# The impact of the COVID-19 pandemic on accidental and suicidal drug intake rates, what has the pandemic changed?

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**Abstract.** – **OBJECTIVE:** The primary aim of this study was to review the patients admitted to pediatric emergency service with a history of accidental and suicidal drug intake within the first nine months of the pandemic period and the same period a year ago.

PATIENTS AND METHODS: The study is done retrospectively on patients with a history of accidental and suicidal drug intakes between March-December 2019 and March-December 2020.

**RESULTS:** The study included 360 patients. Of 250 (69.4%) patients admitted in 2019, 163 (65.2%) of them were accidental drug intakes, while 87 (34.8%) were suicidal drug intakes. In 2020, of the 110 (30.6%) patients admitted, 73 (66.4%) of them were accidental drug intakes, while 37 (33.6%) were suicidal drug intakes. The ratio of accidental drug intakes to total patient admissions in 2019 and 2020 was 0.23% and 0.33%, respectively ( $\underline{z}$ =-0.44;  $\underline{p}$ =0.65). The ratio of suicidal drug intakes to total patient admissions in 2019 and 2020 was 0.12% and 0.16%, respectively ( $\underline{z}$ =-0.1956;  $\underline{p}$ =0.84), and an increase in the ratio of suicidal drug intakes was observed during the pandemic.

conclusions: With the pandemic, increased cases of neglect because of accidental drug intake and the increase in suicidal drug intake are worrisome. Protecting and improving the mental health of the society, especially of parents and adolescents, is very important in preventing suicide and child neglect and abuse from reaching dangerous levels in pandemics.

Key Words:

COVID-19, Suicide, Drug intoxications, Child, Pediatric emergency.

# Introduction

A novel coronavirus named pneumonia-related Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) was first reported in China, in December 2019. During the following weeks, the virus spread to the entire world¹. The World Health Organization declared a public health emergency of international concern on January 30, 2020, and named this outbreak as COVID-19 on February 12, 2020. They reported the first case in Turkey on March 11, 2020². Schools closed in Turkey on March 16, 2020. With the closure of schools, children received education at home, and with the start of curfew, parents started working from home. With curfew, all children spent more time at home. Cases of domestic accidents and neglect may have increased, especially in the under-five-year age group, or may have decreased as parents spent more time at home.

When we look at the consequences of the pandemic on suicide, it can vary according to the country's public health control measures, socio-cultural and demographic structure, access to patients by face-to-face teleconference, and existing supports<sup>3</sup>. The COVID-19 pandemic can cause anxiety, distress, and potentially depression among children due to COVID-19-related fears, families' economic problems, and limited social contact and activities4. Social contact limitations and taking care of the children while working from home can increase parents' stress. Increasing parent stress can lead to the deterioration of family or parent-child relationships and, finally, can lead to conflicts and violence between family members. Taken together, they may adversely affect the mental health of children and adolescents. leading to an increased risk of suicide.

On the other hand, COVID-19 pandemic can influence child mental health in a positive manner, families can spend more time with their children, can build powerful bonds and can provide them with social support<sup>5</sup>. Family relations might help reduce anxiety and distress of the children

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caused by the COVID-19 crisis and family relations also might prevent them from falling into depression<sup>6,7</sup>. Also, staying home can reduce the stress and pressure coming from academic stress or peer bullying at school<sup>5</sup>. Considering that family and school factors are accepted as the main risk factors, these positive effects may reduce the risk of suicide in children<sup>4</sup>.

The main aim of this study was to compare the rates of the pandemic period and the same period one year ago in patients admitted to the pediatric emergency department with a history of accidental or suicidal drug intake.

#### **Patients and Methods**

All patients between the ages of 0-18 years who were admitted to the University of Health Sciences Ankara Research and Training Hospital, Pediatric Emergency Service between March-December 2019, and March-December 2020 with a history of accidental and suicidal drug intake were included in our study. The patient data (demographic characteristics of the patients, admission complaints, follow-ups in the emergency service, and other services) were filled in the questionnaire forms, which were retrospectively taken from the electronic health records of the same hospital. Patients who left the hospital without permission, refused treatment, and poisoning because of non-drug reasons, were not included in the study.

The ethical consent of the study was taken from the University of Health Sciences Ankara Research and Training Hospital Ethics Committee (Date/number: 28.1.2021/573).

# Statistical Analysis

Statistical analyses were performed using the IBM SPSS version 26 (IBM Corp., Armonk, NY, USA). The variables were investigated using visual (histograms, probability plots) and analytical (Kolmogrov-Simirnov/Shapiro-Wilk's methods test) to determine whether they are normally distributed. Descriptive analyses were presented (using tables of frequencies for the ordinal variables) using medians and minimum-maximum values for the non-normally distributed; non-parametric tests were conducted to compare these parameters, as well as to compare the ordinal variables. The univariate analyses to identify variables associated with patients' outcome (accidental/suicidal drug intake) when the child was admitted to

the pediatric emergency using the Chi-square test was used to compare these proportions in different groups (categorical values) and Mann-Whitney-U tests, where appropriate. Two proportion z-tests were used to compare both the total average of both years and the mean of those who took drugs by accident and by suicidal intent. For the multivariate analysis, the factors identified with univariate analyses were further entered into the logistic regression analyses to determine the independent predictors of patient outcome. Hosmer-Lemeshow goodness of fit statistics were used to assess model fit. A 5% type-I error level was used to infer statistical significance. The significance level was accepted as p<0.05.

#### Results

All children who were admitted to this hospital for any complaint were included in the research. While the total number of admissions to the University of Health Sciences Ankara Research and Training Hospital's pediatric emergency department in 2019-2020 was 120,990, admissions in January-February of both years were excluded from the analysis of periodic admissions because the COVID-19 period began in March (Figure 1). Figure 2 depicts the monthly distribution of accidental and suicidal drug consumption in 2019-2020. The proportion of patients admitted to the hospital because of accidental or suicidal drug intakes compared to the number of total admissions to the hospital did not show a statistically significant change between the two periods change (z=-0.1956; p=0.84). When we analyzed the rates of drug intake in all patients admitted to the pediatric emergency during the COVID-19 period, we found no statistically significant relationship between the rate of those who took drugs accidentally in 2019 and the ratio of those who accidentally took drugs in 2020 (z=-0.44; p=0.65). This was the same for suicidal drug intake (z=-0.1786; p=0.86).

In addition, the duration of emergency observation was significantly higher in accidental drug intakes in 2019 (p=0.022), while there was no statistically significant difference in suicidal drug intakes (0.956). Multiple drug intake was higher in the suicidal group in 2020 compared to 2019 (p=0.010) (Table I).

The mean age of those who took drugs with suicidal intentions was statistically significantly higher than those who accidentally took drugs in months (p<0.001).



Figure 1. Numbers of patients that were included by the year.

Furthermore, when comparing individuals who took drugs with suicidal intentions to those who accidentally took drugs, the time to admission to the emergency service was statistically significantly longer among those who took drugs with suicidal intentions (p < 0.001). The percentages of girls (44.5%) and boys (55.5%) in the group who accidentally took drugs were statistically significantly different from the percentages of females (75.8%) and males (24.2%) in those who took drugs with suicidal intentions (p<0.001). The hours of admission to the hospital were mostly between 00:01-07:59 for those who took drugs with the intention of suicide. while those who accidentally took drugs mostly admission to the emergency service between the hours of 08:00 and 16:00 and these differences were statistically significant (p<0.001). Suicidal multidrug intake was statistically significantly greater than accidental multidrug intake in terms of percentage (p<0.001). 29.5% of drug intakes with suicidal intentions and 10.7% of accidental drug intakes included intakes of antidepressants (*p*<0.001) (Table II).

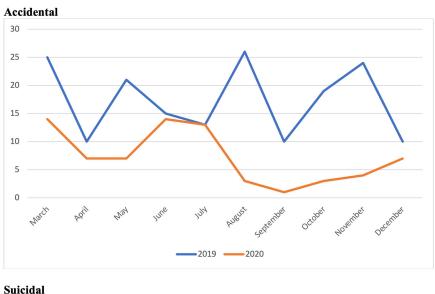
The binary logistic regression analysis was used to assess the elements that contributed to persons consuming medications, the statistically significant factors that were correlated with suicidal drug intakes were multidrug intakes (OR=0.118, 95% CI: 0.28-0.49; *p*=0.004), taking antidepressants (OR=11.81, 95% CI: 1.53-91.07; *p*=0.018), taking anti-hypertensive drugs

(OR=107.88, 95% CI: 3.29-3533; p=0.009), age (calculated in months) (OR=1.54, 95% CI: 1.19-1.99; p=0.001) and admission to the hospital after 16:00 o'clock, mostly suicidal (OR=0.23, 95% CI: 0.11-0.46; p=0.008) which increases the suspicion of taking drugs for suicide compared to taking drugs accidentally (Table III).

# Discussion

Drugs are the most commonly used tools in suicide attempts in the adolescent group, accidental intakes in early childhood also account for a significant portion of emergency service admissions as cases of neglect<sup>8,9</sup>. In this study, where we are evaluating drug intoxications during the pandemic period, the number of our patients admitted to our Pediatric Emergency Service because of accidental and suicidal drug intake has shown significant increases proportionally according to the pre-pandemic period, revealing that the pandemic increases this risk.

Although children have a mild course of COVID-19 disease, they have been the most heavily affected group psychosocially<sup>10</sup>. With the COVID-19 pandemic, the closing of schools, children's staying at home and unexpected unemployment of families became significant causes for child neglect-abuse cases and suicide attempts in the whole world<sup>11</sup>. Closure of schools, quarantine admissions, inability to spend time outdoors,



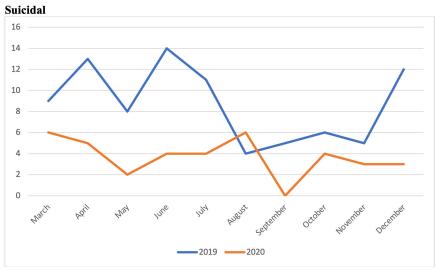


Figure 2. Distribution of accidental and suicidal drug intakes by months in 2019-2020.

staying away from friends and social places, disruptions of eating and sleeping habits, increasing monotony and boredom, fear of contracting the virus, the anxiety of family members catching the virus and losing their lives have become an important risk factor for neuropsychiatric diseases and suicidality<sup>12-14</sup>. In a study conducted with 2,230 primary school students who were quarantined for 3-4 months in China, it was reported that 22.6% showed depressive symptoms, 18.9% showed anxiety symptoms, and 37.3% were worried about catching the virus. This shows how the pandemic can affect children's mental health<sup>15</sup>. Similarly, in a survey study conducted on 5,175 children during the pandemic period in China, it

was found that 12.33% of the participants had depression and 6.26% had anxiety symptoms<sup>16</sup>. In a recent survey study<sup>17</sup> using the suicide screening scale in adolescents admitted to the Pediatric Emergency Service in the USA before and during the pandemic period, suicidal behavior and thoughts were found to be higher during the pandemic period. In a survey study<sup>18</sup> including adolescents and adults in the USA during the pandemic period, it was found that adolescents were more likely to have depression, anxiety, sleep problems, and suicidal tendencies. It is stated that factors such as stress, anxiety, and loneliness caused by the pandemic may increase the susceptibility to substance addiction and cause body

**Table I.** Demographic characteristics according to the reason for drug intake.

		Accid	lental	P	Suicidal		P
		2019 n (%)	2020 n (%)		2019 n (%)	2020 n (%)	
Gender	Female	73 (44.8)	32 (43.8)	0.892	66 (75.9)	28 (75.7)	0.982
	Male	90 (55.2)	41 (56.2)		21 (24.1)	9 (24.3)	
Age (mean±SD)	Month	67.0±41.2	64.5±54.3	0.003	197±40	192±39	0.087
Time before admission	mean±SD	2.13±3.24	3.10±5.43	0.214	4.4±5.7	3.5±3.9	0.393
Observation time in the emergency service (hours)	mean±SD	18.8±12.3	14.6 ±11.8	0.022	19.8±11.8	21.9±18.4	0.956
Admission time	08:00-16:00	60 (36.8)	30 (41.1)		16 (18.4)	10 (27)	
	16:01-23:59	87 (53.4)	36 (49.3)	0.817	49 (56.3)	20 (54.1)	0.497
	24:00-07:59	16 (9.8)	7 (9.6)		22 (25.3)	7 (18.9)	
Admission month	March	25 (9.2)	14 (19.2)		9 (10.3)	6 (16.2)	
	April	10 (6.1)	7 (9.6)		13 (14.9)	5 (13.5)	
	May	21 (12.9)	7 (9.6)		8 (9.2)	2 (5.4)	
	June	15 (9.2)	14 (19.2)		14 (16.1)	4 (10.8)	
	July	13 (8)	13 (17.8)	0.001	11 (12.6)	4 (10.8)	0.376
	August	26 (16)	3 (4.1)		4 (4.6)	6 (16.2)	
	September	10 (6.1)	1 (1.4)		5 (5.7)	0 (0)	
	October	19 (11.7)	3 (4.1)		6 (6.9)	4 (10.8)	
	November	24 (14.7)	4 (5.5)		5 (5.7)	3 (8.1)	
	December	10 (6.1)	7 (9.6)		12 (13.8)	3 (8.1)	
Admission season	Spring	46 (28.2)	28 (38.4)	0.006	30 (34.5)	13 (35.1)	0.837
	Summer	54 (33.1)	30 (41.1)		29 (33.3)	14 (37.8)	
	Autumn	53 (32.5)	8 (11)		16 (18.4)	7 (18.9)	
	Winter	10 (6.1)	7 (9.6)		12 (13.8)	3 (8.1)	
Multidrug intake	Yes	13 (8)	8 (11)	0.457	28 (32.2)	21 (56.8)	0.010
	No	150 (92)	65 (89)	0.457	59 (67.8)	16 (43.2)	0.010
Drug active	Anti-hypertensive	3 (2.9)	3 (4.5)		3 (7)	1 (2.9)	
ingredient	Anti-inflammatory		11 (16.7)		10 (23.3)	7 (20)	
<b>g</b>	Decongestant	1 (1)	0 (0)		3 (7)	1 (2.9)	
	Antibiotic	2 (1.9)	0 (0)	0.085	3 (7)	2 (5.7)	0.303
	Antidepressant	7 (6.8)	11 (16.7)		15 (34.9)	8 (22.9)	
	Epilepsy	1(1)	4 (6.1)		0 (0)	0 (0)	
	Non-toxic	6 (5.8)	6 (9.1)		0 (0)	2 (5.7)	
	Other	54 (52.4)	31 (47)		9 (20.9)	14 (40)	
Admission to	Yes	73 (77.6)	44 (74.6)	0.550	32 (84.2)	6 (15.8)	0.144
another service	No	21 (22.4)	15 (25.4)	0.550	6 (15.8)	10 (30.3)	0.144
Service	Child service	6 (54.5)	5 (33.3)		3 (50)	5 (50)	
	Intensive care	1 (9.1)	5 (33.3)	0.315	2 (33.3)	3 (30)	0.982
	Dispatch	4 (36.4)	5 (33.3)		1 (16.7)	2 (20)	

image. Even before the pandemic, the European Monitoring Center for Drugs and Drug Addiction warned about the use of synthetic opioids, which are 50-100 times more potent than morphine.

The economic and social changes resulting from the pandemic can spin substance use disorder out of control. They have reported that high rates of anxiety and worry related to the pandemic are associated with high rates of substance use. It has been reported that the rates of alcohol and recreational drugs use in the USA and Canada have increased significantly compared to the pre-pandemic period<sup>19</sup>.

**Table II.** Sociodemographic characteristics of all patients who took drugs for accidental or suicidal purposes according to the drug intake reason.

	Accidental n=236 (%)	Suicidal n=124 (%)	χ <b>²/Z</b>	P*
Gender				
Male	131 (44.5)	94 (75.8)	32.24	< 0.001
Female	105 (55.5)	30 (24.2)		
Age (year)	(****)	( - )		
Median (min-max) mean±SD	5.06±3.81	3.37±0.303	-13.923	<0.001*
Age (Month)				
Median (min-max) mean±SD	66.25±45.59	40.12±3.60	-13.897	<0.001*
Admission month				
March	29 (12.3)	15 (12.1)		
April	17 (7.2)	18 (14.5)		
May	28 (11.9)	10 (8.1)		
June	29 (12.3)	18 (16.4)		
July	26 (11)	18 (14.5)	12.10	0.207
August	29 (12.3)	15 (12.1)		
September	11 (4.7)	10 (8.1)		
October	22 (9.3)	5 (4)		
November	28 (11.9)	10 (8.1)		
December	17 (7.2)	8 (6.5)		
Admission time				
08:00-16:00	90 (38.1)	26 (21)		
16:01-24:00	123 (52.1)	69 (55.6)	18.09	< 0.001
24:01-07:59	23 (9.7)	29 (23.4)		
Admission season		· ·		
Spring	74 (31.4)	43 (34.7)		
Summer	84 (35.6)	43 (34.7)	4.34	0.227
Autumn	61 (24.8)	23 (18.5)	4.34	
Winter	17 (7.2)	15 (12.1)		
How long did it take befor	e admission to the hos	spital?		
	Median: 2 (min-max: 1-9)	Median: 2.5 (min-max: 1-10)	-4.721	<0.001*
Year	(IIIII-IIIax. 1-7)	(IIIII-IIIaA. 1-10)		
2019	163 (69.1)	97 (70.3)		
		8/(/0//)		
		87 (70.2) 37 (29.8)	0.046	0.831
2020	73 (30.9)	37 (29.8)	0.046	0.831
2020 Multidrug intake	73 (30.9)	37 (29.8)		
2020 Multidrug intake Yes	73 (30.9)	37 (29.8) 49 (39.5)	0.046 48.65	<0.001
2020 Multidrug intake Yes No	73 (30.9) 21 (8.9) 215 (91.1)	37 (29.8) 49 (39.5) 75 (60.5)		
2020 Multidrug intake Yes No Drug active ingredient	73 (30.9) 21 (8.9) 215 (91.1) n=169	37 (29.8) 49 (39.5) 75 (60.5) <b>n=78</b>		
2020  Multidrug intake Yes No  Drug active ingredient Anti-hypertensive	73 (30.9)  21 (8.9) 215 (91.1) <b>n=169</b> 6 (3.6)	37 (29.8) 49 (39.5) 75 (60.5) <b>n=78</b> 4 (5.1)		
2020  Multidrug intake Yes No  Drug active ingredient Anti-hypertensive Anti-inflammatory	73 (30.9)  21 (8.9) 215 (91.1) <b>n=169</b> 6 (3.6) 40 (23.7)	37 (29.8)  49 (39.5) 75 (60.5) <b>n=78</b> 4 (5.1) 17 (21.8)		
2020  Multidrug intake Yes No  Drug active ingredient Anti-hypertensive Anti-inflammatory Decongestant	73 (30.9)  21 (8.9) 215 (91.1) <b>n=169</b> 6 (3.6) 40 (23.7) 1 (0.6)	37 (29.8)  49 (39.5) 75 (60.5) <b>n=78</b> 4 (5.1) 17 (21.8) 4 (5.1)	48.65	<0.001
2020  Multidrug intake Yes No  Drug active ingredient Anti-hypertensive Anti-inflammatory Decongestant Antibiotic	73 (30.9)  21 (8.9) 215 (91.1)  n=169 6 (3.6) 40 (23.7) 1 (0.6) 2 (1.2)	37 (29.8)  49 (39.5) 75 (60.5)  n=78 4 (5.1) 17 (21.8) 4 (5.1) 5 (6.4)		
2020  Multidrug intake Yes No  Drug active ingredient Anti-hypertensive Anti-inflammatory Decongestant Antibiotic Antidepressant	73 (30.9)  21 (8.9) 215 (91.1)  n=169 6 (3.6) 40 (23.7) 1 (0.6) 2 (1.2) 18 (10.7)	37 (29.8)  49 (39.5) 75 (60.5)  n=78 4 (5.1) 17 (21.8) 4 (5.1) 5 (6.4) 23 (29.5)	48.65	<0.001
2020  Multidrug intake Yes No  Drug active ingredient Anti-hypertensive Anti-inflammatory Decongestant Antibiotic	73 (30.9)  21 (8.9) 215 (91.1)  n=169 6 (3.6) 40 (23.7) 1 (0.6) 2 (1.2)	37 (29.8)  49 (39.5) 75 (60.5)  n=78 4 (5.1) 17 (21.8) 4 (5.1) 5 (6.4)	48.65	<0.001

Continued

**Table II** (continued). Sociodemographic characteristics of all patients who took drugs for accidental or suicidal purposes according to the drug intake reason.

	Accidental n=236 (%)	Suicidal n=124 (%)	χ²/Ζ*	P
Observation time in the emerg	ency service (hours	)		
Median (min-max)	2 (1-5)	3.5 (1-24)	-1.717	0.086*
Admission to another service	n=153	n=71		
Yes	26 (17)	16 (22.5)	0.978	0.323
No	127 (83)	55 (77.5)	0.978	0.323
	n=26	n=16		
Child service	11 (42.3)	8 (50)		
Intensive care	6 (23.1)	5 (313)	1.25	0.534
Dispatch	3 (34.6)	3 (18.8)		

<sup>\*</sup>The Mann-Whitney-U test was used in the analyses since these data were not normally distributed according to the reason for drug intake. Chi-Square test was used when variables were categorical. SD: Standard Deviation.

In a study<sup>20</sup> evaluating adolescents admitted to a children's hospital in France with a suicidal attempt at the beginning of the pandemic, it was found that admission rates decreased significantly. In a study<sup>21</sup> comparing the total suicide rates in the first three months when schools were closed during the pandemic period in Japan to the previous two years, they found that the pandemic did not change the suicide rates. In our study, although suicide admission numbers decreased during the pandemic period, the proportion of suicide ad-

mission to total admissions increased, though the change was not statistically significant.

With the pandemic, the risk of burnout in parents increased significantly, because many parents either lost their jobs or had to work at home while their children also must spend all of their time at home. Burnout would be further exasperated by caregivers and family elders not being able to provide support because of the risks of illness and lockdown measures. Not being able to rely on others for household chores would also

**Table III.** Factors associated with suicidal drug intake.

	Variable	OR (95% CI)	P
Gender	Male	0.662 (0.13-3.31)	0.616
	Female	Reference	
Admission time	08:00-16:00	0.27 (0.28-2.50)	0.247
	16:01-23:59	0.23 (0.11-0.46)	0.008
	24:00-07:59	Reference	
Drug active ingredient	Others	Reference	
	Anti-hypertensive	107.88 (3.29-3533)	0.009
	Anti-inflammatory	8.49 (1.26-57.03)	0.028
	Decongestant	3.54 (0.00-38385)	0.789
	Antibiotic	0.903 (0.065-12.62)	0.940
	Antidepressant	11.81 (1.53-91.07)	0.018
	Epilepsy	0.000 (0.00-0.00)	0.999
	Nontoxic	1.55 (0.04-645)	0.885
Multidrug	Yes	0.118 (0.28-0.49)	0.004
	No	Reference	
Age	Month	1.54 (1.19-1.99)	0.001
	Year	0.01 (0.001-0.184)	0.002
How long did it take before admitting to the hospital?		0.950 (0.843-1.070)	0.950

limit the time parents can dedicate to their children. Lack of time dedicated to children and risk of burnout would increase the dangers of neglect and abuse<sup>22</sup>.

In a study<sup>23</sup> conducted in New York, child neglect and abuse case reports of the 3 months of the pandemic period and the same period one year ago were compared, and they found that there was a significant decrease in the pandemic. However, it has been emphasized that this may not reflect the truth because the cases of neglect and abuse could not be detected due to the schools being closed, which led to the lack of teacher supervision in suspicious cases, and the children did not apply to the hospital unless they had very severe illness symptoms.

To detect the change in neglect and abuse cases with the COVID-19 pandemic, in a study<sup>24</sup> conducted on children under the age of 18 in the USA, the cases of neglect and abuse in emergency service admissions were compared with the previous year and a decrease in admission to emergency services during the pandemic period was detected. In this study, the total number of neglect and abuse-related admissions decreased while the rates of such admissions compared to total admissions increased.

Although the number of patients who were admitted to the emergency service because of accidental drug intakes, which we considered as cases of neglect in our study, decreased like other admissions in the pandemic, it increased proportionally compared to the previous year. In addition, the duration of admission to the emergency service was longer than the previous year, and the rate of hospitalization in the pediatric intensive care unit was found to have increased compared to the previous year. Although many parents spend more time at home with their children during the pandemic, it reveals that the time and attention spent on the child was not enough. While drug intoxications remain important in hospital admissions, due the substance's side effects and harm that cannot be expected by families, incidents of physical-emotional neglect and abuse are unfortunately overlooked.

The limitation of the study is that we conducted it in a single center. Its strength is that it is the first study in the literature to compare suicidal and accidental drug intake in children covering a long period such as nine months before and during the pandemic period. Multi-center studies covering even longer periods at the end of the pandemic would help to achieve more realistic results.

# Conclusions

As a result, with the pandemic, increased cases of neglect because of accidental drug intake and the increase in suicidal drug intake have been worrisome. Protecting and improving the mental health of the society, especially of parents and adolescents, is very important in preventing suicide and child neglect and abuse from reaching dangerous levels during pandemics.

### **Ethics Approval**

The Ethical Consent of the study was given by the University of Health Sciences Ankara Research and Training Hospital Ethics Committee (Date/number: 28.01.2021/573).

#### **Informed Consent**

Informed consent was obtained from all individual participants included in the study.

#### Availability of Data and Materials

All data necessary to support the protocol are available upon reasonable request.

#### **Conflict of Interests**

All the authors declare that they have no conflict of interest.

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### Authors' Contributions

IF, MAT, wrote the main manuscript text, tables, and figures. OB, GI, and SE provided the resources. IF, MAT, and GI conducted the investigation. OB and SE worked on data curation. IF, MAT, GI worked on the conceptualization of the study. All authors approved the publication.

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