Asthma and the Risk of SARS-CoV-2 Infection Among Children and Adolescents

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abstract

OBJECTIVES: Over 6 million pediatric severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have occurred in the United States, but risk factors for infection remain poorly defined. We sought to evaluate the association between asthma and SARS-CoV-2 infection risk among children.

METHODS: We conducted a retrospective cohort study of children 5 to 17 years of age receiving care through the Duke University Health System and who had a Durham County, North Carolina residential address. Children were classified as having asthma using previously validated electronic health record-based definitions. SARS-CoV-2 infections were identified based on positive polymerase chain reaction testing of respiratory samples collected between March 1, 2020, and September 30, 2021. We matched children with asthma 1:1 to children without asthma, using propensity scores and used Poisson regression to evaluate the association between asthma and SARS-CoV-2 infection risk.

RESULTS: Of 46 900 children, 6324 (13.5%) met criteria for asthma. Children with asthma were more likely to be tested for SARS-CoV-2 infection than children without asthma (33.0% vs 20.9%, $P < .0001$). In a propensity score-matched cohort of 12 648 children, 706 (5.6%) children tested positive for SARS-CoV-2 infection, including 350 (2.8%) children with asthma and 356 (2.8%) children without asthma (risk ratio: 0.98, 95% confidence interval: 0.85–1.13. There was no evidence of effect modification of this association by inhaled corticosteroid prescription, history of severe exacerbation, or comorbid atopic diseases. Only 1 child with asthma required hospitalization for SARS-CoV-2 infection.

CONCLUSIONS: After controlling for factors associated with SARS-CoV-2 testing, we found that children with asthma have a similar SARS-CoV-2 infection risk as children without asthma.

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Ms Rao conceptualized and designed the study, conducted the analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Hurst conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Ms Zhao assisted in conducting the analyses and reviewed and revised the manuscript; Drs Goldstein, Thomas, and Lang conceptualized and designed the study and reviewed and revised the manuscript; Dr Kelly conceptualized and designed the study, supervised the analyses, drafted the initial manuscript, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Risk factors for SARS-CoV-2 infection among children remain poorly defined. Current guidelines recommend that individuals with asthma take additional precautions to prevent SARS-CoV-2 infection, but the relationship between asthma and SARS-CoV-2 infection risk and severity in children is unclear.

WHAT THIS STUDY ADDS: Children with asthma were not at increased risk of SARS-CoV-2 infection compared with children without asthma and generally had mild SARS-CoV-2-associated illnesses.

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Current public health guidelines recommend that individuals with certain medical conditions, including moderate to severe asthma, take additional precautions to prevent infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, the etiological agent of coronavirus disease 2019 (COVID-19).[1,2] However, several prior studies suggested that asthma may be associated with a lower susceptibility to SARS-CoV-2 infection and a low risk of severe COVID-19. In 1 of the first epidemiologic studies of the pandemic, only 5 of 548 (<1%) patients hospitalized at Tongji Hospital in Wuhan, China had an asthma diagnosis.[3] Additionally, in a retrospective study of 22 254 individuals tested for SARS-CoV-2 infection in New York City, asthma was less prevalent among individuals testing positive for SARS-CoV-2 than among individuals testing negative for the virus (7% vs 11%).[4] Further, patients with asthma do not appear to be at greater risk of severe COVID-19.[5–7] Notably, these studies focused primarily on adults and were conducted among hospitalized patients or through convenience sampling of individuals presenting for SARS-CoV-2 testing. There is an ongoing need to investigate the association between asthma and SARS-CoV-2 infection risk in population-based studies of children and adolescents among whom asthma is the most common chronic medical condition and a leading cause of hospitalization.[8]

We sought to evaluate SARS-CoV-2 infection risk by asthma status in a cohort of 46 900 children receiving care in a large, integrated health system in central North Carolina. We matched 6324 children with asthma 1:1 to children without asthma using propensity scores and evaluated the association between asthma and the risk of SARS-CoV-2 infection. As a priori-specified secondary objectives, we evaluated the extent to which use of inhaled corticosteroids (ICS), history of severe asthma exacerbations, and the presence of comorbid atopic diseases modified the association between asthma and SARS-CoV-2 infection risk.

METHODS

Setting

This study was conducted in the Duke University Health System (DUHS), a comprehensive medical system consisting of a large academic medical center, 2 community hospitals, a network of primary and urgent care clinics, and both inpatient and outpatient subspecialty services. DUHS is the main health care provider in Durham County, North Carolina, with an estimated 85% of Durham residents receiving care within DUHS.[9] This study was conducted during a 19-month period from March 1, 2020, to September 30, 2021. The study was determined to be exempt human subjects research by the DUHS Institutional Review Board.

Study Population

We identified all children 5 to 17 years of age with a Durham County address and at least 1 health care encounter in DUHS within the 3 years preceding the study period (March 1, 2017, to February 28, 2020). We classified children as having asthma if they met 1 of 3 previously validated electronic health record (EHR)-based definitions during this 3-year period: (1) 2 or more outpatient or emergency health care encounters associated with an International Classification of Diseases, Ninth/Tenth Revision (ICD-9/ICD-10) code for asthma (Supplemental Table 5) and an active prescription for 1 or more medications for asthma (Supplemental Table 6); (2) at least 1 hospital encounter associated with an ICD-9/ICD-10 for asthma and an active prescription for 1 or more medications for asthma; or (3) a problem list entry with an asthma-related ICD-9/ICD-10 code and an active prescription for 1 or more medications for asthma.[10]

Data Collection

We used the Duke University School of Medicine Clinical Research Datamart to abstract patient EHR data.[11] Data recorded included age, gender, race and ethnicity, insurance status, and the neighborhood deprivation index, a metric that incorporates income, education, employment, and housing to create scores for neighborhoods based on socioeconomic disadvantage.[12] Race and ethnicity were derived from the EHR and may represent provider-reported or patient-reported data. Patients were classified as non-Hispanic Black, non-Hispanic White, Hispanic, or other racial or ethnic minority groups, with the last group including individuals listed in the EHR as being of 2 or more races, Asian, American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander, or "other" race. Race or ethnicity were included as a covariate in analyses to account for potential differences in access to testing and outcomes of SARS-CoV-2 infection. To account for differences in health system engagement that could influence observability and likelihood of SARS-CoV-2 testing, we recorded if the child's pediatrician was within DUHS, if the child had a well-child visit in the 2 years before the study period, and the number of health care encounters in DUHS in the 1 year preceding the study period. To identify a subset of children with asthma who were more likely to have an atopic asthma phenotype, we identified comorbid atopic diseases using

ICD-9/ICD-10 codes (Supplemental Table 5). Children were considered to have a history of severe asthma exacerbations if they had an exacerbation that required systemic corticosteroids in the 3 years before the study period. SARS-CoV-2 infection was identified based on positive test results in the EHR.

Statistical Analysis

We described characteristics of the study population by asthma status, by performance of SARS-CoV-2 testing, and by SARS-CoV-2 testing results. We first used Poisson regression with a sandwich variance estimator to evaluate associations between asthma, demographics, insurance type, health system engagement, and neighborhood characteristics with performance of SARS-CoV-2 testing and positive testing in the overall study cohort.[13] Because we identified substantial differences in patient characteristics and SARS-CoV-2 testing rates by asthma status, we used propensity score matching to construct a cohort of children with asthma and control children without asthma closely matched on these variables. We first used logistic regression to evaluate associations between demographics, insurance type, health system engagement, and neighborhood characteristics with asthma status. The predicted covariate values from this model were then used to generate propensity scores for the probability of having asthma for all children in the dataset. We then matched each child with asthma to a single child without asthma using nearest-neighbor matching of propensity scores. Distributions of propensity scores were evaluated for balance across the asthma and control groups (Supplemental Fig 3). For our primary analysis, we used Poisson regression with a sandwich variance estimator to evaluate the association between asthma status and the risk of SARS-CoV-2 infection in the propensity score-matched cohort. Finally, in a priori-specified secondary analyses, we fit modified Poisson regression models to evaluate for effect modification of the association between asthma status and SARS-CoV-2 infection by inhaled corticosteroid (ICS) prescription, recent history of severe asthma exacerbation, and comorbid atopic diseases in the propensity score--matched cohort. All statistical analyses were performed using R version 4.0.2.[14]

RESULTS

Patient Characteristics

Of 46 900 children, 6324 (13.5%) met the criteria for asthma (Fig 1). Characteristics of the unmatched cohort by asthma status are shown in Table 1. Compared with children without asthma, children with asthma were more likely to be male (58% vs 50%, $P < .0001$), to identify as non-Hispanic Black race (56% vs 37%, $P < .0001$), and to have public insurance (59% vs 49%, $P < .0001$). Children with asthma were also more likely to have had a well-child visit within the prior 2 years (73% vs 52%, $P < .0001$), had more health care encounters in the preceding 1 year (median interquartile range [IQR]: 3 [1–6] vs 1 [0–3], $P < .0001$), and were more likely to have a primary care physician in DUHS (99% vs 97%, $P < .0001$). Age and neighborhood deprivation index scores were similar among children with and without asthma.

Factors Associated With SARS-CoV-2 Testing

Overall, 10 566 (22.5%) children had 1 or more tests for SARS-CoV-2 during the study period. Children with asthma were more likely to be tested for SARS-CoV-2 infection than children without asthma (33.0% vs 20.9%, $P < .0001$). Patient race and ethnicity, insurance status, and neighborhood deprivation index scores also differed by SARS-CoV-2 testing status (Table 2). Specifically, children of other racial minority groups or with self-pay insurance status were less likely to be tested for SARS-CoV-2 infection, while children with public insurance and higher neighborhood deprivation index scores (corresponding to lower neighborhood socioeconomic status) were more likely to be tested for SARS-CoV-2. We also observed higher levels of previous health system engagement among children who were tested for SARS-CoV-2 infection. Compared with children who were not tested for SARS-CoV-2, tested children were more likely to have had a well-child visit in the 2 years preceding the study period and were more likely to have a primary care physician in DUHS.

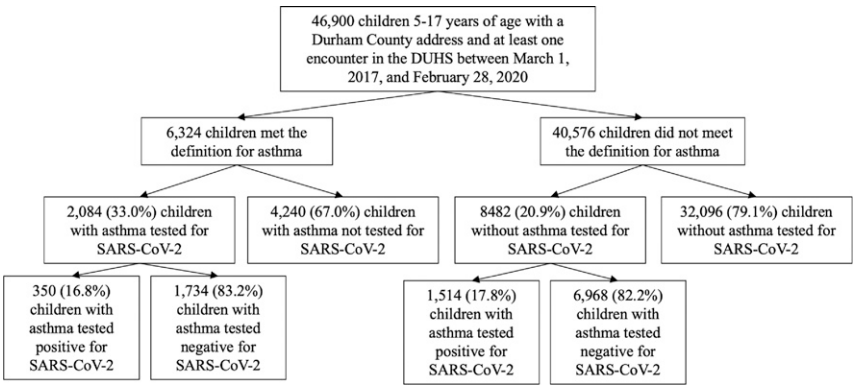

FIGURE 1
Participant flow diagram.

TABLE 1 Characteristics of the Study Population

	Unmatched Cohort (n = 46 900)					Propensity Score-Matched Cohort (n = 12 648)				
	Asthma (n = 6324)		No Asthma (n = 40 576)		SMD	Asthma (n = 6324)		No Asthma (n = 6324)		SMD
	n	(%)	n	(%)		n	(%)	n	(%)	
Median (IQR) age, y	11.0	(8.0–14.0)	11.0	(7.0–14.0)	0.060	11.0	(8.0–14.0)	11.0	(8.0–14.0)	0.007
Gender					0.158					<0.001
Female	2689	42	20 440	50		2689	42	2688	42	
Male	3635	58	20 136	50		3635	58	3636	58	
Race or ethnicity					0.249					0.036
Hispanic	918	15	9843	24		918	15	895	14	
Non-Hispanic Black	3510	56	15 052	37		3510	56	3515	56	
Non-Hispanic White	1315	21	10 932	27		1315	21	1380	22	
Other racial minority groups[a]	408	7	3049	8		408	7	383	6	
Insurance status					0.337					0.037
Private	2334	37	15 722	39		2334	37	2388	38	
Public	3731	59	19 674	49		3731	59	3719	59	
Self-pay	259	4	5180	13		259	4	217	3	
Neighborhood deprivation index					0.081					0.035
1–5	3979	63	27 071	67		3979	63	4056	64	
6–10	2145	34	12 438	31		2145	34	2099	33	
Well-child visit in the prior 2 y	4583	73	21 167	52	0.428	4583	73	4635	73	0.018
Median (IQR) number of encounters in prior year	3	(1–6)	1	(0–3)	0.325	3	(1–6)	3	(1–5)	0.032
Primary care physician in DUHS	6241	99	39 150	97	0.144	6241	99	6249	99	0.101
Tested for SARS-CoV-2 by PCR	2084	33	8482	21	0.274	2084	33	1791	28	0.080

DUHS, Duke University Health System; IQR, interquartile range; SMD, standardized mean difference.

[a] Other racial minority group includes individuals designated in the EHR as being of 2 or more races, Asian, American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander, or other race.

A total of 1864 (4.0%) children tested positive for SARS-CoV-2 infection during the study period, including 350 (5.5%) children with asthma and 1514 (3.7%) children without asthma. Among children tested for SARS-CoV-2 infection, non-White race, public and self-pay insurance, and higher neighborhood

TABLE 2 Factors Associated With SARS-CoV-2 Testing in the Overall Study Population

	Tested (n = 10 566)		Not Tested (n = 36 334)		Relative Risk	
	n	(%)	n	(%)	n	(95% CI)
Asthma status						
Children with asthma	2084	20	4240	12	1.31	(1.24–1.37)
Children without asthma	8482	80	32 094	88	1.00	Ref
Median (IQR) age, y	10.0	(7.0–14.0)	11.0	(7.0–14.0)	1.00	(0.99–1.00)
Gender						
Female	5441	52	17 688	49	1.10	(1.06–1.15)
Male	5125	48	18 646	51	1.00	Ref
Race or ethnicity						
Hispanic	2185	21	8576	24	0.99	(0.93–1.05)
Non-Hispanic Black	4438	42	14 124	39	0.95	(0.90–1.00)
Non-Hispanic White	2932	28	9315	26	1.00	Ref
Other racial minority groups	640	6	2817	8	0.78	(0.71–0.85)
Insurance status						
Public	5706	54	17 699	49	1.10	(1.05–1.16)
Private	4157	39	13 899	38	1.00	Ref
Self-pay	703	7	4736	13	0.85	(0.78–0.92)
Neighborhood deprivation index[a]						
1–5	6768	64	24 282	67	1.00	Ref
6–10	3451	33	11 132	31	1.12	(1.07–1.18)
Well-child visit in the prior 2 y	7494	71	18 256	50	1.75	(1.68–1.83)
Median (IQR) number of encounters in prior y	3	(1–6)	1	(0, 3)	1.02	(1.02–1.02)
Primary care physician in DUHS	10 534	>99%	34 857	96%	7.22	(5.20–10.45)

CI, confidence interval; DUHS, Duke University Health System; IQR, interquartile range; Ref, reference.

[a] Higher values are associated with greater deprivation and lower socioeconomic status.

TABLE 3 Factors Associated With Testing Positive Among Children Tested for SARS-CoV-2

	SARS-CoV-2-Positive (n = 1864)		SARS-CoV-2-Negative (n = 8702)		Relative Risk	
	n	(%)	n	(%)	n	(95% CI)
Asthma status						
Children with asthma	350	19	1734	20	0.91	(0.80–1.02)
Children without asthma	1514	81	6968	80	1.00	Ref
Median (IQR) age, y	11.0	(8.0–14.0)	10.0	(7.0–14.0)	1.04	(1.03–1.05)
Gender						
Female	948	51	4493	52	0.96	(0.87–1.05)
Male	916	49	4209	48	1.00	Ref
Race or ethnicity						
Hispanic	559	30	1626	19	2.18	(1.84–2.59)
Non-Hispanic Black	884	47	3554	41	1.74	(1.49–2.04)
Non-Hispanic White	259	14	2673	31	1.00	Ref
Other racial minority groups	106	6	534	6	1.64	(1.30–2.06)
Insurance status						
Public	1250	67	4456	51	1.41	(1.24–1.60)
Private	462	25	3695	42	1.00	Ref
Self-pay	152	8	551	6	1.30	(1.06–1.59)
Neighborhood deprivation index						
1–5	985	53	5783	67	1.00	Ref
6–10	800	43	2651	31	1.19	(1.08–1.32)
Well-child visit in the prior 2 ys	1244	67	6250	72	1.09	(0.98–1.21)
Median (IQR) number of encounters in prior y	3	(1–5)	3	(1–6)	0.99	(0.98–1.00)
Primary care physician in DUHS	1857	>99	8677	>99	0.95	(0.49–2.23)

CI, confidence interval; DUHS, Duke University Health System; IQR, interquartile range; Ref, reference.

deprivation were associated with positive testing for SARS-CoV-2 infection (Table 3). Of the 1864 children who tested positive for SARS-CoV-2, 34 were hospitalized within 30 days of a positive test, 3 of whom met our criteria for asthma. Eight of these children had COVID-19 as a primary indication for hospitalization (0.5%), including 7 of 1514 children without asthma (0.5%) and 1 child out of 350 children with asthma (0.3%). Additionally, 1 child without asthma was admitted for multisystem inflammatory syndrome in children.

Association Between Asthma and SARS-CoV-2 Infection

We next generated propensity scores for the probability of having asthma for all children and matched each of the 6324 children with asthma to a child without asthma using nearest-neighbor matching of propensity scores. Propensity score matching resulted in a population that was closely matched on patient characteristics (Table 1). In this propensity score-matched cohort, 706 (5.6%) children tested positive for SARS-CoV-2 infection during the study period, including 350 (5.5%) children with asthma and 356 (5.6%) children without asthma (Table 4). In multivariable analyses, SARS-CoV-2 infection risk was similar among children with and without asthma (risk ratio [RR] among children with asthma: 0.98, 95% confidence interval [CI]: 0.85–1.13. We tested for effect modification of this association by prescription of ICS, history of asthma exacerbation requiring systemic corticosteroids in the 3 years before the study period, and

TABLE 4 Associations Between Asthma Status and SARS-CoV-2 Infection in the Propensity Score-Matched Cohort (n = 12 648)

	SARS-CoV-2 Infection				
	n	(%)	Adjusted RR (95% CI)		P
Primary analysis					
Asthma (n = 6324)	350	5.5	0.98	(0.83–1.17)	.82
No asthma (n = 6324)	356	5.6	1.00	Ref	
Effect modification analyses					
Inhaled corticosteroid prescription, n = 4003					
Yes (n = 3238)	168	5.2	0.88	(0.73–1.09)	.27
No (n = 3086)	182	5.9	1.08	(0.89–1.34)	.42
Oral systemic corticosteroids					
Yes (n = 1561)	89	5.7	0.95	(0.71–1.25)	.71
No (n = 4763)	261	5.5	1.00	(0.84–1.18)	.97
Comorbid atopic disease					
Yes (n = 3986)	232	5.8	0.94	(0.79–1.12)	.52
No (n = 2338)	118	5.0	1.07	(0.83–1.38)	.60

Ref, reference.

comorbid atopic diseases. We observed similar risks of SARS-CoV-2 infection among children with asthma who were prescribed ICS (RR: 0.88, 95% CI: 0.73–0.94) and those who did not have a prescription (RR: 1.08, 95% CI: 0.89–1.34). Additionally, we did not observe a difference in the risk of SARS-CoV-2 infection among children with a history of severe asthma exacerbation (RR: 0.95, 95% CI: (0.71–1.25) and children who did not have a history of severe exacerbation (RR: 1.00, 95% CI: 0.84–1.18). Finally, the risk of SARS-CoV-2 infection was similar among children who had a diagnosis of comorbid atopic disease (RR: 0.94, 95% CI: 0.79–1.12) and those who did not have this comorbidity (RR: 1.07, 95% CI: 0.83–1.38).

As observed in other regions of the country, the majority of SARS-CoV-2 infections during the study period occurred in distinct waves; the most recent of which began in August 2021, when genomic surveillance data indicated widespread transmission of the delta variant (Fig 2).[15] Notably, the risk of SARS-CoV-2 infection among children with asthma relative to children without asthma was similar before and during this "third wave" of SARS-CoV-2 infections (Supplemental Table 7).

DISCUSSION

In this population-based study of over 46 000 children in central North Carolina, children with and without asthma had similar risk of SARS-CoV-2 infection. We identified marked differences in the likelihood of children being tested for SARS-CoV-2 by sociodemographic factors. Finally, we found that hospitalization among children with COVID-19 was infrequent, including among children with asthma.

Prior epidemiologic studies have reported inconsistent associations between asthma and SARS-CoV-2 infection risk. A nationwide cohort of 219 959 South Korean adults reported a slightly higher risk of testing positive for SARS-CoV-2 among individuals with asthma,[16] while a study of 400 000 children and adults in Mexico reported a lower prevalence of individuals with asthma among those testing positive for SARS-CoV-2.[17] Moreover, studies of pediatric populations have not identified an increased risk of SARS-CoV-2 infection among children with asthma. A retrospective, single-site EHR-based study in the United States of 7256 children tested for SARS-CoV-2 found that the asthma prevalence among children who tested positive for the virus was approximately the same as the overall pediatric asthma prevalence among children in the network.[18] A study of 7 pediatric health networks in the United States that included 135 794 patients less than 25 years of age tested for SARS-CoV-2 reported a slightly lower SARS-CoV-2 positivity rate among individuals with asthma and other previously diagnosed respiratory conditions.[19] Unlike these prior studies, we accounted for factors influencing the likelihood of children undergoing SARS-CoV-2 testing, including clinical and sociodemographic factors and healthcare utilization patterns that likely influence SARS-CoV-2 testing. Further, our study included data from the summer and fall of 2021, corresponding temporally with widespread transmission of the highly transmissible delta variant.

In addition to finding a similar risk of SARS-CoV-2 infection among children with and without asthma, we did not identify an association between asthma and COVID-19 severity, similar to previous findings in adults and children.[5,20–24] Among 222 children and adolescents hospitalized with COVID-19 in the United States during the first 6 months of the pandemic, the prevalence of asthma was similar to the estimated national prevalence of pediatric asthma.[25] An EHR-based analysis of children undergoing SARS-CoV-2 testing at Children's Hospital of Philadelphia facilities found that asthma was associated with a lower odds of hospitalization for COVID-19.[26] In contrast, a recent nested case-control study of 1392 children in Western Pennsylvania

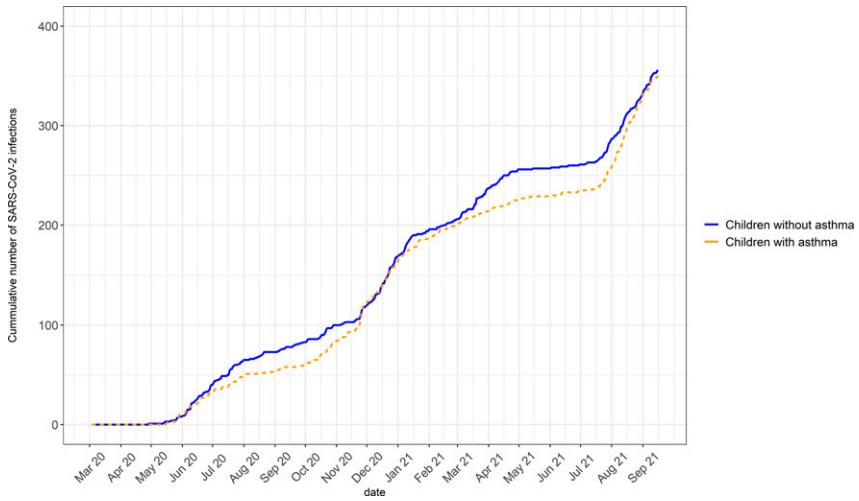

FIGURE 2
Cumulative incidence of SARS-CoV-2 infection among children in the propensity score-matched cohort by asthma status.

found that children with asthma who became infected with SARS-CoV-2 were 4 times more likely to be hospitalized than SARS-CoV-2-infected children without asthma, though length of stay and respiratory support did not differ between these groups.[27] It is also possible that asthma severity could influence SARS-CoV-2 outcomes among children. A study of over 700 000 children in Scotland found that SARS-CoV-2-infected children with poorly controlled asthma were at higher risk of hospitalization for COVID-19.[28] We specifically evaluated SARS-CoV-2 infection risk among children with a history of severe asthma exacerbations but did not identify any difference in SARS-CoV-2 infection risk. Taken together, these data suggest that asthma is not associated with worse outcomes among children and adolescents with SARS-CoV-2 infection.

Although we observed similar rates of SARS-CoV-2 infection among children with and without asthma in our cohort, there are several potential mechanisms by which asthma could influence SARS-CoV-2 infection risk. SARS-CoV-2 entry is mediated by the cell surface proteins that are reported to be expressed at lower levels in individuals with asthma compared with those without asthma, though the data are conflicting regarding associations with different asthma endotypes.[29–33] ICS use could also influence SARS-CoV-2 susceptibility, including through dampening of host inflammatory responses and decreased viral replication.[34,35] Finally, SARS-CoV-2 infection risk might differ among children with asthma because of differences in behavior and risk mitigation strategies due to a perceived risk of severe COVID-19 among children with chronic respiratory conditions.

The availability of SARS-CoV-2 testing to children during the COVID-19 pandemic has been influenced by national and local policies, testing availability, and our evolving understanding of the virus. A study of SARS-CoV-2 testing in North Carolina during the first 3 months of the pandemic identified lower access to testing among Hispanic, non-Hispanic, Black, and other historically marginalized populations, though individuals from these populations were more likely to test positive compared with White individuals.[36] Similarly, a study evaluating testing data from 7 states found that Black individuals were more likely to test positive compared with White individuals, and that test positivity was also associated with socioeconomic status.[37] We found that non-White children were tested at slightly lower rates compared with White children, though non-White children in these groups were more likely to test positive for SARS-CoV-2 than White children. Moreover, we observed that individuals with disadvantaged living conditions or who had public insurance had a higher test positivity rate than individuals who lived in neighborhoods with higher socioeconomic status. Consistent with this finding, a study of children presenting for drive-up testing at an academic medical center reported that families in the highest income quartile tested positive at a lower rate that those from lower income quartiles.[38] These findings highlight significant disparities in SARS-CoV-2 testing accessibility and disease burden among children by race, ethnicity, and socioeconomic status.

Our study has several strengths and limitations. First, our cohort included more than 6000 children with a current asthma diagnosis and active prescriptions for controller medications. While this stringent definition enabled us to have substantial confidence in the diagnosis in children classified as having asthma, children with mild asthma or who did not have active prescriptions for controller medications were likely misclassified as not having asthma. Both asthma and COVID-19 have well-recognized relationships with obesity. Unfortunately, we did not have recent height and weight or body mass index data for nearly half of the children included in this study; thus, we were unable to evaluate the impact of obesity on SARS-CoV-2 infection risk. We relied upon SARS-CoV-2 test results from within the health care system and could not account for SARS-CoV-2 testing performed at other sites. To minimize this possibility, we focused on children who reside in Durham County, for which DUHS provides the vast majority of primary and specialty pediatric services. We assumed that children who were not tested for SARS-CoV-2 did not have the virus; due to limited testing availability and asymptomatic infections, it is likely that some SARS-CoV-2 infections were not identified. We used propensity score matching to account for confounding in demographics associated with asthma status and access to SARS-CoV-2 testing. Finally, we were unable to account for differences in infection prevention and shielding behaviors that may have existed between children with and without asthma.

In summary, despite the continued general precaution regarding asthma and COVID-19, we found no evidence that asthma predisposes children to SARS-CoV-2 infection or severe illness from COVID-19. Importantly, we identified marked disparities in SARS-CoV-2 testing based on sociodemographic factors, highlighting the need for improved access to SARS-CoV-2 testing and care among certain vulnerable pediatric populations. Finally,

further research is needed to evaluate the complex relationships that exist between medical comorbidities, such as asthma and SARS-CoV-2 infection, and to monitor the impact of viral variants and vaccination strategies on SARS-CoV-2 infection among children.

ABBREVIATIONS

CI: confidence interval
COVID-19: coronavirus disease 2019
EHR: electronic health record
ICD: International Classification of Diseases
ICS: inhaled corticosteroids
RR: risk ratio
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

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