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CORRELATION BETWEEN NEUTROPHIL-LYMPHOCYTE RATIO AND LIPID PROFILE IN TYPE-2 DIABETES MELLITUS

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a metabolic disease that can cause low-grade chronic inflammation related to insulin resistance. Recently, neutrophil to lymphocyte has become a potential marker of chronic inflammation. An abnormal lipid profile occurs due to lipotoxicity from insulin resistance. **Objective:** To prove the correlation between NLR and lipid profiles in T2DM patients. **Methods:** An analytic observational study used a cross-sectional approach to 45 medical records of T2DM patients who received treatment at Nasional Diponegoro Hospital Semarang. This study was conducted from October to November 2022. Data was collected by using consecutive sampling. Analysis of the correlation between NLR and lipid profiles used spearman's correlation test. **Results:** The correlation between NLR and HDL cholesterol levels was p=0.035, r=-0.315. The correlation between NLR and cholesterol, LDL cholesterol, and triglyceride levels was p = 0.061, r = -0.281; p = 0.170, r = -0.208; p = 0.563, r = -0.089, respectively. **Conclusion:** There was a weak negative correlation between NLR and HDL cholesterol levels in T2DM patients, but there was no correlation between NLR and other lipid profiles.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a threat to the world population, especially Indonesia. According to the epidemiological data center of the International Diabetes Federation (IDF), people with diabetes in Indonesia in 2021 reached 19.47 million patients. This value increased by 167% when compared to 2011, which reached 7.29 million, and is expected to continue to increase in 2045 to 28.6 million. [1]

The characteristics of T2DM are hyperglycemia that occurs due to insulin resistance, defects in insulin secretion, or both. Insulin resistance results in the body not being able to fully utilize insulin.[1,2] Chronic inflammation in T2DM is associated with endothelial dysfunction and atherosclerosis. Endothelial dysfunction is closely associated with cardiovascular disease. [3,4]

Chronic inflammation can be determined by measuring levels of inflammatory markers, but in daily practice this is difficult to do due to cost limitations, so the neutrophil lymphocyte ratio (NLR) is expected to be an alternative because of its role in indicating acute, chronic inflammation and adaptive immunity.[5]

The neutrophil-lymphocyte ratio has become a potential marker of chronic inflammation in recent years. Chronic inflammation is characterized by an elevated neutrophil count and a decreased lymphocyte count.[3,4] Leukocytosis is a potential pathogenesis responsible for metabolic syndrome and atherosclerosis. Several studies have shown that total leukocyte count as a marker of inflammation is not superior to NLR. Neutrophils, which have a negative effect on endothelial damage, and the role of lymphocytes as anti-atherosclerosis agents are the main points for NLR examination. [3,6-8]

Lousy DM control can increase dyslipidemia, which includes increased triglyceride levels, low-density lipoprotein cholesterol (LDL-C), and

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decreased high-density lipoprotein cholesterol (HDL-C).[2] This is related to chronic inflammation in T2DM, which can affect lipid metabolism. The inhibitor of κappa kinase (IKK) complex will be activated, causing an increase in the hormone leptin, so people with T2DM often experience polyphagia. Excess calories will be stored in the form of fat cells in adipose tissue, but insulin resistance that occurs in adipose tissue will cause the lipogenesis process to be inhibited and an increase in free fatty acids. The increase in free fatty acids will increase the secretion of very low-density lipoprotein 1 (VLDL1) in the liver, which can encourage the formation of small dense low -density lipoprotein (sdLDL) and reduce HDL-C levels.[9] Hypertriglyceridemia is often associated with insulin resistance due to this process.[10]

Research by Eftekharian (2016) and Dudani (2021) showed that NLR and lipid profile affect the disease progression of T2DM. Aboulmakarim's research (2021) showed that NLR and lipid ratios did not significantly correlate with glycemic control in diabetes mellitus. Previous studies discussed the relationship of NLR and lipid profile to T2DM separately, so this study aims to evaluate the correlation between NLR and lipid profile in patients with T2DM. [11-13]

METHOD

The study used a cross-sectional methodology and was an analytical observational study. The participants were T2DM patients who visited the internal medicine clinic of Diponegoro National Hospital from January 2020 to October 2022. The selection of research subjects was carried out by consecutive sampling in accordance with the research criteria. The inclusion criteria of this study were being 18 years old, having a complete medical history, and having a body temperature within the normal range (36.8–37.2 °C). The exclusion criteria were T2DM patients who were pregnant, suffering from hematological malignancies involving the number and function of both neutrophils and lymphocytes, and taking anti lipid drugs.

The neutrophil-lymphocyte ratio was calculated from the differential leukocyte count in the complete blood test. Lipid profiles (total cholesterol, HDL-C, LDL-C, and triglyceride levels) were obtained from the patient's medical records.

The mean ± standard deviation was used to represent normally distributed numerical data, the median (minimum-maximum) for non-normally distributed numerical data, and the frequency (percentage) for categorical data. The Spearman correlation test was used to analyze the data. Research ethics were obtained from the Universitas Diponegoro Health Research Ethics Committee Number 355/EC/KEPK/FK-UNDIP/IX/2022.

RESULTS

This study included 45 subjects, 19 male (42.4%) and 26 female (57.8%), with a mean age of 60.69 years. Table 1 displays the characteristics of the study participants.

Table 1. Subject characteristic data

Subject characteristic	n (%)	Mean± SD	Median (min-max)
Age (year)		60.69 ± 11.29	
Sex			
Male	19 (42.2%)		
Female	26 (57.8%)		
Temperature (°C)			36.5 (36-36.9)
Random blood glucose (mg/dL)			164 (24-912)
Fasting blood glucose (mg/dL)			144 (65-529)
Postprandial blood glucose (mg/dL)			190 (80-589)
Leukocyte (10^3/µl)			10.7 (5.1-25.29)
NLR			4.06 (1.31-22.5)
Total Cholesterol (mg/dL)		199.22 ± 41.55	
HDL-C (mg/dL)		42 ± 14.02	
LDL-C (mg/dL)		124.51 ± 35.24	
Triglyceride (mg/dL)			137 (50-489)
Comorbidity			
Stroke	18 (40%)		
CVD	11 (24.4%)		

Neutrophil lymphocyte ratio and triglycerides were not normally distributed, while total cholesterol, HDL-C, and LDL-C were normally distributed. Random blood glucose varied with a median value of

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164 mg/dl, with the lowest result of 24 mg/dl and the highest value of 912 mg/dl. Fasting blood glucose with a median value of 144 mg/dl and postprandial blood glucose with a median value of 190 mg/dl. Leukocyte count varied from normal count (minimum value 5.1 x 10^3/µL) and leukocytosis (maximum value 25.29 x 10^3/µL). Lipid profile examination results varied from normal range values and dyslipidemia.

Table 2 showed the correlation test between NLR and the lipid profile. The correlation test analysis showed a negative correlation between NLR and HDL-C (p=0.035; r=-0.315) but no correlation with total cholesterol (p=0.061, r=-0.281), LDL-C (p=0.170, r=-0.208), or triglycerides (p=0.563, r=-0.089).

Table 2. Correlation test results between variables

Variables		*r*	*p**
NLR	Total cholesterol	-0,281	0,061
	HDL-C	-0,315	0,035
	LDL-C	-0,208	0,170
	Triglyceride	-0,089	0,563

*Spearman correlation test

According to Figure 1, the scatter plot graph showed a weak correlation between NLR values and HDL-C levels, with a linear R2 value of 0.149.

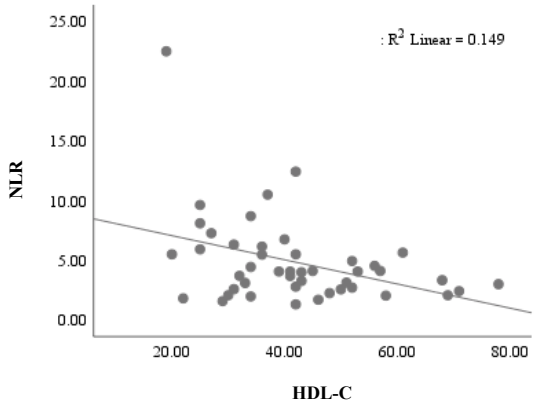

Fig 1. Correlation between NLR and HDL-C

DISCUSSION

Spearman correlation test analysis between NLR values and total cholesterol levels showed that there was no significant correlation (p = 0.061, r = -0.281). According to the findings of a study conducted by Syauqi et al., on the elderly in Taiwan, patients with T2DM and metabolic syndrome had higher NLR, BMI, hip circumference, waist circumference, and waist/hip ratio, while their HDL-C, LDL-C, triglyceride, and total cholesterol levels were lower. The high levels of NLR in this study were associated with gender and physical activity.[14] Meanwhile, different results were found in a study by Mete et al., which showed that there was a very weak positive relationship between NLR and total cholesterol levels (p = 0.003, r = 0.182) in healthy people.[15]

Both studies are different from the results of this study, a possible cause because the subjects in this study mostly had complications in the form of ischemic stroke (n = 18 [40%]). This is based on the research of Quan et al., which suggests that after an ischemic stroke, neutrophils will immediately exit the blood vessels and become the first immune cells to occupy brain tissue. The entry of neutrophils into the brain occurs due to damage to the blood-brain barrier, and if this condition continues, neutrophils will induce thrombus formation and release inflammatory mediators that can cause expansion of the infarction area. Lymphocytes also play a role in causing the expansion of the infarct area and post-ischemic behavioral deficits, but their role is slower than neutrophils. The presence of chronic inflammation and hypercholesterolemia causes the inflammation to be more massive, the area of damage is wider, and neurological deficits occur very quickly.[16] Meanwhile, the first week after an ischemic stroke, there will be a decrease in total cholesterol and LDL-C levels. [17]

Sudden physical activity can increase the inflammatory response, whereas gradual and regular physical activity has anti-inflammatory effects that are useful in chronic disease therapy. An increase in NLR may be indicative of chronic excessive physical activity.[18] Glycemic index control drugs used in T2DM treatment may also influence the study's findings. This is supported by a study by Solymar et al., who found that T2DM patients who received metformin therapy as a glycemic index controller had significantly lower total cholesterol and LDL-C levels, but no changes in HDL-C or triglyceride levels.[19] In addition, metformin can affect chronic inflammatory conditions because it can suppress the inflammatory response by inhibiting NFκB through

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AMPK and inhibiting the formation of AGEs and RAGE expression. [20]

Hyperglycemia conditions in T2DM patients cause AGE formation. Metformin will reduce AGE levels through the reaction between metformin molecules with dicarbonyl AGE precursors such as methylglyoxal. Metformin activates the AMPK pathway, which reduces ROS formation by RAGE suppression, inhibiting AGE-induced apoptosis, and reducing inflammation and fibrotic reactions in tubular cells. [20]

The Spearman test showed an association between NLR value and HDL-C level ($p = 0.035$, $r = -0.315$). The results of this study were in accordance with research by Aboulmakarim et al., which states that there was a negative correlation between NLR and HDL-C ($p = 0.01$, $r = 0.14$). 12 Different results were found in Mete et al.'s study. They report that there was no relationship between NLR and HDL-C levels. 15 According to Omodanisi et al., the lipid profile component that was most affected in T2DM conditions was HDL-C, which increased in triglyceride content in the HDL-C molecule, resulting in increased HDL-C excretion into LDL-C. [21]

Diabetes mellitus is a proinflammatory condition, mediated by increased expression of inflammatory cytokines and adhesion molecules. An increase in NLR will be associated with a decrease in HDL-C levels as an anti-inflammatory agent.[12] Decreased HDL-C levels impair HDL-C function as an inhibitor of cell surface molecule adhesion by activated endothelium. This leads to inhibition of sphingosine kinase and nuclear translocation of NF-κB, resulting in ROS and chemokines induced by oxLDLs. [22]

A decrease in HDL-C levels can occur during inflammation due to structural changes that can be hydrolyzed by lipase enzymes, becoming smaller in size and more rapidly cleared by Apo A-I. LCAT activity in the process of cholesterol esterification becomes lower during inflammation, which can also trigger a decrease in HDL-C.[23]

In vivo studies using mice have shown that HDL-C has an important role in protecting pancreatic β-cells from glucose toxicity and IL-1β. HDL-C also plays a role in increasing insulin activity and glucose uptake in skeletal muscle. Inflammation in T2DM causes changes in the HDL-C proteome. It can eliminate the normal function of HDL-C and turn into proatherogenic. Inflammation also turns HDL-C into proinflammatory particles by increasing the value of the HDL-C inflammatory index >1 which means HDL-C enhances the inflammatory response by oxLDL.[24]

HDL-C levels can also be affected by vitamin B complex supplementation, especially those containing niacin. Niacin can increase HDL-C levels.[25]

The Spearman correlation test between NLR and LDL-C levels showed no significant correlation ($p = 0.17$, $r = -0.208$). Kemba et al.'s study showed that an increase in NLR was associated with an increase in LDL-C levels. [22] Mete et al., in their study using healthy subjects, also reported that there was a relationship between NLR and LDL-C levels (p 0.001, $r = 0.26$).[15] This was related to the function of LDL-C as the main route of cholesterol and phospholipid transport. LDL-C will accumulate and oxidize to form ROS. Oxidized LDL-C (oxLDL) will activate NADPH oxidase, resulting in ROS overproduction and cellular oxidative stress. These ROS then activate the NFκB pathway, resulting in leukocyte recruitment and an increase in neutrophil count.[22] In this study, the different results could be due to comorbid factors in patients. cardiovascular disease can cause metabolic disorders of LDL-C.

Research by Wu et al. showed that LDL-c levels in ischemic stroke patients in China were <70 mg/dL. The risk of ischemic stroke also increases when there is poor control of blood pressure and increased blood glucose levels. Chronic inflammation in T2DM can also cause a decrease in LDL-c levels to be very low by exacerbating the accumulation of cholesterol into macrophages.[26]

T2DM conditions can cause changes in the structure of LDL-C to be small and dense and easily oxidized and glycated.[27] This LDL-C structure is more atherogenic when compared to the normal LDL-C structure because LDL-C with this structure has a longer half-life in plasma and does not attach well to LDL-C receptors, causing these LDL-C particles to be easily oxidized. Increased interaction of small LDL-C particles with scavenger receptors promotes foam cell formation and atherogenesis, while lipoproteins retained in the intima undergo modification under oxidative stress conditions. It is this modification and oxidation of lipoproteins in the intima that triggers a cascade of inflammation and

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plaque formation in the blood vessels.[28] Elevated levels of oxidized LDL-C were found in T2DM patients at risk of cardiovascular disease.[29] These small and dense LDL-C particles due to T2DM are more likely to cause atherosclerosis compared to large and light LDL-C particles. Niacin administration can affect sdLDL levels by increasing the highest diameter of particles and decreasing sdLDL levels.[30]

Spearman correlation test analysis between NLR values and triglyceride levels showed that there was no significant relationship ($p = 0.563$, $r = -0.089$). The results of research by Eftekharian et al. showed that for every increase of 5 units of triglycerides, there was an increase in NLR by 1 unit ($p = 0.012$, $r = 0.21$).[11] Insulin resistance conditions are associated with chronic inflammation, which causes changes in NLR values. Triglyceride accumulation is also associated with insulin resistance. Insulin resistance will inhibit lipolysis in adipose tissue and cause an increase in plasma free fatty acid levels. [31] Meanwhile, the results of a study by Mete et al. found no significant relationship between NLR and triglycerides in healthy people ($p = 0.439$, $r = 0.047$).[15] A decrease in the number of triglycerides occurs in a state of high NLR reported by Syauqy et al. in their study using subjects with metabolic syndrome. [14]

Triglyceride levels in the blood are a balance between synthesis and use. They are influenced by insulin sensitivity, diet, and fasting conditions. Triglycerides can be a very sensitive parameter at a certain point in time but can also be inaccurate when reflecting triglyceridemia in the long term, especially if lifestyle modifications are involved.[32] Research by Ren et al. suggests that there are differences in triglyceride levels based on the duration of diabetes. T2DM in the short term showed that high triglyceride levels were associated with an increased risk of heart and vascular disease complications, but in contrast to prolonged T2DM because a decrease in triglyceride levels actually increases the risk of these complications. [33] This suggests that a decrease in triglyceride levels does not always show good clinical results but can increase the risk of heart and vascular disease complications in T2DM. This study has several limitations. It does not pay attention to the duration of T2DM, drugs or supplements consumed, comorbidity, lifestyle, nutritional status, diet, and physical activity that can affect the development of T2DM.

CONCLUSION

There was a weak negative correlation between NLR values and HDL-C levels in T2DM patients. There was no correlation of NLR with other lipid profiles. Further research needs to be done by considering the duration of DM, comorbidity factors, and patient lifestyle.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Boyko EJ, Magliano DJ, Karuranga S, Piemonte L, Riley P, Saeedi P, et al., editors. 2021.
2. Jamerson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J, editors. Harrison's Principles of Internal Medicines. 20th ed. USA: McGraw-Hill Education; 2018. 2850–2909 p.
3. Wan H, Wang Y, Fang S, Chen Y, Zhang W, Xia F, et al. Associations between the Neutrophil-to-Lymphocyte Ratio and Diabetic Complications in Adults with Diabetes: A Cross-Sectional Study. J Diabetes Res. 2020:1–9.
4. Sun HJ, Wu ZY, Nie XW, Bian JS. Role of endothelial dysfunction in cardiovascular diseases: The link between inflammation and hydrogen sulfide. Front Pharmacol. 2020;10(1568):1–15.
5. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci. 2022;23(7):1–10.
6. Firooz M, Moradi B, Hosseini SJ. Leukocytosis in Diabetic Ketoacidosis; Whether the Time Has Come to Start Antibiotics? A Short Literature Review. Patient Saf Qual Improv J. 2019;7(1):27–8.
7. Bajpai A, Tilley DG. The Role of Leukocytes in Diabetic Cardiomyopathy. Front Physiol. 2018;9(1547):1–12.
8. Wibisana KA, Subekti I, Antono D, Nugroho P. Hubungan antara Rasio Neutrofil Limfosit dengan Kejadian Penyakit Arteri Perifer Ekstremitas Bawah pada Penyandang Diabetes Melitus Tipe 2. J Penyakit Dalam Indones. 2019;5(4):184–8.

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9. Hirano T. Pathophysiology of diabetic dyslipidemia. J Atheroscler Thromb. 2018;25(9):771–82.
10. Ma M, Liu H, Yu J, He S, Li P, Ma C, et al. Triglyceride is independently correlated with insulin resistance and islet beta cell function: A study in population with different glucose and lipid metabolism states. Lipids Health Dis. 2020;19(121):1–12.
11. Eftekharian MM, Karimi J, Safe M, Sadeghian A, Borzooei S, Siahpoushi E. Investigation of the correlation between some immune system and biochemical indicators in patients with type 2 diabetes. Hum Antibodies. 2016;24(1–2):25–31.
12. Aboulmakarim S, Boukhira A, Sayagh S, Chellak S. Association of Lipid Ratios and Neutrophil-lymphocyte Ratio in Type 2 Diabetic Moroccan Patients Without Chronic Kidney Disease. Am J Lab Med. 2021;6(6):107–13.
13. Dudani S, Poodury S, Mangalesh S. Study of neutrophil-lymphocyte ratio (NLR) in recent onset type 2 diabetes mellitus. Bali Med J. 2021;10(1):11–6.
14. Syauqy A, Hsu CY, Rau HH, Chao JCJ. Association of dietary patterns, anthropometric measurements, and metabolic parameters with C-reactive protein and neutrophil-to-lymphocyte ratio in middle-aged and older adults with metabolic syndrome in Taiwan: A cross-sectional study 11 Medical and Hea. Nutr J. 2018;17(1):1–12.
15. Mete B, Sait Değer M, Zoroğlu G. Relationship between blood lipids, inflammation parameters and body composition. Cukurova Med J Cukurova Med J. 2020;45(4):1555–61.
16. Quan K, Wang A, Zhang X, Meng X, Chen P, Li H, et al. Neutrophil to lymphocyte ratio and adverse clinical outcomes in patients with ischemic stroke. Ann Transl Med. 2021;9(13):1047–1047.
17. Weir CJ, Sattar N, Walters MR, Lees KR. Low triglyceride, not low cholesterol concentration, independently predicts poor outcome following acute stroke. Cerebrovasc Dis. 2003;16(1):76–82.
18. Walzik D, Joisten N, Zacher J, Zimmer P. Transferring clinically established immune inflammation markers into exercise physiology: focus on neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and systemic immune-inflammation index. Eur J Appl Physiol. 2021;121(7):1803–14.
19. Solymár M, Ivic I, Pótó L, Hegyi P, Garami A, Hartmann P, et al. Metformin induces significant reduction of body weight, total cholesterol and LDL levels in the elderly – A meta-analysis. PLoS One. 2018;13(11):e0207947.
20. Saisho Y. Metformin and Inflammation: Its Potential Beyond Glucose-lowering Effect. Endocrine, Metab Immune Disord Targets. 2015;15:196–205.
21. Omodanisi EI, Tomose Y, Okeleye BI, Ntwampe SKO, Aboua YG. Prevalence of dyslipidaemia among type 2 diabetes mellitus patients in the Western Cape, South Africa. Int J Environ Res Public Health. 2020;17(23):1–12.
22. Kemba M, Suguna S. Neutrophil-Lymphocyte Ratio: A Risk Predictor in Patients with Type 2 Diabetes Mellitus. Int J Physiol. 2017;5(1):166–70.
23. Feingold KR, Grunfeld C. Effect of inflammation on HDL structure and function. Curr Opin Lipidol. 2016;27(5):521–30.
24. Farbstein D, Levy AP. HDL dysfunction in diabetes: Causes and possible treatments. Expert Rev Cardiovasc Ther. 2012;10(3):353–61.
25. Gordon SM, Amar MJ, Jeiran K, Stagliano M, Staller E, Playford MP, et al. Effect of niacin monotherapy on high density lipoprotein composition and function. Lipids Health Dis. 2020;19(1):1–10.
26. Wu Z, Huang Z, Lichtenstein AH, Liu Y, Chen S, Jin Y, et al. The risk of ischemic stroke and hemorrhagic stroke in Chinese adults with low-density lipoprotein cholesterol concentrations < 70 mg/dL. BMC Med. 2021;19(1):1–11.
27. Pinakesty A, Azizah RN. Correlation Between Lipid Profile with Type 2 Diabetes Mellitus Progression. JIMKI. 2020;8(2):66–72.
28. Sugden M, Holness M. Pathophysiology of diabetic dyslipidemia: Implications for atherogenesis and treatment. Clin Lipidol. 2011;6(4):401–11.
29. Linton MF, Yancey PG, Davies SS, Jerome WG, Linton EF, Song WL, et al. The Role of Lipids and Lipoproteins in Atherosclerosis. In: Feingold KR, Anawalt B, Boyce A, editors.

JURNAL KEDOKTERAN DIPONEGORO
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JKD (DMJ), Volume 14, Number 2, March 2025 : 55-61

Endotext. South Dartmouth (MA): MDText.com, Inc.; 2019 [cited 2022 Dec 20]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK343489/

30. Jin X, Yang S, Lu J, Wu M. Small, Dense Low-Density Lipoprotein-Cholesterol and Atherosclerosis: Relationship and Therapeutic Strategies. Front Cardiovasc Med. 2022;8(2):1–14.
31. Lou M, Luo P, Tang R, Peng Y, Yu S, Huang W, et al. Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. BMC Endocr Disord. 2015;15(1):5841–6.
32. Tirosh A, Shai I, Bitzur R, Kochba I, Tekes-Manova D, Israeli E, et al. Changes in Triglyceride Levels Over Time and Risk of Type 2 Diabetes in Young Men. Diabetes Care. 2008;31(10):2032.
33. Ren Y, Ren Q, Lu J, Guo X, Huo X, Ji L, et al. Low triglyceride as a marker for increased risk of cardiovascular diseases in patients with long-term type 2 diabetes: A cross-sectional survey in China. Diabetes Metab Res Rev. 2018;34(2).