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Impact of COVID-19 pandemic on pediatric patients with epilepsy in Jordan: The caregiver perspective

Miral Al Momani^{a,*}, Basima A. Almomani^b, Philip Sweidan^c, Aladdin Al-Qudah^d, Samah Aburahma^e, Yusra Arafeh^c

^a Department of Pediatrics and Neonatology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

^b Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid, Jordan

^c Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

^d Department of Conservative Dentistry, Faculty of Dentistry, Jordan University of Science and Technology, Irbid, Jordan

e Department of Neuroscience, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

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ABSTRACT

Objectives: The recent COVID-19 pandemic has disrupted care systems around the world. We assessed the impact of COVID-19 lockdown on the care of pediatric patients with epilepsy in Jordan. Potential predictors for seizure control during COVID-19 outbreaks were investigated.

Methods: A cross- sectional survey was conducted on pediatric patients with epilepsy in Jordan, between January and February 2021, via online questionnaires. The collected data included demographic information, epilepsy-related characteristics, views of caregivers and changes in seizure control during COVID-19 outbreak.

Results: A total number of 672 subjects were screened, 276 were eligible, and 154 completed the questionnaire adequately. Two thirds of caregivers (66.2%) reported that the COVID -19 outbreaks prevented their child from getting proper epilepsy care and 28.6% reported difficulty giving the drugs to their child on time because of loss of daily routine. In addition, more than half (55.8%) reported difficulty obtaining antiseizure medicines (ASMs). On the other hand, 77.3% of caregivers reported that seizure status remained unchanged or improved for their children during the COVID-19 and 22.7% reported worsened seizure control. The number of antiseizure medicines taken by patients (p < 0.001), age (p = 0.032), residency area (p = 0.013) and the difficulty in giving the medicine during COVID-19 pandemic (p = 0.002) were the major factors influencing the seizure worsening experienced by patients.

Conclusion: Almost one of every five patients reported worsened seizure control during the outbreak of COVID-19 in Jordan. Moreover, two thirds of caregivers reported poor epilepsy care. This finding highlights the need to implement organized and efficient telemedicine programs devoted to epilepsy care.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a communicable disease caused by the newly emergent SARS-COV-2. The literature was able to uncover several aspects of respiratory and non-respiratory manifestations [2]. Neurological manifestations have been frequently encountered and documented [11]. Mild complaints of anosmia and ageusia have been used to distinguish contracting COVID-19 from the seasonal flu [12]. The most commonly reported serious neurological manifestations in young low-risk patients included encephalitis and strokes [8].

People with chronic illness are a vulnerable population because they are at a higher risk for severe illness from COVID-19. Epilepsy is documented to be the second-greatest neurological disorder burden worldwide [18]. Moreover, findings indicate that severe and potentially injurious seizure behaviors contribute to anxiety and socially avoidant behavior for people with epilepsy [7].

The first COVID-19 case in Jordan was reported on March the 2nd 2020. This was followed by spikes in September and October 2020 [10]. Accordingly, the focus of health services was directed towards COVID-19 management, leaving out abundant numbers of patients

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^{*} Corresponding author at: Department of Pediatrics and Neonatology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan.

E-mail addresses: maalmomani3@just.edu.jo (M. Al Momani), baalmomani1@just.edu.jo (B.A. Almomani), philipsweidan@yahoo.com (P. Sweidan), aqudah@ just.edu.jo (A. Al-Qudah), samahk@just.edu.jo (S. Aburahma), theyusraarafeh@gmail.com (Y. Arafeh).

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without their regular access to health care. This entailed trouble getting their medicines due to several factors including fear of contracting the infection, financial strain, and psychological depression. Around 70% of children with epilepsy with optimal treatment would enter remission if access to medications and regular follow-up were attainable [15]. However, in reality, remission has been difficult to maintain due to the barriers to care that are present during the outbreak.

A study by Rosengard and coworkers in the USA assessed the adult patient's perceived seizure control during the pandemic and reported that 17.5% of responders suffered from worsening seizure control with the majority having more frequent attacks [18]. While other patients with epilepsy suffered from more severe seizures or new-onset seizures [18]. Moreover, both stress (80.6%) and poor sleep attributed to the pandemic were the most reported seizure precipitants by patients with epilepsy [18]. Furthermore, impaired access to epilepsy care including difficulty obtaining antiseizure medicines was more likely to be documented among those who reported worsened seizure control [18]. Another study from Italy that investigated the impact of COVID-19 on patients with epilepsy, reported an increased seizure frequency in 13.2% of patients [19]. In Jordan, focal epilepsies were the most common type of pediatric epilepsy, the structural-metabolic causes were the most common causes of epilepsy [1]. Adding to that, epilepsy originating from genetic causes was commonly attributed to electroclinical syndromes [1]. In contrast to patients with epilepsy from other Arab countries, those from Jordan appear to exhibit the best overall life quality, mainly due to good seizure control [4]. Moreover, a pre-pandemic study in Jordan stated that most of the adult patients with epilepsy did not have any restriction of daily activities due to epilepsy. In addition, more than half of them did not perceive any impact of epilepsy on their daily living [4]. Worldwide, there's a prominent paucity of information regarding the impact of the COVID-19 pandemic on epilepsy [3].

The main goal of this study was to assess the influence of the COVID-19 outbreak on seizure control among pediatric patients with epilepsy in Jordan and whether specific variables (demographics, epilepsy characteristics, and healthcare access) were associated with this change. In addition, the views of patients' caregivers on different issues related to the COVID-19 pandemic were investigated.

2. Methods and materials

2.1. Study design

A cross-sectional survey was conducted on pediatric patients with epilepsy in Jordan during January and February 2021. The online questionnaire was developed using Google Forms and distributed to patients using WhatsApp. A second reminder was sent to those who did not respond to the first message. The list of candidate patients who were diagnosed with epilepsy within the last 5 years (2016-2020) at King Abdullah University Hospital was retrieved from a computerized hospital database. These patients were registered in the pediatric neurology clinic at the hospital. The current study included pediatric patients with epilepsy aged 1-16 years who had their diagnosis confirmed by a neurology consultant, regularly visited the clinic, and were treated with antiseizure medicines for at least 6 months. Newly diagnosed patients, first attack of seizure, those with EEG-confirmed psychogenic nonepileptic seizures (PNES), Dravet syndrome, and SCNA1 phenotypes were excluded from the study. Ethical approval was granted from the Institutional Review Board in Jordan University of Science and Technology. Consent to participate in the study was obtained from participants before filling the questionnaire. Approximately, a total of 10 minutes was required to complete the online survey.

2.2. Questionnaire development

[9, 10] and discussion within the research team. The questionnaire was originally constructed in English and reviewed for face validity by experts in the field. Following that, it was translated to Arabic and examined for clarity through a pilot study (n=5). The questionnaire consisted of 3 main sections covering different themes. The first section covered demographic details such as age, gender, monthly income, residence place, and educational level. The second section included information about epilepsy history such as duration of epilepsy, type of epilepsy, number of anti-seizure medications, and seizure exacerbation during the COVID-19 pandemic. The third section covered the views of caregivers during the COVID-19 outbreak (in terms of access to healthcare services along with possible concerns they had during the pandemic in regard to their child's health).

2.3. Data analysis

After data collection, all the submitted questionnaires were checked for completeness and entered into SPSS. Descriptive statistics of categorical (counts and percentages) and continuous (median and interquartile range) variables were calculated. Univariate analyses were conducted using the appropriate statistical tests (chi-square, Man Whitney) to assess the association between the variables and seizure control. Factors that were investigated as potential predictors for seizure control during COVID-19 were: age of the child, gender, duration of disease, education of caregivers, income, insurance, employment, achievement of seizure control before the outbreak, difficulty getting antiseizure medicines during the pandemic, number of antiseizure medicines, years of medication treatment, difficulty giving the medicinesto your child, type of epilepsy, and presence of the comorbid condition. Factors with < 0.05 on univariate analyses were entered in multivariate analysis using binary logistic regression to calculate odds ratio (OR) and 95% confidence interval (95%CI). The statistical significance level was considered at a p-value < 0.05.

3. Results

3.1. Demographics

Out of 672 patients in the hospital list, 396 were excluded because of having a new-onset seizure, first attack of seizure, not on antiseizure medicine or febrile seizure. Of 276 eligible patients whose caregivers were contacted: 91 did not respond, 2 were reported dead and 10 declined participation. A total number of 173 patients' caregivers filled the survey and a total of 154 complete responses were recorded and included in the analysis.

The average age of children was 10 years old, and more than half of the children were males (55.2%). Approximately, half of the patients' caregivers had school education (52.6%), 47.4% were employed and 74% had a monthly income less than 600 JOD. Moreover, 49.4% of patients were living in a village and a third (36.4%) of patients were not medically insured.

Regarding clinical data; 22.1% of patients had comorbid conditions (such as meningomyelocele, hypothyroidism, iron deficiency anemia, heart failure, failure to thrive, bronchial asthma, mild immune deficiency, diabetes mellitusetc). The average duration of epilepsy among patients was 3 years and 44.2% of them had focal epilepsy. A half of patients (51.3%) used 2 or more antiseizure medicines and 61.7% reported no change on antseizure medicines (dose, duration, type of medication) during COVID-19. Only 1.9% reported that their child with epilepsy had tested positive for COVID-19. However, 12.3% stated that their children might have been infected with COVID-19 without confirming this by any laboratory testing. Detailed demographics and clinical are presented in Table 1.

The questionnaire items were developed based on literature review

Table 1

Demographics and Clinical Data for patients.

Demographics ^a	Number(%)		
Relationship with child			
Father	84 (54.5)		
Mother	70 (45.5)		
Age ^b	10 [5-12.25]		
Gender			
Male	85 (55.2)		
Female	69 (44.8)		
Residency area			
Village	76 (49.4)		
City	78 (50.6)		
Monthly income			
$<600 \text{ JOD}^{\circ}$	114 (74)		
$\geq 600 \text{ JOD}^{\circ}$	40 (26)		
Education			
school education	81 (52.6)		
university education	73 (47.4)		
Employment			
Unemployed	81 (52.6)		
employed	73 (47.4)		
Health insurance			
Not insured	56 (36.4)		
insured	98 (63.6)		
Clinical data			
Comorbid condition in addition to epilepsy			
No	120 (77.9)		
Yes	34 (22.1)		
Duration of disease (years) ^b	3 [1.98-7]		
Type of epilepsy			
Focal	68 (44.2)		
generalized	46 (29.9)		
unclassified	40 (26)		
Number of antiseizure medications(ASMs)			
One medication	75 (48.7)		
\geq two medications	79 (51.3)		
Reported change in seizure control during COVID-19 pandemic			
Stable or better seizure control	119 (77.3)		
Worse seizure control	35 (22.7)		
Type of change on ASMs during COVID-19			
No change	95 (61.7)		
change	59 (38.3)		
Infected with COVID-19 (without testing)			
No	135 (87.7)		
Yes	19 (12.3)		
Tested positive for COVID-19	4 = 4 (00 4)		
No	151 (98.1)		
Yes	3 (1.9)		

^a Data are presented as number (percent) unless otherwise indicated.

^b median [interquartile range].

^c 1 JOD= 1.42 US dollars.

3.2. Views of patients' caregivers on different issues related to COVID-19 pandemic

As shown in Table 2, two-thirds of caregivers reported (66.2%) that the COVID-19 outbreaks prevented their child from getting proper epilepsy care. 28.6% of caregivers reported difficulty giving the drugs to the child on time because of loss of daily routine during the COVID-19 pandemic. In addition, more than half (55.8%) reported difficulty obtaining antiseizure medicines during the pandemic. As shown in Fig. 1, different reasons were reported by caregivers that affected attaining the medicines to their children: 52.3% reported difficulty getting to the hospital to dispense the medicine, 36% pharmacy did not have medicine in stock, and 33.7% financial issues. On a different note, a quarter (25.3%) only believed that their children would benefit from the COVID-19 vaccine and 26% showed their willingness to vaccinate the child if the vaccine was available.

3.3. Level of seizure control of patients with epilepsy during COVID-19

77.3% of caregivers reported that seizure status remained unchanged

Table 2

Views of caregivers on different issues related to COVID-19 pandemic

Views of parents	Number (%)
Do you think that COVID -19 outbreaks prevent your child from	
getting proper epilepsy care?	52 (33.8)
• No	102 (66.2)
• Yes	
Difficulty giving ASMs to the child on time because of loss of daily	
routine during COVID-19 pandemic	110 (71.4)
• No	44 (28.6)
• Yes	
Difficulty obtaining ASMs during the pandemic	
• No	68 (44.2)
• Yes	86 (55.8)
Do you think your child with epilepsy would benefit from the COVID-	
19 vaccine?	115 (74.7)
• No	39 (25.3)
• Yes	
Are you willing to vaccinate your child with epilepsy if it is available?	
• No	114 (74)
• Yes	40 (26)

ASMs: Antiseizure medicines.

or improved for their children during COVID-19 and 22.7% reported worsened seizure control. The results of multivariate analysis are shown in Table 3. The results indicated that patients with \geq 2 ASMs had worsened seizure control compared to those who were taking one medication (OR=10.512, 95%CI=3.105-35.587, p < 0.001). In addition, caregivers who found difficulty in giving ASMs to their child had worsened seizures compared to their counterparts (OR=7.114, 95CI%= 2.004-25.259, p = 0.002). Furthermore, those living in a village had worsened seizures compared to those living in a city (OR=3.585, 95% CI=1.315- 9.776, p = 0.013). On the other hand, older patients had unchanged or improved seizures compared to younger ones (OR=0.889, 95%CI=0.799-0.990, p = 0.032).

4. Discussion

To the best of our knowledge, this is the first study that investigated prevalence and factors affecting seizure control during the COVID-19 pandemic in children with epilepsy. The results of our study revealed three main findings. First, about a quarter of patients with epilepsy had worsened seizure control during the COVID-19 pandemic in Jordan. Second, the major factors influencing the seizure worsening include the number of antiseizure medicines taken by patients, age, residency area, and the difficulty in giving the medicine because of loss of daily routine during the COVID-19 pandemic. Third, more than half of caregivers reported difficulty obtaining antiseizure medicines for their children during the pandemic.

During the COVID-19 pandemic in Jordan, 22.7% of our subjects with epilepsy reported worsened seizure control. On the other hand, the worsening seizure control in previous studies was reported in lower prevalence that varied between 6% and 18% [3, 6, 9, 18, 19]. The high prevalence in our study might be explained by the differences in sample size and age compared to other studies. In addition to that, a high percentage of caregivers reported poor epilepsy care during the COVID-19 pandemic (66.2%). This high percentage was explained by the fact that the lockdown strongly affects daily life, as well as health systems. Therefore, mandatory social distancing and the lack of effective treatments has made telemedicine the safest interactive system between patients and clinicians [16, 20]. Older patients in the present study were found to have more stable seizure control than younger ones (p =0.032). However, age did not reach statistical significance in previous studies [9, 18]. This finding can be explained by the notion that older patients are usually more independent in dealing with and handling their epilepsy and personal duties, and do not need another individual to obtain or administrate their prescribed medications.

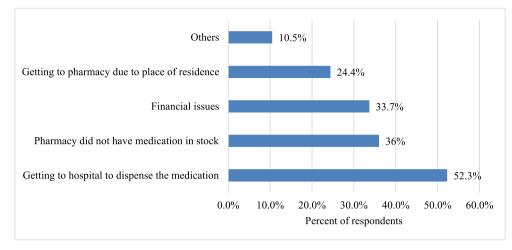


Fig. 1. Reasons behind the reported difficulty in getting antiseizure medicines during the COVID-19 pandemic.

In the current study, patients residing in a villages reported having worsened seizures in comparison to patients residing in cities. This finding is associated primarily with the lower socioeconomic status of individuals residing in a villages [13] and their pre-existing dependence on medical insurances, which primarily covers tertiary hospitals in cities. It has been reported that a higher prevalence of epilepsy and poorer seizure control were associated with low socioeconomic status. Socioeconomic disadvantages among patients with epilepsy might preclude their access to health care including specialty care (because of barriers such as cost and transportation), thus affecting seizure control [13]. Considering the implementation of complete and partial lockdowns and the inability of individuals to freely travel without restrictions between cities, it was likely that subjects could not follow up with their health care providers, where they have been insured. Moreover, the fact that public hospitals and outpatient clinics had to close for months and knowing that 74% of our subjects had a monthly income of less than 600JOD, suggests that it would be difficult for them to seek medical care at the private sector.

In the present study, patients treated with 2 and more antiseizure medicines were associated with worsened seizure control. Remarkably, it was even the strongest predicting factor of seizure worsening (p < 0.001) which is consistent with a study in Italy. This probably reflects a concomitant drug resistance and pre-existing difficulty of seizure control [3].In addition, it has been reported that the number of antiseizure medicines before the pandemic is an indicator of the severity and uncontrollable nature of epilepsy in adult and children studies [3, 6, 14, 17]. Moreover, there is possibility that seizure worsening during the pandemic resulted in prescribing more antiseizure medicines.

In the current study, 71.4% of patients' caregivers reported having given medicine to their children regularly during the COVID-19 period, whereas 28.6% of patients' caregivers reported reduced adherence to ASMs as they found difficulty in giving the medicine to their children on time because of loss of daily routine during COVID-19 pandemic. This high percentage of adequate adherence to ASMs is consistent with two previous studies from Italy [3, 6, 19]. This finding can be due to how the presence of the patients in their homes with their families contributed to better monitoring and administration of antiseizure medicines due to a lack of possible distracting factors (e.g. work, school, or recreational and leisure activities), also, the caregivers may have spent more time in taking care and monitoring their children closely at home, thus, achieving more adherence to ASMs, thus achieving better seizure control [3, 18]. Moreover, we found that difficulty in giving the medication was significantly associated (p = 0.002) with worsened seizure control.

More than half of caregivers (55.8%) reported difficulty obtaining antiseizure medicines (ASMs) for their children. Although this factor did not reach statistical significance in the current study, this number is really concerning and much higher than other countries such as Italy, (12.6% and 15.3% in adult and pediatric studies respectively) [3, 19], and New York (9.6%) where respondents reported difficulty obtaining ASMs [18]. It is worth mentioning that more than half (52.3%) of caregivers who had a problem getting ASMs attributed this to the difficulty in getting to the hospital to dispense the medications due to the implemented lockdown measures. Another reason reported by 36% of caregivers was that the pharmacy did not have medicine in stock. These findings suggest the feasibility to associate the lockdowns and travel restrictions with medication dispensing and thus affecting the appropriate management and health outcomes of chronic diseases, including epilepsy.

A previous study in Jordan reported that only 37.4% of the 3100 participants were willing to take the COVID-19 vaccine [5]. In the current study, 25.3% of caregivers believed that the vaccine will be beneficial for their children and only 26% of participants were willing to give the vaccine to their children. Further assessment to know which sources people are using, and what misconceptions they might have developed regarding the vaccine will be helpful for the development of public awareness programs surrounding this issue.

This study had some limitations. First, it is a cross-sectional questionnaire survey that records the caregivers' experiences at only one point in time and thus the answers are given retrospectively. Moreover, many patients' caregivers do not keep a seizure diary about seizure counts, severity, and hospital visits. Secondly, epilepsy is not a static disease as seizure control has natural fluctuations irrespective of the pandemic, and likely they would have experienced improved or worsened seizure control. Finally, the data was self-reported and subjected to recall and social desirability biases.

5. Conclusion

The novelty of social restriction and lockdowns caused by the COVID-19 pandemic negatively impacted the healthcare system and epilepsy care in Jordan. Among the factors studied, It was found that the number of chronically taken antiseizure medicines is the strongest predicting factor of seizure worsening in pediatric patients. In addition, the other factors affected the seizure control during COVID-19 were age, residency area, and the difficulty in giving the medication. Moreover, large number of caregivers reported an increased in difficulty obtaining antiseizure medicines for their children during the pandemic. These findings highlight the need to improve epilepsy care in Jordan through the implementation of organized and efficient telemedicine programs devoted to epilepsy care. Moreover, the alarming socioeconomic disadvantages that were aggravated by the COVID-19 pandemic should be studied to find ways to limit their effect on access to necessary medical

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Table 3

Factors affecting seizure control during the COVID-19 pandemic.

Factors ^a	Univariate analysis		Multivariate analysis		
	Stable or better seizure control NoN=119	Worse seizure control YesN=35	P value	OR (95% CI)	P value
Age ^b	10 [6-13]	4 [3-11]	0.001	0.889 (0.799- 0.990)	0.032
Gender			0.515		
Male	64 (53.8)	21 (60)			
• Female	55 (46.2)	14 (40)			
Duration of disease ^b	3 [2-7]	3 [1.2-6]	0.442		
Education of parents			0.011		0.058
School education	56 (47.1)	25 (71.4)		Ref	
University education	63 (52.9)	10 (28.6)		0.339 (0.111- 1.039)	
Income			0.026		0.213
• $< 600 \text{ JOD}^{c}$	83 (69.7)	31 (88.6)		Ref	
• $\geq 600 \text{ JOD}^{c}$	36 (30.3)	4 (11.4)		0.423 (0.109-	
				1.640)	
Employment			0.077		
• Unemployed	58 (48.7)	23 (65.7)			
• employed	61 (51.3)	12 (34.3)			
Achievement of seizure control before outbreak			0.072		
• No	35 (29.4)	16 (45.7)			
• Yes	84 (70.6)	19 (54.3)			
Residency area					0.013
• city	66 (55.5)	12 (34.3)		Ref	
• village	53 (44.5)	23 (65.7)		3.585 (1.315- 9.776)	
Health insurance			0.035		0.502
Not insured	38 (31.9)	18 (51.4)		Ref	
• Insured	81 (68.1)	17 (48.6)		1.460 (.483- 4.413)	
Number of ASMs			< 0.001		< 0.001
One medication	70 (58.8)	5 (14.3)		Ref	
• ≥ 2 medications	49 (41.2)	30 (85.7)		10.512 (3.105- 35.587)	
Difficulty giving the medicines to your child on time because of loss of daily			0.001		0.002
routine during COVID-19 pandemic	93 (78.2)	17 (48.6)		Ref	
• No	26 (21.8)	18 (51.4)		7.114 (2.004-	
• Yes				25.259)	
Difficulty obtaining ASMs during the pandemic			0.035		0.941
• No	58 (48.7)	10 (28.6)		Ref	
• Yes	61 (51.3)	25 (71.4)		0.957 (0.303- 3.026)	
Years of medications treatment ^b	3 [1-6]	3.5 [2-5.25]	0.131		
type of epilepsyFocalGeneralized			0.160		
• Unclassified	53 (44.5)	15 (42.9)			
	39 (32.8)	7 (20)			
	27 (22.7)	13 (37.1)			
Presence of comorbid condition			0.129		
• No	96 (80.7)	24 (68.6)			
• Yes	23 (19.3)	11 (31.4)			

CI: confidence interval; OR: odds ratio.

^a Data are presented as number (percent) unless otherwise indicated.

^b median [interquartile range].

 $^{\rm c}~$ 1 JOD = 1.42 US dollars.

care in similar times.

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Declaration of Competing Interest

All named authors declare that they have no potential conflict of interest.

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