

Impacts of the COVID-19 pandemic on Iranian patients with epilepsy

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Objective: To investigate the effects of COVID-19 pandemic on patients' perceptions of hardship in obtaining their drugs and if this pandemic and the social restrictions in response to that has resulted in any changes in their seizure control status. We also investigated factors potentially associated with the perceptions of difficulty in obtaining their drugs (eg, polytherapy vs monotherapy, taking imported drugs, and seizure status worsening).

Methods: We surveyed a random sample of patients with epilepsy, who were registered in our database at Shiraz Epilepsy Center, Iran, on their perceptions on two issues: (a) What has been your experience on obtaining your antiseizure medications in the past 4 weeks (compared to before)? (b) Have you experienced any changes in your seizure control status in the past 4 weeks?

Results: We included 100 patients (53 male and 47 female patients). In response to the question "Have you had any difficulties in the past 4 weeks to obtain your drugs?," 31 people (31%) expressed hardship obtaining their drugs. In response to the question "How has been your seizure control status compared with before?," six people (6%) expressed worsening of their seizure control status in the past 4 weeks. None of the patients reported symptoms of coronavirus infection.

Conclusion: About one-third of patients with epilepsy expressed significant hardship obtaining their drugs after the intensification of the COVID-19 outbreak in Iran. The current COVID-19 pandemic could be considered as a major shock to a nation that has already been under significant pressure (ie, Iran).

KEYWORDS

coronavirus, COVID, epilepsy, pandemic, seizure

1 | INTRODUCTION

Epilepsy is a common chronic neurological disorder. The mainstay of treatment in people with epilepsy (PWE) is antiseizure medication (ASM) therapy.¹ Daily medication regimen with ASM(s) is necessary for PWE, and non-adherence to this treatment strategy may have serious consequences (eg, status epilepticus and death).¹

Recently, the world has been experiencing a catastrophic phenomenon, a pandemic of coronavirus disease (COVID-19) that is caused by SARS-CoV2.² This virus has a high potential for transmission, and implementation of social distancing measures has been advocated in almost all countries to control the outbreak. Iran reported its first confirmed cases of SARS-CoV2 infection on February 19, 2020. As of April 28, 2020, there were 5806 COVID-19 deaths with more than 91 000 confirmed infections in Iran.³ Strict quarantine

measures have not been implemented in response to this outbreak in Iran; however, the government's actions included cancelation of all public events, closure of schools, and shopping centers, and banning of festival celebrations.³ In addition, people have been encouraged by the authorities and the media to stay home and cancel all unnecessary travels. This deadly outbreak has created a lot of anxiety among the people, has disrupted many businesses, and has put the healthcare system under a significant hardship. In addition, the healthcare system in Iran was already under pressure due to reimposition and intensification of the economic sanctions on Iran by the USA.⁴

The aim of the current study was to investigate the effects of COVID-19 pandemic on the patients' perceptions of hardship in obtaining their ASMs and if this pandemic and the social restrictions in response to that has resulted in any changes in their seizure control status. We also investigated factors potentially associated with the perceptions of difficulty in obtaining their ASMs (eg, polytherapy vs monotherapy with ASMs, taking imported ASMs, and seizure status worsening).

2 | METHODS

We surveyed a random sample of PWE, who were registered in our database at Shiraz Epilepsy Center, Iran, on their perceptions on two issues:

1. What has been your experience on obtaining your antiseizure medications in the past 4 weeks (compared to before)?
2. Have you experienced any changes in your seizure control status in the past 4 weeks?

In a phone call interview to 100 randomly selected patients on March 27-31, 2020, we tried to obtain the following information if patients agreed to participate and answer the questions (consented

orally): age, sex, when was your last seizure, what are your drug(s), have you had any difficulties in the past 4 weeks to obtain your drugs, how is your seizure control status compared with before, have you been staying home due to this outbreak, and have you been infected with this coronavirus? (Table 1). We retrieved their demographic and clinical data from our database. We performed univariate analyses using Fisher's exact test for the statistical analyses of the potential association between the perceptions of difficulty in obtaining ASMs and polytherapy vs monotherapy with ASMs, taking imported ASMs, and seizure status worsening. A *P* value < .05 was considered as significant. Shiraz University of Medical Sciences Review Board approved this study.

3 | RESULTS

We included 100 patients in this study (53 male and 47 female patients). Their mean age (\pm standard deviation) was 32 (\pm 13) years (range: 11-75 years), and their age at diagnosis was 21 (\pm 13) years (range: 1-65 years). All included participants were diagnosed with epilepsy before March 2014.

Forty-eight people had focal epilepsy syndromes, 26 persons had idiopathic generalized epilepsies, 22 patients had symptomatic (structural-metabolic) generalized epilepsies, and four people had unclassified epilepsies. Forty-nine patients were seizure-free for more than 1 year, and 51 people reported having one or more seizures in the past 12 months. Forty-one patients were taking one ASM, and 59 people were on polytherapy with two or more ASMs. In 28 people, the drug regimen included one or more imported ASMs, while the rest of the patients were on Iranian made drugs. Fifty-three people have strictly observed the "stay home" advice in the past 4 weeks (Table 1).

In response to the question "Have you had any difficulties in the past 4 weeks to obtain your drugs?," 31 people (31%) expressed

TABLE 1 Answers provided by 100 patients with epilepsy to the questionnaire

Have you had any difficulties in the past 4 wk in obtaining your drugs?	<ol style="list-style-type: none"> 1. No, I have stocked enough medicine: 44 2. No, I could obtain my drugs easily: 25 3. Yes, I have had hardship obtaining my drugs: 31
If you are running out of medicine, what is the reason for that?	<ol style="list-style-type: none"> 1. Pharmacy stores were closed: 0 2. Pharmacy stores did not have my drug available: 22 3. I cannot go buy my medicine, because I am afraid of getting infected with the coronavirus: 1 4. The doctor's office was closed: 8
How has been your seizure control status in the past 4 wk compared with before?	<ol style="list-style-type: none"> 1. Similar to before: 94 2. I had been free of seizures before for more than 12 mo, but I recently (in the past 4 wk) had seizures: 1 3. My seizure frequency has increased (in the past 4 wk) more than two times than before: 5
Have you been staying home due to the COVID-19 outbreak in the past 4 wk?	<ol style="list-style-type: none"> 1. Yes: 53 2. No: 47 (Why: a. 39 people going out for necessary issues; b. 8 people ignored the advices)
Have you had symptoms of (been infected with) COVID-19?	<ol style="list-style-type: none"> 1. Yes: 0 2. No: 100

TABLE 2 Factors potentially associated with experiencing hardship in obtaining antiseizure medications (ASMs)

	Having hardship (N = 31)	No hardship (N = 69)	P value
Polytherapy with ASMs	22 (71%)	37 (54%)	.1
Taking imported ASMs	11 (35%)	17 (25%)	.3
Seizure status worsening	4 (13%)	2 (3%)	.07

hardship obtaining their drugs (Table 1). In response to the question "How has been your seizure control status compared with before?" six people (6%) expressed worsening of their seizure control status in the past 4 weeks. None of the patients reported symptoms of coronavirus infection (and none was tested for the infection). Table 2 shows factors potentially associated with experiencing difficulty in obtaining ASMs among the participants.

4 | DISCUSSION

In this study, we observed that about one-third of PWE expressed significant hardship obtaining their drugs during the past 4 weeks and after the intensification of the COVID-19 outbreak in Iran. More importantly, 6% of the patients expressed worsening of their seizure control status in the past 4 weeks. Seizure control status showed a trend to be worse among those who experienced difficulty obtaining their medicine. In a similar study of 227 patients with epilepsy during the SARS (severe acute respiratory syndrome) outbreak in 2003 in Taiwan, 22% of the people did not receive their medication due to loss of contact with their healthcare providers; 12% of the patients suffered seizure status worsening during the outbreak (including two patients with status epilepticus).⁵ Therefore, it seems that history repeats itself and we should learn to be prepared for any similar circumstances in the future. The observed difficulty obtaining drugs in PWE in the current study and also in the previous outbreak of SARS in 2003 could have multiple reasons; strict quarantine measures in response to the outbreak, financial difficulties due to loss of employment, and disruption in production and distribution of drugs are some of these potential reasons. Experiencing hardship obtaining drugs in people with any chronic medical condition, including epilepsy, creates a lot of anxiety for patients, their caregivers, and their healthcare providers, and may put the lives and well-being of the patients at great risk.^{6,7} In addition, stress by itself is a common seizure trigger reported by PWE.⁸

We observed a similar scenario a couple of years ago and after reimposition and intensification of the economic sanctions on Iran in 2018.⁴ Back then, 53% of the patients expressed significant difficulty and frustration obtaining their drugs and 30% perceived breakthrough seizures or worsening of their seizures after reimposition

of the economic sanctions.⁴ Therefore, the current outbreak has increased hardship on the people, who were already experiencing significant difficulties, and the current COVID-19 pandemic could be considered as a major shock to a nation that has already been under significant pressure.

Since none of our study participants contracted COVID-19, we cannot comment on the potential direct effects of SARS-CoV2 infection on patients with epilepsy. However, neurotropic and neuroinvasive capabilities of coronaviruses have been described in humans and coronavirus infections have been associated with neurological manifestations including seizures and change in mental status.⁹ Some patients with COVID-19 may have non-specific neurological symptoms, such as confusion and headache, and a few may show more specific neurological manifestations, such as seizures.⁹

This study has some limitations including its self-report design. This is a study with a modest objective and a questionnaire that addressed specific issues (not a comprehensive survey since we evaluated a limited number of factors; eg, we did not assess their anxiety/stress). Moreover, patients did not routinely keep a seizure journal (diary) and the changes in their seizure frequency were based on their recall and estimate (the seizure control information was only qualitative).

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CONFLICT OF INTEREST

Ali A. Asadi-Pooya, M.D. received honoraria from Cobel Daruo, RaymandRad and Tekaje; Royalty: Oxford University Press (Book publication). Others received none.

AUTHOR CONTRIBUTIONS

Ali A. Asadi-Pooya, M.D. designed and conceptualized the study; analyzed the data; and drafted and revised the manuscript. Mohsen Farazdaghi, M.D. and Mehdi Bazrafshan, M.D. collected the data and revised the manuscript. The authors conducted the statistical analyses.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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