Jurnal Analis Medika Biosains (JAMBS)
Vol.11, No.1, March 2024, pp. 18 - 22
E-ISSN: 2656-2456
http://jambs.poltekkes-mataram.ac.id/index.php/home
DOI: https://doi.org/10.32807/jambs.v11i1.332

Correlation Of Neutrophil Lymphocyte Ratio (NLR) Value With Incidence Of Tuberculosis Disease In Patients With Diabetes Mellitus

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Article Info

Article history :

Received November 20, 2023
Revised January 17, 2024
Accepted Fabruary 23, 2024

Keyword :

NLR
Tuberculosis
Diabetes mellitus

ABSTRACT

Diabetes mellitus is a non-communicable disease (PTM) that is chronic and can weaken the immune system so that sufferers are 3 times more likely to suffer from pulmonary TB. In chronic infection there is continuous inflammation which is characterized by the presence of neutrophils themselves and will be followed by low lymphocyte values due to immune system pathways that do not work perfectly. The purpose of this study was to determine the correlation between the Neutrophil Lymphocyte Ratio (NLR) and the incidence of Tuberculosis in Diabetes Mellitus patients at the Jorongan Health Center, Probolinggo Regency. This research is a correlative analytic study with a cross sectional approach. A total of 30 samples of diabetes mellitus patients at the Jorongan Health Center from January to April 2023. The NLR examination method was with a hematology analyzer and tuberculosis patients were examined using Molecular Rapid Test. The statistical test uses Spearman's nonparametric test. The results showed that there was a correlation between NLR values and the incidence of tuberculosis in diabetes mellitus patients at the Jorongan Health Center, p = 0.003 and r = 0.521. Further research needs to be carried out involving larger samples and other laboratory tests related to the immune system in patients with diabetes mellitus.

INTRODUCTION

One of the important problems that has a risk of pulmonary tuberculosis is diabetes mellitus (Ministry of Health of the Republic of Indonesia, 2016). Diabetes mellitus is one of the chronic non-communicable diseases (NCDs) that can disrupt the immune system and increase the risk of pulmonary tuberculosis in affected individuals by three times (Ministry of Health, 2015). Numerous studies have shown a significant relationship between diabetes mellitus and tuberculosis.

Those with type 2 diabetes mellitus are more likely to contract tuberculosis than those without. Elevated blood sugar and low insulin levels can have an indirect impact on immune cell activity, particularly on macrophages and lymphocytes. Patients are more susceptible to infection because chemotaxis, phagocytosis and activation of antigen presenting cells are impaired (Sola et al., 2016).

In comparison, patients with uncontrolled diabetes have a higher risk of developing tuberculosis than those with good glycemic control. Type 2 diabetes mellitus affects chemotaxis, phagocytosis, antigen presentation, and cell activation by impairing the function of macrophages, lymphocytes, and monocytes. Low phagocytic activity is followed by decreased macrophage function in type 2 diabetes mellitus patients for antigen presentation. There is a delay in T cell-mediated immune system mechanisms due to decreased dendritic cells and delayed dendritic cells in activating naive T cells. Early phagocytosis of pathogens by neutrophils is no longer important (According to Kumar et al. in 2017; Kumar Nathella and Babu in 2017; Wang et al. in 2018; Rao et al. in 2019).

How to cite:
Istiqomah, I., Suhariyadi, S., & Woelansari, E. (2024). Correlation Of Neutrophil Lymphocyte Ratio (NLR) Value With Incidence Of Tuberculosis Disease In Patients With Diabetes Mellitus. *Jurnal Analis Medika Biosains (JAMBS), 11*(1), 18-23.

Cellular immunity in patients with diabetes mellitus will decrease, as a result Th-1 lymphocytes will decrease and the production of TNF, IL-, and IL-6 will decrease. Mycobacterium tuberculosis bacteria can grow and develop in conditions supported by hyperglycaemia, or high blood sugar levels. Increased concentrations of glycerol and nitrogen, which are growth stimuli for Mycobacterium tuberculosis bacteria, are said by some researchers to increase the risk of infection in cells with reduced cell-protective function (Airliny, 2015).
Hyperglycaemia, one of the symptoms of the chronic disease diabetes mellitus, causes chronic inflammation. Through the process of non-enzymatic protein glycation, glucose oxidation, and increased lipid peroxidation leading to enzyme destruction, these hyperglycemic conditions produce free radicals that create oxidative stress tissues making people more susceptible to it and making them more insulin resistant. White blood cells or also called leukocytes are one of the biomarkers that can be used to measure inflammation in the body. One of the pathogenesis factors of insulin resistance is the number of white blood cells in the body. The main task of leukocytes is to prevent infection and react to the presence of foreign bodies. Neutrophils, lymphocytes, monocytes, eosinophils, and basophils are 5 types of leukocytes that can be easily recognized through a rapid blood test. Leukocytes are made up of 75-90% neutrophils and lymphocytes. As a result of malfunctioning immune system pathways, chronic infections are characterized by ongoing inflammation characterized by the presence of neutrophils themselves and will be followed by low lymphocyte values. according to the research findings of Nurdin et al. Th The type of research used is analytic observational with a cross sectional approach. The research sample was Diabetes mellitus patients with random blood sugar test results > 200 mg/dl. This study began on March 1 to April 30, 2023 at the Jorongan Health Center, Probolinggo Regency.
Researche NLR value can be used as a marker for inflammation in patients with Type 2 Diabetes Mellitus because in 2021, the NLR results were as many as (86.67 percent) samples had an increase in the NLR value. The number of leukocytes, neutrophils, and lymphocytes and the risk of developing DM are interrelated, according to research by Borne Y, Smith J, et al. (2016).

MATERIALS/METHOD

This research was conducted at Jorongan Health Center Surabaya. The type of research used is analytic observational with a cross sectional approach. The research sample was Diabetes mellitus patients with random blood sugar test results > 200 mg/dl. This study began on March 1 to April 30, 2023 at the Jorongan Health Center, Probolinggo Regency.

RESULTS AND DISCUSSION

Based on the results of research conducted at the Jorongan Health Center, Leces District, Probolinggo Regency, from March 1 to April 30, 2023, the following results were obtained:

Table 1. Frequency Distribution Glucose, NLR and Molecular Rapid Test examination results

Value	Gender		Age	
	Male	**Female**	**46 – 55 Years**	**56 – 65 Years**
Glucose Value				
Glucose >200 mg/dL	10 (33,3%)	20 (66,7%)	10 (33,3%)	20 (66,7%)
NLR				
1-3%	7 (23,3%)	20 (66,7%)	9 (30,0%)	18 (60%)
>3%	3 (10%)	0 (0%)	1 (3,3%)	2 (6,7%)
Molecular Rapid Test				
Not Detected	7 (23,3%)	20 (66,7%)	9 (30,0%)	1 (3,3%)
Detected	3 (10%)	0 (0%)	18 (60%)	2 (6,7%)

Based on Table 1, obtained data of 10 (33.3%) male respondents have random blood glucose examination results> 200 mg/dl and 20 (66.7%) female respondents have random blood glucose examination results> 200 mg/dl . In the age group there were 10 (33.3%) respondents were in the age range of 46-55 years and as many as 20 (66.7%) respondents were in the age range of 56-65 years. NLR examination data increased in 3 (10%) male respondents and in 3 (10%) male respondents had positive Molecular Rapid Test results. NLR examination data increased in the age range of 46 - 55 years by 1 (3.3%) and in the age range of 56 - 65 years as much as 2 (6.7%). Whereas on Molecular Rapid Test examination the positive Molecular Rapid Test examination results in the age range of 46 - 55 years were 1 (3.3%) and in the age range of 56-65 years of 2 (6.7%).

Table 2. Correlation Of Neutrophil Lymphocyte Ratio (NLR) Value with Incidence of Tuberculosis Disease

NLR	Molecular Rapid Test		p-Value	r
	Not Detected	Detected		
1-3%	27 (90,0%)	0 (0%)	0,003	0,521
>3%	0 (0%)	3 (10%)		

During the period March to April 2023 there were 30 samples of diabetes mellitus patients at the Jorongan Health Center. The proportion of patients with diabetes mellitus is seen in Table 1 The results show that 20 respondents (66.7%) are women and 10 respondents (33.3%) are male. This is in accordance with the findings of previous research by Rudi, A. Age, History of heredity, gender, and eating habits are factors that affect blood sugar levels, according to research Kwureh (2017). The results showed that, the percentage compared to men, women were higher. Women are more likely to experience overweight because the percentage of their body fat is higher than men, thereby increasing the risk of developing diabetes and obesity (Rudi, et al, 2017). Based on the distribution in the age group, seen from the table 1 states that the age group 46-55 years is 10 people (33.3 %) and the age group 56-65 years as many as 20 people (66.7 %). The same result was shown by Rudi's research. The study stated that the physiology of aging which included a decrease in body function as we get older, including the ability of the hormone insulin to function properly and cause high blood sugar levels, related to age factors (Rudi, 2017).

Based on the frequency of the results of NLR and Molecular Rapid Test examinations based on the age seen in Table 1 obtained data on the results of NLR examination with a male sex of 7 people (23.3%), with normal values and negative Molecular Rapid Test results or not detected. Male sex 3 people (10%) with a value of more than normal, and positive or detected Molecular Rapid Test results. As many as 20 people (66.7%) are female with normal NLR values and Molecular Rapid Test not detected results. Neutrophils are the main components of human peripheral circulation leukocytes, which play a key role in human inflammation and disease defense. Neutrophils reach the location of infection or injury first, followed by executing the phagocytosis program, degranulation, and installing extracellular traps Neutrophils to eliminate attackers. They also issue chemokines and cytokines to draw monocytes from local areas to phagocytes themselves by macrophages and transit signals to activate the following adaptive immunity. Recently, neutrophil subpopulation is also reportedly suppressing immune responses mediated by T cells. Lymphocytes are other main populations of human peripheral circulation leukocytes, which mainly mediates adaptive immunity including T lymphocytes that mediate cellular immunity and B lymphocytes that mediate humoral immunity. The previous study stated that the results showed no significant NLR difference between the population of women and men in each age group, (Sarraf KM et al, 2019).

Based on Table 1 obtained data from NLR examination results increased at 46-55 years of 1 person (3.3%) and in the age range of 56-65 years as many as 2 people (6.7%). The results of previous studies show that NLR is positively correlated to age, the older the age is the higher the results of the NLR (Walsh Sr et al, 2020). Neutrophils are the main components of human peripheral circulation leukocytes, which play a key role in human inflammation and defense. The discovery of the correlation of NLR values and ages and other covariat such as systolic pressure, distolic pressure, body and gender index (Walsh Sr, 2020).

The results of data analysis using crosstab in table 5.4 obtained as many as 27 people (90%) with a value of NLR 1-3% and Molecular Rapid Test not detected examination. As many as 3 people (10%) with a value of NLR> 3% (more than normal) with Molecular Rapid Test detected results. This finding is in line with previous research which states that cellular immunity plays an important role in the pathogenesis of tuberculosis. Previous studies showed that leukocyte physiological immune responses that circulated to various inflammatory events were characterized by increased neutrophils and decreased lymphocytes, TD 4+ T lymphocytes, and macrophages (Hamai A et al, 2019).

Hyperglycemia tends to cause oxidative stress, which causes glucose to be oxidized automatically and produce reactive oxygen species (ROS), or oxygen radicals (Meija, 2018). Protein is used in the process of non-enzymatic gups that produce free radicals of hydrogen peroxide and superoxide when glucose is oxidized. As a result of the disruption of the glycolysis process due to damage to free radicals in the core DNA, the Advanced Glycation End Products (AGE) pathway arises, which is marked by an increase in HBA1C in the blood. Inflammation can also be caused by ROS.

Some studies have shown that patients with diabetes mellitus are higher risk to develop into tuberculosis compared to those that are not 2.5 times (IDF, 2019). The mechanism that underlies the occurrence of this matter, due to the defect of the immune cell function and the hosting defense mechanism (Joen C.Y, 2018). T lymphocytes, neutrophils, and cellular immunity are all influenced by diabetes. When compared to non-DM, TB-DM shows a decrease in the response of cytokine t-helper 1 (TH1), TNF Alpha production, IL-1 Beta production, and IL-6 production. Control and inhibition of bacteria Mycobacterium tuberculosis is very dependent on the cytokine of TH1. Diabetes is more likely to develop into tuberculosis when the number and function of T lymphocytes is reduced. Because of the weakening of the production of reactive oxygen species, phagocyte functions, and cities in diabetics, macrophage functions are also depressed (Laurentia M et al, 2018).

Lymphocyte Neutrophils Ratio (NLR) is the result of dividing the number of lymphocytes with the total number of neutrophils. According to a study, neutrophils are phagocytic cells that often have a significant impact and contribute to infection control, including infections caused by, as one example of mycobacterium tuberculosis in the blood. Because of its short age and inability to react to intracellular pathogens such as mycobacterium tuberculosis bacteria, neutrophils are initially believed not to play a role in the infection of the bacterium Mycobacterium tuberculosis. Neutrophils played an important role since the first day of mycobacterium tuberculosis bacterial infection until the development of granuloma, according to research in recent years. Mycobacterium tuberculosis bacteria cause the biphasic neutrophil response. The initial value increased on the first day after infection, decreased, and then increased again after 8 to 15 days (Kim JY, 2019).

Before the correlation test was carried out, a normality test was carried out with the Kolmogorov Smirnov analyst using SPSS. The analysis was followed by a nonparametric spearman correlation test obtained by results based on Table 2 $p = 0.003$ ($p < 0.05$) with the correlation coefficient (r) = 0.521. The significance value of this study is smaller than α (0.05), which means that the NLR value has a significant relationship with the incidence of tuberculosis of diabetes mellitus patients. The findings of this research support previous research conducted by Santos et al. (2018) There is a correlation between the value of NLR and the incidence of tuberculosis in patients with diabetes mellitus. Hyperglycemia causes impaired neutrophil and monocytes function so that chemotactic, phagocytosis and bacterial killing power decreases. Low immune response in a person makes infectious diseases, such as disease, more easily developed caused by mycobacterium tuberculosis bacteria (Santos et al, 2018).

In this study, there are samples that are for quality Molecular Rapid Test examination. This can cause Molecular Rapid Test not detected or negative examination. For this reason, it is hoped that when giving phlegm pots so that researchers or officers can provide counseling on how to issue good phlegm.

Since some time, molecular technology has been used in the diagnosis of TB. However, the method used is too complicated for standard examinations in developing countries. Its application in countries with limited resources is difficult because the stages of processing specimens and DNA extraction. At present Molecular Rapid Test examination with the Genexpert MTB/RIF examination is a molecular examination using Nycleic Acid Amplification Technology (NAAT) technology that can diagnose TB and resistance to rifampicin within 2 hours (Kemenkes, 2017).

CONCLUSIONS

Based on the results of the study, it can be concluded that the average NLR results in diabetes mellitus patients in the Jorongan Health Center with an average tilapia of 2.18%, the results of Molecular Rapid Test examination in patients with diabetes mellitus in the Jorongan Puskesmas 90% not detected and 10% detected, there is a correlation between The value of NLR with the incidence of tuberculosis in patients with diabetes mellitus ($p = 0.003$).

REFERENCE

ADA. (2018). American Diabetes Association (ADA) Standards of Medical Care in Diabetes: Classification And Diagnosis Of Diabetes. Diabetes Care, 41(Supplement 1), 13–27. https://doi.org/10.2337/dc18-Sint01

American Diabetes Association. (2020). Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care, 43(January), S14–S31.

Anggraini NWP, Sulistyowati S. Low neutrophil-to-lmphocyte ratio decreases risk of coronavirus disease in

pregnant women. Universa Med. 2020;39(2):88. doi:10.18051/univmed.2020.v39.88-96
Anggraeni, dini siti. 2020. Stop Tuberkulosis. Bogor: Penerbit Cita Insan Madani.
Angger, A. (2020). Buku Ajar : Diabetes Dan Komplikasinya (A. Guepedia (ed.)). The First On-Publisher in Indonesia.
A.Viktor Hoffbrand, dkk. 2018. Kapita selecta Hematologi Edisi 7. Jakarta
Ciccullo A, Borghetti A, Zileri Dal Verme L, et al. Neutrophil-to-lymphocyte ratio and clinical outcome in COVID-19: a report from the Italian front line. Int J Antimicrob Agents. 2020;56(2). doi:10.1016/j.ijantimicag.2020.106017 26. Rosyanti L, Hadi I. Respon Imunitas dan Badai Sitokin Severe Acute
Crofton John, Norman Horne dan Fred Miller. 2019. Tuberkulosis Klinis. Jakarta: Widya Medika.
Depkes RI. 2018. Pedoman Nasional Penanggulangan Tuberkulosis, Jakarta: Dirjen P2M&PL.
Dinkes. 2020. Profil Kesehatan Kabupaten Probolinggo 2020 : Dinas Kesehatan Kabupaten Probolinggo.
Lestari, Zulkarnain, & Sijid, A. (2021). Diabetes Melitus: Review etiologi, patofisiologi, gejala, penyebab, cara pemeriksaan, cara pengobatan dan cara pencegahan. Prosiding Seminar Nasional Biologi, 7(1), 237–241.
Nanda Dkk (2018). Pengaruh Intervensi Tahu Kedelai Hitam Kaya Serat Terhadap Glukosa Darah Dan Inflamasi Responden Diabetes Tipe 2, J.Teknol dan Industri Pangan.
Nizar, Muhamad. 2010. Pemberantasan dan Penanggulangan Tuberkulosis. Yogyakarta: penerbit Gosyen Publising.
PERKENI. (2021). Pedoman Pengelolaan dan Pengelolaan Diabetes Melitus Tipe 2 Dewasa di Indonesia. In Global Initiative for Asthma (pp 1-119).
Puskesmas Jorongan. 2017. Sop pengambilan sampel darah. Puskesmas Jorongan
Puskesmas Sumberasih. 2018. Sop penggunaan Molecular Rapid Test. Puskesmas Sumberasih
Rudy, B., & Richard, D. (2018). Buku Pegangan Diabetes Edisi Ke 4 (Barrarah Bariid (ed.)).
Sadaat, M., Rumana, K., Hossain, S., Masud, P., Sultana, S., & Khanam, R. (2019). Diabetes & Metabolic Syndrome : Clinical Research & Reviews Association Between Physical Activity And Diabetic Complications Among Bangladeshi Type 2 Diabetic Patients. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, Vol 13, No 1, page 806–809. Https://Doi.Org/10.1016/J.Dsx.2018.11.069
Spartano, N. L., Davis-Plourde, K. L., Himali, J. J., Murabito, J. M., Vasan, R. S., Beiser, A. S., & Seshadri, S. (2019). Self-Reported Physical Activity And Relations To Growth And Neurotrophic Factors In Diabetes Mellitus : The Framingham Offspring Study. Journal Of Diabetes Research. Retrieved From Https://Doi.Org/10.1155/2019/2718465
Subiyanto. 2019. Diabetes Melitus Tipe 2. Jakarta.
World Health Organization, 2018. World Health Organization Global report. WHO. 24 : 10- 11
Yuhelma, Hasneli, Y., & Nauli, F. A. (2018). Identifikasi Dan Analisis Komplikasi Makrovaskuler Dan Mikrovaskuler Pada Pasien Diabetes Mellitus, Hlm 569–579. Universitas Riau.
Zheng, Y., Ley, S. H., & Hu, F. B. (2018). Global Aetiology And Epidemiology Of Type 2 Diabetes Mellitus And Its Complications. Nature Reviews Endocrinology, 14(2), 88–98. https://doi.org/10.1038/nrendo.2017.151
Zulkifli Amin, Asril Bahar. 2016. Tuberkulosis Paru, Buku Ajar Ilmu Penyakit Dalam. Jakarta: UI