Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Seizure: European Journal of Epilepsy 94 (2022) 136–141

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Epilepsy is overrepresented among young people who died from COVID-19: Analysis of nationwide mortality data in Hungary

Réka A. Horváth [a], Zsófia Sütő [a], Balázs Cséke [a], Dániel Schranz [a], Gergely Darnai [a,b,c], Norbert Kovács [a,b], Imre Janszky [d,e], József Janszky [a,b,*]

[a] Department of Neurology, Medical School, University of Pécs, Rét u. 2, H-7623 Pécs, Hungary
[b] MTA-PTE Clinical Neuroscience MRI Research Group. Hungary, Ifjúság u. 20., H-7624 Pécs, Hungary
[c] Department of Behavioral Sciences, Medical School, University of Pécs, Rét u. 2, H-7623 Pécs, Hungary
[d] Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Håkon Jarls gate 11 and Mauritz Hanssens gate, 7491 Trondheim, Norway
[e] Regional Center for Health Care Improvement, St Olav's Hospital, Trondheim, Norway

ARTICLE INFO

Keywords:
Epilepsy
COVID-19
Age
Death
Intellectual disability
Hungary

ABSTRACT

Background: : Studies examining epilepsy as a COVID-related death risk have come to conflicting conclusions. Our aim was to assess the prevalence of epilepsy among COVID-related deaths in Hungary.
Methods: Each COVID-19 infection case is required to be reported on a daily basis to the National Public Health Center of Hungary. This online report includes the beginning and end of the infection, as well as information on comorbidities. Death during infection is regarded as COVID-related. The anonymized data of each deceased patient are published on an information website (www.koronavirus.gov.hu) and provides up-to-date information on each patient with the date of death, the patient's sex, age, and chronic illness.
Results: There were 11,968 patients who died of COVID-19 in Hungary between 13 March 2020 and 23 January 2021. Among 11,686 patients with no missing values for comorbidities, 255 patients had epilepsy (2.2%). Epilepsy was much more common among those who died at a young age: 9.3% of those who died under the age of 50 had epilepsy, compared with only 1.3% in those over the age of 80. The younger an age group was, the higher was the prevalence of epilepsy.
Conclusion: Patients who died of COVID-19 under the age of 50 were 10 to 20 times more likely to have epilepsy than what would have been expected from epidemiological data. Our results highlight the need for increased protection of young people with epilepsy from COVID-19 infection and the development of a vaccination strategy accordingly.

1. Introduction

The COVID-19 epidemic erupted in 2019 has increased mortality worldwide, especially in European countries [1]. The best established risk factors for death due to COVID-19 are older age, hypertension, diabetes, obesity, and malignancy [2, 3, 4].

Little is known about the risk of people with epilepsy (PWE) dying from COVID-19. Cabezudo-García et al. found that epilepsy was an independent risk factor for COVID-related death, with an odds ratio (OR) of 5.1 for mortality [5]. Other studies found no association between epilepsy and mortality from COVID-19 [6,7,8]. Clift et al. found a 1.6 hazard ratio for death from COVID-19 in PWE [4]. The difference in the estimates of the effect of epilepsy on COVID-19 mortality can be explained by different testing protocols, health facility structure of different countries as well as difference in population characteristics (including age, sex, socioeconomic status, and comorbidities) in these studies.

One of the key comorbidities may be intellectual disability (ID). Young people with ID who got COVID-19 have a higher case-fatality rate compared to young people without intellectual disability, suggesting that a disproportionate percentage of adults with ID dying at younger ages due to COVID-19 [9]. A non-per-reviewed study (published only on

* Corresponding author at: Department of Neurology, Medical School, University of Pécs, Rét u. 2, H-7623 Pécs, Hungary
E-mail addresses: horvath.reka@pte.hu (R.A. Horváth), suto.zsofia@pte.hu (Z. Sütő), cseke.balazs@pte.hu (B. Cséke), schranz.daniel@pte.hu (D. Schranz), darnai.gergely@pte.hu (G. Darnai), kovacs.norbert@pte.hu (N. Kovács), imre.janszky@ntnu.no (I. Janszky), janszky.jozsef@pte.hu (J. Janszky).

https://doi.org/10.1016/j.seizure.2021.11.013
Received 31 August 2021; Received in revised form 27 October 2021; Accepted 17 November 2021
Available online 1 December 2021

preprint site medRxiv at the time of the preparation of this manuscript) suggested that ID may increase the chance of COVID-related death by 8-fold [10]. Analyzing comorbidities of 82 COVID-related deaths in ID patients, Perera et al. found that epilepsy was the most frequent co-morbidity (almost half of their cohort had epilepsy) [11]. In Down syndrome (DS), there may be a 10-fold increased risk for COVID–related death [12] or hospitalization [13]. Moreover, a non-per-reviewed study (published only on preprint site medRxiv at the time of the preparation of this manuscript) found that hospitalized DS patients were on average 10 years younger than non-DS patients and 50% of them had epilepsy [13]. In contrast, the estimated prevalence of epilepsy in Down syndrome is 15–17% in general [14,15].

In this study, we analyzed the data of all 11,968 patients who died of COVID-19 in Hungary from March 2020 to January 23, 2021. Our aim was to assess the prevalence of epilepsy in those who have died of COVID-19 and whether this prevalence was different across different age groups.

2. Methods and materials

2.1. COVID-19 epidemic in Hungary

A special feature of the COVID-19 epidemic in Hungary was that the incidence of COVID-19 in the first wave of the epidemic (March–June 2020) was low, which was also reflected in the low COVID-related mortality. In contrast, the second wave, which began in September 2020, was much stronger, severely straining the healthcare capacities.

Overall, at the population level, COVID-related mortality was very high in Hungary. According to data as of March 23, 2021, the COVID-related mortality rate is 191 per 100,000 inhabitants, which is the 5th worst figure in the ranking of countries in the world [16]. The epidemic persists at the time of writing of this paper.

2.2. Analysis of the Hungarian COVID-related death data

In Hungary, each COVID-19 infection case is required to be reported on a daily basis to the *National Public Health Center*. The report is provided by GPs (if the patient is not hospitalized) or epidemiological services and physicians working in COVID centers of the hospitals (if the patient is hospitalized). This online report includes the beginning and end of the infection, and also if the patient dies during the infection. Serious chronic disorders of the patients - which were present before infection - should be reported on the basis of ICD-10. For this report, COVID-19 infection is defined as positive PCR or rapid antigen test or a typical clinical picture. Death during infection is regarded as COVID-related.

The anonymized data of each deceased patient are published on the information website of the National Public Health Center (www.koronavirus.gov.hu). This website contains only the data of the deceased patients related to COVID-19 infection. Deceased patient data can be freely downloaded from this website. Thus, the published database provides up-to-date information on each patient with the date of death, the patient's sex, age, and chronic illness. An epileptic patient can be considered any patient in whom it was included in the comorbidities. The database does not contain information on the type or etiology of epilepsy. Our study conforms with World Medical Association Declaration of Helsinki. The approval of local ethics committee was not needed as anonymized patient data is freely available on the information website of the National Public Health Center.

In our study, we analyzed data from patients who died in relation to COVID-19 between March 13, 2020 (when the first patient died of confirmed COVID-19) and January 23, 2021 (when we closed the data collection). We examined the prevalence of epilepsy in this population and the association of epilepsy with ID, DS, history of stroke, and brain tumor as known comorbidities for adult epilepsy and known risks factors for COVID-related death [4].

2.3. Statistical methods

For the analysis of the categorical data, Chi-square or Fisher's exact tests were carried out. For continuous variables, the independent samples Student's t was used. To identify which variables were associated with epilepsy independently, a logistic regression analysis was performed. All statistical analyses were performed using the IBM SPSS software package (version 27, IBM Inc., Armonk, NY, USA).

2.4. Data availability and ethical consideration

The individual data are published in a public anonymized database (www.koronavirus.gov.hu) accessible to everyone. Request for output of statistical analyses will be available from the corresponding author, [JJ], upon reasonable request.

3. Results

According to the data published on www.koronavirus.gov.hu, 11,968 patients died of COVID-19 in Hungary between 13 March 2020 and 23 January 2021: 50.8% of them were men, 49.2% were women. The average age was 75.7, (range: 18–104) years. We have available information on chronic disease in 97.6% of the deaths (data were missing in 282 cases). Among 11,686 patients with no missing values for comorbidities, 255 patients had epilepsy (2.2%). Table 1 shows the characteristics of patients with and without epilepsy who died from COVID-19. Young age, male sex, intellectual disability (ID), Down syndrome (DS), brain tumor, and history of stroke were associated with the presence of epilepsy. There was no difference in mortality between waves 1 and 2 of the epidemic. Epilepsy was present in 33% of ID patients (28 out of 84) and DS patients (5 out of 15) who died of COVID-19.

Because previous studies [9,13] have shown that ID and DS occurred primarily in younger age groups among those who died from COVID-19, therefore, in the present study, the presence of epilepsy and epilepsy-associated disorders were analyzed separately in different age groups.

Epilepsy was much more common among those who died at a young age: 9.3% of those who died under the age of 50 had epilepsy, compared with only 1.3% in those over the age of 80. As predicted, COVID-related death in ID was also strongly age-dependent: ID was present in 10% of deaths occurred under the age of 50 and only in 0.1% of those who died

Table 1
Basic characteristics of epilepsy vs. non-epilepsy patients who died from COVID-19.

	All patients[a] $N = 11,686$	Epilepsy patients $N = 255$	Patients without epilepsy $N = 11,431$	*p value*
Age (y, mean±SD)	75.73±11	68.24±15	75.89±12	<0.001
	N (% of all patients)	N (% of epilepsy patients)	N (% of patients without epilepsy)	
Male sex	5912 (50.6%)	150 (58.8%)	5762 (50.4%)	<0.01
Died during the first wave[b]	674 (5.8%)	12 (4.7%)	662 (5.8%)	0.45
Intellectual disability	84 (0.7%)	28 (11.0%)	56 (0.5%)	<0.001[c]
Down syndrome	15 (0.13%)	5 (2.0%)	10 (0.09%)	<0.001[c]
Brain tumor[d]	55 (0.5%)	8 (3.1%)	47 (0.4%)	<0.001[c]
History of stroke	1072 (9.2%)	56 (22.0%)	1016 (8.9%)	<0.001

[a] Only patients without missing information on chronic diseases were included.
[b] Wave 1: March 2020-May 2020, wave 2: September 2020-January 23, 2021.
[c] Fisher's exact test was used.
[d] All types of brain tumors were included (primary, metastasis).

over the age of 80 (see Table 2). Table 2 shows that the younger an age group was, the higher was the prevalence of epilepsy.

Because epilepsy and ID were strongly associated with each other (see Table 1), and in both cases, mortality was age-dependent (see Table 2), this might suggest that this age dependence was merely due to the frequent co-occurrence of ID and epilepsy. Therefore, in the next step, we excluded patients with ID and again looked at the prevalence of epilepsy by age groups. Fig. 1 shows that this age-dependency was also present in the non-ID population: 5.3% of patients under 50 years of age had epilepsy.

The high number of deaths may reflect an endemic infection in 1–1 care facility / hospital, but unfortunately no direct information was available on this issue. To approach the issue at some level, we hypothesized that infection in a care facility may be characterized by a higher mortality rate for a given time period, so we also looked at mortality broken down by months. In the months with prominent COVID-related mortality (October, November, December in 2020; January in 2021), the incidence of epilepsy among deaths was 2.0–2.5%, i.e., we did not see outstanding fluctuations in mortality rates according to month. Similarly, there was no outstanding mortality according to month for ID and other epilepsy-associated disorders either (see Supplementary Table S1).

Because there were more men than women among the deceased epilepsy patients, we looked at the sex differences in the total population, in those who died with epilepsy, and with epilepsy-associated disorders (Supplementary Table S2). The majority of people over 80 years of age who died from COVID-19 were women, while in the other age groups the majority were men. In epilepsy, male predominance was most pronounced in the under-50 and 60–69 age groups, while there was no sex difference in the other age groups, where the female-to-male ratio was around 50%.

We performed a multivariable logistic regression in order to identify which variables were associated with epilepsy independently. All variables shown in Table 1 were included except for Down syndrome as all patients with DS also had ID. Age was divided into two categories: age<50 vs age≥50. Logistic regression analysis showed that the ***intellectual disability*** ($p<0.001$, odds ratio for epilepsy [OR]= 19.3, 95% confidence intervals [CI]: 11.4 – 32.9)***, brain tumor*** ($p<0.001$, OR= 6.7, 95% CI:3.1–14.8)***, history of stroke*** ($p<0.001$, OR= 3.2, 95% CI:2.3–4.3)***, age<50*** ($p<0.001$, OR= 2.8, 95% CI:1.8–4.5), *and* ***male sex*** ($p = 0.02$, OR= 1.36, 95% CI:1.1–1.8) were independently associated with presence of epilepsy in this COVID-related death population**.**

4. Discussion

The main findings of our study is that (1) There were 255 people with epilepsy (PWE) who died due to COVID-19 between March 13, 2020 and January 23, 2021; which means that epilepsy occurred in 2.2% of COVID-related deaths in Hungary. (2) Epilepsy was much more common among those who died at a young age: 9.3% of those who died under the age of 50 had an epilepsy, compared with only 1.3% in those over the age of 80.

Prevalence of epilepsy in high-income countries is about 0.52% [17]. According to a systematic review, the median prevalence of epilepsy in Europe is 0.52% (ranging 0.33% to 0.78% according to different countries) [18]. Unfortunately, we do not have Hungarian epidemiological data on epilepsy. Of the countries in the Eastern part of Europe ("post-communist region"), epidemiological studies on epilepsy have been performed in Croatia [19] and Estonia [20]. Tables 3-5 show the epilepsy prevalence in Europe, Croatia, and Estonia by age. Comparing these prevalence data with our COVID-related death data, it can be seen that the prevalence of epilepsy in the *overall* COVID-related death population was slightly higher than expected. Conversely, *patients who died of COVID-19 under the age of 50 were 10 to 20 times more likely to have epilepsy than what would have been expected from epidemiological data* (Tables 3-5). This is in agreement with a systematic review which found that 10% of children critically ill due to COVID-19 had epilepsy [21].

The effect of epilepsy on mortality is age-dependent. PWE have a higher risk of premature death than the general population [22]. The overall standardized mortality ratio (SMR) in epilepsy is between 1.7 and 3 [22,23,24]. All-cause mortality in epilepsy is most marked in the younger age groups [22,24]: the SMR in adult PWE in the 40–60 age group is 2-times higher than in older (>60 years) age groups [22,24]. This can be explained by that epilepsy in the elderly is more benign, usually responds better to antiepileptic drugs [25,26], and some causes of deaths specific to epilepsy typically occur at a younger age. For example, one of the leading causes of death from epilepsy, the SUDEP (sudden unexplained death in epilepsy) is strongly age-dependent: nearly 90% of SUDEP cases occur under the age of 50 [27,28].

Some studies suggest that the risk factors for COVID-19 mortality in young age may be different from those in old age. For example, severe obesity increases mortality 5.1-fold in the under-50 age group, while only 1.6-fold in the over-50 age group [29]. COVID-related death predominantly affects the elderly [2,3]. Therefore, young adult deaths due to COVID-19 are less represented in epidemiological studies: In the first wave of COVID infection in the U.S., only 2.9% of deaths were among those under 45 years of age [30]. Thus, a disease which increases mortality in young adulthood but not in older ages may not appear as a risk factor in COVID-19 mortality studies that are not stratified for age. To the best of our knowledge, no studies investigated COVID-related mortality in epilepsy specifically among younger adults. This may be one of the reasons why previous studies examining epilepsy as a COVID-related death risk have come to conflicting conclusions [4,5,6,7,8]. Concerning our study, COVID-related death in young adults was also relatively rare: only 2.86% of cases were under 50 years of age. However, because we had access to data of almost 12,000 COVID-related deaths, we were able to examine COVID-related mortality by age groups.

One of the explanations of our findings may be the indirect effect of epilepsy on infections. The main feature of COVID-19 is pneumonia. Pneumonia is one of the leading causes of premature death in PWE in all age groups with a cause-specific SMR of 4–6 [22,23,24,31]. Some authors suggest that epilepsy and antiepileptic drugs may lead to suppression of the immune system with a subsequent risk of more severe infections [22, 32]. Another explanation may be that some epilepsy-related comorbidities are also risk factors for COVID-related death. Previous studies [9,13] and our own data also show that intellectual disability (ID) is overrepresented among young deaths in COVID-19. Because epilepsy and ID are strongly associated with each other, this might suggest that the high prevalence of epilepsy in young adults who died of COVID-19 is merely due to the frequent

Table 2
Prevalence of epilepsy and epilepsy-related comorbidities among the deceased patients in different age groups.

Age groups	Number of all patients	Epilepsy (N,% of all patients in the age group)	Intellectual disability	Down syndrome	Brain tumor	history of stroke
all age groups	11,686	255 (2.2%)	84 (0.7%)	15 (0.13%)	55 (0.5%)	1072 (9.2%)
age 49 or younger	334	31 (9.3%)	33 (9.9%)	9 (2.7%)	5 (1.5%)	13 (3.9%)
50–59 years	696	33 (4.7%)	21 (3%)	5 (0.72%)	6 (0.9%)	36 (5.2%)
60–69 years	2189	66 (3%)	13 (0.6%)	1 (0.047%)	13 (0.6%)	159 (7.3%)
70–79 years	3517	61 (1.7%)	12 (0.2%)	0 (0%)	20 (0.6%)	336 (9.6%)
≥80 years	4950	64 (1.3%)	5 (0.1%)	0 (0%)	11 (0.2%)	528 (10.7%)

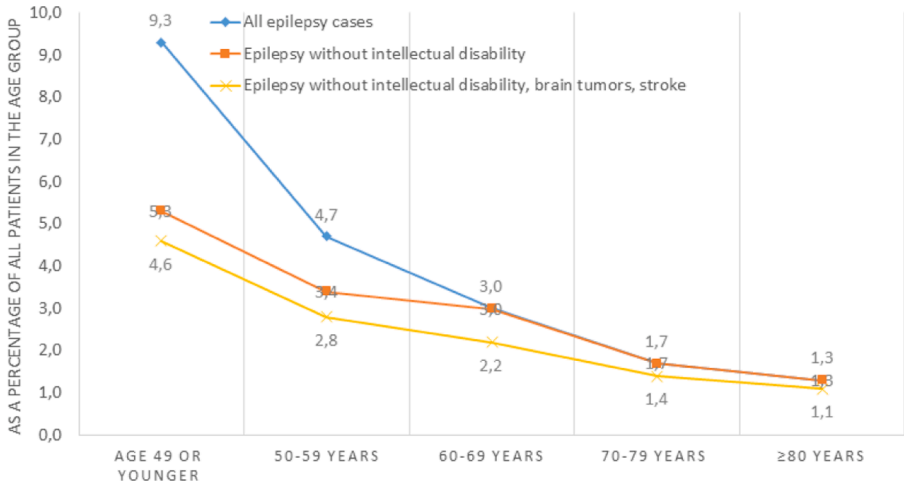

Fig. 1. Prevalence of epilepsy in different age groups with and without comorbidities.

Table 3
Comparison of prevalence of adult epilepsy in Europe vs. presence of epilepsy in Hungarian COVID-related deaths in different age groups (using the data from Table 3 from **reference 18**)[18].

Age groups	Estimated prevalence of epilepsy in Croatia	Patients with epilepsy among those who died of COVID-19 in Hungary (% of all patients in the particular age group)
19–45 years	0.5% (CI:0.47–0.53)	10.5% ($N = 21/200$)
46–65 years	0.47% (CI:0.44–0.5)	4.1% ($N = 77/1877$)
>65 years	0.44% (CI:0.41–0.48)	1.6% ($N = 157/9608$)

Table 4
Comparison of prevalence of adult epilepsy in Croatia vs. presence of epilepsy in Hungarian COVID-related deaths in different age groups (using the data from Table 2 from **reference 19**)[19].

Age groups	Estimated prevalence of epilepsy in Croatia	Patients with epilepsy among those who died of COVID-19 in Hungary (% of all patients in the particular age group)
19–45 years	0.5% (CI:0.47–0.53)	10.5% ($N = 21/200$)
46–65 years	0.47% (CI:0.44–0.5)	4.1% ($N = 77/1877$)
>65 years	0.44% (CI:0.41–0.48)	1.6% ($N = 157/9608$)

Table 5
Comparison of prevalence of adult epilepsy in Estonia vs. presence of epilepsy in Hungarian COVID-related deaths in different age groups (using the data from Table 1 from **reference 20**)[20].

Age groups	Estimated prevalence of epilepsy in Estonia	Patients with epilepsy among those who died of COVID-19 in Hungary (% of all patients in the particular age group)
20–29	0.43% (CI:0.33–0.53)	4% ($N = 1/25$)
30–39	0.57% (CI:0.45–0.69)	12.9% ($N = 9/70$)
40–49	0.6% (CI:0.46–0.74)	8.8% ($N = 21/239$)
50–59 years	0.61% (CI:0.47–0.75)	4.7% ($N = 33/696$)
60–69 years	0.63% (CI:0.48–0.78)	3.0% ($N = 66/2189$)
70–79 years	0.22% (CI:0.1–0.34)	1.7% ($N = 61/3517$)
≥80 years	0.48% (CI:0.23–0.73)	1.3% ($N = 64/4950$)

co-occurrence of ID and epilepsy. However, if we exclude ID cases from our COVID-related death population, the prevalence of epilepsy is 5.3% in the under-50 age group (Fig. 1), which is still an order of magnitude higher than the prevalence of adult epilepsy in general population of the same age. In our study, 11% of all PWE had ID, while the occurrence of ID was 43% among those PWE who died under age 50. Conversely, epilepsy was present in 33% of ID patients died of COVID-19. In the study of Perera et al., epilepsy was present in 44% of ID patients who died of COVID-19 [11], which is twice as much as expected in a general sample of ID people where the prevalence of epilepsy is around 22% [33]. These suggest that both epilepsy and ID might increase the risk of death due to COVID-19 but, we cannot rule out that the co-occurrence of epilepsy and ID further increases the risk of death than the two conditions alone.

Some other epilepsy-related comorbidities beyond ID may also play a role. Brain tumors are one of the main causes of adult epilepsy, while neoplasms are risk factors for COVID-related death [2]. Stroke is the probably the leading cause of epilepsy in adulthood [34], moreover, epilepsy increases the risk of subsequent stroke [35]. History of stroke is a risk factor for COVID-related death [4]. However, if we exclude cases with ID, stroke, and brain tumor from our COVID-related death population, the prevalence of epilepsy is still 4.6% in the under-50 age group which is still an ca. 8-times higher than the expected prevalence of epilepsy in this age group (Fig. 1), indicating that these comorbidities alone cannot explain the overrepresentation of epilepsy among young adults died of COVID-19.

Cabezudo-García et al. found a marked increase in the fatality rate only in those PWE who were hospitalized, suggesting that only PWE with COVID-19 severe enough to require hospitalization were vulnerable [5]. This may raise the possibility of that care for epilepsy in hospital-based COVID centers was inadequate, as an epilepsy specialist could not always be involved in care due to the high workload. In our study, however, there was no apparent differences in prevalence of epilepsy among COVID-related deaths during Wave 1 (March–June 2020, which barely burdened health care in Hungary) vs. the Wave 2 (September 2020-January 2021 which had a heavy load on health capacities) (Table 1). There were no outstanding fluctuations in mortality rates by month (Supplementary Table S1). However, we shall emphasize that the number of deaths during Wave 1 was very low, making such comparisons difficult.

We found that there were nearly 40% more men than women among PWE who died of COVID-19. This may be due to the fact that epilepsy is generally more common in men [18], and partly because epilepsy may be more severe in men [36]. However, the sex difference may also reflect that the majority of those who died of COVID-19 at a young age were men in our study population (Supplementary Table S2).

5. Limitations

(1) There are no available reliable epidemiological data on epilepsy in Hungary. Hungary is located in Eastern-Central Europe (“post-communist region”). The prevalence of epilepsy in the immediate neighbor Croatia and in Estonia (both are located in the same region of Europe as Hungary) is similar, and does not differ significantly from general European prevalence of epilepsy [18, 19,20]. Thus, we can assume that the epilepsy prevalence data in Hungary may also be similar.

(2) The diagnosis on chronic disorders in people who died of COVID-19 was provided to the National Public Health Center by GPs or physicians working at the COVID centers, so the diagnosis of epilepsy may not be completely reliable, although in Hungary the diagnosis of epilepsy in general is made by neurologists, often with the involvement of epilepsy centers [37].

(3) We examined the absolute number of COVID-related deaths, thus, our study does not provide any direct information on whether epilepsy is a risk factor for COVID-related death. The absolute number of COVID-related deaths in epilepsy depends on the incidence rate of the infection in the population, individual susceptibility to a serious infections and the probability of fatal outcome of a serious illness. At the same time, however, the absolute number of deaths may demonstrate the magnitude of the effect of COVID-19 pandemic on epilepsy community in a country in many ways better than separate data on susceptibility, predisposition to a serious illness and the risk of a death during serious illness. The absolute number of deaths were those that highlighted that young PWE may be much more affected by COVID-19 than previously thought, as nearly 10% of young deaths had epilepsy, 10–20 times more than what we could have expected from epidemiological studies. The exact mechanism of the causal relationship between death of young adult epileptic patients and COVID-19 infection cannot be established with certainty based on our results.

(4) The database does not contain information on the type or etiology of epilepsy, thus we have no results on mortality data for different subgroups of epileptic patients [38].

6. Conclusions

Based on our data,epilepsy is overrespresented among among young patients who died from COVID-19.

Our results highlight the need for increased protection of young PWE from COVID-19 infection and the development of a vaccination strategy accordingly. We suggest that the risk factors for COVID-19 mortality in young adults may be different than in the general population. Further studies are needed that should focus specifically on COVID-19 mortality in young adults.

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Financial disclosure

RAH, ZS, BC, DS, GD, IJ have nothing to disclose. **NK** received <1000 EUR consultation fees from Hungarian subsidiaries of Medtronic. Boehringer Ingelheim. Novartis. GlaxoSmithKline. UCB, Krka and Abbvie. Regarding this study, the author did not receive any corporate funding. **JJ** received <1000 EUR consultation fees from Hungarian subsidiaries of UCB, Richter and Gerot. Regarding this study the author did not receive any corporate funding

Conflicts of Interest

None

Acknowledgments

This study was supported by the Hungarian Brain Research Program (2017-1.2.1-NKP-2017-00002), NKFIH EFOP-3.6.2-16-2017-00008 government-based funds. Our research was partly financed by the Higher Education Institutional Excellence Program of the Ministry of Human Capacities in Hungary, within the framework of the 5th thematic program of the University of Pécs, Hungary (20765/3/2018/FEKUSTRAT).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.seizure.2021.11.013.

References

[1] Nørgaard SK, Vestergaard LS, Nielsen J, Richter L, Schmid D, Bustos N, et al. Real-time monitoring shows substantial excess all-cause mortality during second wave of COVID-19 in Europe, October to December 2020. Euro Surveill 2021;26(2): 2002023. https://doi.org/10.2807/1560-7917.ES.2021.26.1.2002023.

[2] Booth A, Reed AB, Ponzo S, Yassaee A, Aral M, Plans D, et al. Population risk factors for severe disease and mortality in COVID-19: a globalsystematic review and meta-analysis. PLoS One 2021;16(3):e0247461. https://doi.org/10.1371/journal.pone.0247461.

[3] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054–62. https://doi.org/10.1016/S0140-6736(20)30566-3.

[4] Clift AK, Coupland CAC, Keogh RH, Diaz-Ordaz K, Williamson K, Harrison EM, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 2020;371:m3731. https://doi.org/10.1136/bmj.m3731.

[5] Cabezudo-García P, Ciano-Petersen NL, Mena-Vázquez N, Pons-Pons G, Castro-Sánchez MV, Serrano-Castro PJ. Incidence and case fatality rate of COVID-19 in patients with active epilepsy. Neurology 2020;95(10):e1417–e25. https://doi.org/10.1212/WNL.0000000000010033.

[6] Balestrini S, Koepp MJ, Gandhi S, Rickmann HM, Shin GY, Houlihan CF, et al. Clinical outcomes of COVID-19 in long-term care facilities for people with epilepsy. Epilepsy Behav 2021;115:107602. https://doi.org/10.1016/j.yebeh.2020.107602.

[7] Granata T, Bisulli F, Arzimanoglou A, Rocamora R. Did the COVID-19 pandemic silence the needs of people with epilepsy? Epileptic Disord 2020;22(4):439–42. https://doi.org/10.1684/epd.2020.1175.

[8] Asadi-Pooya AA, Emami A, Akbari A, Javanmardi F. COVID-19 presentations and outcome in patients with epilepsy. Acta Neurol Scand 2021. https://doi.org/10.1111/ane.13404. Published online Feb 16 2021.

[9] Turk MA, Landes SD, Formica MK, Goss KD. Intellectual and developmental disability and COVID-19 case-fatality trends: triNetX analysis. Disabil Health J 2020;13(3):100942. https://doi.org/10.1016/j.dhjo.2020.100942.

[10] Williamson E.J., McDonald H.I., Bhaskaran K., Davy S., Schultze A., Tomlinson R., et al. Risks of covid-19 hospital admission and death for people with learning disability: population based cohort study using the OpenSAFELY platform.BMJ, 2021; 374: n1592. doi: 10.1136/bmj.n1592.

[11] Perera B, Laugharne R, Henley W, Zabel A, Lamb K, Branford D, et al. COVID-19 deaths in people with intellectual disability in the UK and Ireland: descriptive study. BJPsych Open 2020;6(6):e123. https://doi.org/10.1192/bjo.2020.102.

[12] Clift AK, Coupland CAC, Keogh RH, Hemingway H, Hippisley-Cox J. COVID-19 mortality risk in down syndrome: results from a cohort study of 8 million adults [published online ahead of print, 2020 Oct 21]. Ann Intern Med 2020:M20–4986. https://doi.org/10.7326/M20-4986.

[13] Malle L, Gao C, Bouvier N, Percha B. Bogunovic D (2020) COVID-19 hospitalization is more frequent and severe in down syndrome and affects patients a decade younger. medRxiv 2020. https://doi.org/10.1101/2020.05.26.20112748. 05.26.20112748.

[14] Johannsen P, Christensen JE, Goldstein H, Nielsen VK, Mai J. Epilepsy in Down syndrome–prevalence in three age groups. Seizure 1996;5(2):121–5.

[15] Prasher VP. Epilepsy and associated effects on adaptive behaviour in adults with Down syndrome. Seizure 1995;4(1):53–6. https://doi.org/10.1016/s1059-1311(05)80079-2.

[16] NY times: Coronavirus world map: tracking the global outbreak, Updated Updated March 23, 2021, 2:29 PM. E.T., Accessed March 23, 2021https://www.nytimes.com/interactive/2020/world/coronavirus-maps.html.

[17] Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, et al. Prevalence and incidence of epilepsy: a systematic review and meta-analysis of international studies. Neurology 2017;88(3):296–303. https://doi.org/10.1212/WNL.0000000000003509.

[18] Forsgren L, Beghi E, Oun A, Sillanpää M. The epidemiology of epilepsy in Europe - a systematic review. Eur J Neurol 2005;12(4):245–53. https://doi.org/10.1111/j.1468-1331.2004.00992.x.
[19] Bielen I, Cvitanovic-Sojat L, Bergman-Markovic B, Kosicek M, Planjar-Prvan M, Vuksic L, et al. Prevalence of epilepsy in Croatia: a population-based survey. Acta Neurol Scand 2007;116(6):361–7. https://doi.org/10.1111/j.1600-0404.2007.00881.x.
[20] Oun A, Haldre S, Mägi M. Prevalence of adult epilepsy in Estonia. Epilepsy Res 2003;52(3):233–42. https://doi.org/10.1016/s0920-1211(02)00234-6.
[21] Williams N, Radia T, Harman K, Agrawal P, Cook J, Gupta A. COVID-19 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review of critically unwell children and the association with underlying comorbidities. Eur J Pediatr 2021;180(3):689–97. https://doi.org/10.1007/s00431-020-03801-6.
[22] Neligan A, Bell GS, Johnson AL, Goodridge DM, Shorvon SD, Sander JW. The long-term risk of premature mortality in people with epilepsy. Brain 2011;134(Pt 2):388–95. https://doi.org/10.1093/brain/awq378.
[23] Granbichler CA, Oberaigner W, Kuchukhidze G, Bauer G, Ndayisaba JP, Seppi K, et al. Cause-specific mortality in adult epilepsy patients from Tyrol, Austria: hospital-based study. J Neurol 2015;262(1):126–33. https://doi.org/10.1007/s00415-014-7536-z.
[24] Lhatoo SD, Johnson AL, Goodridge DM, MacDonald BK, Sander JW, Shorvon SD. Mortality in epilepsy in the first 11 to 14 years after diagnosis: multivariate analysis of a long-term, prospective, population-based cohort. Ann Neurol 2001;49(3):336–44.
[25] Brigo F, Lattanzi S, Zelano J, Bragazzi NL, Belcastro V, Nardone R, et al. Randomized controlled trials of antiepileptic drugs for the treatment of post-stroke seizures: a systematic review with network meta-analysis. Seizure 2018;61:57–62. https://doi.org/10.1016/j.seizure.2018.08.001.
[26] Timmons S, Sweeney B, Hyland M, O'Mahony D, Twomey C. New onset seizures in the elderly: aetiology and prognosis. Ir Med J 2002;95(2):47–9.
[27] Devinsky O, Spruill T, Thurman D, Friedman D. Recognizing and preventing epilepsy-related mortality: a call for action. Neurology 2016;86(8):779–86. https://doi.org/10.1212/WNL.0000000000002253.
[28] Thurman DJ, Hesdorffer DC, French JA. Sudden unexpected death in epilepsy: assessing the public health burden. Epilepsia 2014;55(10):1479–85. https://doi.org/10.1111/epi.12666.
[29] Klang E, Kassim G, Soffer S, Freeman R, Levin MA, Reich DL. Severe obesity as an independent risk factor for COVID-19 mortality in hospitalized patients younger than 50. Obesity (Silver Spring) 2020;28(9):1595–9. https://doi.org/10.1002/oby.22913.
[30] Wortham JM, Lee JT, Althomsons S, Latash J, Davidson A, Guerra K, et al. Characteristics of persons who died with COVID-19 — United States, February 12–May 18, 2020. MMWR Morb Mortal Wkly Rep 2020;69:923–9. https://doi.org/10.15585/mmwr.mm6928e1.
[31] Tian N, Shaw EC, Zack M, Kobau R, Dykstra H, Covington TM. Cause-specific mortality among children and young adults with epilepsy: results from the U.S. National child death review case reporting system. Epilepsy Behav 2015;45:31–4. https://doi.org/10.1016/j.yebeh.2015.02.006.
[32] Nowak M, Bauer S, Haag A, Cepok S, Todorova-Rudolph A, Tackenberg B, et al. Interictal alterations of cytokines and leukocytes in patients with active epilepsy. Brain Behav Immun 2011;25(3):423–8. https://doi.org/10.1016/j.bbi.2010.10.022.
[33] Robertson J, Hatton C, Emerson E, Baines S. Prevalence of epilepsy among people with intellectual disabilities: a systematic review. Seizure 2015;29:46–62. https://doi.org/10.1016/j.seizure.2015.03.016.
[34] Redfors P., Holmegaard L., Pedersen A., Jern C., Malmgren K (2020) Long-term follow-up of post-stroke epilepsy after ischemic stroke: room for improved epilepsy treatment. Seizure 76:50–55. doi: 10.1016/j.seizure.2020.01.009.
[35] Cleary P, Shorvon S, Tallis R. Late-onset seizures as a predictor of subsequent stroke. Lancet 2004;363(9416):1184–6. https://doi.org/10.1016/S0140-6736(04)15946-1.
[36] Janszky J, Schulz R, Janszky I, Ebner A. Medial temporal lobe epilepsy: gender differences. J Neurol Neurosurg Psychiatry 2004;75(5):773–5. https://doi.org/10.1136/jnnp.2003.020941.
[37] Halász P. Management of epilepsy in Hungary. Acta Neurol Scand Suppl 1995;162:24–6. https://doi.org/10.1111/j.1600-0404.1995.tb00495.x.
[38] Pack AM. Epilepsy overview and revised classification of seizures and epilepsies. Continuum (Minneap Minn) 2019;25(2):306–21. https://doi.org/10.1212/CON.0000000000000707. PMID: 30921011.