

IMMUNE RESPONSE OF INDIVIDUALS WITH OVERWEIGHT AND OBESITY AFTER RE-EXPOSURE TO SARS-COV-2: SCOPE REVIEW PROTOCOL**RESPUESTA INMUNOLÓGICA DE INDIVIDUOS CON SOBREPESO Y OBESIDAD TRAS LA REEXPOSICIÓN AL SARS-COV-2: PROTOCOLO DE REVISIÓN DE ALCANCE****RESPOSTA IMUNOLÓGICA DE INDIVÍDUOS COM SOBREPESO E OBESIDADE APÓS REEXPOSIÇÃO AO SARS-COV-2: PROTOCOLO DE REVISÃO DE ESCOPO**¹Lorrane de Farias Marques²Maria Hellen Ferreira Brasil³Viviane Cordeiro de Queiroz⁴Dilyane Cabral Frade⁵Bárbara Iansã de Lima Barroso⁶Ana Cristina de Oliveira e Silva

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Submission: 08-04-2025**Approval:** 01-10-2025**ABSTRACT**

Introduction: COVID-19, caused by SARS-CoV-2, resulted in more than 7 million deaths globally and more than 700 thousand in Brazil, with variable clinical manifestations according to the patients' immune response. The dysregulation of the immune response, often associated with the "cytokine storm", contributes to the severity of the disease, especially in obese individuals. **Objective:** To identify scientific evidence on the immune response of individuals with obesity after re-exposure to SARS-CoV-2 antigens. **Method:** This is a scope review protocol, which will be conducted according to the guidelines of the Joanna Briggs Institute (JBI) and Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). The information bases that will be used: Medline via (PubMed), Embase (Excerpta Medica Database - Elsevier), Web of Science, Scopus (Elsevier) and Latin American and Caribbean Health Sciences Literature (LILACS) via Virtual Health Library (BVS), ProQuest (global database of dissertations and theses), Catalog of theses and dissertations and Brazilian digital library of theses and dissertations (BDTD), using the descriptors in health. Articles will be exported to the reference manager Rayyan QCRI, where two independent reviewers will carry out screening, identification and evaluation of studies. In case of disagreement, a third reviewer will be consulted, as recommended by the JBI. It will include original studies available in full and free of charge, in any language and without time cut, that answer the guiding question. Duplicate articles will be deleted. Results will be presented according to PRISMA-ScR guidelines. The protocol was registered in the Open Science Framework (OSF).

Keywords: Immunological Response; Obesity; Covid-19; Reexposure to SARS-CoV-2.

RESUMEN

Introducción: La COVID-19, causada por el SARS-CoV-2, resultó en más de 7 millones de muertes globalmente y más de 700 mil en Brasil, con manifestaciones clínicas variables según la respuesta inmunológica de los pacientes. La disregulación de la respuesta inmune, a menudo asociada con la "tormenta de citocinas", contribuye a la gravedad de la enfermedad, especialmente en individuos obesos. **Objetivo:** Identificar evidencia científica sobre la respuesta inmune de individuos obesos tras la reexposición a antígenos del SARS-CoV-2. **Método:** Se trata de un protocolo de revisión del alcance, que será conducido según las directrices del Joanna Briggs Institute (JBI) y Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). Las bases de información que serán utilizadas: Medline vía (PubMed), Embase (Excerpta Medica Database - Elsevier), Web of Science, Scopus (Elsevier) y Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS) vía Biblioteca Virtual en Salud (BVS), ProQuest (banco global de disertaciones y tesis), Catálogo de tesis y disertaciones y Biblioteca digital brasileña de tesis y disertaciones (BDTD), utilizando los descriptores en salud. Los artículos serán exportados al gestor de referencias Rayyan QCRI, donde dos revisores independientes llevarán a cabo la selección, identificación y evaluación de los estudios. En caso de discrepancia, se consultará a un tercer revisor, como recomienda el JBI. Se incluirán estudios originales disponibles en su totalidad y de acceso gratuito, en cualquier idioma y sin recorte temporal, que respondan a la pregunta orientadora. Artículos duplicados serán excluidos. Los resultados se presentarán según las directrices de PRISMA-ScR. El protocolo fue registrado en el Marco de Ciencia Abierta (OSF).

Palabras clave: Respuesta Inmunológica; Obesidad; Covid-19; Reexposición al SARS-CoV-2.

RESUMO

Introdução: A Covid-19, causada pelo SARS-CoV-2, resultou em mais de 7 milhões de mortes globalmente e mais de 700 mil no Brasil, com manifestações clínicas variáveis conforme a resposta imunológica dos pacientes. A disregulação da resposta imune, frequentemente associada à "tempestade de citocinas", contribui para a gravidade da doença, especialmente em indivíduos com obesidade. **Objetivo:** Identificar evidências científicas sobre a resposta imune de indivíduos com obesidade após reexposição a antígenos do SARS-CoV-2. **Método:** Trata-se de um protocolo de revisão do escopo, que será conduzido conforme as diretrizes do Joanna Briggs Institute (JBI) e Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). As bases de informação que serão utilizadas: Medline via (PubMed), Embase (Excerpta Medica Database - Elsevier), Web of Science, Scopus (Elsevier) e Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) via Biblioteca Virtual em Saúde (BVS), ProQuest (banco global de dissertações e teses), Catálogo de teses e dissertações e Biblioteca digital brasileira de teses e dissertações (BDTD), utilizando os descritores em saúde. Os artigos serão exportados para o gerenciador de referências Rayyan QCRI, onde dois revisores independentes realizarão triagem, identificação e avaliação dos estudos. Em caso de divergência, um terceiro revisor será consultado, conforme preconiza o JBI. Serão incluídos estudos originais disponíveis na íntegra e de acesso gratuito, em qualquer idioma e sem recorte temporal, que respondam à questão norteadora. Artigos duplicados serão excluídos. Os resultados serão apresentados conforme orientações do PRISMA-ScR. O protocolo foi registrado na Open Science Framework (OSF).

Palavras-chave: Resposta Imunológica; Obesidade; Covid-19; Reexposição ao SARS-CoV-2.



INTRODUCTION

Covid-19 is a disease caused by the SARS-CoV-2 virus and, according to the World Health Organization, there have been more than 7 million deaths worldwide since the beginning of the pandemic⁽¹⁾. In Brazil, the total number of deaths exceeded 700,000 cumulative cases⁽²⁾.

The severity of COVID-19 is divided into three main stages: critical, which involves acute respiratory distress syndrome (ARDS), sepsis or septic shock, requiring life support such as mechanical ventilation or vasopressure therapy; severe, characterized by oxygen saturation below 90%, severe pneumonia or signs of respiratory difficulty, including the use of accessory muscles and a breathing rate above 30 per minute; and not severe, with no signs of severity or critical case criteria⁽³⁾.

The immune response plays a crucial role in defense against SARS-CoV-2 and is closely associated with the severity of the infection. In certain cases, the immune response to SARS-CoV-2 may become unregulated and excessive. This process results in an exacerbated production of pro-inflammatory cytokines, such as Interleukin 6 (IL-6) and Interferon γ (IFN γ), characterizing the cytokine storm⁽⁴⁾.

This intense inflammatory phenomenon compromises the homeostasis of the organism and can lead to significant tissue damage, particularly in the lungs, where destruction of alveolar tissue and impairment of gas exchange occurs. The cytokine storm is associated with the development of severe complications, such as acute respiratory distress syndrome (ARDS) and

multiple organ failure. The immune dysregulation observed in these cases is one of the main determinants of Covid-19 severity⁽⁵⁾.

In addition, the severity of COVID-19 and the deregulation of the immune response are especially related to populations at risk, such as obese individuals. Obesity is a multifactorial chronic condition characterized by excessive accumulation of body fat and classified as a public health problem⁽⁶⁾.

The clinical diagnosis of obesity is based on the estimation of body mass index (BMI) which is calculated by the formula: $BMI = \text{weight/height}^2$ (kg/m²). In this sense, the nutritional status can be classified into: Overweight when BMI is between 25.00 – 29.99; Obesity grade I with BMI between 30.00 – 34.99. Obesity grade II when BMI between 35.00 – 39.99; and Obesity grade III when the BMI is greater than 40.00⁽⁷⁾.

The degree of obesity is proportional to the damage caused to the organism and, among these compromises, the Immune System suffers relevant impacts, occurring dysregulation of responses. This fact seems to be associated with a close interaction with adipose tissue, since this tissue houses several innate and adaptive immune cells and the adipocytes secrete various signaling molecules, including adipokines⁽⁸⁾.

The adipokines are signaling molecules produced by adipocytes, among them, leptin has an important role in stimulating pro-inflammatory processes, promoting the production of cytokines such as IL-6, IL-12, IL-18 and TNF α . On the other hand, there are

adipokines that may have an anti-inflammatory role, such as adiponectin, however, their roles are not fully elucidated⁽⁹⁾.

The impairment of immune function by obesity, therefore, may lead to a less efficient immune response and affect the severity of diseases such as Covid-19. In this context, overweight appears as a determining factor for the severity of infection and has a direct impact on the immune response, which reinforces the vulnerability of this population mainly in more severe stages of the disease^(10, 11).

Based on this analysis, this work is justified by the need to deepen the understanding of immunological mechanisms in obese individuals infected with SARS-CoV-2. Whereas COVID-19 has become an endemic condition, and still represents a risk for the vulnerable population and given the understanding of how this condition affects the immune response being crucial to prevent serious complications and guide management strategies that can minimize impacts on public health and reduce associated mortality, The following question arises: what is the scientific evidence available in the literature about the immune response in obese individuals reexposed to SARS-CoV-2 antigen? Therefore, the scope review guided by this protocol will aim to: Know the immune response of overweight and obese individuals after reexposure to SARS-CoV-2 antigens.

METHOD

This is a scoping review protocol, which will be carried out in accordance with the JBI recommendations and the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)⁽¹²⁾. The protocol was registered in the Open Science Framework (OSF registries - DOI 10.17605/OSF.IO/JZ3GD) and is described according to the items in the Template for Scoping Review Protocols⁽¹³⁾.

The guiding question of the review was formulated based on the strategy that takes into account the population, the concept and the context of the object of study, following the acronym PCC, being P = Population (Adults with obesity), C = Concept (Immunological Response) and C = Context (Exposure to SARS-CoV-2 antigen). Thus, the following question was asked: What scientific evidence is available in the literature about the immune response in obese individuals reexposed to SARS-CoV-2 antigen?

The descriptors were identified through the lists available in the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH). The following search strategies will be used:

Chart 1 – Search Strategy Test. João Pessoa, Paraíba, Brazil, 2025.

Databases	Search strategy
Medline through PUBMED	("Immunity"[MeSH Terms] OR "immune response*" [Title/Abstract] OR "immune process*" [Title/Abstract]) AND ("covid 19"[MeSH Terms] OR

	"covid 19"[Title/Abstract] OR "covid 19 pandemic*"[Title/Abstract] OR "sars cov 2 infection*"[Title/Abstract] OR "Coronavirus Disease 2019"[Title/Abstract] OR "Coronavirus Disease-19"[Title/Abstract] OR "covid 19 virus disease*"[Title/Abstract] OR "covid 19 virus infection*"[Title/Abstract]) AND "Obesity"[MeSH Terms]
<i>Embase</i>	('immunity'/exp OR 'immune response':ti,ab,kw OR 'immune process':ti,ab,kw) AND ('covid 19':ti,ab,kw OR 'covid 19 pandemic':ti,ab,kw OR 'sars cov 2 infection':ti,ab,kw OR 'coronavirus disease 2019':ti,ab,kw OR 'coronavirus disease-19':ti,ab,kw OR 'covid 19 virus disease':ti,ab,kw OR 'covid 19 virus infection':ti,ab,kw) AND 'obesity'/exp
<i>Web of Science</i>	TS=("Immunity" OR "Immune Response*" OR "Immune Process*") AND TS=("Obesity") AND TS=("COVID-19" OR "COVID 19" OR "COVID-19 Pandemic*" OR "SARS-CoV-2 Infection*" OR "Coronavirus Disease 2019" OR "Coronavirus Disease-19" OR "COVID-19 Virus Disease*" OR "COVID-19 Virus Infection*")
SCOPUS	TITLE-ABS-KEY ("Immunity" OR "Immune Response*" OR "Immune Process*") AND TITLE-ABS-KEY ("Obesity") AND TITLE-ABS-KEY ("COVID-19" OR "COVID 19" OR "COVID-19 Pandemic*" OR "SARS-CoV-2 Infection*" OR "Coronavirus Disease 2019" OR "Coronavirus Disease-19" OR "COVID-19 Virus Disease*" OR "COVID-19 Virus Infection*")
LILACS through BVS	("Immunity" OR "Imunidade" OR "Inmunidad") AND ("Obesity" OR "Obesidade" OR "Obesidad") AND ("COVID-19" OR "Doença por Coronavírus 2019" OR "Infecção pelo SARS-CoV-2" OR "Pandemia COVID-19" OR "Doença por Novo Coronavírus de 2019")
ProQuest	TS=("Immunity" OR "Immune Response*" OR "Immune Process*") AND TS=("Obesity") AND TS=("COVID-19" OR "COVID 19" OR "COVID-19 Pandemic*" OR "SARS-CoV-2 Infection*" OR "Coronavirus Disease 2019" OR "Coronavirus Disease-19" OR "COVID-19 Virus Disease*" OR "COVID-19 Virus Infection*")
Catalog of theses and dissertations	(Imunidade OR Resposta Imunológica OR Processo Imunológico) AND Obesidade AND COVID-19
Brazilian Digital Library of Theses and Dissertations (BDTD)	(Imunidade OR Resposta Imunológica OR Processo Imunológico) AND Obesidade AND COVID-19

Source: Created by the authors, 2024.

Articles found in databases will be exported to the reference manager Rayyan QCRI, widely used in scope reviews⁽¹⁴⁾. After export, two independent reviewers (first and last author) will eliminate duplicates and read the titles and abstracts to decide on inclusion or exclusion in the sample. At the end, they will compare their results. It will be established

among these reviewers that whenever the title and summary of the studies are not enlightening about the contemplation of the subject, it should be included for the next phase of the research, which will be read in full for decision on inclusion or exclusion in the sample.

It should be noted that the process will be conducted blindly, as provided by the tool itself,

to avoid decision biases. The pre-selected articles will be fully analyzed by the same two authors, and in case of disagreement, a third author will be consulted, acting as arbitrator. This third author has previous experience in the subject and will be responsible for reviewing points of divergence and issuing the final opinion, ensuring methodological consistency and reliability of the selection process.

After the selection of relevant articles, a data collection form will be built in Microsoft Excel version 2015, which will be filled with data from each article of the final sample of the study. This form will include information on article title, country, year of publication, study objectives, study type, participants characteristics and immune response characteristics.

The information relevant to the objective will be extracted using an electronic spreadsheet that includes the variables author/ year, title, database and information relevant to the theme. The results will be presented in tables and tables. The selection process of articles will be detailed by means of the PRISMA-ScR flow chart⁽¹⁵⁾.

The results of this scoping review are expected to allow to map and synthesize, in a comprehensive way, the available evidence on the immune response of overweight and obese individuals after exposure to SARS-CoV-2 antigen. The identification and analysis of the immunological characteristics of this population could provide fundamental subsidies for the understanding of the immunological vulnerabilities associated with overweight,

contributing to the design of more effective preventive and therapeutic strategies against Covid-19 and future viral threats with a similar profile.

In addition, the findings may support public health policies aimed at protecting risk groups, especially in contexts of endemic disease transition, and will provide theoretical and practical support for the conduct of new clinical and laboratory studies. Thus, this review will not only fill relevant gaps in the current scientific literature, but may also positively influence clinical care, protocol formulation and public health planning in the face of epidemics or pandemics involving exacerbated inflammatory response.

REFERENCES

1. World Health Organization. Covid-19 epidemiological update – 15 July 2024, Edition 169. Geneva: WHO; 2024
2. Ministério da Saúde (BR). Covid-19 no Brasil [Internet]. Brasília-DF: Ministério da Saúde; 2024. [cited 2025 Jan 13]. Available from: https://infoms.saude.gov.br/extensions/covid-19_html/covid-19_html.html.
3. World Health Organization. Clinical management of Covid-19: living guideline. Geneva: WHO; 2023 [Internet]. [cited 2025 Jan 15]. Disponível em: <https://iris.who.int/bitstream/handle/10665/372288/WHO-2019-nCoV-clinical-2023.2-eng.pdf?sequence=1>
4. Nezhad MG, Jami G, Kooshkaki O, Chamani S, Naghizadeh A. The role of inflammatory cytokines (Interleukin-1 and Interleukin-6) as a potential biomarker in the

- different stages of covid-19 (Mild, Severe, and Critical). *J Interferon Cytokine Res.* 2023;43(4):147-63. doi: <https://doi.org/10.1089/jir.2022.0185>
5. Alefishat E, Mousa M, Albreiki M, Jelinek HF, Halwachi ZA, Khalili M, et al. Genetic variants and serum profiles of cytokines in covid-19 severity. *Shock.* 2022;59(1):58-65. doi: <https://doi.org/10.1097/shk.00000000000002043>
 6. World Health Organization. WHO acceleration plan to stop obesity. Geneva: WHO; 2023
 7. Liu X, He M, Li Y. Adult obesity diagnostic tool: a narrative review. *Medicine (Baltimore).* 2024;103(17):37946-53. doi: <https://doi.org/10.1097/md.000000000000037946>
 8. Zhou Y, Wang Y, Wu T, Zhang A, Li Y. Association between obesity and systemic immune inflammation index, systemic inflammation response index among us adults: a population-based analysis. *Lipids Health Dis.* 2024;23(1):1-11. doi: <https://doi.org/10.1186/s12944-024-02240-8>
 9. Taylor EB. The complex role of adipokines in obesity, inflammation, and autoimmunity. *Clin Sci (Lond).* 2021;135(6):731-52. doi: <https://doi.org/10.1042/cs20200895>
 10. Almond M, Farne HA, Jackson MM, Jha A, Katsoulis O, Pitts O, et al. Obesity dysregulates the pulmonary antiviral immune response. *Nat Commun.* 2023;14(1):1-14. doi: <https://doi.org/10.1038/s41467-023-42432-x>
 11. Ritter A, Kreis NN, Louwen F, Yuan J. Obesity and covid-19: molecular mechanisms linking both pandemics. *Int J Mol Sci.* 2020;21(16):5793. doi: <https://doi.org/10.3390/ijms21165793>
 12. Aromataris E, Lockwood C, Porritt K, Pilla B, Jordan Z. *JBIM Manual for evidence synthesis.* JBI; 2024. doi: <https://doi.org/10.46658/JBIMES-24-01>
 13. Joanna Briggs Institute. Template for scoping reviews protocols [Internet]. Adelaide: JBI; 2020 [cited 2025 Jan 20]. Available from: <https://jbi.global/scoping-review-network/resources>
 14. Mak S, Thomas A. Uma introdução às revisões de escopo. *J Grad Med Educ.* 2022;14(5):561-4. doi: <https://doi.org/10.4300/JGME-D-22-00620.1>
 15. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. Extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med.* 2018;169:467-73. doi: <https://doi.org/10.7326/M18-0850>

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Authorship Criteria (Author Contributions)

Lorrane de Farias Marques

1. Contributes substantially to the conception and/or planning of the study; 2. Obtains, analyzes, and/or interprets the data; 3. Provides writing and/or critical review and final approval of the published version.

Maria Hellena Ferreira Brasil

1. Contributes substantially to the design and/or planning of the study; 2. Obtaining, analyzing, and/or interpreting the data; 3. Contributes substantially to the writing and/or critical review and final approval of the published version.

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Ana Cristina de Oliveira e Silva

1. contributed substantially to the conception and/or planning of the study; 2. to the collection, analysis, and/or interpretation of data; 3. as well as to the writing and/or critical review and final approval of the published version.

Declaration of Conflict of Interest

"Nothing to declare."

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