

# **NEUTROPHIL-TO-LYMPHOCYTE RATIO IS SIGNIFICANTLY INCREASED IN CENTRAL OBESITY**

**Muh Taufiq<sup>1)</sup>, Yolanda Ngabito<sup>2)</sup> Titin Dunggio<sup>3)</sup>**

Bina Mandiri University Gorontalo

E-Mail: moh.taufik@ubmg.ac.id

## **ABSTRACT**

The Neutrophil-to-Lymphocyte Ratio (NLR) is a biomarker closely associated with systemic inflammation, particularly in conditions like central obesity. Given that central obesity leads to increased NLR, which in turn raises the risk of metabolic syndrome, including cardiovascular disease, conducting this study is deemed highly necessary, especially in regions with a high prevalence of central obesity, such as Gorontalo City, Indonesia. This study was designed as a cross-sectional analysis. A total of 100 respondents, categorized as Central Obese (CO) and Non-Central Obese (Non-CO), were evaluated for their NLR. Obesity categories were assessed based on the Asia-Pacific criteria. Statistical analysis revealed significant differences in NLR between those with and without central obesity, for both men and women (with p-values of 0.020 and 0.004, respectively). Overall, the findings suggest that NLR is significantly higher in individuals with central obesity compared to those without. Future studies should focus on assessing the correlation between NLR and other metabolic disease risk factors.

**Keywords:** NLR, Central Obesity

## **INTRODUCTION**

The world is currently facing a significant growth in the central obese population. Central obesity (OS), also called abdominal or visceral obesity, is a condition of fat accumulation in the abdominal area that threatens health status. It is directly linked to hypertension, dyslipidemia, metabolic syndrome, diabetes and coronary heart disease [1]. The prevalence of central obesity from year to year has continued to increase from 2012 to 2021, especially in the 20 to 30s age group. It is noted that the accumulated prevalence of central obesity in productive age (18-45 years) is 66.4%, which means that more than half of the world's population in productive age is centrally obese [2]. Therefore, blood glucose, lipids, and blood pressure should be detected early in adults with normal BMI but in the central obesity category to reduce the

prevalence of hypertension, diabetes, and hyperlipidemia [3].

People with a normal BMI can also be centrally obese, and this is a much higher risk factor for metabolic syndrome compared to being morbidly obese. Furthermore, several studies have shown that waist circumference is more closely associated with cardiovascular disease mortality than those with a BMI > 30 [3].

Subclinical chronic inflammation that occurs in central obesity leads to an increase in pro-inflammatory cytokines such as IL-6, hepsidin, NLR and others [4]. The neutrophil-lymphocyte ratio (NLR) is one of many biomarkers that are closely related to systemic inflammation as occurs in central obesity [4]. NLR reflects the balance between neutrophil-mediated inflammation

and lymphocyte-mediated immune response. Elevated NLR has been shown to be associated with various pathological conditions, including atherosclerosis, plaque instability, and vascular dysfunction [5].

There are various possible mechanisms that may explain the association between elevated NLR and the risk of cardiovascular events. Neutrophils secrete inflammatory mediators that can lead to degeneration of the blood vessel wall. In contrast, lymphocytes regulate the inflammatory response and have an antiatherosclerotic role where regulatory T cells, a subclass of lymphocytes, have an inhibitory effect on atherosclerosis [6].

Considering the impact of central obesity that results in an increase in NLR and leads to an increased risk of metabolic syndrome events including cardiovascular disease, this study is considered very necessary to be carried out, especially in areas with a high central obesity base, one of which is in Gorontalo City, Indonesia.

## RESEARCH METHODS

This study used a cross-sectional design with an analytic observational method. A total of 100 respondents, consisting of 25 OS males (WC > 90 cm), 25 non-OS males (WC < 90 cm), 25 OS females (WC > 80 cm) and 25 non-OS females (WC < 80 cm) performed NLR calculations taken from the results of flow cytometry-based complete hematological examination.

### 2.1. Determination of Respondents

Before the determination of respondents, sorting was carried out based on the inclusion criteria set; (1) Men / Women are not experiencing chronic or acute diseases that can cause changes in NLR values, (2) Normal uric acid levels, (3) Do not smoke and (4) Have Waist Circumference (WC) above normal (Men: > 90 cm and Women: > 80 cm) according to central obesity criteria

for Asia-Pacific. Non-centrally obese men and women were used for comparison.

### 2.2. Waist Circumference Measurement

Respondents who fit the inclusion criteria 1, 2 and 3 were then measured Waist Circumference (WC). Waist Circumference measurements are carried out referring to the standards set out in the WHO guidelines related to Waist Circumference and Waist-Hip Ratio. Report of a WHO Expert Consultation [7][7].

### 2.3. Complete Hematology Analysis

Respondents who met the inclusion criteria had their venous blood drawn with K3-EDTA vacuum tubes to obtain whole blood specimens. The specimen was homogenized and examined with a Sysmex XN-1000 hematology analyzer instrument. The complete hematology examination data were taken only the leukocyte count parameters, namely %Neutrophils and %Lymphocytes.

### 2.4. NLR calculation

After collecting the %Neutrophils and %Lymphocytes data of the respondents, the NLR value was calculated referring to the following formula [8]:

$$NLR = \frac{\%Neutrofil}{\%Limfosit}$$

### 2.5 Data Analysis

Data from the calculation of the NLR of OS respondents were then compared with the NLR of non-OS respondents using the Unpaired sample T-Test statistical test to examine the relationship between NLR and central obesity.

## RESULTS AND DISCUSSION

### Results

The results of the calculation of the NLR value of OS and non-OS respondents as a whole can be seen in the following table:

Table 1. NLR Value of OS and Non-OS Respondents

Respondent Category Object of Analysis :

Tabel 1. Nilai NLR Responden OS dan Non-OS

Kategori Responden	Obyek Analisis				
	WBC (sel/ $\mu$ L)	Neutrofil (%)	Limfosit (%)	NLR	WC (cm)
	Nilai Rata-Rata ( $\bar{x}$ )				
Pria OS	7,8	63,7	23,7	2,7	102
Pria Non-OS	5,8	50,2	38,6	1,32	77
Wanita OS	7,2	62,2	26,2	2,4	96
Wanita Non-OS	5,4	50,4	37,1	1,4	68

The data in the table above shows the mean of the objects analyzed in this study. It was found that the mean WBC, % Neutrophils, % Lymphocytes, NLR and WC of OS males were successively greater than the mean WBC of non-OS males. In line with these findings, the same was found for OS females compared to non-OS females.

### 3.1 NLR of OS and non-OS Men

#### NLR value calculation results

The results are comprehensively divided into 4 objects, namely the comparison of NLR of OS Men and non-OS Men, the comparison of NLR of OS Women and non-OS Women, the comparison of NLR of OS and non-OS as a whole and the correlation of NLR with WC.

### 3.1 NLR Pria OS dan Pria non-OS

Data hasil perhitungan nilai NLR Pria OS dan Pria non-OS dapat dilihat pada tabel berikut :

Tabel 2. NLR Pria OS dan Pria non-OS

Kategori Responden	NLR			WC (cm)			Sig. (Unpaired Sample t-Test)
	$\bar{x}$	Min	Max	$\bar{x}$	Min	Max	
Pria OS	2,7	2	3,4	102	93	104	0,02
Pria non-OS	1,3	1	1,8	77	68	84	

The statistical review clearly states that there is a significant difference between the NLR of OS men and Non-OS men (Sig < 0.02). In line with what was found, the findings of Bagyura et al (2023) also explained that there was a significant difference between NLR in OS and Non-OS cases. This is due to the activation of the inflammatory response due to excessive oxidative stress generated by fat accumulation in adipose tissue [9].

### 3.2 NLR of OS Women and Non-OS Women

Data from the calculation of the NLR values of OS Women and Non-OS Women can be seen in the following table:

Table 3. NLR of OS Women and Non-OS Women

Kategori Responden	NLR	WC (cm)	Sig. (Unpaired Sample t-Test)

	<i>Test)</i>					
	$\bar{x}$	M in	M ax	$\bar{x}$	M in	M ax
Wanita OS	2, 4	2	3, 6	9 6	80	11 7
Wanita non- OS	1, 4	1	1, 9	6 8	60	75

0,004

Similar to the previous findings in the male group, the statistical review stated that there was a significant difference between the NLR values of OS Women and Non-OS Women (Sig. <0.05). Fauziah et al in 2023 also found the same thing. The study, which focused on OS and Non-OS Women, stated

there was a significant correlation between NLR and waist circumference in the above respondent groups. Central obesity, both in men and women, causes sufferers to undergo molecular and cellular changes that affect systemic metabolism starting with an increase in free fatty acids (FFA) throughout the body along with the release of glycerol from adipocytes, followed by the production of proinflammatory cytokines in adipose tissue that stimulate the release of neutrophils and monocytes into the circulation and into inflammatory areas in large numbers, which further affects the proportion of leukocyte types [10]. The mechanisms underlying sub-clinical chronic inflammation in central obesity conditions are not yet fully understood. Some studies suggest that different stages of adiposity (overweight, obese, and severely obese) lead to the accumulation of myeloid cells, including macrophages and neutrophils. Obesity may alter the compartmental structure of hematopoietic cells which may lead to an increase in granulocyte progenitors and macrophages [11].

Neutrophil-to-Lymphocyte Ratio (NLR) may be elevated in central obesity as this condition is often associated with chronic low-grade inflammation. Central obesity, E-ISSN: 2746-167X, Vol. 5, No. 1, Mart. 2024 – pp.5 7-61

which is characterized by fat accumulation around the abdomen, triggers the release of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-6, and leptin from adipose tissue. These cytokines stimulate the inflammatory response by increasing the number of neutrophils in circulation and reducing the number of lymphocytes, which overall increases the NLR ratio [2]. This chronic inflammation plays an important role in various obesity-related diseases, such as cardiovascular disease and type 2 diabetes. Thus, increased NLR in central obesity not only reflects the presence of inflammation but could also be an indicator of risk for further complications associated with obesity [12].

### Conclusion

NLR is significantly higher in Central Obesity compared to Central Non-Obesity. The mechanism underlying this in both men and women is basically the same, namely due to a sub-clinical chronic inflammatory response that triggers the release of pro-inflammatory cytokines and further stimulates the release of neutrophils. In the future, it is necessary to assess the correlation between NLR and other metabolic disease risk factors, such as cardiovascular disease risk, hyperlipidemia and others..

### Acknowledgments

Our deepest gratitude to Heri Kurnia van Gobel as the Owner of Avicena Clinical Laboratory who has contributed to providing hematology examination facilities that are very important for the continuity of this study.

### REFERENCES

- [1] E. Israel, K. Hassen, M. Markos, K. Wolde, and B. Hawulte, "Central Obesity and Associated Factors Among Urban Adults in Dire Dawa Administrative City, Eastern Ethiopia," *Diabetes, Metab. Syndr. Obes.*, vol. 15, no. February, pp. 601–614, 2022, doi: 10.2147/DMSO.S348098.

<https://journals.ubmg.ac.id/index.php/JHTS>

- [2] S. M. Jeong *et al.*, “2023 Obesity Fact Sheet: Prevalence of Obesity and Abdominal Obesity in Adults, Adolescents, and Children in Korea from 2012 to 2021,” *J. Obes. Metab. Syndr.*, vol. 33, no. 1, pp. 27–35, 2024, doi: 10.7570/jomes24012.
- [3] W. Y. Feng, X. D. Li, J. Li, Y. Shen, and Q. Li, “Prevalence and risk factors of central obesity among adults with normal bmi in shaanxi, china: A cross-sectional study,” *Int. J. Environ. Res. Public Health*, vol. 18, no. 21, 2021, doi: 10.3390/ijerph182111439.
- [4] D. Khanna, S. Khanna, P. Khanna, P. Kahar, and B. M. Patel, “Obesity: A Chronic Low-Grade Inflammation and Its Markers,” *Cureus*, vol. 14, no. 2, 2022, doi: 10.7759/cureus.22711.
- [5] Q. C. Wang and Z. Y. Wang, “Comparative analysis of neutrophil-to-lymphocyte ratio and remnant cholesterol in predicting cardiovascular events and mortality in general adult population,” *Sci. Rep.*, vol. 13, no. 1, pp. 1–8, 2023, doi: 10.1038/s41598-023-49403-8.
- [6] T. Angkananard, T. Anothaisintawee, M. McEvoy, J. Attia, and A. Thakkinstian, “Neutrophil Lymphocyte Ratio and Cardiovascular Disease Risk: A Systematic Review and Meta-Analysis,” *Biomed Res. Int.*, vol. 2018, 2018, doi: 10.1155/2018/2703518.
- [7] World Health Organisation (WHO), “Methods for measuring waist and hip circumference,” in *WHO / Waist Circumference and Waist–Hip Ratio. Report of a WHO Expert Consultation*, 8th ed., no. December, WHO, Ed., Geneva: WHO Library Cataloguing-in-Publication Data, 2011, pp. 5–7. [Online]. Available: <http://www.who.int>
- [8] A. Buonacera, B. Stancanelli, M. Colaci, and L. Malatino, “Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases,” *Int. J. Mol. Sci.*, vol. 23, no. 7, 2022, doi: 10.3390/ijms23073636.
- [9] Z. Bagyura *et al.*, “Neutrophil-to-Lymphocyte Ratio Is an Independent Risk Factor for Coronary Artery Disease in Central Obesity,” *Int. J. Mol. Sci.*, vol. 24, no. 8, pp. 1–11, 2023, doi: 10.3390/ijms24087397.
- [10] H. Fauziah, S. Aprianti, S. W. Hartono, and S. Jalaluddin, “Analysis of Neutrophil-to-Lymphocyte Ratio between Obese and Non-Obese Women,” vol. 06, no. 04, pp. 20–23, 2023.
- [11] E. Rodríguez-Rodríguez, M. D. Salas-González, R. M. Ortega, and A. M. López-Sobaler, “Leukocytes and Neutrophil–Lymphocyte Ratio as Indicators of Insulin Resistance in Overweight/Obese School-Children,” *Front. Nutr.*, vol. 8, no. May, pp. 1–8, 2022, doi: 10.3389/fnut.2021.811081.
- [12] C. H. Lin, Y. H. Li, Y. Y. Wang, and W.D.Chang, “Higher Neutrophil-to-Lymphocyte Ratio Was Associated with Increased Risk of Chronic Kidney Disease in Overweight/Obese but Not Normal-Weight Individuals,” *Int. J. Environ. Res. Public Health*, vol. 19, no. 13, pp. 1–13, 2022, doi: 10.3390/ijerph19138077.