Title: Use of Imaging Technology to Assess the Effect of COVID-19 on Retinal Tissues: A Systematic Review

First author and corresponding Author: Orlaith E McGrath, orlaith.mcgrath@mft.nhs.uk

Affiliations: 1. The University of Manchester, Manchester, UK.

2. Manchester Royal Eye Hospital, NHS Central Manchester University Hospitals, Manchester, UK.

Last Author: Tariq M Aslam

Affiliations: 1. School of Pharmacy and Optometry, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK.

2. Manchester Royal Eye Hospital, NHS Central Manchester University Hospitals, Manchester, UK.

Study	Funding	Study Type	Time post covid	Cohort size (Cases, Controls)	Covid Severity	Study group OCT findings	Study group OCTA findings	Study Group Fundus Photography/ Fundus Autofluorescence findings
Abrisham i et al.	Financial support of the Vice-Chancellor of Research of Mashhad University of Medical Sciences	Case- Control	At least 14 days from symptoms	31, 23	Mild (71%), Severe (29%)		Reduced mean SCP VD and DCP VD; decreased blood flow in the SCP and DCP.	
Beni et al.	Nil	Case- Control	40-95 days post symptom onset	51,37	Moderate		Moderate- intensity SARS-CoV-2 pneumonia had altered peripapillary and macular vessel density	x
Burgos- Blasco et al.	Nil	Case- Control	38.8 days ± 13.3	29,61	Mild	Increase in peripapillary RNFL thickness (global and sectoral)	х	Nil of note
Cennamo et al.	Nil	Case- Control	6 months post hospital discharge	40,40	Moderate		Significant reduction in SCP and DCP VD and Radial	

Banderas García et al.	Nil	Case- Control	8.5 months	56,19	Mild (18) moderate (21) severe (17)		Peripapillary Capillary plexus (RPC) in all sectors; more significant impairment of the DCP than the SCP Persistent reduction in the central vascular area over time in patients with moderate and severe disease
Gonzalez Zamora et al.	Research grants from the "Instituto de Salud Carlos III/European Regional Development Fund (ERDF)" and RD16/0008/0011, OFTARED: Enfermedades oculares: "Prevención, detección precoz, tratamiento y rehabilitación de las	Case- Control	14 days post hospital discharge	25,25	Mod to severe	VCIPL thinning	Thinner ganglion cell layer and thicker retinal nerve fibre layer

patologías oculares".

Guemes Villahoz et al.	Nil	Case- Control	88 days post diagnosis	66,29	Intrathrombotic, no thrombotic event		Lower VD and perfusion density compared to healthy controls	
Hazar et al.	Financial Support: National Medical Research Council Singapore Open Fund Large Collaborative Grant: NMRC/LCG/004/20 18	Case- Control	1 month post-hospital discharge	50,55	Mild to moderate		VD is low in some sectors in both superficial and deep layers, but no change in FAZ	
Invernizzi et al.	Nil	Case- Control	30 days from symptom opnset	54,133	Mild (74%), severe (26%)			Dilated fundus veins (27.7%), CWS (7.4%), retinal haemorrhages (9.25%), Higher MAD and MVD
Oren et al.	Nil	Case- Control	14 to 30 days post symptoms	35,25	Mild	Increased CMT,reduce d GCL and INL thickness	x	
Savastan o et al.	Nil	Case- Control	36.1 days post discharge	70,22	Moderate to severe		Reduced perfusion density and a reduced	

Szkodny et al.	Nil	Case- Control	1-4 months post diagnosis	156,98	Mild to severe	Nil significant found	perfusion flow index of the RPC Nil significant found VD was	
Turker et al.	Nil	Case- Control	Within 1 week post hospital discharge	27,27	Moderate		considerably lower and significantly higher choriocapillar is flow area	
Zapata et al.	Nil	Case- Control	36 days post hospital discharge, 60d post diagnosis	96,27	Mild (24) moderate (24) severe (21)		values The decreased central retina VD was related to COVID-19 infection severity	
Brantl et al.	Nil	Case Series	3 months	21	Mild to Moderate	Nil of note after 3 months of follow up	Nil of note after 3 months of follow up	
Byparedd y et al.	Nil	Case Series	6 days	138	Mild to moderate(hospitalise d)			Nil of note found on examination (1 patient had a retinal streak

Costa et al.	Scholarship from the "Conselho Nacional de Desenvolvimento Científico e Tecnológico" (CNPq) for working with COVID-19 research projects	Case Series	82±36.4 days post symptom onset	64	Mild to moderate (n = 7), severe (n = 33), critical (n = 24)(hospitalised)	haemorrhage, likely incidental) N=2 showed discrete white- yellowish dots in the posterior pole, leading to hypo-reflective changes at the RPE level, outer segment, and ellipsoid layers.
Landecho et al.	Nil	Case Series	14 days post- hospital discharge	27	Moderate Severe, post-hospital discharge	cotton wool spots in six of 27 eyes (22%)
Lani Louzada et al.	Nil	Case Series	2 to 14 days post symptom onset	25	Moderate Severe, (hospitalised)	microhemorrhage s, flame-shaped haemorrhage and nerve fibre layer infarcts
Marinho et al.	Nil	Case Series	Mean 44 days post covid diagnosis	18	Mild to severe	Hyper- autofluorescence findings were present in 6 patients, Hypo- autofluorescence in 14 patients and six patients had mixed pattern lesions.

Pereira et al.	Nil	Case Series	11.5 days	18	Severe (hospitalised)			Flame hemorrhages (n = 4) CWS (n = 4) Flame hemorrhages and CWS (n = 1) Peripheral hemorrhages (n = 2) Acute retinal ischaemia (n=1)
Pirraglia et al.	Nil	Case Series	21.5 days post hospitalisatio n	46	Mild to severe (hospitalised)	х	x	No sign of retinal involvement seen
Sim et al.	Nil	Case Series	16 days post- diagnosis	108	Mild (not hospitalised)			

Study	Study Type	Age	Covid Severity	Ocular Symptoms	Monocular?	ОСТ	ОСТА	Fundus Photography/Fundus autofluorescence	Fundus Exam
Conrady et al.	Case Report	40		Visual loss	Monocular	White-dot-like outer retinopathy	White-dot- like outer retinopathy	white-dot-like outer retinopathy	
Dumitrascu et al.	Case Report	48	Severe	Acute visual loss	Monocular	Acute macular neuroretinopathy			Incomplete OAO
Gascon et al.	Case Report	53	Mild	acute loss of vision	Monocular	and paracentral acute middle maculopathy			

Gonzalez-	Case			Arcuate VF			SCP ischemia which corresponds to the arcuate scotoma observed on		
Lopez et al.	Report	50	Mild	defect	Monocular		VF testing		
Ortiz-Egea et al.	Case Report	42	Mild	Scotoma		Hyperreflective, placoid band at the GCL and IPL acute posterior	J		
Olguín- Manríquez	Case					multifocal placoid pigment		Multiple yellow- white placoid lesions	
et al.	Report	35	Mild	Visual loss		epitheliopathy Inner retinal thinning temporal to the fovea in both eyes, and focal	Bilateral areas of nonperfusion	involving the fovea	
Ortiz-						disruptions of the	at the level of	Weak hyper	
Seller et	Case			Retro-		outer retinal	the	autofluorescence of	
al. Virgo and	Report	51	Mild	orbital pain	Binocular	layers	choriocapillaris	lesions	
Mohamed et al. Virgo and	Case Report	37	Mild	Paracentral scotoma		PAMM			
Mohamed	Case			Paracentral					
et al. Acharya et	Report Case	32	Mild	scotoma		AMN			
al.	Report	60	Severe	Visual loss	Monoocular	X	Х	X	CRAO

Serous macular
Case Reduced detachment and
Sheth et al. Report 52 vision Monocular significant CMO x

BRVO, HRVO

BRVO, HRVO

x not done

RNFL Retinal Nerve Fiber Layer

RPC radial peripapillary capillary

MAD Mean Artery Diameter

MVD Mean Vein Diameter

SCP Superficial Capillary Plexus

CMO cystoid macular oedema

FAZ Foveal Avascular Zone

VD Vessel Density

CWS Cotton Wool Spots

OAO Ophthalmic Artery Occlusion

CRAO Central Retinal Artery Occlusion

BRVO Branch Retinal Vein Occlusion

HRVO Hemiretinal Vein Occlusion

PAMM Paracentral Acute Middle Maculopathy

AMN Acute Macular Neuroretinopathy