



The Impact of Social Distancing for COVID-19 Upon Diagnosis of Kawasaki Disease

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mitigation policies have been associated with profound decreases in diagnoses of common childhood respiratory infections. A leading theory of etiology of Kawasaki disease (KD) is that it is triggered by presently unidentified ubiquitous respiratory agent. We document that mitigation policies instituted in mid-March 2020 were associated with strikingly fewer diagnoses of KD in April-December 2020 compared with the same period in the previous 8 years ($P = .01$), a >67% decline. This finding supports the hypothesis that KD is caused by a respiratory-transmitted agent.

Key words. COVID-19; Kawasaki disease; mitigation; respiratory transmission; social distancing.

Hatoun et al [1] recently examined the impact of coronavirus disease 2019 (COVID-19) childhood mitigation (social distancing, masking, and school closures) upon the transmission of several childhood infectious diseases. These investigators used electronic health record data from a large Massachusetts pediatric primary care network to analyze the weekly incidence of 12 common infectious diagnoses from in-person and telemedicine encounters in 2019 and 2020. They documented striking declines in rates of diagnosis of a broad variety of respiratory viral and bacterial and viral enteric illnesses in children 0-17 years old during the mitigation period. They concluded that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mitigation policies led to profound decreases in common childhood illness diagnoses due either to bona fide declines in these conditions or to parental choice not to seek medical care.

A leading theory regarding the etiology of Kawasaki disease (KD) is that an as yet unidentified ubiquitous respiratory infectious agent triggers KD in genetically susceptible hosts generally early in life, and a protein epitope of a putative viral etiologic agent has recently been identified [2]. We hypothesized that the transmission of such an agent might also be reduced during a time of coronavirus mitigation in children, leading to a decrease in the number of KD cases.

We explored the frequency of KD diagnoses during 2020 before and after the closure of schools and the introduction of other social distancing measures in mid-March 2020 in Illinois (including the closure of all public and private schools on March 17 and a stay-at-home order on March 20) compared with 8 previous years (2012-2019) at our large children's hospital in Chicago and an affiliated institution.

METHODS

We accessed records of the Center for Kawasaki Disease at Lurie Children's Hospital for cases of KD diagnosed from January 1, 2020, to March 31, 2020 (pre-social distancing), and from April 1, 2020, to December 31, 2020 (social distancing period), and for the corresponding dates from 2012 to 2019. Similar data were accessed from our affiliated institution Central DuPage Hospital, which is located 30 miles west of Chicago and is staffed by an Infectious Diseases physician (B. G.) linked to Lurie Children's Hospital and Northwestern University Feinberg School of Medicine. Confidence intervals (CIs) and P values were calculated based on t distributions ($df = 7$). The Center for Kawasaki Disease at Lurie Children's Hospital has maintained detailed prospective records of KD cases for over 30 years, and we provide all inpatient and outpatient care.

RESULTS

As shown in Figure 1, the number of cases of KD diagnosed in the January to March pre-social distancing period of 2020 was 13 (95% CI from 2012 to 2019, 13.0, 21.7), which is comparable to the corresponding period in 2012-2019. In striking contrast, the number of KD cases diagnosed from April to December 2020, the coronavirus mitigation period, was significantly lower, with 15 cases, than the number of cases diagnosed annually from April to December in 2012-2019 (2012-2019 mean = 46.6; 95% CI: 41.5, 51.7; $P = .01$). To take into account the slight decrease in KD cases from January to March 2020 compared with previous years, we calculated the ratio of incidence from April to December cases divided by January to March cases. There was again a substantial decrease in April-December cases in 2020 with the incidence ratio of 1.15 (95% CI from 2012 to 2019 ratios is 1.86, 4.15; $P = .008$). These findings are parallel to the findings of Hatoun et al [1] for common respiratory and enteric viral and some bacterial infection diagnoses during the months of mitigation.

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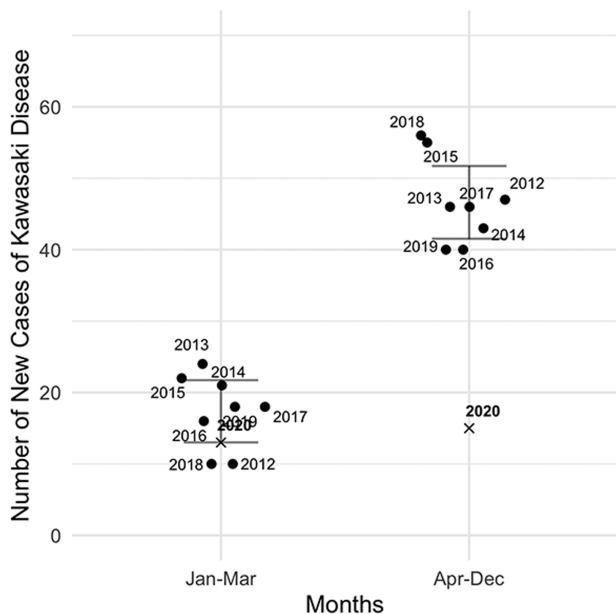


Figure 1. The number of Kawasaki disease diagnoses from 2012 to 2020 with mean and 95% confidence intervals is shown in vertical columns for January 1 to March 31 and April 1 to December 31, with 2020 numbers shown by X and years 2012–2019 shown by black circles. The April 1 to December 31, 2020, value is significantly lower than the corresponding 2012 to 2019 data ($P = .008$), while the January 1 to March 31, 2020, value is not significantly different from previous years.

Thus, this finding supports the hypothesis that KD is triggered by a common childhood infectious respiratory agent [2, 3]. To assess the possibility that the decreased number of KD cases during the April-December 2020 mitigation was the result of parents not bringing their febrile children to our center for care, we examined the number of distinct patient emergency department visits and admissions for acute pyelonephritis (International Classification of Diseases [ICD]-10 code = 590.1, 590.11, 590.8, N10, 599, and N39.0) from 2016 to 2020 and we found no decrease corresponding to the mitigation period.

DISCUSSION

Hatoun et al reported that COVID-19-related childhood mitigation social distancing measures including closure of schools, stay-at-home advisory, and use of masks coincided with marked reduction in childhood diagnoses of many common infectious diseases. The most pronounced declines were observed in infections transmitted by the respiratory route, with influenza, croup, and bronchiolitis essentially disappearing during the social distancing period [1].

We found that the number of cases of KD in early 2020 (January-March) was comparable to the number in the same months the 8 previous years but that the number of KD diagnoses during the 2020 social distancing era (April-December) was very significantly lower

than in the comparable period of 2012-2019, less than one-third of the number previously observed ($P = .008$). This finding supports the hypothesis that the agent of KD is transmitted via the respiratory route and that transmission of the agent is also reduced by coronavirus mitigation practices. Although COVID-19 mitigation efforts could potentially diminish acquisition of a hypothesized toxin “blowing in the wind,” a theory of KD etiology proposed by some, we do not believe that the wind theory is compatible with the epidemiologic features of KD such as winter-spring predominance, very young age distribution, and rarity of recurrent cases. Instead, these are classic epidemiologic features of infections due to ubiquitous pathogens transmitted via the respiratory route such as measles in the pre-vaccine era.

During April-December 2020, we also cared for 41 patients with multisystem inflammatory syndrome in children (MIS-C). We do not believe that there was diagnostic confusion regarding MIS-C and KD in these children. These patients with MIS-C had a median age of 10 years, were all COVID antibody positive, and the vast majority had hypotension, marked lymphopenia, and thrombocytopenia. None fulfilled the classic diagnostic criteria for KD. In 6 of these 41 patients, right coronary artery and left anterior descending coronary artery Z scores were 2.6 to 3.7 during the acute illness, and all normalized within 1-2 weeks. These features are in marked contrast to children with KD, who are much younger, do not manifest lymphopenia, and who experience peak coronary artery dilation 2-3 weeks after the fever onset, during a time that they generally appear well [4, 5].

An alternative potential explanation for this finding would be that ill children during the coronavirus mitigation period have not been brought for medical care by parental choice. In the study by Hatoun et al [1], a relatively small decrease in diagnosis of urinary tract infection, an infectious but noncontagious condition, led those authors to suggest that care-seeking behavior had a relatively modest effect, if any, on the other observed declines. In our study, diagnoses of pyelonephritis were unaffected by COVID-19 mitigation measures. At least one recent study has assessed the impact of COVID-19 mitigation upon an important noninfectious pediatric disease. Tittel et al [6] found that there was no change in the incidence of diagnoses of pediatric type 1 diabetes in Germany during the COVID-19 lockdown in 2020 compared with the corresponding period in 2011-2019. This study may suggest that parents are not electing to keep more seriously ill children at home during COVID-19 mitigation efforts. For the diagnosis of KD, we also believe that change in care-seeking behavior is unlikely to contribute significantly to the striking decline in cases, primarily because of the severity of the KD clinical presentation, which is characterized by prolonged fever, rash, and other features, including marked irritability. We did not observe an increase in delayed presentations of KD during April-December 2020, as might be expected if parents were not seeking care in a timely fashion. One of the 13 patients was diagnosed on illness day 10, none any later.

In conclusion, the dramatic reduction in children presenting with KD during the coronavirus mitigation period in Chicago (a more than two-thirds decline) supports the hypothesis that the etiologic agent is transmitted via the respiratory route.

Notes

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Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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