

The immune response of SARS-CoV-2 vaccine in population with obesity: a systematic review



Nur Arafah^{1*}, Gatot Soegiarto^{1,2}, Laksmi Wulandari³

¹Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;

²Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;

³Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;

*Corresponding author:

Nur Arafah;
Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia;
nur.arafah15@gmail.com

Received: 2023-02-05

Accepted: 2023-04-22

Published: 2023-05-09

ABSTRACT

Background: COVID-19 vaccines involve a humoral response to produce a neutralizing antibody that could protect subjects from severe COVID-19 infection. However, obesity tends to lower the immune response to the COVID-19 vaccine. Therefore, we conducted a systematic review to determine the immune response of various types of COVID-19 vaccines in a population with obesity.

Methods: We conducted a systematic review based on The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement. Using keywords, we search studies from Taylor & Francis, PubMed, ScienceDirect, Cochrane, and EBSCOHost.

Results: We included eight cohort studies with 21,280 subjects after thorough selection and appraisal. Four studies stated that obesity was related to lower antibody titer post-SARS-CoV-2 vaccination, even though one study stated that obesity was not associated with long-term immune response. Another prospective cohort study involving approximately nine million populations stated that SARS-CoV-2 vaccination provided similar protection against COVID-19 compared to normoweight when underweight was a risk factor for lower protection. One study found that antibody titer wanes faster in obesity compared to normoweight. In addition, another study found lower antibody titer in obese men, whereas no significant findings were found in obese women.

Conclusion: Therefore, it should be noted that COVID-19 vaccination in an obese population tends to provide a lower immune response regardless of vaccine type and doses are given. This should inform clinicians who want to administer the COVID-19 vaccine to obese populations.

Keywords: COVID-19, Efficacy, Immune, Obesity, Vaccine.

Cite This Article: Arafah, N., Soegiarto, G., Wulandari, L. 2023. The immune response of SARS-CoV-2 vaccine in population with obesity: a systematic review. *Bali Medical Journal* 12(2): 1522-1527. DOI: 10.15562/bmj.v12i2.4170

INTRODUCTION

Coronavirus disease (COVID-19) vaccines are hallmark prevention for COVID-19, which has caused a worldwide pandemic. It was known to prevent COVID-19 by inducing the production of neutralizing antibodies. Neutralizing antibodies are produced by the immune response which involves T cells. Administered vaccines turned CD8+ and CD4+ T cells into functional and memory cells. Those cells conjoin with type I interferon to stimulate CD4+ T follicular helper cells to turn B cells into plasma cells which produce antibodies. In addition to the initial immune response, the secondary immune response, which is enhanced by the booster vaccine, involves the production of memory B and T cells before previous exposure. This mechanism created trained immunity and long-term immunological memory.^{1,2}

In general, COVID-19 vaccines provide good immunity against COVID-19 infection. However, several factors affect the immunogenicity of the vaccine, for instance, chronic conditions such as hypertension, including the host's nutritional status. Obesity is proven to improve the severity of infection while decreasing humoral response toward the COVID-19 vaccine.^{3,4} These phenomena are observed as people with obesity have ongoing chronic inflammation alongside impaired immune responses. Obese people tend to have impaired cytokine production, less functional natural killer cells, and an imbalance of CD8+ and CD4+ T cells, which could lead to decreased immune response toward COVID-19 vaccines.^{5,6} Obesity has been observed to wane immune response not only in COVID-19 vaccination but to other vaccination. People with obesity produced less immune responses when compared

to normoweight, which were given the hepatitis B vaccine.⁵ Obesity is also linked with the development of diabetes and hypertension, which also affects the COVID-19 immune response and the severity of the infection.⁷ An initial study by Faizo AA et al. proposed a hypothesis of COVID-19 vaccine immunogenicity in obese patients. The study stated that there was a slightly significant reduction of the population achieving neutralizing antibody response in obese subjects when compared to controls, with a response rate of 82.19% and 97.83%, respectively. The results were hypothesized to be caused by the reduced humoral response in obese patients.⁸

There has been evidence of the impact of obesity on the COVID-19 immune response. However, no synthesis of those studies has ever been created. Therefore, we would like to conduct a systematic review of the antibody response of COVID-19

vaccines in populations with obesity to determine immune response and provide better insights to clinicians who would like to administer the COVID-19 vaccine to these populations. In addition, we would like to provide a better analysis of immune response based on different types of vaccines, thus could provide an immune response profile on each type of vaccine.

METHODS

We conducted a systematic review based on The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.⁹ We determine population, intervention, control, and outcome (PICO) as follows: population of obesity, the intervention of SARS-CoV-2 vaccine administration, control of none (single-armed study), and outcome of the immune response. We search studies from Taylor & Francis, PubMed, ScienceDirect, Cochrane, and EBSCOHost using keywords in Table 1. All studies were selected using criteria with inclusion criteria as follows: (1) clinical trials; (2) including obese population; (3) any SARS-CoV-2 vaccination as intervention; (4) outcome related to immune response. In addition, the following exclusion criteria were applied: (1) patients with end-stage diseases which could affect immune response; (2) patients with immunodeficiency or impairment of immunocompetence; (3) written in a language other than English. Selected studies were included and appraised using critical tools by The Joanna-Briggs Institute, which concluded the study for inclusion or exclusion.¹⁰ Included studies were extracted for characteristics and results, further analyzed qualitatively with results reported below. All processes were done by XX independent reviewers (AA, BB, CC) using keywords in Table 1 for searching and the criteria above for selection. If there is any discrepancy in search or selection findings, a discussion will be conducted to conclude.

RESULTS

We found eight studies, after a thorough search based on Figure 1, which were considered to be included after critical appraisal, as seen in Table 2. Six studies

Table 1. Keywords for studies searching.

Journal	Keywords
PubMed	((“Obesity” [MeSH]) OR (“Body Mass Index” [MeSH])) AND (“COVID-19 Vaccines” [MeSH])
Taylor & Francis	(“COVID-19 Vaccine”) AND (“Body Mass Index” OR “Obesity” OR “Obese”)
ScienceDirect	(“COVID-19 Vaccine”) AND (“Body Mass Index” OR “Obesity” OR “Obese”) – Filter: Research Articles
Cochrane	(“COVID-19 Vaccine”) AND (“Body Mass Index” OR “Obesity” OR “Obese”)
EBSCOHost	(“COVID-19 Vaccine”) AND (“Body Mass Index” OR “Obesity” OR “Obese”)

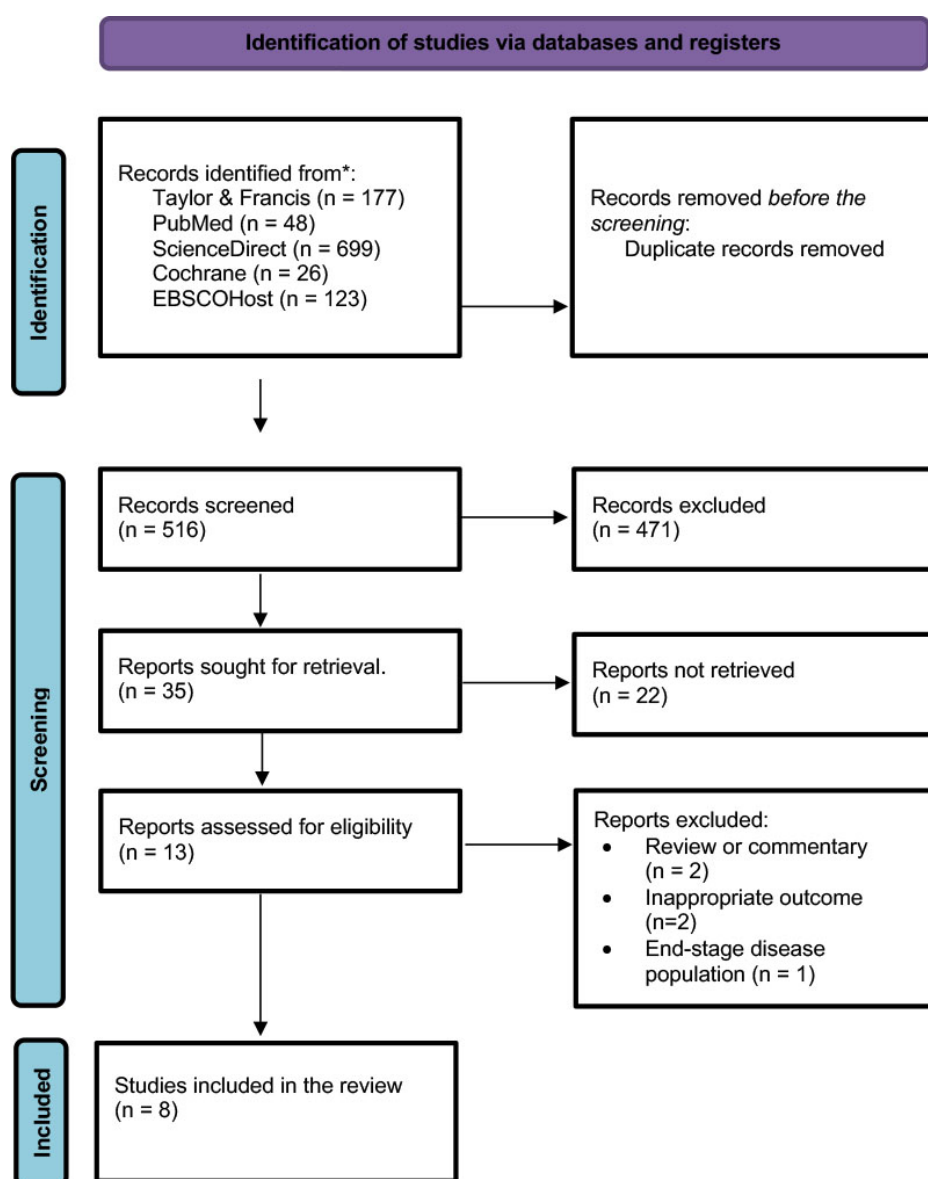


Figure 1. Searching scheme for selected studies.⁹

were conducted in Europe and others in Asia, including 21,280 subjects with dosage administration varying from one to three doses. Patients were follow-up with minimal 2 weeks after administration

of the last dose. Further characteristics, including comorbidities of subjects, were explained further in Table 3.^{8,11-17}

Several studies stated that obesity was related to lower antibody titer post-SARS-

Table 2. Critical appraisal results of selected studies.¹⁰

Study	Type	Appraisal Aspect*											Conclusion	
		1	2	3	4	5	6	7	8	9	10	11		
Alharbi JK et al. ¹¹	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included
Golec M et al. ¹²	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included
Herzberg J et al. ¹³	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included
Kara Z et al. ¹⁴	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included
Malavazos AE et al. ¹⁵	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included
Faizo AA et al. ⁸	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included
Watanabe M et al. ¹⁶	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included
Yamamoto S et al. ¹⁷	C	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	Included

*Based on The Joanna Briggs Institute's critical appraisal tools; Y=Yes; NA: Not Assessed

CoV-2 vaccination, even though one study stated that obesity was not associated with long-term immune response.^{8,12-14,16-19} Study by Malavazos found that antibody titer wanes faster in obesity than normoweight.¹⁵ In addition, Yamamoto S et al. found that lower antibody titer was found in obese men, whereas no significant findings were found in obese women, as seen in Table 4.¹⁷

DISCUSSION

Studies demonstrated lower antibody production in obese populations receiving the SARS-CoV-2 vaccine of any type. Faizio AA et al. showed reduced antibodies response in obese individuals (82.19%) compared to individuals with normal weight (97.83%).⁸ Herzberg J et al. also found that even though there was no significant difference in antibody ratio after nine months, change of initial antibody response, and T cell response between groups, there was significantly lower neutralizing antibody between obese and normal weight subjects with the percentage of 58.68 and 70.07, respectively.¹³ Watanabe M et al. also showed lower antibody titers in obese populations measured by high waist circumference ($R = -0.324$, $p = 0.004$).¹⁷

This phenomenon accounted for excessive body fat in obese populations. Body fat consists of adipose tissue rich in angiotensin-converting enzyme 2 (ACE-2) receptors. SARS-CoV-2 uses the ACE-2 receptor to gain entry to cells to replicate and produce disease. Thus the presence of the ACE-2 receptor in adipose tissue could improve infection possibility and reduce the effectiveness of vaccination.¹⁷

In addition, adipose tissue impairs the immune response.¹⁹ Excessive adiposity could impair B cells, which enhance humoral immunity and provide pro- and anti-inflammatory responses towards diseases. It is also important for producing cytokines, chemokines, and antigen-presenting cells. Therefore, there is a significant reduction of immune response in populations with obesity.²⁰ It is also documented in vaccination of tetanus, influenza, and hepatitis B.²¹⁻²³

Underlying mechanisms are still a hypothesis, including impairment of lymphoid tissue physiology, discoordination between adaptive and innate immunity, lack of antigen-presenting cells, and impairment of the ability to contain the pathogen.^{24,25} These mechanisms also explained that COVID-19 vaccine response tends to wane faster in obese populations compared to normal populations, with a risk ratio of 2.44 fold and 1.82 fold, respectively.¹⁵ However, generally, the COVID-19 vaccine response also tends to wane over time. A study by Levin EG et al. found that IgG antibodies decreased consistently over time, and neutralizing antibodies decreased rapidly in the first three months of vaccination using BNT162b2 COVID-19 vaccines.²⁶ Therefore, obesity should be considered as more antibodies will be depleted compared to the general population with normal weight.

Not only impairs COVID-19 vaccine effectiveness, but obesity also improves the chance of getting a severe COVID-19 infection. It is noted as obesity is correlated to other comorbidities such as diabetes, cerebrovascular diseases, cardiovascular

diseases, and pulmonary disorders.²⁷⁻³⁵ Obese patients also tend to have higher inflammatory activity, which could damage organs earlier in the disease compared to patients with normal weight.²⁸ Therefore, another study noted an improvement in risk for hospitalization by 5 to 10 percent for each increase of 1 kg/m² BMI.²⁹ This could also be explained by obesity which improves lung burden and thus could impact more when a pulmonary disease such as COVID-19 strikes.³⁰⁻³²

Even though obesity could affect damper immunogenicity after COVID-19 vaccination and could worsen COVID-19 progression, COVID-19 vaccines were reported to protect obese patients. Butsch WS et al. reported that COVID-19 vaccines with different types (Pfizer, Moderna, Janssen/Johnson, AstraZeneca) successfully protected obese populations. Its efficiency did not differ significantly between obese and non-obese populations.^{30,31} This was further confirmed by Golec M et al. and Piernas C et al., which studied nine million populations in England and stated that COVID-19 vaccination provided significant protection for obese populations for severe COVID-19 infection and death by COVID-19 with a risk ratio of 0.32 and 0.26 folds, respectively.^{12,34,35}

There were other factors contributing to COVID-19 vaccine effectiveness on obese populations. A study by Kara Z et al. showed significant differences in antibodies level was observed in obese populations without prior SARS-CoV-2 infection but not in obese populations which not naïve towards SARS-CoV-2 infection, regardless of the administration of either BNT162b2

Table 3. Characteristics of Selected Studies.

Study	Year	Location	Vaccine Received*			Dose(s)	Follow-up* (weeks)	Sample Size	Age (Years)	Male (%)	DM (%)	HT (%)	Dyslipidemia (%)	Smoking (%)	Obesity (%)	BMI Cut-Off (kg/m ²)
			A	B	C											
Alharbi JK et al. ¹¹	2022	Saudi Arabia	V	V		1	17091	33	59.62	9.37	11.21	5.90	NS	3.53	30	
Golec M et al. ¹²	2022	Poland	V			2	243	47.42	23.05	30.04	NS	NS	18.52	18.11	30	
Herzberg J et al. ¹³	2022	Germany	V			2	184	46.32	26.6	NS	NS	NS	28.2	16.3	30	
Kara Z et al. ¹⁴	2022	Turkey	V		V	2	80	42	16	34	25	NS	NS	61.5	40	
Malavazos AE et al. ¹⁵	2021	Italy	V			2	1060	41.42	37.74	1.42	9.15	5.15	15.75	11.13	30	
Faizo AA et al. ⁸	2022	Saudi Arabia	V	V	V	2	119	18-61	56.2	NS	NS	NS	NS	NS	30	
Watanabe M et al. ¹⁶	2022	Italy	V			3	68	29	39.5	2.4	15.3	7.1	31.7	9.5	30	
Yamamoto S et al. ¹⁷	2022	Japan	V			2	2435	36.6	29.90	NS	NS	NS	NS	9.8	25	

Abbreviations: A = AstraZeneca vaccine (ChAdOx1-SARS-COV-2); B = Pfizer-BioNTech vaccine (bnt162b2); C = Moderna vaccine (mRNA-1273); D = CoronaVac vaccine (Sinovac); BMI = body mass index; DM=Diabetes mellitus; HT=Hypertension; NS=Not stated. * After the last dose.

Table 4. Results of included studies.

Study	Vaccine Received*				Results
	A	B	C	D	
Alharbi JK et al. ¹¹	V	V			Obesity was associated with post-vaccination infection (p<0.01)
Golec M et al. ¹²	V				Obesity was not associated with long-term immune response (p=0,77)
Herzberg J et al. ¹³	V				Obesity provided a negative effect on antibody persistence (p<0.01)
Kara Z et al. ¹⁴	V			V	The antibody of severe obesity was lower compared to normoweight (p=0.001). The antibody of patients with severe obesity was higher in the BNT162b2 group compared to Corona Vac (p<0.001)
Malavazos AE et al. ¹⁵	V		V		Antibody drop was more remarkable in obesity compared to normoweight (p<0.01)
Faizo AA et al. ⁸	V		V		Significantly lower serum neutralizing antibody in obese populations compared to control populations (p<0.01)
Watanabe M et al. ¹⁶	V		V		Central obesity was associated with lower antibody titers (p=0.004)
Yamamoto S et al. ¹⁷	V		V		Antibody was going lower with higher BMI among men (p=0.03) but not among women (p=0.62)

Abbreviations: A = AstraZeneca vaccine (ChAdOx1-SARS-COV-2); B = Pfizer-BioNTech vaccine (bnt162b2); C = Moderna vaccine (mRNA-1273); D = CoronaVac vaccine (Sinovac).

or CoronaVac vaccine.¹⁴ In addition, a study by Yamamoto S et al. found that antibody titers of spike IgG decreased alongside increasing BMI in men but not women.¹⁷ Therefore, various variables which could affect the immune response to the COVID-19 vaccine, other than obesity, should be well-noted before giving COVID-19 vaccinations.

This initial qualitative study systematically analyses the impact of obesity on the COVID-19 vaccine response. However, this study was limited to data quantity as we do not have enough evidence to make a quantitative analysis possible. Therefore, there is still a possibility for meta-analysis, which involves quantitative analysis, to be conducted. We recommend conducting more high-quality studies to provide pooled analysis that yields better evidence levels for better practice.

CONCLUSION

COVID-19 vaccine provided a limited immune response in obese populations compared to normal populations. However, COVID-19 vaccination still protects against severe COVID-19 and death by COVID-19 in these populations. Therefore, it is recommended that obese populations take the COVID-19 vaccine per protocol.

CONFLICT OF INTEREST

The authors declare no conflict of interest in the making of this manuscript.

ETHICAL CONSIDERATION

No ethical clearance is needed as we conduct a study of the literature.

FUNDING

The authors are responsible for the study's funding without involving a grant, scholarship, or any other funding resource.

AUTHOR CONTRIBUTION

PPN was involved in writing the manuscript. GS and LW supervised and revised all manuscripts. All authors prepare the manuscript and agree for this final version to be submitted to this journal.

ACKNOWLEDGMENT

The authors would like to thank all the authors of included studies for contributing to this field for further research and advancement.

REFERENCE

- Teijaro JR, Farber DL. COVID-19 vaccines: Modes of immune activation and future challenges. *Nat Rev Immunol.* 2021;21(4):195–197.
- Yao Y, Jeyanathan M, Haddadi S, Barra NG, Vaseghi-Shanjani M, Damjanovic D et al. Induction of autonomous memory alveolar macrophages requires T cell help and is critical to trained immunity. *Cell.* 2018;175(6):1634–1650.
- Soegiarto G, Wulandari L, Purnomosari D, Dhia FK, Ikhwan GH, Tri HS, et al. Hypertension is associated with antibody response and breakthrough infection in health care workers following vaccination with inactivated SARS-CoV-2. *Vaccine.* 2022;40(30):4046.
- Kabir A, Lotfi S, Farsi F, Pazouki A. Impact of body mass index on immunogenicity of hepatitis B vaccine in bariatric surgery candidates: a retrospective study. *Diabetes Metab Syndr Clin Res Rev.* 2021;15(5):102254
- Fan W, Chen XF, Shen C, Guo ZR, Dong C. Hepatitis B vaccine response in obesity: a meta-analysis. *Vaccine.* 2016;34(40):4835–4841
- Daryabor G, Kabelitz D, Kalantar K. An update on immune dysregulation in obesity-related insulin resistance. *Scand J Immunol.* 2019;89(4):e12747
- Mitsunaga T, Ohtaki Y, Seki Y, Yoshioka M, Mori H, Suzuka M, et al. The evaluation of factors affecting antibody response after administration of the BNT162b2 vaccine: a prospective study in Japan. *PeerJ.* 2021;9(1):e12316
- Faizo AA, Qashqari FS, El-Kafrawy SA, Barasheed O, Almashjary MN, Alfelali M, et al. A potential association between obesity and reduced effectiveness of COVID-19 vaccine-induced neutralizing humoral immunity. *J Med Virol.* 2023;95(1):e28130.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow C, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Systematic Reviews.* 2021;10(1):89.
- Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews: addressing questions of prevalence. *Int J Health Policy Manag.* 2014;3(3):123–812.
- Alharbi JK, Al-Tawfiq JA, Alghnam S, Alwehaibe A, Alasmari A, Alsagaby SA, et al. Outcomes of single dose COVID-19 vaccines: eight month follow-up of a large cohort in Saudi Arabia. *J Infect Public Health.* 2022;15(5):573–577.
- Golec M, Fronczek M, Zembala-John J, Chrapiec M, Konka A, Węstyryk K, et al. Early and longitudinal humoral response to the SARS-CoV-2 mRNA BNT162b2 vaccine in healthcare

workers: significance of BMI, adipose tissue, and muscle mass on long-lasting post-vaccinal immunity. *Viruses.* 2022;14(5):868.

- Herzberg J, Fischer B, Lindenkamp C, Becher H, Becker A, Honarpisheh H, et al. Persistence of immune response in health care workers after two doses BNT162b2 in a longitudinal observational study. *Front Immunol.* 2022;13(1):839922.
- Kara Z, Akcin R, Demir AN, Dinc HO, Taskin HE, Kocazeybek B, et al. Antibody response to SARS-CoV-2 vaccines in people with severe obesity. *Obes Surg.* 2022;32(9):2987–2993.
- Malavazos AE, Basilico S, Iacobellis G, Milani V, Cardani R, Boniardi F, et al. Antibody responses to BNT162b2 mRNA vaccine: infection naïve individuals with abdominal obesity warrant attention. *Obesity (Silver Spring).* 2022;30(3):606–613.
- Watanabe M, Balena A, Tuccinardi D, Tozzi R, Risi R, Masi D, et al. Central obesity, smoking habit, and hypertension are associated with lower antibody titres in response to COVID-19 mRNA vaccine. *Diabetes Metab Res Rev.* 2022;38(1):e3465.
- Yamamoto S, Mizoue T, Tanaka A, Oshiro Y, Inamura N, Konishi M, et al. Sex-associated differences between BMI and SARS-CoV-2 antibody titers following the BNT162b2 vaccine. *Obesity (Silver Spring).* 2022;30(5):999–1003.
- Gomez-Zorita S, Milton-Laskibar I, Garcia-Arellano L, Gonzalez M, Portillo MP. An overview of adipose tissue ACE2 modulation by diet and obesity – potential implications in COVID-19 infection and severity. *Int J Mol Sci.* 2021;22(15):7975.
- Moscogiuri G, Pugliese G, Laudisio D, Castellucci B, Barrea L, Savastano S, et al. The impact of obesity on immune response to infection: plausible mechanisms and outcomes. *Obes Rev.* 2021;22(6):e13216.
- Mauri C, Bosma A. Immune regulatory function of B cells. *Annu Rev Immunol.* 2012;30(1):221–241.
- Green WD, Beck MA. Obesity impairs the adaptive immune response to influenza virus. *Ann Am Thorac Soc.* 2017;14(5):406–409.
- Park HL, Shim SH, Lee EY, Cho W, Park S, Jeon HJ, et al. Obesity-induced chronic inflammation is associated with the reduced efficacy of influenza vaccine. *Hum Vaccin Immunother.* 2014;10(5):1181–1186.
- Liu F, Guo Z, Dong C. Influences of obesity on the immunogenicity of hepatitis B vaccine. *Hum Vaccin Immunother.* 2017;13(5):1014–1017.
- Stefan N. Metabolic disorders, COVID-19, and vaccine-breakthrough infections. *Nat Rev Endocrinol.* 2022;18(2):75–76.
- Kanneganti T, Dixit VD. Immunological complications of obesity. *Nat Immunol.* 2012;13(8):707–712.
- Levin EG, Lustig Y, Cohen C, Fluss R, Indenbaum V, Amit S, et al. Waning immune humoral response to BNT162b2 COVID-19 vaccine over 6 months. *N Engl J Med.* 2021;385(24):e84.
- Ko JY, Danielson ML, Town M, Derado G, Greenlund KJ, Kirley PD, et al. Risk factors

- for coronavirus disease 2019 (COVID-19) – associated hospitalization: COVID-19-associated hospitalization surveillance network and behavioral risk factor surveillance system. *Clin Infect Dis*. 2021;72(11):e695–703
28. Ledford H. How obesity could create problems for a COVID vaccine. *Nature*. 2020;586(7830):488–489
 29. Sattar N, Valabhji J. Obesity as a risk factor for severe COVID-19: summary of the best evidence and implications for health care. *Curr Obes Rep*. 2021;10(3):282–289.
 30. Kompaniyets L, Goodman AB, Belay B. Body mass index and risk for COVID-19-related hospitalization, intensive care unit admission, invasive mechanical ventilation, and death – United States, March–December 2020. *MMWR Morb Mortal wky Rep*. 2021;70(10):355–361.
 31. Pranata S, Vranada A, Armiyati Y, Samiasih A, Aisah S, Kurnia A, et al. Inflammatory markers for predicting severity, mortality, and need for intensive care treatments of a patient infected with covid-19: a scoping review. *Bali Medical Journal*. 2023;12(1):324–330.
 32. Wijaya T, Hsieh PP, Melinda F, Suarca IK. Hypercoagulation state in infant with COVID-19: a case report. *Indonesia Journal of Biomedical Science*. 2022;16(1):66–69.
 33. Butsch WS, Hajduk A, Cardel MI, Donahoo WT, Kyle TK, Standord FC et al. Obesity (Silver Spring). 2021;29(10):1575–1579
 34. Piernas C, Patone M, Astbury NM, Gao M, Sheikh Z, Khunti K et al. Associations of BMI with COVID-19 vaccine uptake, vaccine effectiveness, and risk of severe COVID-19 outcomes after vaccination in England: a population-based cohort study. *Lancet Diabetes Endocrinol*. 2022;10(8):571–580.
 35. Herawati S, Kandarini Y, Mulyantari NK, Prabawa IPY. Correlation of Neutrophil to Lymphocyte Ratio with Interleukin-10 in Diagnosis and Monitoring of Coronavirus Disease-19 Patients. *Open Access Macedonian Journal of Medical Sciences*. 2022;10(B):63-66.



This work is licensed under a Creative Commons Attribution