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The relationship between atherogenic index of plasma and major risk factors of cardiovascular disease in obese and non-obese individuals

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ABSTRACT

Objectives: Obesity is a health problem with gradually increasing prevalence and directly contribute to the development of cardiovascular disease (CVD). We aimed to investigate the relationship between atherogenic index of plasma (AIP) and major risk factors of CVD in obese and non-obese individuals.

Methods: This analytical case-control study was carried out on 501 individuals. Obese patients were included in the case group and normal-overweight individuals were included in the control group. The groups were similar in terms of ages and gender. Detailed medical background of the participants was recorded and antropometric parameters were measured. High-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, total cholesterol, triglyceride, fasting blood glucose (FBG) and insulin were measured. AIP risk categories were created according to published epidemiological data: AIP < 0.1 is associated with low risk, 0.1-0.24 with moderate risk, and > 0.24 with high risk.

Results: There was a statistically significant relationship between obesity, male gender, older age, smoking, insulin resistance, high waist circumference, elevation of the blood pressure, FBG and high CVD risk ($p < 0.005$). CVD risk in males were 6.254 times more than in females [OR = 6.254, 95% CI; (2.287-17.107)], CVD risk in obese was 3.436 times more than in none-obese and CVD risk in individuals with insulin resistance was 5.560-fold increase than individuals without insulin resistance [OR = 5.560, 95% CI; (3.069-10.070)] ($p < 0.001$).

Conclusions: Our findings showed that increasing in AIP is associated with obesity and other cardiovascular risk factors. Therefore, AIP can be used as a simple, economic and non invasive marker to identify for CVD risk.

Keywords: Obesity, cardiovascular disease, atherogenic index of plasma, insulin resistance

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Cardiovascular diseases (CVD) are the leading causes of morbidity and mortality worldwide [1]. According to the recent Turkish Statistical Institute recording system in our country, cardiovascular diseases ranked first in all causes of death with 40.4 % in 2014 [2]. The main risk factors for the development of CVD are: modifiable (hypertension, smoking, obesity, elevated total cholesterol or low-density lipoprotein-cholesterol (LDL-C) concentrations, reduced levels of high-density lipoprotein-cholesterol (HDL-

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C), type 2 diabetes) and nonmodifiable (age, sex, genetic predisposition) [3]. The American Heart Association (AHA) has classified obesity as a major, modifiable risk factor for CVD in 1988 (4). The risk of CVD is significantly increased in obese patients, regardless of other risk factors. In particular, abdominal obesity is recognized as an independent risk factor of obesity-related diseases and death [5].

Atherogenic dyslipidemia that often accompany obesity is also associated cardiovascular diseases. Atherogenic dyslipidemia is characterized by low levels of HDL-C, high levels of triglycerides and LDL-C [6]. Although the concentrations of LDL-C continue to hold a principal role in the association of lipids to CVD, the atherogenic potential of a high TG: HDL-C molar ratio is now recognized by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III [7]. Atherogenic index of plasma (AIP), a new marker of atherogenicity, has been shown to significantly increase with cardiovascular risk. It has been suggested that AIP < 0.1 is associated with low risk, 0.1-0.24 with moderate risk, and > 0.24 with high risk (8).

As AIP is a strong marker to predict the risk of atherosclerosis and CVD, we aimed to investigate the relationship between AIP and major risk factors of CVD in obese and non-obese individuals.

METHODS

Study Design, Setting and Population

This analytical case-control study was constituted of 501 individuals aged 18 and older between 25.04.2017 and 01.08.2017. The study population was chosen randomly from the patients who applied with any problem to Family Medicine Outpatient Clinic. At first, the female and male subjects were matched according to their ages and gender. After calculating their body mass indexes (BMIs), the participants were categorized as nonobese and obese. Obese patients were included in the case group and normal-overweight individuals were included in the control group. In the previous studies, obesity prevalence in our country was found to be 35% [9]. In our study, the number of the subjects that had to be included in the study was calculated by using $n = t^2.p.q/d^2$ formula because the number of the individuals in the universe was not known. According to this calculation, 501 individuals aged 18 and older were included in our study.

Exclusion Criteria

Those with CVD, hypertension, diabetes mellitus, liver and kidney failure; patients who have been diagnosed with hyperlipidemia previously and who use antihyperlipidemic drugs; those who were pregnant, lactating women, and those who did not agree to participate in the study were not included in the research.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Medical Faculty (Number: 2017/896) before participation in this study. All of the participants were volunteers. The participants were duly informed and written, and oral consent was obtained from volunteers according to the Principles of the Helsinki Declaration.

Collection of Data

The questionnaire prepared by the researcher was filled in with face to face interview technique. The question form was prepared to determine demographic features (age, gender, marital status, occupation, education, smoking status etc.). Of all the patients, systolic (SBP) and diastolic blood pressures (DBP) were measured by a sphygmomanometer in the supine position after at least 5 min of resting.

Major Risk Factors of CVD

The cardiovascular risk factors of the patients were determined in the direction of the 2018 guideline of the European Society of Cardiology.

Risk Factors

- Male sex
- Smoking
- Waist circumference (female) > 88 cm
- Waist circumference (male) > 102 cm
- BMI ≥ 30 kg/m2
- HOMA-IR ≥ 2.5
- Systolic blood pressure ≥ 140 mmHg
- Diastolic blood pressure ≥ 90mmHg
- Fasting blood glucose ≥ 100mg/dl

Antropometric Measurements

Anthropometric parameters including height, weight, and waist circumference (WC) were measured. Weight was measured while subjects wore only light clothing; height was assessed without shoes, back squared against the wall tape, eyes looking straight ahead using a stadiometer. WC (at the smallest point between lower costal and 10th rib border) was determined using a nonelastic fiberglass measuring tape. All of these measurements were done by the same researcher. BMI was calculated by dividing body weight in kilograms to square of body height in meters and expressed in units of (kg/m2). They were classifed as normal weight if BMI value was between 18.50-24.99 kg/m2, overweight if BMI value was between 25.0-29.99 kg/m2 and obese if it was higher than 30.0 kg/m2. According to WHO obesity criteria, waist circumference cut off value was accepted to be 88 cm in women and 102 cm in men [10]. Waist circumference was measured using a non-flexible tape, in the standing position and in midway between the lowest rib and the superior border of iliac crest.

Laboratory Analyses

In all subjects, a fasting blood sample was collected in the morning after fasting at least 10-12 h for analysis of the following biochemical parameters using standard techniques: Total cholesterol (TC), TG, LDL-C, HDL-C, FBG and insulin.

Atherogenic Index of Plasma (AIP)

AIP was calculated as the logarithmically transformed ratio of TG to HDL-C [log (TG/HDL-C)] measured in mmol/L. AIP risk categories were created according to published epidemiological data: AIP < 0.1 is associated with low risk, 0.1-0.24 with moderate risk, and > 0.24 with high risk [8].

Insulin Resistance

Homeostasis model assessment as an index of insulin resistance (HOMA-IR) test which was developed by Matthews *et al*. [11] is a simple test to show insulin resistance. For insulin resistance, HOMA-IR was calculated with the formula below by using fasting plasma glucose and insulin levels. Cut-off value of HOMA-IR was taken as 2.5. HOMA-IR = Serum glucose (mg/dL) × plasma insulin (μU/mL) / 405.

Statistical Aanalysis

While evaluating the results obtained in the study, SPSS 20.0 packet program was used for statistical analyses. Descriptive statistics for continuous variables were given in terms of average and standard deviation; and descriptive statistics for categorical data were given in terms of frequency and percentage. To compare quantitative data in doublet groups; student-t test was used if they corresponded normal distribution hypothesis and Mann-Whitney U test was used if they did not correspond normal distribution hypothesis and if they showed a skew distribution. Chi square test was used to compare categorical data. Results were evaluated at 95% confidence interval and significance was evaluated in $p < 0.05$ level.

RESULTS

Of all the participants, 372 (74.3%) were female, 129 (25.7%) were male, the mean age was 35.47 ± 10.91 years (34.16 ± 10.75 years in female, 39.26 ± 10.48 years in male), 389 (77.6%) were married, 164 (32.7%) primary school graduate, 192 (38.3%) university graduate, 203 (40.5%) were housewives. The frequency of smoking was 16.6% (n = 83). Of the participants, 127 (25.3%) were normal weight, 150 (29.9%) were overweight and 224 (44.7%) were obese.

When sociodemographic characteristics were compared with obesity; the prevalence of obesity was significantly higher in individuals aged 35 years and older ($p = 0.005$). The prevalence of obesity in individuals who were married, had low education and who were non-working were higher. This difference was statistically significant ($p < 0.001$). There was not a significant relationship between obesity and smoking ($p > 0.05$) (Table 1).

When investigating the relationship between BMI and insulin resistance; insulin resistance in obese group was significantly higher than normal weight group. This difference was statistically significant ($p < 0.001$). Systolic ($p < 0.001$) and diastolic ($p = 0.007$) blood pressures in obese group were significantly higher than non obese group. In the obese group, the risk of CVD was significantly higher than in the non-obese group ($p <0.001$) (Table 1).

When we compared with FBG, serum lipids and BMI

in our study; while the levels of FBG ($p < 0.001$), total cholesterol ($p = 0.026$), LDL-C ($p = 0.004$) and triglyceride ($p < 0.001$) were significantly higher, the level of HDL-C ($p < 0.001$) was significantly lower in the obese group (Table 2).

The CVD risk was significantly higher in individuals aged 35 years and older ($p = 0.003$), in smokers ($p = 0.002$), in male gender ($p < 0.001$) and

Table 1. Comparison of sociodemographic characteristics and BMI

Sociodemographic characteristics	Non-obese group (n = 277)		Obese group (n = 224)		χ^2	*p* value
	n	%	n	%		
Age						
< 35 years	157	61.3	99	38.7	7.722	**0.005**
≥ 35 years	120	49.0	125	51.0		
Gender						
Female	214	57.5	158	42.5	2.926	0.087
Male	63	48.8	66	51.2		
Marital status						
Married	193	49.6	196	50.4	22.670	**< 0.001**
Single	84	75.0	28	25.0		
Education level						
≤ Secondaryeducation	74	33.9	114	66.1	71.126	**< 0.001**
≥ High schooleducation	203	71.7	80	28.3		
Working status						
Working	193	68.9	87	31.1	47.767	**< 0.001**
Non-working	84	38.0	137	62.0		
Smoking						
Yes	52	62.7	31	37.3	2.181	0.140
No	225	53.8	193	46.2		
HOMA-IR						
<2.5	250	64.8	136	35.2	61.102	**< 0.001**
≥2.5	27	23.5	88	76.5		
Systolic blood pressure						
<140 mmHg	251	60.3	165	39.7	25.267	**< 0.001**
≥140 mmHg	26	30.6	59	69.4		
Diastolic blood pressure						
< 90 mmHg	263	57.0	198	43.0	7.239	**0.007**
≥ 90 mmHg	14	35.0	26	65.0		
AIP						
<0.1 low CVD risk	75	80.6	18	19.4		
0.1-0.24 moderate CVD risk	59	66.3	30	33.7	42.669	**< 0.001**
>0.24 high CVD risk	143	44.8	176	55.2		

AIP = atherogenic index of plasma, CVD = cardiovascular disease, BMI = body mass index, HOMA-IR = homeostasis model assessment as an index of insulin resistance

Table 2. Comparison of FBG and serum lipids in obese and non-obese groups

Parameters	Non-obese group (n = 277)	Obese group (n = 224)		
	Mean ± SD	Mean ± SD	t	*p value*
FBG (mg/dL)	91.11 ± 9.00	94.85 ± 9.03	-4.624	**< 0.001**
Total cholesterol (mg/dL)	185.42 ± 41.14	193.53 ± 39.57	-2.231	**0.026**
LDL-C (mg/dL)	114.12 ± 36.53	123.13 ± 33.25	-2.854	**0.004**
HDL-C (mg/dL)	49.40 ± 12.17	43.62 ± 9.26	5.862	**< 0.001**
Triglyceride (mg/dL)	105.72 ± 59.76	135.57 ± 67.80	-5.233	**< 0.001**

FBG = fasting blood glucose, HDL-C = high-density lipoprotein-cholesterol, LDL-C = low-density lipoprotein-cholesterol

Table 3. Comparison of sociodemographic characteristics and CVD risk

Sociodemographic characteristics	Low/moderate CVD risk AIP ≤ 0.24 (n = 182)		High CVD risk AIP > 0.24 (n = 319)		χ^2	*p value*
	n	%	n	%		
Age						
< 35 years	109	42.6	147	57.4	8.843	**0.003**
≥ 35 years	73	29.8	172	70.2		
Gender						
Female	164	44.1	208	55.9	37.599	**< 0.001**
Male	18	14.0	111	86.0		
Smoking						
Yes	18	21.7	65	78.3	9.219	**0.002**
No	164	39.2	254	60.8		
WC (female)						
≤ 88 cm	102	60.0	68	40.0	32.164	**< 0.001**
> 88 cm	62	30.7	140	69.3		
WC (male)						
≤ 102 cm	14	25.0	42	75.0	10.057	**0.002**
> 102 cm	4	5.5	69	94.5		
Obesity						
BMI < 30 kg/m^2	134	48.4	143	51.6	38.879	**< 0.001**
BMI ≥ 30 kg/m^2	48	21.4	176	78.6		
HOMA-IR						
<2.5	168	43.5	218	56.5	37.646	**< 0.001**
≥2.5	14	12.2	101	87.8		
SBP						
< 140 mmHg	169	39.4	260	60.6	12.136	**< 0.001**
≥ 140 mmHg	13	18.1	59	81.9		
DBP						
< 90 mmHg	170	36.8	292	63.2	0.565	0.452
≥ 90 mmHg	12	30.8	27	69.2		
FBG						
< 100 mg/dl	158	40.0	237	60.0	10.887	**< 0.001**
≥ 100mg/dl	24	22.6	82	77.4		

BMI = body mass index, CVD = cardiovascular disease, FBG = fasting blood glucose, DBP = diastolic blood pressure, HOMA-IR = homeostasis model assessment as an index of insulin resistance, SBP = systolic blood pressure, WC = waist circumference

Table 4. Comparison of some parameters and CVD risks (AIP > 0.24).

Parameters		OR	%95 CI		*p value*
			Lower	Upper	
Gender	Female	1	2.838	8.331	**< 0.001**
	Male	4.862			
WC (female)	≤ 88 cm	1	2.207	5.199	**< 0.001**
	> 88 cm	3.387			
WC (male)	≤ 102 cm	1	1.775	18.629	**0.002**
	> 102 cm	5.570			
Obesity	BMI < 30 kg/m^2	1	2.311	5.109	**< 0.001**
	BMI ≥ 30 kg/m^2	3.436			
HOMA-IR	< 2.5	1	3.069	10.070	**< 0.001**
	≥ 2.5	5.560			

AIP = atherogenic index of plasma, BMI = body mass index, CVD = cardiovascular disease, HOMA-IR = homeostasis model assessment as an index of insulin resistance, WC = waist circumference

Table 5. Correlations of some parameters in obese and non-obese groups

PARAMETERS		1	2	3	4	5	6
1. AIP	r	1					
	p						
2. Age (year)	r	0.190	1				
	p	**< 0.001**					
3. BMI (kg/m²)	r	0.354	0.165	1			
	p	**< 0.001**	**< 0.001**				
4. WC (cm)	r	0.456	0.293	0.819	1		
	p	**< 0.001**	**< 0.001**	**< 0.001**			
5. Insulin	r	0.266	-0.102	0.311	0.275	1	
	p	**< 0.001**	**0.024**	**< 0.001**	**< 0.001**		
6. HOMA-IR	r	0.261	-0.070	0.299	0.258	0.983	1
	p	**< 0.001**	0.112	**< 0.001**	**< 0.001**	**< 0.001**	

AIP = atherogenic index of plasma, BMI = body mass index, HOMA-IR = homeostasis model assessment as an index of insulin resistance, WC = waist circumference

in individuals with insulin resistance ($p < 0.001$) (Table 3).

CVD risk in males were 6.254 times more than in females [OR = 6.254, 95% CI; (2.287-17.107)], and this difference was found to be statistically significant ($p < 0.001$). CVD risk in individuals with insulin resistance was 5.560-fold increase than individuals without insulin resistance [OR = 5.560, 95% CI; (3.069-10.070)] and this difference was found to be highly statistically significant ($p < 0.001$). The odds ratios of the other parameters were shown in Table 4.

When the correlation between AIP and waist circumference is examined; AIP was correlated with waist circumference (r = 0.456, $p < 0.001$) (Table 5). When linear regression analysis is performed; 20.8% of the increase in AIP is attributed to the increase in waist circumference ($R^2 = 0.208$, $p < 0.001$) (Figure 1).

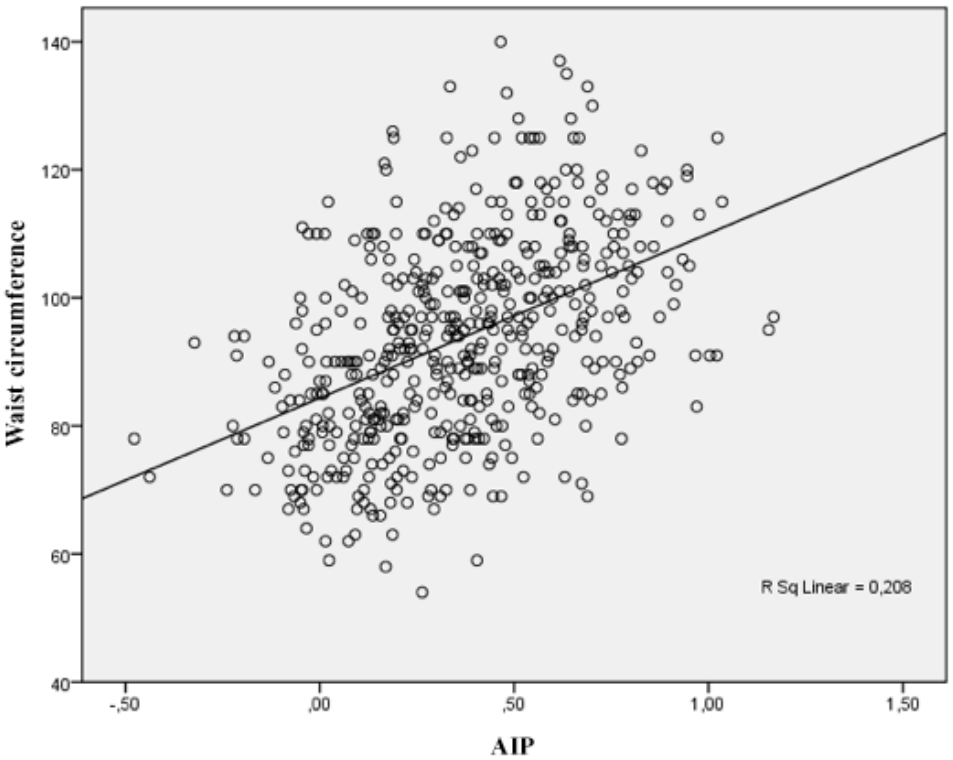

Figure 1. Linear regression analysis between waist circumference and AIP. R^2= Regression determinant coefficient (R2=0.208, $p < 0.001$)

DISCUSSION

Before mentioning the conclusions, the limitations of the study should be considered. Although the overall sample was relatively large, we reached a small group. In addition, although a quite close match, this study group is not entirely representative of the Turkish population. The study includes only the citizens of Konya. The most important limitation of our study is that the physical activity and nutritional status have not been assessed.

Obesity is a complicated and multifactorial disease which provides a basis for many diseases, reduces life quality and longevity of individuals and it causes deaths. Overweight and obesity directly contribute to the development of cardiovascular diseases and type 2 diabetes mellitus. For this reason, it has become an important public health concern on a global scale [12]. In this study, we assessed the correlation between AIP and the major risk factors of CVD in obese and non-obese individuals.

When we looked at the relation between obesity and cardiovascular risks in our study, it was seen that as BMI increased, cardiovascular risk increased as well. Cardiovascular risk in obese individuals was 3.436 times more than in none-obese individuals. Chhezom *et al*. [12] found out in their study that obese individuals had significantly higher cardiovascular risk. It was discovered in many studies that waist circumference as a marker of abdominal obesity is a better marker to reveal cardiovascular risk than BMI [13]. In our study, there was a significant relation between WC and cardiovascular risks. Shen *et al*. [14] showed that there was a positive relationship between waist circumference and AIP in their studies. Ying Lee *et al*. [15] stated in their meta-analysis study that preventing abdominal obesity is especially more important to reduce cardiovascular risk.

The strongest independent risk factor for CVD development is age. It was discovered in our study that cardiovascular risk in individuals above 35 years of age is 4.862 times more than in ones under 35 years of age. In women in premenopausal period, CVD is seen 10 years later compared to men. The reason of this delay is attributed to protective effect of estrogen [16]. The risk increases in women during premenopausal period but this risk is lower than in men when making an evaluation between age groups. In the study performed by Yıldız *et al*. [16] in our country, it was shown that cardiovascular risk increases significantly in postmenopausal women compared to premenopausal women. The studies indicate that cardiovascular risk in men is significantly higher than in women in all groups of age [17, 18]. We also determined that cardiovascular risk is 5.570 times more in men than in women.

In our study, cardiovascular risk in smokers was significantly higher than in non-smokers. Smoking increases CVD risk 2-3 times and causes the risk to increase more by interacting with other risk factors. Smoking stimulates sympathetic nervous system, increases blood pressure and reduces oxygen delivery in myocardium. Besides, it has also effects on atherosclerosis. A decrease is observed in events related to CVD when smoking is given up [19].

It has long been known that hypertension plays an important role in pathogenesis of coronary artery disease and other cardiovascular diseases. Hypertension is responsible for 35% of all atherosclerotic cardiovascular events [20]. In our study, CVD risk is significantly higher in individuals whose systolic blood pressure was higher. Onat [21], stated in their study that high blood pressure increases cardiovascular risk significantly.

In our study, we determined that cardiovascular risk was 5.560 times more in individuals with high insulin resistance. Insulin resistance makes a significant contribution to atherosclerosis even before the occurrence of overt diabetes. In meta-analysis studies, it was seen that increased insulin and fasting blood glucose in non-diabetic patients increase CVD risk significantly [22, 23]. It was found out in our study that CVD risk was significantly higher in individuals with high FBG. Similiar to our study, Oluyombo *et al*. [24] showed that as FBG level increases, cardiovascular risk increases in individuals as well. The studies indicate that mortality risk related to cardiovascular events in diabetic patients was 2-6 times more than in non-diabetic patients [25].

CONCLUSION

FBG, insulin resistance, high waist circumference, elevation of the blood pressure, LDL-C, total cholesterol, triglyceride in obese group were

significantly higher than non obese group. Only, the level of HDL-C was significantly lower in the obese group. AIP, a new marker of atherogenicity, has been shown to significantly increase with cardiovascular risks. AIP could be a convenient and practical approach for assessment of CVD risks in public health settings and primary health centers. In this study, there was a statistically significant relationship between obesity, male gender, older age, smoking, insulin resistance, high waist circumference, elevation of the blood pressure, FBG and AIP > 0.24 (high CVD risk).

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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