REVIEW

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Pediatric asthma control during the COVID-19 pandemic: A systematic review and meta-analysis

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Abstract

Background: With the onset of the coronavirus disease 2019 (COVID-19) pandemic, many experts expected that asthma-associated morbidity because of severe acute respiratory syndrome coronavirus 2 infection would dramatically increase. However, some studies suggested that there was no apparent increasing in asthma-related morbidity in children with asthma, it is even possible children may have improved outcomes. To understand the relationship between the COVID-19 pandemic and asthma outcomes, we performed this article.

Methods: We searched PubMed, Embase, and Cochrane Library to find literature from December 2019 to June 2021 related to COVID-19 and children's asthma control, among which results such as abstracts, comments, letters, reviews, and case reports were excluded. The level of asthma control during the COVID-19 pandemic was synthesized and discussed by outcomes of asthma exacerbation, emergency room visit, asthma admission, and childhood asthma control test (c-ACT).

Results: A total of 22,159 subjects were included in 10 studies. Random effect model was used to account for the data. Compared with the same period before the COVID-19 pandemic, asthma exacerbation reduced (odds ratio [OR] = 0.26, 95% confidence interval [CI] = [0.14–0.48], $Z = 4.32$, $p < 0.0001$), the odds of emergency room visit decreased as well (OR = 0.11, 95% CI = [0.04–0.26], $Z = 4.98$, $p < 0.00001$). The outcome of asthma admission showed no significant difference (OR = 0.84, 95% CI = [0.32–2.20], $Z = 0.36$, $p = 0.72$). The outcome of c-ACT scores were not analyzed because of the different manifestations used. Overall, c-ACT scores reduced during the pandemic.

Conclusion: Compared to the same period before the COVID-19 pandemic, the level of asthma control has been significantly improved. We need to understand the exact factors leading to these improvements and find methods to sustain it.

KEYWORDS
asthma control, children, COVID-19, systematic review and meta-analysis

Ze Yang and Xiang Wang co-first authors.

1 | INTRODUCTION

The novel coronavirus disease (COVID-19), which is associated with significant morbidity and medical complications induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread sparking alarm worldwide.[1,2] In June 2020 WHO declared COVID-19 a global pandemic which has made many countries to shut down their borders.[3] Asthma has become the most common chronic respiratory disease in children.[4–6] Because respiratory viruses are a common trigger of poor asthma control and exacerbations, many experts expected an increase in respiratory morbidity among patients with asthma.[7–9] However, some studies suggested that there was no apparent increase in asthma-related morbidity in children with asthma,[10] it is even possible that due to reduced exposures due to confinement, such children may have improved outcomes.[11]

The main objective of this study was to identify how is asthma in children during the COVID-19 pandemic controlled compared with the time before it.

2 | MATERIALS AND METHODS

2.1 | Data source

We searched PubMed, Embase, and Cochrane Library for the updated articles published from the inception of each database to August 1, 2021. when duplicate publications were identified, we chose the most complete and recent trial. Two investigators (Z.Y. and X.W.) independently retrieved all the related studies in the databases and excluded duplicate publications. The combined text and medical subject heading (MeSH) terms were cross-searched using MeSH and free word as follows: (Asthma[Mesh] OR Allergic asthma[Title/Abstract] OR Bronchial asthma[Title/Abstract] OR Asthma control[Title/Abstract] OR Asthma admission[Title/Abstract] OR Asthma exacerbation[Title/Abstract] OR asthma Emergency room visit[Title/Abstract]) AND (COVID-19[Mesh] OR COVID-19 Virus Disease[Title/Abstract] OR COVID-19 Virus Infection[Title/Abstract] OR 2019-nCoV Infection[Title/Abstract] OR Coronavirus Disease-19[Title/Abstract] OR 2019 Novel Coronavirus Disease[Title/Abstract] OR 2019-nCoV Disease[Title/Abstract] OR SARS Coronavirus 2 Infection[Title/Abstract] OR SARS-CoV-2 Infection[Title/Abstract] OR (COVID-19 Pandemic[Title/Abstract]) AND (Child[Mesh] OR Children[Title/Abstract]). We also reviewed abstracts and presentations from major conference proceedings up to June 1, 2021 to ensure that no additional studies were overlooked.

2.2 | Inclusion and exclusion criteria

Our meta-analysis is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement and had been registered at the International Prospective Register of Systematic Reviews (number: CRD42021266458).[12] Studies that met the following criteria were included: (1) the aim of the primary studies: comparing the level of asthma control the year of the pandemics with the year before the pandemics; (2) children and adolescents aged < 19 years; (3) the population are diagnosed as asthma; and (4) the background of the study is COVID-19 pandemic. We did not include abstracts, reviews, case reports, letters, duplicate publications, or studies with incomplete or unidentified data.

2.3 | Quality assessment and data extraction

Two independent investigators (Z.Y. and X.W.) evaluated the quality of all studies according to an 11-item checklist that was recommended by the Agency for Healthcare Research and Quality (AHRQ)[13] subjectively. "0" will be scored if it was answered No or Unclear and "1" will be given to the answer Yes. The quality of articles was assessed as follows: "0–3" means low quality, "4–7" means moderate quality, and "8–11" means high quality. The following information was extracted: first author, publication time, study design, source of population, mean age or age range, the sample size, and outcomes.

2.4 | Statistical analysis

A random-effect model was used to estimate the asthma exacerbation, asthma admissions, emergency room visits. Pooled odds ratio (OR) and 95% confidence intervals (95% CI) were calculated to report dichotomous data and mean difference (MD) with 95% CI were used to report continuous data. Statistical heterogeneity was considered to be present when $p < 0.1$ or $I^2 > 50\%$. Sensitivity analysis was used to analyze the source of heterogeneity. Publication bias was evaluated visually by funnel plots and considered significant when $p < 0.05$ in either Begg's test or Egger's test when the inclusion was more than 10 articles. Revman 5.4 was also used to conduct different analyses and all statistical tests.

3 | RESULTS

3.1 | Search results

Our initial search yielded 143 articles in total, 20 of which were removed for duplication. After screening titles and abstracts, further 41 items were taken away. Eighty-two articles were reviewed, among which 10 were included in this meta-analysis. No further study was identified by manual search. The flow diagram of studies selection was shown in Figure 1.

3.2 | Study characteristic

Ten studies,[14–23] with 22,159 subjects were included for the final meta-analysis. The sample size of the studies ranged from 16 to 18,912. The age of participants ranged from 2 to 18 across all studies. Outcomes in the studies are shown as follows: asthma exacerbation, asthma admissions, emergency room visits, and childhood asthma control test (c-ACT).
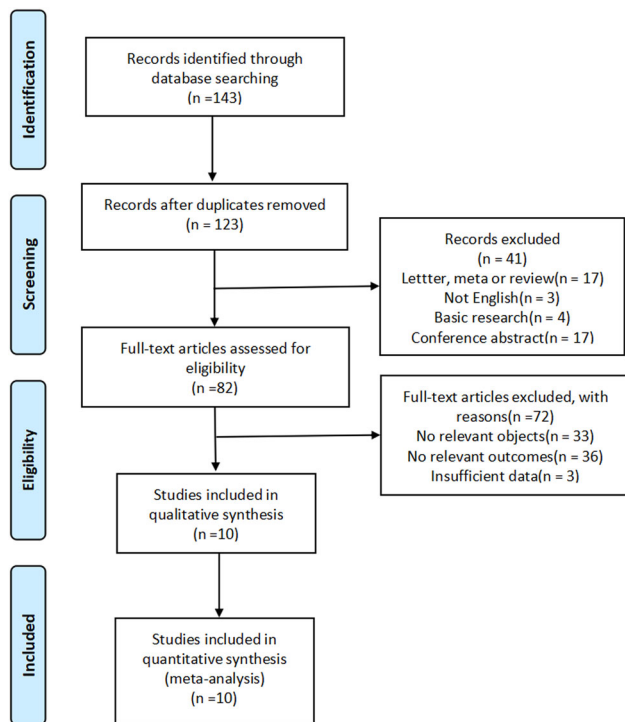
FIGURE 1 PRISMA flow diagram of the study selection process [Color figure can be viewed at wileyonlinelibrary.com]

The main characteristics of the 10 articles were summarized in Table 1. AHRQ scores suggested that all studies scored at 8–9 as high quality.[14]

3.3 | Asthma exacerbation

Four studies[14,15,20,20,23] were included in this outcome, with 835 cases during COVID-19 pandemic, and 945 cases before COVID-19 pandemic. Heterogeneity test analysis suggested that there was heterogeneity (I^2 = 75%, p = 0.007) (Figure 2A). Sensitivity analysis suggested that after removing Ochoa-Avilés et al.'s research,[20] the heterogeneity disappeared (I^2 = 0%, p = 0.75). The random effects model was used. The meta-analysis demonstrated there was significant difference between two groups (OR = 0.26, 95% CI = [0.14–0.48], Z = 4.32, p < 0.0001) (Figure 2B).
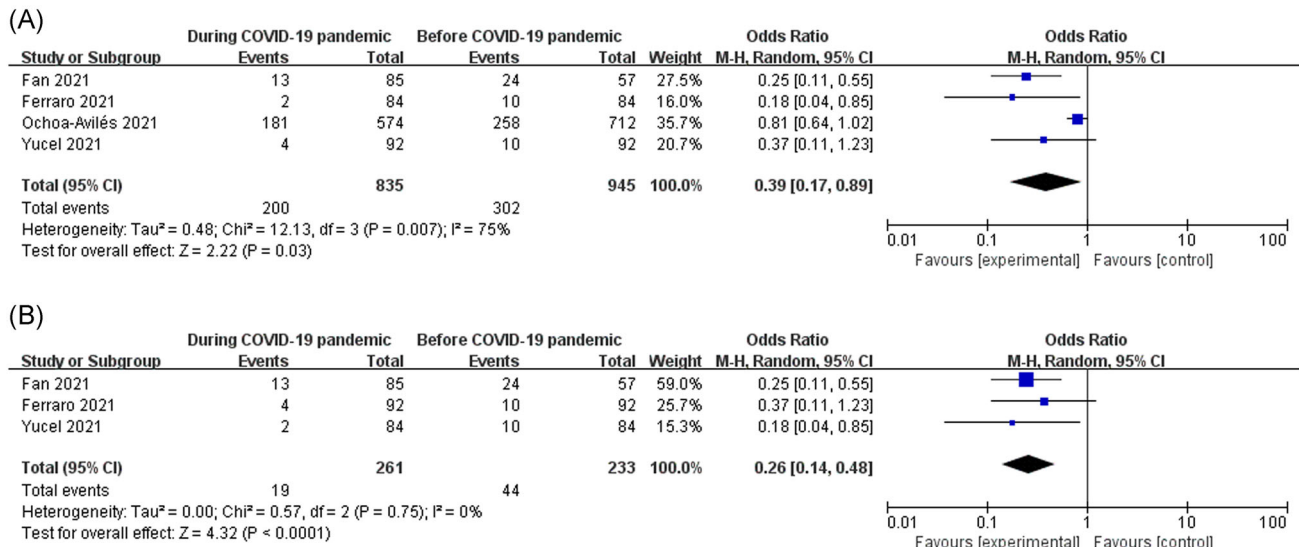
3.4 | Asthma admission

Five studies[16,17,19,19,21,22] were included in this outcome. The meta-analysis showed that there was no significant difference between two groups in asthma admission (OR = 0.84, 95% CI = [0.32–2.20], Z = 0.36, p = 0.72) (Figure 3). Heterogeneity test analysis suggested there was high heterogeneity (I^2 = 91%, p < 0.00001), so random effects model was used.
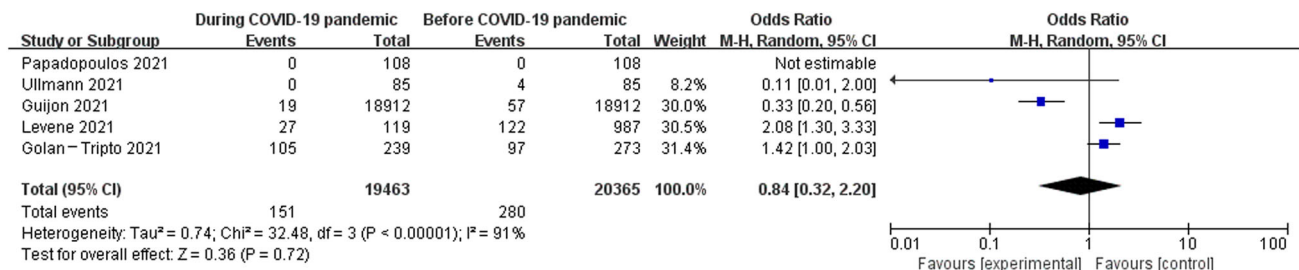
3.5 | Emergency room visit

Three studies[15,20,22] were included in this outcome. Heterogeneity test analysis suggested that there was no heterogeneity (I^2 = 0%, p = .87). The meta-analysis demonstrated there was significant difference between two groups(OR = 0.11, 95%CI = [0.04,0.26], Z = 4.98, P < 0.00001)

TABLE 1 Characteristics of the 10 studies included in the meta-analysis

Study	Source of population	Mean age or age range (AVG)	Sample size (boys/girls)	Outcomes	Quality score
Fan et al.[14]	China	8.2 (5.2–14.2)	85(70/15)	①	8
Ferraro et al.[15]	Italy	12 ± 3	92 (67/25)	①③	8
Golan-Tripto et al.[16]	Israel	2–18	512	②	8
Guijon et al.[17]	America	9.6 ± 4.6	18,912(10951/7961)	②	8
Jia et al.[18]	China	8	16(9/7)	④	8
Levene et al.[19]	America	7	4925(2466/2459)	②	8
Ochoa-Avilés et al.[20]	Ecuador	9.1 ± 2.9	213(110/103)	①③	8
Papadopoulos et al.[21]	15 countries	10	1054(662/392)	②③④	8
Ullmann et al.[22]	Italy	4.2 ± 1.1	85(48/47)	②③④	9
Yucel et al.[23]	Turkey	8.5	84	①④	8

Note: ①Asthma exacerbation; ②Asthma admissions; ③Emergency room visits; ④childhood asthma control test (c-ACT).

(A)

(B)

FIGURE 2 (A) Forest plots for comparison of asthma exacerbation between COVID-19 pandemic and before it. (B) Sensitivity analysis for comparison of asthma exacerbation between COVID-19 pandemic and before it. CI, confidence interval; COVID-2019, coronavirus disease 2019 [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 3 Forest plots for comparison of asthma admission between COVID-19 pandemic and before it [Color figure can be viewed at wileyonlinelibrary.com]
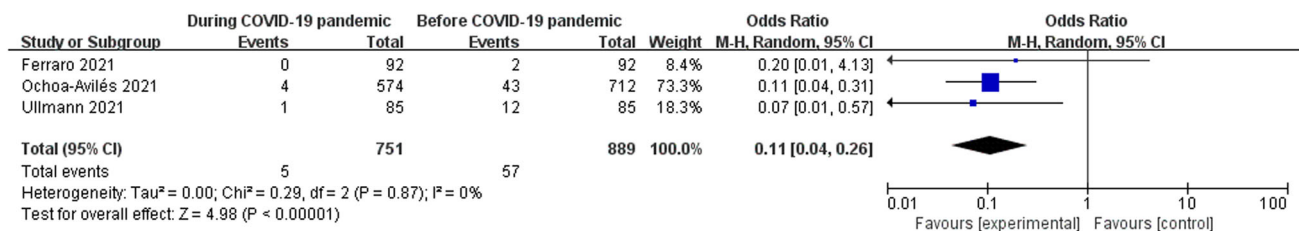
FIGURE 4 Forest plots for comparison of emergency room visit between COVID-19 pandemic and before it. CI, confidence interval; COVID-2019, coronavirus disease 2019 [Color figure can be viewed at wileyonlinelibrary.com]

(Figure 4), during COVID-19 pandemic, the emergency room visits of asthma were lower than that before COVID-19 pandemic.

3.6 | c-ACT

The outcome of c-ACT scores were not analyzed, which was mainly because of the different manifestations used. Overall, compared with the same period before COVID-19 pandemic, c-ACT scores reduced during the pandemic.

3.7 | Publication bias

We cannot use the funnel plot to reflect publication bias because all outcomes are included of fewer than 10 articles.

4 | DISCUSSION

The current systematic review provides a quantitative estimate of the asthma control of the current ongoing COVID-19 pandemic in children. The COVID-19 outbreak and the measures taken to it have had significant influences on asthma control among children. We have shown that the level of asthma control was significantly improved during the COVID-19 pandemic compared to the same period before it, with a reduction of asthma exacerbation, and emergency room visits. One reason for these results is probably associated with the lockdown measures during COVID-19 pandemic, which limits viral disease transmissions, reduces the possible exposure to asthma triggers, such as viral infections, outdoor allergens, physical activities, and air pollution.[24–26] It might also be explained by caregivers' afraid to bring children to the hospital because of the risk of exposure to SARS-Co-V2.[27] And increased treatment adherence is also an important factor. Caregivers are afraid of going to the hospital in the special time, so they pay more attention to their health than that before the pandemic and treat their children's asthma in time, and take the treatment actively, thus the times of visits to the hospital has decreased and the frequency of asthma exacerbation has also decreased. Anyway, these results mean less medication and healthcare resources are used in the control of children's asthma.

There was no significant difference between the two groups in asthma admission. A study of Levene et al.[19] mentioned that intentional avoidance of ED visits may lead to a delay for their asthma care, thus increasing the number of admission people. Guijon et al.'s study[17] showed different conclusions, they found asthma admission was decreased in the COVID-19 pandemic compared with the time before it, the main reasons were similar with asthma exacerbation and emergency room visit decreasing mentioned above.

For those probable infected with COVID-19, the study[28] found no differences between them and those without infection in asthma control or severity.

The outcome of c-ACT scores was not analyzed, though many articles included it. It was mainly because of the different manifestations used. For example, Papadopoulos et al.[21] use a number of people to show improved scores. Jia et al.[18] use the number of people whose scores were greater or equal to 20 which means good control. Ullmann et al.[22] use the exact scores directly. Yucel et al.[23] use the ratio of a score less than 20. It is hard to unite these outcomes. This is a problem that needs to be unified in the follow-up studies. Overall, c-ACT scores suggested a reduction in asthma symptoms during the pandemic.

Although the current meta-analysis results show that the control of asthma in children has been improved during pandemics, we are still concerned about the question that will childhood asthma worsen if the pandemic continues for a very long time? Because asthma control has largely benefited from the lockdown measure. A long time of lockdown means asthma control of patients with indoor allergen sensitization might be worse. Confounding factors such as increased exposure to indoor allergens, such as house dust mites (HDMs), molds, pet allergens, and decreased exposure to seasonal outdoor allergens such as pollens may have both negative and positive effects respectively on asthma. Besides, according to articles reported already, the pandemic period has no significant effect on children's asthma control. However, there are only a few studies that reported it, thus we can't get the conclusion exactly. We are also concerned about whether further studies will report asthma control being worse with a long time of the pandemic.

After the pandemic disappearing, children suffering from asthma and their caregivers should still reduce exposure to asthma triggers like viral infections, outdoor allergens, and air pollution, at the same time increase treatment adherence, just do what they underwent in the pandemic, thus restoring maintain and promote effective asthma management for children, this is the meaning of our writing this article.

Our review has several limitations. First, the sample size of this meta-analysis was relatively small. As a result, the unknown risk of bias caused by incomplete data could constrain our results. Second, our results are based on observational studies, which are susceptible to design bias, selection bias, and residual confounding. Third, in this study was that heterogeneity across the studies was substantial, which could be attributed to different definitions of severity used or sample size. Despite these limitations, this meta-analysis provides information on the association between children's asthma control and the COVID-19 pandemic.

5 | CONCLUSION

In summary, compared to the same period before the COVID-19 pandemic, the level of asthma control has been significantly improved. We need to understand the exact factors leading to these improvements and find methods to sustain them. This meta-analysis can guide children and their caregivers to restore, maintain and promote effective asthma management during, and more importantly, after the pandemic.

AUTHOR CONTRIBUTIONS
Ze Yang: conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); resources (equal); software (equal); supervision (equal). **Xiang Wang**: conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); software (equal); supervision (equal). **Xigang Wan**: data curation (equal); formal analysis (equal); investigation (equal); software (equal). **Menglei Wang**: resources (equal); software (equal). **Zonghua Qiu**: supervision (equal); validation (equal). **Jiali Chen**: validation (equal); visualization (equal). **Manhao Shi**: visualization (equal); writing original draft (equal). **Shiyi Zhang**: supervision (supporting); writing review & editing (supporting).

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material (References) of this article.

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