IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 10 Ser.11 (October. 2020), PP 50-53
www.iosrjournals.org

The eye, is it a target of the novel coronavirus 2019 (nCOV-19)?

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Abstract: *The Covid-19 currently responsible for the Severe Acute Respiratory Syndrome-Cov-2 (SARS-CoV-2) pandemic, affects other organs apart from the respiratory system including digestive, liver and nervous systems. Nevertheless, although coronavirus are known to cause various eye diseases in animals; its ocular implications in humans have been little studied. Our reviews, is focus on the main manifestations of coronavirus-related eye disease in animals before reviewing the evidence in the literature concerning coronavirus-related eye disease in humans and there practical implications in ophthalmology.*

Key words: *Corona virus, COVID-19, severe acute respiratory syndrome coronavirus-2, eye infection*

Date of Submission: 15-10-2020 Date of Acceptance: 31-10-2020

I. Introduction:

Coronaviruses (CoVs) are known to cause various eye diseases in animals. However, their ocular implications in humans have been little studied. Currently with the Covid-19 pandemic, the study of these non-respiratory manifestations is of great importance. It may lead to symptoms indicative of infection or other modes of transmission, which have a major impact on our daily practices in medicine and ophthalmology.

In this reviews, we will focused on the main manifestations of coronavirus-related eye disease in animals before reviewing the evidence in the literature and the most up-to-date information concerning coronavirus-related eye disease in humans.

II. Coronaviruses :

Coronaviruses belong to the subfamily of Coronaviridae, they are a viruses surrounded by a crown-shaped protein capsule hence their name "corona" (Fig.1) [1]. They are characterized by a very long single RNA (more than 29,800 nucleotides) (Fig.2) [1, 2], which exposes to intrinsic mutations and facilitates the interspecies transmission phenomenon or "crossing the species barrier" as well as rapid adaptation to the new host [3, 4].

There are four genera of CoVs: AlphaCoV, BetaCoV, GammaCov and DeltaCov. AlphaCov and BetaCov mainly infect mammals, while GammaCov and DeltaCov mainly infect birds [1]. Ubiquitously, humans are infected by alpha-CoV (HCoV-229E; HCoVNL63) and Beta-CoV (HCoV-OC43; HKU1). In good standing they are responsible for a moderate respiratory infections in immunocompetent individuals [1, 5].

Zoonotic CoVs can evolve into strains capable of infecting humans resulting in fatal SARS. It's the case of the current novel betaCoV named nCoV-19 responsible for the current SARS-CoV-2 pandemic, probably originated in nasophus bats and was then transmitted to humans via pangolin [1, 5, 6].

The pathogenic mechanism of ocular disease is not yet fully understood. However SARS-CoV-2 shares the same host receptor with SARS-CoV of the human angiotensin-converting enzyme 2 (ACE2) receptor, suggesting a similar transmission route. The ACE2 has been also identified on ocular surface, cornea, humor aqueous, retina and epithelium choroid. Hence, more research exploring the hypothesis of SARS-CoV-2 ocular infection through ACE2 has to be conducted [7, 8, 9].

In animals, CoVs cause systemic damage and ocular disease. Understanding the ocular manifestations of animal CoV infections may provide insights into the spectrum of ocular diseases that CoVs can cause.

III. Cov-Related Eye Damage In Animals:

CoV affect with varying intensity different organs in birds and mammals. Feline CoV (FCoV) is an Alphacoronavirus that affects both domestic and wild cats. Classified into two biotypes, feline enteric CoV (FECV) and feline infectious peritonitis virus (FIPV). For the most is a FECV, responsible for a generally mild infection associated sometimes with self-limiting diarrhoea [10]. FIPV is responsible of a multisystem

impairment with poor prognosis characterized by a fibrinous and granulomatous serositis, protein-rich serous effusion in body cavities and granulomatous lesions.

FIPV is also responsible for various ocular segments inflammation including conjunctivitis, anterior uveitis and retinitis [11, 12]. It has been suggested that the underlying pathogenic mechanism is a vasculitis triggered by the infected monocytes and macrophages [11]. Viral isolates from conjunctival swabs also contained live FCoV, suggest that ocular tissues and secretions were potentially infectious as well [12].

The Murine coronavirus (M-CoV) is a coronavirus that causes an epidemic murine illness with high mortality, especially among colonies of laboratory mice. Some strains have been extensively utilized to create models of human disease including multiple sclerosis, pneumonitis and viral hepatitis [13, 14]. On the ophthalmological side, the intravitreal inoculation of M-CoV induce a retinal degeneration, known as the experimental CoV retinopathy (ECOR) and it used to examine genetic and host immune responses that may contribute to retinal disease [15]. In relate of the hypothesis about the viral-induced inflammation behind multiple sclerosis, the M-CoV-A59 has been used to induce and studied
the viral-induced optic neuritis models [16].

IV. Cov-Related Eye Damage In Humans:

After the epidemic of SARS-CoV-1 recognised in Guangdong Province in China and in Hong Kong in March 2003 [17], several studies was conducted to understand the different manifestations and transmission modes of CoV in humans.

Ophthalmologically, studies have focused on tears as one of the body fluids that can potentially harbour the CoV. Proposed theories include the conjunctiva as a site for direct inoculation from infected droplets, or by migration of the infection from the upper respiratory tract through the nasolacrymal duct or even by diffusion of a blood-borne infection from the lacrimal gland [9].

In 2003, in Singapore, Loon SC and coll., seek to isolate the SARS-Cov in tears by a reverse transcription-polymerase chain reaction (RT-PCR) analysis. From eight patients eventually proved to be probable SARS (8/36), only three patients (37.5%) yielded positive RT-PCR results in tears, while none of the SARS suspect patients had a positive RT-PCR result [18]. In same period, the prospective interventional case series study conducted in Hong Kong by Chan and coll. [19], about 17 confirmed SARS CoV-1, among which, five (29.4%) were positive for SARS-CoV by RT-PCR with the samples from nasopharynx or stool. In all tear and conjunctival scraping samples, no SARS-CoV virus could be detected by RT-PCR or isolated by viral culture. Authors attributed these negative results to one of three reasons. Firstly, RT-PCR testing or viral culture is known to be very specific but lacks sensitivity. Secondly, it is possible that the virus and its genetic material were only present for a brief period of the disease, and the samples were not collected at the right time. Thirdly, the virus might not be present in tears at all.

In 2005, a French retrospective study analyzing nasal swabs from 18 children with Covs (HCoV-NL63) positive respiratory diseases between 2000 and 2003 reported that 17% of these children (3 cases/18) had developed conjunctivitis [20].

Currently, in conjunction with the SARS-CoV-2 pandemic, especially with the emergence of anecdotal reports about conjunctivitis like a first presentation of disease, the crucial issue about manifestations and transmission modes of CoV in humans has again come to the fore [21, 22].

In china, at the epicenter of the pandemic, 9 cases (0.8%) of conjunctivitis are reported in the cohort involving 1099 Covid-19 patients confirmed in 30 hospitals in China [23]. In the Xia and coll. prospective interventional case series study about 30 patients confirmed novel coronavirus pneumonia (NCP) [24], the RT-PCR was positive in both tear and conjunctival secretions from the same only patient with conjunctivitis. Autors speculate that SARS-CoV-2 may be detected in the tears and conjunctival secretions swab in NCP patients with conjunctivitis.

In the recent case series conducted by Ping and coll. [25]. authors reported ocular symptoms in 12 (31.6%) of 38 hospitalized patients for COVID-19 in Hubei. Among 38 patients, only 2 (5.2%) patients had positive results on RT-PCT by a conjunctival swab as well as by nasopharyngeal swabs. Among the 12 patients with ocular symptoms, there were 4 cases judged as moderate, 2 cases judged as severe, and 6 cases judged as critical. The authors suggested that ocular symptoms appear almost in patients with severe pneumonia [25].

On another side, in the recent series of Xian and coll. [26], only two patients (2.78%) with conjunctivitis were identified from 72 patients a confirmed COVID-19. From those two patients, Covid-19 RNA fragments were found in ocular discharges by RT-PCR in only one patient [26]. And in the study conducted by Jun and coll. [27], using both culture and RT-PCR in 64 samples of tears taken from 17 patients confirmed COVID-19. Neither viral culture nor RT-PCR detected the virus in tears [27]. Authors suspect that the incidence of SARS-CoV-2 infection through the ocular surface is extremely low.

V. Conclusion:

In all large-scale research has not yet been done, and new data is emerging daily, but taken together, these data proof a potential eye tropism of SARS-CoV-2, especially if patient has a confirmed novel coronavirus pneumonia with conjunctivitis. The risk of viral transmission through ocular secretions is low, while the nosocomial infection of SARS-CoV-2 through the eyes after occupational exposure is a potential route.

Eye care providers and their assistants may be more susceptible to infection due to the nature and proximity of the ophthalmic examination and eye care. So they are encouraged to use slit lamp breath shields and should counsel patients to speak as little as possible when sitting at the slit lamp to reduce the risk of virus transmission. Disinfection and sterilization practices should be employed for shared clinic equipment such as tonometers, trial frames, and contact lenses for laser procedures [28, 29].

Finally, all eye care providers are invited to fully comply with the practical ophthalmological society's recommendations to reduce the risk of infection or transmission of SARS-COV-2 infection in a working environment [30, 31].

Figures:

Figure.1: Coronavirus nCOV-19 in electron microscopy the crown appearance is due to the presence of high spicules made of the surface protein [1].

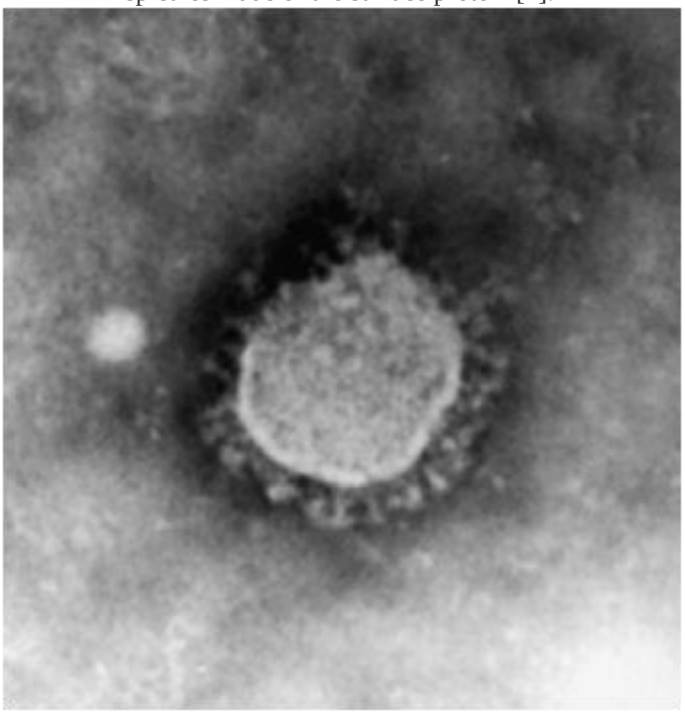
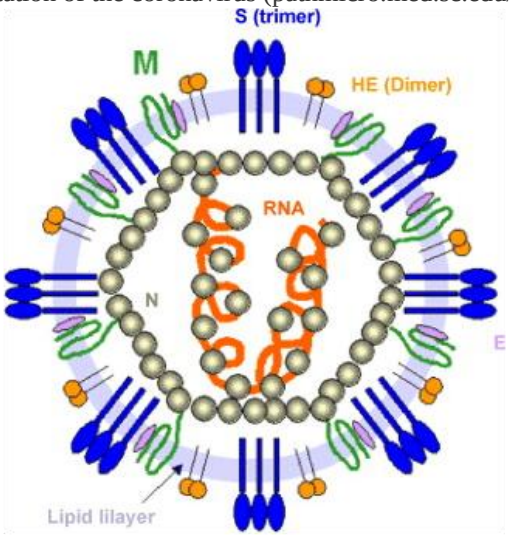


Figure.2: Schematic representation of the coronavirus (pathmicro.med.sc.edu/virol/coronaviruses.htm.) [4].



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Moulay Omar Moustaine, et. al. " The eye, is it a target of the novel coronavirus 2019 (nCOV-19)?." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(10), 2020, pp. 50-53.