259.
- [22]. Chary MA, Barbuto AF, Izadmehr S, Hayes BD, Burns MM. COVID-19: Therapeutics and Their Toxicities. J Med Toxicol. 2020;16(3):284–94.
- [23]. Defence Order No. (2) [Internet]. Pm.gov.jo. 2021. Available from: http://www.pm.gov.jo/upload/files/Order-Defense-2.pdf

- [24]. Bronstein AC, Spyker DA, Cantilena LRJ, Green JL, Rumack BH, Heard SE. 2007 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 25th Annual Report. Clin Toxicol (Phila). 2008 Dec;46(10):927–1057.
- [25]. Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino J. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol. 1998;36(3):205–13.
- [26]. Detailed Toxicology Information From POISINDEX [Internet]. [cited 2021 Sep 2]. Available from: https://www.micromedexsolutions.com/micromedex2/4.77.0/WebHelp/Document_help/Toxi cology_Management_document.htm
- [27]. Pollard MS, Tucker JS, Green HDJ. Changes in Adult Alcohol Use and Consequences During the COVID-19 Pandemic in the US. JAMA Netw open. 2020 Sep;3(9):e2022942.
- [28]. Neufeld M, Lachenmeier DW, Ferreira-Borges C, Rehm J. Is Alcohol an "Essential Good" During COVID-19? Yes, but Only as a Disinfectant! Alcohol Clin Exp Res [Internet]. 2020;44(9):1906–9. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/acer.14417
- [29]. PHE. Monitoring alcohol consumption and harm during the COVID-19 pandemic. 2021; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data /file/1002627/Alcohol and COVID report.pdf
- [30]. The Ontario Drug Policy Research Network, The Office of the Chief Coroner for Ontario/Ontario Forensic Pathology Service, Public Health Ontario, Centre on Drug Policy Evaluation. Preliminary Patterns in Circumstances Surrounding Opioid-Related Deaths in Ontario during the COVID-19 Pandemic. 2020;(November):1–24. Available from:

BMJ Open

Drug Test Resul	Its Before and Afte	er the US Dec	claration of a Nat	tional Emergency
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	stry RD. Dog Bite ced Prevention. J		0 0	pronavirus Disease-2019: A
[35] Albals D Yeh	va A Issa R Faw	adleh A Retr	ospective assess	ment of acute poisoning
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Center, 2014 to Table 1: Incidence and Pattern May). Total Number of Cases Class of Exposure	2018-Part I. Pharr ns of Toxic exposures and p Drugs Household Cleaners* Alcohol* Pesticides Hydrocarbons* Food Insect bites Domestic Animals bites* Heavy Metals Toxic Gases (chlorine)* Scorpion stings Snake bites Toxic Plants Ingestion Inhalation Dermal Paranteral Ocular	2019 Number of Cases 285 141 (49%) 32 (11%) 12 (4%) 20 (7%) 16 (6%) 17 (6%) 14 (5%) 4 (1%) 9 (3%) 2 (1%) 11 (4%) 5 (2%) 2 (1%) 12 (4%) 46 (16%) 3 (1%) 2 (1%)	COVID-19 Lockdown Number of Cases 544 321 (59%) 83 (15%) 37 (7%) 20 (4%) 17 (3%) 14 (3%) 15 (3%) 11 (2%) 12 (2%) 8 (1%) 5 (1%) 0 (0%) 446 (82%) 18 (3%) 56 (10%) 3 (1%) 13 (2%)	ng COVID-19 Lockdown and 2019 (Ma % of Δ 91% 128% 159% 208% 0% 6% -18% 7% 175% 33% 330% -300% -55% -100% -55% -100% 50% 0% 50%
Center, 2014 to Table 1: Incidence and Pattern May). Class of Exposure Route of Exposure	2018-Part I. Pharr 2018-Part I. Pharr ns of Toxic exposures and p Drugs Household Cleaners* Alcohol* Pesticides Hydrocarbons* Food Insect bites Domestic Animals bites* Heavy Metals Toxic Gases (chlorine)* Scorpion stings Snake bites Toxic Plants Ingestion Inhalation Dermal Paranteral Ocular Others* Work	2019 Number of Cases 285 141 (49%) 32 (11%) 12 (4%) 20 (7%) 16 (6%) 17 (6%) 14 (1%) 9 (3%) 2 (1%) 11 (4%) 5 (2%) 2 (1%) 3 (1%) 2 (1%) 3 (1%) 5 (2%)	COVID-19 Lockdown Number of Cases 544 321 (59%) 83 (15%) 37 (7%) 20 (4%) 17 (3%) 14 (3%) 15 (3%) 11 (2%) 8 (1%) 5 (19%) 0 (0%) 1 (0%) 446 (82%) 18 (3%) 55 (10%) 3 (1%) 13 (2%) 8 (1%) 2 (0%)	ng COVID-19 Lockdown and 2019 (Ma % of A 91% 128% 159% 208% 0% 6% -18% 7% 175% 339% 300% -55% -100% -55% -100% 22% 0% 50% 22% 0% 559% 167%

https://www.publichealthontario.ca/-/media/documents/o/2020/opioid-mortality-covid-surveillance-report.pdf?la=en

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Suicidal Unintentional Occupational Medical Consultation* Therapeutic* Intentional Medical Error Bite/Sting 0-5 y 6-10 y	36 (12) 168 (5) 9 (35) 14 (5) 16 (6) 3 (19) 8 (35) 31 (11) 142 (5)	9%) %) %) %) %)	33 (6 406 (7 0 (0) 14 (3 35 (6 31 (6 22 (4 3 (1)	5%) %) %) %) %) %) %) %)		% % % %		
Occupational Medical Consultation* Therapeutic* Intentional Medical Error Bite/Sting 0-5 y 6-10 y	9 (35 14 (5 16 (6 3 (15 8 (35 31 (1)	%) %) %) %) %)	0 (0) 14 (3 35 (6 31 (6 22 (4	%) %) %) %) %) %) %) %) %) %)	-100 0% 119 933 175	% 6 % %		
Therapeutic* Intentional Medical Error Bite/Sting 0-5 y 6-10 y	16 (6 3 (19 8 (39 31 (1)	%) %) %)	35 (6 31 (6 22 (4	9%) 9%) 9%)	119 933 175	%		
Intentional Medical Error Bite/Sting 0-5 y 6-10 y	3 (19 8 (39 31 (11	%)	31 (6	%) %)	933 175	%		
Medical Error Bite/Sting 0-5 y 6-10 y	8 (39)	%)	22 (4	%)	175			
Bite/Sting 0-5 y 6-10 y	31 (11					%		
0-5 y 6-10 y		1%)	3 (1	%)		175%		
6-10 y	142 (5				-90	%		
6-10 y		0%)	332 (6	1%)	134	0/6		
	142 (50%) 18 (6%) 4 (1%) 15 (5%)		332 (61%) 29 (5%) 15 (3%)		<u>61%</u> 275%			
11-15 y								
16-20 y			30 (6		100%			
21-50 y	92 (32		104 (1		13%			
>50 y	14 (5%)		34 (6%)		143%			
						1		
						Female % o		
Drugs	84 (51%)	(48%)	198 (64%)	123 (53%)	136%	116%		
Pesticides	10 (6%)		9 (3%)	11 (5%)	-10%	10%		
Toxic Plants	2 (1%)	0 (0%)	0 (0%)	1 (0%)	-100%	NA		
Scorpion stings	6 (4%)	5 (4%)	4 (1%)	1 (0%)	-33%	-80%		
Snake bites	4 (2%)	1 (1%)	0 (0%)	0 (0%)	-100%	-100%		
Insect bites					-45%	200%		
						300%		
						20%		
	. ,	(15%)				100%		
						0%		
						NA 29%		
						243%		
Alcolloi	5 (578)	7 (076)	13 (478)	24 (1076)	100 /6	24378		
General public	93 (3	3%)	156 (29%)	68'	%		
vil Defense Directorate					170%			
	· · · ·							
Health Care Workers	84 (2	9%)	96 (1	8%)	14	%		
Non (No offect)	26 (0	09/)	201 (270/)	(72	0/		
					<u> </u>			
					-31%			
					-24%			
Death			0 (0%)		0%			
Jumber of Admissions	15 (5%) 7 (47%)		54 (10%) 30 (56%)		260	%		
hildren from 0-5 Years					329%			
80 out of 108 cases 119 out of 292 cases (41%)		2 cases (41%)	-33%					
	>50 y Drugs Pesticides Toxic Plants Scorpion stings Snake bites Insect bites Insect bites Insect bites (oxic Gases (chlorine) Heavy Metals Household Cleaners Hydrocarbons omestic Animals bites Food Alcohol General public vil Defense Directorate (911) Health Care Workers Non (No effect) minor Moderate Severe Death Jumber of Admissions hildren from 0-5 Years	>50 y 14 (5 Male Male Drugs 84 (51%) Pesticides 10 (6%) Toxic Plants 2 (1%) Scorpion stings 6 (4%) Snake bites 4 (2%) Insect bites 11 (7%) Heavy Metals 4 (2%) Household Cleaners 14 (8%) Hydrocarbons 10 (6%) omestic Animals bites 4 (2%) Food 10 (6%) Alcohol 5 (3%) General public 93 (3) vil Defense Directorate (911) 108 (3) Health Care Workers 84 (2 Non (No effect) 26 (5) minor 95 (3) Moderate 131 (4) Severe 33 (1) Death 0 (0) Mumber of Admissions 15 (5) hildren from 0-5 Years 7 (4)	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	>50 y 14 (5%) 34 (6%) 143 Male Female Male Female Male % of Λ Drugs 84 (51%) 57 (48%) 198 (64%) 123 (53%) 136% Pesticides 10 (6%) 10 (8%) 9 (3%) 11 (5%) -10% Toxic Plants 2 (1%) 0 (0%) 0 (0%) 1 (0%) -33% Snake bites 4 (2%) 1 (1%) 0 (0%) 0 (0%) -100% Insect bites 11 (7%) 3 (3%) 6 (2%) 9 (4%) -45% Toxic Plants 2 (1%) 0 (0%) 0 (0%) -100% -100% Insect bites 11 (7%) 3 (3%) 6 (2%) 9 (4%) -45% Toxic Gases (chlorine) 1 (1%) 4 (1%) 4 (2%) 300% -100% Heavy Metals 4 (2%) 18 47 (15%) 36 (15%) 236% Hydrocarbons 10 (6%) 6 (5%) 11 (4%) 24 (2%) 75% Food 10 (6%) 7 (6%) 5 (2%)		

Figure 1: Class of Exposure

This chart shows the difference in classes of exposure when comparing the period of 2019 to COVID-19 lockdown.

Figure 2: Route of Exposure

This chart shows changes in routes of exposure in both studied periods.

Figure 3: Site of Exposure

In this chart, changes in sites of exposure are shown.

Figure 4: Reason of Exposure

Reasons for exposure for both periods are set side by side, showing variance.

Figure 5: Gender Variation

This chart shows the prevalence of toxic exposures across different age groups. roc.

Figure 6: Distribution across Age Groups

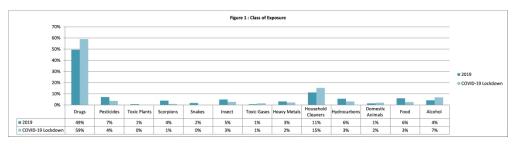
In this chart, a correlation between different exposure classes and gender is highlighted

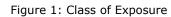
Figure 7: Source of Calls

This chart shows the difference in the source of calls in both studied periods.

Figure 8: Medical Outcome Including Admission

Changes in medical outcomes are shown in this chart. It also includes changes in the percentage of admissions and percentage of children admitted during both periods





353x89mm (300 x 300 DPI)

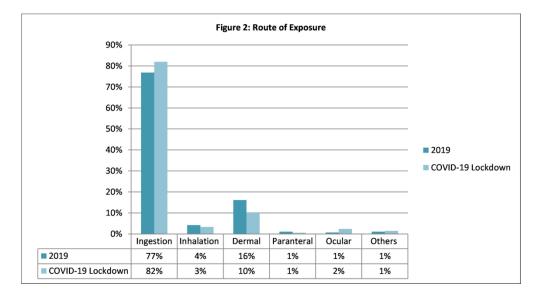
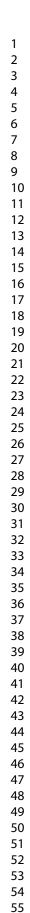


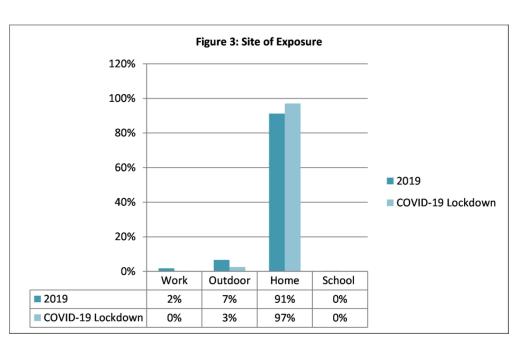
Figure 2: Route of Exposure

182x98mm (300 x 300 DPI)

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60





146x90mm (300 x 300 DPI)

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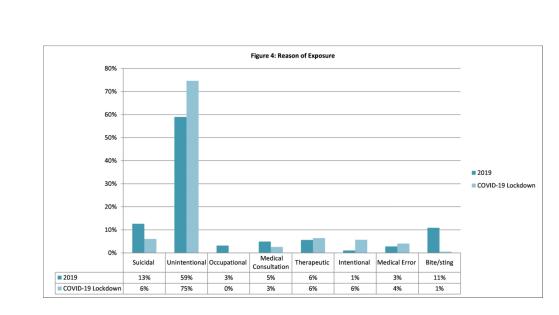


Figure 4: Reason of Exposure

250x126mm (300 x 300 DPI)

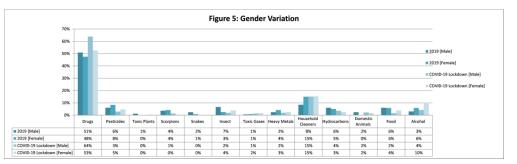


Figure 5: Gender Variation

383x114mm (300 x 300 DPI)

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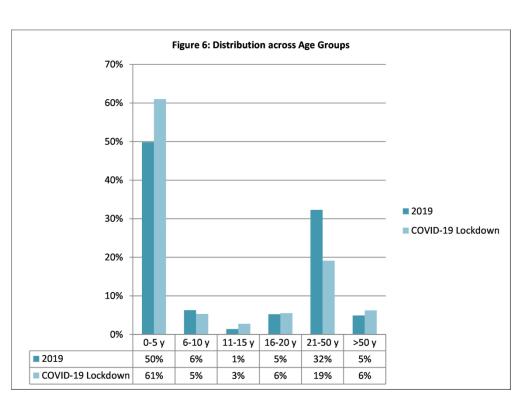
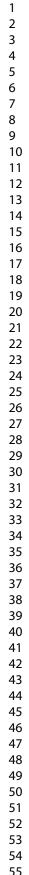


Figure 6: Distribution across Age Groups

165x118mm (300 x 300 DPI)





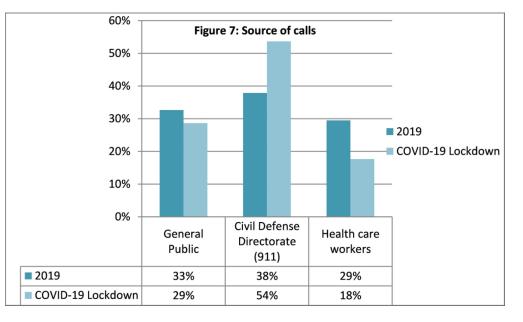


Figure 7: Source of Calls

140x82mm (300 x 300 DPI)

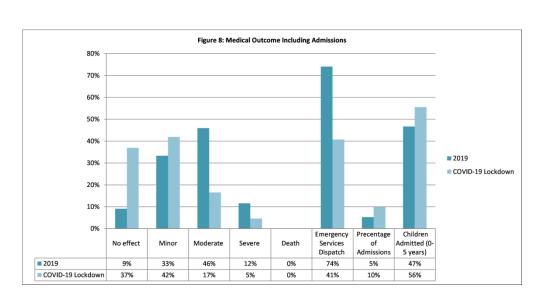


Figure 8: Medical Outcome Including Admissions

238x121mm (300 x 300 DPI)

STROBE Statement-checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Pag No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the	1,2
		abstract	
		(b) Provide in the abstract an informative and balanced summary of what	2
		was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of	5,6,
6		recruitment, exposure, follow-up, and data collection	- , - ,
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods	_
		of selection of participants. Describe methods of follow-up	
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and	_
		methods of case ascertainment and control selection. Give the rationale for	
		the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and	_
		methods of selection of participants	
		(b)Cohort study—For matched studies, give matching criteria and number of	_
		exposed and unexposed	
		<i>Case-control study</i> —For matched studies, give matching criteria and the	_
		number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders,	5,6
		and effect modifiers. Give diagnostic criteria, if applicable	
D-4-	8*	For each variable of interest, give sources of data and details of methods of	5,6,
Data	0		
Data sources/measurement	0	assessment (measurement). Describe comparability of assessment methods if	
	0	assessment (measurement). Describe comparability of assessment methods if there is more than one group	
sources/measurement		there is more than one group	5
sources/measurement Bias	9	there is more than one group Describe any efforts to address potential sources of bias	5
sources/measurement Bias Study size	9 10	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at	
sources/measurement Bias	9	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If	
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
sources/measurement Bias Study size	9 10	there is more than one groupDescribe any efforts to address potential sources of biasExplain how the study size was arrived atExplain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why(a) Describe all statistical methods, including those used to control for	
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (a) Describe all statistical methods, including those used to control for confounding	7
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions	7
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one groupDescribe any efforts to address potential sources of biasExplain how the study size was arrived atExplain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why(a) Describe all statistical methods, including those used to control for confounding(b) Describe any methods used to examine subgroups and interactions(c) Explain how missing data were addressed	7
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one groupDescribe any efforts to address potential sources of biasExplain how the study size was arrived atExplain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why(a) Describe all statistical methods, including those used to control for confounding(b) Describe any methods used to examine subgroups and interactions(c) Explain how missing data were addressed(d) Cohort study—If applicable, explain how loss to follow-up was	7
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) Cohort study—If applicable, explain how loss to follow-up was addressed	7
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and	7
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed	7
sources/measurement Bias Study size Quantitative variables	9 10 11	there is more than one group Describe any efforts to address potential sources of bias Explain how the study size was arrived at Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and	7

Continued on next page

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	-
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and	7
data		information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	-
		Case-control study—Report numbers in each exposure category, or summary	-
		measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	8,9,10
Main results 1	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and	8,9,10
		their precision (eg, 95% confidence interval). Make clear which confounders were	
		adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	-
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a	-
		meaningful time period	
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and	-
		sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or	15
		imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	10-14
		multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other informati	ion		
Funding	22	Give the source of funding and the role of the funders for the present study and, if	16
-		applicable, for the original study on which the present article is based	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.