



The prevalence of ophthalmic manifestations in COVID-19 and the diagnostic value of ocular tissue/fluid

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Dear Editor,

The World Health Organization (WHO) has declared rapid infection of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) across the globe as a pandemic on March 11, 2020. Although the main mode of SARS-CoV-2 transmission is predominantly respiratory, several studies have suggested that exposure of unprotected eyes to the virus may also cause novel coronavirus pneumonia (NCP) [1, 2]. In agreement, a recent animal study also confirmed that macaque's conjunctiva inoculated with SARS-CoV-2 lead to the development of mild interstitial pneumonia [3], implying that ocular tissues and fluid may be a potential alternative mode of SARS-CoV-2 transmission. So far, there have been varying reports regarding the prevalence of ocular manifestations among COVID-19-infected patients [2, 4–9]. Hence, in order to summarize the current evidence, a meta-analysis was conducted to estimate the prevalence of ocular manifestations among COVID-19-infected patients. In addition, the diagnostic value of ocular tissue/fluid in detecting SARS-CoV-2 was also evaluated.

A comprehensive literature search was conducted from PubMed, Scopus, Web of Science, and Google scholar. Keywords such as “ocular/eye/ophthalmology,” “coronavirus 2019/COVID-19,” “2019-nCoV,” and “SARS-CoV-2” were used singularly or in combination without applying language restriction and dated up to April 4, 2020. Criteria of studies included in this meta-analysis were (1) observational studies that

reported ocular symptoms among COVID-19-infected patients and (2) comparing diagnostic outcomes between ocular tissue and fluid (conjunctival swab/tears) and nasopharyngeal swab or sputum in detecting SARS-CoV-2 by polymerase chain reaction (PCR) analysis. Seven studies were included in this meta-analysis [2, 4–9]. Prevalence estimates of ocular manifestations were calculated from six studies [2, 4, 5, 7–9] (Table 1). Heterogeneity was evaluated with the I^2 statistic, in which an I^2 value over 50% was considered an indicator of substantial heterogeneity. If heterogeneity existed, the random-effects model was then used; otherwise, the fixed-effects model was applied. A funnel plot and Begg's test were used to investigate the publication bias if the pooled effect size consisted of 10 or more studies. The value of 0.05 was indicative of the statistical significance.

The prevalence of ocular manifestations among COVID-19-infected patients ranged from 2 to 32%. The random-effects model was used due to heterogeneity ($I^2 = 69.62\%$, $p = 0.006$). The overall pooled prevalence of ocular manifestations among COVID-19-infected patients was 5.5% (42/735 subjects, 95% CI 1.6–9.4%; Fig. 1). The pooled sensitivity and specificity were calculated from six studies [2, 4–7, 9]. Although the pooled specificity was high (100%, 95% CI 0–100), the pooled sensitivity of ocular tissue/fluid in detecting SARS-CoV-2 was very low (0.6%, 95% CI 0.1–5.1) in comparison with standard sample collection from nasopharyngeal swab/sputum (Table 1).

Therefore, in this current analysis, we emphasize that ocular symptoms have relatively low prevalence among COVID-19-infected patients. Interestingly, it seems that the ophthalmic manifestations appear to be associated with the disease severity of COVID-19 [5, 8]. And although ocular tissue/fluid is useable for SARS-CoV-2 detection, the procedure may not be useful for diagnostic purposes in the clinical setting. Despite the findings, ocular transmission of SARS-CoV-2 remains a crucial issue that requires vigilance of protecting the ocular surface and by wearing protective equipment during ophthalmic examination and handling of ocular fluids by the physician or health care worker.

Zulvikar Syambani Ulhaq and Gita Vita Soraya contributed equally to this work.

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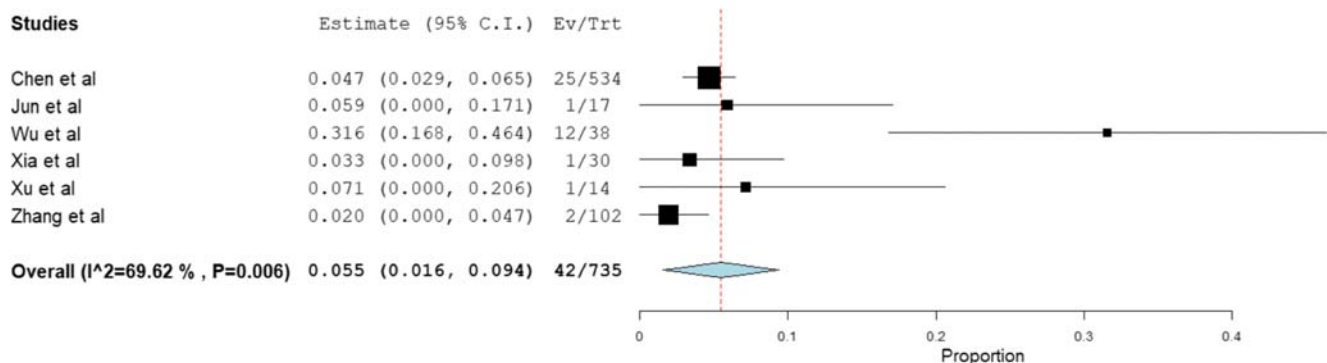
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Table 1 Characteristics of included study in this meta-analysis

Study	Location	No. of cases	Women (%)	Age	Ocular symptoms		PCR SARS-CoV-2	
					Yes	No	CS/tears	NP/sputum
Chen et al. [8]	China	534	NR	40/50 (mean)	25	509	NR	371
Deng et al. [6]	China	114	54	61.4 (mean)	NR	114	0	90
Jun et al. [4]	Singapore	17	NR	NR	1	16	0	17
Wu et al. [5]	China	38	34	68 (median)	12	26	2	11
Xia et al. [7]	China	30	30	54.5 (mean)	1	29	0	29
Xu et al. [9]	China	14	50	48 (mean)	1	13	0	14
Zhang et al. [2]	China	102	50	57.63 (mean)	2	100	1	72

CS, conjunctival swab; NP, nasopharyngeal swab; NR, not reported; PCR, polymerase chain reaction

**Fig. 1** Forest plot of the 6 studies estimating the pooled prevalence of ocular manifestations among COVID-19-infected patients

Compliance with ethical standards

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

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