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Original Article

Ophthalmology Section

Ocular Diseases Presenting in Post-COVID-19 Patients: A Cross-sectional Study Conducted at a Tertiary Institute in Andhra Pradesh, Southern India

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ABSTRACT

Introduction: The Coronavirus Disease-2019 (COVID-19) pandemic, which started in December 2019, has rapidly spread across the globe. Although the prevalence of COVID-19 disease has significantly decreased, there are cases of post-COVID-19 complications affecting multiple organ systems, including the eyes.

Aim: To evaluate ocular diseases presenting in post-COVID-19 patients and their association with demographic profiles, duration of post-COVID-19, and the type of treatment received.

Materials and Methods: A descriptive cross-sectional study was conducted over a four-month period (August 2021 to November 2021) in the Department of Ophthalmology at AIIMS, Mangalagiri, Guntur, Andhra Pradesh, India. The study focused on post-COVID-19 patients who had been affected by COVID-19 no more than three months prior. Patients who were not post-COVID-19 and those who had contracted COVID-19 during the first wave were excluded from the study. The patients' clinical history and symptoms were documented. Visual acuity, intraocular pressure, and detailed anterior and posterior segment findings were recorded for all patients. The study aimed to assess post-COVID-19 ocular complications and any potential associations with hospital stays, steroid intake, or oxygen inhalation on eye diseases. Mean and median calculations were performed for continuous variables, and a Chi-square test was used to study associations. Statistical Package for Social Sciences (SPSS) version 25.0 was employed, and a p-value <0.05 was deemed significant.

Results: In the present study, males constituted 41 (62.1%) and females constituted 25 (37.9%), with a male-to-female ratio of 1.64:1. The majority of patients 23 (34.8%) were above 50 years old. Most patients 24 (36.4%) developed eye diseases one month after their COVID-19 infection. Out of 66 patients, 11 (16.7%) were diabetic, 8 (12.1%) were hypertensive, and 40 (60.6%) had no associated co-morbidities. During their COVID-19 illness, 53 (80.3%) patients underwent home isolation and received supportive treatment, while 13 (19.7%) patients were hospitalised. The most common ocular disease observed was conjunctivitis 39 (59.1% of patients) following post-COVID-19. Additionally, 4 (6%) patients developed central serous chorioretinopathy, 4 (6%) developed refractive errors, 5 (7.6%) experienced persistent headaches, and 2 (3%) developed orbital mucormycosis.

Conclusion: The present study presents ophthalmic manifestations in post-COVID-19 patients. Conjunctivitis was found to be the most common ocular disease, more prevalent one month after the COVID-19 infection. COVID-19 retinopathy was the most common posterior segment complication, especially in patients above 50 years old and three months post-COVID-19.

Keywords: Conjunctivitis, Coronavirus disease-2019 retinopathy, Orbital mucormycosis, Persistent headaches, Posterior segment complication, Refractive errors

INTRODUCTION

The COVID-19 pandemic, which began in Wuhan City, China, in December 2019, soon spread across the globe [1,2]. Over time, there have been small strides made in understanding the disease, its management, and vaccination [3,4]. Although COVID-19 cases have declined tremendously, there are still instances of post-COVID-19 complications involving multiple organ systems, including the eyes. There has been a subsequent rise in cases of orbital mucormycosis [5], viral conjunctivitis [6], and presentations of decreased vision in post-COVID-19 patients. Additionally, vision-threatening neuro-ophthalmic disorders, higher ocular surface disease index scores, and lower Schirmer test results [7] have been noted in patients following hospitalisation for COVID-19. Exposure keratitis has also been found in patients admitted to Intensive Care Unit (ICU) units [8].

In the current scenario, almost four years have passed since the occurrence of the first case of COVID-19 in Wuhan city. The authors are now seeing post-COVID-19 vaccine uveitis, simultaneous onset of Graves' disease and ocular myasthenia gravis, along with dry eye syndromes and orbital mucormycosis [9,10]. Greenhalgh T et al., recently coined a new entity called Post-COVID-19 Syndrome, which is defined as extending beyond three weeks from the onset of the first COVID-19 symptom, and Chronic COVID-19 as symptoms extending beyond 12 weeks [11]. There are only case reports and a few studies from different parts of the world, such as Egypt, China, Syria, Malaysia, Poland, and Saudi Arabia, which have documented acute COVID-19 and post-ocular symptoms and isolated post-COVID-19 manifestations pertaining to parts of the eye, such as nerve palsy, retina, ocular surface, and refractive errors [12-17]. There are only a few case series and studies from India which have documented post-COVID-19 ocular manifestations [8,18]. However, in all the available literature [8,12-18], there is no exact and comprehensive documentation of ocular diseases persisting after post-COVID-19, and various ocular ailments resulting from acquiring various treatments for COVID-19, especially in South India. The present study aimed to address this gap.

Therefore, the present study aimed to analyse various ocular diseases reported after post-COVID-19 and study their association with the duration, age, gender, co-morbidities, hospitalisation, medication, oxygen intervention, and hypothesise a relevant possible explanation for the aetiopathogenesis of the ocular diseases pertaining to post-COVID-19.

MATERIALS AND METHODS

This was a cross-sectional descriptive study conducted on post-COVID-19 patients who were affected by COVID-19 not more than three months prior in the Department of Ophthalmology at All India Institute of Medical Sciences (AIIMS), Mangalagiri, Guntur, Andhra Pradesh, India. Approval from the Institutional Ethics Committee board was obtained before conducting the study (IEC no- AIIMS/MG/IEC/2022-23/147). Strict ethical guidelines indicated in the Declaration of Helsinki were followed in the present study, and the present study did not involve any financial issues. Verbal consent was obtained from the patients. The study was conducted over four months, from September 2021 to December 2021.

Inclusion criteria: The study population included patients presenting with ocular ailments, who were post-COVID-19 for not more than three months, of all age groups and both genders.

Exclusion criteria: Patients who were not post-COVID-19 and those who were post-COVID-19 during the first wave were excluded. The reason being the first COVID-19 wave occurred in India in March 2021, and the second COVID-19 wave occurred in February 2021, with a time lapse of more than six months between the onset of the two waves. The present study aimed to study ocular diseases presenting in post-COVID-19 patients within three months only, hence post-COVID-19 patients from the first wave were excluded from the present study.

Sample size calculation: Anticipating that 22% of the subjects would develop eye disease within three months of a COVID-19 infection (based on pilot data of patients attending the hospital with post-COVID-19 ocular complications), with 10% absolute precision and 5% level of significance, the sample size was calculated using the estimation of single proportion formula {$n \geq z1-\alpha/2P(1-P)/d^2$, with Z at 5% level of significance-1.96, anticipated proportion (P)=0.22, 1-P=0.78, and absolute precision (d)=0.1}.

Study Procedure

This resulted in a sample size of 66. A total of 66 patients were enrolled during the study period after obtaining prior consent. The date of COVID-19 positivity and the date of onset of symptoms were noted. All ocular diseases of presenting patients were recorded, and their clinical demographic profile was documented through proper examination, and the results were analysed. Discrete variables such as gender, hospital admission, oxygen requirement, and continuous variables such as age, blood sugar levels, blood pressure, duration of post-COVID-19, etc., were recorded. The patients' clinical history and symptoms were recorded. All the patients had their visual acuity recorded using Snellen charts, and intraocular pressure recorded using Goldmann Applanation Tonometry. Detailed anterior segment examination was performed under a slit lamp. Fundus findings were recorded using a +90D lens, and further investigations were conducted wherever necessary.

STATISTICAL ANALYSIS

The continuous variables were summarised with mean and standard deviation or median with interquartile range based on the normality of the data. Normality was assessed using the Kolmogorov-Smirnov test. Categorical variables were summarised with frequency and proportion. The association of gender and various age groups with ocular disease and other clinical parameters was assessed using the Chi-square/Fisher's -exact test with SPSS software version 25. A p-value of <0.05 was considered statistically significant.

RESULTS

In the present study, out of 66 patients who presented with ocular diseases following post-COVID-19, males constituted 41 (62.1%) and females constituted 25 (37.9%), with a male-to-female ratio of 1.64:1. The age of the patients ranged between 20 to 60 years, and most of the patients 23 (34.8%) were above 50 years, as summarised in [Table/Fig-1]. In the present study, most patients who had developed eye diseases following COVID-19 fell within one month of the COVID-19 attack 24 (36.4%), followed by within less than one month of the COVID-19 attack 20 (30.3%) [Table/Fig-1]. Out of the 66 patients who presented with various eye diseases following post-COVID-19 of less than one month to three months duration, 11 were diabetics (16.7%), 8 patients were hypertensive (12.1%), and 40 patients (60.6%) had no associated co-morbidities [Table/Fig-1]. A total of 53 patients (80.3%) had undergone home isolation during their COVID-19 time and had received supportive treatment, and 13 patients (19.7%) were hospitalised [Table/Fig-1].

Parameters	Frequency	Percentage
Age group		
20-29 years	13	19.7%
30-39 years	17	25.8%
40-49 years	13	19.7%
50 years and above	23	34.8%
Total	66	100.0%
Duration of post-COVID-19		
Less than a month	20	30.3%
One month	24	36.4%
More than 1 month and less than 2 months	9	13.6%
More than 2 months and less than 3 months	12	18.2%
3 months	1	1.5%
Total	66	100.0%
Co-morbidities		
Diabetes mellitus	11	16.7%
Hypertension	8	12.1%
Both diabetes and hypertension	5	7.6%
Others	2	3.0%
No co-morbidities	40	60.6%
Total	66	100.0%
Home/hospital admission		
Home isolation	53	80.3%
Hospital admission	13	19.7%
Total	66	100.0%
Treatment		
Oxygen	1	1.5%
Steroids	25	37.9%
Oxygen and steroids	5	7.6%
Steroids and remdesivir	1	1.5%
No treatment	34	51.5%
Total	66	100.0

[Table/Fig-1]: Demographic details of the patients.

Ocular diseases: The most common ocular disease was conjunctivitis (39 patients) following post-COVID-19. Eight patients had developed central serous chorioretinopathy, and four members developed refractive errors. Five patients developed persistent headaches, and two patients developed Orbital Mucormycosis. All the symptoms were more common in males [Table/Fig-2], except for retinopathy, which showed equal frequency in both genders. However, the higher incidences in the male gender were not statistically significant.

Association between ocular diseases and age distribution [Table/Fig-3]: Conjunctivitis and COVID-19 retinopathy were more frequent in individuals over 50 years of age. However, this association was not statistically significant. Association between ocular diseases and the type of treatment received (details shown in [Table/Fig-4]): Refractive error was more frequent in individuals receiving steroids, and this association was statistically significant.

Ocular disease	Male n=41 (%)	Female n=25 (%)	p-value*
Ocular headache	4 (9.7%)	1 (4%)	0.642
Proptosis	1 (2.4%)	1 (4%)	1.000
Conjunctivitis	22 (53.6%)	17 (68%)	0.250
Ophthalmoplegia	1 (2.4%)	0	1.000
Herpes zoster ophthalmicus	0	1 (4%)	0.379
COVID-19 retinopathy	4 (9.7%)	4 (16%)	0.465
Preseptal cellulitis	2 (4.8%)	0	0.522
Optic nerve involvement	1 (2.4%)	0	1.000
Mucormycosois	1 (2.4%)	1 (4%)	1.000
Decreased near vision	1 2.4 (%)	0	1.000
Chronic sinusitis	0	1 (4%)	0.379
Refractive error	3 (%)	1 (4%)	1.000
Dry eye	2 (4.8%)	0	0.522

[Table/Fig-2]: Table showing association between ocular diseases and gender.
*The association of gender with ocular disease was assessed using Chi-square/Fisher's-exact test

Association between ocular diseases and post-COVID-19 duration [Table/Fig-5]: Conjunctivitis was more frequent in individuals who were one month post-COVID-19, and this association was statistically significant. COVID-19 retinopathy was more frequent in individuals who were 2-3 months post-COVID-19, and this association was statistically significant. Similarly, refractive error was more frequent in individuals who were less than one month post-COVID-19, and this association was statistically significant.

Association between ocular diseases and co-morbid diseases [Table/Fig-6]: Proptosis and mucormycosis were more frequent in diabetics, and this association was statistically significant. Ophthalmoplegia and optic nerve involvement were seen in one patient each and were more common in patients with diabetes and hypertension, and hemiplegia patients, respectively.

Association between ocular diseases and the place of treatment [Table/Fig-7]: The most common symptom in patients under home isolation during COVID-19 and presenting post-COVID-19 was conjunctivitis, followed by ocular headache and COVID-19

Ocular diseases	20 to 29 years (n=13)	30 to 39 years (n=17)	40 to 49 years (n=16)	Above 50 years (n=23)	Total (n=66)*	p-value
Ocular headache	1 (7.7)%	2 (11.8%)	2 (12.5%)	0	5 (7.6%)	0.328
Proptosis	0	0	1 (6.2%)	1 (4.3%)	2 (3.0%)	0.565
Conjunctivitis	10 (76.9)%	9 (52.9%)	7 (43.7%)	13 (56.5 %)	39 (59.1%)	0.535
Ophthalmoplegia	0	0	0	1 (4.3%)	1 (1.5%)	0.594
Herpes zoster ophthalmicus	0	0	0	1 (4.3%)	1 (1.5%)	0.594
COVID-19 retinopathy	0	2 (11.8%)	2 (12.5%)	4 (17.4%)	8 (12.1%)	0.471
Preseptal cellulitis	0	0	1 (6.2%)	1 (4.3%)	2 (3.0%)	0.565
Optic nerve involvement	0	0	1 (6.2%)	0	1 (1.5%)	0.247
Mucormycosois	0	0	1 (6.2%)	1 (4.3%)	2 (3.0%)	0.565
Decreased near vision	0	1 (5.9%)	0	0	1 (1.5%)	0.403
Chronic sinusitis	0	1 (5.9%)	0	0	1 (1.5%)	0.403
Refractive error	1 (7.7%)	1 (5.9%)	1 (6.2%)	1 (4.3%)	4 (6.1%)	0.971
Dry eye	1 (7.7%)	1 (5.9%)	0	0	2 (3.0%)	0.465

[Table/Fig-3]: Association between ocular diseases and age-wise distribution.
*some patients had more than one symptom

Ocular diseases	Oxygen inhalation	Steroids	Inj. Remedesvir	Both oxygen and steroids	Supportive treatment	Total (n=66)*	p-value
Ocular headache (n=5)	0	1 (20%)	0	0	4 (80%)	5 (7.6%)	0.757
Proptosis (n=2)	0	0	1 (50%)	0	1 (50%)	2 (3.0%)	0.219
Conjunctivitis (n=39)	1 (2.6%)	15 (38.5)	3 (7.7%)	0	20 (51.3%)	39 (59.1%)	0.709
Ophthalmoplegia (n=1)	0	0	0	0	1 (100%)	1 (1.5%)	0.916
Herpes zoster ophthalmicus (n=1)	0	0	0	0	1 (100%)	1 (1.5%)	0.916
COVID-19 retinopathy (n=8)	0	3 (37.5%)	1 (12.5%)	0	4 (50%)	8 (12.1%)	0.966
Preseptal cellulitis (n=2)	0	1 (50%)	0	0	1 (50%)	2 (3.0%)	0.990
Optic nerve involvement (n=1)	0	1 (100%)	0	0	0	1 (1.5%)	0.797
Mucormycosois (n=2)	0	0	1 (50%)	0	1 (50%)	2 (3.0%)	0.219
Decreased near vision (n=1)	0	1 (100%)	0	0	0	1 (1.5%)	0.797
Chronic sinusitis (n=1)	0	0	0	0	1 (100%)	1 (1.5%)	0.916
Refractive error (n=4)	0	2 (50%)	0	1 (25%)	1 (25%)	4 (6.1%)	0.002
Dry eye (n=2)	0	1 (50%)	0	0	1 (50%)	2 (3.0%)	0.990

[Table/Fig-4]: Association between ocular diseases and type of treatment received.

Ocular diseases (n)	Less than one month	One month	>One month to <Two months	>Two months to <three months	3 months	p-value
Ocular headache (5)	1 (20%)	1 (20%)	1 (20%)	2 (40%)	0	0.690
Proptosis (2)	1 (50%)	1 (50%)	0	0	0	0.901
Conjunctivitis (39)	10 (25.7%)	20 (51.3%)	4 (10.2%)	5 (12.8%)	0	0.036*
Ophthalmoplegia (1)	0	1 (100%)	0	0	0	0.777
Herpes zoster ophthalmicus (1)	1 (100%)	0	0	0	0	0.674

COVID-19 retinopathy (8)	1 (12.5%)	0	2 (25%)	5 (62.5%)	0	0.005*
Preseptal cellulitis (2)	2 (100%)	0	0	0	0	0.315
Optic nerve involvement (1)	0	0	1 (100%)	0	0	0.169
Mucormycosois (2)	1 (50%)	1 (50%)	0	0	0	0.901
Decreased near vision (1)	0	0	0	1 (100%)	0	0.334
Chronic sinusitis (1)	1 (100%)	0	0	0	0	0.674
Refractive error (4)	2 (50%)	0	1 (25%)	0	1 (25%)	0.001*
Dry eye (2)	1 (50%)	0	1 (50%)	0	0	0.490

[Table/Fig-5]: Association between ocular diseases and post-COVID-19 duration.

Ocular diseases	Diabetes	Hypertension	Diabetes and hypertension	Other systemic diseases, a) Hemiplegia b) Sjogren's syndrome	No. of co-morbidities	p-value
Ocular headache (5)	1 (20%)	1 (20%)	0	0	3 (60%)	0.926
Proptosis (2)	2 (100%)	0	0	0	0	0.035
Conjunctivitis (39)	4 (10.3%)	4 (10.3%)	1 (2.7%)	3 (7.7%)	27 (69%)	0.425
Ophthalmoplegia (1)	0	0	1 (100%)	0	0	<0.005*
Herpes zoster ophthalmicus (1)	1 (100%)	0	0	0	0	0.279
COVID-19 retinopathy (8)	1 (12.5%)	3 (37.5%)	0	1 (12.5%)	3 (37.5%)	0.178
Preseptal cellulitis(2)	1 (50%)	0	0	0	1 (50%)	0.757
Optic nerve involvement (1)	0	0	0	1 (100%)	0	0.015
Mucormycosois (2)	2 (100%)	0	0	0	0	0.035
Decreased near vision (1)	0	0	0	0	1 (100%)	0.956
Chronic sinusitis (1)	0	0	0	0	1 (100%)	0.956
Refractive error (4)	1 (25%)	0	0	0	3 (75%)	0.863
Dry eye (2)	0	1 (50%)	0	0	1 (50%)	0.551

[Table/Fig-6]: Association between ocular diseases and co-morbid diseases.

retinopathy. Meanwhile, the most common symptom in patients under hospital stay during COVID-19 and presenting post-COVID-19 was conjunctivitis, followed by COVID-19 retinopathy and refractive errors.

Ocular diseases	Home isolation	Hospitalisation	p-value
Ocular headache (5)	5 (100%)	0	0.574
Proptosis (2)	1 (50%)	1 (50%)	0.358
Conjunctivitis (39)	32 (82%)	7 (18%)	0.668
Ophthalmoplegia (1)	1 (100%)	0	1.000
Herpes zoster ophthalmicus (1)	1 (100%)	0	1.000
COVID-19 retinopathy (8)	5 (62.5%)	3 (37.5%)	0.185
Preseptal cellulitis (2)	2 (100%)	0	1.000
Optic nerve involvement (1)	1 (100%)	0	1.000
Mucormycosois (2)	1 (50%)	1 (50%)	0.358
Decreased near vision (1)	1 (100%)	0	1.000
chronic sinusitis (1)	1 (100%)	0	1.000
Refractive error (4)	2 (50%)	2 (50%)	0.171
Dry eye (2)	2 (100%)	0	1.000

[Table/Fig-7]: Association between ocular diseases and place of treatment.

DISCUSSION

In the present study, most patients who had developed eye diseases following COVID-19 disease presented one month after the COVID-19 attack or a lesser duration, constituting 24 (36.4%) and 20 (30.3%) patients, respectively. This is similar to the study done by Tohamy D et al., in which patients who developed eye diseases recovered from COVID-19 within one month [12]. Very few patients developed eye disease following three months or more after the COVID-19 attack. The probable explanation can be the effect of coronavirus pathogenesis in ocular tissues, and the exaggeration of immunological activity may diminish along with the time since the COVID-19 attack. However, the exact reason is not yet known.

In the present study, anterior segment diseases like conjunctivitis (39 patients, 59.1%) and dry eyes (two patients, 3%) were more common in post-COVID-19 patients who did not have any co-morbidities (28 patients). Conjunctivitis was present in 30.7% with co-morbidities vs 79.3% without co-morbidities, and who had acquired mild COVID-19 infection and had undergone home isolation only, with supportive treatment alone (conjunctivitis (n=39)-82% with home isolation vs 18% with hospitalisation, dry eye (n=2) 100% with home isolation vs 0% hospitalisation). Posterior segment diseases like central serous chorioretinopathy, retinal haemorrhages, etc., were found in eight patients, and 37.5% of these had used steroids during their treatment.

In a study done by Costa IF et al., dry eye diseases were also reported in patients who had suffered from mild to moderate COVID-19 only [19]. In a similar study done by Wan KH et al., the authors noticed an association between dry eye-related disease and post-COVID-19 status [13]. They have documented an OR of 0.91 (95% CI 0.84-0.98) for ocular surface symptoms like dry eye within four weeks following diagnosis in patients with a lower viral load.

In the present study, five patients who had persistent headaches were mild cases and had received supportive treatment in home isolation. The majority (3 patients) of them did not have any co-morbidities. The presence of headache in post-COVID-19 patients was also noted in the study by Costa IF et al., [19]. Membrilla JA et al., also observed that headache occurred in patients who had mild COVID-19 in the acute stage [20]. The probable reason could be the accumulation of SARS-COV-2 Ribonucleic Acid (RNA) virus in the trigeminal nerve (nerve endings in the conjunctiva and cornea), which may trigger immune reactivity of Angiotensin Converting Enzyme 2 (ACE2) in cerebral blood vessels and cerebral endothelium, leading to the activation of a cascade of inflammatory reactions and the release of glutamate, resulting in persistent headaches.

Ophthalmoplegia was present in one male patient who received supportive treatment, with one month of post-COVID-19 duration and had both diabetes and hypertension co-morbidities. A similar

case of complete ophthalmoplegia in a diabetic patient who had received steroid treatment was reported by Hajjar D et al., [14]. In the present study, the patient was on supportive treatment only. Only III and IV cranial nerves were involved, and very few cases of ophthalmoplegia are reported in the literature to date. The probable cause is that an immunological reaction could have been triggered in the patient who had both diabetes and hypertension co-morbidities and was already on supportive therapy.

In the present study, four patients (two male and two female) had developed Central Serous Chorioretinopathy (CSR). Three patients had taken steroids in their treatment and one had received an injection of Remdesivir. The majority (4) of them developed CSR after three months of the post-COVID-19 attack. Three of them were hypertensives, and one of them had diabetes. One patient was in home isolation, and three were hospitalised during the COVID-19 attack. The majority of them were above 50 years of age. A similar case had been reported by Sanjay S et al., in an Asian Indian female who developed CSR unilaterally after using steroids [21]. Sharifi A et al., also reported a similar case of CSR in a 49-year-old female patient who was treated with injections of Remdesivir and Dexamethasone [22]. Mohd-Alif WM et al., in their study reported bilateral CSCR in a patient who had received both intravenous and oral corticosteroids as treatment during COVID-19 infection [15]. The exact aetiology and pathology of CSCR in post-COVID-19 patients are yet to be understood. However, three possible explanations for developing CSCR are as follows: 1) Use of steroids, as per treatment protocols, could have led to the development of Unilateral CSCR in the post-COVID-19 stage, after four weeks to two months; 2) SARS-COV-2 may lead to endotheliitis, escalating to hyperpermeability of the choriocapillaris, endothelial dysfunction, and retinal pigment epithelial pump dysfunction, finally leading to CSCR; 3) Psychological stress faced by the patients during the COVID-19 stage, and mostly hypertensive co-morbidity may have led to CSCR in the post-COVID-19 stage.

Four patients presented with cotton wool spots and retinal haemorrhages, which were similar to the Polish study done by Szkodny D et al., [7], but in the present study, two patients who presented with subtle haemorrhages and cotton wool spots were hypertensives. It is not clear whether cotton wool spots were due to hypertensive retinopathy or COVID-19. However, one patient with haemorrhages did not have any co-morbidity, and the other patient with few cotton wool spots had Hemiplegia as a co-morbid factor. These retinal findings may be attributed to the immunological effect caused by the coronavirus, but the exact mechanism is unclear to date.

In the present study, one female patient had Herpes Zoster Ophthalmicus (HZO) after mild COVID-19 (less than one-month duration, under home isolation), and had been diabetic for the past 20 years. Pourazizi M et al., had reported a similar case of HZO in a 25-year-old female following moderate to severe COVID-19 [16]. The probable explanation is that, as the patient was already immune-compromised due to long-standing diabetes, SARS-CoV-2 attack could have reactivated Herpes. Immune dysfunction of T cells and immune dysregulation following COVID-19 may be an acceptable pathogenesis, but a lot of research should be done to understand the exact mechanism.

In the present study, two patients had orbital mucormycosis. Both developed orbital mucormycosis within one month of acquiring COVID-19 infection, similar to the study by Ponce-Rosas L et al., [23]. In our study, both patients had long-standing diabetes as a co-morbidity, similar to other studies on Rhino-orbital mucormycosis in post-COVID-19 patients, such as those by Arjun R et al., Ponce-Rosas L et al., Desai EJ et al., and Mobeen H et al., [18,23-25]. One patient had undergone hospitalisation and was administered Injection Remdesivir, similar to the study by Mobeen H et al., and one had received supportive treatment in home isolation [25]. In these two patients, there was a decrease in vision, restriction of eye movements, and unilateral proptosis. One patient had undergone orbital exenteration, and the other patient recovered with Amphotericin. Both modalities of treatment were reported by Arjun R et al., and Desai EJ et al., [18,24]. The age of both patients affected by orbital mucormycosis in the present study was above 40 years, middle-aged, and old, which is similar to Ponce-Rosas L et al., [23]. Long-standing diabetes and middle to older age of patients should have made the patients more vulnerable to getting orbital mucormycosis following post-COVID-19 sequelae. In the present study, none of the patients had taken steroids as part of COVID-19 treatment, which is in contrast to Mobeen H et al.'s study [25]. In studies reported by Arjun R et al., few patients who had suffered from orbital mucormycosis didn't receive steroids as part of their treatment but were long-standing diabetics, which is similar to the present study [18]. The most common similarity in all the studies quoted above and the present study is that all the patients were diabetics, suffered from moderate COVID-19, and were middle-aged patients. Probably, immune compromise by diabetes, already attacked by COVID-19, and hospitalisation may reactivate the invasive fungus, leading to lethal orbital mucormycosis. However, the sample size in the present study was small (two patients out of 66), but the risk factors of acquiring orbital mucormycosis coincided with other studies. It can be concluded that long-standing diabetes is undoubtedly a major risk factor for developing orbital mucormycosis in post-COVID-19 patients.

In the present study, four patients developed refractive error following post-COVID-19 infection. Among them, all three were males. Two patients had received steroids, and one patient had both oxygen and steroids as part of the treatment protocol for COVID-19 disease, with a significant p-value of 0.002. The duration of acquiring refractive error post-COVID-19 was less than one month in two patients, similar to the Alrashidi study and with a significant p-value of 0.001 [17]. All patients had no co-morbidities, with two in home isolation and two in hospitalisations. The probable explanation for developing refractive error post-COVID-19 in non refractive error patients is the development of abnormalities in the tonic mechanism of accommodation. However, much research has to be done in this area to have a better understanding of the mechanism.

Limitation(s)

The study is limited by the fact that the hypotheses made on disease pathogenesis were based solely on observations and cannot be proven without experimental or analytical studies to confirm or disapprove the hypotheses. Additionally, the study is limited by its sample size and requires studies with larger sample sizes.

CONCLUSION(S)

This paper presents ophthalmic manifestations in post-COVID-19 patients thus approving the hypothesis. Conjunctivitis was the most common ocular disease, more common after one month of post-COVID-19. COVID-19 retinopathy was the most common posterior segment complication, more common in patients above 50 years and two to three months post-COVID-19. Around one-tenth of patients had persistent headache post-COVID-19. Ophthalmoplegia and central serous retinopathy were noted in a few patients who had received supportive treatment and presented with co-morbidities.

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