





BRIEF COMMUNICATION

Status epilepticus admissions during the COVID-19 pandemic in Salzburg—A population-based study

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Abstract

Several emergencies were admitted less frequently to the hospital during the coronavirus disease 2019 (COVID-19) pandemic. To investigate whether this also occurred with status epilepticus (SE) we compared admissions due to first SE from March to April 2020 (“Time of COVID,” TOC) with January to February 2020 (“pre-COVID,” preCOV). We also compared admission numbers in TOC and preCOV with the respective 2-month periods in 2018 and 2019 in a retrospective cohort analysis. Two investigators independently searched the hospital patient database for various forms of SE. There was no significant change in the 2-month incidences of first SE in the city of Salzburg from preCOV of 6.1 (95% confidence interval [CI] 2.9–12.3) to TOC of 6.9/100 000 adults (95% CI 3.4–13.3). Admission numbers did not differ significantly from previous years. Estimated adjusted incidence was in line with a recent 5-year epidemiological study in Salzburg. However, a trend toward less-frequent nonconvulsive SE (NCSE) and loss of female predominance were indirect hints of underdiagnosing SE. In contrast to other medical conditions, SE most often presents clinically with impaired consciousness, which may promote admission to emergency

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departments even in times of lock-down. Further research of medical support of women and patients with NCSE during pandemic-related restrictions is warranted.

KEYWORDS

epidemiology, incidence, protection, risk, wristband

1 | INTRODUCTION

During the coronavirus disease 2019 (COVID-19) pandemic, several emergencies were reportedly admitted to hospital less frequently.^{1,2} Previous studies documented a decline of admissions during lockdown by 48% for acute myocardial infarction,^{1,3} and 37.7% for stroke in some areas⁴ for several reasons, such as fear of infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).^{1,3,4} Status epilepticus (SE) is a life-threatening neurological condition in which seizure activity exceeds its usual duration and requires urgent medical treatment.⁵ However, no studies have so far focused on SE during the COVID-19 pandemic.

We investigated whether SE was diagnosed less frequently at our neurological university hospital during the first peak of the COVID-19 pandemic in Austria and the nation-wide lockdown measures.

2 | METHODS

In Austria, the first period of high incidence of SARS-CoV-2 infections occurred in March and April 2020 (“Time of COVID,” TOC).⁶ At its peak on March 26th, a total of 1064 new infections per day were recorded, with 10% of peak being reached on March 11th and decreased to 10% on April 17th.⁶ A nationwide lockdown was introduced on March 16, 2020, as a government measure to minimize viral transmission.⁶

We performed a retrospective cohort analysis to investigate whether the number of adults (18 years or older) admitted with first SE changed during March 1 to April 30, 2020, (“Time of COVID,” TOC) compared with January 1 to February 29, 2020 (“pre-COVID,” preCOV), and the respective 2-month periods in 2018 and 2019 at the Department of Neurology, Christian Doppler University Hospital, Salzburg. Two investigators independently searched the patient database for “status epilepticus,” “nonconvulsive” SE (NCSE), and “aphasic” SE in outpatient and inpatient reports, consultations, and electroencephalography (reports). Our center is the only neurology department in the region and is linked to all other hospitals in the city of Salzburg by liaison and EEG services.

In the city of Salzburg (census code 50101), the 2-month incidences in TOC and preCOV were calculated by division of all adults with first SE in the respective 2-month period by the number of adults on January 1, 2020.^{7,8} Admission numbers with first SE in the city of Salzburg referring to the 2-month

periods January-February and March-April in a particular year were compared by calculating their admission ratio (AR). An AR close to 1.0 indicated no change. Quotients of admission ratios (QARs) were determined to compare ARs from different years. A QAR of 1.0 indicated no change in ARs from two different years (eg, 2020 vs 2019). Fisher exact tests (categorical variables) and *t* tests (metric variables) with an unadjusted two-sided level of 0.05 were applied to assess for significant changes in patient characteristics for all first SE during preCOV and previous study months taken together compared with TOC.

We divided all first SE in the city of Salzburg during the four study months of each year by the adult population of the respective year and multiplied by 3.0 to obtain extrapolated annual crude incidences.^{7,8} For comparison with a recent 5-year epidemiological study in Salzburg, we performed an age and gender adjustment of all first SE in the city of Salzburg during all 12 study months (based on Salzburg 2020) to the reference population of Austria 2016, which was used in the 5-year study.⁷⁻⁹ All calculations were performed using the statistical software R.¹⁰ This study obtained approval by the ethics committee (District of Salzburg, 1094-2020). Patient informed consent was waived in this retrospective non-interventional study in accordance with Austrian law.

3 | RESULTS

We identified 188 adults with SE during the study period, that is, January to April in 2018, 2019, and 2020; 140 (74.5%) had a first episode of SE, and 46 of these (32.9%) were inhabitants of the city of Salzburg.

Demographic and clinical characteristics of adults with first SE in the entire catchment area during TOC compared with preCOV, 2018, and 2019 are presented in Table 1. There were no statistically significant differences. Women constituted 37.5% of NCSE in TOC compared with 71.7% in preCOV ($P = .101$). No patient with SE had COVID-19.

The admissions of first SE in the entire catchment area in TOC compared to preCOV showed an AR of 1.05 (21 vs 20). This did not differ significantly from the ARs in previous years (2018 vs 2020: QAR = 1.47, 95% confidence interval [CI] 0.60-3.64; 2019 vs 2020: QAR = 0.81, 95% CI 0.32-2.05). Two-month admission numbers are displayed in Figure 1.

When analyzing the incidences of first SE in the population of city of Salzburg, we did not find a significant change

TABLE 1 Demographic data of patients with first status epilepticus in the entire catchment area in “Time of COVID” compared with all investigated months before COVID-19

	First SE in time of COVID N = 21	First SE in PreCOVID, and January to April 2018 and 2019 N = 119	P value*
Age: median, range	69; 22-97	71; 20-96	.386
Gender, female, N, %	8 (38.1)	69 (58.0)	.102
Salzburg City inhabitants	9 (42.9)	37 (31.1)	.319
Convulsive SE, i.e., bilateral tonic clonic	7 (33.3)	35 (29.4)	.797
Myoclonic SE without coma	0 (0.0)	2 (1.7)	1
Focal motor SE	6 (28.6)	22 (18.5)	.373
NCSE			
Total	8 (38.1)	60 (50.4)	.349
Female	3 (37.5 ^a)	43 (71.7 ^a)	.101
Pre-existing epilepsy	9 (42.9)	43 (36.1)	.627
Acute	5 (23.8)	39 (32.8)	.611
Remote	11 (52.4)	61 (51.3)	1
Cerebrovascular	6 (28.6)	43 (36.1)	.623
Traumatic brain injury	0 (0.0)	7 (5.9)	.594
Progressive	4 (19.0)	13 (10.9)	.287
Epilepsy syndrome	1 (4.8)	3 (2.5)	.482
Unknown cause	0 (0.0)	3 (2.5)	1

Abbreviations: NCSE, nonconvulsive SE; PreCOVID, January and February 2020; SE, status epilepticus; Time of COVID, March and April 2020.

^aPercentages refer to N within subgroup (ie, NCSE).

*Fisher exact tests (categorical variables) and t tests (metric variables).

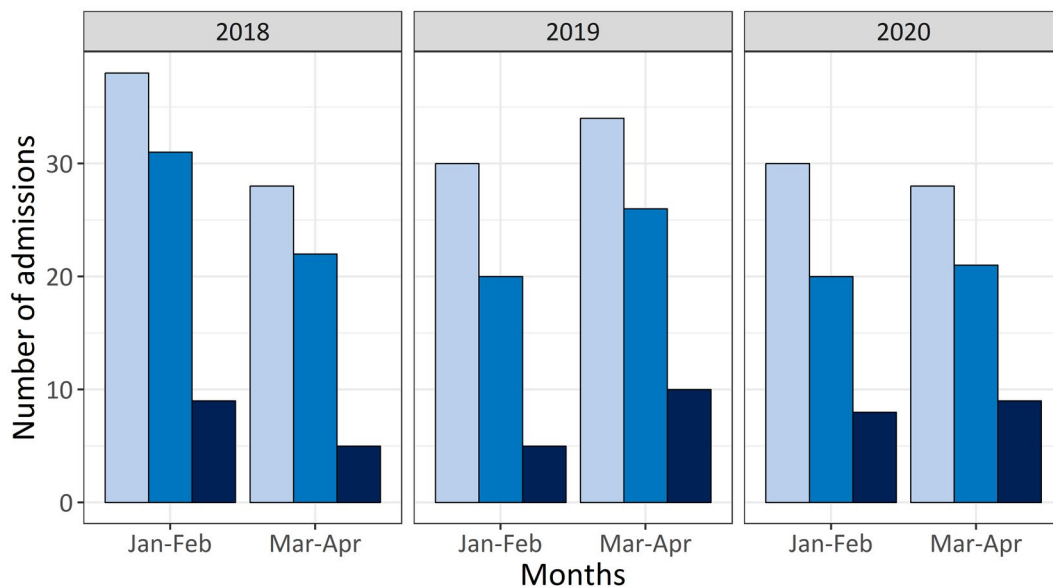


FIGURE 1 Number of adults with status epilepticus in the respective 2-month period in a particular year. Note, that January and February had 60 d together in 2020. The light blue bars represent all admissions with SE in the entire catchment area, medium blue bars indicate all admissions with first SE in the entire catchment area, dark blue bars indicate all admissions with first SE resident in the city of Salzburg

of the 2-month incidences from preCOV of 6.1 (95% CI 2.9-12.3) to TOC of 6.9 (95% CI 3.4-13.3).

The extrapolated crude annual incidence of first SE in the city of Salzburg for 2018, 2019, and 2020 were 32.5 (95% CI 23.9-44.0), 34.6 (95% CI 25.7-46.4), and 39.0 (95% CI 29.5-51.3)/100 000 adults. The crude annual incidence of all first SE over the whole study period was 35.2/100 000 adults in Salzburg 2020, which was 33.9/100 000 adults after age and gender adjustment to Austria 2016.

4 | DISCUSSION

The frequency of first SE in Salzburg did not change in the 2 months of the first peak of COVID-19 compared with previous months. In the time of first peak of COVID, there was a loss of female predominance, and a non-significant increase in focal motor SE and decrease in NCSE.

We found no statistically significant difference between the 2-month incidence of first SE in Salzburg during TOC of 6.9 (95% CI 3.4-13.3) compared to preCOV of 6.1 (95% CI 2.9-12.3)/100 000 adults. The number of admissions also did not change when compared to the corresponding months in 2018 and 2019. The extrapolated annual incidence of first SE in Salzburg 2018 (32.5, 95% CI 23.9-44.0), 2019 (34.6, 95% CI 25.7-46.4), and 2020 (39.0, 95% CI 29.5-51.3) and the age- and gender-adjusted incidence over the whole study period of 33.9/100 000 adults matched well with the annual incidence of 36.1/100 000 adults (95% CI 26.2-48.5) found in a recent epidemiological 5-year study performed in the same study area of city of Salzburg.⁹

We also searched for subtle signs of underdiagnosis of SE and investigated the semiology and gender predominance. We found a non-significant increase in focal motor SE and relatively less NCSE. Within the subgroup of NCSE, women comprised only 37.5% in TOC compared to 71.7% in all previous investigated months, and 77.6% in the 5-year study.⁹ In all first SE, women constituted only 38.1% in TOC compared to 58.0% in all previous investigated months and 56.0% in the 5-year study.⁹ We wonder whether we underdiagnosed SE despite constant admission incidence of first SE. We concluded that especially women and people with NCSE need higher efforts and awareness for appropriate management. From an epidemiological point of view, we recommend meticulous investigation of gender structures to validate incidence data.⁸ A potential underdiagnosis of SE might have been compensated by other factors: COVID-19 may involve the central nervous system (CNS) either directly or indirectly due to cerebrovascular accidents caused by endothelial alterations or hyperactivity of the immune system.¹¹ However, we identified no patient with both COVID and SE in our study. Only a few cases of COVID-19-related SE were published so far^{12,13}; thus we

do not expect an increase of SE due to direct SARS-CoV-2 involvement.

Our results are in striking contrast to stroke, where admissions declined during lockdown by 37.7% in a large study from China.⁴ Telestroke consultations fell by 48% in a large tertiary care center in Philadelphia (United States).² Similarly, admissions for acute myocardial infarction fell by 14.6% and 48% during the COVID-19 pandemic in several countries.^{1,3,14}

The reasons for this discrepancy are far from clear. As a potential SE-specific factor, clinical presentation of SE drew attention to the patients either by prominent motor semiology or by quantitatively or qualitatively impaired consciousness in NCSE. In times of COVID-19, relatives may have been more sensitive to changes in a person's behavior, as they wished to provide more support and protection to family members. However, the social isolation of many of the elderly, who lived alone or with only limited social contacts, was accentuated by the lockdown measures. In addition, the complication of NCSE in this elderly population by pneumonia or other infections may have led to their admittance to internal medicine departments rather than the neurological emergency room. Both effects might contribute to the reduction of reported SE in women, as women prevail in this age group for epidemiological reasons.^{8,9} In addition, the functional impairment of CNS performance during SE prevented patients from expressing their wish concerning admittance to hospital. Thus one can assume that a patient with SE was admitted as early as SE was suspected. Patients with acute stroke might have refrained from actively seeking or accepting help due to neglect or anosognosia. Patients with cardiac disorders were able to decide if and when to attend the emergency department (ED). Reasons that patients chose not to present to an ED include fear of SARS-CoV-2 infection in hospital,^{14,15} competing for care with individuals who might need it more urgently,¹⁶ or financial burden due to loss of employment.¹⁶

Several factors may limit the generalizability of our data. Health services were restructured to secure treatment for both COVID-19 and non-COVID-19 patients. The density of intensive care beds in Austria was high compared with that of other European countries (28.9/100 000 persons), with no shortage during TOC.^{6,17} All measures were communicated via the media to reassure people. However, these measures could not prevent a 39.4% decrease in admissions of patients with acute myocardial infarctions in a nationwide Austrian survey.¹⁸ Local measures may be of higher importance. In the District of Salzburg (558 410 inhabitants), one hospital was declared as a "COVID-19 Hospital," whereas all other hospitals served as non-COVID hospitals, including Christian Doppler University Hospital. However, we dedicated neurologists to the COVID-19 Hospital to guarantee rapid access to neurological assessment. Personal protection equipment (PPE) was

also made available for EEG technicians. All patients were screened based on a checklist and body temperature was measured. The intensive care unit and stroke unit screened all admitted patients for SARS-CoV-2 with a mucosal swab test. The individual risk determined different fast and secure pathways inside the hospital and potentially also isolation until testing negative for SARS-CoV-2. All patients were equipped with a colored wristband to clearly indicate the appropriate PPE to staff members. A local task force weekly adapted all measures as needed. Generalization to entire Austria or countries with different health care systems should be performed with caution.

In an Italian study, one third of patients with epilepsy raised complaints about issues with epilepsy management, but only 71% of these patients reached the treating physician.¹⁹ In our study, the percentage of pre-existing epilepsy did not change significantly in TOC, possibly because of our approach to proactively call all patients scheduled in our epilepsy outpatient facility and to provide safe personal meetings to those with complex problems.

Admissions due to SE might differ in countries that were affected by COVID-19 without a preparation time (eg, Italy or Spain in contrast to Austria), and therefore reported results may not be representative for other European countries.

The number of admissions might have decreased during holidays as a potential source of bias. However, this possible effect applies to all 2-month periods of this study, as “January and February” always included one week of “Christmas holidays,” whereas “March and April” always included “Easter holidays.”

Furthermore, subgroup sizes were small, and admission numbers had to be extrapolated for comparison with previous incidence estimates.

In conclusion, our retrospective population-based study did not reveal reduced admission or a drop in incidence during the first peak of COVID in Salzburg. Incidences were also in line with our recent epidemiological 5-year study.⁹ We therefore assume that clinical presentation of SE promotes admissions to EDs even in times of lockdown, as opposed to other medical conditions. Further research of medical support of women and patients with NCSE during pandemic-related restrictions is warranted.

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CONFLICTS OF INTEREST

Markus Leitinger reports travel grants from UCB Pharma and speaker’s honoraria from Eisai, unrelated to the present work. Alexandra Rohrachner received travel support and speaker’s honoraria from Eisai, unrelated to the present work. Gudrun Kalss received travel support and speaker’s honoraria from Eisai and UCB, unrelated to the present work. Eugen Trinka reports paid consultancy for UCB, Eisai, Bial, Medtronic, EVER Pharma, Biogen, Takeda, LivaNova, NewBridge, Sunovion, GW Pharmaceuticals, Marinus, and Arvelle; research funding (directly, or to his institution) from GSK, Biogen, Eisai, Novartis, Red Bull, Bayer, and UCB; speaker’s honoraria from Bial, Böhringer Ingelheim, Eisai, EVER Pharma, GSK, LivaNova, NewBridge, Novartis, Sanofi, Sandoz, and UCB. ET is the CEO of Neuroconsult Ges.m.b.H. ET receives grants from the Austrian Science Fund (FWF), Österreichische Nationalbank, and the European Union, unrelated to the present work. Kai-Nicolas Poppert, Matthias Mauritz, Fabio Rossini, Georg Zimmermann, Giorgi Kuchukhidze, Julia Höfler, Pilar Bosque-Varela, Rudolf Kreidenhuber, Kamila Volna, Caroline Neuray, Teia Kobulashvili, Claudia A. Granbichler, and Uwe Siebert report no conflicts of interests.

ETHICAL PUBLICATION STATEMENT

“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.”

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