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Association between pediatric asthma and positive tests for SARS-CoV-2 in the District of Columbia

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Clinical Implications

- For urban children and adolescents, little is known regarding whether current asthma is associated with an increased or decreased risk of SARS-CoV-2 test positivity. We found no association between current pediatric asthma and positive tests in such a population.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test positivity among patients with asthma has not been well studied,[1] especially among urban, minority, and under-resourced children and adolescents, a population with a disproportionately higher prevalence of both asthma[2] and coronavirus disease 2019 (COVID-19).[3] Recent research suggests that pediatric patients with asthma may be protected with a lower risk of SARS-CoV-2 test positivity,[4,5] possibly related to a lower expression of the gene encoding angiotensin-converting enzyme 2 (ACE2).[6] In addition, SARS-CoV-2 testing among children with current asthma may be subject to referral bias.[4] Specifically, clinicians may test children with current asthma at a lower threshold (with milder symptoms, after more limited exposure, or because asthma symptoms can mimic those of COVID-19), yielding a misleadingly lower rate of test positivity. We therefore hypothesized that the proportion of positive tests for SARS-CoV-2 in children and adolescents with current asthma in the District of Columbia (DC) (an urban, largely minority, and under-resourced population) would be lower than the proportion among those without asthma. We further hypothesized that this difference would persist after controlling for the presence of COVID-19 symptoms or exposure.

We assembled a cross-sectional case series of all DC residents aged 2 to 17 years tested for SARS-CoV-2 by nasopharyngeal polymerase chain reaction at Children's National Hospital (CNH) in Washington, DC from March 13 to November 19, 2020. We included only first test results for all patients to reduce the effect of an individual testing rate on test positivity. In a subset of these participants, we were able to determine the presence or absence of COVID-19 symptoms or exposure. Symptomatic/exposed patients were identified from a previously described drive-through and walk-up testing site.[3,7] Children tested at this site were referred by a physician if there was concern for COVID-19 symptoms or exposure.[3,7] Asymptomatic and unexposed patients were identified from CNH's pre-procedural testing clinic. Children tested in this clinic did not have COVID-19 symptoms or known exposure and were tested as a precaution before a planned medical procedure. Participants with current asthma were identified from a previously described population-based registry of DC children with asthma.[8] Persistent asthma was defined by any of the following in the preceding 12 months: $\geq$2 or more asthma-related emergency department visits, $\geq$1 asthma-related hospitalizations, prescription for an asthma controller medication, or any International Classification of Diseases (Tenth Edition) code for persistent asthma. All children with current asthma who did not meet criteria for persistent asthma were classified as intermittent asthma.

Three multivariable logistic regression analyses were performed. The first determined the independent association between current asthma and positive tests for SARS-CoV-2 among all participants. The second identified predictors of a positive test only among participants with current asthma (both those with persistent asthma and intermittent asthma). The third model assessed the role of referral bias by controlling for the presence or absence of COVID-19 symptoms or exposure in the subpopulation with that variable defined. Results are reported as odds ratios (with 95% confidence intervals [CIs]) adjusted for age, sex, race/ethnicity, insurance status, and asthma status. CNH's institutional review board approved the study.

A total of 5906 participants were tested for SARS-CoV-2 including 1471 (24.9%) with current asthma, of whom 801 (13.6% of total) had persistent asthma. The 1471 children with current asthma tested for COVID-19 represent 9.4% of all children with current asthma in DC according to the city-wide pediatric asthma registry.[8] Compared with all DC children with current asthma, those tested for COVID-19 were significantly more likely to be younger, non-Black or Hispanic, publicly insured, and have persistent asthma. Of the entire study population, 18% (1066/5906) had defined COVID-19 symptoms or exposure. This group consisted of 412 patients with symptoms or exposure (tested at a drive-through site) and 654 asymptomatic and unexposed patients (tested pre-procedure) (Table I).

Of all 5906 participants tested, 410 (6.9%) were positive for SARS-CoV-2, including 8.3% (122/1471) of all those with current asthma, 7.5% (60/801) of those with persistent asthma, and 6.5% (288/4435) of those without asthma. African American (AA) race, Hispanic ethnicity, and public insurance were associated with a positive test in the entire cohort, and AA race and Hispanic ethnicity were associated in the subset with asthma (Table II).

There was no association between current asthma and positive tests in the total population (adjusted odds ratio [aOR] = 1.05, 95% CI = 0.83-1.31) (Table II). In addition, having persistent asthma was not associated with SARS-CoV2 positivity when compared with not having asthma (aOR = 0.98, 95% CI = 0.73-1.31) or having intermittent asthma (aOR = 0.86, 95% CI = 0.59-1.26). In the subpopulation with defined COVID-19 symptoms or exposure (n = 1066), there was also no association between current asthma and positive tests (aOR = 1.03, 95% CI = 0.57-1.85) (Table II). Furthermore, we demonstrated no difference in COVID-19 test positivity by current asthma status in the subset of 654 asymptomatic children tested in the pre-procedural clinic (current asthma = 1%, no asthma = 0.5%; P = .69).

TABLE I. Demographics of DC children aged 2-17 years tested for SARS-CoV-2 between March 13 and November 19, 2020

	Entire population				Subpopulation with defined COVID-19 Symptoms or exposure			
Characteristic	**Total (N = 5906)**	**Asthma (N = 1471)**	**No asthma (N = 4435)**	***P* value***	**Total (N = 1066)**	**Asthma (N = 248)**	**No asthma (N = 818)**	***P* value***
Mean age, SD (median)	8.50 (4.82, 8.00)	8.94 (4.51, 9.00)	8.35 (4.91, 8.00)	<.001	8.11 (4.65, 7.00)	8.61 (4.47, 8.00)	7.96 (4.69, 7.00)	.05
Age group (y), N (%)								
2-11	4044 (68.5)	989 (67.2)	3055 (68.9)	.238	777 (72.9)	172 (69.4)	605 (74.0)	.15
12-17	1862 (31.5)	482 (32.8)	1380 (31.1)		289 (27.1)	76 (30.6)	213 (26.0)	
Sex,† N (%)								
Male	2997 (50.7)	830 (56.4)	2167 (48.9)	.001	574 (53.8)	148 (59.7)	426 (52.1)	.05
Female	2904 (49.2)	641 (43.6)	2263 (51.0)		492 (46.2)	100 (40.3)	392 (47.9)	
Race/ethnicity, N (%)								
Caucasian, non-Hispanic; other; or unknown	2053 (34.8)	283 (19.2)	1770 (39.9)	.001	397 (37.2)	66 (26.6)	331 (40.5)	.001
African American	3054 (51.7)	1007 (68.5)	2047 (46.2)		496 (46.5)	146 (58.9)	350 (42.8)	
Hispanic	799 (13.5)	181 (12.3)	618 (13.9)		173 (16.2)	36 (14.5)	137 (16.7)	
Insurance, N (%)								
Private	1831 (31.0)	183 (12.4)	1648 (37.2)	.001	301 (28.2)	41 (16.5)	260 (31.8)	.001
Public	3683 (62.4)	1205 (81.9)	2478 (55.9)		618 (58.0)	190 (76.6)	428 (52.3)	
Other/unknown	392 (6.6)	83 (5.6)	309 (7.0)		147 (13.8)	17 (6.9)	130 (15.9)	
COVID-19 symptoms or exposure, N (%)								
No					654 (61.4)	154 (62.1)	500 (61.1)	.78
Yes					412 (38.6)	94 (37.9)	318 (38.9)	

SD, Standard deviation.

*Univariate comparison (*t*-test or χ^2) between groups with and without asthma.

†Five participants in total population identified as nonbinary.

TABLE II. Associations of demographic and clinical variables with positive tests for SARS-CoV-2 among DC residents aged 2-17 years

	All participants (N = 5906)		Participants with asthma (N = 1471)		Participants with defined COVID-19 symptoms/exposure (N = 1066)	
Variable	Positive test, N (%)	aOR (95% CI)*	Positive test, N (%)	aOR (95% CI)*	Positive test, N (%)	aOR (95% CI)†
Current asthma						
No asthma	288 (6.5)	Reference			56 (6.8)	Reference
Asthma	122 (8.3)	1.05 (0.83-1.31)			23 (9.3)	1.03 (0.57-1.85)
Persistent asthma						
No asthma	288 (6.5)	Reference			56 (6.8)	Reference
Persistent asthma	60 (7.5)	0.98 (0.73-1.31)			10 (7.6)	1.14 (0.55-2.34)
Age group (y)						
2-11	278 (6.9)	Reference	82 (8.3)	Reference	52 (6.7)	Reference
12-17	132 (7.1)	0.96 (0.77-1.20)	40 (8.3)	1.00 (0.66-1.50)	27 (9.3)	1.13 (0.66-1.95)
Sex						
Male	211 (7.0)	Reference	70 (8.4)	Reference	39 (6.8)	Reference
Female	199 (6.9)	0.97 (0.79-1.19)	52 (8.1)	0.97 (0.66-1.44)	40 (8.1)	1.07 (0.65-1.78)
Race/ethnicity						
Caucasian, non-Hispanic; other; or unknown	55 (2.7)	Reference	9 (3.2)	Reference	9 (2.3)	Reference
African American	238 (7.8)	1.95 (1.39-2.73)	76 (7.5)	2.30 (1.10-4.76)	43 (8.7)	2.91 (1.29-6.57)
Hispanic	117 (14.6)	4.10 (2.86-5.89)	37 (20.4)	7.06 (3.22-15.50)	27 (15.6)	7.00 (2.92-16.79)
Insurance						
Private	44 (2.4)	Reference	8 (4.4)	Reference	8 (2.7)	Reference
Public	333 (9.0)	2.55 (1.78-3.66)	106 (8.8)	1.35 (0.62-2.93)	55 (8.9)	2.67 (1.16-6.19)
COVID-19 symptoms or exposure‡						
No (n = 654)					6 (0.9)	Reference
Yes (n = 412)					73 (17.7)	26.6 (11.2-62.9)

CI, Confidence interval; *aOR*, adjusted odds ratio.
*Multivariable logistic regression with adjustment for age, sex, insurance, race/ethnicity, and asthma status.
†Multivariable logistic regression with adjustment for age, sex, insurance, race/ethnicity, asthma status, and COVID-19 symptoms/exposure.
‡Children without COVID-19 symptoms/exposure were the subset of patients who had been tested in the CNH pre-procedural testing clinic. Children with COVID-19 symptoms/exposure were the subset of patients who were tested at the drive-through and walk-up testing site for symptomatic/exposed children.

We found no significant negative or positive association between current asthma and a positive test for SARS-CoV-2 in a large population of urban and largely under-resourced children and adolescents from a city with a prevalence of pediatric asthma 50% higher than the national mean.[9] This finding remained unchanged after controlling for the presence of COVID-19 symptoms or exposure in a subpopulation, suggesting that it is unlikely that having current asthma precipitated a referral bias causing clinicians or families to test patients with asthma at a lower threshold of symptoms or exposure or those with mild asthma exacerbations. Finally, we found no difference when we examined the proportion of COVID-19 test positivity by current asthma status in the subset of asymptomatic children, a group that did not experience testing bias because all children presenting to the pre-procedural testing clinic were tested.

Limited data from other mechanistic[6] and population-based studies[4,5] have suggested that asthma may be protective against SARS-CoV-2 test positivity. Jackson et al[6] reported lower expression of the ACE2 gene in nasal epithelial cells of 11-year-old urban children with asthma or atopy (high IgE levels). Bailey et al[4] reported test results from 135,794 patients <25 years old from 8 US academic pediatric centers and noted a significant negative association between asthma and positive tests (standardized ratio = 0.86, 95% CI = 0.80-0.91). However, their population had far fewer AA and Hispanic participants than ours (26% vs 65.2%, respectively) and far fewer participants with public insurance (36% vs 62.4%, respectively). This study also did not control for COVID-19 symptoms or exposure. In a study of 37,469 Israelis (including 602 patients aged 5-19 years), Green et al[5] found a lower odds of positive tests among people with asthma (aOR = 0.73, 95% CI = 0.61-0.90). Their population also differed markedly from ours, and it included only patients referred for testing because of symptoms or exposure.

Consistent with prior data among children and adolescents,[3,4] minority racial/ethnic status and public insurance were associated with positive tests. These disparities are troubling and should drive increased public health efforts to slow transmission of the virus in such populations through social distancing, masks, and vaccinations. However, given that we did not find current asthma to be associated with SARS-CoV-2 positivity, a diagnosis of asthma alone may not be a reason to keep a child from attending school. This may be especially relevant given the social inequities affecting racial and ethnic minority children that are inherent to the pandemic.

There are several limitations. First, our tested group is drawn from a single urban population. Results may differ in other populations. Second, we are unable to adjust for propensity to be exposed to the virus and be tested for it. For the latter, however, we were able to demonstrate similar results in a small subset of patients without testing bias, the pre-procedural testing group.

Third, it is possible that if children were tested too early during their illness course, they could have had a false-negative COVID test result. However, this should affect both children with and without asthma equally. Finally, we were unable to distinguish between symptoms and exposure in the drive-through cohort.

In conclusion, we believe that the risk of SARS-CoV-2 positivity may vary across specific patient groups with asthma. Clinicians should not assume that current asthma protects against COVID-19, and they should refer their pediatric patients with asthma for testing for SARS-CoV-2 using the same criteria as they use for their patients without asthma.

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