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Original Article

The role of plasma atherogenic index in patients with NAFLD

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A B S T R A C T

Background Plasma atherogenic index (PAI) is a novel index investigated in recent years related to cardiovascular disease and atherosclerosis. The role of PAI is not clear in non-alcoholic fatty liver disease (NAFLD). This study aimed to examine the role of PAI in patients with NAFLD and its relationship with metabolic components.

Material and Methods This study was designed as a retrospective study, and the patients' files admitted to the Internal Medicine unit were retrospectively scanned. Within the scope of the study, demographic and laboratory data of the groups with and without NAFLD were compared.

Results A total of 234 patients were evaluated, 159 of which were NAFLD (age: 39.52 ± 10.38 years) and 75 controls (age: 38.07 ± 12.11 years) ($p = 0.374$). PAI level was statistically significantly higher in the NAFLD group compared to the control group (p = 0.006). In the whole group correlation analysis, PAI level and body mass index ($p < 0.001$, r = 0.363), waist circumference ($p < 0.001$, r = 0.366), systolic blood pressure ($p < 0.001$, r = 0.333), diastolic blood pressure ($p = 0.001$, r = 0.210), ALT ($p < 0.001$, r = 0.312), AST ($p = 0.005$, r = 0.182), fasting plasma glucose ($p = 0.017$, r = 0.157) and insulin resistance ($p < 0.001$, r = 0.302) values were positively correlated.

Conclusions PAI level was higher in patients with NAFLD; this index was associated with other metabolic components, especially insulin resistance. This indicates that the PAI level may be associated with clinical progression in the pathogenesis and course of the disease.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide, and its prevalence is estimated at 25%. The prevalence of NAFLD has been increasing in recent years due to increased risk factors such as obesity, inactivity, metabolic syndromes (MetS) and type 2 diabetes mellitus (T2DM). The majority of NAFLD patients are asymptomatic, and it is usually found incidentally during routine investigations. Ultrasonography (USG) is the most commonly used imaging method for diagnosis.[1]

The development of hepatic steatosis characterizes NAFLD without significant alcohol consumption or other secondary causes of steatosis (e.g. chronic viral hepatitis, medications, other chronic liver diseases, etc).[2] Excessive liver fat accumulation is the main reason, which is induced by increased uptake of fatty acids (FA) and triglyceride (TG) from circulation, upregulated de novo lipogenesis, and the saturation of FA oxidation and very low-density lipoprotein (VLDL).[3] However, the evidence explaining the direct role of individual blood lipid profiles in steatosis is controversial. Studies have shown atherogenic dyslipidemia in 20-80% of NAFLD.[4] Hence, NAFLD is considered a risk factor for atherosclerotic heart disease.

The plasma atherogenic index (PAI) is a new quantitative index used as a powerful marker of dyslipidemia. Several studies have revealed the high accuracy of PAI in strongly predicting the risk of atherosclerosis and have also been linked with MetS.[5-6] Recently, PAI has been investigated as a potential predictive marker for detecting NAFLD, but the results are controversial. This study explores PAI's role in NAFLD and its relationship with metabolic components.

MATERIAL AND METHODS

Study design and population

This retrospective study collected data from the routine health check-up (including liver USG) of 2,500 subjects aged over 20 years in the policlinic of Balıkesir University Hospital Internal Medicine Outpatient Clinic from 2020 to 2022 after excluding duplicate patients. The exclusion criteria were age < 18, a history of excessive alcohol consumption, malignancy, and chronic disease. The Ethics Committee of Balıkesir University approved this study, and it was carried out according to the ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent amendments.

Anthropometric and clinical parameters

Patients' baseline characteristics such as age, gender, height, weight, waist circumferences (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP) and laboratory measurements such us including fasting plasma glucose (FPG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), TG, aspartate aminotransferase (AST), alanine aminotransferase (ALT), glomerular filtration rate (GFR), haemoglobin (Hb) were extracted from medical records on their visit.

Insulin resistance was measured using the homeostatic model assessment of insulin resistance (HOMA-IR).[7] PAI was calculated as the logarithmic transformation of the TG-to-HDL-C ratio.[8] Body mass index (BMI) was calculated by body weight in kilograms divided by height in square meters. Regarding US criteria for NAFLD, the diagnosis was made when at least two of three findings were reported by a trained radiologist: diffusely echogenic liver (known as "bright liver"), vascular blurring, and narrowing of the hepatic veins.[9]

Statistical analysis

All data were expressed as mean ± standard deviation (SD). The Shapiro-Wilk test was used for the normality analysis of continuous variables. Independent samples t-test was used in univariate analyses since continuous variables assumed normality. Similarly, Pearson correlation was used in the correlation analysis as it provided the assumption of normality of continuous variables. Results with a p-value less than 0.05 were considered statistically significant.

RESULTS

A total of 159 patients with NAFLD (mean age: 39.52 ± 10.38 years) and 75 healthy control (mean age: 38.07±12.11 years) subjects were included (p = 0.374). The anthropometric, clinical and laboratory parameters of all groups were shown in Table 1. Patients with NAFLD had significantly higher BMI, WC, SBP, DBP, HOMA-IR, ALT (p = 0.001 for all) and glucose (p = 0.025) levels than the healthy controls.

Table 1. Comparison of clinical and biochemical features of patients with NAFLD and healthy controls.

Variables	NAFLD group (n: 159)	Control group (n: 75)	*p* - value
Age (years)	39.52 ± 10.38	38.07 ± 12.11	0.374
BMI (kg/m^2)	30.86 ± 4.92	25.49 ± 4.55	0.001*
WC (cm)	102.11 ± 12.49	88.31 ± 12.46	0.001*
SBP (mmHg)	119.98 ± 12.02	113.48 ± 11.66	0.001*
DBP (mmHg)	76.93 ± 8.85	71.33 ± 7.71	0.001*
Hb (g/dL)	13.81 ± 1.57	13.71 ± 1.70	0.650
FPG (mg/dL)	97.82 ± 11.72	94.37 ± 10.43	0.025
HOMA-IR	2.99 ± 2.53	1.79 ± 2.33	0.001*
eGFR (mL/min)	93.97 ± 12.44	91.36 ± 15.60	0.206
TC (mg/dL)	200.5 ± 40.23	194.20 ± 36.21	0.233
LDL-C (mg/dL)	121.11 ± 35.17	119.21 ± 32.10	0.682
ALT (IU/L)	27.52 ± 22.83	19.31 ± 10.60	0.001*
AST (IU/L)	21.51 ± 10.71	20.57 ± 10.88	0.538
PAI	0.39 ± 0.31	0.29 ± 0.26	0.006*

NAFLD: non-alcoholic fatty liver disease, BMI: body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, Hb: haemoglobin, FPG: fasting plasma glucose, HOMA-IR: homeostatic model assessment-insulin resistance, eGFR: estimated glomerular filtration rate, TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, ALT: alanine aminotransferase, AST: aspartate aminotransferase, PAI: plasma atherogenic index.

The data was given in mean ± standard deviation (SD). *$p < 0.05$, statistically significant.

The PAI level was statistically significantly higher in patients with NAFLD (0.39 ± 0.31) compared to the control group (0.29 ± 0.26, p = 0.006).

In the whole group correlation analysis, PAI level and BMI ($p < 0.001$, r = 0.363), WC ($p < 0.001$, r = 0.366), SBP ($p < 0.001$, r = 0.333), DBP ($p = 0.001$, r = 0.210), ALT ($p < 0.001$, r = 0.312), AST ($p = 0.005$, r = 0.182), FPG ($p = 0.017$, r = 0.157) and HOMA-IR ($p < 0.001$, r = 0.302) values were positively correlated (Figure 1).

DISCUSSION

NAFLD is the most common chronic liver disease worldwide and is directly associated with an increased risk of CVD. On the other hand, many studies in the current literature have stated that PAI is related to cardiovascular diseases (CVD). However, the role of PAI in the pathogenesis of NAFLD is unclear and may be associated with an increased risk of CVD in this patient group. In this study, we aimed to investigate the level of PAI in patients with NAFLD, and the PAI level was significantly higher in patients with NAFLD compared to the control group. Furthermore, the level of PAI was positively associated with metabolic components such as BMI, WC, SBP, DBP and HOMA-IR. As well as PAI level was associated with liver enzymes.

In a study by Xie *et al.*10, PAI levels were significantly higher in patients with NAFLD compared to the control group. Also, PAI level was a significant predictor of fatty liver.[10] In another study by Dong *et al.*[11], in non-obese Chinese and Japanese participants, it was found that PAI level was observed to be higher in patients with NAFLD, and it was emphasized that PAI could be a novel screening indicator for NAFLD in non-obese individuals. Furthermore, in a study by Fadaei *et al.*[12], the level of PAI was found to be high in patients with NAFLD, and it was determined that PAI showed a positive association with carotid intima-media thickness. In light of these data, we found that the PAI level was significantly higher in patients with NAFLD compared to the control group in this study. In addition, our study showed that increased PAI level was positively correlated with metabolic components such as BMI, WC, SBP and DBP. These variables are directly associated with an increased risk of CVD, and our findings suggest that the increased PAI levels may reflect the unhealthy metabolic profile, NAFLD

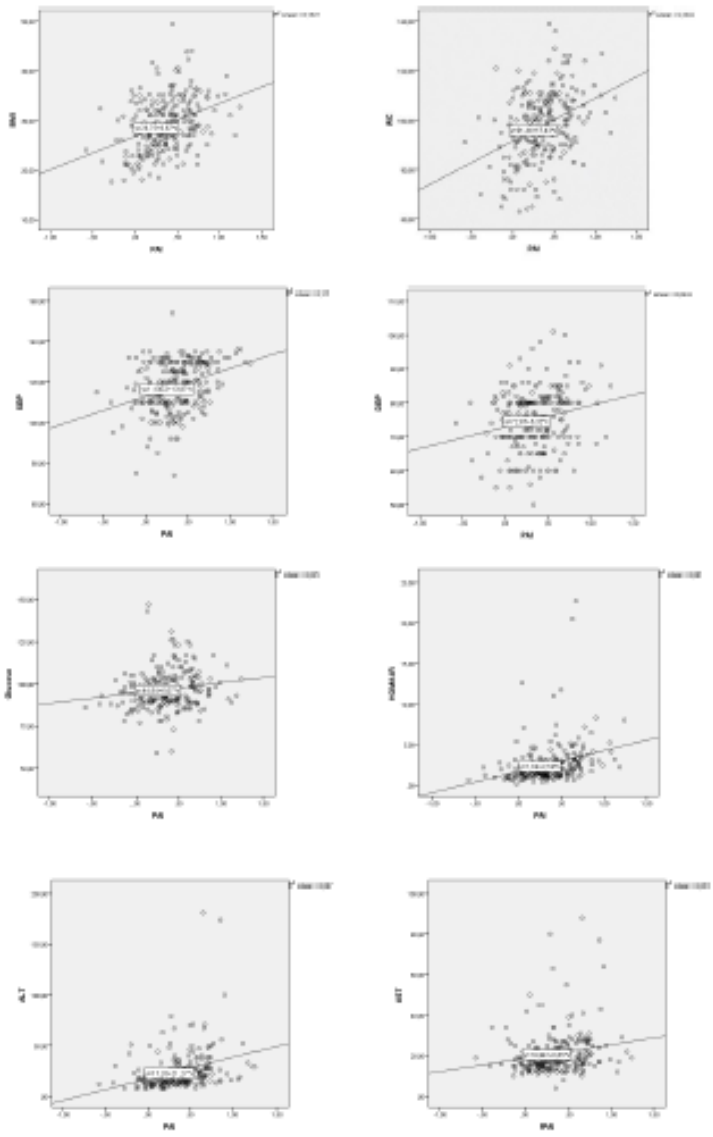

Figure 1. Graphs of significant correlations between PAI and variables.

and even CVD.

In the current literature, a few studies have indicated that insulin resistance may be a predictive factor for fibrosis in patients with NAFLD. Kessoku *et al*.[13] found that HOMA-IR increased depending on the degree of hepatic fibrosis in biopsy-proven NAFLD patients with T2DM. On the other hand, 361 biopsy-proven Japanese NAFLD patients without T2DM were evaluated by Fujii *et al*.[14] They reported that a HOMA-IR level above 2.9 independently predicts hepatic fibrosis. In our study, PAI level showed a significant correlation with HOMA-IR. In addition, our study observed a significant positive correlation between PAI and liver enzymes such as ALT and AST. In the future, PAI may be a promising novel index to predict fibrosis in patients with NAFLD because it correlates with HOMA-IR.

There were a few limitations in this study. Firstly, this study was single-centre and did not reflect the general population. Secondly, the diagnosis of NAFLD was determined by the USG, and liver biopsy, which was the gold standard method, could not be used. Finally, insulin resistance was assessed with HOMA-IR but not with the gold standard hyperinsulinemic-euglycemic clamp technique.

CONCLUSIONS

As a result, PAI level was higher in patients with NAFLD compared to the healthy controls. Furthermore, the increase in PAI level was positively

correlated with the deterioration of metabolic components and liver enzymes. Therefore, PAI may predict liver damage and increased risk of CVD in patients with NAFLD.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Balikesir University Medical School, Balikesir, Turkey (Decision number: 2022/87, date: 12.08.2022).

Authors' Contribution

Study Conception: AK, HS; Study Design: AK, HS; Literature Review: AK, HS; Critical Review: AK, HS; Data Collection and/or Processing: AK, HS; Analysis and/or Data Interpretation: AK, HS; Manuscript preparing: AK, HS.

REFERENCES

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016 Jul;64(1):73-84. doi: 10.1002/hep.28431.

2. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol. 2016 Jun;64(6):1388-402. doi: 10.1016/j.jhep.2015.11.004.

3. Mato JM, Alonso C, Noureddin M, Lu SC. Biomarkers and subtypes of deranged lipid metabolism in non-alcoholic fatty liver disease. World J Gastroenterol. 2019 Jun 28;25(24):3009-20. doi: 10.3748/wjg.v25.i24.3009.

4. Souza MR, Diniz Mde F, Medeiros-Filho JE, Araújo MS. Metabolic syndrome and risk factors for non-alcoholic fatty liver disease. Arq Gastroenterol. 2012 Jan-Mar;49(1):89-96. doi: 10.1590/s0004-28032012000100015.

5. Chang Y, Li Y, Guo X, Dai D, Sun Y. The association of ideal cardiovascular health and atherogenic index of plasma in rural population: A cross-sectional study from Northeast China. Int J Environ Res Public Health. 2016 Oct 19;13(10):1027. doi: 10.3390/ijerph13101027.

6. Zhang X, Zhang X, Li X, Feng J, Chen X. Association of metabolic syndrome with atherogenic index of plasma in an urban Chinese population: A 15-year prospective study. Nutr Metab Cardiovasc Dis. 2019 Nov;29(11):1214-9. doi: 10.1016/j.numecd.2019.07.006.

7. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28:412-9. doi: 10.1007/BF00280883.

8. Niroumand S, Khajedaluee M, Khadem-Rezaiyan M, Abrishami M, Juya M, Khodaee G, Dadgarmoghaddam M. Atherogenic index of Pplasma (AIP): A marker of cardiovascular disease. Med J Islam Repub Iran. 2015 Jul 25;29:240.

9. Hamaguchi M, Kojima T, Itoh Y, Harano Y, Fujii K, Nakajima T, Kato T, Takeda N, Okuda J, Ida K, Kawahito Y, Yoshikawa T, Okanoue T. The severity of ultrasonographic findings in nonalcoholic fatty liver disease reflects the metabolic syndrome and visceral fat accumulation. Am J Gastroenterol. 2007 Dec;102(12):2708-15. doi: 10.1111/j.1572-0241.2007.01526.x.

10. Xie F, Zhou H, Wang Y. Atherogenic index of plasma is a novel and strong predictor associated with fatty liver: a cross-sectional study in the Chinese Han population. Lipids Health Dis. 2019 Sep 12;18(1):170. doi: 10.1186/s12944-019-1112-6.

11. Dong BY, Mao YQ, Li ZY, Yu FJ. The value of the atherogenic index of plasma in non-obese people with non-alcoholic fatty liver disease: a secondary analysis based on a cross-sectional study. Lipids Health Dis. 2020 Jun 23;19(1):148. doi: 10.1186/s12944-020-01319-2.

12. Fadaei R, Meshkani R, Poustchi H, Fallah S, Moradi N, Panahi G, Merat S, Golmohammadi T. Association of carotid intima media thickness with atherogenic index of plasma, apo B/apo A-I ratio and paraoxonase activity in patients with non-alcoholic fatty liver disease. Arch Physiol Biochem. 2019 Feb;125(1):19-24. doi: 10.1080/13813455.2018.1429475.

13. Kessoku T, Yoneda M, Sumida Y, Eguchi Y, Fujii H, Hyogo H, Ono M, Kawaguchi T, Nakajima A; Japan Study Group of NAFLD. Insulin resistance correlated with the severity of liver histology in Japanese NAFLD patients: a multicenter retrospective study. J Clin Gastroenterol. 2015 Feb;49(2):169-70. doi: 10.1097/MCG.0000000000000186.
14. Fujii H, Imajo K, Yoneda M, Nakahara T, Hyogo H, Takahashi H, Hara T, Tanaka S, Sumida Y, Eguchi Y, Chayama K, Nakajima A, Nishimoto N, Kawada N; Japan Study Group of Nonalcoholic Fatty Liver Disease. HOMA-IR: An independent predictor of advanced liver fibrosis in nondiabetic non-alcoholic fatty liver disease. J Gastroenterol Hepatol. 2019 Aug;34(8):1390-5. doi: 10.1111/jgh.14595.

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