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Novel markers in predicting non-alcoholic liver fatty and metabolic syndrome in obese children and adolescents: Atherogenic index of plasma and monocyte / high-density lipoprotein cholesterol ratio

Obez çocuk ve adölesanlarda metabolic sendrom ve non-alkolik karaciğer yağlanmasını öngörmede yeni belirteçler: Plazma aterojenik indeks ve monosit / yüksek dansiteli lipoprotein kolesterol oranı

Edip Ünal [1], Yusuf Kenan Haspolat [1]

[1] Dicle University Faculty of Medicine, Department of Pediatric Endocrinology, Diyarbakir, Turkey

ORCID ID of the author(s)
EÜ: 0000-0002-9809-0977
YHP: 0000-0003-1930-9721

Corresponding author / Sorumlu yazar:
Edip Ünal
Address / Adres: Dicle Üniversitesi Tıp Fakültesi, Pediatrik Endokrinoloji Anabilim Dalı, Sur, Diyarbakır, Türkiye
E-mail: edip76@yahoo.com

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Abstract

Aim: The aim of this study is to investigate the relationship between metabolic syndrome (MetS), insulin resistance, waist circumference (WC) and non-alcoholic fatty liver disease (NAFLD) with atherogenic index of plasma (AIP) and monocyte/ high-density lipoprotein cholesterol ratio (MHR) among obese children and adolescents.

Methods: The cross-sectional study consisted of 172 obese and 63 healthy children. Anthropometric and biochemical parameters [Weight, height and BMI SDS, WC, Complete blood count, aspartate-aminotransferase (AST), alanine-aminotransferase (ALT), insulin, glucose, total cholesterol (TC), high-density lipoprotein (HDL-C), triglyceride (TG) and low-density lipoprotein (LDL-C), homeostasis model assessment-insulin resistance (HOMA-IR), AIP, MHR] were assessed. The AIP was classified into three groups: Low (<0.11), intermediate (0.11–0.21) and high (>0.21) risk. The MetS definition proposed by the International Diabetes Federation was adopted.

Results: BMI SDS, WC, HOMA-IR, TC, TG, LDL-C, AST, ALT, AIP, and MHR parameters were significantly higher among the obesity group (P<0.05 for each). The MetS was analyzed in 146 obese children older than 10 years of age and found positive in 49 (33.6%) children. The mean AIP and median MHR were significantly higher in the group with MetS than in the group without (P<0.001, P=0.017, respectively). A significant positive correlation was determined between AIP and WC, HOMA-IR, TG, ALT, MHR, and steatosis degree (r=0.34, P<0.001, r=0.289, P<0.001, r=0.863, P<0.001, r=0.292 P<0.001, r=0.447, P<0.001, r=0.298, P<0.001 respectively).

Conclusion: Both AIP and MHR are simple, cheap, and easily calculable parameters. The AIP might be used as an effective marker to predict MetS, abdominal obesity, NAFLD and IR in obese children. In addition, the high MHR in obese children may be associated with an increased risk of cardiovascular disease and MetS.

Keywords: Atherogenic index of plasma, Monocyte to HDL cholesterol ratio, Obesity, Metabolic syndrome, Children

Öz

Amaç: Bu çalışmada obezitesi olan çocuk ve adölesan hastalarda plazma aterojenik indeks (PAİ) ve monosit / HDL oranı (MHO) ile metabolik sendrom (MS), insülin direnci (İD), bel çevresi (BÇ) ve non-alkolik karaciğer yağlanması (NAKY) arasındaki ilişkinin araştırılması amaçlanmıştır.

Yöntemler: Çalışma kesitsel olup, 172 obez çocuk hasta ile 63 sağlıklı kontrol hastası içermekteydi. Antropometrik ve biyokimyasal parametreler [ağırlık, boy, beden kitle indeksi (BKİ) standart deviasyon skoru (SDS), BÇ, hemogram, aspartat transaminaz (AST), alanin transaminaz (ALT), insulin, glukoz, total kolesterol (TC), yüksek-dansiteli lipoprotein kolesterol (HDL-C), trigliserid (TG), düşük-dansiteli lipoprotein kolesterol (LDL-C), HOMA-IR, PAİ ve MHO] değerlendirildi. Plazma aterojenik indeks; düşük (<0,11), orta (0,11–0,21) ve yüksek (>0,21) risk diye üç gruba ayrıldı. Metabolik sendrom tanımı Uluslararası Diyabet Fedarasyonuna göre yapıldı.

Bulgular: Obez hasta grubunda BKİ SDS, BÇ, HOMA-IR, TC, TG, LDL-C, AST, ALT, PAİ değeri ve MHO anlamlı ölçüde yüksek saptandı (her biri için P<0,05). On yaş üzeri 146 hastada MS araştırıldı ve 49 hastada (%33,6) pozitif saptandı. Ortalama PAİ ve ortanca MHO değeri obez ve MS'u olanlarda, obez ve MS'u olmayanlara göre anlamlı ölçüde yüksek saptandı (p değeri sırasıyla; <0,001, 0,017). Plazma aterojenik index ile BÇ, HOMA-IR, TG, ALT, MHO ve karaciğerin yağlanma derecesi arasında anlamlı pozitif korelasyon saptandı (r=0,34, P<0,001, r=0,289, P<0,001, r=0,863, P<0,001, r=0,292, P<0,001, r=0,447, P<0,001, r=0,298, P<0,001 sırasıyla).

Sonuç: Hem PAİ hem de MHO basit, ucuz ve kolay hesaplanabilen parametrelerdir. Obez çocuklarda PAİ değerinin, abdominal obezite, NAKY, İD ve MS'u öngörmede bir belirteç olarak kullanılabilir. Ayrıca obez çocuklarda yüksek MHO'nın artmış kardiyovasküler hastalık riski ve MS ile ilişkili olduğu düşünülebilir.

Anahtar kelimeler: Plazma aterojenik indeks, Monosit/HDL-C oranı, Obezite, Metabolik sendrom, Çocuklar

Introduction

Childhood obesity is one of the most serious public health issues of the 21st century, with rapidly increasing worldwide prevalence. According to 2016 World Health Organization (WHO) data, there are more than 42 million overweight children under the age of 5 years. Obesity increases the risk for both diabetes and cardiovascular diseases (CVD) by provoking insulin resistance and impaired glucose tolerance, leading to hypertension, dyslipidemia, and Non-alcoholic fatty liver disease (NAFLD) [1]. One of the most important risk factors for CVD is dyslipidemia. It has been shown that both a decrease in high density lipoprotein cholesterol (HDL-C) and an increase in total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) levels contribute to the progression of atherosclerosis [2]. The atherogenic index of plasma (AIP) value is a proven good marker to determine the risk of atherosclerosis and CVD [3,4]. The AIP value is calculated through logarithmic transformation of the number obtained from the division of the plasma TG level by the HDL-C level.

Similar to the AIP value, the Monocyte/HDL Ratio (MHR) has also been proven as a useful prognostic marker, especially for atherosclerotic cardiovascular diseases, hypertension and metabolic syndrome, as the value is elevated in those diseases [5-8]. Monocytes and macrophages play a significant role during atherosclerotic plaque development and monocytes in large numbers are known to trigger the development of plaque. It has also been previously reported that HDL-C inhibits the expression of inflammation adhesion molecules in endothelial cells [9].

Most studies that have evaluated the relationship of both AIP and MHR with CVD have been conducted on adults [3,4]. The aim of this study is to investigate the relationship between metabolic syndrome (MetS), insulin resistance (IR), waist circumference (WC) and NAFLD with AIP and MHR among children and adolescents with obesity.

Materials and methods

The study included patients aged 7-18 years, who presented at the Pediatric Endocrinology Polyclinic of Dicle University Medical Faculty. Patients were excluded from the study if obesity was associated with hypothyroidism, Cushing syndrome, growth hormone deficiency, chronic corticosteroid drug usage, genetic or neuromuscular reasons. Body weight, weight standard deviation scores (SDS), height, height SDS, Body Mass Index (BMI), BMI SDS and WC measurements were obtained and recorded for all patients. Height was measured using a Harpenden stadiometer with sensitivity of 0.1 cm and weight was measured using scales with sensitivity of 0.1 kg (SECA, Hamburg, Germany).

Venous blood samples were obtained from all patients after 12 hours of fasting. Complete blood count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), insulin, fasting blood glucose, TC, HDL-C, TG and LDL-C levels were examined from the blood samples.

Steatosis was investigated in all patients on abdomen ultrasonography (USG) performed by a single experienced radiologist. The diagnosis of hepatic steatosis was based on the criteria defined by Saverymuttu et al. [10] and the severity was classified as grade 1: mild, grade 2: moderate, and grade 3: severe, according to the degree of fatty infiltration. Control group was assembled from individuals visiting the outpatient clinics for routine check-up, who were not diagnosed with obesity and had normal results for physical examination.

Written informed consent was obtained from the parents of the patients for publication of this paper. This study was approved by Ethics Committee of Dicle University Medicine of Faculty (Document number: 25.03.2016/158).

Definitions

Body mass index was calculated with the formula: Body weight/height^2. Body Mass Index values >95% according to age and sex were considered obesity. Acquired BMI values were compared with the normal reference values in Turkish public society [11]. The waist circumference was measured at the level of the midpoint between the spina iliaca anterior superior and arcus costalis and then compared with the age-related reference values for Turkish children [12].

Metabolic syndrome was defined according to the International Diabetes Federation (IDF) criteria which was adapted for children and adolescents [13]. It is suggested that MetS cannot be diagnosed children below the age of 10 years by the IDF. For children between 10 and 16 years of age, the diagnosis of MetS required the presence of abdominal obesity and the two or more of the following factors: (a) hypertriglyceridemia (>150 mg/dL); (b) low HDL-C (<40 mg/dL); (c) increased fasting glucose (≥ 100 mg/dL); (d) elevated blood pressure (the online calculator program was developed by Demir et al [14] and it was used for evaluation of blood pressure). The percentile curves established for Turkish children were used for waist circumference. A waist circumference ≥90th percentile was considered abdominal obesity [12].

The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) value was calculated with the formula of fasting insulin (mcU/ml) X fasting glucose (mg/dl) / 405. The HOMA-IR values were considered positive at >2.67 in prepubertal boys, >2.22 in prepubertal girls, >5.22 in pubertal boys and >3.82 in pubertal girls [15]. Monocyte/HDL ratio was calculated by division of total monocyte number acquired by complete blood count to serum HDL value. The AIP value was calculated by logarithmic transformation of the number acquired by division of plasma TG value to HDL value. The AIP value was considered low risk at values <0.11, moderate risk at values between 0.11 and 0.21 and high risk at values >0.21 according to the references of previous studies [16,17].

Statistical analysis

SPSS 20.0 statistical package program was used to analyze the data of this study. Measured variables were stated as mean (standard deviation (SD)) values, and categorical variables as number (n) and percentage (%). Conformity of the data to normal distribution was assessed with the Kolmogorov Smirnov and Shapiro Wilk tests. For numerical comparisons, the independent sample t-test, or Mann-Whitney U-test were used according to normality of distribution of the measured parameters. Spearman or Pearson correlation analysis was used

to identify the associations between variables. The patient group was separated into three subgroups as low, moderate, and high according to the AIP values and ANOVA test was used to compare the data of those three groups. The Kruskal-Wallis test was used for non-normally distributed parameters (TG, HDL-C, BMI, ALT and MHR). A receiver operating characteristics (ROC) curve analysis was performed for determination of the best cut-off value for AIP in prediction of MetS. In addition, ROC analysis was performed for AIP, TG and HDL-C to differentiate which parameter is more useful in predicting MetS in obese patients. The AIP-HDL, AIP-TG and HDL-TG ROC curves were compared using pROC package analysis in R version 4.0.0 Arbor Day program. In all statistical tests, $P<0.05$ was considered statistically significant.

Results

A total of 235 children including 172 obese patients and 63 normal weight healthy control subjects were included in this study. No statistically significant difference was determined between the patient and control groups with respect to age and gender. The BMI SDS, WC, systolic blood pressure, HOMA-IR, TC, TG, LDL-C, AST, ALT, AIP value and MHR ratio parameters were significantly higher in the obese patient group compared to the control group ($P<0.05$ for each), and HDL-C was significantly lower ($P<0.001$). The anthropometric data and laboratory test results of the patient and control groups are presented in Table 1. According to the AIP value, 113 (65.7%) children in the patient group were classified as having low risk, 21 (12.2%) as moderate risk and 38 (22.1%) as high risk. The three groups were similar in terms of BMI SDS, systolic blood pressure, TC, LDL-C and AST (p values: 0.072, 0.225, 0.213, 0.253, 0.233, and 0.180, respectively), but significantly different with regards to WC, HOMA-IR, TG, HDL-C, ALT and MHR (p values: <0.001, <0.001, <0.001, <0.001, 0.004, and <0.001, respectively) (Table 2).

The International Diabetes Federation criteria for MetS were analyzed in 146 obese children older than 10 years of age. Metabolic syndrome was diagnosed in 49 children, which accounted for 33.6% of the group. While the mean AIP value was 0.25 (0.23) and the median MHR value was 13.6 in the group with MetS, the mean AIP value was -0.76 (0.20) and the median MHR value was 12.52 (4.62-25.6) in the non-MetS group ($P<0.001$, $P=0.017$, respectively).

In the ROC analysis, the optimum cut-off value for AIP in predicting MetS was 0.065 (AUC: 0.884, sensitivity 85%, specificity 75%, $P<0.001$) (Figure 1). In predicting the development of MetS, AUC values for AIP, TG and HDL-C were 0.884 (95% Cl: 0.824-0.943, $P<0.001$), 0.815 (95% Cl: 0.742-0.887, $P<0.001$), and 0.787 (95% Cl: 0.701-0.873, $P<0.001$), respectively. There was a significant difference between AIP-HDL and AIP-TG ROC curves ($P=0.01$, $P=0.02$, respectively), while HDL-TG ROC curves were similar ($P=0.65$) (Figure 2).

A significant positive correlation was detected between the AIP value and WC, HOMA-IR, TG, ALT, MHR, and steatosis degree (r=0.34, $P<0.001$, r=0.289, $P<0.001$, r=0.863, $P<0.001$, r=0.292 $P<0.001$, r=0.447, $P<0.001$, r=0.298, $P<0.001$ respectively). A significant negative correlation was detected between AIP and HDL-C (r=-0.650, $P<0.001$). No significant correlation existed between the AIP value and BMI SDS, systolic blood pressure, diastolic blood pressure, TC, LDL-C, and AST (r=0.067, $P=0.381$, r=0.073, $P=0.339$, r=0.124, $P=0.118$, r=0.112, $P=0.144$, r=0.660, $P=0.391$, r=0.144, $P=0.06$ respectively) (Table 3).

Table 1: Comparison of anthropometric and laboratory data of obese patients and healthy control group

	Patient Group (n:172)	Control Group (n:63)	*P*-value
Age (month)	159.77 (30.05)	161.23 (24.60)	0.074*
BMI (kg/m^2)	29.55 (21.1-46.6)	19.36 (14.2-25.48)	<0.001**
BMI SDS	2.58 (0.62)	-0.30 (1.05)	<0.001*
WC (cm)	97.35 (11.79)	70.44 (9.06)	<0.001*
SBP (mmHg)	118.35 (14.68)	114.21 (7.83)	0.034 *
DBP (mmHg)	76.55 (11.89)	75.95 (5.66)	0.751*
Glucose (mg/dl)	89.61 (6.63)	90.33 (8.47)	0.498*
Insulin (µIU/mL)	23.43 (11.35)	11.84 (4.47)	<0.001*
HOMA-IR	5.17 (2.62)	2.66 (1.02)	<0.001*
TC (mg/dl)	165.41 (29.91)	152.88 (24.22)	0.003*
TG (mg/dl)	114.5 (38-324)	81 (36-130)	<0.001**
LDL (mg/dl)	91.19 (27.20)	79.78 (21.35)	0.003*
HDL (mg/dl)	48.35 (27.7-90)	55.6 (34.5-91.70)	<0.001**
AST (U/L)	23.42 (8.40)	19.9 (6.36)	0.003*
ALT (U/L)	21 (7-109)	13 (6-29)	<0.001**
AIP	0.04 (0.27)	-0.20 (0.20)	<0.001*
MHR	12.66 (4.66-29.8)	10.6 (4.20-22.60)	0.003**

BMI-SDS: body mass index-standard deviation score, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, HOMA-IR: homeostasis model assessment of insulin resistance, TC: total cholesterol, TG: triglyceride, LDL: low density lipoprotein, HDL: high density lipoprotein, AST: aspartate aminotransferase, ALT: alanine aminotransferase, AIP: atherogenic index of plasma, MHR: monocyte to high-density lipoprotein cholesterol ratio, *independent t test, **Mann–Whitney U test; data are given as mean (SD) or median (Interquartile Range 25th–75th percentile)

Table 2: Comparison of anthropometric and laboratory characteristics of low, moderate and high-risk AIP groups

Parameters	Low risk (group 1), mean (SD)	Moderate risk, (group 2) mean (SD)	High risk (group 3) mean (SD)	*P*-value
Age (month)	157.82 (30.06)	159.66 (29.20)	161.84 (27.84)[b]	0.084*
BMI SDS	2.50 (0.58)	2.69 (0.58)	2.75 (0.71)	0.072*
WC (cm)	94.53 (9.67)	100.90 (12.63)[a]	104.68 (13.66)[b]	<0.001*
SBP (mmHg)	117.23 (14.54)	117.86 (11.24)	121.97 (16.42)	0.225*
DBP (mmHg)	75.83 (11.68)	74.52 (12.23)	79.34 (12.11)	0.213*
HOMA-IR	4.62 (2.37)	5.84 (2.52)	6.45 (2.93)[b]	<0.001*
TC (mg/dl)	163.32 (26.06)	175.04 (38.20)	166.28 (34.98)	0.253*
TG (mg/dl)	91.77 (33.27)	152.14 (28.58)[a]	214.97 (103.06)[b,c]	<0.001**
LDL (mg/dl)	89.94 (24.95)	100.69 (32.74)	89.66 (29.93)	0.233*
HDL (mg/dl)	53.76 (11.11)[a,b]	45.70 (8.74)[c]	38.76 (7.22)	<0.001**
AST (U/L)	22.69 (7.63)	26.24 (12.32)	24.05 (7.83)	0.180*
ALT (U/L)	22.04 (10.46)	30.62 (23.51)[a]	29.82 (16.56)[b]	0.004**
AIP	-0.14 (0.18)	0.15 (0.03)[a]	0.35 (0.18)[b,c]	<0.001**
MHR	12.52 (4.07)	14.75 (5.32)	17.14 (6.06)[b]	<0.001**

[a]: between low risk and moderate risk, [b]: between low risk and high risk, [c]: between moderate risk and high risk, *One way Anova test, **Kruskal Wallis test

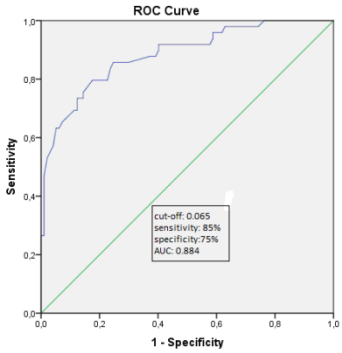

Figure 1: The ROC analysis for AIP in prediction of the metabolic syndrome

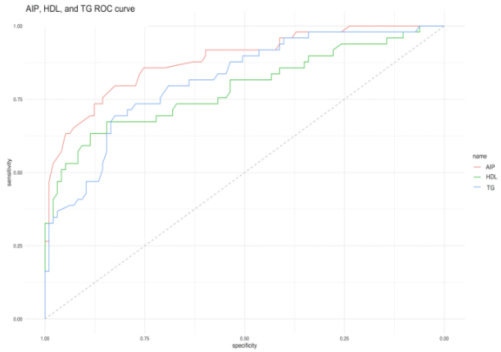

Figure 2: Comparison of AIP-HDL, AIP-TG and HDL-TG ROC curves

Table 3: Pearson correlation analysis between AIP and other parameters

Parameters	r	*P*-value
Age (month)	0.213	0.05
BMI SDS	0.067	0.381
WC (cm)	0.341	<0.001
SBP (mmHg)	0.073	0.339
DBP (mmHg)	0.124	0.118
HOMA-IR	0.289	<0.001
TC (mg/dl)	0.112	0.144
TG (mg/dl)	0.863	<0.001
LDL (mg/dl)	0.660	0.391
HDL (mg/dl)	-0.650	<0.001
AST (U/L)	0.144	0.060
ALT (U/L)	0.292	<0.001
MHR	0.447	<0.001
Liver steatosis degree	0.298	<0.001

A significant positive correlation was detected between MHR value and TC, TG and ALT (r=0.212, *P*=0.008, r=0.216, *P*=0.007, r=0.167, *P*=0.038 respectively). On the other hand, MHR and HDL-C were significantly negatively correlated (r=-0.650, *P*<0.001) (Table 4).

Steatosis was determined in 64 (37.2%) patients in the obesity group. The mean AIP value was 0.084 (0.038) in the subjects with steatosis and -0.043 (0.022) in those without. The difference between those two groups was statistically significant (*P*=0.003). Steatosis was grade 1 in 45 (70.3%) of the 64 steatotic subjects, grade 2 in 16 (25%) and grade 3 in 3 (4.7%). A significant positive correlation was determined between AIP value and steatosis grade (r=0.298, *P*<0.001).

Table 4: Spearman correlation analysis between MHR and other parameters

Parameters	r	*P*-value
Age (month)	0.033	0.679
BMI SDS	-0.053	0.510
WC (cm)	0.119	0.138
SBP (mmHg)	-0.050	0.535
DBP (mmHg)	0.011	0.889
HOMA-IR	0.059	0.473
TC (mg/dl)	0.212	0.008
TG (mg/dl)	0.216	0.007
LDL (mg/dl)	-0.047	0.561
HDL (mg/dl)	-0.650	<0.001
AST (U/L)	0.069	0.393
ALT (U/L)	0.167	0.038
Liver steatosis degree	0.153	0.056

Discussion

Clinical and epidemiological studies conducted on children, adolescents and adults have revealed that body fat distribution is associated with cardiovascular risk factors. Various parameters are used to evaluate fat distribution of body. One of those parameters is BMI, which is recommended for use in defining obesity and overweight status in children aged >2 years and adolescents. However, BMI is not an accurate reflection of the composition and distribution of fat throughout the body. Waist circumference has been reported to be a better marker than BMI for cardiovascular risk factors and visceral fat tissue [18]. In the current study, no significant difference was determined between the low, moderate, and high-risk groups according to the AIP value in terms of BMI SDS, whereas a significant difference was detected in WC. Moreover, there was no significant correlation between AIP and BMI SDS, whereas a positive significant correlation was determined between AIP and WC. Based on this correlation between AIP and WC in our study, it can be suggested that AIP might be used as an efficient marker for cardiovascular risk factors and abdominal obesity predictions in obese children and adolescents. There are very few studies that have investigated the relationship between AIP values and abdominal obesity in children. Nonetheless, a previous study conducted with children reported comparable results with our study, which stated elevated levels of AIP values among obese cases and a positive significant correlation between AIP and WC [19]. In addition, a study conducted on adults have also revealed a positive correlation between AIP and WC [20].

Some studies in adults have shown that AIP can be used as a marker to predict the development of MetS [21,22]. However, to the best of our knowledge, there is no study evaluating the relationship between AIP and MetS in pediatric patients. In our study, it was shown that the AIP value was significantly higher in the group with MetS. In ROC analysis, the optimum cut-off value for AIP in predicting metabolic syndrome was 0.065 (AUC: 0.884; sensitivity 85%; specificity 75%; *P*<0.001). In addition, we showed that the AUC value for AIP was greater in predicting MS development and AIP could be more meaningful than TG and HDL-C in predicting MS with respect to ROC curves.

Previous studies have shown dyslipidemia to be a risk factor for CVD. Furthermore, the relationship between CVD and lipid parameters such as TC, LDL-C and TG is well known. Moreover, it is also accepted that lipid ratios such as TC/HDL-C and LDL-C/HDL-C are predictors for CVD [2,3]. Because of small particle size, small density LDL particles (sdLDL) can penetrate the arterial walls, easily accumulate to be stored and oxidized to turn into OxLDL, when compared to LDL particles. When OxLDL is phagocyted with macrophages, macrophages turn into foam cells and cause atherosclerosis and cardiovascular disease. Recent studies have suggested the clinical utilization of sdLDL particles as a marker to predict atherosclerosis [4]. However, because of the complicated detection method and expensive costs, the detection of sdLDL is limited in clinical applications. AIP was first defined as a strong sensitive index that reflects the interaction between atherogenic and protective lipoproteins by Dobiasova and Frohlich in 2001 [17]. In that study, AIP value was inversely correlated with the circumference of LDL-C particles and reflected the size of the sdLDL particles [17]. Likewise, previous studies conducted with adults revealed that AIP value is a more reliable marker for CVD risk factors compared to traditional lipid parameters and lipid ratios [4,23]. However, there are not adequate studies on this issue in children. In our study, TC, LDL-C, TG, AIP values were significantly higher, and HDL-C was significantly lower in obese patients compared to the control group.

The parameter of IR in obese children is related to cardiovascular and metabolic risk, and IR is known to have a role in the development of endothelial dysfunction metabolism [24]. In the current study, the AIP value of the patient group was higher than that of the control group. Moreover, the HOMA-IR value was significantly higher in the high-risk group according to AIP value compared to the low-risk group and a positive correlation was determined between AIP and HOMA-IR. There are very few studies which have evaluated the relationship between AIP and IR in children. Two previous studies conducted on obese children reported a positive correlation between AIP and HOMA-IR, similar to the current study [19,25]. The detection of a positive correlation between AIP and HOMA-IR in both the current study and the two previous studies indicates that AIP might be used as a marker to predict insulin resistance in childhood obesity.

Non-alcoholic fatty liver disease is the most frequent chronic liver disease seen in children. NAFLD prevalence has been reported to vary between 1.7% and 85% in studies conducted on obese children [26]. It is thought to be caused by primary metabolic dysfunctions which are triggered by prevalent symptoms such as oxidative stress, insulin resistance and inflammatory cytokines [27]. Very few studies in literature have evaluated the relationship between AIP value and NAFLD in obese patients [20, 28]. One of the previous studies of adults with NAFLD revealed a significantly higher AIP value in the patient group than in the control group and a positive correlation between AIP value and Carotis intima media thickness of the patients [28]. Another study of adults separated the obese patients into three groups as low, moderate, and high-risk according to the AIP value. That study reported a significant difference in ALT values between the groups and higher steatosis prevalence in the moderate and high-risk groups [20]. In the current study, NAFLD was detected in 37.2% of the obese patients, and AIP values were significantly higher in the obese patients with NAFLD than those without. Moreover, a significant positive correlation was detected between the AIP value, steatosis degree and ALT level. Therefore, AIP value can be considered for use as a marker for NAFLD in obese children. To the best of our knowledge, this is the first study which evaluated the relationship between NAFLD and AIP in obese children.

Monocyte activation is a factor known to play a role in chronic inflammation and cardiovascular diseases [5]. It has also been reported that HDL-C might prevent macrophage migration as it has anti-inflammatory, antioxidant, and antithrombotic effects [5]. Previous studies have suggested that MHR might be used to predict the development and prognosis of CVD [29, 30]. However, all those studies were conducted on adults. To the best of our knowledge, there is no study in literature which has investigated the relationship between obesity and MHR in children. Monocyte/HDL ratio was significantly higher in obese patients in the current study. In the group with MetS, the median MHR was significantly higher than those without MetS. MHR was high in the AIP high-risk group and a positive correlation was detected between AIP value and MHR, MHR, TC, and TG, whereas a negative correlation was found between MHR and HDL-C. An elevated MHR value can be related with CVD risk in obese children.

Limitations

This study had some limitations. First, it was a cross-sectional study, and the study population was small. Second, the results of the study could not definitively provide a causal relationship between AIP and NAFLD. In addition, the monocyte count was calculated automatically from the peripheral blood sample, and it was not compared with other inflammatory biomarkers.

Conclusion

Both AIP and MHR are simple, cheap, and easily calculated parameters, and AIP might be an effective marker to predict MetS, abdominal obesity, NAFLD and IR in obese children. The AIP and MHR calculations might also be beneficial in the determination of the CVD risk, as MHR was significantly high in obese children and a significant correlation existed between AIP and MHR. However, the findings of this study must be supported by future studies, as there are very few studies on this subject, and this was the first such study for some of the findings.

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