

COVID-19 and Acute Otitis Media in Children: A Case Series

Journal of Primary Care & Community Health
Volume 13: 1–6
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DOI: 10.1177/21501319221082351
journals.sagepub.com/home/jpc



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Abstract

Background: The association of SARS-CoV-2 with acute otitis media (AOM) in children is poorly understood. **Methods:** Cases were identified as a subpopulation within the NO TEARS prospective AOM study in Denver, CO from March to December 2020. Children enrolled were 6 to 35 months of age with uncomplicated AOM; those with AOM and SARS-CoV-2 were included. Data was obtained from electronic medical records and research case report forms. **Results:** A total of 108 patients enrolled in the NO TEARS study from May 2019 through December 2020 (all subsequently tested for SARS CoV-2). During the COVID-19 pandemic study period (March-December 2020), 16 patients enrolled, and 7 (43.6%) were identified with AOM/COVID-19 co-infection. Fever was present in 3 of 7 children (29%). Four children (57%) attended daycare. Only 2 children (29%) had SARS CoV-2 testing as part of their clinical workup. Mean AOM-SOS[®] scores were similar among SARS CoV-2 positive and negative patients with no statistical significance with two-sided *t*-tests: 13.6 (± 4.5) versus 14.2 (± 4.9) at enrollment, 1.4 (± 1.8) versus 4.2 (± 4.9) on Day 5, and 0.6 (± 0.9) versus 2.5 (± 6.1) on Day 14. Among the 7 cases, no child had an AOM treatment failure or recurrence within 3 to 14 or 15 to 30 days respectively. Of the 6 patients with completed bacterial and viral testing, a bacterial pathogen was identified in all 6, and a viral pathogen in 3 (50%). **Conclusions:** COVID-19 and AOM can co-exist. Providers should maintain a high index of suspicion for COVID-19 even in patients with clinical AOM and should not use a diagnosis of AOM to exclude COVID-19.

Keywords

SARS-CoV-2, ear infection, viral infection, coinfection

Dates received: 30 December 2021; revised: 3 February 2022; accepted: 4 February 2022.

Introduction

Viruses are known to contribute significantly to the development of acute otitis media (AOM) and AOM patients with some concurrent viral infections have higher severity of symptoms compared to those without.¹ A prior case series of adults with COVID-19 and concurrent AOM suggests that severe AOM symptoms and hearing loss may be more common among COVID-19 associated AOM than typical AOM.^{2,3} The association of SARS-CoV-2 (the virus that causes COVID-19) with AOM, the frequency of this co-infection and presenting symptoms of COVID-19 associated AOM in children are poorly understood. We describe 7 cases of children with AOM and SARS-CoV-2 detected that were followed for 30 days post diagnosis and completed comprehensive laboratory evaluations for other otopathogens.

Methods

Cases were identified as a subpopulation of children enrolled in the NO TEARS prospective AOM study at Denver Health (DH), Denver, CO from March to December 2020 (enrollment was halted April-September due to the pandemic). The NO TEARS study aims to improve care for children with AOM by evaluating the clinical failure rate of amoxicillin

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and assessing the correlation of nasopharyngeal (NP) organisms with clinical outcomes. The study enrolls children 6 to 35 months of age with uncomplicated AOM who are prescribed amoxicillin. Patients with complicated infections defined as: tympanic membrane rupture at diagnosis, more than 2 doses of systemic antibiotics in the preceding 30 days, concurrent competing bacterial diagnosis that could necessitate a systemic antibiotic, are immunocompromised, have concurrent steroid use, underlying ear abnormality (cleft palate, Down syndrome, prior sensorineural hearing loss or current tympanostomy tubes), or are not diagnosed during an in-person encounter are excluded.

Children who were 6 to 35 months of age with SARS-CoV-2 detected by polymerase chain reaction assay (PCR) and provider-diagnosed AOM were included in the case series.

Data, including demographics, clinical symptoms, exam findings, and laboratory results were obtained by electronic medical record review and from research case report forms. All patients enrolled in the study completed surveys on the day of enrollment and on days 5, 14, and 30 after enrollment. Enrollment, day 5, and day 14 surveys included the Acute Otitis Media Severity of Symptom (AOM-SOS[®]) scale (used with permission of University of Pittsburgh Medical Center, Pittsburgh, PA), a method developed for measuring symptoms of AOM in young children.

At enrollment (within 24 h of diagnosis) all patients had a NP ESwab[™] (Copan Diagnostics; Murrieta, CA) obtained. From the NP swab, culture for otopathogens including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Staphylococcus aureus* was completed using standard techniques within 24 h of enrollment. Qualitative PCR evaluation for *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, *S. aureus*, and 12 respiratory viruses including SARS-CoV-2 (see Table 2) (Quidel Lyra[®] Direct SARS-CoV-2, San Diego, CA) was completed in batches on previously frozen extracted aliquots (stored at -70°C in Amies media). Testing specimens after extended and proper storage has been shown to not negatively impact results.⁵ Samples were tested retrospectively in the research laboratory on frozen samples. Of the 7 patients included in this case series, 1 had not yet had otopathogen and respiratory viral PCR testing completed. Patients enrolled after September 2020 also had an oropharyngeal swab collected and tested in real-time for SARS-CoV-2 in the DH clinical microbiology laboratory (Abbott RealTime[®] SARS-CoV-2 Assay, Chicago, IL). Descriptive statistics were used to summarize the data. Comparison of AOM-SOS[®] scores between SARS-CoV-2 positive and negative patients were completed using or two-sided *t*-tests with alpha of $<.05$ considered statistically significant.

The Colorado Multiple Institute Review Board reviewed the study and caregivers provided informed consent prior to enrollment.

Results

Demographics and Medical History

A total of 108 patients were enrolled in the NO EARS study from May 2019 through December 2020. During the COVID-19 pandemic study period (March-December 2020), 16 patients were enrolled, and 7 (43.6%) had SARS-CoV-2 detected. All patients enrolled before March 2020 were negative for SARS-CoV-2. AOM demographic and clinical features are shown in Table 1. The median age of the patients was 16 months (range 7-30 months). Two patients (29%) had prior medical conditions, one had wheezing and prenatal drug exposure, the other had prematurity. Five children had no prior history of AOM. Four of the children (57%) attended daycare.

Clinical Course

The most commonly reported symptoms in children with SARS-CoV-2 identified were ear pain/tugging (6, 86%), runny nose (6, 86%), increased fussiness/irritability (6, 86%), cough (5, 71%), and not eating or drinking normally (5, 57%). Fever was only present in 3 children (29%). No child had AOM treatment failure or recurrence as defined by a need for a new antibiotic within 3 to 14 or 15 to 30 days, respectively. Two children (29%) reported diaper rash and diarrhea as adverse events from antibiotics. Previous studies have shown that mean AOM-SOS[®] scores when AOM is diagnosed can range from 3.71 to 6.39, compared with 0.96 at visits when AOM is not diagnosed.^{6,7} In this case series, mean AOM-SOS[®] scores were similar among the SARS CoV-2 positive and negative patients: 13.6 (± 4.5) versus 14.2 (± 4.9) at enrollment, 1.4 (± 1.8) versus 4.2 (± 4.9) on Day 5, and 0.6 (± 0.9) versus 2.5 (± 6.1) on Day 14. Differences in mean AOM-SOS[®] scores between SARS-CoV-2 positive and negative patients were not statistically significant with two-sided *t*-tests.

Microbiology Results

Of the 7 patients with SARS-CoV-2 identified, only 2 patients were identified as part of routine clinical care. SARS-CoV-2 was retrospectively identified by testing of research samples in the remaining 5 patients (71%). Five patients had testing completed only in the research laboratory, 1 had testing completed in both the research and clinical laboratories, and 1 had testing completed only in the clinical laboratory. The 5 patients identified exclusively by the study were enrolled in March 2020 when clinical testing availability for SARS-CoV-2 was limited. Culture and PCR results are shown in Table 2. Concurrent bacterial pathogens were identified in all children, except the child whose NP swab had not yet had otopathogen and respiratory viral

Table 1. Clinical Features of Children With Concurrent SARS-CoV-2 and AOM.

| Category | Characteristic | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 |
|-----------------------|---------------------------------|-----------------------|--------|--------|--------|----------------|----------------|--------|
| Demographics | Age (months) | 30 | 29 | 16 | 8 | 11 | 7 | 24 |
| | Gender-Male | + | | + | | + | + | + |
| | Race other than white | + ^a | | | | + ^b | | |
| | Hispanic | + | | + | + | + | + | |
| | Public Insurance | + | | + | + | + | + | + |
| Medical history | Past medical problems | | | | | + ^c | + ^d | |
| | 2+ doses PCV | + | + | | + | + | | + |
| | Smoke exposure | + | | | + | | | |
| | Breastfeeding | + | + | + | | + | | + |
| | Daycare attendance | | + | + | | + | | + |
| Clinical presentation | Ear pain/tugging | + | + | + | + | | + | + |
| | Nasal congestion | + | + | + | + | + | | + |
| | Fussiness/irritability | + | + | + | + | + | | + |
| | Cough | + | | + | + | + | | + |
| | Reduced oral intake | | | + | + | + | | + |
| | Eye redness/pain/discharge | | | + | | + | | |
| | Fever- subjective or over 100.4 | | | + | | + | + | |
| | Vomiting | | | | | | + | |
| | Diarrhea | | | | | + | | |
| | Reduced urine output | | | | + | | | |
| | Bilateral infection | | | | | + | | |
| | Outcomes | AOM-SOS ^{®e} | | | | | | |
| Diagnosis | | 10 | 6 | 10 | 18 | 15 | 18 | 18 |
| Day 5 | | 0 | 0 | 0 | 4 | 4 | 0 | 2 |
| Day 14 | | 0 | 0 | 2 | 2 | 0 | 0 | 0 |
| Treatment failure | | No | No | No | No | No | No | No |
| Recurrence | | No | No | No | No | No | No | No |

PCR testing completed in the research laboratory. Additional viral pathogens were identified in 3/6 (50%) children tested.

Discussion

AOM and SARS-CoV-2 can coexist and a diagnosis of either should not be used to exclude the other. Children in this case series with concurrent AOM and COVID-19 did not have a higher severity or more prolonged symptoms than SARS-CoV-2 negative children with AOM. Only 2 patients had SARS-CoV-2 testing as part of routine clinical care bringing to question whether providers are under-testing for SARS-CoV-2. Consistent with prior studies, most children had multiple pathogens identified by their NP swab tests.^{8,9} This occurred during a period where few other circulating respiratory viruses were identified. And since viruses tend to precipitate bacterial growth, it may be plausible that SARS-CoV-2 contributed to AOM in these children.

Though infection prevention measures including masking, hand hygiene, and social distancing during the COVID-19 pandemic have resulted in a significant reduction in the frequency of common pediatric infections including AOM,

these cases demonstrate that SARS-CoV-2 is evident in children with AOM.^{10,11} The clinical presentations of these children with AOM and SARS-CoV-2 were similar to the typical presentations of either AOM or mild COVID-19 disease. No child identified in this case series had complications from either infection. However, children with complicated AOM were excluded from the primary prospective study so we cannot make generalized conclusions regarding severity of symptoms in children with concurrent SARS-CoV-2 and AOM.

Importantly, only 2 patients had SARS-CoV-2 testing completed as part of routine clinical care, all other patients were exclusively tested as part of the research. The lack of testing may be explained by limited testing capacity during the early phases of the pandemic; however, robust testing systems were quickly established and available. This has significant public health impact, particularly since 4 of these patients were enrolled in daycare, which could have resulted in increased community transmission of SARS-CoV-2. Thus, providers should not use a diagnosis of AOM to exclude COVID-19. This also applies to other common pediatric bacterial and viral infections like influenza and conjunctivitis, which can occur concurrently with COVID-19.¹² Additionally,

Table 2. Laboratory Findings of Children With Concurrent SARS-CoV-2 and AOM.

| Laboratory test ^a | Specific pathogen | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 |
|------------------------------|---|---------------------|--------|--------|--------|--------|--------|------------------|
| SARS-CoV-2 PCR | Clinical SARS CoV-2 PCR (Abbott) | | | | | | + | + |
| | Research SARS-CoV-2 PCR (Quidel) | + | + | + | + | + | + | NYT ^b |
| Respiratory Viral PCR | Adenovirus | | | | | + | | NYT |
| | Influenza A | | | | | | | NYT |
| | Influenza B | | | | | | | NYT |
| | Parainfluenza 1 | | | | | | | NYT |
| | Parainfluenza 2 | | | | | | | NYT |
| | Parainfluenza 3 | | | | | | | NYT |
| | RSV | | | | | | | NYT |
| | Human Metapneumovirus | | | | + | | | NYT |
| | Rhinovirus | + ^c | | | | | + | NYT |
| | Coronavirus spp. (not SARS-CoV-2 or MERS) | | | | | | | NYT |
| | MERS | | | | | | | NYT |
| | Enterovirus | + | | | | | | NYT |
| | Bacterial PCR | <i>S.pneumoniae</i> | + | + | + | | + | |
| <i>H. influenzae</i> | | + | + | + | + | | + | NYT |
| <i>M. catarrhalis</i> | | + | | + | | + | | NYT |
| <i>S. aureus</i> | | | | | + | | + | NYT |
| Culture | <i>S. pneumoniae</i> | | + | + | + | + | | – ^d |
| | <i>H. influenzae</i> | + | + | + | + | + | | – |
| | <i>M. catarrhalis</i> | | | + | | | | – |
| | <i>S. aureus</i> | | | | + | | | – |

^aAll testing completed using NP swabs collected at enrollment.

^bNYT- not yet tested.

^cInconclusive.

^dCulture completed after receiving 1 dose of antibiotics.

oropharyngeal Group A Streptococcus carriage is common and could be incidentally detected in a child with COVID-19.¹³ Because the clinical presentation of COVID-19 and other common pediatric infections have significant overlap,¹² health care staff should exercise caution by using personal protective equipment and testing symptomatic patients for SARS-CoV-2, even if other diagnoses are suspected.

It is unclear how often children with SARS-CoV-2 infections develop AOM. Because young children have difficulty communicating symptoms, it is likely that AOM is underdiagnosed during SARS-CoV-2 infections. This is particularly likely with the shift to telemedicine during the pandemic because AOM cannot be reliably diagnosed without a physical exam. Fortunately, AOM frequently self-resolves, even if bacterial in etiology, and untreated AOM poses minimal risk for complications.^{14,15} Nevertheless, providers who are evaluating children for respiratory illnesses via telemedicine should discuss return-to-clinic guidelines for children who are not improving or are worsening, and examine children in-person who are not improving or when there is concern for AOM that would necessitate antibiotic treatment.

It cannot be discerned if SARS-CoV-2 was the organism responsible for AOM in these cases or if it was

detected incidentally. Since most AOM episodes follow viral upper respiratory infections and the frequency of pathogens other than SARS-CoV-2 during this time period was low, we suspect that SARS-CoV-2 was directly associated with the development of AOM in these children. The angiotensin-converting enzyme-2 (ACE2) receptor, which is the known cellular entry point for SARS-CoV-2 is highly expressed among ciliated cells in the Eustachian tube and could readily facilitate spread to the middle ear.^{16,17} Similar to other studies, nearly all children had bacterial otopathogens detected.^{8,9} We were limited in that testing for otopathogens was only completed on NP specimens and not middle ear fluid and that 1 child had SARS-CoV-2 testing only completed in the clinical laboratory using the Abbott assay (and not the research laboratory) at the time of this publication. Prior studies demonstrate a correlation between otopathogens detected in the nasopharynx and those present in middle ear fluid during AOM episodes (negative predict value 92%, positive predictive value 37%-67%).⁸ However, up to half of healthy children will have one or more otopathogens detected in the nasopharynx. Therefore, we cannot say definitively if SARS-CoV-2 or bacterial otopathogens detected by the NP swabs were present in the middle ear.

In contrast to prior findings in adult patients, we found that children in this case series with SARS-CoV-2 detected and AOM did not have higher severity of symptoms on presentation compared to other children with AOM who were negative for SARS-CoV-2.³ Though not statistically significant given the small sample size, AOM-SOS[®] scores were lower on days 5 and 14 for those with SARS-CoV-2, compared to those without and were consistent with a normal state of health by day 5.⁴ No child with AOM and SARS-CoV-2 had treatment failure, recurrence, or complications from either COVID-19 or AOM. Thus, the primary role of testing for SARS-CoV-2 in children with AOM is likely to advise families on isolation and quarantine requirements to reduce virus transmission rather than to guide clinical management.

Though the long-term effects of the COVID-19 pandemic remain to be seen, it is likely that as children return to daycare and school we will increasingly observe respiratory illnesses that include COVID-19, other viral pathogens, and common childhood infections such as AOM, at times simultaneously. Though this study is small, it points to the need for future studies to better characterize the frequency and characteristics of SARS-CoV-2 and other co-infections in order to guide clinical care and testing.

Authors' Note

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Acknowledgments

Holly M. Frost conceptualized and designed the study, provided subject matter support, analyzed and interpreted data, drafted the initial manuscript, and critically reviewed and revised the manuscript. Thesia Sebastian provided subject matter support, assisted with data collection, analyzed and interpreted the data, drafted the initial manuscript, and critically reviewed and revised the manuscript. Amy Keith and Melanie Kurtz assisted with data collection and analysis, and critically reviewed and revised the manuscript. Samuel R. Dominguez, Sarah K. Parker, and Timothy C. Jenkins provided subject matter support, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by The Gerber Foundation (PI: Frost); and H.F. receives salary support from the Eunice Kennedy Shriver

National Institute of Child Health & Human Development of the National Institutes of Health [K23HD099925].

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Role of the Funder

The funder had no role in the design, conduct, or reporting of the project.

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