

Letter to the Editor: Are severe COVID-19 patients more susceptible to conjunctivitis?

Dear Editor,

We read with interest the article by Loffredo et al¹ [Reference citation was changed on June 17, 2020 after initial publication online.] of conjunctivitis and COVID-19: a meta-analysis. We appreciate the article's suggestions on protection in ophthalmic diagnosis and treatment but believe that the data and conclusions in meta-analysis need further study, the reasons are as follows: First, the original meta-analysis included three studies²⁻⁴ one of which the data processing of Wu et al^2 may not be consistent with the original text. Wu et al² found conjunctivitis in 12 of the 38 patients. Among these 12 patients, there were four cases judged as moderate, two cases judged as severe, and six cases judged as critical. Therefore, according to the guideline of PC-NCP,⁵ the proportion of severe COVID-19 should be 8 of 15 and that of not severe COVID-19 should be 4 of 23. However, the data of this meta-analysis are 2 of 15 and 1 of 23, respectively. Second, in a study by Guan et al,³ [Reference citation was changed on June 17, 2020 after initial publication online.] there is a great difference between the severe and not severe sample sizes, which is larger than that in the other two included studies. The probability of conjunctivitis in patients with ['not' was deleted on June 17, 2020 after initial publication online.] severe COVID-19 was 4 of 173, and the not ['not' was added on June 17, 2020 after initial publication online.] severe COVID-19 is 5 of 926. Although the conclusion remains unchanged after this study is removed, it seems that large sample size differences between studies may lead to publication bias. However, there is no denying that this analysis is still very meaningful, especially when there are few reports on relevant research. [Text 'Although...research' was added on June 17, 2020 after initial publication online.] COVID-19 patients may have conjunctivitis, and

even the first symptom of some cases is conjunctivitis.⁶⁻⁸ However, it is not clear whether the onset of conjunctivitis is different for COVID-19 patients with different severe conditions.

Based on the above thinking, we searched PubMed and CNKI for articles on COVID-19 and conjunctivitis with the words of COVID-19, 2019-CoV, SARS-CoV-2, and conjunctivitis. The severity of COVID-19 was distinguished according to PC-NCP guidelines, the incidence of conjunctivitis in patients with severe and not severe COVID-19 was included. A total of 62 studies were searched, 37 studies were read in full after duplication, and 4 studies were included (Figure 1).^{2,4,9,10} Meta-analysis showed that the probability of conjunctivitis (log odds ratio [It was changed on June 17, 2020 after initial publication online.] = -0.84; 95% confidence interval, [-1.66, -0.01]; P = .05) between severe patients and not severe patients was statistically significant, ['not' was delete from here on June 17, 2020 after initial publication online.] severe COVID-19 patients seem to be more likely to develop conjunctivitis. It can be seen that the results of our metaanalysis are consistent with those of the original meta-analysis. To a certain extent, we have confirmed the great possibility of the original analysis results. [Text 'To a...results' was added on June 17, 2020 after initial publication online.]

Inevitably, our meta-analysis also has certain limitations, such as too few documents and factors of the reporting population. Therefore, whether the patient has conjunctivitis or not is not necessarily related to the severity of COVID-19, this controversial issue may require further study. But when it is unknown whether conjunctival infection exists and whether it has an early warning effect on some systemic diseases, it is necessary to improve prevention and is also an important measure to facilitate treatment and avoid further spread.

not severe severe								Log Odds-Ratio	Weight
Study	Yes	No	Yes	No				with 95% Cl	(%)
Wu, P	4	19	8	7		-	-	-1.69 [-3.17, -0.2	1] 47.05
Xia, J	1	20	0	9				— 0.33 [-2.96, 3.6	2] 3.77
Hong, N	6	18	9	23				-0.16 [-1.36, 1.04	4] 34.02
Ye, Y	2	27	1	0				-3.50 [-6.95, -0.04	4] 15.16
Overall							•	-0.84 [-1.66, -0.0	1]
Heterogeneity: I ² = 42.94%, H ² = 1.75									
Test of θ	= θ _j : Q	(3) =	5.26,	p = 0	15				
Test of θ	= 0: z =	= -1.9	98, p =	= 0.05					
					-10	-5	Ó	5	

Fixed-effects Mantel-Haenszel model

Meng Liu¹ 🕩

- Cheng Dai²
- Xiaodong Lv³
- Binzhong Li¹

¹School of Basic Medicine, North Sichuan Medical College, Nanchong, China ²Department of Ophthalmology, Affiliated Hospital of North Sichuan Medical College, Nanchong, China ³Department of Clinical Medicine, North Sichuan Medical College, Nanchong, China

Correspondence

Meng Liu, School of Basic Medicine, North Sichuan Medical College, 637000 Nanchong, China. Email: 13658105660@163.com

ORCID

Meng Liu (D) http://orcid.org/0000-0002-9066-2993

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