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Retrospective analysis of the relationship between neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and glycemic regulation in patients with type 2 diabetes mellitus followed up at an internal medicine outpatient clinic

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Ethics Committee Approval
The study was approved by Balıkesir University Faculty of Medicine Clinical Research Ethics Committee (March 22, 2023 and 2023/35). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Type 2 diabetes mellitus (T2DM) is a common chronic disease with an increasing incidence worldwide and its effects are being seen in many countries. Insulin resistance is the main factor in the pathophysiology. T2DM leads to an increase in mortality and morbidity due to macrovascular and microvascular complications. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are effective parameters in monitoring the inflammatory response. The primary aim of this study was to investigate glycemic control in patients with type 2 diabetes by focusing on their correlation with inflammatory markers, such as NLR and PLR, glycated hemoglobin (HbA1c), and fasting blood glucose levels.

Methods: The present study was carried out in 2022 within the purview of the Internal Medicine Clinic at Balikesir İvrindi State Hospital. Data from the initial annual consultations of patients with T2DM, either newly diagnosed or previously diagnosed and visiting for follow-up, were utilized. Our study excluded patients under the age of 18 and those diagnosed with cirrhosis, heart failure, type 1 diabetes mellitus, malignancy, epilepsy, acute infection, pregnancy, or chronic inflammatory disease. We further excluded those on medications including steroids, antivirals, anticonvulsants, antipsychotics, antithyroids, and chemotherapeutic drugs that impact the leukocyte count. Based on their HbA1c levels, patients were systematically categorized into two distinct cohorts: those with controlled blood sugar (HbA1c ≤7%) and those with uncontrolled blood sugar (HbA1c >7%). In the ambit of this study, we incorporated data from 205 patients. We employed a cross-sectional study that retrospectively examined the correlation between NLR, PLR, and glycemic regulation in T2DM patients. SPSS 22.0 software was used to perform statistical calculations.

Results: It was observed that patients with poor glycemic control had longer disease durations and this disparity bore statistical significance (P=0.005). Patients exhibiting poor glycemic control demonstrated elevated levels of CRP (C-reactive protein), a difference that reached statistical significance (P=0.003). The group exhibiting poor glycemic control demonstrated a notable elevation in NLR, indicating statistical significance (P=0.001). Although it was not statistically significant, PLR was found to be higher in patients with uncontrolled T2DM (P=0.441).

Conclusion: This research investigates the correlation between HbA1c levels and inflammatory markers, specifically NLR and TLR, in T2DM patients who exhibit poor control of glycemia. Our findings highlight the potential of these markers as indicators of glycemic control, thus emphasizing the need for integrated strategies for managing inflammation and improving glycemic control in T2DM patients. The novelty of this area of research contributes to the scarcity of available literature, underlining the importance and timeliness of this study. Based on our findings, we suggest an increased focus on regular monitoring of inflammatory markers, for instance NLR and PLR, to assess the glycemic control in T2DM patients. The significant correlation of these markers with HbA1c levels implies that they could potentially serve as useful tools in personalizing diabetes management strategies, leading to improved patient outcomes. Not only does our research contribute to filling this knowledge gap, but it also underscores the potential for utilizing inflammatory markers in tracking disease progression and optimizing treatment efficacy in T2DM.

Keywords: neutrophil lymphocyte ratio, platelet lymphocyte ratio, type 2 diabetes mellitus

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease that causes multi-organ involvement and dysfunction. The most important feature is that it occurs with insulin resistance [1]. The global incidence of T2DM continues on an upward trend, with projections indicating an estimated prevalence of around 10.4% by the year 2040 [2]. T2DM causes a significant increase in mortality and morbidity due to chronic macrovascular and microvascular complications. Coronary artery disease, peripheral vascular disease, and cerebrovascular disease are prominent as macrovascular complications, while nephropathy, retinopathy, and neuropathy are defined as microvascular complications [3]. Hyperglycemia and insulin resistance cause stimulation of inflammatory processes. Markers of inflammation, specifically C-reactive protein (CRP) and interleukin-6 (IL-6), are noted to be significantly elevated in T2DM [4].

The ratio was obtained by dividing the absolute neutrophil count by the absolute lymphocyte count in the complete blood count is expressed as the neutrophil-lymphocyte ratio (NLR). It is an easily calculable and low-cost marker. This ratio stands as a crucial marker of systemic inflammatory response [5]. NLR independently prognosticates ventricular dysfunction, and is notably correlated with the severity and mortality outcomes in coronary artery disease [6]. The elevated NLR value has been shown to be correlated with a reduced overall survival duration in many cancers [7]. Moreover, empirical evidence underscores a significant association between NLR and the occurrence of diabetic nephropathy [8]. NLR may increase in T2DM patients, and this increase may indicate the inflammatory burden of T2DM [9]. The ratio of the absolute platelet count divided by the absolute lymphocyte count in the complete blood count is expressed as the platelet-lymphocyte ratio (PLR). PLR may be utilized as an inflammatory marker in rheumatologic diseases and chronic obstructive pulmonary disease [10,11]. There are studies showing that the PLR value can also be used as an inflammatory marker in T2DM patients [12,13]. The high level of inflammation has been observed in uncontrolled T2DM patients, as evaluated in the existing literature. Additionally, it is known that NLR and PLR values are associated with inflammation. The objective of this study is to clarify the association between NLR and PLR values, and reveal their potential influence on glycemic control among patients diagnosed with T2DM.

Materials and methods

Study design

This research was conceived as a retrospective, cross-sectional study, in the Internal Medicine Clinic of Balikesir İvrindi State Hospital between January 2022 and December 2022. After obtaining approval from the local ethics committee (2023/35, 22/03/2023), the study was initiated by accessing the patients' records by retrospectively scanning the hospital and laboratory systems. This research was performed with patients who visited the Internal Medicine Outpatient Clinic. All newly diagnosed or previously diagnosed T2DM patients were incorporated into the study. The first application of each patient in 2022 was considered. Patients with diagnoses of cirrhosis, heart failure, type 1 diabetes mellitus, malignancy, epilepsy, acute infection, pregnancy, chronic inflammatory disease, and patients under the age of 18 were excluded from the study. Those using steroids, antivirals, anticonvulsants, antipsychotics, antithyroids, and chemotherapeutic drugs that affect the leukocyte count were also excluded from the study. The total patient count for the study was established at 205. T2DM patients were divided into two groups: those with controlled blood glucose levels (HbA1c ≤7%) and those without (HbA1c >7%). The study was performed ensuring ethical conformity with the principles expounded in the Declaration of Helsinki.

Participant selection

The sample size calculation was performed utilizing G*Power 3.1, a software program created by Franz Faul at the University of Kiel, Germany. Setting the Type I error rate at 0.05 and confidence level at 90%, it was determined that a minimum sample size of 140 was necessary.

Data collection

All participants' demographic attributes, clinical details, and laboratory data were accumulated from their individual medical documents. Demographic characteristics and clinical and laboratory data of all participants were obtained from their respective medical records. In addition to their age, gender, T2DM disease duration, biochemical data such as alanine aminotransferase (ALT), fasting blood glucose, aspartate aminotransferase (AST), glycated hemoglobin (HbA1c), CRP, urea, creatinine, total protein, triglyceride (TG), albumin, total cholesterol, globulin, high-density lipoprotein (HDL), low-density lipoprotein (LDL), neutrophil count (NEU), white blood cell (WBC), platelet count (Plt), hemoglobin count (Hgb), lymphocyte count (LYM), iron, ferritin, and total iron binding capacity values were examined. NLR and PLR were evaluated by taking the ratio of the absolute neutrophil count and the absolute platelet count to the absolute lymphocyte count, respectively, from the evaluation of the complete blood count.

Statistical analysis

Data compiled during the investigation were recorded using the IBM SPSS 22.0 (SPSS INC, Chicago, IL, USA) software, and further statistical analyses were then conducted. In terms of descriptive statistics, continuous variables were denoted as mean (standard deviation), while categorical variables were presented as percentages. The normality of distribution within the groups was examined using both the Kolmogorov-Smirnov and Shapiro-Wilk tests. When comparing the two groups, numerical data following a normal distribution were assessed via the Student's t-test, while the Mann-Whitney U test was employed for numerical data exhibiting a non-normal distribution. The Chi-square test was applied to compare independent groups with categorical variables. Spearman's correlation analysis was deployed to identify linkages between continuous variables. Findings with *P*-values less than 0.05 were interpreted as statistically significant.

Results

Eighty-four cases with controlled blood sugar (HbA1c ≤%7) and 121 cases with uncontrolled blood sugar (HbA1c >%7) were used in this research. Table 1 presents the

demographic characteristics and laboratory parameters of the enrolled cases. The mean age of controlled T2DM patients was 64.6 (11.9) and the average age of uncontrolled T2DM patients was 65.5 (9.7). This distinction was determined to be statistically inconsequential (*P*=0.573). Fifty-eight (69%) of the controlled T2DM patients were female, while 26 (31%) were male; 79 (65.3%) of the uncontrolled T2DM patients were female, while 42 (34.7%) were male. No statistically significant difference was observed among controlled and uncontrolled patients in terms of gender (*P*=0.574). The mean duration of T2DM was determined to be 4.9 (3.2) years for controlled patients and 6.1 (3.2) years for uncontrolled patients. It was determined that the detected difference was statistically significant (*P*=0.005). A comparative analysis of fasting blood sugar values revealed an average of 140.7 (44.4) for the controlled group and an average of 228.8 (103.2) for the uncontrolled group (*P*<0.001). CRP values were determined to be an average of 1.04 (1.9) in the controlled group and 1.2 (1.8) in the uncontrolled group. Statistical analysis revealed that this discrepancy was significant (*P*=0.003). When compared to controlled T2DM patients, uncontrolled T2DM patients demonstrated significantly elevated NLR levels. This difference was found to carry statistical significance upon evaluation (*P*=0.001). TLR was lower in controlled T2DM patients compared to uncontrolled patients; however, this observation did not reach the threshold of statistical significance (*P*=0.441).

Table 1: Demographic characteristics and laboratory parameters of the study population

Parameter	Controlled T2DM (HbA1c ≤%7) (n=84) Mean (SD)	Uncontrolled T2DM (HbA1c >%7) (n=121) Mean (SD)	*P*-value
Age	64.6 (11.9)	65.5 (9.7)	0.573
Gender (Female/Male) n(%)	58 (69%)/26 (31%)	79 (65.3%)/42 (34.7%)	0.574
Duration of T2DM (years)	4.9 (3.2)	6.1 (3.2)	0.005
FPG (mg/dl)	140.7 (44.4)	228.8 (103.2)	<0.001
AST (U/L)	20.6 (12.9)	20.5 (12.9)	0.703
ALT (U/L)	18.7 (9.3)	19.3 (10.6)	0.918
Urea (mg/dl)	39 (18.2)	39 (21.4)	0.828
Creatinine (mg/dl)	1.1 (0.7)	1.1 (0.7)	0.806
Total Protein (g/dl)	7.6 (0.5)	7.5 (0.7)	0.401
Albumin (g/dl)	4.2 (0.3)	4.2 (0.4)	0.795
Globulin (g/dl)	3.3 (0.4)	3.3 (0.5)	0.999
Triglycerides (mg/dl)	165.6 (99.7)	182.1 (100.7)	0.173
Total Cholesterol (mg/dl)	201 (41.3)	208.6 (48.3)	0.503
LDL (mg/dl)	111 (33.9)	116.7 (38.5)	0.492
HDL (mg/dl)	57.4 (16.2)	57.1 (16.3)	0.908
CRP (mg/dl)	1.04 (1.9)	1.2 (1.8)	0.003
Iron (mg/dl)	65.1 (32.4)	72.3 (46.6)	0.580
TIBC (mg/dl)	336 (70.4)	349.2 (70.4)	0.304
Ferritin (ng/ml)	72.5 (163.8)	80.3 (155.5)	0.349
Hgb (g/dl)	13.2 (1.8)	13.6 (1.9)	0.056
WBC (10^3/µL)	8.1 (2.5)	8.2 (2.5)	0.717
NEU (#)	5.4 (2.0)	5.8 (2.3)	0.182
LYM (#)	1.7 (0.7)	1.5 (0.6)	0.007
PLT (10^3/µL)	251.6 (74.7)	231.1 (75.7)	0.060
NLR	3.3 (1.7)	4.5 (4.0)	0.001
TLR	164.7 (104.3)	171.3 (102.1)	0.441

T2DM: Type 2 diabetes mellitus HbA1c: glycated hemoglobin FBG: fasting blood glucose AST: aspartate aminotransferase ALT: alanine aminotransferase LDL: low-density lipoprotein HDL: high-density lipoprotein CRP: C-reactive protein TIBC: total iron binding capacity Hgb: hemoglobin count WBC: white blood cell count NEU: neutrophil count LYM: lymphocyte count PLT: platelet count NLR: neutrophil-to-lymphocyte ratio TLO: platelet-to-lymphocyte ratio

The correlation rates between HbA1c and other parameters are shown in Table 2. A high level of relationship was discerned between fasting blood sugar and HbA1c, and a low level of a relationship was discerned between NLR and HbA1c. This difference was found to carry statistical significance upon evaluation (Rho=0.642, *P*<0.001; Rho=0.177, *P*=0.011). A moderate level of correlation was found between TLR and HbA1c, but this was statistically insignificant (Rho=0.400, *P*=0.567). An inverse correlation of moderate strength between lymphocyte count and HbA1c was statistically validated (Rho=-0.207, *P*=0.003).

A high level of association was noted between NLR and TLR, and this was statistically validated (Rho=0.697, *P*<0.001). A low level of a link could be seen between NLR and fasting blood sugar, which was confirmed to be statistically meaningful. (Rho=0.235, *P*=0.001). A correlation of lower magnitude was additionally found between TLR and fasting blood sugar, but this was statistically insignificant (Rho=0.132, *P*=0.060). A low level of correlation was found between fasting blood sugar and triglycerides, and a moderate level of correlation was observed between age and duration of T2DM, and these were statistically significant (Rho=0.257, *P*<0.001; Rho=0.398, *P*<0.001).

Table 2: Correlation analysis between HbA1c and laboratory parameters

	HbA1c	
	Rho	***P*-value**
Age	-0.002	0.98
FPG (mg/dl)	0.642	<0.001
NLR	0.177	0.011
TLR	0.400	0.567
Duration of T2DM (years)	0.114	0.103
AST (U/L)	-0.117	0.930
ALT (U/L)	-0.056	0.421
Urea (mg/dl)	-0.011	0.881
Creatinine (mg/dl)	0.026	0.716
Total protein (g/dl)	-0.044	0.548
Albumin (g/dl)	-0.034	0.636
Globulin (g/dl)	0.014	0.850
Triglycerides (mg/dl)	0.136	0.053
Total cholesterol (mg/dl)	0.066	0.353
LDL (mg/dl)	0.024	0.733
HDL (mg/dl)	0.013	0.852
CRP (mg/dl)	-0.031	0.666
Iron (mg/dl)	0.025	0.752
TIBC (mg/dl)	0.066	0.412
Ferritin (ng/ml)	0.020	0.824
Hgb (g/dl)	0.082	0.242
WBC (10^3/µL)	0.046	0.510
NEU (#)	0.127	0.700
LYM (#)	-0.207	0.003
PLT (10^3/µL)	-0.135	0.540

HbA1c: glycated hemoglobin FBG: fasting blood glucose NLR: neutrophil-to-lymphocyte ratio TLR: platelet-to-lymphocyte ratio AST: aspartate aminotransferase ALT: alanine aminotransferase LDL: low-density lipoprotein HDL: high-density lipoprotein CRP: C-reactive protein TIBC: total iron binding capacity Hgb: hemoglobin count WBC: white blood cell count NEU: neutrophil count LYM: lymphocyte count PLT: platelet count

Discussion

Recently, several reports have shown that the progression of T2DM is significantly impacted by the presence of chronic inflammation [14]. Chronic inflammation plays a pivotal role in the pathogenesis of T2DM and metabolic syndrome, exerting its influence through immunological inflammatory mechanisms and contributing to the advancement of the disease [15,16]. The excessive secretion of some mediators (IL-1, IL-6, TNF-a, and CRP) and damage to the endothelium cause the complications of T2DM [17]. T2DM causes microvascular and macrovascular complications. These complications are the most important factors in increasing mortality and morbidity [18]. Blood glucose control is crucial in preventing complications. For many adult patients without pregnancy, the glycemic target in blood sugar control is set at HbA1c ≤7 [19].

There are many studies showing that glycemic control worsens as the duration of T2DM increases. The main reasons for this include the lack of regular follow-ups, failure of patients to pay attention to their diets, and poor medication adherence [20]. There are also studies on the worsening of glycemic control with the diagnosis of T2DM at a young age and the length of disease duration [21,22]. In the scope of our research, we

discerned a correlation that holds statistical significance between the length of T2DM affliction and poor glycemic control. CRP elevation is often observed in relation to inflammation. As glycemic control deteriorates, CRP levels increase [23]. Our investigation demonstrated a statistically significant correlation between an augmentation in CRP levels and compromised glycemic control. There are studies showing a linear relationship between high triglyceride levels and high HbA1c levels [24]. In addition to its relationship with glycemic control, high HbA1c levels are also considered to be an effective indicator of lipid profile [25]. Although not statistically significant, our study showed that the group with poor glycemic control had high levels of triglycerides and LDL.

NLR can be used as a non-invasive, easy, and economical indicator in the evaluation of systemic inflammation. This indicator can be easily obtained through complete blood count analysis. Some studies have shown a relationship between NLR and T2DM [26]. Others have shown that as glycemic control deteriorates, NLR levels increase [27]. In our investigation, a statistically meaningful increase in NLR was noted in T2DM patients lacking effective glycemic control.

Research has suggested that T2DM patients have inadequate lymphocyte proliferation. One study indicated that there may be an increase in NLR due to a decrease in lymphocyte count caused by hyperglycemia [28]. In our study, the lymphocyte count was lower in T2DM patients with uncontrolled disease, and this was statistically significant. Several research investigations have identified a positive association between HbA1c and WBC counts in patients afflicted with T2DM [29]. Other studies suggest that elevated WBC counts are associated with impaired insulin sensitivity in T2DM patients [30]. In our study, WBC count was found to be higher in uncontrolled T2DM patients; however, this difference did not reach the threshold of statistical significance.

Research has shown an increase in TLR ratio in relation to increased platelet count in T2DM patients [31]. Our study found that TLR was high in patients with poor glycemic control, but this was determined to be statistically insignificant.

Limitations

There are some limitations in the current study. First, the possibility of error cannot be ruled out, since laboratory measurements were made only once. Second, because the study design was retrospective, patients could not be reached to measure height, weight, and body mass index, which affect NLR and other parameters. Third, the single center where the study was conducted is a factor limiting the external validity of those measured. In addition, sampling sizes and sampling groups were obtained from only one region; therefore, data from different situations and larger sampling groups need to be validated before the outcomes of this research can be generalized to a larger sample.

Conclusion

T2DM is a chronic, multisystemic disease whose impact extends beyond hyperglycemia to a broader range of complications including inflammatory pathologies. The association of inflammation with T2DM underscores the relevance of inflammatory markers, such as NLR and TLR, as potential indicators of glycemic control in individuals with T2DM. Our study illuminates a possible relationship between the levels of HbA1c and values of NLR and TLR, particularly in patients presenting poor glycemic control. This association amplifies the significance of managing inflammation alongside improving glycemic control as integral strategies in T2DM management. Given the relatively novel nature of research within this area, there is a noticeable paucity of studies exploring these relationships. Thus, our findings fill a critical gap in the existing literature, serving as a robust platform for further investigations. In light of these insights, it becomes increasingly evident that integrating the monitoring of inflammatory markers into the treatment regimen could provide a more comprehensive understanding of disease progression and treatment efficacy in T2DM. As such, we anticipate that future research endeavors will further elucidate the mechanistic links between inflammation, NLR and TLR values, and glycemic control, thereby refining therapeutic strategies for T2DM and mitigating its associated complications.

References

1. Tinajero MG, Malik VS. An Update on the Epidemiology of Type 2 Diabetes: A Global Perspective. Endocrinol Metab Clin North Am. 2021 Sep;50(3):337-55. doi: 10.1016/j.ecl.2021.05.013.
2. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract. 2017 Jun;128:40-50. doi: 10.1016/j.diabres.2017.03.024.
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018 Feb;14(2):88-98. doi: 10.1038/nrendo.2017.151.
4. Wang X, Bao W, Liu J, Ouyang YY, Wang D, Rong S, et al. Inflammatory markers and risk of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2013 Jan;36(1):166-75. doi: 10.2337/dc12-0702.
5. Sen BB, Rifaioglu EN, Ekiz O, Inan MU, Sen T, Sen N. Neutrophil to lymphocyte ratio as a measure of systemic inflammation in psoriasis. Cutan Ocul Toxicol. 2014 Sep;33(3):223-7. doi: 10.3109/15569527.2013.834498.
6. Dong CH, Wang ZM, Chen SY. Neutrophil to lymphocyte ratio predict mortality and major adverse cardiac events in acute coronary syndrome: A systematic review and meta-analysis. Clin Biochem. 2018 Feb;52:131-6. doi: 10.1016/j.clinbiochem.2017.11.008.
7. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014 May 29;106(6):dju124. doi: 10.1093/jnci/dju124.
8. Khandare SA, Chittawar S, Nahar N, Dubey TN, Qureshi Z. Study of Neutrophil-lymphocyte Ratio as Novel Marker for Diabetic Nephropathy in Type 2 Diabetes. Indian J Endocrinol Metab. 2017 May-Jun;21(3):387-92. doi: 10.4103/ijem.IJEM_476_16.
9. Duman TT, Aktas G, Atak BM, Kocak MZ, Erkus E, Savli H. Neutrophil to lymphocyte ratio as an indicative of diabetic control level in type 2 diabetes mellitus. Afr Health Sci. 2019 Mar;19(1):1602-6. doi: 10.4314/ahs.v19i1.35.
10. El-Gazzar AG, Kamel MH, Elbahnasy OKM, El-Naggar ME. Prognostic value of platelet and neutrophil to lymphocyte ratio in COPD patients. Expert Rev Respir Med. 2020 Jan;14(1):111-6. doi: 10.1080/17476348.2019.1675517.
11. Gasparyan AY, Ayvazyan L, Mukanova U, Yessirkepov M, Kitas GD. The Platelet-to-Lymphocyte Ratio as an Inflammatory Marker in Rheumatic Diseases. Ann Lab Med. 2019 Jul;39(4):345-57. doi: 10.3343/alm.2019.39.4.345.
12. Abdallah A., Abdelaziz A., El-Sayed E., Emran T. Study of neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) as a predictor inflammatory marker for diabetic nephropathy in type 2 diabetic patients. The Egyptian Journal of Hospital Medicine, 72(7), 4800-7. doi: 10.21608/ejhm.2018.10137
13. Atak B, Aktas G, Duman TT, Erkus E, Kocak MZ, Savli H. Diabetes control could through platelet-to-lymphocyte ratio in hemograms. Rev Assoc Med. 2019 Jan;65(1):38-42. doi: 10.1590/1806-9282.65.1.38
14. Rohm TV, Meier DT, Olefsky JM, Donath MY. Inflammation in obesity, diabetes, and related disorders. Immunity. 2022 Jan 11;55(1):31-55. doi: 10.1016/j.immuni.2021.12.013.
15. Cho Y, Lee SY. Useful Biomarkers of Metabolic Syndrome. Int J Environ Res Public Health. 2022 Nov 15;19(22):15003. doi: 10.3390/ijerph192215003.
16. Dolapoğlu N, Yürekli BPŞ, Eker MÇ, Elbi H. Relationship Between Serum Agouti-Related Peptide Levels and Metabolic Syndrome in Euthymic Bipolar Patients. Noro Psikiyatr Ars. 2020 Oct 11;58(1):16-20. doi: 10.29399/npa.25005.
17. Liu C, Feng X, Li Q, Wang Y, Li Q, Hua M. Adiponectin, TNF-α and inflammatory cytokines and risk of type 2 diabetes: A systematic review and meta-analysis. Cytokine. 2016 Oct;86:100-9. doi: 10.1016/j.cyto.2016.06.028.
18. Goyal R, Jialal I. Diabetes Mellitus Type 2. 2022 Jun 19. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 30020625.
19. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. On behalf of the American Diabetes Association. 6. Glycemic Targets: Standards of Care in Diabetes-2023. Diabetes Care. 2023 Jan 1;46(Suppl 1):S97-S110. doi: 10.2337/dc23-S006.
20. Hartz A, Kent S, James P, Xu Y, Kelly M, Daly J. Factors that influence improvement for patients with poorly controlled type 2 diabetes. Diabetes Res Clin Pract. 2006 Dec;74(3):227-32. doi: 10.1016/j.diabres.2006.03.023.
21. Al-Eitan LN, Nassar AM, Saadeh NA, Almomani BA. Evaluation of Glycemic Control, Lifestyle and Clinical Characteristics in Patients with Type 2 Diabetes Treated at King Abdullah University Hospital in Jordan. Can J Diabetes. 2016 Dec;40(6):496-502. doi: 10.1016/j.jcjd.2016.04.009.
22. Al-Ma'aitah OH, Demant D, Jakimowicz S, Perry L. Glycaemic control and its associated factors in patients with type 2 diabetes in the Middle East and North Africa: An updated systematic review and meta-analysis. J Adv Nurs. 2022 Aug;78(8):2257-76. doi: 10.1111/jan.15255.
23. Luc K, Schramm-Luc A, Guzik TJ, Mikolajczyk TP. Oxidative stress and inflammatory markers in prediabetes and diabetes. J Physiol Pharmacol. 2019 Dec;70(6). doi: 10.26402/jpp.2019.6.01.

24. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. Clin Exp Med. 2007 Mar;7(1):24-9. doi: 10.1007/s10238-007-0121-3.
25. Al Quran TM, Bataineh ZA, Al-Mistarehi AH, Zein Alaabdin AM, Allan H, Al Qura'an A, et al. Prevalence and Pattern of Dyslipidemia and Its Associated Factors Among Patients with Type 2 Diabetes Mellitus in Jordan: A Cross-Sectional Study. Int J Gen Med. 2022 Oct 4;15:7669-83. doi: 10.2147/IJGM.S377463.
26. Bilgin S, Aktas G, Zahid KM, Atak BM, Kurtkulagi O, Duman TT, Savli H. Association between novel inflammatory markers derived from hemogram indices and metabolic parameters in type 2 diabetic men. Aging Male. 2020 Dec;23(5):923-7. doi: 10.1080/13685538.2019.1632283.
27. Sefil F, Ulutas KT, Dokuyucu R, Sumbul AT, Yengil E, Yagiz AE, et al. Investigation of neutrophil lymphocyte ratio and blood glucose regulation in patients with type 2 diabetes mellitus. J Int Med Res. 2014 Apr;42(2):581-8. doi: 10.1177/0300060513516944.
28. Chang FY, Shaio MF. Decreased cell-mediated immunity in patients with non-insulin-dependent diabetes mellitus. Diabetes Res Clin Pract. 1995 May;28(2):137-46. doi: 10.1016/0168-8227(95)00168-8.
29. Tong PC, Lee KF, So WY, Ng MH, Chan WB, Lo MK, et al. White blood cell count is associated with macro- and microvascular complications in Chinese patients with type 2 diabetes. Diabetes Care. 2004 Jan;27(1):216-22. doi: 10.2337/diacare.27.1.216.
30. Buyukkaya E, Karakas MF, Karakas E, Akçay AB, Tanboga IH, Kurt M, et al. Correlation of neutrophil to lymphocyte ratio with the presence and severity of metabolic syndrome. Clin Appl Thromb Hemost. 2014 Mar;20(2):159-63. doi: 10.1177/1076029612459675.
31. Akinsegun A, Akinola OD, Sarah JO, Olajumoke O, Adewumi A, Majeed O, et al. Mean platelet volume and platelet counts in type 2 diabetes: mellitus on treatment and non-diabetic mellitus controls in Lagos, Nigeria. Pan Afr Med J. 2014 May 12;18:42. doi: 10.11604/pamj.2014.18.42.3651.