# ASSERTION OF A DIDACTIC ILLUSTRATIVE SCHEME OF THE HYPERINFLAMMATORY RESPONSE IN COVID-19

Marcos Jessé Abrahão Silva<sup>1,\*</sup>, Layana Rufino Ribeiro<sup>2</sup>, Maria Isabel Montoril Gouveia<sup>2</sup>, Beatriz dos Reis Marcelino<sup>2</sup>, Karla Valéria Batista Lima<sup>2</sup>, Luana Nepomuceno Gondim Costa Lima<sup>2</sup>

<sup>1</sup> Graduate Program in Epidemiology and Health Surveillance (PPGEVS) of the Evandro Chagas Institute (IEC), Ananindeua, PA, Brazil.

<sup>2</sup> Bacteriology and Mycology Section of the Evandro Chagas Institute (IEC), Ananindeua, PA, Brazil.

\* E-mail: jesseabrahao10@gmail.com

### **1. INTRODUCTION/AIMS**

COVID-19 is a multisystemic disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The immunopathogenic conditions of the hyperinflammatory response that cause systemic inflammation are extremely linked to its severity (Zhou et al., 2020). This work aims to answer the research problem, "What pathogenic aspects of COVID-19 are involved in the progression of the hyperinflammatory response?" and to create a didactic illustrative scheme using an explanatory figure for the hyperinflammatory response of patients with COVID-19.

#### 2. METHODS

This is a systematic review using the PUBMED, LILACS, MEDLINE, and SCIELO databases through articles of the types of clinical trials, case-controls, *in vitro* trials, case reports, cohort, case-control, cross-sectional studies, reviews, and experimental studies between May 2020 and July 2022 with the following search terms in conjunction with "AND": "SARS-CoV-2"; "COVID-19"; "ARDS" and "Cytokine Storm". The quality appraisal and risk of bias were assessed by the JBI checklists and the Cochrane Collaboration's RoB 2.0 and ROBINS-I tools, respectively, and the risk of bias for *in vitro* studies by a pre-defined standard in the literature. From this, the schematic construction was made on paper with office supplies, and, therefore, its digitization and painting in Adobe Photoshop CS6 program.

### **3. RESULTS AND DISCUSSION**

The search resulted in 39 articles. The main actors in this response denote SARS-CoV-2 Spike proteins, cellular proteases, leukocytes, cytokines, and proteolytic cascades. Figure 1 shows the main findings of the hyperinflammatory response in COVID-19 patients. This present work and this Figure have been published in *Viruses* Journal (MDPI) as our article (DOI: 10.3390/V15020553) (Silva et al., 2023).



**Figure 1.** Hyperinflammatory response in patients with COVID-19.

It describes the stages of immune processes in the human body from viral entry into the alveolar epithelial cell (A), the processes of adhesion and recognition by APCs (B), the activation of cell signaling pathways (C), secretion of inflammatory mediators by immune cells responsible for the generation of cytokine storms (D), the recruitment of co-stimulatory molecules of this inflammation (E), activation of proteases, inflammasomes, and coagulation factors (F), as well as the elevation of the patient's clinical parameters that reflect pathological complications (G), which can be related to either local or systemic damage and lead to death (H-I). This didactic illustrative scheme for the hyperinflammatory response to COVID-19 is based on the results of this work. They are represented in chronological order of events by letters (A-Z).

## **4. CONCLUSIONS**

Therefore, the hyperinflammatory response causes several unfavorable outcomes in patients, and systemic inflammation caused largely by the dysregulation of the immune response should be controlled for their recovery.

#### **CONFLICTS OF INTEREST**

The authors declare no conflict of interest.

### REFERENCES

Zhou, F.; Yu, T.; Du, R.; Fan, G.; Liu, Y.; Liu, Z.; Xiang, J.; Wang, Y.; Song, B.; Gu, X.; et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet* **2020**, *395*, 1054–1062. Silva, M.J.A.; Ribeiro, L.R.; Gouveia, M.I.M.; Marcelino, B.d.R.; Santos, C.S.d.; Lima, K.V.B.; Lima, L.N.G.C. Hyperinflammatory Response in COVID-19: A Systematic Review. *Viruses* **2023**, *15*, 553. https://doi.org/10.3390/v15020553