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Impact of COVID-19 pandemic in pediatric patients with epilepsy with neuropsychiatric comorbidities: A telemedicine evaluation



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ABSTRACT

Objective: The objective of this study was to evaluate care needs, emotional and behavioral changes, and parental stress indices in a cohort of pediatric patients with epilepsy with neurocognitive and emotional comorbidities at the time of the coronavirus disease 2019 (COVID-19) pandemic.

Methods: This is a prospective observational study involving pediatric patients with epilepsy with neurocognitive and emotional comorbidities. Included patients were admitted to our hospital between August 2019 and February 2020 for epilepsy and neuropsychiatric assessment, and Child Behavior Checklist (CBCL) questionnaires were filled in by parents. Those patients and their families accepted to participate in a phone follow-up visit in April–May 2020 and to refill CBCL and Parenting Stress Index–Short Form (PSI-SF) questionnaires.

Descriptive statistics for demographic and clinical data, CBCL questionnaire scores before and during the COVID-19 pandemic, and PSI-SF scores have been computed. Moreover, results of a short phone survey on the psychological burden during COVID lockdown have been reported.

Results: This study provides the parental-proxy report of emotional and behavioral profile changes of 23 pediatric patients with epilepsy and neurocognitive and emotional comorbidities during the COVID-19 pandemic. Concerns for therapy monitoring at the time of lockdown emerged in 43% of families, and 30% of patients showed worries for an altered contact with the referring medical team.

Patients with neurocognitive comorbidities were more likely to exhibit behavioral problems, especially externalizing problems compared with patients with a diagnosis of anxiety/depression.

Conclusion: Our data suggest the importance to monitor disease trajectory and behavior and affective symptoms with telehealth strategies to provide effective care to patients and their families.

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1. Introduction

Novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2), has been responsible for the pandemic of the highly contagious coronavirus disease 2019 (COVID-19) [1,2]. Italy, with deep involvement of the region of Lombardia, has been one of the epicenters. In the absence of specific and effective therapies, as a primary intervention to contain the infection spread, the Italian government tried to limit the human-to-human transmis-

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sion by engaging the population to adhere to severe travel and daily-life restrictions. Therefore, social, educational, and productive activities have been suspended, leading to the so-called lockdown. Notably, restrictions on hospital admissions, standard clinical activity, and general healthcare services not related to the COVID-19 emergency became part of the containment strategy, thus leading to the interruption of nonurgent hospitalizations and exams. Although these measures were successful in arresting the outbreak, they represented a further consequence of the pandemic for patients and their families as well as for clinicians [3]. From the beginning of March 2020 till the end of May 2020, the standard clinical activity in our tertiary-level center dramatically changed because of the impossibility of providing outpatient visits, hospitalizations, or electroencephalographic exams except for emergencies. Treatment adjustments have been conducted only in few cases and on a clinical basis; no blood tests nor weaning of ongoing





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medications became feasible. As a consequence, the email and phone correspondence with patients and their families substantially increased by the beginning of the lockdown, and telemedicine emerged as the unique alternative to follow patients and to manage nonurgent epilepsy-related problems. Thus far, the comorbid diagnosis of epilepsy itself or other neurological disorders has not emerged as a specific risk factor for susceptibility for COVID infection [4,5], and the same can be said for antiseizure medications (ASMs). Nevertheless, COVID-19 could affect everyone and cause additional concerns for those patients with chronic conditions. Actually, patients with a chronic disease and preexisting behavioral disorders, mood disorders, sleep disorders, and neuropsychological fragilities once exposed to the lockdown might undergo further risks. In this regard, it should be considered that patients with epilepsy are often affected by cognitive and behavioral or affective [6] problems that can worsen quality of life and adversely affect long-term psychosocial functioning [7]. More specifically, a prevalence of 12–26% for mood disorders in children and adolescents with epileptic syndromes is reported [8], and Caplan and colleagues have estimated the presence of any current anxiety symptomatology in 35% of youth with epilepsy [9]. Indeed, patients with epilepsy and their families might face problems arising from the modified school and social activities and abrupt interruption of clinical follow-up. This study aimed to highlight the importance of estimating the impact of the COVID comorbidities. Sociodemographic characteristics, epilepsy-related clinical features, affective symptoms, and parental stress indices have been collected. Consistently, the main objective of this study was to assess the presence and trajectories of affective symptoms and behavioral problems at the time of COVID pandemic in outpatients compared with baseline.

2. Methods

2.1. Participants and procedures

Twenty-three patients diagnosed as having epilepsy and neurocognitive and emotional comorbidities were enrolled during April-May 2020. Patients were included in the study if they had a diagnosis of epilepsy associated with neurocognitive and emotional comorbidities and at least one follow-up visit as inpatient or outpatient in our center, August 2019 and February 2020, during which Child Behavior Checklist (CBCL) guestionnaires had been compiled by parents. Patients were not considered eligible for the study if they had a moderate or severe intellectual disability (intelligence quotient [IQ] < 55). Patients were divided into two groups according to comorbidity: neurocognitive comorbidities (specific learning disorder, attention-deficit, neuropsychological fragilities) in group 1 and internalizing problems (anxiety, depression) in group 2. For further analyses, the population was divided into two groups according to IQ level (IQ > 85 vs IQ < 85) and into two groups according to the timing of comorbidity and epilepsy diagnosis (last 12 months vs more than 1 year). Sociodemographic and clinical variables were obtained from the medical charts. Parents were reached through a phone follow-up visit and were asked to complete self-report questionnaires on stress indices and selfreport questionnaires on patients' affective and behavioral symptoms and to answer to a short telephone survey aimed at exploring the psychological burden of the disease. The parents of all the participating patients gave informed consent, and the study was approved by the local ethical committee.

2.2. Measures

2.2.1. Sociodemographic and clinical variables

Sociodemographic variables included patients' sex, age, and residence. Clinical variables included main diagnosis, history of epilepsy duration, current seizure frequency, ASMs treatment, comorbidities and date of comorbidity diagnosis, presence of a rehabilitation/psychotherapy before and after February 2020, and usual follow-up frequency at our center before the COVID-19 emergency.

2.2.2. CBCL questionnaire

The CBCL [10] is a screening tool commonly used to identify clinical, borderline, and normative behaviors in children. It contains 118 items rated on a Likert scale, where 0 = not true. 1 = sometimes true, and 2 = very true or often true. Child Behavior Checklist scoring provides a total problem score, two broadband scores (internalizing and externalizing problems), and the following eight subscale scores: Anxious/Depressed, Withdrawn/ Depressed, and Somatic complaints (together: internalizing or emotional problems); Rule-breaking behavior and Aggressive behavior (together: externalizing or behavioral problems); and Social problems, Thought problems, and Attention problems. T scores on the broadband scales between 59 and 64 are considered to fall within a borderline clinical range, while T scores of 64 and higher fall within the clinical range. For syndrome scales, these cutoff scores are 65 for the borderline range and 70 for the clinical range. Child Behavior Checklist scores of the evaluation at t0 (September 2019-February 2020) and CBCL scores of the evaluation at t1 (April-May 2020) were compared for each patient.

2.2.3. Parenting Stress Index-Short Form questionnaire

The Parenting Stress Index–Short Form (PSI-SF) is a brief version of the Parenting Stress Index [11], a widely used measure of parenting stress.

The questionnaire is divided into the following three subscales of 12 items each: (1) Parental distress (PD) related to conflicts with partner, social support, life restrictions; (2) Parent–child dysfunctional interactions (PCDI) about parents' impression on interaction with their children also compared with other children; and (3) Difficult child (DC) related to parents' perception of their children's self-regulatory abilities. Scores can be calculated for each subscale by summing scores of the 12 items, with possible scores ranging from 12 to 60. A total score is calculated by summing the three subscale scores, with possible scores ranging from 36 to 180. Higher scores indicate higher levels of parental stress.

All families of included patients were asked to fill out a PSI-SF questionnaire at t1.

2.2.4. Phone survey

Short ad hoc questions were asked during a phone follow-up visit at t1 to receive information on the following issues: concerns about the underlying disease (therapy monitoring, worsening of seizures with COVID infection, changes in contact with the referring specialist), sleep disturbance, difficulties in adhering to the new scholastic arrangement, and social disconnection (see Table A).

2.3. Plan of analysis

Descriptive statistics for sociodemographic and clinical data as well as for questionnaire scores were computed.

To test differences between groups based on the different types of comorbidity (neurocognitive comorbidities vs internalizing problems), IQ (IQ \geq 85 vs IQ < 85), and time of comorbidity (last 12 months vs more than 1 year), χ square test was employed for categorical variables and Kruskal–Wallis rank-sum test when the variable was numeric.

The differences between t0 and t1 in CBCL scores were tested with a paired *t*-test or a paired Wilcoxon rank-sum test (depending on the result of a Kolmogorov–Smirnov normality test).

Table 1

Demographic and clinical features of the cohort (23 subjects).

Gender	
Male	9 (39.2%)
Female	14 (60.8%)
Age	
Mean, range	Mean: 13 years; range: 9–17 years
History of disease	
Comorbidity diagnosis	Mean: 15 months; range: 3–60 months
Epilepsy diagnosis	Mean: 55 months; range: 11–
	148 months
Epilepsy type	
Focal epilepsy	11 (48%)
Generalized epilepsy	12 (52%)
Seizure frequency	
Weekly/monthly	5 (21.8%)
Sporadic	18 (78.2%)
Follow-up frequency	
Biannually	8 (34.8%)
Quarterly/bimonthly	15 (65.2%)
Comorbidity type	
Group 1: neurocognitive	13 (56.5%)
disorders	Specific learning disorder (8)
	Attention-deficit (3)
	Neurocognitive fragilities (2)
Group 2: internalizing disorders	9 (43.5%)
	Anxiety (5)
	Depression (4)
Intelligence quotient	
$IQ \ge 85$	16 (69.57%)
IQ < 85	7 (30.43%)

To analyze differences between groups and time points in CBCL scores, nonparametric repeated measure analysis of variance (ANOVA) was employed, and p-values of the interaction are reported.

For all the statistical tests performed, a significance level of 0.05 is set.

3. Results

3.1. Demographics and clinical history

A descriptive analysis of sociodemographic and clinical history data of the overall population is reported in Table 1.

Among the 23 patients (M: 9, F: 14; median age: 13 years; range: 9–17 years), the most frequent diagnosis was focal epilepsy (48%). Twenty-one patients were under ASMs (12 monotherapy; 9 polytherapy). Four patients (17%) were affected by drug-resistant epilepsy. Seizure frequency varied from weekly to sporadic.

Usual clinical follow-up was performed with a frequency varying from bimonthly to biannual. Four patients were undergoing rehabilitation at t0, none was able to continue that therapy at t1. Of the 7 patients undergoing psychotherapy at t0, only three were able to keep on with the treatment at t1.

Seven patients had a relatively recent diagnosis of epilepsy (last 2 years). Sixteen patients received the diagnosis of neuropsychiatric comorbidity in the last year.

3.2. Phone survey

Among the patients included in the study, none has been affected by COVID-19 infection. Three patients (13%) had a family member affected by COVID-19: all cases resolved with a hospitalization. Concerns for therapy monitoring at the time of lockdown emerged in 43% of families. None expressed concerns for a possible worsening of seizures by contracting COVID-19. The 30% of patients showed worries for an altered contact with the referring medical team.

As far as school activities were concerned, 39% of patients demonstrated difficulties in following the provided school program, manifesting attention and homework organization problems (30%), thus requiring an increased parents' assistance. Patients showing major difficulties related to homework organization and following provided school problems belonged to group 1 (χ^2 (1) = 4.32, p-value = 0.038).

Seventeen percent of patients showed reduced contact with peers, with a major proportion in group 2.

No significant sleep disturbance was reported.

3.3. PSI-SF

No clinically relevant scores emerged. The subscale with more elevated scores was the DC scale, related to parents' perception of their children's self-regulatory abilities, where in 9 cases, a score greater than 20 was obtained. That datum was mainly represented in group 2 (t (18.97) = 1.78, p-value: 0.09) (Fig. 2). Scores in the remaining subscales ('PCDI' and 'DC') tended to be higher in group 1 (Table 2).

3.4. CBCL questionnaire

The median and range of CBCL scores obtained in the two groups of patients are shown in Table 2.

Each patient included had some borderline and clinical scores at t0. A tendency towards an increase of 'total external problems' scores from t0 to t1 and a decrease of 'internal problems' scores from t0 to t1 was recorded in the overall population.

The profile of group 1 diverges from the one of group 2. In group 1, increased scores are registered in 'total external', 'attention problems', 'aggressive behavior', 'anxious-depressed'. In group 2, a decrease of 'aggressive behavior', 'rule-breaking behavior', 'with-drawal', 'attention', 'total external', and 'social problems' has emerged. In particular, by comparing the two groups' profiles, total external problems generally increased at t1 in group 1 compared with group 2 with a positive trend (statistic (1) = 2.96, p-value: 0.085), and aggressive behavior worsened in group 1 compared with group 2 at t1 (statistic (1) = 9.27, p-value: 0.002) (Fig. 1a, b).

Table 2			
Descriptive statistics	(median	and	range).

	Group 1 (n = 14)	Group 2 (n = 9)
CBCL TO		
CBCL total	Mdn = 56.5 [47– 70]	Mdn = 59 [53– 70]
CBCL internalizing	Mdn = 61 [48-70]	Mdn = 65 [52– 73]
CBCL externalizing	Mdn = 52.5 [43– 69]	Mdn = 54 [51– 62]
CBCL T1		
CBCL total	Mdn = 60 [50–73]	Mdn = 57 [36– 72]
CBCL internalizing	Mdn = 58.5 [50– 72]	Mdn = 62 [33– 73]
CBCL externalizing	Mdn = 56.5 [50– 75]	Mdn = 51 [34– 73]
PSI-SF	,	,
PSI total	Mdn = 44 [10–91]	Mdn = 51 [3– 70]
Parental distress	Mdn = 11.5 [1– 39]	Mdn = 12 [0– 19]
Parent-child dysfunctional	Mdn = 12.5 [3-	Mdn = 13 [1-
interaction	30]	21]
Difficult child	Mdn = 19.5 [4– 28]	Mdn = 23 [2- 41]

Note. Group 1, neurocognitive disorder; Group 2, internalizing disorder; Mdn, median; CBCL, Child Behavior Checklist; PSI, Parenting Stress Index.



a. 'Total external' item scores at t0 and t1 for group 1 (red) and group 2 (light blue)





Fig. 1. a. 'Total external' item scores at t0 and t1 for group 1 (red) and group 2 (light blue).b. 'Aggressive behavior' item scores at t0 and t1 for group 1 (red) and group 2 (light blue). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Anxiety/depression scores increased at t1 for patients with a diagnosis of comorbidity from more than 1 year compared with the rest with a positive trend (statistic (1) = 2.91, p-value: 0.088).

Social problems increased at t1 for patients with a diagnosis of comorbidity from more than 1 year (statistic (1) = 5.60, p-value: 0.018).



Fig. 2. PSI-SF DC scores at t1 for group 1 (red) and group 2 (light blue). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

The history of epilepsy disease as well as the IQ level did not turn out to be significant contributors to emotion and behavior changes.

4. Discussion

The present study aimed at assessing possible changes in emotions and behavior in pediatric patients with epilepsy and neuropsychiatric comorbidities and exploring parental stress index during the COVID-19 pandemic. Those aspects have been examined through telemedicine visits, standardized questionnaires, and an ad hoc survey. Results obtained were analyzed considering different comorbidity types (group 1 vs group 2), different IQ (IQ \geq 85 vs IQ < 85), and timing of comorbidity and epilepsy diagnosis (last 12 months vs more than 1 year).

The recent pandemic has led to an impairment of usual healthcare assistance with significant consequences both for medical operators and patients. In a scenario where COVID-19 is threatening human being's health, connections are reduced or impaired, and everyday life is subverted for individuals and families; subjects are exposed to major risks. We hypothesized that patients with a chronic disease such as epilepsy and neurocognitive and emotional comorbidities might represent a special at-risk category. It is now recognized that to enable early intervention and therapy, children and teens with epilepsy should be periodically screened for cognitive and affective and behavioral comorbidities. As proposed by Wagner et al. [12], the clinician should promote the integration of comorbidities screening into the routine follow-up. On the other hand, it is well known that children and adolescents are often reluctant to report spontaneously the potential presence of depressive and anxious symptoms with the clinician. All patients included in the study were used to adhere to a regular clinical follow-up in our center. During the scheduled visits, patients and their parents are usually asked to report about behavior and affective symptoms; moreover, all the patients with epilepsy undergo an extensive neuropsychological evaluation yearly since patients with epilepsy are at risk for a variety of neurocognitive comorbidities [13]. Thus, a regular in situ follow-up has a clinical and therapeutic value both for patients and their families. With the temporary suspension of this service, we attempted to provide alternative follow-up and psychological support with telehealth, trying to both monitor patients' disease trajectory and behavior with the concurrent pandemic and to alleviate concerns.

In the recent consensus paper of French et al. [14], epileptologists have been invited to administer as much care as possible at home to reduce risk exposure. Among the other indications included in the consensus, it has been suggested to lower the threshold to provide emergency rescue medication to promote medication compliance and preventive measures. In the population herein reported, concerns for therapy monitoring at the time of lockdown emerged in 43% of families. We tried to address this concern by promoting support indications for a favorable lifestyle as well as constant compliance. Our patients did not manifest the concern for a potential worsening of seizures with COVID-19 infection; however, none of the included patients presented recognized risk factors for COVID-19 exposure, and only 3 patients had a close family member affected by the virus. Beyond the epilepsy care, handling with comorbidities and difficulties arising from the routine interruption, often without the availability of rehabilitation and therapies (in our population, psychotherapy was suspended in the majority of cases during lockdown), represented a critical issue. Thus, reassurance to patients and families became fundamental.

As far as school activities were concerned, 39% of patients presented difficulties in following provided school program, manifesting attention and homework organization problems (30%), thus requiring an increased parents' assistance. Patients showing major difficulties related to homework organization and adherence to provided school program, as predictable, belonged to the group with neurocognitive comorbidity. This reflects the difficulty of coping with new learning setup, without usual supports, especially for patients for whom school functioning represents a critical issue independently from COVID-19 conditions [15].

The profile of emotion and behavior changes of our patients, trackable through CBCL questionnaires administered before and during the COVID-19 pandemic, offers some insights. A different characterization emerged comparing patients with neurocognitive comorbidity and patients with internalizing problems through time: patients belonging to the first group generally appeared more at risk since a trend of increased scores was registered, in particular in total external problems, and aggressive behavior. In this respect, it must be highlighted that at the time when CBCL questionnaires have been compiled, patients were just getting used to the new scholastic activities provided, and very often, support teacher assistance was not guaranteed.

Child Behavior Checklist scores of patients with internalizing problems, in general, did not show significant changes at t1, remaining stable compared with t0 scores. A partial decrease of internalizing problems has been recorded at t1 for this group: this could be justified by a temporarily reduced exposure to social issues that usually trigger anxiety and feelings of inadequacy in those patients. Similar findings have been described in adult populations; Shanahan et al. [16] have found an improvement of internalizing symptoms in the lockdown period, and Zheng et al. [17] have reported how lockdown measures and psychological distance had a buffer effect on social anxiety in pandemic regions, with the mediating role of psychological distancing. Nevertheless, in group with neurocognitive comorbidity, the scores at PSI-SF DC scale which reflects parents' perception of their children selfregulatory abilities - turned out to be higher compared with the scores obtained in the other subscales of PSI-SF and mildly greater than scores obtained in the same scale in group with internalizing problems. This result might possibly refer to parents' awareness of the innermost fragilities of their child, despite the absence of evident behavioral changes registered.

The history of epilepsy disease did not turn out to be a significant contributor in emotion and behavior changes, whereas a longer history of comorbidity seemed to be related to an increased possibility of anxiety/depression and social problems manifestation at t1.

It is fairly early for an estimation of the burden of the COVID-19 pandemic. Certainly, patients included in the study will deserve special attention in the future, together with all patients with atrisk factors for mental health such as the presence of epilepsy as a chronic disease and neuropsychiatric comorbidities. In this regard, knowledge and understanding of the experiences of patients and their families during quarantine are crucial to minimizing the negative effects. We will monitor these patients in the medium and long term.

As suggested by French et al. [14], we try to keep considering a comprehensive care plan, promoting the importance of routine maintenance and contacts with peers, regular medications, and adequate sleep. For this purpose, the use of telemedicine tools for communication between patients and their families has to be implemented in the emergency interventions.

This study presents some limits. The population analyzed is small and not that representative since patients enrolled belonged exclusively to a tertiary center. Moreover, parents' reports could reflect parents' reactions and emotions being less objective compared with direct patients' assessment. In literature, parentproxy reports are often used to assess behavior and make inferences about psychiatric affection [8] but the importance of assessing children directly should be kept in mind. However, we believe that the depicted profile could have been of interest. Finally, the employed standardized questionnaires characterize well the affective and behavioral symptoms, as well as parental stress indices, but are not specific diagnostic tools.

5. Conclusions

This study reports subclinical affective and behavioral changes during the COVID-19 pandemic in patients with a diagnosis of epilepsy and neuropsychiatric comorbidity. It is possible to speculate that patients included in the study, especially the ones with neurocognitive comorbidities, had disease concerns and an impairment in regular daily activity during the COVID-19 pandemic. Beyond comorbidity type, a history of comorbidity emerged as possible contributors to the worsening of affective and behavior problems. Patients with a chronic disease such as epilepsy and comorbidities should deserve special attention during and after the COVID-19 emergency, with a special focus on their scholastic and social functioning.

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Declaration of competing interest

None of the authors has any conflict of interest to disclose.

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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