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The prevalence of central retinal vein occlusion was observed in middle age patients with post-covid syndrome multicenter study

Sanaa Ahmed[1*], Ahmed Elmahdy[2], Eglal Kenawy[3], Marwa Abdulrehim[4], Samar Shoeir[5], Ghada Elmohaseb[6], Eman Youssef[7], Eman Bayoumy[7], Marwa Byomy[8]**

[1]Ophthalmology Department, Al-Zahraa Hospital, Al-Azhar University, Cairo, Egypt; [2]Ophthalmology Department, El-Hussein, University Hospital, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.; [3]Internal Medicine Department, Al-Azhar University Hospital, Faculty of Medicine for Boys, Al-Azhar University Assiut Branch, Egypt.; [4]Internal Medicine Department, Al-Azhar University Hospital, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt.; [5]Ophthalmology Department, Al Fayoum Ophthalmology Hospital, Al Fayoum, Egypt.; [6]Internal Medicine Department, Al-Azhar University, Faculty of medicine for Girls, Al-Azhar University, Cairo, Egypt; [7]Biochemistry Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt; [8]Clinical Pathology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

***Corresponding author:** Sanaa Ahmed Mohamed, Ophthalmology Department, Al-Zahraa Hospital, Al-Azhar University, Cairo, Egypt.

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ABSTRACT

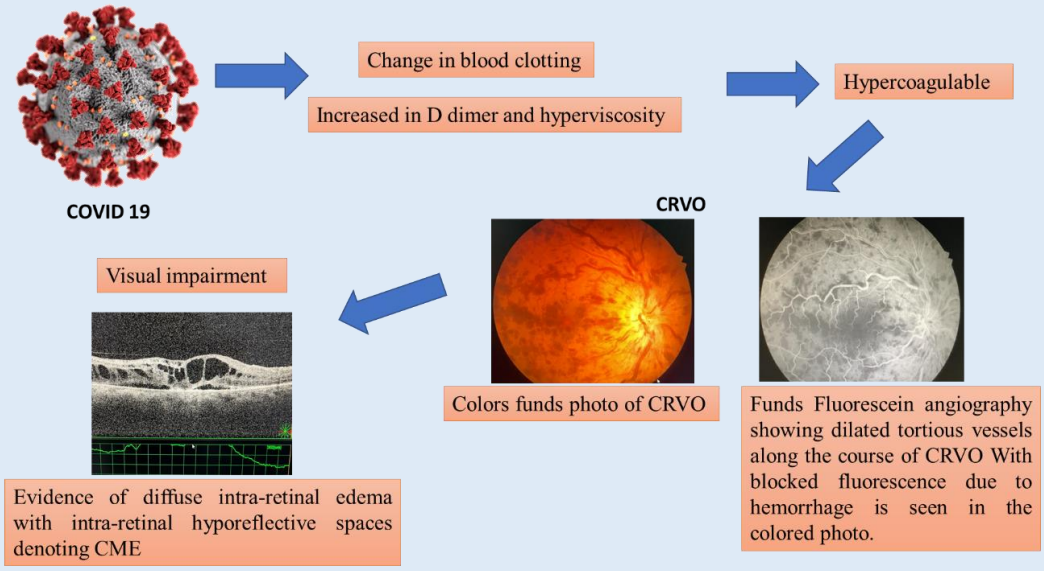
Background: The World Health Organization pronounced the Coronavirus disease (COVID-19) a pandemic on March 11, 2020. Patients with COVID-19 are more likely to have multisystem thromboembolic events, such as deep vein thrombosis and pulmonary emboli**.** This study estimates the clinical characteristics of patients with central retinal vein occlusion (CRVO) post-COVID-19 infection in three governorates of Egypt**.**

Methods: A retrospective randomized study was conducted at Al-Azhar University Hospitals. We revised medical records for patients presented to Ophthalmology departments with CRVO. We considered all patients above 30 years old of both sexes without risk factors for central vein occlusion.

Results: Central retinal vein occlusion was observed in post-COVID syndrome at younger ages, rather than the ordinary cases. The most presenting symptoms were fever, dyspnea, and a cough with significant hypoxia and elevated D-dimer level.

Conclusion: Our study asserts the importance of more investigation into ocular complications associated with COVID-19. Physicians should be vigilant for acute visual symptoms in COVID-19 patients. Patients presenting with thromboembolism should be screened for COVID-19 infection as a presumed etiology. D-dimer may have an important prognostic value for disease severity. Anti-coagulant medications may be required on a long-term basis after COVID-19 infections.

Keywords: acute visual symptoms, ophthalmic evaluation, thromboembolism



INTRODUCTION

Post-acute COVID syndrome are the implications that are presented during or post-infection with COVID-19. The syndrome presents for 12 weeks or more and is only referred to as a kind of viral infection [1-3]. The common symptoms of post-COVID infection include dyspnea, fatigue, chest pain and the recent appearance of other clinical manifestations, such as neurological manifestations which are rare, as well as thromboembolic complications, like Guillain-Barré syndrome. In contrast, the long-term consequences of this infection are still unclear [4-6].

The post-COVID syndrome pathogenesis is multifactorial. There are many mechanisms that may be involved in different manifestations. For instance, long-term inflammation possesses a key effect on the pathogenesis of COVID infection. Other mechanisms include thromboembolism, immune-mediated vascular and neural disorders [7, 8]. 1500 Since the initial stage of the pandemic, significant coagulopathy, multiple infarctions and antiphospholipid antibodies have been reported in COVID-19 patients [9].

Severely ill patients and those who require ICU admission may have a 20 % risk of venous

thromboembolism (VTE) [10-12]. The validity of thrombotic manifestations is suggested by recent reports as an early symptom of COVID-19 [13]. Additionally, many investigations were published on case reports to document retinal vein occlusions after COVID [14-19]. The incidence of central retinal vein occlusion (RVO) is the second most common vascular disorder after diabetic retinopathy [20]. The vein occlusion can be divided into two types: branchial and central. The occlusion site is at the optic nerve's lamina cribrosa [21]. CRVO is further divided into ischemic and non-ischemic, each of which has ramifications for prognosis and treatment [22]. The pathogenesis of central retinal occlusion is believed to follow the principles of Virchow's triad for thrombo-embolic mechanisms, involving hypercoagulability, stasis and vessel damage [23]. The central retinal artery and vein share a posterior adventitial sheath posterior to the lamina cribrosa at the arteriovenous crossing, so that atherosclerotic changes of the artery may compress the vein and accelerate CRVO [24].

Few studies were conducted to evaluate the relationship between central retinal vein occlusion and post-COVID syndrome in limited cases (case studies) [4, 16, 17]. In contrast, this relation to a large number of patients was not evaluated. Therefore, a systematic review summarizes 55 publications describing 10 patients diagnosed with central retinal vein occlusion (CRVO) secondary to COVID-19 [25]. The study aimed to evaluate the relationship between central retinal vein occlusion (CRVO) in patients with post-COVID syndrome in three different governorates in Egypt. The assessment may help to decrease the risk of blindness after COVID-19 infection.

MATERIALS AND METHODS

Materials: Twenty-six patients complaining of diminution of vision have been classified into three groups according to admitted time in the hospitals in three waves: wave one from March to August 2020, wave two from December 2020 to April 2021, and wave three from June to December 2022-- with over 1500 of total patient admission in our hospitals. We reported all available information of patients, including age, sex, history of ocular/system diseases, and history of confirmed COVID-19 infection (Clinically, in the form of fever, cough, diarrhea, myalgia, and/or anosmia together with positive radiological findings and/or positive PCR nasal swab) within the last 120 days, history of contact with a proven case of COVID-19 within the last 120 days, and the use of any medications, especially anti-coagulants or aspirin.

Study design: A retrospective cohort randomized study was conducted at Al-Azhar University Hospitals (Al-Zahraa and El-Hussein, Assiut, Hospitals) in Cairo and Assiut, Egypt. As a result, we revised medical records for patients presented to Ophthalmology departments with CRVO between March 2020 and December 2021. Those patients had pretested at outpatient clinics of Ophthalmology Departments by diminution of vision without risk factors, except for a history of COVID-19 infection.

Inclusion criteria: We considered all patients above 30 years old of both sexes without risk factors for central vein occlusion.

Exclusion criteria: We excluded patients with autoimmune disorders, hyper/hypothyroidism, pregnant females, and females receiving oral contraceptive medication.

Ethical considerations: The study adhered to the principles of the Al-Azhar Medical Research Ethical Committee (No. 0000052), according to the Declaration of Helsinki. Patients gave their written agreement to the use of their information in the study and the researchers

de-identified patient data before including it in the database.

METHODS

Laboratory investigations: We evaluated available laboratory results that included CBC (lymphocyte% neutrophil %, platelet count, and Hb), CRP, Ferritin, serum urea, serum creatinine, Alanine aminotransferase, aspartate aminotransferase, serum sodium, serum potassium, blood glucose level, arterial blood gases, D-dimer and anti-COVID-19. IgG and IgM antibodies were conducted by rapid test Artron COVID-19 IgM/IgG Antibody Test, Artron Laboratories, Canada).

Ophthalmological examination and investigations*:* Data of ophthalmological evaluation were reported, including uncorrected visual acuity test, best corrected visual acuity, IOP measurement, slit-lamp biomicroscopy, fluorescein angiography, and OCT macular assessment. *Statistical analysis:* SPSS (V. 28.0, IBM Corp., USA) was performed for the data. In addition, descriptive statistics, and frequency of the studied variables [26]. Test Variance analysis carried out quantitative results with the Levene test's parametric and non-parametric distribution. For data with normal distribution, One-Way ANOVA was applied [27].

RESULTS: The descriptive statistics of demographic and vital data are depicted in Table 1. The study included 26 different patients, 9 females (34.6%) and 17 males (65.4%), with ages ranging from 40-65 years old (main age 54.92 ± 7.66) (Table 1). One patient had a history of hypertension. All patients gave a history of confirmed COVID-19 diagnosis within the last 120 days. There were only 4 patients with a history of ICU admittance (15.4%). The most presenting symptoms were fever (76.9%), cough (73.1%), and dyspnea (61.5%) (Table 1). All patients had positive anti-COVID-19 IgG antibodies denoting exposure to the previous infection of COVID-19, Although the elevated level of CRP (median (IQR) 44 (24 – 96)), D-Dimer (median (IQR) 0.72 (0.6 0.6– 0.8)) and serum ferritin {median (IQR) 555 (199 – 1347) had been noted in other laboratory investigations, the results are shown in Table 2. These results indicated that CRVO could affect COVID patients younger than 50 years.

Laboratory investigation results showed that all patients had positive anti-COVID-19 IgG antibodies, denoting exposure to the previous infection of COVID-19. The D-dimer range was 0.1 - 4. Other laboratory findings are reported in Table 2.

Table 1. Demographic and clinical data of The Twenty-six Post COVID Cases

clinical data	**No.**	**%**	Demographic and vital data		**No. = 26**
Dyspnea	16	61.5%	Age /year	Mean±SD	54.92 ± 7.66
Cough	19	73.1%		Range	40 – 65
Sputum	4	15.4%	Sex	Male	17 (65.4%)
Fever	20	76.9%		Female	9 (34.6%)
Chest pain	7	26.9%	Site of admission	Ward	22 (84.6%)
Gastritis	8	30.8%		ICU	4 (15.4%)
Diarrhea	7	26.9%	Systolic blood pressure	Mean±SD	123.46 ± 14.13
Sore throat	2	7.7%		Range	100 – 140
Rhinitis	2	7.7%	Diastolic blood pressure	Mean±SD	75.38 ± 8.11
Hypertension	1	3.8%		Range	70 – 100
Diabetes mellitus	0	0.0%	Pulse	Mean±SD	96.00 ± 13.76
Other symptoms or chronic diseases	0	0.0%		Range	64 – 112

Table 2. Laboratory Data of The Twenty-Six Post COVID Cases

Blood glucose (mg/dl)	**Mean±SD**	**116.52 ± 24.42**
	Range	72 – 158
Blood urea (mg/dl)	Median (IQR)	27 (23 – 50)
	Range	14 – 101
Serum creatinine (mg/dl)	Median (IQR)	1.2 (0.9 – 1.5)
	Range	0.7 - 7
HB (g/dl)	Mean±SD	12.59 ± 1.17
	Range	10 - 14.1
Total WBC count thousands/cmm	Median (IQR)	5.9 (4.4 – 7.8)
	Range	2.9 - 27.5
Absolute lymphocytic count /10^9/L	Median (IQR)	1.3 (0.8 – 1.6)
	Range	0.3 - 3.7
Absolute Neutrophils count / 10^9/L	Mean±SD	3.5 (2.5 – 6.9)
	Range	0.8 - 23.6
Platelet count thousands/cmm	Median (IQR)	243 (169 – 302)
	Range	88 - 650
Monocytes percentage %	Median (IQR)	0.5 (0.294 – 0.616)
	Range	0.1 - 2
C reactive protein (mg/dl)	Median (IQR)	44 (24 – 96)
	Range	15 - 205
D dimer (mg/dl)	Median (IQR)	0.72 (0.6 – 0.8)
	Range	0.1 - 4
Serum ferritin (ng/ml)	Median (IQR)	555 (199 – 1347)
	Range	120 - 1872
Na (mmol/dl)	Median (IQR)	135.75 ± 3.87
	Range	131 - 144
K (mmol/dl)	Mean±SD	3.47 ± 0.49
	Range	2.7 - 4
AST (U/L)	Median (IQR)	31.5 (22 – 45.5)
	Range	6 - 200
ALT (U/L)	Median (IQR)	22 (15 – 27)
	Range	3 - 240
PH	Mean±SD	7.42 ± 0.08
	Range	7.23 - 7.52
PCO_2 / mmhg	Mean±SD	37.60 ± 9.79
	Range	21 - 67
PO_2 / mmhg	Mean±SD	67.25 ± 20.73
	Range	27 - 106
HCO_3 mmol/l	Mean±SD	25.05 ± 5.99
	Range	13 - 38.9
SO_2 %	Mean±SD	90.86 ± 7.92
	Range	62 - 98

Hb; hemoglobin, WBC: White blood cells, Na; sodium, K; potassium, AST; Aspartate Transferase, ALT; Alanine Aminotransferase, IQR; Interquartile range, SD; standard deviation

Ophthalmic examination results showed that there was a BCVA range of 0.1-1 (Decimal equivalent), an IOP range of 10-21mm Hg, one patient had a sclerotic lens, and another one had a cataractous lens. In regard to a fundus examination, all cases had unilateral CRVO, the other eye showed no abnormality in 25 patients, and 1 patient had hypertensive retinopathy (grade 3). OCT Examination showed a central retinal thickness range of 313-659 (mean 462.93±110.8). FFA examination proved that only 5 patients were ischemic, while the remaining 21 were non-ischemic (Table 3).

Table 3. Ophthalmology Parameters of The Twenty-Six Post COVID Cases

Parameters	Mean±SD	No. = 26
V/A	Mean±SD	0.40 ± 0.20
	Range	0.1 - 1
IOP	Mean±SD	14.35 ± 3.57
	Range	10 - 21
EYE	Os	11 (42.3%)
	Od	15 (57.7%)
AS	NAD	23 (88.5%)
	Mild Flare	2 (7.7%)
	Mudey Ires	1 (3.8%)
Pupil	RRR	16 (61.5%)
	RAPD	5 (19.2%)
	Slugesh	5 (19.2%)
Lens	Clear	9 (34.6%)
	IMSC	3 (11.5%)
	N Scleroses	5 (19.2%)
	Psdophkia	3 (11.5%)
	PCIOL	3 (11.5%)
	Catractus	3 (11.5%)
Fundus	CRVO	26 (100.0%)
FFA	Non-Ischemic	21 (80.8%)
	Ischemic	5 (19.2%)

BCVA: best corrected visual acuity, IOP: intraocular pressure, AS: anterior segment, CRVO: central retinal vein occlusion, NAD: No abnormality detected, OCT: ocular coherence tomography, Os: Left eye, Od: Right eye, FFA: fundus fluorescein angiography, RRR: Round Regular Reactive, IMSC: Immature senile cataract, RAPD: Relative afferent pupillary defect.

Furthermore, no statistically significant difference had been noted between patient groups regarding age, sex, site of admission, blood pressure and pulse (Table 4). However, in the wave three patients' group, a statistically significant difference had been noted in presenting symptoms like dyspnea, cough, sputum, chest pain, gastritis, diarrhea, anemia, and hypoxia.

The most presenting symptoms were dyspepsia (100%) P value (< 0.023), cough (100%) P value < 0.005, especially in the 3rd wave patients, while gastritis and diarrhea were the next symptoms (88.9%) $p < 0.001$ and (77.8%) $p < 0.001$ respectively in the 3thrd wave patients. Anemia $p < 0.001$, low oxygen saturation $p < 0.001$, and hypoxia $p < 0.02$ were the most laboratory findings in the 3rd wave patients (Table 5).

Table 4. Comparison between The Three Studied Groups Regarding Demographic and Vital Data

		Wave 1	Wave 2	Wave 3	Test value	P-value
		No. = 10	No. = 7	No. = 9		
Age/year	Mean±SD	56.50 ± 8.41	52.29 ± 8.10	55.22 ± 6.72	0.61*	0.55 NS
	Range	40 – 65	41 - 61	42 - 62		
Sex	Male	9 (90.0%)	3 (42.9%)	5 (55.6%)	4.63*	0.09 NS
	Female	1 (10.0%)	4 (57.1%)	4 (44.4%)		
Site of admission	Ward	9 (90.0%)	7 (100.0%)	6 (66.7%)	3.72*	0.15 NS
	ICU	1 (10.0%)	0 (0.0%)	3 (33.3%)		
Systolic blood pressure/mmhg	Mean±SD	121.00 ± 12.87	118.57 ± 14.64	130.00 ± 14.14	1.61‡	0.22 NS
	Range	110 - 140	110 - 140	100 - 140		
Diastolic blood pressure/mmhg	Mean±SD	75.00 ± 5.27	74.29 ± 7.87	76.67 ± 11.18	0.17‡	0.84 NS
	Range	70 – 80	70 - 90	70 - 100		
Pulse	Mean±SD	95.50 ± 19.39	89.57 ± 6.97	101.33 ± 12.54	1.51‡	0.24 NS
	Range	64 - 112	79 - 100	78 – 109		

P > 0.05: Non-significant (NS); ‡: One Way ANOVA test; *: Chi-square test

Table 5. Comparison Between the three studied groups regarding significant clinical and laboratory data

Parameters		**Wave 1**	**Wave 2**	**Wave 3**	**Test value***	**P-value**
		No. = 10	**No. = 7**	**No. = 9**		
Dyspnea	No	6 (60.0%)	4 (57.1%)	0 (0.0%)	8.62*	0.013 S
	Yes	4 (40.0%)	3 (42.9%)	9 (100.0%)		
Cough	No	2 (20.0%)	5 (71.4%)	0 (0.0%)	10.61*	0.005 S
	Yes	8 (80.0%)	2 (28.6%)	9 (100.0%)		
Sputum	No	10 (100.0%)	7 (100.0%)	5 (55.6%)	8.93*	0.012 S
	Yes	0 (0.0%)	0 (0.0%)	4 (44.4%)		
Chest pain	No	8 (80.0%)	7 (100.0%)	4 (44.4%)	6.57*	0.037 S
	Yes	2 (20.0%)	0 (0.0%)	5 (55.6%)		
Gastritis	No	10 (100.0%)	7 (100.0%)	1 (11.1%)	21.83*	<0.001 HS
	Yes	0 (0.0%)	0 (0.0%)	8 (88.9%)		
Diarrhea	No	10 (100.0%)	7 (100.0%)	2 (22.2%)	18.09*	<0.001 HS
	Yes	0 (0.0%)	0 (0.0%)	7 (77.8%)		
HB g/dl	Mean±SD	13.13 ± 0.97	13.52 ± 0.65	11.56 ± 0.73	13.39‡	<0.001
	Range	11.7 - 14.1	12.2 - 13.9	10 - 12		HS
PO_2	Mean±SD	62.57 ±4.50	98.20 ± 7.53	52.00 ± 12.04	42.44‡	<0.001
	Range	54 -67	89 – 106	27 - 65		HS
SO_2	Mean±SD	91.86 ±3.02	96.14 ± 4.49	85.38 ± 10.00	4.81‡	0.020
	Range	88 -95	86 – 98	62 - 93		S

P <0.05: Significant (S); P <0.01: Highly significant (HS), ‡: One Way ANOVA test; *: Chi-square test

There is no significant difference between groups regarding V/A, IOP, eye, AS, and FFA. There are significant differences between groups regarding pupil and lens (Table 6).

Table 6. Comparison between the three studied groups regarding ophthalmology parameters

		Wave 1	Wave 2	Wave 3	Test Value	P-Value
		No. = 10	No. = 7	No. = 9		
V/A	Mean±SD	0.35 ±0.18	0.34 ± 0.16	0.51 ± 0.24	2.05‡	0.15
	Range	0.1 -0.6	0.1 - 0.6	0.3 – 1		NS
IOP	Mean±SD	14.00 ±3.71	13.57 ± 2.70	15.33 ± 4.12	0.54‡	0.59
	Range	10 -19	10 - 17	10 – 21		NS
Eye	OS	4 (40.0%)	1 (14.3%)	6 (66.7%)	4.46*	0.11
	OD	6 (60.0%)	6 (85.7%)	3 (33.3%)		NS
AS	NAD	9 (90.0%)	7 (100.0%)	7 (77.8%)	5.60*	0.23
	Mild Flare	0 (0.0%)	0 (0.0%)	2 (22.2%)		NS
	Mudey Ires	1 (10.0%)	0 (0.0%)	0 (0.0%)		
Pupil	RRR	10 (100.0%)	3 (42.9%)	3 (33.3%)	10.31*	0.036
	RAPD	0 (0.0%)	2 (28.6%)	3 (33.3%)		S
	Slugesh	0 (0.0%)	2 (28.6%)	3 (33.3%)		
Lens	Clear	4 (40.0%)	2 (28.6%)	3 (33.3%)	23.68*	0.009
	IMSC	0 (0.0%)	2 (28.6%)	1 (11.1%)		S
	N Scleroses	3 (30.0%)	0 (0.0%)	2 (22.2%)		
	Psdophkia	3 (30.0%)	0 (0.0%)	0 (0.0%)		
	PCIOL	0 (0.0%)	0 (0.0%)	3 (33.3%)		
	Catractus	0 (0.0%)	3 (42.9%)	0 (0.0%)		
Fundus	CRVO	10 (100.0%)	7 (100.0%)	9 (100.0%)	-	-
FFA	Non-Ischemic	10 (100.0%)	5 (71.4%)	6 (66.7%)	3.93*	0.140
	Ischemic	0 (0.0%)	2 (28.6%)	3 (33.3%)		NS

P > 0.05: Non-significant (NS); P <0.05: Significant (S), ‡: One Way ANOVA test; *: Chi-square test

IOP: intraocular pressure, AS: anterior segment, CRVO: central retinal vein occlusion, NAD: No abnormality detected, OCT: ocular coherence tomography, Os: Left eye, Od: Right eye, FFA: fundus fluorescein angiography, RRR: Round Regular Reactive, IMSC: Immature senile cataract, RAPD: Relative afferent pupillary defect.

DISCUSSION

This study aimed to assess the relationship between central retinal vein occlusion (CRVO) in patients with post-COVID syndrome. COVID-19 is now understood as a thromboembolic disease affecting multiple organs, with the possibility of a thrombotic issue as the earliest presentation [13, 28, 29]. Two possible major mechanisms explain the incidence of vascular damage in COVID-19 disease. Firstly, a viral infiltration of the endothelial cells with COVID-19 leads to a pseudo-vasculitis state. Secondly, the incidence of hypercoagulable conditions, which elevated D-dimer and abnormal coagulation profile, can characterize platelet number and function. Those mechanisms could analyze the association between the probable impact on retinal vascular flow, the circulation of COVID-19 infection and the incidence of a retinal vascular disorder [30, 31].

Since the COVID-19 pandemic announcement, patients presented with recent vascular disorders have been investigated for COVID-19, according to health authorities' recommendation guidelines. Such patients are subjected to a full history of confirmed COVID-19 infection, symptoms suggestive of COVID-19 infection, contact with confirmed COVID-19 patients within the last 4 months, or both conditions. In addition, patients were also subjected to necessary radiological investigation and tested for coagulation profile, Anti-COVID-19 IgM, and IgG antibodies (Ab).

Ocular manifestations of COVID-19 were widely reported as conjunctivitis, retinal vein occlusions, retinal vasculitis, granulomatous uveitis (anterior), choroiditis, retinal detachment, and retinal vasculitis [14, 18]. In our case series, all cases had a history of positive COVID-19 infection over three months and showed positive anti-COVID-19 IgG Ab. In addition, all cases had negative anti-COVID-19 IgM Ab, denoting that none of the reported cases had an acute COVID-19 infection at the time of presentation. One of our reported cases (3.8%) had a systemic disease and hypertension and was known to predispose to retinal vein occlusions. In contrast, other cases had no history of chronic systemic diseases with elevated D dimer, CRP, serum ferritin and decreased Absolute lymphocyte count.

In the herein study, D-dimer highest positive titers were reported in patients with ischemic CRVO. Elevated D-dimer levels have shown a strong positive correlation to clinical severity, prognosis, and complications associated with COVID-19 infection concerning thrombotic sequelae such as pulmonary embolism, stroke, DIC, limb, and digit infarctions [9]. This result agrees with Acharya, et al. [13], who suggested that elevated D-dimer measurement can be used as a predictor of coagulopathy in COVID-19. In addition, the same authors indicated that higher D-dimer levels are directly linked to increased mortality.

COVID-19-positive patients may have around a 20% risk of venous thromboembolism (VTE) and a 3% risk of stroke. The liability of VTE is increased in patients needing intensive care treatment more CU than other patients [13]. Mao, et al. [32] pointed out that nervous system manifestations are significantly more common in serious infections, rather than in mild infections (45.5% vs. 30.2%, $P = 0.02$). Such manifestations include acute cerebrovascular disease, ischemic stroke, and cerebral hemorrhage. Nevertheless, serious conditions put the patient at a higher risk for complications. In our study, all cases with a confirmed COVID-19 infection required hospital admission, four of which were in the ICU. Furthermore, CRVO was reported 3-8 weeks after COVID-19 infection, suggesting that a strong relationship between COVID-19 and vascular eye diseases occurs not only during the active infection but also after the recovery. Occasionally, patients may have passed the infection period, unaware of their ocular symptoms.

In the current investigation, there are wide ranges in the ages of patients. This result is indirectly depicted in the previous case studies. For instance, Sheth, et al. [14] reported a case of RVO in a left eye observed after a COVID infection in a 52-year-old man complaining of decreased visual acuity. This case was observed 10 days after detecting his positive test for SARS-CoV-2. The report refers to the mechanism of thrombo-inflammatory status due to a "cytokine storm" to explain the systemic manifestations of COVID-19. Other reports presumed acute COVID-19 infection as an etiology for CRVO. Infection was confirmed after presentation with ocular symptoms. Venkatesh, et al. [16] reported a 56-year-old female health worker who reported a diminution of vision in her left eye (6/18), the fundus was suggestive of CRVO, and the patient presented with cystoid macular edema in OCT. On the other hand, Walinjkar, et al. [15] reported a case of CRVO in a 17-

years old girl with a confirmed COVID-19 infection 21 days prior to visual symptoms.

Venkatesh, et al. [16] indicated that the laboratory work-up showed an elevation of ESR, D-dimer levels, positive SARS-CoV-2 IgG, and negative IgM. Such case started the treatment with little-dose aspirin of 150 mg/day, and the vision improved over a period of 1 month to (6/6). Yahalomi, et al. [17] found blurry vision and light flashes in the left eye of a 33-year-old man with no other neurological symptoms. This patient suffered from shortness of breath, dry cough and fatigue for a period of three weeks, which ended about 2 weeks before the ocular symptoms. Ophthalmic examination and investigation emphasized a left eye CRVO. During admission, a negative RT-PCR was assessed for SARS-CoV-2. The same case exhibited negative IgM and positive IgG responses for SARS-CoV-2, which indicated recovery from COVID-19.

Marinho, et al. [18] reported 12 adult cases between 25-69 years old with retinitis developed 11–33 days after COVID-19 onset. Virgo and Mohamed [33] reported a COVID-19 patient with an acute macular neuro-retinopathy and a paracentral acute middle maculopathy. Insausti-García, et al. [34] reported a young male patient who recently recovered from COVID-19 and was diagnosed with Papillophlebitis. Walinjkar [35] reported a case of combined central retinal artery occlusion and CRVO with confirmed COVID-19 infection, diagnosed after the presentation. These reports, together with our observations, indicate the risk for retinal vasculopathy should be considered in all cases of COVID-19 infection regardless of disease severity and risk that may extend for several weeks after recovery. Fever, dyspnea, gastritis, and diarrhea all other symptoms can affect the nutrition state of the patients during the disease and may last for a period of time after recovery [36-37]. Supplantation with vitamins, like zinc and vitamin D, needs further studies to evaluate its role in preventing and curing the disease [38-40].

It should be noted that in our study the reported patients received anti-coagulant medications during active COVID-19 infection and were prescribed low-dose aspirin for 8 weeks after recovery. Three patients were receiving low-dose aspirin at the time of presentation. However, they developed CRVO. This may result in questions about preventing vascular thrombosis after COVID-19 regarding medications required, prophylactic doses, and duration of treatment, especially in middle-aged patients without risk factors for thrombosis

This study has several limitations, including its retrospective nature and inherent variance in the assessment approach taken by each investigator. Depending on the clinical discretion of the investigator, this factor may have the greatest impact on outcomes. In addition, as a result of the small sample size and the absence of a control group, we cannot directly compare our findings with those from other populations and studies. It is also possible that the ongoing COVID-19 pandemic has hindered regular clinical care.

CONCLUSION

Patients presenting thromboembolism should be screened for COVID-19 infection as a presumed etiology. Middle aged patients without risk factors to thromboembolic manifestation were in danger after COVID -19 infection. D-dimer may have an important prognostic value for disease severity. Anti-coagulant medications may be required on a long-term basis after COVID-19 infections even in those who did not present risk factors for thromboembolism. Further studies should be conducted on ocular complications accompanied by

COVID-19. Ophthalmic specialists should consider acute visual symptoms in COVID-19 patients.

List of abbreviations: BCVA: best corrected visual acuity, IOP: intraocular pressure, AS: anterior segment, CRVO: central retinal vein occlusion, NAD: No abnormality detected, OCT: ocular coherence tomography, Os: Left eye, Od: Right eye, FFA: fundus fluorescein angiography, RRR: Round Regular Reactive, IMSC: Immature senile cataract, RAPD: Relative afferent pupillary defect.

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