

Review Article

CLINICAL CHANGES IN EYE DUE TO COVID - 19 PANDEMIC- A REVIEW

Abstract: -COVID-19 is a coronavirus disease caused by the SARS-CoV-2 subtype. It was first reported in 2019. Since it has been around the world, it has affected over 5,000,000 people and has caused over 300,000 deaths. Coronaviruses have attracted global attention due to the emergence of severe respiratory syndrome infections such as SARS and MERS in 2003. They were triggered by the introduction of the coronavirus in humans. The ongoing COVID-19 pandemic is a reminder of the evolution of organisms. For SARS-CoV-2 and COVID-19, the two viruses have the same angiotensin converting enzyme 2 (ACE2). The human-to-human transfer of SARS-CoV-2 occurs through respiratory droplets and contact with the mucous membranes. Eye protection is often required to prevent the spread of SARS-CoV-2. Human-to-person transmission of SARS-coV-2 occurs through respiratory droplets and contact with the body's mucous membranes. Eyewitnesses have raised concerns that the disease could be transmitted through the ocular surface. Several patients with COVID-19 exhibited ocular abnormalities. Several studies have shown that patients with COVID-19 exhibited ocular anomalies. Further studies suggest that this infection may have a relationship with SARSCoV-2 infection. SARS-CoV-2 is a respiratory illness that has caused thousands of fatalities globally. It has been named COVID-19. SARS-CoV-2 is a respiratory illness that has caused more than 4 million cases and 280,000 deaths globally since it emerged in 2003. The SARS-CoV-2 virus has caused a global epidemic. It has infected over four million people and killed around 280,000 others since it emerged in 2001. Cases of pneumonia were reported in December 2019 in Wuhan, China. The infections were caused by the SARS virus.

Keyword: - Covid-19, Conjunctivitis, respiration, droplets.

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INTRODUCTION

COVID-19 is a coronavirus disease caused by the SARS-CoV-2 subtype. It was first reported in 2019. Since it has been around the world, it has affected over 5,000,000 people and has caused over 300,000 deaths.¹ Coronaviruses have attracted global attention due to the emergence of severe respiratory syndrome infections such as SARS and MERS in 2003. They were triggered by the introduction of the coronavirus in humans.² The ongoing COVID-19 pandemic is a reminder of the evolution of organisms. For SARS-CoV-2 and COVID-19, the two viruses have the same angiotensin converting enzyme 2 (ACE2).³ The human-to-human transfer of SARS-CoV-2 occurs through respiratory droplets and contact with the mucous membranes. Eye protection is often required to prevent the spread of SARS-CoV-2.⁴ Human-to-person transmission of SARS-CoV-2 occurs through respiratory droplets and contact with the body's mucous membranes. Eyewitnesses have raised concerns that the disease could be transmitted through the ocular surface.⁵

Several patients with COVID-19 exhibited ocular abnormalities.⁶ Several studies have shown that patients with COVID-19 exhibited ocular anomalies. Further studies suggest that this infection may have a relationship with SARS-CoV-2 infection.⁶⁻⁸ SARS-CoV-2 is a respiratory illness that has caused thousands of fatalities globally. It has been named COVID-19.⁸⁻¹⁰ SARS-CoV-2 is a respiratory illness that has caused more than 4 million cases and 280,000 deaths globally since it emerged in 2003.¹¹⁻¹⁵ The SARS-CoV-2 virus has caused a global epidemic. It has infected over four million people and killed around 280,000 others since it emerged in 2001.¹⁶⁻²⁰ Cases of pneumonia were reported in December 2019 in Wuhan, China. The infections were caused by the SARS virus. The first known physician to report similarities between the symptoms of the illness and the virus was Dr. Li Wenliang.²¹⁻²⁴ A new RNA betacoronavirus was

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found to be the main cause of the human disease. It was initially believed that the virus was introduced by bats. Human infections usually occur through coughing or sneezing.²⁵⁻²⁸

Coronaviruses can infect a wide range of mammals and birds. They can also cause respiratory failure in humans. Two human CoVs, which were known to cause respiratory failure, were eradicated after SARS-CoV2.^{29,30} Coronaviruses are mainly involved in the transmission of diseases among animals. Two human CoVs have been known to cause respiratory failure.³¹⁻³³ One case report describes the positive PCR result of a tear sample for SARS-CoV, while other tests did not find evidence of viral load in the samples.³⁴⁻³⁶ Non-structural proteins are responsible for the viral infection and the replication of pathogens. For instance, the surface spike glycoprotein enables the attachment of host cells to the virus.³⁵⁻⁴⁰ Their primary target is the lung epithelial cells. Binding to the same cellular receptor can cause severe infections in the upper respiratory tract and lower respiratory tract. Currently, the reverse transcriptase-PCR (RT-PCR) is the most widely used diagnostic test for COVID-19. However, neither a vaccine nor an antiviral treatment is available.³⁷⁻⁴⁰

There are seven known human coronaviruses that can cause mild respiratory infections in humans. The most dangerous kinds of coronaviruses are SARS-CoV-2 and SARS-CoV-3. They can also cause life-threatening illnesses.⁴¹⁻⁴³ Human coronaviruses have been known to cause ocular diseases. The first known example of this was the HCoV-NL63 subtype, which was isolated from a child with respiratory illness.⁴⁴⁻⁴⁸ In a case series, the authors did not find evidence of ocular complications in the patients with SARS-CoV infection. They also did not detect evidence of the virus' pathogenesis in these cases.⁴⁹⁻⁵¹ Since the outbreak started, a growing number of clinical reports of COVID-19 patients have been published. These reports include various symptoms, such as hyperemia, chemosis, and ocular congestion.⁵²⁻⁵⁵

Subconjunctival hemorrhage, pseudomembranes, and impaired vision were also reported in COVID-19. It is possible that SARS CoV-2 can infiltrate the ocular surface and cause conjunctivitis.⁵⁶⁻⁵⁹ Subconjunctival hemorrhage, pseudomembranes, and impaired vision were also reported. Although the incidence of COVID-19 is low, evidence suggest that SARS-CoV-2 can infect the ocular surface.⁶⁰

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A 29-year-old nurse in an emergency department presented with persistent bilateral conjunctivitis and a watery discharge on the second day of her fever. A 30-year-old male patient was also diagnosed with COVID-19.⁶¹⁻⁶⁵ The acute onset of ocular symptoms with progressive hyperemia and watery discharge was associated with the SARS-CoV-2 infection. It was confirmed that the symptoms were viral conjunctivitis. The varying characteristics and definitions of conjunctivitis in different reports may have contributed to the different findings. Due to the potentially dangerous nature of the condition, some cases of conjunctivitis were performed using telemedicine or penlight examinations.⁶⁶⁻⁷⁰ Conjunctivitis is a common eye disorder that can be caused by a variety of infectious or noninfectious causes.^{71,72}

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Conjunctivitis is often caused by non-infectious causes. In most cases, it is diagnosed as differentially if the affected patient has no ocular virus testing.⁷³ The chemosis and conjunctival congestion exhibited by COVID19 individuals are like the symptoms of conjunctivitis. They can be caused by various factors such as mechanical ventilation, electrolyte imbalance, and fluid overload.⁷⁴ Also, prolonged exposure to sunlight may affect the development of COVID-19. In addition, prolonged exposure to low levels of vitamin D may affect the development of COVID-19.⁷⁵

It has been reported that the ACE2 protein is expressed in the retina and in aqueous humor. Also, coronaviruses can cause neuritis and retinopathy in animal models.⁷⁶ The authors did not test for

SARSCoV-2 in the patients' bodies or the ocular surface. Instead, they focused on the coronavirus's potential to infect intraocular tissues.⁷⁷There is no known therapy for treating ocular SARS-CoV-2 infections. However, some treatment agents such as antibiotics, eye drops, and artificial tears have been utilized.⁷⁸Most of the mild symptoms experienced during the SARS-CoV-2 pandemic were mild, and they did not cause sight-threatening complications.⁷⁹There is no known therapy for treating ocular SARS-CoV-2 infections. However, some treatment agents such as antibiotics, eye drops, and artificial tears have been utilized.⁸⁰It has been hypothesized that the coronavirus can cause proliferative diseases in animal models. Also, it has been observed that patients with COVID-19 exhibited no visual disturbance and no intraocular inflammation.⁸¹The authors did not test for the presence of SARS-CoV-2 in the body of COVID-19 patients. It is possible that the virus can also infect the intraocular tissues of COVID-19 patients.⁸²

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Most of the ocular manifestations in COVID-19 were mild, and they recovered in a relatively short time.⁸³RTPCR-based testing for SARS-CoV2 is commonly performed in ocular specimens by amplifying the virus RNA using RT-qPCR in tears or fluids. This method can also be used for other applications. The detection of SARS-CoV2 in conjunctival or tear specimens can be done depending on the viral load and shedding profile of the samples. Viral loads in conjunctival specimens were lower than those in the other types of specimens after conjunctivitis onset. They showed that the decrease was undetectable for days 5 to 7 after onset.⁸³

It has been hypothesized that SARS-CoV-2 can appear on the ocular surface during the onset of conjunctivitis. In a study, researchers detected the presence of SARSCoV-2 RNA in the ocular swabs of a patient with COVID-19. Then, they observed a five-day clinical effect after inoculating human tissue with the first positive specimen of SARS-CoV-2 cells. This effect was

triggered by the inoculating cells. Although the effects of SARS-CoV-2 RNA and Vero E6 cells were not detected in tear samples from COVID-19 patients, the low viral loads were still found to be negative. Although it is possible that the results were obtained due to the contamination of testing items, further studies are needed to determine if SARS-CoV-2 can be transmitted through the eyes. In three cases, positive conjunctival swab samples were detected for COVID-19. Two of the patients did not exhibit ocular symptoms.⁸⁰ Ocular swab samples were positive for 2 weeks in this patient, even though the former became negative. These observations indicate that the ocular surface could harbor SARS-CoV-2 without entering the cells. Although the ocular surface is a less likely route of infection for SARS-CoV-2 than the conjunctiva, it could still be infected through ophthalmic practice. The SARS-CoV-2 S protein is a key component of the coronavirus's infection pathway, which involves binding to host cells. It can also enhance the binding of the ACE2 protein.⁸⁴

SARS-CoV-2's S protein is cleaved by the serine 2 protease, which is activated by the transmembrane protease. It exhibits a different viral shedding pattern than that of SARS-CoV. The expression of ACE2 in the body can be used to identify potential infection routes caused by SARS-CoV-2. This protein is widely expressed in various organs, including the lungs, ileum, and colon. Through single-cell RNA-sequencing, they discovered that the ACE2 protein was expressed in the eye's various cell types. This finding supports the notion that the cell type that appears on the surface of the ocular is not differentiated. The expression levels of the two genes were lower in the eyes than in the lungs, which suggests that they could lower the risk of SARS-CoV-2 transmission. The expression level of human Ace2 and TMPRSS2 in the conjunctiva was significantly higher in comparison to that in the cornea. The results of this study support the notion that the cornea has the highest expression of these proteins for SARS-CoV-2

infections.⁸³The distribution of ACE2 on the ocular surface has been suggested as a potential entry point for SARS-CoV-2 into the eye. In an ex vivo study, human conjunctival explant cultures were extensively infected with SARS-CoV-2. The presence of ace2 on the surface led to the spread of the infection.⁸³The distribution of ace2 on the ocular surface has been suggested as a possible route of SARS-CoV-2 infection. Hui and his colleagues investigated the presence of SARS-CoV-2 in human explant cultures with higher infectious viral titers than those of SARS-CoV. Ocular surface is closely associated with the respiratory tract through the nasolacrimal system. It is composed of the tear film and the keratographia. The nasolacrimal system is a route that allows viruses to spread between the eyes and the upper respiratory tract. In two of four confirmed SARS cases, the specimens tested positive. None of the stool or swab samples from these patients were positive.⁸³ Viral loads were detected in the conjunctival swabs of macaques after they were inoculated using the intratracheal route. They also found no viral loads in the nasopharyngeal swabs of the animals. The authors proposed that SARS-CoV-2 could infect the surface cells of the nasopharyngeal tract and enter the respiratory tract through the secretion of the nasolacrimal system. The rapid emergence of COVID-19 has raised concerns about the transmission of the SARS-CoV-2 coronavirus. This infection can be transmitted through the contact with an eye or respiratory droplets. Due to the increasing number of cases of SARS-CoV-2 infections, the need for healthcare workers to protect their eyes is becoming more prevalent. Reports have been issued to inform ophthalmological clinics about the importance of protecting patients and healthcare providers from possible exposure to an infectious disease.⁸⁵

Other symptoms of COVID-19 infection have also been screened. In patients with acute conjunctivitis infections, the symptoms can be seen in several different forms of illness. It is important that healthcare workers protect themselves from the harmful effects of ultraviolet

radiation by wearing masks and performing good hand hygiene. Aside from these, healthcare workers also need to wear goggles and face shields.⁸⁵

To minimize the risk of transmission of droplets, the use of slit lamps has been suspended. The use of non-touch tonometry machines has been restricted to prevent the aerosolization of drugs.

1. EYE COMPLICATIONS DURING COVID-19

1.1.CONJUNCTIVITIS

Since SARS-CoV-2 can cause respiratory failure, most of the treatment and diagnostic efforts are focused on the respiratory tract. However, other symptoms such as fever, muscle aches, and tears in the eyes can also be caused by the disease.⁸⁶⁻⁸⁹ Conjunctival infection was reported to be a contributing factor to the COVID-19 outbreak. The viral RNA found in the patients' tears suggested that the infection was caused by the COVID-19 virus.⁹⁰⁻⁹² The presence of the ACE-2 receptor on the ocular surface could serve as a portal of entry for viral infection. This protein is a key component of the cell surface protease enzymes (TMPRSS2) that can allow access to host cells.⁹³⁻⁹⁵ The presence of the ACE-2 receptor on the ocular surface could serve as a portal to enter an infected cell. This factor and the cell surface protease enzyme TMPRSS2 are known to bind with the virus and allow it to enter the host cell.⁹⁶⁻¹⁰¹

A study has shown that the expression of TMPRSS2 in conjunctival and pterygium samples is not consistent. It has been hypothesized that the presence of this protein triggers the systemic infection. It is also believed that the severity of the response is not equal in all patients. This condition, which is known as a macrophage activated syndrome, can trigger both an immunological and inflammatory response. It is possible that SARS-CoV-2 exhibits a low conjunctival replication. However, it can still infect the conjunctiva through infected tears that travel through the nasolacrimal ducts. This infection could be initiated using an unidentified

receptor. It is possible that the SARS-CoV-2 virus conjunctival the conjunctiva through infected tears, which can then be transmitted to the nasopharyngeal area. Infestation of the skin with the virus could also cause a low conjunctival replication. COVID-19 conjunctivitis is like other viral forms. It usually presents with various symptoms, including fever, dilated pupils, and inflamed epiphora. At present, there are no reported cases of vision-threatening events. In a study, a patient with monoliteralkeratoconjunctivitis was described as the first symptom of COVID-19.¹⁰¹

Although the exact number of cases of COVID-19 conjunctivitis is still unknown, it is believed that around 31.6% of patients have the condition. In most cases, the viral load is higher than the threshold of test detection.¹⁰² It is possible that patients who have already started antiviral therapy may have developed the infection through tears. Also, some of them may have developed ocular symptoms before the swab.¹⁰³ It is possible that the only disease-specific symptom of COVID-19 is conjunctivitis. In this case, the presence of SARS-CoV-2 RNA isolated on the normal conjunctiva of COVID-19 patients could indicate a viral spreading.¹⁰⁴

The symptoms of COVID-19 have been self-limiting. They are caused by the virus' ability to infect the ocular surface cells. It is important to avoid getting infected with this disease and to maintain a safe and effective infection control program.¹⁰⁵⁻¹⁰⁷

1.2.KAWASAKI DISEASE

Kawasaki disease is a chronic and usually self-limiting vesicular disease that usually affects young children. It causes fever, oropharyngeal changes, and polymorphous rash. Although the exact cause of KD is still not known, it has been theorized that an infectious agent could trigger a cascade reaction. Several studies have reported an increase in the number of cases of severe kapital depression (KD) in children. The prevalence of this condition was also found to be 80%. According to some authors, a severe form of KD has a 30-fold increased incidence of being

diagnosed with COVID-19 serology. Other studies also suggest that there are unusual clusters of cases in the US and UK.¹⁰⁸The first case of COVID-19 infection in a 6-month-old girl was observed in a setting of fever and minimal breathing symptoms. The KD is especially relevant to ophthalmologists due to its possible ocular involvement. Most of the time, it shows signs of iridocyclitis or punctate keratitis.¹¹⁰As the SARS-CoV-2 epidemic spreads globally, it is expected to create new cases of Kawasaki-like disease in the US. This condition could cause diabetic retinopathy and other eye diseases.¹¹¹

1.3.DIABETIC RETINOPATHY.

Due to the global outbreak of coronavirus, many countries have adopted isolation policies. These policies may cause patients to adopt a sedentary lifestyle, which can impair their insulin sensitivity and worsen their lipid metabolism. The increasing prevalence of diabetes mellitus may have unforeseen effects on public health. This could result in an increase in the number of visits to an ophthalmologist for eye complications due to diabetes. The policies that restrict patients' physical activity and sedentary behavior can have detrimental effects on their health. The pandemic may have unforeseen effects on public health, such as an increase in the number of people with diabetes and other eye complications. This could have consequences for public health, such as the worsening of diabetes or the onset of new cases of diabetes. It is also possible that the coronavirus pandemic could lead to an increase in severe cases of diabetes retinopathy.¹¹²

1.4.RETINAL FINDINGS.

A recent report analyzed optical coherence tomography findings in 12 patients infected with SARS-CoV-2 and revealed hyperreflective lesions in the inner plexiform layers of the eye.¹¹³⁻¹¹⁶ Results of an OCT angiography and a ganglion cell complex analysis were normal. Four patients

presented with subtle cotton-wool spots or microhemorrhages on the retinal arcade.¹¹⁷ Concerns have been raised about the interpretation of hyperreflective areas in patients with COVID-19 microcircular damage. It has been hypothesized that these areas may represent normal retinal vessels.¹¹⁸ The complement system activation is a known cause of ocular vascular damage. This condition is characterized by unusual cases of hemolytic uremic syndrome.¹¹⁹ It is also known that high serum levels of C3, which is known to increase the risk of developing diabetes and other neurodevelopmental diseases, can also be linked to an increase in the levels of ACE receptors.¹²⁰ COVID-19 can target vascular pericytes that are expressing ACE-2, which could cause microvascular damage and ocular circulation involvement. This impairs the function of the vascular endothelial cells.¹²¹

1.5.NEURO-OPHTHALMOLOGICAL COMPLICATIONS

COVID-19 has been known to cause neuro-ophthalmological complications such as polyneuritis, Guillain-Barré syndrome, and meningitis. Cases of individuals with COVID-19 have been reported in the literature. According to investigators, COVID-19 could be triggered by factors that contribute to the onset of Oculomotor nerve palsy. Although animal models suggest that optic neuritis could develop in COVID-19 patients, the literature has not yet revealed cases of this condition. Also, the prevalence of respiratory distress syndrome in COVID-19 patients is likely to increase.¹²²⁻¹²³

2. OCULAR COMPLICATIONS IN INTENSIVE CARE UNIT PATIENTS

A study conducted in Italy revealed that out of 1,591 COVID-19 patients, only 9% were admitted to intensive care units (ICUs).¹²⁴ These individuals tend to develop ocular complications.¹²³ Intensified care in an intensive care unit is associated with an increased incidence of eye-related complications.¹²⁵ In most cases, these complications occur in the

posterior segment and ocular surface disorders. Only one case of central retinal artery occlusion has been reported during this review, and this was caused by COVID-19.¹²⁶ The role of thrombophilic factors in the pathogenesis of CVODs is still controversial. Future research may reveal an increased incidence of vascular occlusives during the COVID-19 pandemic.¹²⁷

2.1. OCULAR SURFACE DISORDERS

Surface disorders are the most common ocular complications that occur in the intensive care unit (ICU). They can range from mild to severe infectious keratitis. Most critically ill patients in the intensive care unit (ICU) experience surface disorders, which can range from mild to severe infectious diseases. The most common causes of these conditions include exposure to various multiresistant bacteria, and the use of antibiotics.¹²⁸⁻¹²⁹

In ventilated patients, the main surface defense mechanisms of the eye are impaired. This impairs the ability of the orbicularis to contract. This leads to lagophthalmos.¹³⁰ Airway pressure and oxygen masks can dry the surface of the eye. In most cases, exposure keratopathy occurs in patients who have been sedated for more than 48 hours.¹³² Airway Pressure and Oxygen masks can cause a drying effect on the eye surface. Exposure keratopathy occurs in up to 44% of intensive care unit patients and up to 60% of those sedated for longer periods.¹³³

Conjunctival chemosis is usually seen in patients with acute respiratory distress syndrome (ARDS). It can cause lagophthalmos and reduce ocular surface lubrication. The risk factors for developing this condition include decreased venous return and increased hydrostatic pressure.¹³⁴

In mechanically ventilated individuals, the increase in central venous pressure can also cause subconjunctiva hemorrhage. This condition is usually benign but can lead to surface disorders.

An increase in the central venous pressure can also cause subconjunctival hemorrhage, which is a benign condition that usually goes unnoticed. In mechanically ventilated individuals, the end-

expulsive pressure can also increase and lead to subconjunctival hemorrhage.¹³⁵ A study published in the Journal of Allergy and Infectious Diseases revealed that among 134 patients who underwent respiratory support, at least 77% were colonized by at least a few bacterial species other than those with normal flora.¹³⁶

2.2.RARE OCULAR COMPLICATIONS

It has been observed that prone position ventilation can prevent the development of acute ischemic optic neuropathy. However, prolonged exposure to a prolonged exposure to a high level of oxygen deprivation can lead to the development of this condition.¹³⁸⁻¹⁴⁰ The prone position can also reduce the perfusion acting on two mechanisms. It can increase the IOP by up to 40 mmHg and increase venous pressure by up to 0.5 mmHg.¹⁴¹ Other systemic conditions such as diabetes and arterial hypertension can also affect the blood flow to the ocular surface. This impairs the ability of the eye to perform its usual function. This condition is characterized by the sudden appearance of bilateral or uni-lateral macular pre-retinal hemorrhages. It usually appears due to the increasing intrathoracic pressure.¹⁴² It has been known that valsalva can also occur due an intubation or a high end-expulsive pressure. An acute angle closure is a potentially sight-threatening condition that can be triggered by various factors.¹⁴³ Some of these include the usual medications and the prone position. An acute angle closure can occur in an ICU patient if the patient has underlying risk factors such as diabetes, high end-expulsive pressure, or an unstable or inverted heart rate.¹⁴⁴ Currently, anticholinergics and systemic drugs are known to cause this type of event. This syndrome has been reported to occur in 2% of central venous catheterization patients.¹⁴⁶⁻¹⁴⁶ It was most likely caused by trauma to the central nervous system or an expanding hematoma. In patients with COVID-19, endophthalmitis has been considered a rare but significant clinical feature of the viral infection.¹⁴⁷ Staff members should be aware of the signs of

possible eye-related complications, such as visual impairment and blindness, and should refer them to an ophthalmologist when needed.¹⁴⁸

3. OCULAR SIDE EFFECTS OF DRUGS USED FOR THE TREATMENT OF COVID-19

Currently, there are no pharmacological treatments for COVID-19. However, some drugs are being studied for their potential use.¹⁵⁴

3.1. ANTIMALARIAL DRUGS

The anti-malarial drugs CQ and HCQ are commonly used to treat various conditions, such as malaria and amebiasis. They have also been studied in animal models to develop an immunological response against SARS-CoV-2. A study in China showed that CQ reduced the exacerbations of pneumonia and promoted viral-negative seroconversion. In COVID-19, this treatment led to better clinical recovery and reduced hospitalizations. A study conducted by Gautret et al. showed that treating HCQ in patients with COVID-19 led to viral load reduction and disappearance.¹⁵⁵ In addition, these drugs have anti-SARSCoV-2 and anti-SARSCoV-2 effects. They can inhibit the growth of cells that are infected with SARSCoV-2 and SARSCoV-2 by suppressing the terminal glycosylation of the ACE-2 receptor. COVID-19 is an anti-SARSCoV-2 and SARSCoV-2 monoclonal antibody that blocks the terminal glycosylation of the ACE-2 receptor. It is administered at a dose of 1,000 mg daily for 4 or 7 days.^{156,157}

The clinical picture of CQ and HCQ ocular toxicity shows whorl-like intraepithelial deposits and posterior subcapsular lens opacity. It is also characterized by a bilateral Maculopathy that shows progressive loss of visual acuity and RPE atrophy. The clinical picture of CQ and HCQ ocular toxicity shows whorl-like intraepithelial deposits that are usually reversible. There is also a bilateral Maculopathy that shows the presence of a ring of RPE depigmentation. CQ and HCQ maculopathy is not reversible, and it can progress even after stopping drug assumption. The most critical risk factor for developing these conditions is excessive daily dosage. Most of the patients

treated with COVID-19 for COVID-19 receive higher-than-recommended doses of CQ and HCQ. This increased risk of ocular toxicity increases with prolonged use of HCQ. Most of the patients who received COVID-19 for COVID-19 received potentially toxic doses. The duration of therapy is also an important factor to consider when choosing a drug for treating ocular toxicity. Two studies showed that patients receiving HCQ had a 25% to 40% increase in the incidence of retinopathy within 2 years. No reports of retinal toxicity have been reported in patients receiving CQ or HCQ.¹⁵⁸ A two-year study on patients receiving 800 to 1,000 mg/day of HCQ showed that 60% of them experienced vision problems within 1-2 years. The study did not find evidence of drug toxicity being observed under 2 weeks of CQ.¹⁵⁹

3.2.ANTIVIRAL DRUGS

Both lopinavir and ritonavir are known to reduce the COVID-19 infection in humans. Lopinavir and Ritonavir are commonly used as part of an HIV infection-fighting strategy known as COVID-19. These two drugs are formulated in a combination to inhibit the P450 3A4 enzyme.¹⁵⁵ Lopinavir/ritonavir is a therapy that can reduce the viral load in COV-19 patients. Although it has been shown to improve the efficacy of the virus, its safety has been limited. In one study, researchers described a rare but devastating vision loss caused by ritonavir. The drug was commonly used for treating HIV positive individuals with vision loss. It can also cause visual changes that can deceive people with compromised vision. There can also be changes in the pigments in the mid-peripheral retina. Intricate intraretinal deposits can also form. Pigment changes in the mid-peripheral retina can also occur. Also, loss of the ellipsoid zone and outer retinal layers can also cause OCT to be affected. The shortest time before diagnosis for COVID-19 patients is 19 months. The duration of treatment is usually 5 to 7 days. The shortest time

before diagnosis for COVID-19 patients is 19 months. For HIV cases, the recommended dosage of lopinavir/ritonavir is 400/100 mg twice daily.¹⁶⁰

3.3. IMMUNOMODULATORY DRUGS

Interferons are a class of drugs that can be used to treat COVID-19. Among the IFN subtype's most promising characteristics is their ability to trigger an immunological response against COVID-19.¹⁶¹⁻¹⁶² Interferon-associated retinopathy is a type of visual impairment that can manifest with various microvascular irregularities and cotton-wool spots. It usually appears 3 to 5 months after treatment.¹⁶³ Although the ocular findings of patients with interferon-associated retinopathy were reversed after cessation of treatment, they still exhibited significant deficits in visual quality.¹⁶⁴

Currently, there are no published studies on the use of anti-IL-1 and anti-IL-6 inhibitors in patients with chronic wasting syndrome (COVID-19). However, some studies have shown an association between high doses of anakinra and progressive nystagmus.¹⁶⁵

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