

## Route of COVID-19 Ocular Transmission and its Impact

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There is heightened anxiety and inquisitiveness regarding the global public health threat caused by coronavirus disease-2019 (COVID-19) which became a pandemic in 2019 - 2020 [1], with China being the epicenter of transmission. As of April, 01-2020, the World Health Organization (WHO) numbers released for the COVID-19 outbreak situation was approximately 827,419 confirmed cases and nearly 40,777 deaths [2].

The Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is the etiology for COVID-19. According to the U.S. National Library of Medicine, the corona viruses are heterogenous group of viruses that primarily affects the respiratory and intestinal tract particularly of animals. The domestic animals serve as intermediate hosts for the CoV-2. This virus with its unique ability of rapid recombination and mutation is able to target the human population and induce mass mortality through human-human transmission and by causing fatal pneumonia. COVID-19, which is primarily a respiratory disease affecting the lungs, has now been identified with extra-pulmonary manifestations in human populace.

### Route of transmission

The novel corona virus-19 (2019-nCoV) was originally thought to be transmitted from animal reservoir specifically bats, as per the CDC report [3,4]. The virus spread through small respiratory or naso-pharyngeal droplets produced by an infected person through their coughs or sneezes [5]. These viruses replicate primarily in epithelial cells of the lower respiratory tract and to a lesser extent in the upper respiratory tract. So, according to researchers, the common transmission routes of this novel coronavirus are either via direct transmission by cough, sneeze, and droplet inhalation or by contact transmission via mucous membranes of the oral and nasal cavity [6]. As per the recent clinical surveillance, coronavirus infection presents another mode of transmission through direct contact of eyes with infected droplets [7]. The conjunctival samples from confirmed and suspected cases of 2019-nCoV suggests that the transmission is not restricted to the respiratory tract, but eye exposure could be an effective way for the entry of virus into the body [8,9]. Earlier, it was seen that in patients presumed or diagnosed with SARS, had positive results from their tear samples and RNA of SARS-CoV was identified in tears [10], although a direct ocular transmission has not been demonstrated in these group of patients. Previously, human coronavirus NL63 (HCoV-NL63) was first identified in infants with bronchiolitis [11,12].

In a related research letter published recently, it is shown that bronchoalveolar lavage, biopsy of lung, sputum and blood samples contained live virus in 1,070 specimens from 205 infected patients [13]. Studies have shown that corona virus can be transmitted directly or indirectly through body fluids like saliva. Moreover, not only the public are exposed to this deadly virus but cases have been reported amongst the medical/health care workers and dental care settings. The dental patients and professionals carry the high risk of infection based on the professional services, including direct communication with patients and frequent exposure to saliva, blood, nasal secretions and other body fluids from the infected or asymptomatic patients. They can be exposed to pathogenic viruses and bacteria that infect the oral cavity and respiratory tract like 2019-nCoV. Another article underscore that the health-care workers fall into high-risk category of acquiring this novel disease through unprotected eye contact [14,15]. It is inferred that, in spite of the protective suit and N95 respirator, the likelihood of transmission through unshielded ocular surface is high [16]. In the clinic setup the ophthalmologists, are more susceptible to these infections as they involve in close physical examination during patient consultation and screening procedures. A fecal-oral trans-

mission route has also been indicated by latest studies upon analyzing the stool samples from patients [17-20]. However, these plausible transmission routes need to be further studied and validated.

### Clinical features

Coronavirus has been found to be highly transmissible and has a significant mortality rate, exclusively in the aged, immune-compromised and those individuals with coexisting disorders (for e.g. diabetics, cardiovascular disease and other respiratory illness like Asthma [21]. The exact incubation period for this infection is unknown at this moment, but the WHO reported between 2 and 10 days, while it expectedly takes 4-7 days before the actual onset of symptoms [22]. The primary symptoms that patients presents with include typical respiratory sickness including, cough, sore-throat, shortness of breath, and high fever. Other symptoms reported may include headache, myalgia/fatigue and rare diarrhea [9]. As per the available literature, apart from the characteristic respiratory signs of illness, few patients presented with ocular manifestations viz. conjunctival hyperemia, chemosis and increased tear/lacrimal secretions [12,23]. This indicates the probable high risk of ocular transmission of this novel virus. It should be taken into account that, given the pathogenicity of this virus in animal species, there is a potential for ocular complications such as retinitis or neuritis. However, no cases have been reported so far.

### Pathophysiology

Hitherto, not many studies have elucidated the molecular basis of the pathogenicity of 2019-nCoV. However, since the novel virus is phylogenetically related to SARS- associated coronaviruses, molecular studies postulates that SARS-CoV-2 could bind to human Angiotensin-Converting Enzyme II (ACE2), using it as a receptor to enter/invade the respiratory and lung epithelial cells [14,24,25]. These receptors are found in the lower respiratory tract of humans. It is interesting to note that, the alpha 2-3-linked sialic acid receptors, implicated in human influenza infections are abundant in conjunctival, corneal epithelium while the naso-lacrimal epithelia has alpha 2-3-linked and 2-6 linked sialic acid receptors [25]. Furthermore, the expression of ACE2 receptors seems to be high in oral sites like the tongue followed by buccal and gingival tissues [26]. Besides, epithelial cells of the salivary gland ducts were identified as targets of SARS- CoV infection as they showed positivity for ACE2 receptors [6]; comparable to nCOVID-19 virus. This advocate that the novel coronavirus could potentially exploit the ocular, nasal and oral mucous- membrane surface as their route of transmission and replication. The spike glycoprotein is determined as a significant determinant of virus entry into host cells [27]. This spike glycoprotein attaches the virion to the host cell membrane and enable the coronaviruses to first replicate in epithelial cells of the respiratory and gastric cells leading to cytopathic changes, followed by the replication and release of virus [28]. I believe that, considering the diverse mode of transmission and cell-entry through receptor binding, successive dissemination of COVID- viral particles to distant sites is plausible through systemic circulation and/or by mobile immune cells. It could possibly induce more complications by induction or exaggeration of existing local and remote diseases. However, further studies warranted.

Few previous studies have demonstrated elevated levels of proinflammatory cytokines in serum associated with pulmonary inflammation and extensive lung damage in SARS and MERS patients [29,30]. Similarly, new studies have indicated higher leukocyte numbers, high IL1 $\beta$ , IFN $\gamma$ , IP10, and MCP1, GCSF, levels probably leading to activated T-helper-1 (Th1) cell responses, in corona-infected patients. The findings from this particular study suggest 'cytokine storm' linked with disease severity [9]. These interpretations are expected to aid in assessing the disease severity and therapeutic applications [31].

Based on the contemporaneous clinical outcomes, no treatment options for COVID-19 has been clinically proven to be effective so far. Amidst this pandemic crisis, studies are underway in many laboratories to probe the exact pathophysiology of this novel viral disease and arrive at appropriate therapeutic measures. Hence, in this scenario, containment of the virus through proposed preventive measures are in great demand in all the public and professional sectors. The probability of eye infection and the ocular route as a potential source of

infection should be significantly considered. I urge that all the healthcare professionals and other frontline workers use overall personal protective equipment and eye protection without any compromise, while in close contact with patients for personal and global safety.

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