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Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report

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PURPOSE To evaluate ocular manifestations and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) prevalence in the tears of children with coronavirus disease 2019 (COVID-19).

METHODS A total of 27 pediatric patients with confirmed COVID-19 infection hospitalized from March 16 to April 15, 2020, at the Bambino Gesù Children's Hospital were enrolled in the study. At admission, all patients showed ocular manifestations. Reverse transcriptase–polymerase chain reaction from nasopharyngeal and conjunctival swabs were performed every 2-3 days before discharge.

RESULTS Of the 27 patients, 4 (15%) were asymptomatic, 15 (56%) showed respiratory symptoms, and 8 (30%) had gastrointestinal symptoms. At admission, nasopharyngeal swabs were positive for COVID-19 in all patients; on the second swabs, 7 children (26%) tested negative, and 20 remained positive for COVID-19. Ocular manifestations consistent with mild viral conjunctivitis were observed in 4 patients (15%). At first conjunctival swab, 3 patients (11%), 1 symptomatic and 2 asymptomatic for ocular infection, had positive findings for COVID-19; 2 became negative on the second test and 1 on the third.

CONCLUSIONS In our study cohort, ocular manifestations of COVID-19 seem to have had a milder clinical course in pediatric patients than in adults. Despite the low prevalence and rapid regression of viral presence in the conjunctiva, SARS-CoV-2 transmission through tears may be possible, even in patients without apparent ocular involvement. (J AAPOS 2020;24: 212-215)

Since its onset in December 2019 in Wuhan (Hubei Province, China) the coronavirus disease 2019 (COVID-19) has quickly spread across the globe, causing a global pandemic, according to the World Health Organization (WHO).[1] The pathogen of COVID-19 is a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that can cause multiple system infections but mainly respiratory tract infections, such as severe acute respiratory syndrome.[2,3] The most common signs and symptoms include fever, cough, fatigue, myalgia, dyspnea, diarrhea.[4,5]

Compared with adults, children with COVID-19 seem to have lower incidence, shorter course of disease, and a more favorable clinical presentation and prognosis.[6,7] The transmission route of this novel coronavirus (SARS-CoV-2) remains unclear, and most authors report that it occurs mainly through direct contact or respiratory droplets.[4] Previous studies have investigated the viral presence in tears of patients with SARS-CoV-1 and SARS-CoV-2, reporting controversial results.[8-14] All of these studies were performed in adult patients. In this study we evaluated ocular involvement and the SARS-CoV-2 virus shedding in tears of 27 pediatric patients admitted to the Bambino Gesù Children's Hospital (BGCH) COVID Center in order to better understand the pathogenicity of SARS-CoV-2 in children's eyes.

Subjects and Methods

This study was approved by the Bambino Gesù Children's Hospital Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Informed consent to the procedure

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was obtained for each patient. This prospective observational case series study included 27 pediatric patients (7 females; mean age, 84 months; age range, 8 days to 210 months) with infection confirmed by nasopharyngeal swab COVID-19 nucleic acid test.

All patients were hospitalized from March 16 to April 15, 2020, at BGCH in the COVID-dedicated inpatient service created for the management of the SARS-COV-2 pandemic. Clinical data, including demographic information, contact history, clinical symptoms, and laboratory findings were reviewed and analyzed. Ocular symptoms and signs were also recorded. Real-time reverse transcriptase–polymerase chain reaction (RT-PCR) tests (GeneXpert, Cepheid, Sunnyvale, CA; 250 copies/mL sensitivity, 100% specificity) from nasopharyngeal and conjunctival swabs were performed on admission and repeated every 2-3 days before discharge; the microbiological surveillance was discontinued after two consecutive negative samples.

Swabs to collect tears and conjunctival secretions were performed from the lower eyelid fornix without topical anesthesia to avoid possible contamination of the specimen. Follow-up for each patient continued through April 15, 2020. The laboratory tests were performed in accordance with the guidelines and in laboratories identified for COVID-19 detection by the Italian Health Ministry.

Results

Clinical and demographic data of patients are summarized in Table 1. On admission, 23 patients were symptomatic: 15 patients (56%) showed respiratory symptoms (cough or dyspnea with or without fever), and 8 patients (30%) had gastrointestinal symptoms (vomiting and/or diarrhea with or without fever). No systemic symptoms were detected in 3 newborns whose mothers were infected. Average time from symptoms to admission was 7 days (range, 0-19).

On hospital admission, nasopharyngeal swab to COVID-19 tested positive in all patients. The swabs were repeated on average 4 times (range, 2-8) before discharge. Of the 27 children, 7 had negative findings for COVID-19 on second nasopharyngeal swab, and 20 had positive results.

Of the 27 patients, 4 (15%) had ocular manifestations consistent with viral conjunctivitis, characterized by mild conjunctival hyperemia and secretion; of these, 1 patient tested positive for SARS-CoV-2 on RT-PCR from conjunctival swab, whereas no signs of viral shedding were found in the other 3. Clinical resolution of conjunctivitis was achieved in all patients 3-5 days after onset. Two more patients had positive findings for SARS-CoV-2 in their conjunctival swab without developing clinical signs

Table 1. Patients characteristics

			Systemic symptoms			Ocular	Pharyngeal swab		Conjunctival swab	
Case	Age, mos	Days S–A[a]	Fever	Respiratory	Gastrointestinal	manifestations	First	Second	First	Second
1	52	12	+	–	+	–	Pos	Pos	Pos	Neg
2	6	6	+	–	+	–	Pos	Pos	Neg	Neg
3	8	14	+	+	+	–	Pos	Pos	Neg	Neg
4	204	5	+	+	–	–	Pos	Pos	Neg	Neg
5	12	8	+	+	–	–	Pos	Pos	Neg	Neg
6	168	6	+	+	–	–	Pos	Pos	Neg	Neg
7	210	6	+	+	–	–	Pos	Pos	Neg	Neg
8	192	2	+	–	–	–	Pos	Pos	Neg	Neg
9	216	7	+	+	–	–	Pos	Neg	Neg	Neg
10	25	8	+	+	+	–	Pos	Neg	Neg	Neg
11	133	9	+	+	–	+	Pos	Pos	Neg	Neg
12	84	19	–	+	–	–	Pos	Pos	Neg	Neg
13	1	5	–	–	–	–	Pos	Pos	Neg	Neg
14	1	3	–	+	+	–	Pos	Neg	Neg	Neg
15	1	6	+	–	+	–	Pos	Neg	Neg	Neg
16	1	8	–	–	–	–	Pos	Neg	Neg	Neg
17	180	1	+	+	–	+	Pos	Pos	Pos	Pos
18	81	6	+	–	+	+	Pos	Pos	Neg	Neg
19	137	11	+	–	+	–	Pos	Pos	Neg	Neg
20	180	16	–	+	–	–	Pos	Pos	Neg	Neg
21	81	1	–	–	–	–	Pos	Pos	Neg	Neg
22	108	3	–	–	–	–	Pos	Pos	Neg	Neg
23	76	0	+	–	–	–	Pos	Pos	Neg	Neg
24	69	11	–	+	–	+	Pos	Pos	Neg	Neg
25	34	5	–	+	–	–	Pos	Pos	Pos	Neg
26	183	2	+	+	–	–	Pos	Neg	Neg	Neg
27	156	9	+	–	–	–	Pos	Neg	Neg	Neg

[a]Days from onset of symptoms to admission.

of conjunctivitis. Three patients (11%) had positive findings for COVID-19 on first conjunctival swab; of these, the 2 asymptomatic cases became negative at the second swab (3 days) and the symptomatic case at the third (6 days), while remaining positive on nasopharyngeal swabs.

Additionally, the nasopharyngeal swab was negative on average 8 days (range, 2-17 days) from onset of symptoms, whereas conjunctival swab became negative in all patients on average in 4 days (range, 3-6 days).

Discussion

The novel COVID-19 caused by SARS-CoV-2 emerged in December 2019 in Wuhan, China.[2] Virologic data has demonstrated that individuals carry potentially infectious SARS-CoV-2 particles in their nasopharyngeal secretions, thereby very likely contributing to COVID-19 transmission; therefore, positive SARS-CoV-2 RNA swabs are indicative of active infection.[15] The epidemiology and clinical course of SARS-CoV-2 seems to differ in childhood compared with adults, with a mean lower incidence and milder symptoms in the pediatric population.[6,16,17]

Several reports have investigated ocular involvement in adult patients with COVID-19 infection.[8-14] Wu and colleagues[14] evaluated 38 adult patients with clinically confirmed COVID-19 reporting that one-third of patients with more severe systemic manifestations had conjunctivitis despite a low prevalence of positive findings for SARS-CoV-2 in their conjunctival swabs. Xia and colleagues[12] confirmed this evidence as viral RNA in tear fluid, and conjunctival secretion was found in the only patient affected by conjunctivitis of 30 adults with SARS-CoV-2 infection examined. Additionally, a viral replication has been recently reported in tear fluid of a COVID-19 patient with conjunctivitis after clinical resolution of symptoms and clearance of conjunctival and nasal swabs, indicating ocular mucosa as a site of sustained viral replication and consequently a source of contagion. Zhou and colleagues[18] observed that in adults symptoms and findings, when present, were mild.

On the contrary, Seah and colleagues[13] found that in 17 adult patients with ocular symptoms, including red eye, tearing, blurring of vision, discharge, and color desaturation, there was no evidence of SARS-CoV-2 shedding in tear fluid in all patients through the course of the disease, suggesting a low risk of infection transmission through tears.

The current evaluated a cohort of pediatric patients with COVID-19 infection. Ocular involvement consistent with conjunctivitis was found only in 3 of 27 children and appeared to have a mild clinical course that resolved in a few days. This finding accords with the more benign systemic manifestation of the disease reported for pediatric patients compared with adults. Only a single patient affected by conjunctivitis was positive by swab testing. This apparent discrepancy could be explained by the timing of the test, which may not have been coincidental with the viral maximal load, or by the limited quantity of tear and conjunctival secretions collected, determining an insufficient sample concentration for RT-PCR detection of the virus. However, as in with previous studies, our data showed only a small prevalence of positive swabs in patients with manifest signs of conjunctivitis.

Nevertheless, ocular viral shedding was found in 3 patients, suggesting, as other authors have reported for adult populations, that transmission through tears is possible in children. Furthermore, of the 3 patients with positive conjunctival swabs, only 1 child presented ocular manifestations, indicating that viral load may be present in tears even in asymptomatic patients.

Another issue is the difference between nasopharyngeal and ocular viral shedding trends. In our patients, the conjunctival swab became negative in all patients much sooner than did the nasopharyngeal swab. In most of the cases, patients with persistent positive nasopharyngeal swab over days maintained a negative conjunctival swab, confirming that the viral load in the tear fluid is less than in other biological specimens and that the eye is relatively preserved in comparison with other organs. In consideration of these findings, conjunctival swab should not be considered a valuable diagnostic test of COVID-19, particularly in children. Nevertheless, despite the low prevalence and rapid regression of viral presence in the conjunctiva, transmission through tears is theoretically possible, even if the ocular contagious phase in children seems to be relatively brief. This contrasts with the evidence of long viral persistence and replication in conjunctiva recently reported in adults, but it might be explained by the milder manifestation of the disease in the pediatric population.

Of the children hospitalized for COVID-19, identification of SARS-COV-2 RNA from ocular secretions was uncommon. Of the 3 children (11%) found to have SARS-COV-2 RNA in tears, 2 were without ocular signs or symptoms and 1 had mild conjunctivitis. PCR-based shedding of SARS-CV-2 tended to clear faster from tears than from oropharyngeal secretions (median, 4 vs 8 days), although the ranges were wide, with sizable overlap (2-17 vs 3-6 days, resp.).

This study has some limitations, including its relatively small sample size. Another is the uncertainty of the efficacy of RT-PCR as a technique for diagnosing SARS-CoV-2 in tears.[8,19] False-negative results, usually due to sample contamination or insufficient sample concentration for RT-PCR virus detection, could not be ruled out, mainly in children whose poor compliance may hinder the collection of tears and conjunctival secretion. To decrease false negatives, we repeated the test at least twice for each patient before discharge.

In conclusion, our preliminary data confirms the relatively milder symptoms experienced by pediatric patients and supports the possible presence of viral load in tears and conjunctival secretion. Thus, although pediatric ocular manifestations in COVID-19 seem to be mild, there is still

a risk of transmission. Although SARS-CoV-2 prevalence is low in tears and may disappear, potential ocular transmission must be considered by clinicians treating pediatric patients, in whom disease effects may be milder and eye involvement mostly asymptomatic but hand-to-face contact is common.

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