



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Contents available at [ScienceDirect](#)

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation



Letter to the Editor

Retinal findings in COVID-19 patients with diabetes mellitus



Noemi Guemes-Villahoz^{a,*}, Barbara Burgos-Blasco^a, Juan Donate-Lopez^b,
Julian Garcia-Feijoo^b

^a Department of Ophthalmology, Hospital Clínico San Carlos, Madrid, Spain

^b Department of Ophthalmology, Instituto de investigación sanitaria del Hospital Clínico San Carlos (IsISSC), IIORC, Universidad Complutense, Spain

To the editor,

We read with great interest the correspondence by Dr. Raony and Dr. Saggiore de Figueiredo, describing the possible role of CD147 in retinal findings observed in coronavirus disease 2019 (COVID-19) patients with diabetes mellitus (DM) [1]. Recent experimental and clinical findings suggested transmembrane glycoprotein CD147, also termed Basigin, may represent a novel receptor for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) entry into host cells [2]. Since CD147 is expressed at moderate-to-high levels in human retina [3] and has also proven to be an essential molecule for blood-retinal barrier impairment in streptozotocin-induced diabetic mice [4], the authors suggested an intriguing hypothesis.

At present we are passing through a phase of slow and difficult understanding of the clinical spectrum and the emerging short- and long-term complications caused by SARS-CoV-2 infection. In this sense, the retinal involvement has drawn attention as a possible biomarker of microangiopathy in COVID-19 patients [5]. Marinho et al. reported cotton wool spots (CWS) and microhemorrhages in patients with COVID-19 [6]. However, these findings have been strongly questioned by other authors [7]. Additionally, Landecho et al. recently reported CWS in 6 out of 27 patients evaluated 14 days after hospital discharge due to COVID-19 bilateral pneumonia [5].

CWS represent retinal nerve fiber layer infarcts and may appear in a broad spectrum of diseases, such as diabetic

retinopathy and hypertensive retinopathy among others [5]. As arterial hypertension and DM are common comorbidities encountered in hospitalized patients with COVID-19, it is unclear if CWS represent a true retinal microangiopathy associated with SARS-CoV-2 infection, retinal lesions prior to infection or simply clinical abnormalities related to uncontrolled diseases during the infection.

Our research team has conducted several studies in COVID-19 patients [8–10]. We evaluated a larger sample that included 80 laboratory-confirmed COVID-19 patients (160 eyes). Clinical characteristics of the patients are shown in Table 1. Examination was performed 30 days (28–32) after COVID-19 diagnosis. Every patient underwent fundus examination and optical coherence tomography (OCT). Funduscopy examination of all patients was unremarkable, not revealing cotton wool spots nor retinal hemorrhages.

Considering these contradictory data, further research on COVID-19 retinal outcomes is warranted. We commend the authors on the interesting hypothesis. Whether SARS-CoV-2 infection may precipitate or exacerbate retinal lesions in patients with DM in the short- or long-term requires to be carefully evaluated.

Funding

No funding has been received for the preparation of this manuscript.

* DOI of original article: [10.1016/j.diabres.2020.108280](https://doi.org/10.1016/j.diabres.2020.108280)

* Corresponding author at: Hospital Clinico San Carlos, Ophthalmology Department, Calle del Prof Martín Lagos, s/n, 28040 Madrid, Spain.

E-mail address: noemiguemes@gmail.com (N. Guemes-Villahoz).

<https://doi.org/10.1016/j.diabres.2020.108395>

0168-8227/© 2020 Elsevier B.V. All rights reserved.

Table 1 – Demographic and clinical characteristics of COVID-19 patients.

Variable	N=80
Sex	
Male. No (%)	39 (48,8)
Female. No (%)	41 (51,3)
Age. Mean (SD)	55,8 (8,7)
Medical history	
AH. No (%)	20 (25,0)
DM. No (%)	6 (7,5)
DL. No (%)	21 (26,3)
Clinical severity	
Mild. No (%)	27 (33,8)
Moderate. No (%)	20 (25,0)
Severe. No (%)	33 (41,3)

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

- [1] Raony Í, Saggiore de Figueiredo C. Retinal outcomes of COVID-19: Possible role of CD147 and cytokine storm in infected patients with diabetes mellitus. *Diabetes Res Clin Pract* 2020;165:108280.
- [2] Wang K, Chen W, Zhou Y-S, Lian J-Q, Zhang Z, Du P, et al. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein. *bioRxiv* [Internet]. 2020 Jan 1;2020.03.14.988345. Available from: <http://biorxiv.org/content/early/2020/03/14/2020.03.14.988345.abstract>.
- [3] Hamashima K, Gautam P, Lau KA, Khiong CW, Blenkinsop TA, Li H, et al. Potential modes of COVID-19 transmission from human eye revealed by single-cell atlas. *bioRxiv* [Internet]. 2020 Jan 1;2020.05.09.085611. Available from: <http://biorxiv.org/content/early/2020/05/14/2020.05.09.085611.abstract>.
- [4] Arima M, Cui D, Kimura T, Sonoda K-H, Ishibashi T, Matsuda S, et al. Basigin can be a therapeutic target to restore the retinal vascular barrier function in the mouse model of diabetic retinopathy. Available from. *Sci Rep* [Internet] 2016;6:38445. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27917946>.
- [5] Landecho MF, Yuste JR, Gándara E, Sunsundegui P, Quiroga J, Alcaide AB, et al. COVID-19 retinal microangiopathy as an in vivo biomarker of systemic vascular disease? *J Intern Med* [Internet]. 2020 Jul 30; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32729633>.
- [6] Marinho PM, Marcos AAA, Romano AC, Nascimento H, Belfort R. Retinal findings in patients with COVID-19. *Lancet* (London, England) [Internet]. 2020;395(10237):1610. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32405105>.
- [7] Vavvas DG, Sarraf D, Sada SR, Elliott D, Ehlers JP, Waheed NK, et al. Concerns about the interpretation of OCT and fundus findings in COVID-19 patients in recent Lancet publication. *Eye (Lond)* [Internet]. 2020 Jul 9; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32647303>.
- [8] Burgos-Blasco B, Güemes-Villahoz N, Donate-Lopez J, Vidal-Villegas B, García-Feijóo J. Optic nerve analysis in COVID-19 patients. *J Med Virol* [Internet]. 2020 Jul 10; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32648939>.
- [9] Güemes-Villahoz N, Burgos-Blasco B, Arribi-Vilela A, Arriola-Villalobos P, Vidal-Villegas B, Mendez-Fernandez R, et al. SARS-CoV-2 RNA detection in tears and conjunctival secretions of COVID-19 patients with conjunctivitis. *J Infect* [Internet]. 2020 Jun 3; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32504746>.
- [10] Güemes-Villahoz N, Burgos-Blasco B, Vilela AA, Arriola-Villalobos P, Luna CMR, Sardiña RC, et al. Detecting SARS-CoV-2 RNA in conjunctival secretions: is it a valuable diagnostic method of COVID-19? *J Med Virol* [Internet]. 2020 Jun 24; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32579256>.