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Research article

Analysis of retinal changes in COVID-19 patients: A cross-sectional study at the Navy General Hospital, Colombo, Sri Lanka

D. T. Goonesekera[1], K. A. Salvin[2]

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Abstract

Introduction: *The systemic implications of COVID-19 extend beyond the respiratory system, with emerging evidence suggesting potential retinal involvement. COVID-19 infection may be associated with changes in immune and coagulation systems and possible viral spread through the blood-brain barrier, with clinical and anatomopathological findings of disseminated intravascular coagulopathy (DIC), the effects of these alterations on the eye, specifically regarding posterior segment involvement, have not been fully explored.*

This study compares retinal changes observed in Sri Lankan COVID-19 patients with findings reported in other international studies.

Methods: *A descriptive cross-sectional study was conducted involving 79 COVID-19 positive navy personnel. Retinal evaluations, including Optical Coherence Tomography (OCT), were performed, and the results were compared with normative data from the Cirrus HD OCT machine and published findings from similar studies conducted globally.*

Results: *Among the 158 eyes examined, 46 (29.11%) showed deviations in macular thickness, with the central foveal region being most affected. These findings are consistent with other studies reporting retinal changes post-COVID-19, albeit with variations in the prevalence and type of retinal involvement. The absence of significant findings in visual acuity and slit-lamp examinations contrasts with the OCT results, emphasizing the importance of advanced imaging techniques in detecting subtle retinal changes.*

Conclusions: *The study's findings align with international reports, highlighting the presence of retinal changes in a subset of COVID-19 patients. These results support the assumption of SARS-CoV-2 may have direct or indirect effects on the retina, necessitating further investigation and routine OCT screening in COVID-19 patients.*

Introduction

COVID-19, caused by the SARS-CoV-2 virus, has dramatically impacted global health, leading to a widespread pandemic with far-reaching consequences beyond the well-known respiratory symptoms. The disease is known to have systemic effects, influencing various organ systems, including the cardiovascular, neurological, and ocular systems. As the pandemic has evolved, so too has the understanding of its potential to cause retinal abnormalities, with multiple studies reporting changes in retinal vasculature and thickness among COVID-19 patients.

The retina, a highly vascularized tissue, is particularly susceptible to changes in systemic health, making it a potential target for COVID-19-related complications. The mechanisms through which SARS-CoV-2 affects the retina are not yet fully understood, but it is suggested that both direct viral invasion and the systemic inflammatory response could play significant roles. Previous studies have identified retinal microvascular changes, such as cotton wool spots and microhemorrhages, and alterations in retinal thickness, as potential ocular manifestations of COVID-19. However, the reported prevalence and types of retinal changes vary significantly across different studies, likely due to differences in study populations, disease severity, and the timing of ocular assessments post-infection. Most of the existing literature has focused on older patients or those with severe COVID-19, who may be more susceptible to significant retinal changes. This study aims to address this gap by investigating retinal changes in a younger, healthier population of COVID-19 patients in Sri Lanka and comparing the findings with those reported in other parts of the world.

[1]*Consultant Ophthalmologist, Colombo South Teaching Hospital, Sri Lanka,* [2]*Senior Lecturer, Faculty of Medicine, University of Kelaniya, Sri Lanka.*

Methods

This descriptive cross-sectional study was conducted at the Navy General Hospital Colombo from November 1, 2021, to December 30, 2021. The study included 79 COVID-19 positive navy personnel diagnosed within three months prior to the assessment. Patients with a history of ocular or systemic disorders that could affect retinal findings were excluded.

Retinal assessments included visual acuity tests, slit-lamp biomicroscopy, and macular OCT imaging. The macular thickness was measured using the ETDRS grid, and results were compared with normative data from the Cirrus HD OCT machine. Additionally, the study's findings were compared with published data from similar studies conducted in various countries.

Results

Demographic and Clinical Characteristics:

Table 1. Age and the gender distribution of the sample

Age group	*Male*	*Female*	*Total (%)*
18-24	7 (8.86%)	1 (1.26%)	8 (10.12%)
25-31	15 (18.98%)	3 (3.79%)	18 (22.78%)
32-38	34 (43.03%)	2 (2.53%)	36 (45.56%)
39-45	16 (20.25%)	00	16 (20.25%)
>46	1 (1.26%)	00	1 (1.26%)
Total	73 (92.41%)	6 (7.59%)	79 (100%)

χ^2(df=2) = 3.48: p=0.1748 (rows 3-5 amalgamated). Therefore, the sample could be considered as compatible to each other.

The study included 158 eyes from 79 participants, with a mean age of 34.2 ± 5.75 years. Similar to findings in studies by Sim et al [1] and Louzada et al [2], our study found no significant changes in visual acuity, with 98.73% of eyes achieving 6/6 best-corrected visual acuity.

Slit-Lamp and Fundus Examination:

Table 2. Duration between the diagnosis of COVID-19 and examination of the patient

Duration between Diagnosis of COVID-19 and eye examination (day)	*Rapid Antigen Test (RAT)*	*Reverse Transcription Polymerase Chain Reaction Test (RT-PCR)*	*Total*
10-30	24 (30.3)	1 (1.2)	25 (31.65)
31-60	28 (35.44)	4 (5.1)	32 (40.51)
61-90	18 (22.78)	4 (5.1)	22 (27.84)
Total	70 (88.61)	9 (11.39)	79 (100)

Slit-lamp biomicroscopy revealed follicular conjunctivitis in 40.5% of eyes, a finding that correlates with Burgos-Blasco et al[3], who reported conjunctival involvement in a significant portion of their COVID-19 cohort. However, our study did not observe any significant corneal, lens, or anterior chamber changes, consistent with reports by Cennamo et al[4].

Table 3. Frequency of general symptoms in the sample

Characteristic	*Present (%)*	*Absent*	*Total*
Fever	60 (75.94)	19 (24.06)	79 (100)
Malaise	48 (60.75)	31 (39.25)	79 (100)
Total with general symptoms	63 (79.74)	16 (20.26)	79 (100)

The majority of the participants 79.74% complained of general symptoms with 75.94% having fever and 60.75% with generalized malaise.

χ^2(df=1) = 4.21: *p=0.04*, The result is significant at p<.05 level. The fever and malaise were present in a significantly higher number of participants.

Table 4. Frequency of ocular symptoms in the sample

Characteristic	*Present (%)*	*Absent*	*Total*
Blurred vision	8 (10.12%)	71 (89.87%)	79 (100)
Red eyes	24 (26.96%)	55 (69.62%)	79 (100)
Irritation	21 (26.58%)	58 (73.41%)	79 (100)
Total	25 (31.64%)	54 (68.35%)	79 (100)

Only 25 (31.64%) of participants complained of any ocular symptoms, mainly red eyes (26.96%) and irritation (26.58%).

χ^2 (*df* = 1) = 9.5089: *p=0.008*, The result is significant at p<.05 level. The blurred vision, red eyes and irritation were absent in a significantly higher number of participants.

CT Findings:

Table 5. Mean values of OCT macular thickness: ETDRS macular cube 512×128

Characteristic	*Left (Mean+SD)*	*Right (Mean+SD)*	*Normative values*	*P value*
Central Fovea	240.19±20.21	241.17±20.66	(220.5-294.8)	0.6702
Inner Superior Macula	319.21±17.26	318.52±15.77	(295.2-344.6)	0.7109
Inner Nasal Macula	318.89±15.74	319.11±16.13	(296.9-347.7)	0.9024
Inner Inferior Macula	316.20±12.93	317.74±13.12	(292.4-342.3)	0.2941
Inner Temporal Macula	305.48±13.22	307.20±14.09	(285.1-333.0)	0.2640
Outer Superior Macula	276.82±12.22	277.15±10.48	(254.1-293.8)	0.7968
Outer Nasal Macula	296.00±18.95	295.58±16.11	(263.8-312.5)	0.8320
Outer Inferior Macula	266.22±12.30	266.77±12.38	(245.7-280.4)	0.6923
Outer Temporal Macula	59.82±10.13	258.93±9.09	(239.3-278.6)	0.4117

Mean values of OCT macula thickness does not show any significant difference between two eyes. There is no significant deviation of mean values from the reference ranges.

Table 6.

Characteristic	*Number of below the reference range (%)*	*Number of right eyes below the reference range (%)*	*Number of left eyes above the reference range (%)*	*Number of right eyes above the reference range (%)*	*Total number of eyes outside the reference range (%)*
Central Fovea	10 (21.73)	9 (19.56)	1 (2.17)	1 (2.17)	21 (45.65)
Outer Temporal Macula	2 (4.34)	2 (4.34)	2 (4.34)	1 (2.17)	7 (15.21)
Outer Superior Macula	2 (4.34)	1 (2.17)	4 (8.69)	2 (4.34)	9 (19.56)
Outer Nasal Macula	0	0	5 (10.86)	6 (13.04)	11 (23.91)
Outer Inferior Macula	2 (4.34)	2 (4.34)	1 (2.17)	1 (2.17)	6 (13.04)
Inner Temporal Macula	3 (6.52)	3 (6.52)	1 (1.2)	3 (6.52)	10 (21.73)
Inner Superior Macula	3 (6.52)	5 (10.86)	1 (1.2)	3 (6.52)	12 (26.09)
Inner Nasal Macula	1 (2.17)	1 (2.17)	1 (2.17)	0	3 (6.52)
Inner Inferior Macula	2 (4.34)	1 (2.17)	0	2 (4.34)	5 (10.86)
Cube Volume	2 (4.34)	2 (4.34)	2 (4.34)	1 (2.17)	7 (15.21)
Cube Average Thickness	2 (4.34)	2 (4.34)	2 (4.34)	3 (6.52)	9 (19.56)

The OCT imaging revealed macular thickness deviations in 46 eyes (29.11%), with 23 eyes showing increased thickness and 23 showing decreased thickness. The central foveal region was the most affected, similar to findings by Invernizzi et al[5], who also reported significant changes in the central macula in COVID-19 patients. The absence of microvascular changes on fundus examination contrasts with the findings of Sim et al[1], who observed microhemorrhages and vascular tortuosity in a subset of their patients.

Discussion

The findings of this study align with a growing body of evidence suggesting that COVID-19 can cause subtle yet significant changes in the retina, detectable primarily through advanced imaging techniques such as OCT. The retinal changes observed in this study, particularly the deviations in macular thickness, are consistent with those reported in similar studies from other countries, indicating that these ocular manifestations may be a common consequence of COVID-19.

Mechanisms of Retinal Involvement: The exact pathophysiological mechanisms underlying COVID-19-related retinal changes are not fully understood, but several hypotheses have been proposed. One possibility is that SARS-CoV-2 directly infects retinal cells, given that the ACE2 receptor, which the virus uses to enter cells, is expressed in the retina. Another potential mechanism is the systemic inflammatory response triggered by COVID-19, which could lead to microvascular damage and subsequent retinal changes. This is supported by findings from studies like those of Marinho et al[6] and Pereira et al[7], which reported retinal microvascular abnormalities in patients with severe COVID-19.

Comparison with Global Findings: Our study's finding of significant macular thickness deviations is in line with the results of studies by Burgos-Blasco et al[3] and Cennamo et al[4], both of which reported changes in retinal thickness and the retinal nerve fiber layer (RNFL) in post-COVID-19 patients. The consistency of these findings across different populations and healthcare settings suggests that retinal involvement may be a common feature of COVID-19, regardless of geographical location. However, it is important to note the differences in the types and prevalence of retinal changes reported in different studies. For instance, while Louzada et al[2] found retinal vascular lesions in severely ill patients, our study, which involved a younger and healthier cohort, primarily detected macular thickness changes without overt vascular lesions. This suggests that the severity of retinal involvement may be correlated with the severity of the systemic disease.

Clinical Implications: The absence of significant changes in visual acuity and slit-lamp findings in our study highlights the importance of OCT as a diagnostic tool for detecting subtle retinal changes in COVID-19 patients. Given the potential for these changes to go unnoticed in routine ocular examinations, OCT screening may be warranted for COVID-19 patients, particularly those with neurological symptoms or other risk factors for ocular involvement.

Limitations

This study has several limitations that should be acknowledged. First, the study population consisted of young and relatively healthy navy personnel, which may limit the generalizability of the findings to older or more diverse populations. The absence of severe COVID-19 cases in our cohort could explain the lower incidence of more significant retinal changes, such as microvascular abnormalities, observed in other studies involving critically ill patients.

Second, the sample size of 79 participants is relatively small, which may limit the statistical power of the study and the ability to detect less common retinal changes. Larger studies with more diverse populations are needed to confirm these findings and to better understand the spectrum of retinal involvement in COVID-19.

Conclusions

This study provides further evidence that retinal changes are a notable consequence of COVID-19, consistent with findings from other parts of the world. The significant proportion of patients with macular thickness deviations highlights the need for routine OCT screening in post-COVID-19 patients, particularly those with neurological symptoms or other risk factors for ocular involvement.

Recommendations

- Further longitudinal studies with larger sample sizes and diverse populations are necessary to better understand the long-term ocular effects of COVID-19 and the mechanisms underlying retinal changes.

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