



22q11.2 Deletion and Duplication Syndromes and COVID-19

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Received: 7 January 2022 / Accepted: 8 March 2022 / Published online: 18 March 2022

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To the Editor,

Many respiratory viruses are more severe in people with T cell immunodeficiencies and early evidence demonstrating more severe COVID-19 in people with trisomy 21 led to guidance that 22q11.2 deletion syndrome (22q11.2del), along with other syndromes, represents a high-risk condition for severe COVID-19 [1]. We performed a multinational survey (Supplemental Methods) of patients with 22q11.2-related syndromes to understand the spectrum of severity of COVID-19 from 7/7/21 to 12/22/21. The survey included 152 patients with 22q11.2del and 46 with 22q11.2 duplication syndrome (22q11.2dup). Supplemental Table 1 lists the characteristics of the study population. The baseline characteristics of the population were typical for 22q11.2del and 22q11.2dup. 48% were male and 52% were female. The median age was 13 years with a range of 1–66 years of age (8–23; 25–75 percentiles). We wished to understand the overall impact of the pandemic on people with 22q11.2del/dup. Ninety-one percent reported that they had no trouble accessing healthcare during the pandemic. Among the 198 respondents, 42 had had COVID-19 with 41 providing full responses and this group forms the population further analyzed.

Of the 42 patients who had COVID-19, 16 were clinically diagnosed and 26 had a positive test for COVID-19. Thirty-two out of forty-one had 22q11.2del (age range 2–36, mean age of 13 years) and 9 had 22q11.2dup (age range 2–26, mean age of 11 years). Thirty-eight out of forty-one (93%) were not vaccinated. A single patient was hospitalized for only 1 day and only two were seen in the emergency department. The remainder were managed at home. Eight patients took zinc, 28 took vitamin D, and 9 took steroids as part of their treatment. No patients reported taking remdesivir,

convalescent plasma, or the monoclonal antibody cocktail. Fatigue was the most commonly reported symptom at 63%, headache was reported by 54%, and cough by 51% (Fig. 1). The median time for the patient to feel “back to normal” was 2 weeks with a range of 0 to > 12 weeks. Four patients took longer than 12 weeks to feel “back to normal.” For the four patients who took > 12 weeks to feel back to normal, all experienced fatigue, and half had headache, dizziness, difficulty sleeping, and joint/muscle pain.

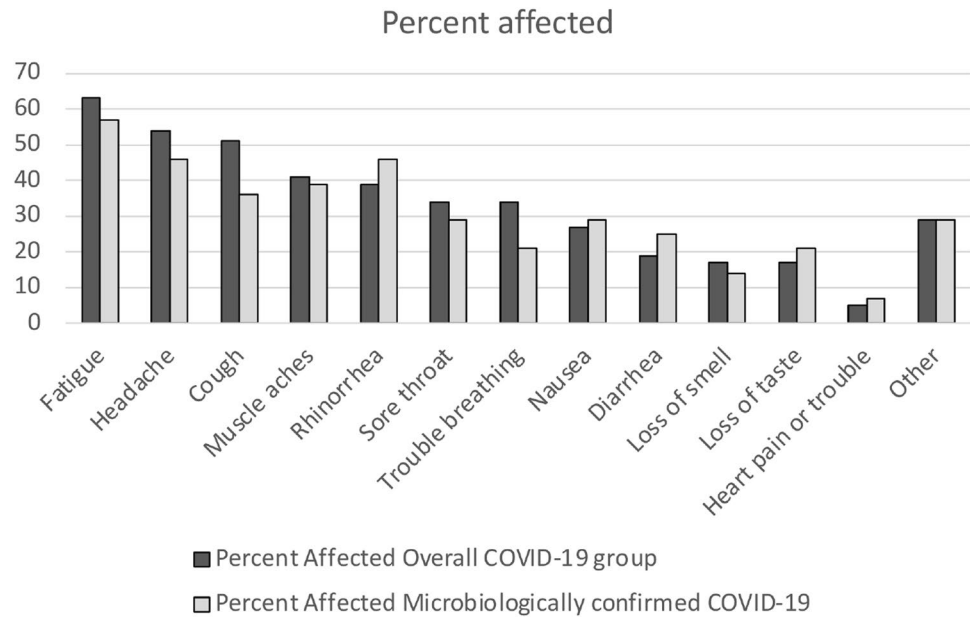
We similarly examined the subset with microbiologically confirmed COVID-19. There were 28 responses recorded as having testing that diagnosed COVID-19. This group included the single person who was hospitalized. This subset reported an average of 19 days until they felt back to normal with a range of 0–100 days and only three were vaccinated. Treatments were similar to the overall COVID-19 group with five patients receiving zinc, 22 patients receiving vitamin D, and 5 patients receiving corticosteroids. Symptoms closely paralleled the overall COVID-19 group (Fig. 1). Comorbidities are listed in the Supplemental Table.

Patients with 22q11.2del/dup do not appear to have the high rate of complications from COVID-19 seen in trisomy 21, another group with developmental delay and frequent cardiac anomalies [2]. Emerging evidence suggests that T cells, which are often diminished in 22q11.2del and occasionally diminished in 22q11.2dup have little impact on the severity of COVID-19 [3]. This has been borne out additionally in model systems where depletion of T cells has a limited effect on clinical recovery [4, 5]. These data are reassuring in that neither the case rate nor the severity appears to be increased in people with 22q11.2del/dup. Only 1/41 patients were hospitalized. Even accounting for the overall young age of this cohort, the patients did surprisingly well, although 4 patients in the overall COVID-19 diagnosed group (10%) had symptoms that lasted > 12 weeks. One troubling aspect of this survey is the high rate of unvaccinated individuals. Over half of the reported infections occurred before vaccination was available even for adults which is a possible explanation for the low vaccination rate.

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Fig. 1 The frequencies of reported symptoms with COVID-19 are displayed for both the overall COVID-19 cohort and the subset who had specific testing confirmation



This is the only survey, as far as we are aware, to focus on 22q11.2del/dup but, as is true for all surveys, it was dependent on motivation for responses which may have skewed the results. While this was distributed internationally, there was a strong bias towards respondents from the USA. Additionally, the dates of reported infections suggest that many predated the appearance of delta strain and certainly do not include omicron strain. Whether these could alter the results is unknown. Nevertheless, this survey provides important information both on the baseline health of people living with 22q11.2del/dup as well as their COVID-19 disease severity. The results are largely reassuring in that while the baseline health suggests significant risk factors for severe disease (hypertension, overweight, psychiatric diagnoses, and immunodeficiency) and in spite of low vaccination rates, the cohort did well with only 41 infections and only one brief hospitalization among those infected. No patient went to the ICU. The CDC does not precisely tabulate hospitalization rates for those < 18 years of age. For those 18–29 years of age in the general population, the hospitalization rate of those known to be unvaccinated and infected by SARS CoV2 is about 6% [6]. Therefore, our rate of 1/41 hospitalized patients (2%) is not higher than expected. The symptoms manifested are also comparable to those described with fatigue, cough and typical upper respiratory tract symptoms experienced by many. Physicians caring for patients and patients and families with 22q11.2 del/dup may be largely reassured by these findings.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10875-022-01246-0>.

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Author Contribution Investigators Sullivan and McDonald-McGinn conceptualized the study, The 22q11.2 COVID group refined the survey instrument, and Mr. Crowley implemented the survey.

Data Availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code Availability Not applicable.

Declarations

Ethical Approval This is an observational study. The Research Ethics Committee at the Children’s Hospital of Philadelphia has confirmed that no ethical approval is required.

Consent to Participate Not applicable, exempted study.

Consent to Publish Not applicable.

Competing Interests The authors declare no competing interests.

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