

ARTIKEL PENELITIAN

**THE CORRELATION BETWEEN NUTRITIONAL STATUS AND  
CD8+ CELL COUNTS IN THE ELDERLY AFTER  
THE SECOND COVID-19 VACCINATION IN PALEMBANG, INDONESIA**

**HUBUNGAN STATUS GIZI DENGAN JUMLAH SEL T CD8+ PADA LANSIA  
SETELAH VAKSINASI COVID-19 KEDUA DI PALEMBANG INDONESIA**

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**ABSTRAK**

**Pendahuluan:** Virus SARS-CoV-2 adalah penyebab penyakit coronavirus (COVID-19). WHO mengklasifikasikan wabah tersebut sebagai pandemi pada 9 Maret 2020. Vaksin COVID-19 telah digunakan secara luas untuk menangani pandemi, namun beberapa kondisi berisiko tinggi yang dapat mengganggu efektivitas vaksin sehingga memerlukan pertimbangan yang cermat. Pasien berusia di atas 60 tahun memiliki risiko lebih besar untuk terkena COVID-19. Karena involusi timus dan transformasi jaringan korteks dan medula menjadi jaringan adiposa yang menyebabkan jumlah sel T CD8+ menurun. Selain itu, status gizi juga mempengaruhi jumlah sel T CD8+. Tujuan dari penelitian ini adalah untuk mengetahui korelasi antara status gizi dan jumlah sel T CD8+ pada pasien usia lanjut setelah vaksinasi COVID-19 sebanyak dua kali.

**Metode:** Studi ini merupakan penelitian pendahuluan dengan desain potong lintang. Pengambilan sampel menggunakan teknik sequential sampling. Pada hari ke-28, setelah pemberian vaksin kedua, dilakukan pengukuran jumlah sel T CD8+ dalam darah dan Mini Nutritional Assessment (MNA) digunakan untuk mengetahui status gizi.

**Hasil:** Sebanyak empat puluh subjek dikumpulkan dari Mei hingga November 2021. Rata-rata jumlah sel T CD8+ 517,32±41,67. Hasil penelitian didapatkan adalah 5 orang (12,5%) berisiko malnutrisi, sedangkan 35 orang (87,5%) berstatus gizi normal.

**Simpulan:** Terdapat hubungan yang signifikan antara status gizi berdasarkan MNA dan kadar CD8+ ( $p < 0,05$ ) dan korelasi positif antara status gizi dengan jumlah sel T CD8+ pada lansia yang mendapatkan vaksinasi covid-19 kedua di Palembang.

**Kata Kunci:** lansia, vaksinasi COVID-19, sel T CD8+, status gizi

**ABSTRACT**

**Introduction:** The SARS-CoV-2 virus is the cause of coronavirus illness (COVID-19). The WHO classified the outbreak a pandemic on March 9, 2020. The COVID-19 vaccine has been widely utilized to manage the pandemic. However, some high-risk conditions that can compromise the vaccine's efficacy require careful consideration. Patients over 60 years old are at a greater risk for COVID-19. Due to the involution of the thymus and the transformation of the cortex and medulla tissue into adipose tissue, CD8+ T cell numbers decline. In addition, undernutrition reduces the number of CD8+ T cells. The purpose of this study is to examine the relationship between nutritional status and CD8+ T cell counts in elderly patients following the second COVID-19 vaccination.

**Methods:** This study is a pilot project employing a cross-sectional design. The sampling employed a technique of sequential sampling. On day 28, following the administration of the second vaccine, the Mini Nutritional Assessment (MNA) and the amount of CD8+ T cells in the blood were utilized to evaluate the nutrition status.

**Results:** Between May and November of 2021, forty subjects were collected. The average number of CD8+ T cells was 517.32±41.67. Therefore, five people (12.5%) were at risk of malnutrition, whereas thirty-five (87.5%) had a normal nutritional status.

**Conclusion:** There is a significant relationship between MNA and CD8+ levels ( $P < 0.05$ ) and a positive correlation between nutritional status and CD8+ T cell counts in the elderly who have received the second covid-19 vaccination in Palembang.

**Key Words:** elderly, COVID-19 vaccination, CD8+ T cells, nutritional status

## INTRODUCTION

COVID-19 is an acute respiratory infection brought on by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The first laboratory-confirmed case of COVID-19 infection occurred in Wuhan, China, on 1 December 2019.<sup>1,2</sup> On March 12, 2020, the World Health Organization (WHO) proclaimed COVID-19 a global pandemic with more than 50 million illnesses and 1.2 million deaths.<sup>3,4</sup> In early 2020, the COVID-19 epidemic had a substantial influence on daily life. Infection with SARS-CoV-2 elicits a cytotoxic response in CD8+ T cells but not in CD4+ T cells, characterized by the simultaneous synthesis of granzymes A and B and perforin in a subpopulation of T cells. Diverse CD8+ effector types Cytotoxic T cells are essential for eradicating infected cells and controlling viruses. CD8+ T lymphocytes with an effector phenotype can destroy target cells by producing and expressing cytotoxic chemicals.<sup>5</sup>

The elderly population has the highest risk of contracting COVID-19. This T cell cytotoxic profile is not detected in COVID-19-infected elderly, particularly those over 80. The absence of a cytotoxic response in elderly patients may explain why COVID-19 is more severe in this age group than in younger people. According to other views, the involution of the thymus in old age reduces the creation of new naive T cells. The function of the thymus, a specialized lymphoid organ

where thymocytes mature into naive T lymphocytes, begins to diminish. This deterioration is believed to be due to abnormalities in the stroma, consistent with histological findings indicating a growth disorder of the thymic epithelial cell structure with age. Consequently, the number of naive T cells accessing the periphery declines with age, as indicated by fewer cells displaying recent thymic emigration markers (such as CD31+ for CD4+ T cells and CD103+ for CD8+ T cells). Memory in the aged is typically characterized by diminished proliferative ability.<sup>6,7</sup>

Vaccination is required to prevent the spread of the COVID-19 virus. When the majority of a community is protected by vaccination, the pathogen's ability to spread is constrained. CD8 T cells are critical to the development of vaccine-induced immunity.<sup>8</sup> Vaccines give an antigenic stimulus, and how the body responds to nutritional status varies from person to person.

A successful immune response following vaccination depends on nutritional status. Nutritional status (both obesity and malnutrition) is critical for immune cell function. T cells influence the role of immune adaptation in obesity and undernutrition (low body mass index). In obesity, this subset of malnutrition-induced alterations in the number and function of T cells may be driven by leptin. The effects of leptin on T cell number and function have been a comprehensive review. Many immune

cells are also responsive to leptin. In addition, expression of the leptin receptor is upregulated following T-cell activation. Besides, undernutrition modifies the quantity and function of CD4+ and CD8+ T lymphocytes, resulting in greater susceptibility to infection and protection against specific kinds of autoimmunity.<sup>9</sup>

The purpose of this study is to examine the relationship between nutritional status and CD8+ T cell counts in the elderly following COVID-19 vaccination twice.

## **METHOD**

This study is a pilot project employing a cross-sectional design. The research subjects were forty individuals aged 60 or older. From May to November of 2021, this study was conducted in multiple Palembang healthcare facilities. Persons above 60 years of age and individuals who have completed the COVID-19 program twice and participated in the study were included in the study samples.

Exclusion criteria included participants with COVID-19 infection during the first and second immunization intervals, subjects hospitalized with a positive SARS CoV-2 PCR Swab test, and subjects who received a second COVID-19 vaccination. However, they exceeded 30 days for the elderly. Simultaneously, dropout criteria include participants who died and those who did not return for the subsequent examination period. In addition, information regarding age, gender, and body mass index were obtained. Blood plasma is the material to be analyzed; 5 mL

will be obtained to assess CD8+ T cells. Plasma blood samples will be analyzed in an accredited and standardized laboratory. Weight, height, and measures of body mass index (BMI) or BMI in patients were also investigated on the samples. WHO classifies BMI as follows: underweight 18, average weight 18.5–22.9, overweight 23–24.9, grade I obesity 25–29.9, and grade II obesity 30. Mini Nutritional Assessment (MNA) is used to determine nutritional status.

## **RESULT**

From May to November 2021, forty participants who met the inclusion and exclusion criteria were recruited. Twenty-five women and fifteen men made up the forty research participants. Five individuals (12.5%) in the sample were at risk of malnutrition, while 35 (87.5%) had a normal nutritional status. The mean CD8+ T cell level in the elderly was  $517.32 \pm 41.67$  cells per microliter (Table 1).

The correlation study revealed that MNA and CD8+ levels were correlated significantly ( $p < 0.05$ ) although positive moderately ( $r = 0.33$ ). (Figure 1).

## **DISCUSSION**

Aging is characterized by a decline in T cell function, which is partially correlated with an increase in a subpopulation of immature T cells. In special populations, such as the elderly, it is essential to consider aspects that can affect it, one of which is nutritional status.<sup>12,13,16</sup>

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**Table 1.** Characteristics of the Subjects (n = 40)

Variables	Median (Range)	n (%)
<b>Gender</b>		
Male		15 (37.5%)
Female		25 (62.5%)
<b>BMI</b>		
Underweight		5 (12.5%)
Normoweight		35 (87.5%)
Overweight/Obese		-
<b>MNA</b>		
At the Risk of Malnutrition		5 (12.5%)
Normal Nutritional Status		35 (87.5%)
Malnourished		-
<b>CD8+ (cell/mm<sup>3</sup>)</b>	517.32±41.67	-

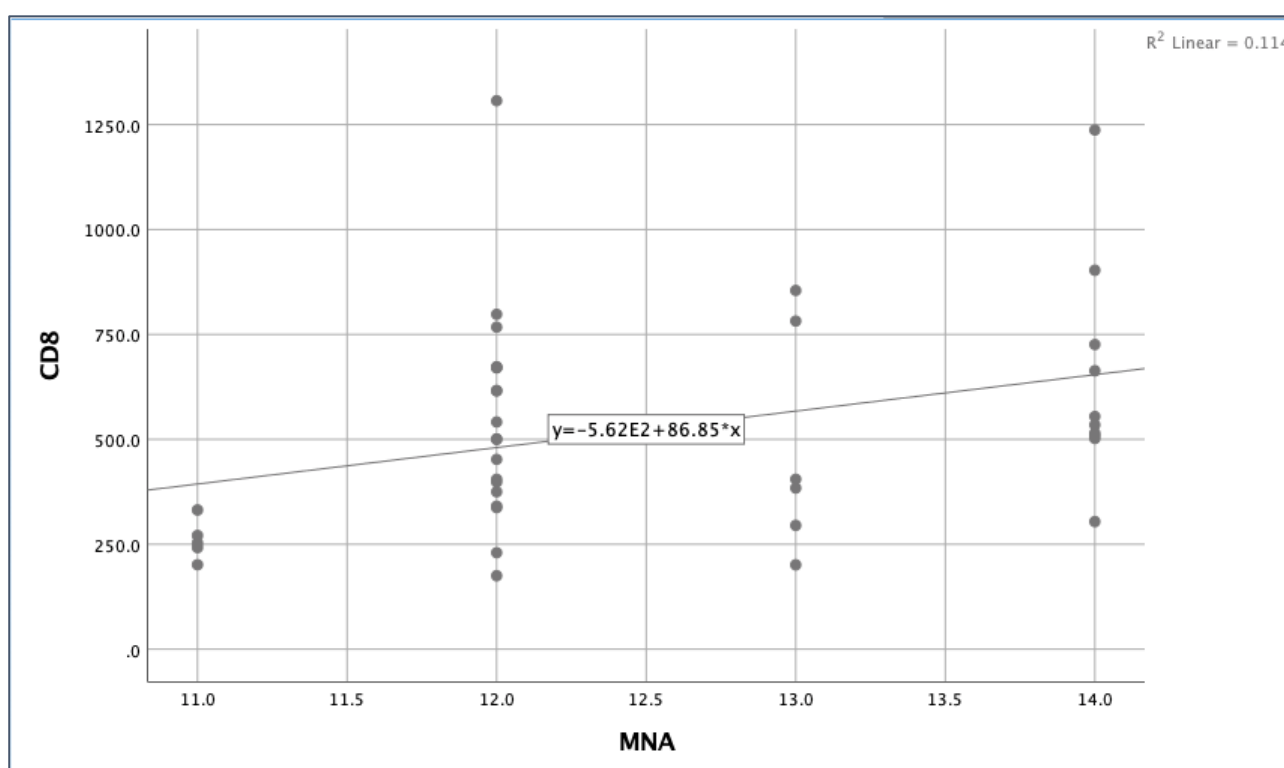


Figure 1. A correlation analysis between MNA and CD8+ levels

Our data reveal increased levels of CD8+ T cells in individuals with normal nutritional status (normal body mass index and mini nutritional assessment) groups and diminished levels of CD8+ T cells in undernutrition (underweight and high-risk malnutrition from mini nutritional assessment) groups. Counts of CD8+ T cells were significantly positively correlated with BMI.

Thus, undernutrition induces alteration in cell-mediated immunity, which could affect individuals' host response to infection. Undernutrition-induced immunodeficiency is known to reduce effective response to vaccines. The immunological response to vaccination can be affected by several factors, including nutritional status, which plays an intrinsic role in the individual's immune

response. Vaccines give an antigenic stimulus; the body's response depends on nutritional status and varies across individuals. Vaccines are more challenging to give and may be less effective at stimulating an immunological response in malnourished individuals due to interference with T-cell survival and proliferation.<sup>10,11</sup> According to Fan S et al., a successful coronavirus vaccination requires adequate nutrition.<sup>11</sup>

According to a study published in *Immunology* by Gerriets VA et al., starvation induces a decrease in adipocyte bulk, which leads to a fall in circulating leptin.<sup>19</sup> Malnourished people simultaneously demonstrate alterations in the quantity and function of CD4+ and CD8+ T lymphocytes, resulting in greater susceptibility to infection and decreased defense. Various types of autoimmunity Leptin can alter the amount of CD4+ T cells and cytokines they produce. This is one way malnutrition can alter the quantity and function of T lymphocytes.<sup>14,15</sup> Based on investigations conducted on 158 women and 90 men, Pellini R et al. reported dissimilar findings. For men who got the BNT162b2 vaccine, there was no statistical difference between BMI and immunological response after vaccination.<sup>9</sup> The other study from Pellini R et al. demonstrates that a single dose of BNT162b2 activates the immune response, and being young and normal-weight correlates positively with this response.<sup>18</sup>

Our study is a pilot project with a small sample size; therefore, a bigger sample size is required to determine the association between

nutritional status and CD8+ and to apply the findings more broadly.

## CONCLUSION

According to this study, there is a positive correlation between nutritional status and CD8+ T cell counts in the elderly who have received the second COVID-19 vaccination in Palembang. Thus, undernutrition induces alteration in cell-mediated immunity, which could affect individuals' host response to infection and increase mortality during the COVID-19 pandemic.

## REFERENCES

1. Wu Y, Chen C, & Chan Y J, (2020). The outbreak of COVID-19: An overview. *Journal of the Chinese Medical Association: JCMA*, 83(3), 217–220. <https://doi.org/10.1097/JCMA.0000000000000270>
2. Hayat O, Loubna K, Mohamed B, Nour E, Hamada I, Nour E, et al, The Pathogenesis of coronavirus disease 2019 (COVID-19): Evaluation and prevention. *Journal of Immunology Research* vol. 2020 1357983. 10 Jul. 2020, doi:10.1155/2020/1357983
3. Rumende CM, Susilo A, Wijaksono C, Santoso WD, Yulianti M, Kurniawan H, et al. Coronavirus disease 2019: Tinjauan literatur terkini. *Jurnal Penyakit Dalam Indonesia*. 2020;7(1):45-67. doi: 10.7454/jpdi.v7i1.415
4. Rauf A, Abu-Izneid T, Olatunde A., Ahmed A, Alhumaydhi F, et al. COVID-19 pandemic: Epidemiology, etiology, conventional and non-conventional therapies. *International Journal Of Environmental Research and Public Health* vol. 17,21 8155. 4 Nov. 2020, doi:10.3390/ijerph17218155
5. Westmeier J, Paniskaki K, Karakose Z, Werner T, Sutter K, Dolff S, et al. Impaired cytotoxic CD8+ T cell response in elderly COVID-19

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- patients. *mBio* vol. 11, 5 e02243-20. 18 Sep. 2020, doi:10.1128/mBio.02243-20
6. Crooke S, Ovsyannikova I, Poland G, Kennedy R. Immunosenescence and human vaccine immune responses. *Immunity & Ageing: I & A* vol. 16 25. 13 Sep. 2019, doi:10.1186/s12979-019-0164-9
  7. Wagner A, Garner-Spitzer E, Jasinska J, Kollaritsch H, Stiasny K, Kundi M, et al. Age-related differences in humoral and cellular immune responses after primary immunisation: indications for stratified vaccination schedules. *Scientific Reports* vol. 8,1 9825. 29 Jun. 2018, doi:10.1038/s41598-018-28111-8
  8. Nogimori T, Suzuki K, Masuta Y, Yagoto M, Ikeda M, Katamaya Y, et al. mRNA vaccine induces cytotoxic CD8+ T-cell cross-reactivity against SARS-CoV-2 Omicron variant and regulates COVID-19 severity, 11 April 2022, PREPRINT (Version 1) available at Research Square [<https://doi.org/10.21203/rs.3.rs-1364513/v1>]
  9. Pellini R, Venuti A, Pimpinelli F, Abril E, Blandino G, Campo F, et al. Initial observations on age, gender, BMI and hypertension in antibody responses to SARS-CoV-2 BNT162b2 vaccine. *EClinicalMedicine* vol. 36 (2021): 100928. doi:10.1016/j.eclinm.2021.100928
  10. Fan S, Teng P, Chew P, Smith G, Copeland L. Food system resilience and COVID-19 - Lessons from the Asian experience. *Global Food Security* vol. 28 (2021): 100501. doi:10.1016/j.gfs.2021.100501
  11. Rayman MP, & Calder PC. Optimising COVID-19 vaccine efficacy by ensuring nutritional adequacy. *The British Journal of Nutrition* vol. 126,12 (2021): 1919-1920. doi:10.1017/S0007114521000386
  12. Lesourd BM, Lainsney C, Salvatore R, Meaume S, Moulias R. Decreased maturation of T-cell populations in the healthy elderly: Influence of nutritional factors on the appearance of double negative CD4-, CD8-, CD2+ cells. *Archives of Gerontology and Geriatrics* vol. 19 Suppl 1 (1994): 139-54. doi:10.1016/s0167-4943(05)80059-7
  13. Diao B, Wang C, Tan Y, Chen X, Liu Y, Ning L, et al. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). *Frontiers in Immunology* vol. 11 827. 1 May. 2020, doi:10.3389/fimmu.2020.00827
  14. Ni L, Ye F, Cheng ML, Feng Y, Deng YQ, Zhao H, et al. Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals. *Immunity* vol. 52,6 (2020): 971-977.e3. doi:10.1016/j.immuni.2020.04.023
  15. Thieme CJ, Anft M, Paniskaki K, Blazquez-Navarro A, Doevelaar A, Seibert FS, et al. The SARS-CoV-2 T-cell immunity is directed against the spike, membrane, and nucleocapsid protein and associated with COVID 19 severity. medRxiv 2020.05.13.20100636
  16. Mazari L, & Lesourd BM. Nutritional influences on immune response in healthy aged persons. *Mechanisms of Ageing and Development* vol. 104,1 (1998): 25-40. doi:10.1016/s0047-6374(98)00047-5
  17. Cohen S, Danzaki K, & MacIver NJ. Nutritional effects on T-cell immunometabolism. *European Journal of Immunology* vol. 47,2 (2017): 225-235. doi:10.1002/eji.201646423
  18. Pellini R, Venuti A, Pimpinelli F, Abril E, Blandino G, Campo F, et al. Early onset of SARS-COV-2 antibodies after first dose of BNT162b2: Correlation with age, gender and BMI. *Vaccines* vol. 9,7 685. 22 Jun. 2021, doi:10.3390/vaccines9070685
  19. Gerriets VA, MacIver NJ. Role of T cells in malnutrition and obesity. *Front Immunol.* 2014;5:379. Published 2014 Aug 11. doi:10.3389/fimmu.2014.00379