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# Incidence of arrhythmias and electrocardiographic abnormalities in symptomatic pediatric patients with PCR-positive SARS-CoV-2 infection, including drug-induced changes in the corrected QT interval

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**BACKGROUND** There is limited data regarding the electrophysiological abnormalities and arrhythmias in children with COVID-19, including those associated with treatment using potentially proarrhythmic hydroxychloroquine (HCQ) and azithromycin (AZN).

**OBJECTIVES** To describe the electrophysiologic findings and arrhythmias associated with pediatric COVID-19 and its treatment.

**METHODS** A single-center retrospective chart review was undertaken and included all patients with (1) symptoms of COVID-19 and (2) PCR-positive nasopharyngeal swabs for SARS-CoV-2 who were placed on continuous telemetry for the duration of their hospitalization during March through May, 2020.

**RESULTS** Thirty-six patients were included in the study. Significant arrhythmias were found in 6 (nonsustained ventricular tachycardia in 5 and sustained atrial tachycardia in 1). All were self-resolving and half prompted prophylactic antiarrhythmic therapy. Patients with significant arrhythmias were likely to have noncardiac comorbidities (4/

6), but these were not more common than in patients without arrhythmias (20/30,  $P = 1$ ). The use of HCQ was associated with statistically significant QTc prolongation ( $413 \pm 19$  ms vs  $425 \pm 16$  ms,  $P = .005$ ). QTc was not statistically different in patients with and without arrhythmias ( $425 \pm 15$  ms vs  $425 \pm 15$  ms,  $P = 1$ ).

**CONCLUSIONS** In pediatric patients with PCR-positive active COVID-19 infection, significant arrhythmias are infrequent, but are more common than expected in a general pediatric population. Comorbidities are not more common in patients with arrhythmias than in patients without arrhythmias. COVID-19 treatment using HCQ is associated with QTc prolongation but was not associated with arrhythmias in pediatric patients.

**KEYWORDS** COVID-19; Pediatric; Arrhythmias; Drug-induced prolonged QT; Hydroxychloroquine

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## Introduction

The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been declared a global pandemic by the World Health Organization and has affected millions of people worldwide.<sup>1</sup> While typically the virus is known to affect the respiratory system, there is adult literature of cardiovascular involvement, including electrophysiologic abnormalities and anecdotal reports of sudden cardiac death.<sup>2-5</sup> Currently, literature regarding electrophysiological abnormalities in children with COVID-19 infection is lacking. In addition,

some of the medications that have been used for treatment of COVID-19 infection, such as hydroxychloroquine (HCQ) and azithromycin (AZN), are known to cause corrected QT (QTc) interval prolongation, therefore potentially predisposing patients to malignant ventricular arrhythmias.<sup>6,7</sup> However, there is little current data on the electrophysiologic consequences of these drugs in the setting of active COVID-19 in pediatric patients.

## Methods

### Study design

This is a single-center retrospective observational study conducted at Cohen Children's Medical Center, located in the COVID-19 epicenter in New York City. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Northwell Institutional Review Board through its COVID-19 Research Consortium.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no conflicts of interest. **Address reprint requests and correspondence:** Dr Sharmeen Samuel, Division of Pediatric Cardiology, Cohen Children's Hospital, 1111 Marcus Ave, 4B, New Hyde Park, NY 11042. E-mail address: [ssamuel21@northwell.edu](mailto:ssamuel21@northwell.edu).

## Study population

All pediatric patients between the ages of 0 and 21 years who were sufficiently medically ill to require hospital admission with confirmed COVID-19 infection by positive result on polymerase chain reaction (PCR) testing of nasopharyngeal specimens between March 1, 2020, and April 30, 2020 were included in the study if they had been placed on continuous telemetry for the duration of their hospitalization. Patients with (1) IgG antibodies for SARS-CoV-2; (2) any known history of known arrhythmias, long QT syndrome, or other channelopathies; or (3) hemodynamically significant congenital heart disease were excluded from analysis. Some patients are included in other Cohen Children's Medical Center COVID reports, but the analyses presented here are original.

## Treatment protocols

As per hospital protocol, COVID-19-specific medications including HCQ with or without AZN were initiated at the discretion of the Infectious Disease team for patients needing supplemental oxygen for hypoxia in the setting of positive SARS-CoV-2, if the baseline QTc was less than 480 milliseconds (ms) measured on lead II via 15-lead electrocardiogram (ECG) or telemetry. All patients were treated with 5 days of HCQ  $\pm$  AZN, with the standard dosing of HCQ being 7 mg/kg/dose (maximum dose 400 mg/dose) on day 1 and 3.5 mg/kg/dose (maximum dose 200 mg/dose) on the subsequent 4 days, and AZN dose being 10 mg/kg/dose (maximum dose 500 mg) on day 1 and 5 mg/kg/dose (maximum dose 250 mg) on subsequent 4 days. Other COVID-19-specific medications such as intravenous immunoglobulin, steroids, remdesivir, anakinra, and tocilizumab were reserved for patients with more severe manifestations and multiple comorbidities. Arrhythmia treatment was at the discretion of the attending electrophysiologist (A.B.).

## Rhythm monitoring and QTc calculations

As part of the treatment protocol, patients underwent baseline 12- or 15-lead ECG, when possible, prior to initiation of treatment and were placed on continuous telemetry rhythm monitoring while on treatment. To reduce contact between health care personnel and COVID-19 patients, ECGs were performed only when there was an absolute clinical indication. ECG interval, axis, and voltage criteria were evaluated via Davignon and colleagues.<sup>8</sup> Otherwise, all rhythm monitoring and QTc calculations were performed using lead II obtained via telemetry. Rhythm tracings were collected daily and independently interpreted by both a pediatric cardiology fellow (S.S.) and a pediatric electrophysiologist (A.B.) in a retrospective fashion for the purposes of research, each blinded to other variables. When there was initial lack of agreement in QTc measurement, tracings were reviewed together and consensus was achieved. All QTc measurements were made from telemetry recordings. Baseline measurements were made shortly prior to therapy with HCQ or AZN. Subsequent manual measurements were made randomly once per

day in the morning, with few exceptions. These daily measurements were recorded and the longest of them is referred to as the longest daily measured QTc. The QTc interval was measured using the Bazett formula ( $QTc = QT/\sqrt{RR}$ ). In patients with conduction abnormalities the QTc was calculated using an adjusted QT (adjusted QT:  $aQT = QT - QRS$  in excess of 100 ms).

Significant arrhythmias included type II second-degree atrioventricular block, complete heart block, nonsustained (ns) or sustained supraventricular/atrial and ventricular tachycardias. Sustained arrhythmias are defined as those lasting more than 30 seconds and/or causing hemodynamic collapse. Single ectopic complexes were recorded but not considered significant arrhythmias. Rates, duration, and factors associated with arrhythmias were also recorded. QTc values of  $>450$  and  $>460$  ms were considered abnormal intervals in males and females, respectively, as per AHA/ACC/HRS recommendations for the standardization and interpretation of the electrocardiogram.<sup>9</sup>

## Analyses

In addition to descriptive analyses, several sub-analyses were performed, including the following: (1) comparisons of QTc prolongation were made between patients who received HCQ with or without AZN, those receiving HCQ alone, patients receiving HCQ with AZN, and those who received neither drug; and (2) comparisons were made between patients who developed significant arrhythmias and those who did not.

## Additional variables

Information including demographics, pre-existing conditions, laboratory data including electrocardiographic and echocardiographic data, cardiac enzymes, respiratory support, need for vasopressors and COVID-19-specific medications used were collected and entered in the project's secure Research Electronic Data Capture (REDCap), hosted by Northwell Health.

## Statistics

Descriptive data are presented as average  $\pm$  standard deviation. Continuous parametric analyses were performed using the Student *t* test. Unpaired tests were used in comparing data from different patients while paired tests were used when comparing data points from the same patient at different times. The Fisher exact test was used for comparing categorical variables between small groups while the  $\chi^2$  test was used for categorical comparisons of larger groups. Clinical correlations were performed using the Pearson correlation.

## Results

Thirty-six patients met criteria for inclusion in the study. Two patients with large ventricular septal defect (VSD) and significant shunts were excluded. No patients were excluded for a channelopathy diagnosis. The demographics of all 36 included patients are presented in Table 1. The majority of

patients were adolescents and there were more boys than girls. Minority children were disproportionately represented. Interestingly, two-thirds of patients had a significant comorbidity, with over a quarter having a hematological or oncologic diagnosis.

Patients were sick for an average of  $5 \pm 6$  days prior to hospitalization and manifested the following symptoms: fever (67%), cough (36%), shortness of breath (24%), chest pain (6%), myalgia (19%), headache (8%), and gastrointestinal symptoms (31%). Elevated troponin T was noted in 8 of 29 (28%) patients, with an average maximum value of  $195 \pm 730$  ng/L, with 1 outlier patient having a maximum level of 4013 ng/L. C-reactive protein was elevated in 28 of 35 (80%) patients, with an average of  $120 \pm 126$  mg/L. Pro-brain natriuretic peptide was elevated in 6 of 14 (42.9%) patients, with an average of  $1545 \pm 2806$  pg/mL. Echocardiograms were performed in 14 patients, 3 of whom had ventricular dysfunction (left ventricular ejection fraction [LVEF]  $<55\%$ ); the average LVEF was  $56\% \pm 8\%$ .

HCQ alone was administered to 16 (44%) patients, a combination of HCQ + AZN was administered to 9 (25%), and 11 (31%) patients received neither medication. Other COVID-19 medications used included intravenous immunoglobulin (3), steroids (4), remdesivir (2), tocilizumab (2), and anakinra (2). Patients were admitted for an average of  $15 \pm 15$  days, with 21 (58%) patients requiring pediatric intensive care unit (ICU) admission, where 12 (33.3%) patients required vasoactive support during their hospital admission. One patient with Walker-Warburg syndrome and multiple

brain anomalies died from complications related to severe respiratory insufficiency.

Twenty-eight patients had at least 1 12-lead ECG and all patients were on continuous telemetry with reviewable strips. Ten patients had significant findings on the 12-lead ECG, including low-voltage QRS complexes (18%), LV hypertrophy (4%), right ventricular hypertrophy (4%), left axis deviation (4%), right axis deviation (4%), and significant ST-segment changes (4%). No patients had second-degree or complete heart block. Three patients had infrequent isolated premature atrial ectopic beats, 1 patient had frequent isolated premature atrial ectopic beats, 1 patient had infrequent isolated late-cycle unifocal premature ventricular ectopic beats (PVCs), and 1 patient had frequent isolated late-cycle unifocal PVCs. Six patients (17%) had significant arrhythmias (Tables 2 and 3). Although all arrhythmias were self-limited and hemodynamically tolerated, prophylactic antiarrhythmic therapy was started in 3 patients. Two patients were started on antiarrhythmics because of recurrence while another was started on labetalol for coexisting hypertension. There was no mortality among patients with significant arrhythmias.

Although there was no association between significant arrhythmias and the presence of comorbid noncardiac medical conditions ( $P = 1$ ), noncardiac comorbidities in children with arrhythmias was common (4/6), with 2 patients having comorbidities and/or associated circumstances known to place the patients at independent risk for arrhythmias, including mediastinal mass and pericardial effusion ( $n = 2$ ) and electrolyte disturbances ( $n = 1$ ). Two others were diagnosed with myocarditis secondary to COVID-19. The maximum troponin level was higher in patients with significant arrhythmias compared to those without ( $753 \pm 1467$  ng/L vs  $50 \pm 85$  ng/L,  $P = .03$ ). However, there was no difference in the proportion of patients with significant arrhythmias who had abnormally elevated troponins compared to the proportion of those without arrhythmias having abnormally elevated troponins (2/6 vs 6/23,  $P = .87$ ). This discrepancy can be explained by a single outlier in the arrhythmia group with very high troponin levels. Other relevant variables such as demographics (age, weight, sex, and race/ethnicity), pre-hospitalization symptoms and duration of symptoms, laboratory variables (pro-brain natriuretic peptide; maximum C-reactive protein, and electrolytes), echocardiographic findings (%EF and presence of LV dysfunction), and significant ECG findings (longest daily measured QTc and baseline ECG abnormalities) were not significantly associated with arrhythmias. There was a trend for arrhythmias to be more common in patients with baseline ECG abnormalities compared to those without these abnormalities (4/6 vs 6/22,  $P = .15$ ). COVID-19 treatment including the use of HCQ with or without AZN was not associated with significant arrhythmias ( $P = .9$ ). Eighty-six percent interobserver agreement was achieved for QTc measurement. In discrepant cases, tracings were reviewed by both interpreters together and consensus was achieved in all remaining tracings. Among the entire study cohort, the average baseline QTc

**Table 1** Demographic characteristics of 36 patients with PCR-positive SARS-CoV-2

Characteristic	Result
Total, n (%)	36 (100%)
Age in years (average $\pm$ SD)	$12.6 \pm 6$ years
•Patients $<12$ years, n (%)	10 (28%)
•Patients $\geq 12$ years, n (%)	26 (72%)
Sex	
•Male, n (%)	20 (57.5%)
•Female, n (%)	16 (44.4%)
Race/ethnicity, n/N (%)	
•African American	11/36 (30%)
•White	3/36 (8.3%)
•Multiracial	10/36 (28%)
•Other races	3/36 (8.1%)
•Unreported race	7/36 (19.4%)
Comorbid conditions, n/N (%)	24/36 (67%)
•Malignancy	6/36 (17%)
•Sickle cell	4/36 (11%)
•Asthma	3/36 (8%)
•Cerebral palsy with seizures	3/36 (8%)
•Obesity	2/36 (5.5%)
Patients on home medications, n/N (%)	20/36 (55.5%)
Patients on QTc-prolonging medications, n/N (%)	2/36 (5.5%)

QTc = corrected QT.

**Table 2** Patient demographic and characteristics pertinent to the finding of arrhythmia

Pt	Age (years)	Arrhythmia	Comorbidities	HcQ ± AZN	QTc prolonged	Echo findings	SF by echo (%)	EF by echo (%)	High-sensitivity troponin T (ng/L)	Circumstances
1	12	Monomorphic VT	Sickle cell disease	No	No	Mild LV dilation with preserved ventricular function	36	59	<6	None
2	20	Monomorphic VT	Lymphoma, mediastinal mass, pericardial effusion	No	No	Large circumferential pericardial effusion	33	69	10	None
3	13	Sustained atrial tachycardia	Myocarditis secondary to COVID-19	No	No	Mild LV dysfunction	32	49	398	High-dose epinephrine and nor-epinephrine drips
4	13	Monomorphic VT	Bloom syndrome, history of testicular cancer	No	No	Mild-to-moderate LV dysfunction	25	46	<6	None
5	17	Monomorphic VT	Myocarditis secondary to COVID-19	No	No	Normal structure and function	31		4013	None
6	16	Monomorphic VT	Acute lymphocytic leukemia, mediastinal mass, pericardial effusion	No	No	Normal structure and function	NA	65	12	HypoMg, HypoK, and HypoCa

AZN = azithromycin; EF = ejection fraction; HcQ = hydroxychloroquine; HypoCa = hypocalcemia, HypoK = hypokalemia, HypoMg = hypomagnesemia; LV = left ventricular; NA = not applicable; Pt = patient; QTc = corrected QT; SF = shortening fraction, VT = ventricular tachycardia.

**Table 3** Arrhythmia characteristics

Pt	Type of arrhythmia	Sustained/nonsustained	Rate (bpm)	Spontaneous termination	Recurrence?	Other ectopy	Antiarrhythmic started	Associated ECG findings
1	Monomorphic VT	Nonsustained	140	Yes	No	No	No	LVH with strain
2	Monomorphic VT	Nonsustained	160	Yes	No	Infrequent unifocal ventricular ectopy	Yes, beta blocker	Low voltage QRS
3	Atrial tachycardia	Sustained	150	Yes	No	No	No	Nonspecific T-wave abnormality
4	Monomorphic VT	Nonsustained	160	Yes	Yes	No	Yes, beta blocker	Normal for age
5	Monomorphic VT	Nonsustained	200	Yes	Yes	Frequent ventricular ectopy, ventricular bigeminy	Yes, amiodarone	Diffuse ST-segment elevation
6	Monomorphic VT	Nonsustained	130	Yes	No	Yes	No	Low-voltage QRS, nonspecific T-wave abnormality

bpm = beats per minute; ECG = electrocardiogram; LVH = left ventricular hypertrophy; Pt = patient; VT = ventricular tachycardia.



was  $412 \pm 19$  ms and the longest daily measured QTc during the hospital course was  $425 \pm 15$  ms. No patients had an abnormal baseline or longest daily measured QTc. Adolescents aged 12–21 years had a statistically significantly longer (but still clinically normal) baseline QTc compared to younger children ( $417 \pm 18$  ms vs  $401 \pm 17$  ms,  $P = .03$ ). Baseline QTc was not different in male vs female patients. Both baseline and longest daily measured QTc were not correlated with EF and were not significantly different in those with LV dysfunction compared to those with normal LV function on echocardiographic evaluation. There was an unexpected trend for the QTc to be shorter in patients with abnormal troponin levels vs those with normal troponin levels ( $416 \pm 17$  ms vs  $428 \pm 14$  ms,  $P = .08$ ).

Baseline QTc was not statistically different for patients who received HCQ alone ( $413 \pm 19$  ms) vs those who also received AZN ( $406 \pm 19$  ms) and vs those who received neither drug ( $417 \pm 18$  ms). Longest daily measured QTc after starting therapy was not different in patients who received HCQ with or without AZN compared to those who received neither drug ( $423 \pm 17$  ms vs  $426 \pm 16$  ms,  $P = .5$ ). However, comparison of baseline to longest daily measured QTc intervals after starting HCQ  $\pm$  AZN showed that the QTc was statistically significantly prolonged (but still clinically normal) for those patients treated with HCQ alone ( $413 \pm 19$  ms to  $425 \pm 16$  ms,  $P = .005$ ), but not for those treated with both drugs ( $406 \pm 19$  ms to  $416 \pm 11$  ms,  $P = .3$ ). This is illustrated in Figure 1. Importantly, the longest daily measured QTc after starting treatment with HCQ with or without AZN occurred after 1 day of treatment in 5, after 2 days in 10, after 3 days in 2, after 4 days in 5, and after 5 days in 3. However, of these, the baseline QTc was longer than the longest daily measured QTc after starting treatment in 5. In 14 patients with posttreatment rhythm strips available, the posttreatment QTc was shorter than the baseline QTc in 8, the same in 1, and longer in 5.

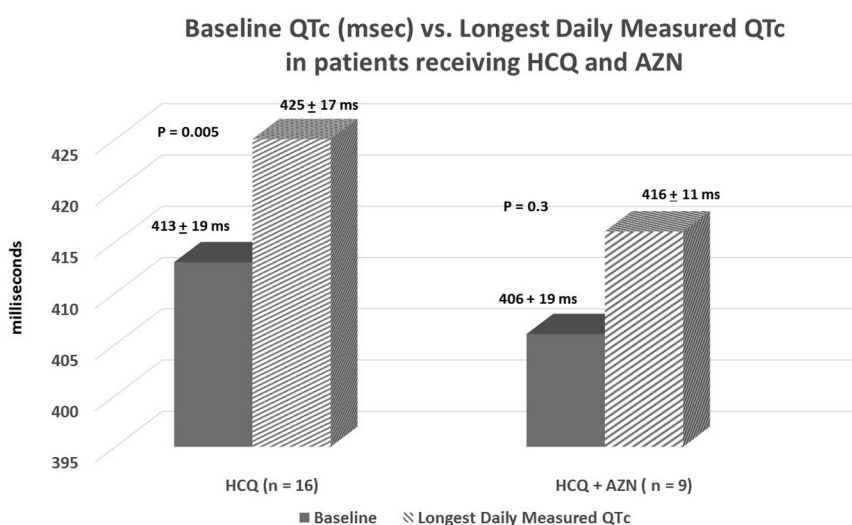
## Discussion

To our knowledge, this is the largest study reporting the electrophysiologic abnormalities in children with COVID-19. There are several main findings of this paper, including the following: (1) significant arrhythmias in pediatric patients with COVID-19 infection are infrequent but occur at incidence higher than expected in a general pediatric population, (2) comorbidities are not more common in COVID-19 patients with arrhythmias, and (3) HCQ is associated with QTc prolongation but is not associated with arrhythmias, despite previous publications.<sup>10,11</sup>

## Arrhythmias

Arrhythmias in the present study occurred more frequently than expected in a general pediatric population. In the current study, 17% of patients had significant arrhythmias, of whom 5 (14% of the study population) had ns VT. In a population of children with structurally normal hearts, less than 2% would be expected to have multifocal PVCs, couplets, or ns VT on ambulatory monitoring.<sup>12</sup> While one could argue that the patients in the present study were monitored for a longer period (5 days) than the average child is monitored in the ambulatory setting, the incidence of ns VT in the present study still seems high. Although no episode required acute intervention for hemodynamic embarrassment, 3 of 5 patients with ns VT received prophylactic therapy and thus may have been prevented from experiencing subsequent episodes with different durations and/or hemodynamic implications.

As more insights are acquired about the novel SARS-CoV-2 virus and the multisystem involvement that occurs with it, the effects of the virus on the cardiovascular system are being revealed. Currently data among adult patients on the incidence of new arrhythmias in patients with COVID-19 infection are limited. Patients with COVID-19 infection may develop arrhythmia owing to acute cardiac injury related



**Figure 1** Bar graphs showing corrected QT (QTc) prolongation associated with the use of hydroxychloroquine (HCQ) or azithromycin (AZN). Baseline QTc (solid bars) is compared to the longest daily measured QTc after initiation of therapy (hashed bars) seen during treatment for each treatment strategy.  $P$  values for paired  $t$  test comparing baseline and longest daily measured QTc after initiation of therapy values for each group are displayed.



to direct myocardial injury from myocarditis, hypoxia-mediated injury, or worsening of preexisting coronary artery disease; as a result of systemic inflammatory response syndrome; or owing to the effects of medications used in the management of COVID-19.<sup>13</sup> In a study from Wuhan by Wang and colleagues,<sup>14</sup> of 138 adult patients who were hospitalized with COVID-19-related pneumonia, arrhythmias were reported in 16.7% of the general cohort and in 44% patients admitted to the ICU. Of the 138 patients, hypertension, cardiovascular disease, and diabetes were present in 43%, 20%, and 10% of patients, respectively.<sup>14</sup> As often found in other clinical circumstances, results obtained from adult studies cannot be directly extrapolated to the pediatric patient population. In our present study, no patient had preexisting cardiovascular morbidity, including ischemic heart disease or hypertension. Although troponin levels were higher in pediatric patients with arrhythmias, there was no increased risk of significant arrhythmias in patients with elevated troponin, suggesting that the association is related to the small number of patients in the study and 1 outlier patient with a severely elevated troponin. This lack of association between abnormal troponin levels and arrhythmias is also different from what has been reported in adults and may be related to the pathophysiologic differences in the etiologies of troponin elevation in adults compared to children.<sup>15</sup>

Although the pediatric population presented here did not have preexisting cardiovascular morbidity, a high proportion of these patients did have other comorbidities. Whether there was a selection bias in that pediatric patients with comorbidities were more likely to be admitted or whether these patients were actually sicker and required hospitalization rather than home management is not clear from our data. Although there was no statistically significant increased risk of arrhythmias in patients with comorbid conditions, 4 of 6 patients with significant arrhythmias had comorbidities that may have independently placed patients at risk for arrhythmias, including mediastinal masses and pericardial effusions in 2, electrolyte derangements in 1, and myocarditis in 2 others. This finding illustrates the point that providers need to be focused on the common associations between arrhythmias while being vigilant for new associations with COVID-19.

Another distinction between adults and children was that in the present study, there was no significant association between arrhythmias and duration of illness or hospitalization, ICU admission, use of vasoactive medications, or mortality. This is in contrast to adult studies that have shown increased morbidity and mortality in patients with COVID-19 infection and cardiovascular complications including arrhythmias.<sup>4,16</sup> This may in part be related to the self-limited nature of the arrhythmias seen in the present study.

### Drug-induced QTc changes with HCQ and AZN in COVID-19

Among the various therapies that have been advocated for the management of COVID-19, HCQ and AZN have been used in the adult and pediatric patient population.<sup>17</sup> However,

HCQ ± AZN has a serious side effect of prolonging QT interval and predisposing patients to ventricular arrhythmias such as torsades de pointes.<sup>18</sup> Although the present pediatric study also found a statistically significantly longer longest daily measured QTc in those patients receiving HCQ, treatment was not terminated in any of the patients in this study, as none of them developed clinically significantly prolonged QTc intervals. In fact, none had QTc intervals that were abnormal and the development of arrhythmias was not associated with QTc prolongation. Although the degree of QTc lengthening found in the present study for those receiving HCQ with or without AZN (12 ms) was shorter than that reported in adult COVID patients receiving HCQ and AZN, the timeline of lengthening (2–4 days in 16 of 20 patients in whom there was lengthening) was similar to that reported in adult studies. In a study by Chorin and colleagues,<sup>19</sup> of 84 adult patients receiving HCQ and AZN for COVID-19 infection, there was prolongation of the QTc from a baseline average of  $435 \pm 24$  ms (mean ± standard deviation) to a maximal average value of  $463 \pm 32$  ms ( $P < .001$ ), which occurred on day  $3.6 \pm 1.6$  of therapy, including a subset of 9 patients who developed severe QTc prolongation of  $>500$  ms; however, no torsades de pointes events were recorded for any patients. It must be acknowledged that it is unclear if the change in QTc seen in the present study was necessarily related to treatment in all patients. Although the longest daily measured QTc occurred during treatment in 80% of patients, it was found that the baseline QTc was longer in 20% of patients treated with HCQ ± AZN and the longest daily measured QTc after treatment was started was not statistically different for those treated with HCQ ± AZN compared to those who received neither drug. Furthermore, there was no difference between baseline QTc and the longest daily measured QTc after treatment was started for those who received both drugs. Thus, routine variation in QTc duration may account for changes in QTc in some patients and may, in part, account for the lack of association with arrhythmias. Though evidence for the efficacy of HCQ and AZN in treating COVID-19 is lacking, it is important to realize that the effects of any treatment must be studied in children as well as adults and not to assume that the risks for children are the same as, less than, or more than that seen in adults.<sup>20</sup>

### Limitations

As a single-center retrospective chart review, this study has several inherent limitations, including a small study cohort, which limited the ability to make statistical comparisons. Because the study was retrospective in nature, certain variables were not obtained in all patients or collected at the same time points in all patients. Management protocols that were instituted during the pandemic were revised frequently for efficacy as well as patient and staff safety, creating variability in dataset completeness at various times during the pandemic. In addition, IgG testing was not available at the beginning of the pandemic. One patient with possible

Kawasaki syndrome, who did not have arrhythmias or QTc prolongation, did not have IgG tested upon admission. However, unlike our subsequent experience and what has been reported with Multisystem Inflammatory Syndrome in Children (MIS-C) patients, this patient's PCR was positive on the first test, suggesting she had active COVID at the time of admission.<sup>2</sup>

## Conclusion

In pediatric patients with PCR-positive active COVID-19 infection, significant arrhythmias are infrequent but occur at an incidence higher than expected in a general pediatric population. Comorbidities are not more common in patients with arrhythmias than in patients without arrhythmias. However, providers still need to be vigilant for comorbidities that may independently place patients at risk for arrhythmias. COVID-19 treatment using HCQ leads to significant QTc prolongation but was not associated with arrhythmias in pediatric patients. The long-term sequelae of arrhythmia development in this population and their impact on outcome needs to be studied.

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