



The COVID-19 pandemic and children with PANS/PANDAS: an evaluation of symptom severity, telehealth, and vaccination hesitancy

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Abstract

The current study assessed the impact of the COVID-19 pandemic on children with PANS/PANDAS, a condition characterized by sudden-onset obsessive-compulsive, tic, or restrictive eating symptoms following infection. We conducted an anonymous survey between February and June 2021 of 254 self-reported caregivers of minors with PANS/PANDAS. Caregivers answered questions regarding PANS/PANDAS symptoms, telehealth care, and intention to vaccinate their child against COVID-19. PANS/PANDAS symptoms during COVID-19 infections were assessed when applicable. Children's OCD symptoms and coercive behaviors towards caregivers, along with the caregivers' mental health, relationship satisfaction, and burden, were assessed using standardized questionnaires. A majority of respondents endorsed a negative impact on their child's friendships, relationships with extended family, hobbies, and academic skills due to the pandemic. Children with suspected or diagnosed COVID-19 experienced new or worsened psychiatric symptoms, particularly mood lability, OCD, and anxiety. Telehealth care was the preferred treatment modality if the child had mild symptoms of PANS/PANDAS. A majority of caregivers reported high levels of relationship dissatisfaction and caregiver burden. As expected, these data suggest an overall negative impact of the COVID-19 pandemic on children with PANS/PANDAS and their caregivers.

Keywords Obsessive-compulsive disorder · Pediatric · Psychiatry · PANS · PANDAS · Tics

Introduction

The SARS-CoV-2 (COVID-19) pandemic has greatly altered daily life for children and families, though the impact for those with preceding mental health difficulties has been especially profound. The pandemic has also negatively impacted the mental health of adults [1], and reports suggest obsessive-compulsive (OCD) symptoms, in particular, have worsened in both adults and children [2–4]. Survey studies show increased anxiety and depressive symptoms in children with OCD during the pandemic [3], and observational studies report that children with preexisting anxiety

disorders are at greater risk of severe illness from COVID-19 [5]. Infection with COVID-19 has been reported to initiate new neuropsychiatric symptoms in adults and children, suggesting this infection may initiate neuronal dysfunction in patients through a currently unknown mechanism [6].

PANDAS, or Pediatric Autoimmune Disorder associated with Streptococcal Infections [7], refers to the abrupt and significant onset of OCD, tic, or restricted eating following a group A streptococcus infection (GAS). Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) describes the acute onset of OCD and/or severe restricted eating, accompanied by at least two ancillary criteria related to cognitive, behavioral, or neurological symptoms [8]. PANS is thought to result from multiple disease mechanisms and etiologies, including an infectious trigger [9]. The prevalence and detailed demographic characteristics of PANS/PANDAS remain unknown, but clinic and survey-based studies have documented a slight male preponderance [7, 10–12].

Previous data suggests that access to care is problematic for children with PANS/PANDAS, and the reported lag between onset of symptoms and age at diagnosis ranges from 0.8 to 4.7 years [13]. Another survey completed by

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caregivers of PANS/PANDAS patients reported a median of 3 providers evaluated a patient before receiving a PANS or PANDAS diagnosis [11]. Additionally, 62.3% of families had traveled more than 50 miles to receive PANS/PANDAS treatment, and 15.6% reported traveling more than 500 miles [11]. Accordingly, the use of telehealth services has increased twenty-fold in the general population during the pandemic, with the highest utilization among adults, patients in metropolitan areas, and patients in counties with lower rates of poverty [14]. Several clinical trials are being conducted to evaluate the efficacy of telehealth interventions for mental health issues in children [15], as the use of telehealth will almost certainly persist once the pandemic ends. Therefore, it is important to understand the utilization of telehealth therapies for PANS/PANDAS treatment and how the adoption of telehealth interventions have affected the clinical course for children with these disorders.

Despite epidemiological data strongly suggesting the opposite, the safety of vaccinations in children continues to be questioned [16]. The consensus recommendations from multiple PANS/PANDAS experts advise that children with PANS/PANDAS should receive all standard childhood vaccines, as well as yearly influenza immunizations. This is based on consensus observations that exacerbations of PANS/PANDAS symptoms following vaccination are uncommon, brief, and manageable with analgesic medications; however, no observational or controlled studies on this topic have been conducted [17]. A consensus statement regarding COVID-19 vaccines from PANS/PANDAS providers has yet to be released, and no specific information on intention or hesitancy towards COVID-19 vaccination among caregivers of PANS/PANDAS children has been published.

We sought to understand the viewpoint of PANS/PANDAS caregivers towards the COVID-19 vaccines, as well as the broader impact of the pandemic on children with PANS/PANDAS. To do so, we created an anonymous survey for caregivers of children with PANS/PANDAS that collected information regarding demographics, health history, telehealth use, and intention to vaccinate their children against COVID-19. Additionally, caregivers were asked to assess the impact of the pandemic on symptoms and symptom severity in their children, along with their social relationships, academic abilities, and involvement in hobbies. We also evaluated the level of caregiver burden, parental anxiety and stress, and pandemic-related financial impacts.

Methods

Data was obtained through an anonymous online survey collected between February 2021 and June 2021. Informed

consent was obtained from all participants in the study. All study procedures were approved by the Institutional Review Board of the recruiting hospital. Caregivers of children with suspected or diagnosed PANS/PANDAS were recruited online through parent advocacy groups for children and families with PANS/PANDAS and OCD. Email invitations were also sent to families who had contacted the hospital's PANS/PANDAS clinic and consented to being contacted for research. Caregivers were included in this study if they self-identified as at least 18 years of age and as a caregiver for a minor with PANS/PANDAS. Data analysis was restricted to respondents who indicated that the child's symptoms included one of the three cardinal symptoms of PANS/PANDAS (i.e., OCD, tics, severe restricted eating) and were triggered by an infection.

Age and gender were reported for both the respondent and the child. Age was measured in years, and gender was self-reported as female, male, or other. Household income was divided into 20 categories from \leq \$20,000 to $>$ \$300,000. Population density of respondent's geographic area was determined using the participant's zip code [18]. A COVID Questionnaire was developed by the study team to assess the children and families' direct contact with the COVID-19 virus, treatment accessibility during the pandemic, use of telehealth services, and perceived stress related to following Centers of Disease Control (CDC) guidelines (i.e., wearing masks, social distancing) for the pandemic. Respondents reported the severity of the child's PANS/PANDAS symptoms during the pandemic on a 7-point scale (see Fig. 1). They also answered questions about the child's relationships with family members, peers, and social and academic engagements using a five-point Likert rating scale (Strong Positive Impact, Somewhat Positive Impact, Neutral, Somewhat Negative Impact, Strong Negative Impact). If respondents endorsed that a child had a suspected or confirmed COVID-19 infection, or multisystem inflammatory symptoms in children (MIS-C), they were asked questions about behavioral symptoms during the infection. Respondent's hopefulness for their child's future and the future in general were assessed on a three-point scale (not at all hopeful, a little hopeful, very hopeful).

Respondents also completed the following psychometric rating scales:

1. *Children's Yale-Brown Obsessive-Compulsive Scale-Parent Report (CY-BOCS-PR)* [20]: The child's current OCD severity was assessed using the CY-BOCS-PR. This 10-item parent-report scale of pediatric OCD symptoms and severity has been shown to have high internal consistency [19].
2. *Coercive Disruptive Behavior Scale for Pediatric OCD (CD-POC)* [21]. The CD-POC was used to assess the

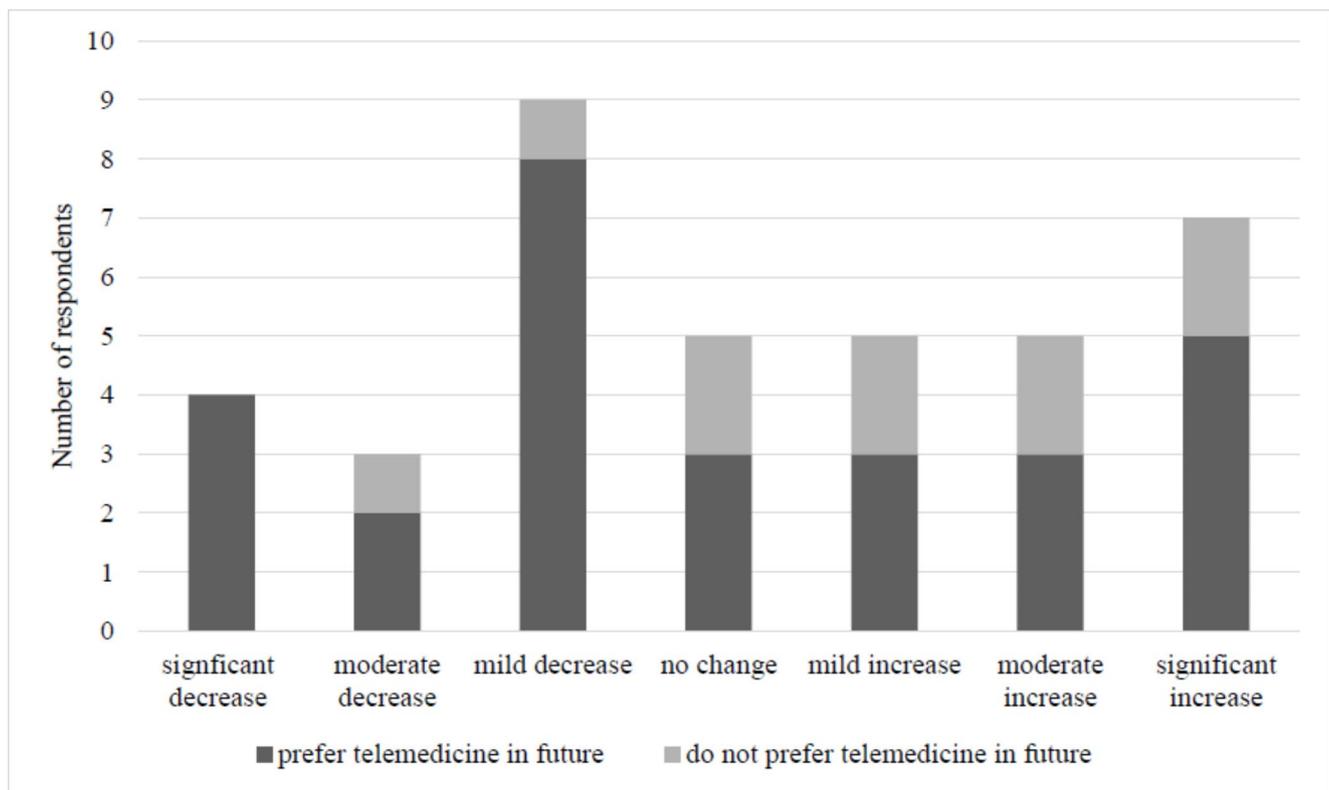


Figure 1 Preference for telemedicine grouped by symptom change over course of pandemic

severity of a child’s coercive behavior in requiring family to engage in OCD-related acts. This 18-item measure has shown high internal consistency [20].

3. *Depression, Anxiety, and Stress Scale (DASS-21)* [21]: Respondents’ symptoms of depression, anxiety, and stress were assessed using the 21-item DASS-21. The DASS-21 has demonstrated high internal consistency (Cronbach’s $\alpha = 0.93$) [22].
4. *Caregiver Burden Inventory (CBI)* [23]: This 24-item questionnaire was used to assess caregiver burden. This self-report measure has been validated for use in a population of caregivers of children and adolescents with PANS/PANDAS [24].
5. *Couples Satisfaction Index (CSI)* [25]: If respondents indicated they were in a relationship, relationship satisfaction was assessed using the 32-item CSI. The CSI has been shown to strong convergent validity and excellent construct validity [25].

All analyses were conducted in SPSS version 24.0 [26]. If a participant was missing an answer to a standardized questionnaire that would significantly impact their total score, the participant was not included in the reporting of that measure. Chi square tests were performed to determine whether there were significant relationships between caretakers’ preference for telehealth and household income or local

population density. A chi-squared test was used to evaluate if PANDAS symptom severity was related to satisfaction with telehealth services. A binary logistic regression using the forced-entry method was used to assess factors for predicting if a respondent planned to vaccinate his/her child when a COVID-19 vaccine became available, with vaccine hesitancy defined as those who answered “No” to the question “Do you plan to vaccinate your child for COVID-19 when a vaccine becomes available?”. Variables were chosen for inclusion based on a literature review of factors associated with vaccine hesitancy. The 81 respondents who entered valid U.S. zip codes and met the definition for vaccine hesitancy above were included in the regression. The continuous covariates were age of the respondent and the proportion of votes for Donald Trump in 2020 in the respondent’s zip code or county. The zip-code-level data was derived from the New York Times [27]; county-level data from CNN [28] was used when zip-code-level was not available. The caregiver’s report of their child’s current immunization status (“Is your child up to date on his/her vaccinations?”) was used as a categorical covariate.

Table 1 Caregiver report of new or exacerbated behavioral difficulties related to COVID-19 infection or MIS-C

Symptom	Child with PANS/PANDAS N (%)		
	Diagnosed COVID-19	Suspected COVID-19	Suspected MIS-C
Total	12	31	9
Sleep	4 (33.33%)	12 (38.71%)	5 (55.56%)
Tics	5 (41.67%)	12 (38.71%)	4 (44.44%)
OCD	5 (41.67%)	18 (58.06%)	5 (55.55%)
Sensory	5 (41.67%)	17 (54.84%)	6 (66.67%)
Mood lability	7 (58.33%)	17 (54.84%)	6 (66.67%)
Behavioral regression	6 (50%)	14 (45.16%)	3 (33.33%)
Urinary Symptoms	3 (25%)	11 (35.48%)	3 (33.33%)
Motor Symptoms	5 (41.67%)	12 (38.71%)	6 (66.67%)
Restricted eating	5 (41.67%)	13 (41.94%)	7 (77.78%)
Depression	3 (25%)	8 (25.81%)	5 (55.55%)
Anxiety	6 (50%)	18 (58.06%)	6 (66.67%)
Hallucinations	2 (16.67%)	2 (6.45%)	2 (22.22%)
Other	2 (16.67%)	4 (12.90%)	1 (11.11%)

Note: MIS-C = multisystem inflammatory disorder in children. No respondents indicated that their child had a diagnosed case of MIS-C.; Responses of caregivers to the question, “What new or exacerbated symptoms did they (the child) exhibit during the course of the illness?”

Results

Data from a total of 254 subjects were included in our analyses (mean age = 45.46 years). The majority of respondents identified as the biological mother of the child (89.4%), followed by adoptive mothers (5.1%) and biological fathers (5.6%). Children with PANS/PANDAS had a mean age of 11.61 years ($SD=3.41$) with a slight male preponderance (60% male, 39% female, 1% other). Infection triggers which initiated PANS/PANDAS were reported by caregivers as strep (66.8%, $N=169$), viral (e.g., common cold, measles) (14.2%, $N=36$), mycoplasma (e.g., pneumonia) (7.5%, $N=19$), or other bacterial infection (not strep) (7.1%, $N=18$), and Lyme (4.3%, $N=11$). Forty-three children had diagnosed or suspected COVID-19 infections. The most commonly endorsed new or exacerbated symptom during confirmed COVID-19 illness was mood lability (58.33%, $N=7$). Mood lability was also reported in over 50% of those with a suspected COVID-19 infection (54.84%, $N=17$), as well as OCD (58.06%, $N=18$), sensory sensitivities (54.84%, $N=17$), and anxiety (58.06%, $N=18$). Similar symptoms were reported in children with suspected MIS-C (see Table 1).

Within the full cohort, respondent endorsements on the COVID Questionnaires suggest that 76.77% of households experienced more stress in the home during the pandemic than pre-pandemic levels. The impact of the pandemic on PANS/PANDAS symptoms, participation in hobbies,

academic skills, and the child’s relationships with others varied greatly from strong negative to strong positive impacts (see Table 2). Almost half (48.48%) of children reportedly did not experience any difference in their ability to receive care for PANS/PANDAS due to the pandemic; 35.86% found it somewhat or much harder to obtain care, and 14.65% found it somewhat or much easier to obtain care. Almost half (44.44%) of children were slightly to overly cautious when following CDC safety guidelines, and 33.34% were more distressed when others were not following safety guidelines (see Table 2). Mean respondent score of the child’s OCD severity, as measured by the CY-BOCS-PR, fell in the moderate range ($M(SD)=17.22(9.18)$), as did the mean severity of coercive behaviors (CD-POC) ($M(SD)=20.11(14.46)$).

Regarding the effect of the pandemic on the respondents, 8.7% of caregivers were previously diagnosed with COVID-19, and another 8.7% had a suspected COVID-19 infection. One respondent required hospitalization related to COVID-19, and one respondent had a member of their household hospitalized. 6% ($N=16$) reported that someone close to them (i.e., coworker, friend, family member) died as a result of a COVID-19 infection or related complication. 33% of respondents ($N=84$) reported being financially impacted by the pandemic (Mild = 36.5%, Moderate = 42.2%, Severe = 20.0%, Extreme = 1.2%). Caregivers’ DASS-21 scores showed mean scores of 6.42 ($SD=7.59$) for anxiety, 14.6 ($SD=9.8$) for stress, and 10.93 ($SD=10.67$) for depression out of a possible total score of 42 per category (higher numbers indicate more severity). The mean CBI score (40.82(20.49)) surpassed the threshold indicating risk of caregiver “burnout” [29]. Caregiver’s reported relationship satisfaction (CSI) indicated relationship dissatisfaction with romantic/domestic partners (98.71(30.88)). The majority of respondents were hopeful for the future of their child with PANS/PANDAS ($N=120$, 47.2%), followed by those that were a little hopeful ($N=66$, 26.0%) and not at all hopeful ($N=10$, 5.5%). Similarly, the majority were “very hopeful” for the future in general ($N=126$, 49.6%), followed by those that were a “little hopeful” ($N=55$, 21.7%) and “not at all hopeful” ($N=14$, 5.5%).

Over 80% of children in the sample received care for PANS/PANDAS via telehealth during the pandemic (83.6%, $N=122$). Of these, when asked about telehealth preference in future, 28.7% ($N=35$) of respondents said that they would prefer telemedicine for PANS/PANDAS treatment in the future, 9.8% said they would not, 0.8% said that question was no longer applicable to their child, and 60.7% said that it would depend on the type of appointment. Respondents who said they preferred telehealth or preferred it depending on the type of appointment were also asked to check all types of appointments they would prefer via telehealth

Table 2 Caregiver report on the effect of the COVID-19 pandemic on PANS/PANDAS symptoms

	Response Options N (%)				
	Strong Negative	Somewhat Negative	Neutral	Somewhat Positive	Strong Positive
PANS/PANDAS symptoms	33 (16.67%)	53 (26.77%)	46 (23.23%)	36 (18.18%)	29 (14.65%)
<i>Relationship with:</i>					
Immediate Family	21 (10.61%)	45 (22.73%)	58 (29.29%)	42 (21.21%)	31 (15.66%)
Extended Family	24 (12.12%)	64 (32.32%)	84 (42.42%)	14 (7.07%)	11 (5.56%)
Respondent	12 (6.06%)	35 (17.68%)	63 (31.82%)	55 (27.78%)	32 (16.16%)
Friends	47 (23.74%)	75 (37.88%)	47 (23.74%)	19 (9.60%)	7 (3.54%)
Participation in Hobbies	68 (34.34%)	69 (34.85%)	32 (16.16%)	18 (9.09%)	10 (5.05%)
Academic Skills	36 (18.18%)	57 (28.79%)	59 (29.80%)	24 (12.12%)	18 (9.09%)
Stress in Home Environment compared to Pre-Pandemic	Less	Neutral	Mild	Moderate	Severe
	23 (11.62%)	22 (11.11%)	57 (28.79%)	61 (30.81%)	34 (17.17%)
Extent to which child is following guidelines*	Resistant to following guidelines*	Not as Cautious as should be	Normal Precautions	Slightly Overcautious	Overly Cautious
	8 (4.04%)	11 (5.56%)	89 (44.95%)	42 (21.21%)	46 (23.23%)
Level of Distress felt by child if others are not following guidelines*	Much Less Distress	Less Distress	No Additional Distress	More Distress	Much More Distress
	12 (6.06%)	17 (8.59%)	102 (51.52%)	43 (21.72%)	23 (11.62%)
Ability to receive PANS/PANDAS care	Much Harder	Somewhat Harder	No Difference	Somewhat Easier	Much Easier
	17 (8.59%)	54 (27.27%)	96 (48.48%)	19 (9.60%)	10 (5.05%)

Note: Questions and response options derived from COVID Questionnaire developed by the lead authors.

*Guidelines refer to the guidelines issued by the Centers for Disease Control to reduce transmission at the time of this survey (e.g., wear a mask, stay 6 feet apart).

for PANS/PANDAS. The treatment type that received the most endorsements was medication management (N=98), following by primary care (N=52), psychiatric assessment (N=38), psychotherapy (N=36), neuropsychological evaluation (N=25), and rheumatology (N=17). Statistical analyses examining whether or not telehealth was preferred for PANS/PANDAS care showed no significant relationship between telehealth preference for future care and respondent's household income, $X^2(18,141) = 21.624, p = 0.249$, or telehealth preference and population density of the respondent's zip code, $t(51) = -1.357, p = 0.181$. When asked if using telehealth during the pandemic had made it easier to obtain care for PANS/PANDAS, 78.7% (N=96) answered yes. The chi-squared test of independence demonstrated a significant relationship between whether a respondent felt telehealth made it easier to obtain care (Yes/No) and PANS/PANDAS symptoms severity during the pandemic, $X^2(3, 120) = 13.812, p = 0.003$. Specifically, caregivers whose children had only mild symptoms during the pandemic were more likely to respond that telehealth made access easier.

Regarding respondents' plans to vaccinate their children with PANS/PANDAS for COVID-19 once a vaccine became available, 25.9% (N=51) of respondents answered that they were not planning to vaccinate their child against

COVID-19, 29.9% (N=59) answered that they were planning to vaccinate their child, and 44.2% (N=87) were unsure. The logistic regression model showed a significant effect of child's previous vaccination status and presidential voting trends in the respondent's geographic area on vaccine hesitancy (i.e., not planning to vaccinate their child for COVID-19). $X^2(3) = 22.797, p < 0.0001$. The model explained 33.02% (Nagelkerke R^2) of the variance and correctly classified 75.3% of cases. Age of the respondent was not a significant predictor in this model ($p > 0.082$). The proportion of votes for the Republican presidential candidate in the 2020 election for the zip code/county where the respondent resided was a significant positive predictor of not planning to vaccinate one's child with the COVID-19 vaccine (OR=25.350, $p = 0.037$). The direction of the interaction showed that as the proportion of votes for the Republican nominee in 2020 in the respondent's zip code or county increased, the likelihood that the respondent was not planning to vaccinate their child with the COVID-19 vaccine also increased. Furthermore, the child's current immunization status for standard childhood vaccinations was a significant negative predictor of not planning to vaccinate against COVID-19 (OR=0.0117, $p < 0.001$). The direction of the interaction suggests that respondents of children who

were not up to date on their childhood immunizations were more likely to say they did not plan to vaccinate their child for COVID-19.

Discussion

The aim of this study was to understand the impact of the pandemic on children with PANS/PANDAS and their families. Using an anonymous survey completed by caregivers of children with PANS/PANDAS, symptom severity, well-being, and use of telehealth, as well as respondent mental health and household impacts, were assessed. Additionally, we collected symptom-level information from a small number of children who had suspected or diagnosed COVID-19 infection. Although the format of this study does not allow for verification of patient diagnoses, it provides an initial evaluation of the impact of the pandemic and COVID-19 infection on patients with PANS/PANDAS.

Our findings reflect a previous finding that caregivers of children with PANS/PANDAS felt symptoms of PANS/PANDAS were negatively impacted by the pandemic [30]. In our sample, the mean OCD severity scores (CY-BOCS-PR) fell in the moderate range, and mean level of coercive behaviors ($M=20.11$) were similar to other samples of children with OCD ($M=16.46$) [31]. Almost half (44.44%) of children in the sample were more cautious than their caregivers expected in following safety guidelines recommended by the CDC. They also reportedly felt more distress than caregiver's would expect when others were not following these guidelines. Similar to previous parental reports of reduced psychological well-being in children during the pandemic [32], the majority of respondents of our survey responded that the pandemic had negative impacts on their child's relationships with friends, extended family, participation in hobbies, and academic skills; however, the majority of respondents felt the pandemic had a positive impact on their relationship with their child. Given the identified perceptions of negative impact, it is important for caregivers and pediatric providers to help children regain mastery in social relationships and important positive indicators for future resiliency [32].

A majority of caregiver's in this study reported high levels of relationship dissatisfaction, burnout, and mild symptoms of stress and depression. This finding is comparable to pre-pandemic levels reported in a similar cohort of PANS/PANDAS caregivers [11]. This suggests caregivers of children with PANS/PANDAS experienced a high level of burn-out both before and during the pandemic, and thus this should continue to be an area of inquiry and appropriate intervention by providers. High levels of caregiver burden and stress are associated with worse outcomes for children

with neurodevelopmental and medical disorders [33, 34], highlighting the importance of addressing these dynamics.

Children who had a COVID infection reported a multitude of symptom exacerbations following their infection (via caregiver report). This is important given the hypothesis that additional infections may trigger symptoms of PANS/PANDAS [7]. No children in this study were reported to have died due to a COVID-19 infection, but future research is needed to understand the impact of COVID-19 infection on symptom exacerbation in this population.

This study also evaluated the impact of the pandemic on the abilities of patients with PANS/PANDAS to access care. While almost half of the sample reported that there was no difference in their ability to receive care, 35% of our sample reported it was somewhat or much harder to receive care. Similar to trends across the U.S. healthcare system [35], the majority of our sample received care for PANS/PANDAS via telehealth during the pandemic. Within that group, 60.7% of caregivers said that their preference for telehealth depended upon the type of appointment their child needed to treat PANS/PANDAS, with the majority preferring medication management as a telehealth-based treatment. Our findings also suggest that telehealth is preferred for patients who have less severe symptoms of PANS/PANDAS.

Approximately 25% of the caregivers sampled reported no current plans to vaccinate their child against COVID-19, similar (28–33%) to parental reports of vaccination refusal in other clinical populations [36, 37]. Our results identified two factors that predicted whether caregivers of children with PANS/PANDAS were not planning to vaccinate their child against COVID-19 once a vaccine becomes available: (1) if they resided in an area with a greater proportion of people who voted for the Republican in the 2020 presidential election, and (2) if their child was previously not up-to-date on immunizations, although respondent age was not a significant predictor. It is possible that rates of vaccine hesitancy in this population could change once vaccines are approved for all ages of children, or if the consequences of infection in children are worsening. For example, parents who were initially unwilling to vaccinate their children (without PANS/PANDAS) for COVID-19 reported willingness to vaccinate if the mortality rates increase [37]. A systematic review found reduced vaccine hesitancy due to interventions such as tailored educational materials, parental reminders, and physician training [38]. Similar to guidelines issued by a consortium of PANS/PANDAS experts regarding vaccination for other diseases [17], guidance from clinical experts based on research should be widely available to caregivers of children with PANS/PANDAS to help them understand the risks and benefits of COVID-19 vaccination for their children.

The generalizability of these findings is limited by several factors of note. Although our anonymous survey allowed us to solicit responses from caregivers across the United States and internationally, this format does not allow for verification of PANS/PANDAS diagnoses in the children of the respondents. Although a standardized measure was used, the patient's OCD severity was also based solely on parent report. While the CY-BOC-PR is highly correlated with clinician reports on the semi-structured version of the CY-BOCS, the CY-POCS-PR has been shown to elicit greater symptom severity than the self-report version [19]. Future research is recommended to assess the impact of telehealth on the efficacy of treatment for PANS/PANDAS, the outcomes and side effects of vaccination for COVID-19 in children with PANS/PANDAS, and whether negative consequences associated with the pandemic, such as increased symptoms, are remedied when the acute phases of the pandemic are over.

While the population of this study included children with both suspected PANS and PANDAS, it is possible that results may differ between these groups. When comparing small cohorts of patients with PANS and PANDAS, no significant differences were detected in age of onset, previous neuropsychiatric symptoms, or psychiatric or autoimmune family history; however, OCD, behavior regression, and somatic symptoms were more common in children with PANS [39]. In the current study, due to the inability to confirm a GAS infection given the anonymous nature of the study, we did not feel we could reliably make a determination of PANS or PANDAS for these analyses. Thus have presented data on all individuals who reportedly presented with symptoms of PANS and/or PANDAS following an infection, but more research should be done to determine whether the COVID-19 infection or the pandemic more widely had differential effects on these subpopulations.

The findings of this study provide valuable implications for clinical care. Providers should be aware that COVID-19 infection in this population may result in an exacerbation of PANS/PANDAS symptoms. Even for children with PANS/PANDAS who did not contract COVID-19, symptoms of PANS/PANDAS may worsened due to factors or stressors from the pandemic. General social and emotional functioning may have been negatively impacted by the pandemic, and thus supports and treatments should be recommended to address these multifaceted issues. It is also noteworthy that caregivers' decisions about whether or not to vaccinate their child for COVID-19 may be influenced by factors outside of medical research about the vaccine. In regards to treatment delivery, we found a subset of caregivers in our study reported more success obtaining care by using telehealth, and providers may want to consider offering both virtual and in-person visits after the pandemic. Our findings also

highlighted the pandemic-related financial burden faced by a subset of families of children with PANS/PANDAS. Social service referrals may be considered for families in which financial constraints may affect access to medical care. Given the high rates of caregiver burden, as well as the minority of respondents who felt hopeless about their child's future, providers should assess for caregiver burnout and sources of hopelessness in order to provide intervention or referrals as indicated.

Overall, this survey study revealed that children with PANS/PANDAS and their families experienced negative impacts from the pandemic as well as some surprising positives, including caregiver perceptions of improved relationships with their child. This sample reported a worsening of PANS/PANDAS symptoms attributed to the pandemic. COVID-19 infection within this sample was reported to result in new symptoms or symptom exacerbation in some children but was not fatal. Future research should evaluate the relationship between COVID-19 infection and neuropsychiatric symptom exacerbation, as this line of inquiry may provide valuable information about the etiology of PANS/PANDAS and post-infectious neuropsychiatric sequelae. Telehealth was widely used by this population but preferred by caregivers of children with mild PANS/PANDAS symptoms. The continuation of telehealth services post-pandemic and the effectiveness of telehealth to treat PANS/PANDAS remains unknown. Future research is warranted to assess the effectiveness of telehealth services for this population. Our data suggests that children's vaccination history and the voting patterns of their geographic area will be important factors as to whether or not their caregiver will consent to their COVID-19 vaccination. As the availability of vaccinations increases and the age of eligibility decreases, we expect that both child-specific and cultural factors will continue to be highly relevant in vaccination decision-making.

Summary

The current study assessed the impact of the COVID-19 pandemic on children with PANDAS/PANS. We conducted an anonymous survey between February and June 2021 of 254 self-reported caregivers of minors with PANS/PANDAS. The majority of respondents felt the pandemic negatively impacted their child's friendships, relationships with extended family, hobbies, and academic skills. Children with suspected or diagnosed COVID-19 experienced new or worsened existing symptoms, particularly mood lability, OCD, and anxiety. Telehealth care was preferred if the child had mild symptoms of PANS/PANDAS. A caregiver's intention to vaccinate their child was significantly associated with the presidential election results in the county the

caregiver resided in, and if the child had received previous vaccines. Respondents reported high levels of relationship dissatisfaction and caregiver burden.

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Declarations

The authors declare that there is no conflict of interest. All procedures in this study were approved by the Internal Review Board (IRB) of the Massachusetts General Hospital (Protocol Number: 2021P003145). All procedures performed were in accordance with the ethical standards of the institution and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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