

# Detection of Covid-19 with Ocular signs, Symptoms, and Rapid Test Standard Q on the Conjunctiva and Tear Film

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**Background** Coronavirus infection (Covid-19) is a recent pandemic outbreak, characterized by transmission through body secretions. Research indicates the presence of the infection in the Oropharynx<sup>2</sup>, encompassing the nasopharynx, establishing a connection to the tear duct pathway (nasolacrimal system). Several studies have reported the presence of the infection in the tears and conjunctival tissues<sup>3</sup>. The objective of this study is to determine the detection of Covid-19 from conjunctival secretions and lacrimal ducts using standard rapid antigen tests. Additionally, the study aims to explore ocular manifestations in individuals diagnosed with Covid-19 using RT-PCR.

**Setting** THABO CROWN PRINCE HOSPITAL

**Study design** Prospective cohort study

**Methodology** Data were collected from 414 patients at risk of contracting Covid-19. A total of 414 patients exhibiting respiratory symptoms indicative of coronavirus disease (Covid-19) received a diagnosis of SARS-CoV-2 through RT-PCR in the PCR group. Subsequently, these subjects underwent evaluation via standard rapid antigen test using conjunctival secretions. Additionally, an ophthalmologist conducted examinations using a handheld slit-lamp microscope.

**Results** The sample group consisted of 414 individuals that exhibit symptoms of entry and susceptibility to Covid-19. Among them, nasal swab RT-PCR, which was considered the gold standard, was performed on 212 people, constituting an incidence rate of 51.21% (95% CI: 46.39-56.02%). The occurrence of Covid-19 in lacrimal secretion was observed in 10 cases (2.42%), with 7 cases (3.30%) identified in the nasal swab RT-PCR positive subgroup. Upon statistical analysis, no statistically significant difference was discerned (P value = 0.290). The sensitivity for the intraocular diagnostic test was determined to be 3.30% (95% CI: 1.58-5.02%). Notably, this study revealed no transmission between medical personnel and patients, and there were no reported fatalities.

**Conclusion:** Within the high-risk group, respiratory symptoms associated with coronavirus (Covid-19) infection can manifest through tears. The diagnosis of Covid-19 was established through both positive and negative results in nasal swabs RT-PCR tests. Consequently, the intraocular Antigen Test Kit (ATK) is deemed inappropriate as a diagnostic tool. Nonetheless, it serves a valuable role in affirming the potential for pathogen contamination in the tear region. Thus, caution is warranted when medical personnel are required to make contact with the patient's conjunctiva and tears.

**Keywords:** Covid-19, SARs-CoV outbreak, Conjunctivitis, Tear film, Antigen test kit

**Conflict of interest declaration:** No conflict of interest

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## Introduction

The current global epidemic, known as "Covid-19", is caused by a single-stranded RNA virus enclosed in a capsule. Originating in Wuhan, China, in December 2019, the virus

presents common symptoms such as fever, cough, shortness of breath, and decreased sense of smell. Less common symptoms include red eyes and diarrhea, with symptoms ranging from 2-14 days post-exposure, and an average incubation period of 5-7 days. The disease can be transmitted through secretions such as mucus, saliva, and tears.

In 2004, Tong et al. investigated the SARs-CoV outbreak, identifying the first discovery of a coronavirus that displayed symptoms of bronchiolitis gastroenteritis and conjunctivitis. Among the 36 patients examined for SARs-CoV in sputum, feces, and tears, they identified three positive PCR RNAs in tears and feces<sup>1,2</sup>. In January 2020, Guangfa Wang, a member among the team of specialists treating Covid-19 patients in Hu'an province, developed keratoconjunctivitis. PCR nasal swab tested positive, stemming potential spread through conjunctival secretions to Wuhan.<sup>3</sup> At the same time, in the early outbreak of Covid-19, Wan Y et al. studied the structure of SARs-CoV and SARS-CoV-2 and found similar profiles, with receptor binding that allows infection entry to host cell via angiotensin-converting-enzyme-2 (ACE2).<sup>4</sup> It is widely known that the renin-angiotensin system (RAS) controls the levels of minerals and enzymes, as well as the mechanism of action of glaucoma drugs, prompting further exploration in this regard.

Several studies in China have reported conjunctivitis in Covid-19 patients, with conjunctivitis prevalence at 0.6%. RT-PCR testing revealed SARS-CoV-2 RNA fragments in tears.<sup>6</sup>

It is well known that Covid-19 is a disease that can spread rapidly via aerosols and, when infected, has potential to cause severe illness or death. When pathogens enter the body, they tend to settle inside the nasal cavity, which connects the nose, mouth, throat, and tear duct. The study focused on the neglected areas pertinent to ophthalmologists and frontline medical personnel, namely conjunctival secretions and tear ducts, which has a point connected to the nasal cavity where the Covid-19 virus usually resides.<sup>5</sup> This study focuses on patients with respiratory symptoms aligning with Covid-19 symptoms according to the criteria for disease screening by the Department of Medical Services,

Ministry of Public Health<sup>7</sup> pending confirmation with nasal swab RT-PCR to assess conjunctiva and tear infection risk. This research serves as a vital pilot study for future investigations, enhancing the safety of medical personnel caring for ophthalmic patients who come to examine their eyes in the outpatient department during this epidemic, where educational evidence in Thailand remains lacking.

## Research Objectives

**Primary Objective:** To study the incidence of Covid-19 from conjunctival secretions and lacrimal ducts using a standard rapid antigen test.

**Secondary Objectives:** Visual signs and symptoms in patients diagnosed with Covid-19 using RT-PCR.

**Study Design** Prospective cohort study

## Materials and Methods

All hospital patients deemed susceptible to SARS-CoV-2 displaying symptoms and history that meet the criteria for Clinical Practice Guidelines for Diagnosis, Care, and Prevention of Hospital Infections in Cases of Coronavirus Disease 2019 (Covid-19) set forth by the Department of Medical Services, Ministry of Public Health<sup>7</sup> (as shown in Figure 1) and underwent RT-PCR diagnostic, resulting in a total of 414 SARS-CoV-2 diagnoses. All participants were informed of the research information and provided informed consent for their involvement in the study. While awaiting RT-PCR results in the surveillance room, high-risk patients would undergo examination using a handheld slit-lamp microscope by an ophthalmologist donned in full PPE, and subsequently analyzed by staff wearing a full PPE suit, along with an analysis staff member. The procedure utilized an antigen test kit (ATK), involving a gentle pull-down of the patient's lower eyelid. The swab was delicately placed on the conjunctiva, where the patients would close their eyes for 15 seconds before reopening them. The same swab method was then applied to the other eye. The swab, now containing tears, was passed on to a staff member for dipping into the test substance for analysis. Following the swabbing process, 0.18% sodium hyaluronate eye drops were applied to prevent dry eye and corneal abrasions in both eyes.

### Inclusion Criteria

Those who have symptoms that meet one of the following criteria:

1. Have at least 2 of the following symptoms: 1) fever 2) cough 3) runny/stuffy nose 4) sore throat 5) mucus or
2. Having any of the symptoms in (1) together with any of the following symptoms: 1) diarrhea 2) muscle pain 3) headache 4) nausea/vomiting 5) diarrhea 6) fatigue 7) a rash; or
3. have one of the following symptoms 1) shortness of breath 2) difficulty breathing 3) abnormal smell/ taste 4) confusion or decreased level of consciousness, or
4. Having any one of the severe respiratory infections: 1) pneumonia/chest x-ray found pneumonia with unknown or unknown cause within 48 hours; or 2) respiratory failure. acute respiratory distress syndrome (ARDS), or
5. The medical examiner suspects that he is infected with the corona virus 2019.
6. Has a history of contact with Covid-19 patients

\*Information from the disease screening criteria of patients in at-risk groups, Department of Medical Services, Ministry of Public Health<sup>7</sup>

### Exclusion Criteria

1. Age less than 10 years
2. A history of regular eyedrops usage
3. Unable to cooperate

### Results

A total of 414 patients who were susceptible to contracting Covid-19 were included in the study. These individuals exhibited respiratory symptoms aligned with Covid-19 criteria for disease screening of at-risk patient groups, Department of Medical Services, Ministry of Public Health.<sup>7</sup> General population information revealed a predominant presence of females, constituting 57.49% of the samples. Furthermore, the majority fell within the age range of 10-30 years, representing a significant 81.88%. The details are presented in Table 1.

**Table 1:** Demographic data of the sample (n = 414 people)

	Number	Percentage
<b>Data SEX</b>		
male	176	42.51
female	238	57.49
Total	414	100
<b>Age (Year)</b>		
Less than 10	7	1.69
between 10-30	339	81.88
more than 30	68	16.43
<b>Nasal RT-PCR</b>		
Positive	202	48.79
Negative	212	51.21

**Table 2:** shows the results of the Rapid antigen test in the lacrimal region and the symptoms detected. \*tear ATK=rapid antigen test result with lacrimal secretion, Conjunctivitis=conjunctivitis, eye drop use=has a history of using eye drops

	Number	Percentage
<b>Tear ATK</b>		
Positive	10	2.42
Negative	404	97.58
<b>Conjunctivitis</b>		
Positive	7	98.31
Negative	407	1.69
<b>Eye drop use</b>		
yes	2	99.52
no	412	0.48

From the overall population of 414 individuals exhibiting symptoms and are at risk of contracting Covid-19, 212 individuals were identified as infected when subjected to nasal swab RT-PCR (considered the gold standard diagnosis test). This indicates an incidence rate

of 51.21% (95% CI: 46.39-56.02) as illustrated in Table 1. Notably, 202 subjects had displayed symptoms and at risk were not subjected to nasal swab RT-PCR testing, accounting for 48.79%. This underscores the heightened vulnerability of the respiratory tract to coronavirus transmission.

**Table 3:** shows the incidence of confirmed Covid-19 infections using the nasal swab RT-PCR method.

			95% CI
<i>Sensitivity</i>		3.30%	1.58% 5.02%
<i>Specificity</i>		98.51%	97.35% 99.68%
<i>Positive predictive value</i>		70.00%	65.59% 74.41%
<i>Negative predictive value</i>		49.26%	44.44% 54.07%
<i>Prevalence</i>	Pr	51.21%	46.39% 56.02%

This is due to the nasopharynx being the focal point for accumulation of coronavirus and the nexus for lacrimal secretions. The study encompassed 414 individuals with respiratory symptoms, revealing that 10 individuals, representing 2.42%, tested positive for Covid-19 in the tear area using ATK. This group comprised of 7 positive cases when tested via nasal swabs RT-PCR and 3 negative cases (false positive), as outlined in Table 2.

Keratoconjunctivitis cases have also been reported in China. Conjunctivitis constitutes to 0.6% of patients diagnosed with Covid-19. RT-PCR testing of tears revealed SARS-CoV-2 RNA fragments<sup>6</sup>, aligning with symptoms observed in this study. The 7 cases of conjunctivitis accounted for 1.69% of all the respiratory symptoms.

Upon preliminary research data, the population baseline data were statistically calculated to determine the correlation.

The chi-square test indicated no statistically significant correlation between Covid-19 from the tear area with ATK and the nasal swab RT-PCR test. The infected group was tested with intraocular ATK to determine if the infection was present in this group, where 7 cases of Covid-19 were identified, representing 3.30% (P value = 0.29). The sensitivity of the intraocular ATK as a diagnostic test was determined to be 3.30% (95% CI: 1.58-5.02%), which is low sensitivity, as delineated in Table 3.

Consequently, intraocular ATK testing could not serve as a diagnostic tool. However, the research highlights a 2.42% prevalence of coronavirus in the tear area among patients

with suspected symptoms of Covid-19. This underscores the importance of surveillance for medical personnel, particularly ophthalmologists who are exposed to patients eyes in their clinical duties.

Given that conjunctivitis is a prevalent symptom in patients infected with the coronavirus, statistical calculations demonstrated a 2.36% association with nasal swab RT-PCR results. This underscores the significance of timely treatment for patients exhibiting conjunctivitis, and it emphasizes the need for ophthalmologists to exercise caution and protective measures during eye examinations for such patients, as indicated in Table 4.

**Table 4:** shows the correlation between nose swab PCR and ocular symptoms.

Nasal swab PCR	Ocular symptoms Negative	Conjunctivitis Positive	Total (N)
negative	200	2	202
positive	207	5	212
total	407	7	414
<b>Pearson chi2 (+)</b>	= 1.1652	Pr = 0.280	

### Discussion

It is widely acknowledged that coronavirus disease (Covid-19) remains a burgeoning field of study with many aspects yet to be thoroughly explored, such as species of infection, distribution, and treatment. This research aims to emphasize the significance of understanding the transmission of the infection from patients to medical personnel, particularly highlighting the vulnerability of ophthalmologists, who must engage in face-to-face examinations involving constant eye contact. The study identified a 2.42% incidence of infection in the tear area among patients at risk or exhibiting respiratory symptoms associated with Covid-19 diagnosis. This finding aligns with findings of Zhou et al., who reported the incidence of viral RNA in the lacrimal duct and conjunctival sac at 3.5-5.2%.<sup>8</sup> Discrepancies exist, however, as the meta-analysis by Ulhaq et al. indicated a lower incidence of SAR-CoV-2 from biopsy and eye secretions, at 0.6%.<sup>9</sup>

Due to limitations in PCR diagnostics in Thailand, it is not possible to carry out a lacrimal test for PCR. Consequently, the researcher opted for the ATK test, signifying its sensitivity in initial screening.

In addition, tear diagnosis is a novel method in the world today, and while similar research results are intriguing, their reliability remains a subject of question. Despite the low incidence of infection in lacrimal secretions<sup>10</sup>, the potential for this to serve as another source of infection remains unknown. The researcher underscores the necessity for additional multi-center studies to obtain a more substantial sample size, recognizing the importance of the present findings as a foundation for future research endeavors.

## Conclusion

This stems from the nasal cavity being the initial site of Covid-19 accumulation, where secretions, including mucus and sputum, converge, along with the proximity of the lacrimal tract junction near the nasal turbinate. Symptoms indicative of coronavirus susceptibility were identified in the tear area. However, it is crucial to note that the tear test cannot serve as a substitute for diagnosing Covid-19 in the nasal cavity or saliva. Despite the limitation, medical personnel are advised to exercise caution when contacting the patients' tear area as an additional protective measure. This is underscored by the prevalence of Covid-19 around the tear area, reaching 2.42% among patients with suspected symptoms of Covid-19. Furthermore, the study revealed the presence of conjunctivitis symptoms in high-risk patients exhibiting symptoms comparable to coronavirus, serving as a crucial indicator for ophthalmologists to look out when examining patients with such symptoms.

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