



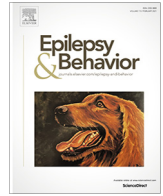
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## Brief Communication

## Is the risk of COVID-19 contraction increased in patients with epilepsy?

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## ABSTRACT

**Objective:** The aim of the current study was to investigate the rates of contracting COVID-19 in various populations to provide evidence on the susceptibility of patients with epilepsy (PWE) to contracting symptomatic COVID-19.

**Methods:** We surveyed a random sample of three groups of people: patients with epilepsy, people with psychiatric problems, and a group of the general population. The survey included four general questions (age, sex, education, and medical/psychiatric problem) and four COVID-19 specific questions (contracting COVID-19, relatives with COVID-19, wearing a face mask, and frequent hand washings).

**Results:** Three hundred and fifty-eight people were surveyed (108 healthy individuals, 154 patients with epilepsy, and 96 patients with psychiatric problems). Thirty-eight (11%) people had a history of COVID-19 contraction. The only factor that had a significant association with COVID-19 contraction was a relative with COVID-19 (Odds Ratio: 5.82; 95% Confidence Interval: 2.85–11.86;  $p = 0.0001$ ). Having epilepsy did not increase the risk of COVID-19 contraction.

**Conclusion:** Symptomatic COVID-19 does not seem to be more likely in PWE. The single most important factor associated with contracting COVID-19 is a close relative with this infection. Isolation of people with SARS-CoV-2 infection and observation of their close contacts may reduce the risk of secondary infections.

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## 1. Introduction

Since the beginning of 2020, the world has been experiencing a devastating and fatal pandemic of a coronavirus disease (COVID-19) caused by SARS-CoV-2 [1]. This virus primarily targets the human respiratory system; however, a severe illness characterized by acute respiratory distress syndrome, multi-organ failure, neurological involvement, and death may happen [1,2]. Major risk factors for a more severe illness have been identified as older age, chronic respiratory problems, diabetes mellitus (DM), and hypertension, among others [1]. Patients with epilepsy (PWE) may have any of these medical comorbidities [3]. In addition, one study suggested that the cumulative incidence of COVID-19 in PWE was higher compared with that in people without epilepsy and the total case fatality rate was also higher in PWE compared to that in those without epilepsy [4]. On the other hand, in another study, among 5700 PWE, who were managed at the studied centers, only 14

patients tested positive for SARS-CoV-2, without any impacts on their epilepsy [5].

Therefore, the evidence on the susceptibility of PWE to contracting COVID-19 is scarce and contradictory. The aim of the current study was to investigate the rates of contracting symptomatic COVID-19 in various populations to provide evidence on the susceptibility of PWE to contracting symptomatic COVID-19.

## 2. Methods

In this cross-sectional study, we surveyed a random sample (easy sampling, based on consecutive referrals) of three groups of people during September 2020: people with epilepsy (referring to the neurology clinic at Shiraz University of Medical Sciences), people with psychiatric problems (people with depression or anxiety referring to the psychiatry clinic at Shiraz University of Medical Sciences), and a group of the general population without a history of any chronic medical/psychiatric problems. Shiraz is the largest city in south Iran with a population of 1,650,000 [6]. Shiraz University of Medical Sciences is a major university in the nation and is a main medical referral center for many people (around 20

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million) living in south Iran. The inclusion criteria were adults ( $\geq 18$  years), literacy ( $>5$  years of education), and any of the above medical/psychiatric problems (or none). The exclusion criteria included intellectual disability, psychosis, and unwillingness to participating in the study.

The survey included four general questions [age, sex, education (school vs. college), and medical/psychiatric problems]. It also included four COVID-19 specific questions [contracting COVID-19 since the start of the pandemic (self-declared), relatives (i.e., spouse, children, siblings, parents) with COVID-19 since the start of the pandemic (self-declared), wearing a face mask in crowded places, and frequent hand washings (10 times or more per day; arbitrarily)]. The COVID-19 specific questions were based on self-declarations for two reasons: the survey was anonymous and also for the convenience.

Statistical analyses were performed using independent *t*-test, Fisher's exact test, Pearson chi-square test, and Bonferroni correction test. Variables with a *p* value  $<0.1$  in univariate tests were assessed in a logistic regression model. Odds ratio and 95% confidence interval (CI) were calculated. A *p* value (2-sided) less than 0.05 was considered as significant. The Shiraz University of Medical Sciences Review Board approved this study.

### 2.1. Availability of data and materials

The dataset is confidential and could not be shared.

## 3. Results

The total number of participants was 358 people (108 healthy individuals, 154 patients with epilepsy, and 96 patients with psychiatric problems). Since the survey was anonymous and voluntarily, we do not know the number of people who refused to participate. The mean age of the participants was 32 years (standard deviation: 12 years) (range: 18–82 years). They included 209 women and 149 men. Totally, 38 (11%) people had a history of COVID-19 contraction. Table 1 shows the associated factors with contracting COVID-19 in this study. The only factor that had a significant association with COVID-19 contraction was close contact with another person with this disease (a relative with COVID-19). Having epilepsy did not increase the risk of COVID-19 contraction compared to that in healthy individuals and those with psychiatric problems. Hand washing frequency showed a trend to be associated with contracting COVID-19.

We then analyzed the association between contracting COVID-19 and variables with a  $P < 0.1$  in a binary logistic regression model. The model that was generated by regression analysis was significant ( $p = 0.0001$ ) and could predict contracting COVID-19 in 89% of the patients. Within this model, a history of a relative with COVID-19 (OR: 5.82; 95% CI: 2.85–11.86;  $p = 0.0001$ ) was significantly associated with contracting COVID-19.

**Table 1**  
Factors associated with contracting COVID-19.

	People with COVID-19 (N = 38)	People without COVID-19 (N = 320)	P value
Sex (Female: Male)	21: 17	188: 132	0.72
Mean age $\pm$ Standard deviation (years)	31 $\pm$ 11	32 $\pm$ 12	0.74
Education (college)	17 (45%)	147 (46%)	1.00
Chronic disease (none, epilepsy, psychiatric)	16: 14: 8	92: 140: 88	0.23
Relatives with COVID-19	21 (55%)	53 (17%)	<b>0.0001</b>
Not wearing a face mask in crowded places	3 (8%)	23 (7%)	0.74
No frequent hand washings (10 times or more per day)	24 (63%)	149 (47%)	0.06

\*After Bonferroni correction, a significant predictive value is 0.007. The significant *p* values are in bold.

## 4. Discussion

While our study is limited due to the lack of confirmation of the COVID-19 contraction by scrutinizing the test results (some patients, who declared to have, may not have had COVID-19 and vice versa, milder versions of COVID-19 would have been undercounted), we can conclude that PWE appear to be at no higher risk for developing symptomatic COVID-19 than our other control groups. This observation corroborates a previous report [5]. However, these two studies contradict another report that suggested an increased risk of contracting COVID-19 in PWE [4]. The results of the latter study were obtained based on a small number of PWE (21 persons) and should be interpreted with caution. Furthermore, there is no plausible biological reason to assume that PWE are at increased risk of contracting viral infections, including COVID-19; such evidence does not exist for influenza or other viral infections, to the best of our knowledge. Having said that, some special populations with epilepsy may be at higher risk of contracting (severe) COVID-19 and other infections; being on immunosuppressive therapy (e.g., for autoimmune epilepsy, organ transplantation, etc.) is an example [7]. Furthermore, we do not really know if PWE show a similar severity of COVID-19 illness when they have comorbidities such as diabetes, hypertension, etc. Finally, PWE may have vitamin D deficiency, [8] and this may be a risk factor for a more severe illness with COVID-19 [9]. These are interesting avenues for further studies. Many patients with epilepsy may develop bone density problems due to anti-seizure medications (ASMs) [10]. This study was not designed to assess ASM or other medication use and the COVID-19 risk and severity. However, given the observations and data on Vitamin D status and COVID-19 severity [9], if some patients with epilepsy were advised to be receiving vitamin D supplementation to mitigate the ASM-induced bone density loss, it would be interesting to compare this group with patients with epilepsy who are not on Vitamin D supplementation with regard to the COVID-19 risk and severity. In general, our recommendation in Iran for vitamin D supplementation in our patients with epilepsy has been to prescribe daily supplements for those who are taking enzyme-inducing ASMs or valproate for more than a couple of years.

In the current study, we also observed that the single most important factor associated with contracting COVID-19 was a close relative to this infection (OR: 5.82). A previous study suggested that the household secondary attack rate of COVID-19 is about 12% if household contacts are defined as all close relatives, and 17% if household contacts only include those at the same residential address as the case. On average, a COVID-19 patient infected 0.5 of their close contacts. Had isolation not been implemented, this number would increase to 0.6 [11].

Therefore, isolation of people with SARS-CoV-2 infection and observation of their close contacts (including those with epilepsy), in addition to population-based measures, may reduce the risk of secondary infections and curb the spread of COVID-19 [12].

## Contributions

Ali A. Asadi-Pooya: Designed and conceptualized the study; analyzed the data; drafted and revised the manuscript.

Others: Collected the data; revised the manuscript.

## Disclosures

Ali A. Asadi-Pooya, M.D.: Honoraria from Cobel Daruo, RaymondRad, Sanofi, Actoverco, and Tekaje; Royalty: Oxford University Press (Book publication). Others: none.

## Role of the funding source

Shiraz University of Medical Sciences had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yebeh.2020.107734>.

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