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A review on ocular manifestations in Covid-19 and an Ayurvedic overview

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ABSTRACT

COVID-19 has become a global pandemic from December 2019 resulting in 3.8 million deaths worldwide. The extra pulmonary manifestations of the virus are unpredictable and varied. The ocular manifestations like conjunctivitis, keratitis, uveitis etc. were observed in the patients during the course of the disease, which is being reviewed and summarized in this article. Here an effort is made to collect all the possible data regarding the ocular presentation of COVID-19 and an overview of the disease through Ayurveda.

Key words: COVID-19, Global Pandemic, Ayurveda, Ocular Manifestations

INTRODUCTION

The first case of COVID-19, caused by novel corona virus or Severe Acute Respiratory Syndrome Corona Virus-2 (SARS CoV-2) was identified in Wuhan, China, in December 2019. The disease has since spread worldwide, leading to an ongoing pandemic. Symptoms of COVID-19 are variable, but often include fever, cough, headache, fatigue, breathing difficulties and loss of smell and taste.^[1] The respiratory tract probably is not the only route for this viral infection, some authors hypothesized that COVID-19 droplets, or infected hands, can also contaminate the conjunctiva, that could represent the initial site for the spread of the

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infection.^[2] Several clinical symptoms have also been frequently reported among COVID-19 patients apart from symptoms of respiratory tract infection, which include gastrointestinal symptoms such as diarrhea, abdominal pain, low appetite and vomit,^[3] others have shown renal and ocular symptoms also.^[4]

Most clinical research works on SARS-CoV-2 have concern about respiratory manifestations: however, a growing body of evidence has raised concern about the ocular complications caused by SARS-Cov-2. In 2003, SARS was tested positive in the tear samples of patients, in Singapore^[5] and also few cases were found with the same evidence in China, which gives initial evidence of ocular manifestations. The reported ocular manifestations of the infection vary greatly and include dry eye, foreign body sensation, itching, blurring of vision, conjunctivitis, chemosis and photophobia. Some studies have reported conjunctivitis as an early sign for COVID-19 diagnosis.[6]

The better knowledge about ocular manifestation of the virus is required for prevention of transmission of the disease and for a better diagnosis. This is a review article showing probable ocular presentations observed in people, along with the other symptoms of COVID-19.

MATERIALS AND METHODS

Data collected from different research works. Case studies and articles, throughout the world, done on ocular manifestation in COVID-19.

Evidence of Cov in Ocular Manifestations

The first evidence of ocular manifestation of Covid-19 was observed in China. In 2004, towards the end of the CoV crisis. a new human coronavirus was identified. This was the HCoV-NL63. The virus was first isolated from a 7-month-old child before being identified in seven additional individuals. During the infection, the child had symptoms and physical examination findings of bronchiolitis and conjunctivitis.^[7]

Mode of Transmission

The exact pathophysiology of the ocular manifestation is not very well understood, but the proposed theories include the conjunctiva being the direct inoculation site of SARS-CoV from infected droplets, the migration of upper respiratory tract infection through the nasolacrimal duct or even haematogenous infection of the lacrimal gland.^[8] Also haematogenous and lymphatic routes were also explained in the posterior segment manifestations.

Ocular Symptoms

The different ocular symptoms are manifested in conjunctiva, cornea, sclera, anterior chamber, retina and optic nerve which is being discussed here.

Conjunctiva

Conjunctivitis is one of the main ocular manifestations of Covid-19. Even though the rate of ocular symptoms in Covid -19 is less, among those symptoms, conjunctivitis is most commonly reported. These symptoms include redness of eyes, ocular irritation, foreign body sensation, mucoid discharge, eye lid swelling and congestion.

In a study conducted in China in 2019, out of 38 patients with clinically confirmed COVID-19, 12 of them were found to have symptoms of conjunctivitis, including hyperaemia, epiphora and conjunctival secretions. Among them, 2 patients showed positive findings in their conjunctival specimens also.^[9]

A cross sectional study conducted on 301 patients, at a hospital in Spain, 35 of them was diagnosed with acute conjunctivitis. Most of the patients presented with mucopurulent discharge, tearing and foreign body sensation and with no complaints of blurry vision.^[10]

A 2year 10months old child, showed positive for covid-19 in nasopharyngeal swab on Feb 17 2020, presented with conjunctivitis and eyelid dermatitis as the symptom. The child was asymptomatic for the initial 7days after being tested as positive and later ophthalmic symptoms were manifested. Once the treatment was started as per the protocol for COVID-19, the symptoms disappeared in 5 days.^[11]

A case of haemorrhagic conjunctivitis with chemosis was observed, with the formation of pseudo membrane in a 46-year-old male patient. The patient developed mild respiratory symptoms initially, later presented with the ocular symptoms. He was treated with topical antibiotics and the symptoms resolved within 4weeks.^[12] Few cases were also reported with conjunctivitis as the only presenting complaint. They developed no fever, general malaise or any respiratory symptoms throughout the course of their illness.^[13]

Cornea

There are no much cases reported on corneal manifestations of covid-19. A case was reported in Canada, with conjunctivitis along with other upper respiratory tract symptoms like rhinorrhoea, nasal congestion and cough during the initial days. Later, changes were observed in the cornea with development of numerous discrete areas of subepithelial infiltrates with overlying epithelial defects. The patient was given oral valacyclovir 500mg TID and Moxifloxacin eye drops one drop QID. This patient did not present with conjunctivitis as previously cases, reported for COVID-19 but as keratoconjunctivitis.^[14]

Sclera

The scleral involvement of COVID infection is not very common. Following are the two different cases of episcleritis which was reported as a presenting and initial symptom of COVID-19 infection.

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A 29year old man, with redness and foreign body sensation in left eve and on further examination revealed, a sectoral nasal conjunctival and episcleral injection with clear cornea. Three days later person developed systemic symptoms like headache shortness of breath, cough and fever and the naso pharyngeal swab test turned out to be positive for COVID-19. The patient was given oral Azithromycin OD, TID, 500mg paracetamol 1g topical flurometholone 0.1% and vitamin supplements. After 5 days, all the symptoms were relieved and the patient was discharged.¹⁵This shows that episcleritis was one of the initial presenting symptoms in COVID-19.

Another case reported, had met the criteria of nodular episcleritis. A 31-year-old lady, had presented with systemic symptoms like myalgia and cough without fever. The nasopharyngeal swab was detected to be positive for COVID-19. After seven days of onset, patient presented with ocular symptoms like redness, epiphora, photophobia without any visual impairment. Patient presented a slightly elevated epibulbar area, which was then diagnosed as nodular episcleritis. Treated with artificial tears and flurometholone 5 times a day, for 3 days and tapered during the following weeks, the ocular symptoms resolved once the patient RT-PCR test turned out to be negative for COVID-19.^[16]

Uvea and Lens

Beyond the ocular surface, acute anterior uveitis was also reported in association with COVID-19. A case was reported in Italy, with symptoms of bilateral hyperaemia, unilateral photophobia and blurred vision in right eye, associated with systemic symptoms of Covid-19. On further evaluation, it was diagnosed as acute anterior non-granulomatous uveitis characterized by diffuse pigmentary and whitish precipitates over anterior capsule of crystalline lens and initial anterior lens opacity which explains the blurred vision. The initial hyperaemia was treated with antibiotic drops, later treated with Tropicamide 10mg/ml solution 3 times daily to prevent the adhesions. A combination of Chloramphenicol 0.5% and betamethasone 0.2% eye drops 3 times daily, 0.6% PVP-I eye drops 2 times daily and antiseptic lubricants

were given and also 0.02% sodium hypochlorite was nebulized on periocular skin 2 times a day. Complete regression of symptoms occurred after one month of topical therapy.^[17]

Retina

OCT evaluation of the Covid-19 patients, showed hyper reflective lesions at the level of ganglion cell and inner plexiform layer more prominently at the pappillomacular bundle in both eyes, in 12 patients. Among those, 4 patients presented with subtle cotton wool spots and micro haemorrhages. These patients presented normal visual acuity and pupillary reflexes, with no signs of any ocular inflammations.^[18]

In a study by Invernizzi.et.al, it was found that out of 54 patients, 5 of them showed retinal haemorrhages, cotton wool spots were seen in 4 patients and drusen in 6 patients. On fundoscopic examination, dilated veins were observed in 15 patients and tortuous vessels in 7 patients. In this study, it was found that both retinal arteries and veins were larger compared to unexposed subjects and the diameter of veins was larger in more severe cases.^[19] In a similar study which included MRI findings of 129 patients from 16 hospitals from March 4th to May 1st 2020, 9 patients showed abnormal MRI findings with one or more nodules in the posterior pole of the globe. Nodules were bilateral and mostly located in the macular region in all cases in association with extra macular nodules.^[20]

Optic Nerve

Most of the neuro ophthalmic manifestations were observed in association with demyelinating disease. Corona virus infection can cause infection of central nervous system characterized by inflammatory demyelination studied in animal models. The lesions tend to mimic multiple sclerosis and of other neurological disease in humans in many aspects.^[21]

The corona virus is a neurotropic and neuro invasive virus which can affect the peripheral as well as central nervous system, which could possibly a reason for the neuro-ophthalmic manifestation of COVID-19. The virus can reach the central nervous system through

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various pathways which include, haematogenous or lymphatic route.^[22]

A 44-year-old male patient, reported with pain around the right eye that had progressed to the left eye with bilateral loss of vision, diagnosed as optic neuritis after two weeks of covid infection. Patient was given methylprednisolone 1g every 24 hours for 5days.Patient was discharged with complete restoration of vision in the left eye but not in right eye. Here the possibilities of Multiple sclerosis or other auto immune diseases were ruled out.[23]

Part involved	Signs and symptoms
Conjunctiva	Redness
	Foreign body sensation
	Itching
	Epiphora
Cornea	Epithelial erosions
Sclera	Redness
	Watering
	Photophobia
	Elevated epibulbar area
Uvea	Blurrness of vision
	Hyperemia
	Photophobia
Lens	Pigmentary and whitish precipitates over anterior capsule
	Lens opacities
	Blurred vision
	Micro haemorrhage
Retina	Cotton wool spots
	Drusen
	Tortuous vessels
	Enlarged venous capillaries
	Macular nodules
Optic nerve	Bilateral loss of vision

Examination

A detailed history taking is important for a proper diagnosis. Also, a complete and thorough examination of the eye is very much essential. Assessing the visual acuity to rule out any visual disturbances and a thorough slit lamp examination of the anterior segment to confirm conjunctivitis, scleritis or any corneal pathologies. The retinal or optic nerve changes are to be evaluated at the initial stage, through a proper fundoscopy and OCT if necessary. Visual field defects are to be ruled out clinically through confrontation tests.

Detection of presence of Covid-19 virus in the tear samples is done by sweeping the lower eyelid fornices with a swab to collect the tears to confirm the diagnosis. CT or MRI can be done to evaluate optic neuritis, field defects or other neurological symptoms. Also details regarding the other symptoms like fever, headache, cough, breathlessness is to be assessed and evaluated for a better diagnosis.

DISCUSSION

Although the respiratory system is involved principally, COVID-19 infection can also produce complications in other anatomical sites. Though ocular manifestations are present, it is not often seen as the initial symptom of covid-19. Conjunctivitis has been considered as the most commonly seen ocular symptom and is also seen as initial presenting symptom in Covid-19. The presence of virus in tear samples serves as a source of transmission of infection to others. The long-standing conjunctivitis has been shown to affect cornea also which has further led to keratitis. Since the symptoms of conjunctivitis are similar to those caused due to other viruses, diagnosis of COVID-19 infection may be missed. Episcleritis was not widely found as a presenting symptom in Covid-19. Episcleritis is seen as one of the ocular symptoms in some of the viral infections pertaining to different viral groups like herpes zoster, Ebola and chikungunya. Given the relationship between immune disorders that induce vascular inflammation in episcleritis and the high-rate incidence of thrombotic complications reported in intensive care unit patients with COVID-19, the pathophysiological theory that could explain the relationship between COVID-19 and episcleritis may include immuno-vascular factors and/or coagulation disorders.^[15] Uveitis can be found in association with other viral infections like HIV, cytomegalovirus, herpes herpes simplex and dengue. zoster, Non-

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granulomatous uveitis may be an acute or chronic exudative inflammation of uveal tissue, usually occurring due to either to a physical and toxic insult to the tissue or as a result of different hypersensitivity reactions.^[24] The changes in lens and its capsule were also observed in association with the uveitis. In retinal manifestation, authors have summarized that COVID-19 can induce changes at the level of retina, mostly affecting the retinal vasculature, especially veins, it can also either trigger or exacerbate the already present inflammatory/demyelinating disease in a person.^[12]

In Ayurveda, the concept of epidemic can be understood under the topic Janapadodhwamsa. Vitiation of factors like Vayu (air), Jala (water), Desha (land) and Kala (season) which are common to the entire population, can affect a large number of people together and cause similar kind of symptoms in them.^[25] Also, the concept of communicable diseases is understood in Avurveda as Samkramika Rogas. The different modes of transmission of diseases are "Gatra Samsparshat (physical contact), Nishwasat (inspiration of expired air), Sahabhojanat (eating together), Sahashayyasanat (sleeping together), Vastra Malyanulepanat (sharing clothes, cosmetics etc)". These are explained for the diseases like Kushta (skin diseases), Jwara (fever), Sosha (tuberculosis) and *Netrabhishyanda*(conjunctivitis).^[26] Netra Abhishyanda is one of the 76 diseases of eye explained in avurvedic classics and is said to be the root cause of all eye diseases.^[27] All inflammatory conditions of eye ball take their origin in Abhishvanda which involves Sroto Syandana and Sravana^[28] in its pathogenesis which can be understood as increased permeability of capillaries leading to excessive discharge. The inflammation can be caused due to Agantuja Nidana (external origin due to bacteria, viruses etc.) which involves vitiation of predominantly Pitta and Rakta Doshas involving the different Mandalas (layers of eye). When Abhishyanda is left untreated it can lead to different other diseases like Adhimanta (uveitis, glaucoma), Akshipaka (endophthalmitis, panophthalmitis) etc.

The features of *Abhishyanda* include *Toda* (pain), *Daha* (burning sensation), *Srava* (discharge), *Asru* (watering

from eyes), Sangharsha (foreign body sensation), Kandu (itching) etc.^[29] according to the predominance respective *Doshas*. The management of of Abhishyanda at an earlier stage is important so as to prevent the disease to progress and involve the deeper ocular tissues. It has been mentioned that treatment modality of Abhishyanda can be adopted in all the 76 diseases of eye. The management mainly includes Shodhana (purificatory procedures) which include Virechana (purgation), Raktamokshana (bloodletting), Nasya (nasal drops) and Kriyakalpas (topical ocular therapeutics). When the infection is identified at the level of anterior segment where the inflammatory signs are present, it can be well controlled and managed with topical procedures like Aschyotana (eye drops), Seka (eye irrigation), Bidalaka (application of medicated paste over the closed eyes excluding over the closed eyes).^[30] Similar treatment is followed for other inflammatory conditions like episcleritis (Sirotpata), keratitis (Shukra), uveitis and optic neuritis also. Whereas procedures like Tarpana and Putapaka (retention of medicated liquid in conjunctival sac) can be adopted, once the inflammatory signs are relieved and are more preferred in posterior segment diseases like Optic neuritis. So the drugs which are Pitta Rakta Hara in nature like Triphala (Embilica officinalis, Terminalia bellirica, Terminalia chebula),^[31] *qlabra*),^[32,34] Yashtimadhu (Glycyrrhiza Nimba (Azadiracta indica),^[34] Shiqru (Moringa oleifera),^[35] Tulasi (Ocimum Sanctum),^[36] Haridra(Curcuma longa),^[37] Daruharidra (Berberis aristata),^[38] Lodhra (Symplocos racemosa)^[39]etc., which also possess excellent anti- inflammatory, anti-viral and antibacterial properties have to be included while carrying out these procedures A case of Viral keratitis (disciform keratitis), which was successfully managed with topical ayurvedic ocular therapeutics by using the drugs like Triphala, Yashtimadhu, Lodhra, Kumari (Aloe Vera) and many other herbs having antiviral properties has been reported^[40] which confirms that these drugs possess antiviral properties which can be efficiently used in managing ocular manifestations of COVID-19. If the ocular manifestations are associated with systemic symptoms like fever, respiratory symptoms etc. they

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can be well managed with internal antiviral *Ayurvedic* medications.

CONCLUSION

Ocular manifestations in humans are typically rare, and conjunctivitis seems to be the most common among them. Although there are increasing numbers of associated ocular findings in patients positive for the COVID-19. These should not be overlooked as it can be an active source for transmission of the virus. As it is said "prevention is better than cure", a regular practice of Dinacharya (daily regimen) like Gandusha or Kavala (gargling/oil pulling), Pratimarsha Nasya (nasal instillation of medicine), Netra Prakshalana (eye wash),^[41] and Ritu Charya (seasonal regimen) like ritu Shodhana (seasonal purification of the body) etc. and following proper Ahara (dietetics) according to different Ritus (season)^[42] mentioned in Ayurvedic classics can prevent the infections like COVID-19 to a greater extent. Also, it is very essential for the health care providers to protect themselves from transmission by wearing a face shield, goggles, wearing gloves and masks irrespective of the patients.

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