



Decreased incidence of acute hemorrhagic conjunctivitis associated with enhanced public health intervention during the COVID-19 epidemic in China, 2020

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Abstract

Outbreaks of acute hemorrhagic conjunctivitis (AHC) are associated with a high disease burden. In this study, we investigated the association between enhanced public health intervention and the incidence of AHC during the COVID-19 pandemic in China. A total of 212,526 AHC cases were reported in China during 2015–2020. The overall yearly incidence rate and number of AHC cases decreased by 23.08% and 22.15%, respectively, during the COVID-19 epidemic, compared with the previous 5 years (all $p < 0.001$). Significant reductions in AHC incidence were found both during the emergency period and after the relaxation of emergency measures in 2020 compared to the previous 5 years (22.22% and 28.00% reduction, respectively; $p < 0.001$). Enhanced public health initiatives during the COVID-19 pandemic in China were therefore associated with lower transmission of pathogens causing AHC.

Introduction

The COVID-19 global pandemic is one of the most extensive and serious crises to afflict humanity in a century. China was one of first countries to suffer the devastating effects of COVID-19 disease, and in response to this threat, the national and local governments launched numerous non-pharmaceutical enhanced public health interventions to curb the spread of this novel virus. As one component, various local governments issued school closures and delayed school

openings, and these school protocols remained in effect throughout the emergency stage (January to April 2020).

Ocular manifestations are not uncommon in COVID-19 patients, and these may appear with severe systemic manifestations [5]. Ocular surface cells, including conjunctiva, are susceptible to infection by SARS-CoV-2 and could therefore serve as possible transmission portals for the virus [4]. The most common viral disease of the ocular surface is acute hemorrhagic conjunctivitis (AHC), which is caused primarily by enterovirus 70, coxsackievirus A24 variant (CA24v), and adenovirus 11. AHC predominately affects school children and is highly contagious. The enhanced public health interventions against COVID-19 have been reported to have reduced the occurrence of seasonal influenza, norovirus

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infections, and enterovirus infections in Australia, France, Japan, and other countries [1, 2, 7, 9, 10]. The aim of the present study was to retrospectively evaluate AHC activity during the COVID-19 pandemic in China to determine whether a similar reduction occurred in AHC in response to public health measures.

Methods

All data used in this study were deidentified; therefore, institutional review board approval was not required. We extracted the number of suspected, clinically diagnosed, and confirmed cases, the number of deaths, and the incidence data for AHC by month and year for the period of 2015–2020 from the National Health Commission of the People's Republic of China. Two proportional tests were applied to measure the statistical differences in average monthly/yearly incidence over the years. The distribution differences of the monthly average incidence of AHC for 2020 vs. each year from 2015 to 2019 were examined using the Mann-Whitney test. The tests were performed and plots were made using R software 4.1.1. (<https://cran.r-project.org/bin/windows/base/>).

Results

We included all suspected, clinically diagnosed, and confirmed AHC cases. A total of 212,526 AHC cases were reported in mainland China from January 1, 2015 to December 31, 2020. Separately, from 2015 to 2019, 183,893 AHC cases were reported, resulting in a yearly average of 36,779 cases and a yearly average incidence of 2.67 per 100,000 people. In 2020, a total of 28,633 AHC cases were reported, with a yearly incidence of 2.05 per 100,000. The overall yearly incidence rate and number of AHCs in 2020 decreased by 23.08% and 22.15%, respectively, compared with the previous 5 years (all $p < 0.001$).

The average monthly cases and incidence of AHC in 2015–2019 were 3065 and 0.22 per 100,000 people, respectively (Table 1). By contrast, the average monthly cases and incidence in 2020 were 2386 and 0.17 per 100,000 people, respectively (Table 1). The average monthly incidence rate of AHC decreased by 22.73% (95% CI: -27.79% to -18.39%), from 0.22 to 0.17 per 100,000 ($p < 0.001$) during the 2020 COVID-19 epidemic compared to the previous 5 years in China (Table 1).

Table 1 Changes in the average monthly incidence rates of AHC in the emergency response stage (January to April 2020) and the routine response stage (May to December 2020) compared with the previous five years in China

Stages	Month	2015-2019		2020		Monthly incidence Change (%) (95%CI) (2020 vs 2015-2019)	p value
		Average number of monthly new cases	Average monthly incidence	Number of monthly new cases	Monthly incidence		
Emergency Stage	January	2178	0.16	2139	0.15	-6.25 (-8.83 to 2.93)	0.32
	February	1854	0.13	1672	0.12	-7.69 (-17.13 to -4.65)	<0.001
	March	2717	0.20	2011	0.14	-30.00 (-31.80 to -21.93)	<0.001
	April	2985	0.22	2230	0.16	-27.27 (-30.90 to -21.47)	<0.001
Total emergency period		2433	0.18	2013	0.14	-22.22 (-23.60 to -12.91)	<0.001
Routine Stage	May	3441	0.25	2468	0.18	-28.00 (-33.49 to -24.77)	<0.001
	June	3931	0.28	2788	0.20	-28.57 (-34.00 to -25.87)	<0.001
	July	4221	0.31	2796	0.20	-35.48 (-38.43 to -30.69)	<0.001
	August	3704	0.27	2561	0.18	-33.33 (-35.86 to -27.53)	<0.001
	September	3324	0.24	2549	0.18	-25.00 (-28.72 to -19.73)	<0.001
	October	2857	0.21	2298	0.16	-23.81 (-25.44 to -15.65)	<0.001
	November	2823	0.20	2538	0.18	-10.00 (-16.24 to -6.13)	<0.001
	December	2744	0.20	2583	0.18	-10.00 (-12.17 to -1.80)	0.008
Total routine period		3381	0.25	2573	0.18	-28.00 (-29.26 to -20.36)	<0.001
Yearly Sum		3065	0.22	2386	0.17	-22.73 (-27.79 to -18.39)	<0.001

Note: 95%CI=95% confidence interval.

We defined monthly **incidence** (per 100,000) as the number of monthly incident cases divided by the population size.

Changes = $(x_1 - x_2) / x_2 \times 100\%$; x_1 : average monthly **incidence** in 2020; x_2 : average monthly **incidence** in the previous five years (2015–2019). “-” = decreased trend. The p-value for emergency or routine stage was computed through two proportional tests.

The five-year average population in 2015–2019 was 1,379,750,092 in China, and the population in 2020 was 1,396,537,448 in China.

The Mann-Whitney test (Fig. 1A and B) indicated a significantly lower mean monthly incidence in 2020 (0.17 per 100,000) than in 2015, 2016, 2017, 2018, or 2019 (0.21, 0.21, 0.21, 0.23, and 0.25 per 100,000, respectively; Fig. 1A and B). The distributions of the monthly incidence for 2020 vs. each year from 2015 to 2019 were all statistically significant (all p values < 0.05). Similar results were observed for the mean monthly cases between 2020 and the years from 2015–2019 (all p < 0.05) (Fig. 1C and D).

China declared a shift in COVID-19 control measures from an emergency state (2020 emergency period: January to April 2020) to a routine period (May to December 2020), so we also compared the AHC incidence in these two periods to the same periods in previous years. During the 2020 emergency period, the average monthly incidence of

AHC was lower compared to the same period in 2015–2019 (0.14 vs. 0.18 per 100,000, a 22.22% reduction [95% CI: -23.60% to -12.91%, p < 0.001]) (Table 1). During the 2020 routine period, the average monthly incidence of AHC was 0.18 per 100,000 population, while this value was 0.25 per 100,000 population during the same period in 2015–2019 (a reduction of 28.00% [95% CI: -29.26% to -20.36%], p < 0.001) (Table 1). A decreasing trend was also found in each month of 2020 compared to the same period in 2015–2019, with a fast decrease seen in July (0.31 to 0.20 per 100,000, 35.48% reduction [95%CI: -38.43% to -30.69%], p < 0.001) (Table 1).

During the 2015 to 2019 period, we diagnosed only one AHC-related death, while two AHC-related deaths were reported in 2020 in the whole of China.

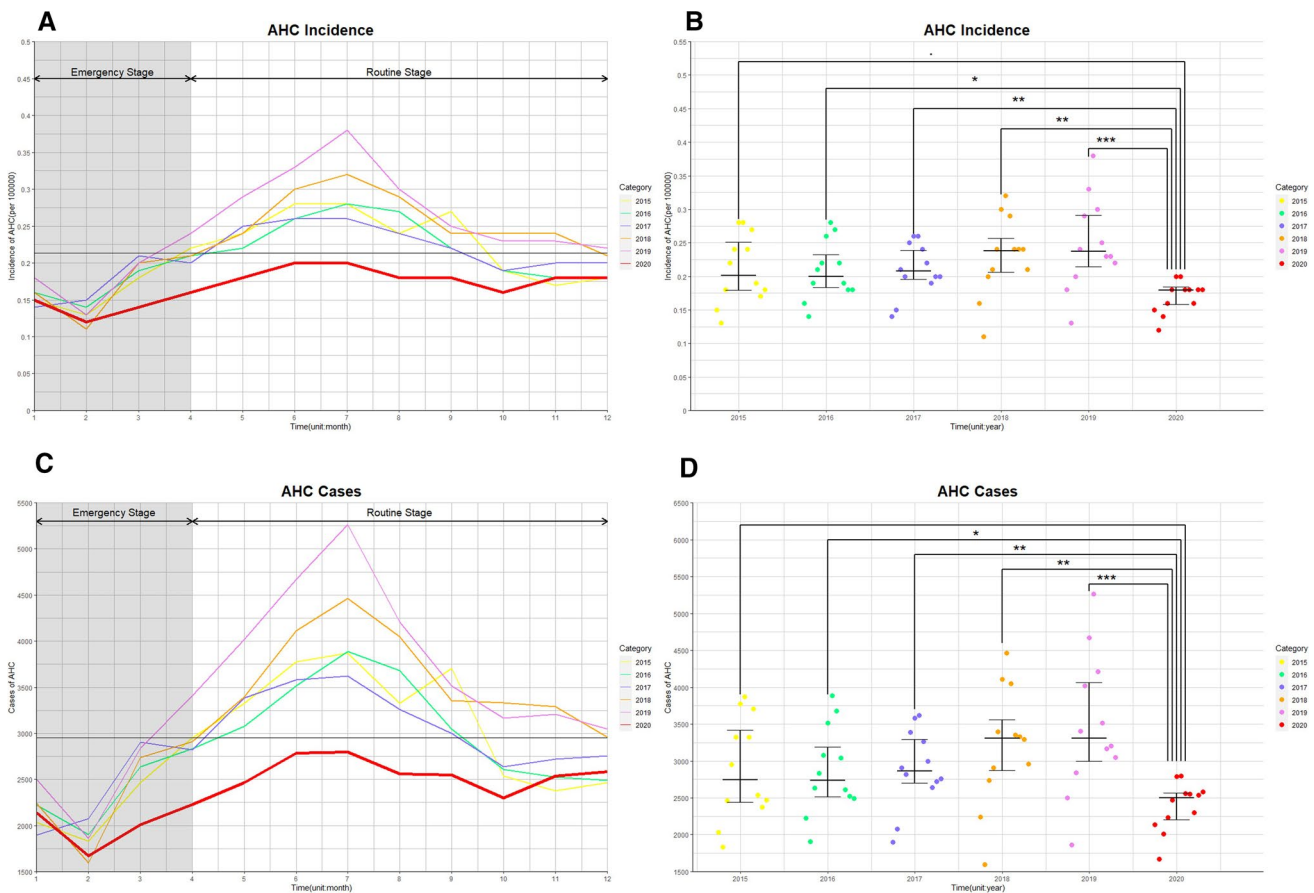


Fig. 1 Comparison of the monthly incidence and monthly number of cases of acute hemorrhagic conjunctivitis between 2015, 2016, 2017, 2018, 2019, and 2020 in China. (A) The monthly incidence distribution of AHC from 2015 to 2020. Black dashes indicate the average monthly incidence of AHC from 2015 to 2019. (B) Comparison of the mean monthly incidence distribution in 2020 to the distributions in 2015 to 2019 using the Mann-Whitney test (***, p < 0.0001; **, $0.001 < p < 0.01$; *, $0.01 < p < 0.05$; $0.05 < p < 0.1$). Black lines indicate P25, P50, and P75, respectively, from the upper and lower quartiles. The dots indicate the monthly incidence from January to

December in different years. The grey rectangle represents the emergency response period in China in 2020. (C) The monthly number of cases of AHC during 2015 to 2020; Black dashes indicate the average monthly cases of AHC during 2015 to 2019. (D) Comparison of mean monthly cases in 2020 to those in 2015 to 2019 using the Mann-Whitney test (***, p < 0.0001; **, $0.001 < p < 0.01$; *, $0.01 < p < 0.05$). The grey rectangle represents the emergency response period in China in 2020. Black lines indicate P25, P50, and P75, respectively, from the upper and lower quartiles. The dots indicate the number of monthly cases from January to

Discussion

We observed a marked decline in the overall incidence and number of AHC cases in 2020 compared to the previous five years in China. Our findings were consistent with the reported declines in other infectious diseases in England, Taiwan, France, and other countries [1, 6, 9]. Recent studies have shown that conjunctivitis could be one manifestation of COVID-19, with an overall rate of 1.1% in COVID-19 patients [8]. However, the reduction in AHC cases observed in this study was not related to increased COVID-19, because none of the AHC cases in this study were related to COVID-19 [8]. Rather, the decreased occurrence might be more attributable to strict compliance with enhanced public health interventions.

As with the SARS-CoV-2 virus, enteroviruses can be transmitted from person to person by direct or indirect contact or the faecal-oral route, but respiratory transmission can also occur [9]. During the emergency response to the COVID-19 pandemic, the lockdown of cities, closure of schools, and delayed school opening, followed by a large increase in the proportion of out-of-school children, may have drastically reduced the circulation of AHC-associated pathogens [9]. Secondly, the implementation of health education promoted students' hygiene awareness, including wearing masks, hand washing, and social distancing, during the routine and emergency stages [3]. In addition, health care avoidance was evident, as fewer patients visited clinics due to concerns about contracting SARS-CoV-2. Strict nosocomial infection control measures for the coronavirus pandemic and increasing clinical guidelines for ophthalmology practices might also have helped to disrupt AHC transmission and outbreaks [11]. Our findings suggest that the COVID-19 pandemic and its consequences significantly decreased the occurrence of AHC in children in 2020 compared to the previous 5 years in China. The beneficial effect of the implementation of public health measures and awareness were observed even after those measures were lifted in the routine period in 2020, highlighting long-term effects.

This study is limited in the sense that it only examines data from overall populations from China. Further, the ability to compare referrals in 2020 to previous data on age- and gender-specific populations, especially in children, as well as to assess pathogen-specific data, are needed to reduce this limitation.

Conclusions

The highly contagious AHC, which primarily affects children, showed a significant reduction in incidence and number of cases in China in 2020 compared to the previous five years. The most likely explanation is that public health measures, strict nosocomial control, and personal behaviour changes due to fears of COVID-19 infection in 2020 led to this reduction. This suggests that surveillance of childhood infectious diseases other than AHC should be conducted if an increase in incidence of infectious diseases is observed when the COVID-19 restrictions are lifted in the future.

Author contributions LZ, XG, and SL conceived and designed the study. LZ, XG, and SL made substantial contributions in reviewing the design of the study and acquiring the data. XG, HJ, and NZ conducted acquisition and statistical analysis of the data. LZ and XG drafted the manuscript. WX and SL supervised the study and critically revised the manuscript. WC took part in the revision. All authors gave final approval of the version to be submitted.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All data used in this study were deidentified; therefore, institutional review board approval was not required.

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