MEANDROS MEDICAL AND DENTAL JOURNAL
March 2025 (1):129:135

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1614618

Research Article

INVESTIGATION OF INFLAMMATION RATES (NEUTROPHIL/LYMPHOCYTE) AND HEMOGRAM RESULTS IN THE STAGES OF NON-ALCOHOLIC FATTY LIVER DISEASE

Mehmet Ali GÜL [1]*, Duygu TOZCU YILMAZ [2], Mustafa ÇAPRAZ [3]

[1]Department of Medical Biochemistry, Faculty of Medicine, Amasya University, Amasya, Türkiye
[2]Department of Physiology, Faculty of Medicine, Amasya University, Amasya, Türkiye
[3]Department of Internal Diseases, Faculty of Medicine, Amasya University, Amasya, Türkiye
*Correspondence: mehmetali.gul@amasya.edu.tr

Received: *08 January 2025*
Revised: *02 February 2025*
Accepted: *07 February 2025*
Published: *20 March 2025*

ABSTRACT

Objective: Non-alcoholic fatty liver disease (NAFLD) is a chronic condition characterized by excessive fat accumulation in the liver accompanied by inflammation. This study aims to know the diagnostic value of NLR (neutrophil to lymphocyte ratio) in stages of NAFLD.

Materials and Methods: A retrospective case-control study was performed, including 49 NAFLD patients with NAFLD Grade 1, 48 with NAFLD Grade 2, 52 with NAFLD Grade 3, and 103 healthy control (HC) individuals. Neutrophil/Lymphocyte ratios as well as RBC, HGB, HCT, MCHC, MPV, WBC, NEUT#, RDW-CV, BASO%, MCH, LYMPH%, PDW, PCT, NLR, EO%, RDW-SD, MONO%, PLT, MCVvalues were examined.

Results: As the disease stages progressed (G3), a significant decrease ($p=0.005^*$) in MPV values and a significant increase ($p<0.05^\#$) in NLR values were observed. No statistically significant difference was found between the groups in RBC ($p=0.061$), HCT ($p=0.097$), MCHC ($p=0.747$), MCV ($p>0.05$), MCH ($p>0.05$), PDW ($p>0.05$), PCT ($p>0.05$), MONO ($p>0.05$) and EO ($p>0.05$) parameters.

Conclusion: MPV and NLR may be considered as effective biomarkers for monitoring the progression of NAFLD and evaluating the inflammatory status of patients.

Keywords: Non-Alcoholic Fatty Liver Disease, Neutrophil/Lymphocyte, Mean platelet volume

MEANDROS MEDICAL AND DENTAL JOURNAL
March 2025 (1):129:135

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1614618

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is recognized as the most prevalent form of chronic liver disease worldwide and defined as the accumulation of fat above 5% of hepatocytes or liver weight that is not caused by alcohol intake or secondary causes (1). The incidence of NAFLD is increasing due to the increase in obesity and diabetes and the lack of effective treatment methods. Global NAFLD incidence was eported at approximately 4.600/100.000 person years, with higher rates observed in men, individuals who are overweight or obese, and a more than threefold increase in incidence from 2000 to 2015 (2, 3). Although the development of non-alcoholic ateatohepatitis (NASH) is a multifaceted process that remains incompletely understood, in the pathogenesis of the disease; the 'two-hit' theory, which includes several stress factors, has been replaced by the 'multiple hit' model, which includes many factors such as lipotoxicity, innate immune system activation and microbiome (4). Type 2 diabetes mellitus, obesity and dyslipidaemia are among the risk factors for NAFLD (5). NAFLD progresses in four main grading: Simple Fatty Liver (Steatosis), NASH, Fibrosis, and Cirrhosis (4). Liver biopsy is used as the gold standard for identification of NAFLD by evaluation of the degree of fibrosis and inflammation. However, this method may have serious risks such as bleeding and bile leakage. Although various inflammatory biomarkers have been used as both prognostic and predictive biomarkers in NAFLD, they have limitations (6).

Although some associations have been identified between certain blood cells and NAFLD, the exact role of blood cells in NAFLD has not been fully elucidated (7). Inflammation causes a stress response in hepatocytes, may lead to lipid accumulation and therefore may lead to steatosis. Studies have highlighted the significant presence of inflammatory factors in NAFLD, this study aimed to investigate the inflammatory indicators neutrophil to lymphocyte ratio (NLR) and Platelet/Lymphocyte ratios in the grades of NAFLD (8).

NLR is an easily accessible and low-cost indicator. The use of NLR in the prognosis of diseases such as chronic kidney disease and some cancers has increased over time (9). The NLR is considered an indicator of systemic inflammation. In NAFLD, fatty liver and inflammation may affect the immune response. An increase in this ratio may indicate increased inflammation and disease progression. However, there are few studies on whether this ratio differs between NAFLD stages. his study aims to analyze and compare the NLR, which has the potential to provide important information in terms of diagnosis and management of the disease, in NAFLD stages and to examine its status in healthy subjects.

MATERIALS AND METHODS

The study was planned as a retrospective study and was conducted by accessing the clinical files of individuals who applied to Amasya University Sabuncuoğlu Şerefeddin Training and Research Hospital between 2020-2024 and met the inclusion criteria for our study and evaluating the data from the hospital archive. According to the diagnoses in the patient file information, staging information of NAFLD was obtained. Separate groups were created for each staging. (Grade 1, Grade 2, Grade 3, Grade 4). A control group consisting of healthy individuals was created. Routine hematology and other information of the individuals included in the groups was obtained from the hospital archive. (RBC, HGB, MCV, MCH, HCT, MCHC, MPV, PLT, NLR, RDW-CV, BASO%, WBC, PCT, EO%, RDW-SD, LYMPH%, NEUT#, PDW, MONO%) Individuals with a history of alcohol consumption (those who consume more than 20 grams of alcohol per day). Individuals with anemia, leukemia or other hematological diseases, under age 18 and those receiving anti-inflammatory, immunosuppressive or hormone therapy were not included in the study. Amasya University Non-Interventional Clinical Research Ethics Committee approval was received for the study (2024/144).

Statistical analyses

Statistical analyses were conducted using SPSS software version 25 (SPSS Inc., Chicago, IL, USA). The normality of continuous variables was assessed visually (histograms and Q-Q plots) and analytically (Kolmogorov-Smirnov/Shapiro-Wilk tests).

Variables showing normal distribution according to the Shapiro-Wilk test were analyzed using one-way ANOVA, and homogeneity of variances was evaluated by Levene's Test. When $p > 0.05$, variances were considered homogeneous, and Tukey Post-Hoc Test was applied for pairwise comparisons. Results for normally distributed variables are presented as mean ± standard deviation (SD). For variables that did not show normal distribution, the Kruskal-Wallis test was used, and results were reported as median and interquartile range (IQR). For pairwise comparisons in non-normally distributed data, the Mann-Whitney U test was applied.

Qualitative variables were compared using the Chi-square test, and results were expressed as n (%). A p-value < 0.05 was considered statistically significant.

MEANDROS MEDICAL AND DENTAL JOURNAL
March 2025 (1):129:135

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1614618

Table 1: Descriptive Statistics of Hematological Parameters and Comparisons Between Groups

	HC (n=103)	G1 (n=49)	G2 (n=48)	G3 (n=52)	p-values
Age (years)	55.87 ± 7.8	55 ± 12.09	55.4 ± 12.1	52.6 ± 12.7[a]	**0.02***
Gender (n/%)	M: 49/47.6 F: 54/52.4	M: 34/69.4 F: 15/30.6	M: 31/64.6 F: 17/35.4	M: 31/59.6 F: 21/40.4	0.56[†]
RBC	4.94 ± 0.5	4.70 ± 0.63	4.77 ± 0.53	4.86 ± 0.52	0.061*
HGB	14.04 ± 1.7 [d]	13.32 ± 1.55	13.44 ± 1.83	13.98 ± 1.73	**0.037***
HCT	42.55 ± 4.57	41.15 ± 4.67	40.80 ± 4.7	42.29 ± 4.67	0.097*
MCHC	33.04 ± 1.27	32.86 ± 1.63	32.89 ± 1.41	33.10 ± 1.29	0.747*
MPV	10.48 ± 0.99	10.36 ± 1.2	10.16 ± 0.99	9.84 ± 1.15[d]	**0.005***
WBC	6.61 (2.35)	7.09 (2.59)	7.67 (1.89) [a,b]	7.47(2.40)	**<0.05[#]**
MCV	87 (6.4)	87 (5.3)	86 (6.5)	86.7 (6.7)	>0.05[#]
MCH	28.9 (2.9)	28.9 (2.8)	28.4 (2.3)	29.5 (2.6)	>0.05[#]
PLT	235 (66)	228 (101)	254 (105) [b]	262 (89) [b]	**<0.05[#]**
RDW-SD	40.6 (3.3)	43.2 (6)[a]	43 (5.68) [a]	41.8 (4.25) [a,b]	**<0.05[#]**
RDW-CV	12.8 (1.2)	13.8 (2.39) [a]	13.7 (1.55) [a]	13.1 (1.5) [a,c]	**<0.05[#]**
PDW	12.6 (3.2)	13.2 (4.2)	12.1 (4.7)	13.2 (4.9)	>0.05[#]
PCT	0.25 (0.1)	0.24 (0.1)	0.26 (0.08)	0.26 (0.11)	>0.05[#]
NEUT#	3.7 (1.67)	4.1 (1.98)	4.47 (1.58) [a]	4.2 (1.35) [a]	**<0.05[#]**
LYMPH%	2.3 (0.7)	1.9 (1.05) [a]	2.3 (1.04) [b]	2.3 (1.24) [b]	**<0.05[#]**
NLR	1.57 (0.78)	1.9 (1.03) [a]	1.89 (1.32) [a]	1.88 (1.2)	**<0.05[#]**
MONO%	0.5 (0.21)	0.45 (0.25)	0.6 (0.26)	0.5 (0.21)	>0.05[#]
EO%	0.13 (0.1)	0.13 (0.14)	0.15 (0.13)	0.15 (0.11)	>0.05[#]
BASO%	0.3 (0.4)	0.3 (0.2)	0.4 (0.3) [a,b]	0.4 (0.3) [a,b]	**<0.05[#]**

a: Compared to HC. b: compared to G1. c: compared to G2. d: compared with other groups.*One-way ANOVA, #Kruskall-Wallis, †Ki-square test.
M: Male, F: Female, HC: healthy controls, G. grade; red blood cells (RBC), white blood cell (WBC), platelet (PLT), hemoglobin (HGB), hematocrit (HCT), neutrophil (NEUT#), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), red cell distribution width-coefficient of variation (RDW-CV), red cell distribution width-standard deviation (RDW-SD), platelet distribution width (PDW), plateletcrit (PCT), lymphocyte (LYMPH), eosinophil (EO), lymphocyte percentile (LYM%), monocyte percentile (MONO%), eosinophil percentile (EOS %), basophil percentile (BASO%), neutrophil lymphocyte ratio (NLR). MPV. mean platelet volume; NLR. neutrophil lymphocyte ratio.

RESULTS

A statistically significant difference was found between the groups in age values (p = 0.02). In the post-hoc analysis, a significant difference was found between HC and G3; the mean age was highest in the Grade 3 group. According to the results of the Chi-Square test, there was no significant difference in gender distribution between the groups (p = 0.56). The proportion of males appears to be higher in the G1 and G2 groups.

No statistically significant difference was found between the groups in RBC (p=0.061), HCT (p=0.097), MCHC (p=0.747), MCV (p>0.05), MCH (p>0.05), PDW (p>0.05), PCT (p>0.05), MONO (p>0.05) and EO (p>0.05) parameters. HGB (a significant difference was found between the groups (p = 0.037); however, no significant difference was found in post hoc analysis. Especially the HGB value of the HC group was higher than the other groups. A significant difference was found between the groups in MPV values (p = 0.005). The results are shown in Table 1. Especially in the G3 group, MPV value was lower than the other groups. There was a significant difference between the groups in WBC values (p < 0.05). In the pairwise comparison made by Mann Whitney- U test, WBC values were found to be significantly higher in the G2 group compared to the HC group and the G1 group. A significant difference was found between the groups in PLT values (p < 0.05). In the pairwise comparison made by Mann Whitney- U test, it was significantly higher in G2 and G3 groups compared to G1 group. A significant difference was found between the groups in NLR values (p < 0.05). In the pairwise comparison made with Mann Whitney- U test, NLR values were significantly higher in G1 and G2 groups compared to HC group. It is shown in the Figure 1a, b, c, d, e. A significant difference was found between the groups in BASO values (p < 0.05). In the pairwise comparison made with Mann Whitney- U test, especially in G2 and G3 groups, BASO value is significantly higher than HC and G1 groups

MEANDROS MEDICAL AND DENTAL JOURNAL
March 2025 (1):129:135

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1614618

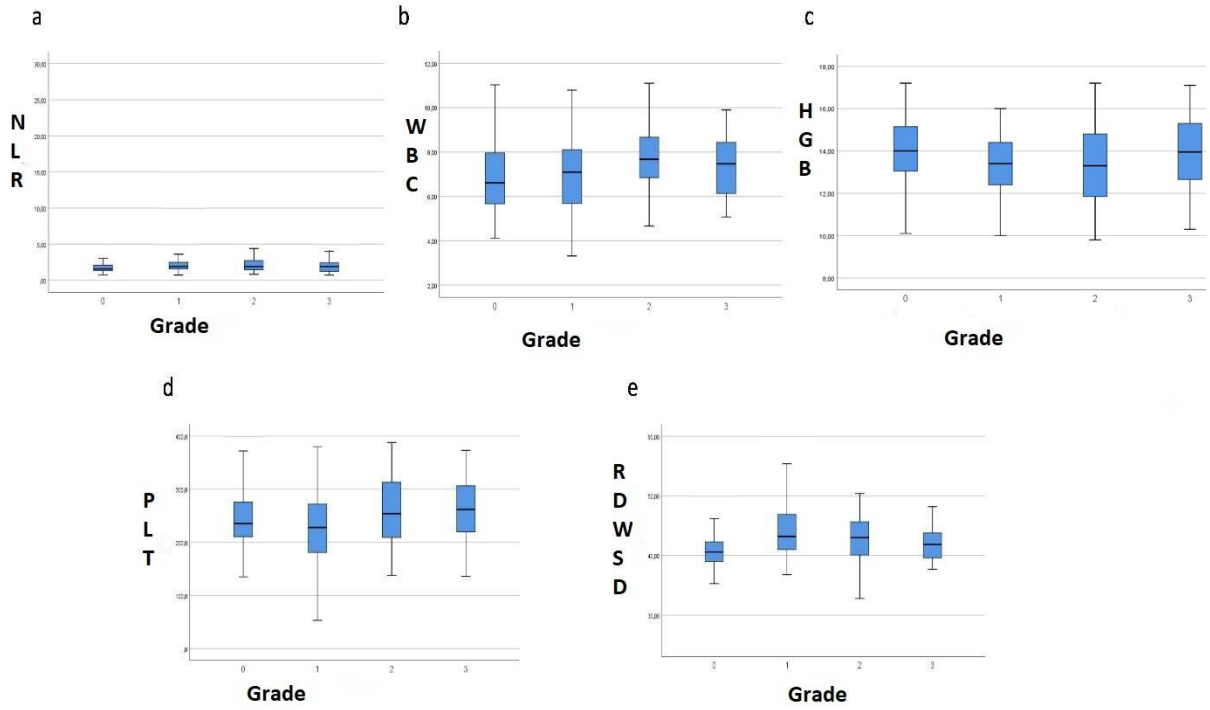

Figure 1 a: Comparison of NLR results according to NAFLD grades,**b:** Comparison of WBC results according to NAFLD grades, **c:** Comparison of HGB results according to NAFLD grades, **d:** Comparison of PLT results according to NAFLD grades e: Comparison of RDWSD results according to NAFLD grades, a: Compared to HC. b: compared to G1. c: compared to G2. d: compared with other groups.

.

DISCUSSION

Metabolic dysfunction-associated liver disease (MASLD) is a substance-independent condition with microvesicular steatosis in ⩾5% of liver cells, including several disease classes such as NASH, liver cirrhosis, non-alcoholic fatty liver and fibrosis (10). The incidence of the disease is increasing and studies on it also reveal its relationship with other diseases. While NAFLD accounts for 40% of deaths from cardiovascular disease, research shows that this disease can increase cardiovascular risk independently of typical risk factors and impacts up to 70% of diabetic patients (11). Recent studies have shown that NAFLD is higher in men and obese individuals, has increased three-fold between 2000 and 2015, treatment options are limited, and prevention of NAFLD should continue to be the focus of public health strategies (2).
Additionally, this procedure is costly, prone to significant sampling error considering the ratio of the obtained sample to liver volume, has poor reproducibility, and is susceptible to post-analytical errors during interpretation (12, 13).

This study demonstrated that changes in haematological parameters become prominent in the progressive stages of NAFLD and these changes have the potential to shed light on the pathophysiology of the disease. In particular, significant increases in WBC, RDW-SD, RDW-C, NEUT and LYMP values suggest that inflammation and systemic immune response could contribute significantly to the progression of NAFLD. In our study, significant decrease in MPV values (p= 0.005*) and a significant increase in NLR values (p<0.05#) were observed as the disease stages progressed (G3). These two parameters indicate that platelet functions and inflammatory processes should be evaluated together in the progression of NAFLD. However, parameters such as RBC and HGB remained constant, suggesting that red blood cells and heemoglobin may be less affected by the stages of the disease. Decreased MPV may reflect changes in platelet activation and potentially microvascular dysfunction. Lower MPV values may be associated with progression of inflammation and liver fibrosis. Increased NLR indicates exacerbation of systemic inflammation and the emergence of a neutrophil-dominated immune response. This finding supports that

inflammation is a fundamental mechanism in the pathogenesis of NAFLD.

NAFLD is a major health concern and is projected to become the primary reason for liver transplantation within the next decade (14). As a result of cumulative meta analysis of NAFLD studies and a meta-analysis of changes in metabolism-related parameters, Akdas et al. showed that NAFLD patients have a high risk of metabolic dysfunction and that most of the Turkish NAFLD patients identified in previous studies may have MASLD. Also Akdas et al. showed that elevated levels of ferritin, hemoglobin, creatinine, CRP, and ESR, along with metabolism disorders related wtih glucose, hyperlipidemia, impaired liver function, and high blood pressure values, were observed in NAFLD patients in Türkiye (15). It has been shown how important NAFLD is and how it causes various changes in metabolism. In another metanalysis study, Shavakhi et al. showed that NLR may be suitable biomarker to help in the prediction and prevention of NASH and fibrosis in patients with NAFLD (16).

NLR ratio has the advantage of simple calculation. It is considered potential noninvasive markers for predicting advanced disease. In parallel with our work, Abdel-Razik et al. found that NLR ratio was higher in NASH group than in non-NASH patients (17). In their study, Wenyi et al. showed that there were negative correlations between high NLR levels and patients with NAFLD exhibiting severe inflammatory activity and substantial fibrosis (18). Otherwise, a large cohort study by Kara et al. revealed that NLR was not linked to the severity of NAFLD.- (19). Although a large study on this condition, Kara et al.'s study had limitations: The study group mainly included mild NAFLD cases, limiting its applicability to severe cases (19).

In contrast to the literature which found a correlation between non-alcoholic steatohepatitis and NLR, Acar et al. did not find a correlation between simple fatty liver disease and NLR in their study (20). Wang et al. reported that NLR levels were positively linked to the the extent of liver fibrosis in individuals with NAFLD (21). But the initial stage of the disease or between other stages was not examined. In a case-control study conducted by Duan et al in children with NAFLD, they found that NLR showed no significant difference between the two study groups (22). Karaoğullarından et al., in contrast to our study, showed that MPV was notably higher in the NAFLD group compared to the control group. Additionally, Kocabay et al. indicated that there was no difference in MPV levels between NAFLD patients and the control group (23, 24).

In the study conducted by Alavarez et al., NAFLD patients who experienced cardiovascular events (CE) were retrospectively examined and compared with NAFLD patients who did not experience CE. It was found that the overall change in MPV level was higher in the CE group compared to the non CE group. They suggested that this finding might indicate MPV as a potential marker for elevated cardiovascular risk in NAFLD patients (25).

MPV and NLR represent different but interrelated aspects of NAFLD. MPV indicates microvascular damage and coagulopathy processes through changes in platelet activity, while NLR provides information about the severity of systemic inflammation. The combined assessment of these two parameters provides a valuable approach to understanding the critical roles played by both inflammatory and haemostatic processes in the progression of NAFLD.

CONCLUSION

In conclusion, the combined assessment of MPV and NLR can be considered as effective biomarkers to monitor the progression of NAFLD and evaluating the inflammatory status of patients. Validation of these parameters in clinical applications may provide a better understanding of both their diagnostic and prognostic value.

Acknowledgments
We would like to express our gratitude to the staff and clinicians of Amasya University Sabuncuoğlu Şerefeddin Training and Research Hospital.

Authorship contributions
GUL MA.; Consept, Design, Data Collection, Analysis and Interpratation, Literature Search, Writing-Original Draft. TOZCU D.; Consept, Design, Data Collection, Analysis, Writing-Original Draft. CAPRAZ M.; Concept, Design, Data Collection, Writing-Original Draft.

Data availibity statement
The data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

Declaration of competing interest
The authors declared no conflict of interest.

Ethics
The Amasya University Non-Interventional Clinical Research Ethics Committee evaluated the study's compliance with ethical principles and obtained ethical approval (2024/144).

Funding
This work has not received any funding support.

REFERENCES

1. Idalsoaga F, Kulkarni AV, Mousa OY, Arrese M, Arab JP. Non-alcoholic Fatty Liver Disease and Alcohol-Related Liver Disease: Two Intertwined Entities. Frontiers in medicine. 2020;7:448. Epub 2020/09/26. doi: 10.3389/fmed.2020.00448. PubMed PMID: 32974366; PubMed Central PMCID: PMCPMC7468507.

2. Le MH, Le DM, Baez TC, Wu Y, Ito T, Lee EY, et al. Global incidence of non-alcoholic fatty liver disease: A systematic review and meta-analysis of 63 studies and 1,201,807 persons. J Hepatol. 2023;79(2):287-95. Epub 2023/04/12. doi: 10.1016/j.jhep.2023.03.040. PubMed PMID: 37040843.

3. Manikat R, Ahmed A, Kim D. Up-to-date global epidemiology of nonalcoholic fatty liver disease. Hepatobiliary Surg Nutr. 2023;12(6):956-9. Epub 2023/12/20. doi: 10.21037/hbsn-23-548. PubMed PMID: 38115930; PubMed Central PMCID: PMCPMC10727827.

4. Maurice J, Manousou P. Non-alcoholic fatty liver disease. Clin Med (Lond). 2018;18(3):245-50. Epub 2018/06/03. doi: 10.7861/clinmedicine.18-3-245. PubMed PMID: 29858436; PubMed Central PMCID: PMCPMC6334080.

5. European Association for the Study of the L, European Association for the Study of D, European Association for the Study of O. EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. Diabetologia. 2016;59(6):1121-40. Epub 2016/04/08. doi: 10.1007/s00125-016-3902-y. PubMed PMID: 27053230.

6. Kopec KL, Burns D. Nonalcoholic Fatty Liver Disease: A Review of the Spectrum of Disease, Diagnosis, and Therapy. Nutr Clin Pract. 2011;26(5):565-76. doi: 10.1177/0884533611419668. PubMed PMID: WOS:000295222800008.

7. Zhu N, Wang X, Zhu H, Zheng Y. Blood cell parameters and risk of nonalcoholic fatty liver disease: a comprehensive Mendelian randomization study. BMC Med Genomics. 2024;17(1):102. Epub 2024/04/24. doi: 10.1186/s12920-024-01879-7. PubMed PMID: 38654378; PubMed Central PMCID: PMCPMC11040836.

8. Miele L, Alberelli MA, Martini M, Liguori A, Marrone G, Cocomazzi A, et al. Nonalcoholic fatty liver disease (NAFLD) severity is associated to a nonhemostatic contribution and proinflammatory phenotype of platelets. Transl Res. 2021;231:24-38. Epub 2020/11/11. doi: 10.1016/j.trsl.2020.11.003. PubMed PMID: 33171266.

9. Solak Y, Yilmaz MI, Sonmez A, Saglam M, Cakir E, Unal HU, et al. Neutrophil to lymphocyte ratio independently predicts cardiovascular events in patients with chronic kidney disease. Clin Exp Nephrol. 2013;17(4):532-40. doi: 10.1007/s10157-012-0728-x. PubMed PMID: WOS:000323511000008.

10. Maurice J, Manousou P. Non-alcoholic fatty liver disease. Clinical Medicine. 2018;18(3):245-50. doi: https://doi.org/10.7861/clinmedicine.18-3-245.

11. Sinn DH, Kang D, Chang Y, Ryu S, Gu S, Kim H, et al. Non-alcoholic fatty liver disease and progression of coronary artery calcium score: a retrospective cohort study. Gut. 2017;66(2):323. doi: 10.1136/gutjnl-2016-311854.

12. Asil M, Dertli R. The Neutrophil-to-Lymphocyte Ratio as A Noninvasive Marker in Patients with Biopsy-Proven Non-Alcoholic Steatohepatitis. Istanb Med J. 2016;17(4):131-5. doi: 10.5152/imj.2016.74755. PubMed PMID: WOS:000391011900004.

13. Lesmana CRA, Kencana Y, Rinaldi I, Kurniawan J, Hasan I, Sulaiman AS, et al. Diagnostic Value of Neutrophil to Lymphocyte Ratio in Non-Alcoholic Fatty Liver Disease Evaluated Using Transient Elastography (TE) with Controlled Attenuated Parameter (CAP). Diabet Metab Synd Ob. 2022;15:15-22. doi: 10.2147/Dmso.S330526. PubMed PMID: WOS:000742778300003.

14. Neuschwander-Tetri BA. Non-alcoholic fatty liver disease. Bmc Medicine. 2017;15. doi:10.1186/s12916-017-0806-8. PubMed PMID: WOS:000396072300001.

15. Akdas S, Yazihan N. From NAFLD to MASLD: Meta-analysis and systematic review of NAFLD patients in Turkiye in terms of metabolic profile and MASLD potential. Hepatology forum. 2024;5(3):126-38. Epub 2024/07/15. doi: 10.14744/hf.2023.2023.0042. PubMed PMID: 39006144; PubMed Central PMCID: PMCPMC11237240.

16. Shavakhi M, Nourigheimasi S, Dioso E, Goutnik M, Lucke-Wold B, Khanzadeh S, et al. Prognostic Role of Neutrophil to Lymphocyte Ratio in Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis. Canadian Journal of Gastroenterology and Hepatology. 2022;2022(1):1554079. doi: https://doi.org/10.1155/2022/1554079.

17. Abdel-Razik A, Mousa N, Shabana W, Refaey M, ElMahdy Y, Elhelaly R, et al. A novel model using mean platelet volume and neutrophil to lymphocyte ratio as a marker of nonalcoholic steatohepatitis in NAFLD patients: multicentric study. Eur J Gastroenterol Hepatol. 2016;28(1):e1-9. Epub 2015/10/16. doi: 10.1097/meg.0000000000000486. PubMed PMID: 26469357.

18. WenYi J, Ting Q, PiaoPiao Y, JinMing W. Association Between Neutrophil-to-Lymphocyte Ratio with Inflammatory Activity and Fibrosis in Non-alcoholic Fatty Liver Disease. The Turkish journal of gastroenterology : the official journal of Turkish Society of Gastroenterology. 2022;33(1):53-61. Epub 2022/01/19. doi: 10.5152/tjg.2022.20715. PubMed PMID: 35040788; PubMed Central PMCID: PMCPMC9128444.

19. Kara M, Dogru T, Genc H, Sertoglu E, Celebi G, Gurel H, et al. Neutrophil-to-lymphocyte ratio is not a predictor of liver histology in patients with nonalcoholic fatty liver disease. Eur J Gastroenterol Hepatol. 2015;27(10):1144-8. Epub 2015/06/11. doi: 10.1097/meg.0000000000000405. PubMed PMID: 26062078.

20. Acar, T., Adibelli, Z. H. (2017). Nötrofil/Lenfosit Oranının Abdominal Yağ Dağılımı, Karaciğer Yağlanması ve Karaciğer Hacmine Olan Etkisi. Konuralp Tip Dergisi, 9(2),73-77.

21. Wang Y, Guo S, He Y, Zhang Q, Zhou N, Wang D, et al. Relationship between Neutrophil-to-Lymphocyte Ratio and Liver Fibrosis in Nonalcoholic Fatty Liver Disease Among Adults in the United States: Data from the National Health and Nutrition Examination Survey 2017-2018. The Turkish journal of gastroenterology : the official journal of Turkish Society of Gastroenterology. 2024;35(4):335-42. Epub 2024/08/11. doi: 10.5152/tjg.2024.23231. PubMed PMID: 39128078; PubMed Central PMCID: PMCPMC11114246.

22. Duan Y, Luo J, Pan X, Wei J, Xiao X, Li J, et al. Association between inflammatory markers and non-alcoholic fatty liver disease in obese children. Frontiers in Public Health. 2022;10. doi: 10.3389/fpubh.2022.991393.

23. Karaoğullarindan Ü, Üsküdar O, Odabaş E, Saday M, Akkuş G, Delik A, et al. Is mean platelet volume a simple marker of non-alcoholic fatty liver disease? Indian Journal of Gastroenterology. 2023;42(2):219-25. doi: 10.1007/s12664-022-01330-8.

24. Kocabay G, Karabay CY, Kalayci A, Colak Y. Mean platelet volume in patients with non-alcoholic fatty liver disease: is mean platelet volume ready as a surrogate marker? Clinical Chemistry and Laboratory Medicine (CCLM). 2014;52(11):e249-e52. doi: doi:10.1515/cclm-2014-0303.

25. Alvarez L, Cipher D, Weideman RA, Brown G. Mean platelet volumes in non-alcoholic liver disease (NAFLD): is there a relationship to cardiovascular events? Gastroenterology & Hepatology. 2016;5(5):325-9. doi: 10.15406/ghoa.2016.05.00157.