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ORIGINAL RESEARCH

Comparison of Visceral Adiposity and Plasma Atherogenicity Indices, Which are Cardiovascular Risk Markers in Hypothyroid Patients and Healthy Controls

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Purpose: Hypothyroidism increases the risk of cardiovascular disease. In recent years, it has been suggested that the Visceral Adiposity Index (VAI) and the Plasma Atherogenicity Index (PAI) may serve as markers of cardiovascular risk. This study aimed to investigate the potential utility of VAI and PAI as predictors of increased cardiovascular risk in patients with hypothyroidism.

Patients and Methods: A retrospective analysis was conducted on 134 participants, including 85 hypothyroid patients and 49 individuals with normal thyroid function who visited the Family Medicine Clinic of Konya Training and Research Hospital between March 2016 and June 2017. Sociodemographic characteristics, anthropometric measurements, blood lipid profiles, and thyroid hormone levels were analyzed for all participants. VAI and PAI levels were calculated.

Results: Among the participants, 111 (82.8%) were female, and 23 (17.2%) were male. In the hypothyroid group, triglycerides (TG) ($p=0.001$), Visceral Adiposity Index (VAI) ($p<0.001$), and Plasma Atherogenic Index (PAI) ($p<0.001$) were significantly higher, in contrast high-density lipoprotein (HDL) ($p<0.001$) was substantially lower than in the control group. Patients were divided into three categories based on PAI levels: low, moderate, and high risk. Compared to the moderate-risk group, the high-risk group had higher weight ($p=0.007$), BMI ($p=0.012$), WC ($p=0.001$), TG ($p<0.001$), VAI ($p<0.001$), and PAI ($p<0.001$), but lower HDL ($p<0.001$). PAI showed a positive correlation with age, weight, BMI, WC, systolic and diastolic blood pressure, thyroid-stimulating hormone (TSH), TG, total cholesterol, and VAI, and a negative correlation with HDL.

Conclusion: This study demonstrates that cardiovascular risk is increased in hypothyroid patients, VAI and PAI are reliable markers for assessing cardiovascular disease risk in this population. These findings may aid primary care physicians in early identification and management of cardiovascular risk in hypothyroid patients. Limitations include the retrospective design and limited male representation in the sample.

Keywords: hypothyroidism, cardiovascular risk, visceral adiposity index, plasma atherogenic index

Introduction

Hypothyroidism is one of the most common endocrine disorders encountered in primary care, affecting 4.3% of the population. Studies report that the prevalence of subclinical hypothyroidism can reach up to 10%.[1–3] Hypothyroidism is associated with an increased risk of obesity and cardiovascular diseases (CVDs).[4–7] Factors contributing to this increased risk include dyslipidemia, hypercoagulability, endothelial dysfunction, platelet abnormalities, impaired fibrinolysis, visceral obesity, and systemic inflammation.[4,8–12]

Visceral adipose tissue is known to pose a greater risk for cardiovascular diseases compared to subcutaneous fat.[13,14] In primary care, simple methods such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio, and waist-to-height ratio are commonly used to assess visceral obesity. However, BMI is influenced by factors such as age, gender, and increased muscle mass. Furthermore, it does not distinguish between different fat tissue compartments.

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Similarly, waist circumference varies depending on ethnicity and lifestyle and cannot differentiate between visceral and subcutaneous fat.

Advanced imaging techniques, such as magnetic resonance imaging (MRI), computed tomography (CT), dual-energy X-ray absorptiometry (DEXA), and bioelectrical impedance analysis, provide more accurate insights into body fat distribution. However, their clinical use in primary care is limited due to cost, radiation exposure, and time requirements. Recently, the Visceral Adiposity Index (VAI) has been proposed as a mathematical model that incorporates anthropometric measurements like BMI and WC, along with biochemical parameters such as triglycerides (TG) and high-density lipoprotein (HDL) cholesterol. VAI is recognized as a reliable indicator of visceral fat dysfunction and a valuable tool for determining cardiometabolic risk.[15]

Another emerging marker is the Plasma Atherogenic Index (PAI), defined as the logarithmic ratio of plasma TG to HDL cholesterol levels.[16] PAI is a more sensitive cardiovascular risk marker compared to traditional lipid parameters. Notably, PAI can indicate increased atherogenicity even when lipid levels are within normal ranges.[17–20]

This study aimed to evaluate VAI and PAI levels in hypothyroid patients and healthy controls, compare these markers, and explore their relationships with anthropometric measurements, blood lipid levels, and thyroid hormones.

Materials and Methods

This retrospective study evaluated 85 patients diagnosed with hypothyroidism and 49 healthy individuals with normal thyroid function tests who met the exclusion criteria. The participants visited the Family Medicine Clinic at the University of Health Sciences, Konya Training and Research Hospital, between March 2016 and June 2017. The control group consisted of healthy individuals who attended the clinic for routine screenings, with 49 meeting the criteria during the study period. Participants with missing data were excluded from the study. Hypothyroidism was defined as a TSH level >10 μIU/mL, or a TSH level between 4–9.9 μIU/mL with free T4 levels <0.89 ng/mL. The control group comprised individuals with similar age and sex distributions, TSH levels between 0.5–3.99 μIU/mL, and normal free T4 levels.

Ethical approval was obtained from the Ethics Committee of Selçuk University (Decision No. 2020/80). Sociodemographic characteristics, anthropometric measurements (height, weight, waist circumference, blood pressure), and biochemical parameters (total cholesterol, HDL, TG, TSH, and free T4 levels) were collected from patient records. Body mass index (BMI) was calculated as weight (kg) / height² (m²). Total cholesterol, HDL, TG, TSH, and T4 levels were evaluated. VAI was calculated using different formulas for men and women.[20] In men: (Waist Circumference / (39.68 + (1.88 × BMI))) × (Triglycerides / 1.03) × (1.31 / HDL), in women: (Waist Circumference / (39.58 + (1.89 × BMI))) × (Triglycerides / 0.81) × (1.52 / HDL).[15]

PAI: log ([TG (mmol/L)] / [HDL (mmol/L)]).[21] Patients were divided into three categories based on PAI levels: those with a PAI below 0.11 were classified as low-risk, between 0.11 and 0.24 as moderate-risk, and above 0.24 as high-risk.[22,23]

The study excluded individuals with diabetes, those using steroids or lipid-lowering medications, pregnant or breastfeeding women, individuals with liver or kidney failure, endocrine disorders, malignancies, and patients under 18 or over 65 years of age.

Statistical Methods

The statistical analyses of the data obtained in the study were performed using the SPSS 22 software package at a significance level of $\alpha = 0.05$. Categorical variables were presented as frequencies and percentages, while numerical variables were expressed as means, standard errors, medians, and interquartile ranges. For single groups, descriptive statistics and normality tests (Kolmogorov–Smirnov and Shapiro–Wilk tests) were used to assess the distribution of continuous data. Continuous variables, such as gestational age, were expressed as mean ± standard and analyzed using Student's *t*-test or one-way ANOVA for normally distributed data. The Mann–Whitney *U*-test and Kruskal–Wallis variance analysis were used for non-normally distributed variables. Statistical significance was set at $P < 0.05$ (two-tailed). Bonferroni correction was used for pairwise comparisons. Correlation levels were determined using Pearson and Spearman correlation analyses.

Results

A total of 134 individuals, including 85 hypothyroid patients and 49 controls, were retrospectively analyzed. Of these, 111 (82.8%) were female, and 23 (17.2%) were male. The mean age of the participants was 39.66 ± 1.12 years. Compared to the control group, patients with hypothyroidism had significantly higher weight ($p<0.001$), BMI ($p<0.001$), and waist circumference ($p=0.002$). While there were no significant differences in age or height between the patient and control groups, triglycerides (TG) ($p=0.001$), Visceral Adiposity Index (VAI) ($p<0.001$), and Plasma Atherogenic Index (PAI) ($p<0.001$) were significantly higher in the hypothyroid group, whereas HDL cholesterol levels were significantly lower ($p<0.001$). There were no statistically significant differences between the two groups in terms of total cholesterol, systolic blood pressure, or diastolic blood pressure ($p>0.05$) (Table 1).

Patients were categorized into three groups based on PAI levels: low, moderate, and high risk. When groups were compared in pairs and as a whole, in the moderate-risk group compared to the low-risk group, TG ($p<0.001$), VAI ($p<0.001$), and PAI ($p<0.001$) were higher, while HDL ($p=0.008$) was lower. In the high-risk group compared to the moderate-risk group, weight ($p=0.007$), BMI ($p=0.012$), waist circumference ($p=0.001$), TG ($p<0.001$), VAI ($p<0.001$), and PAI ($p<0.001$) were higher, while HDL ($p<0.001$) was lower. In the high-risk group compared to the low-risk group, age ($p<0.001$), weight ($p<0.001$), BMI ($p<0.001$), waist circumference ($p<0.001$), systolic blood pressure ($p=0.001$), diastolic blood pressure ($p<0.001$), T4 ($p=0.015$), total cholesterol ($p=0.015$), TG ($p<0.001$), VAI ($p<0.001$), and PAI ($p<0.001$) were higher, while HDL ($p<0.001$) was lower (Table 2).

A positive correlation was identified between PAI and age, body weight, BMI, waist circumference, systolic and diastolic blood pressure, TSH, TG, total cholesterol, and VAI, while a negative correlation was observed with HDL. Similarly, a positive correlation was found between VAI, indicative of visceral fat dysfunction, and age, body weight, waist circumference, systolic and diastolic blood pressure, TSH, TG, total cholesterol, BMI, and VAI, while a negative correlation was noted with HDL cholesterol (Table 3).

Table 1 Comparison of Study Parameters Between Hypothyroid and Control Groups

	Control Group (n=49)	Hypothyroidism Group (n=85)	p
Age (year)	40.12±1.98	39.56±1.73	0.886
Height (cm)	162.36±1.03	163.80±1.02	0.678
Weight (kg)	67.72±2.11	80.04±2.55	**<0.001**
BMI (kg/m^2)	25.70±0.78	29.80±0.89	**<0.001**
Waist circumference (cm)	91.26±2.97	99.62±1.84	**0.002**
Systolic blood pressure (mmHg)	115.10±2.64	117.39±3.61	0.814
Diastolic blood pressure (mmHg)	73.19±1.82	74.27±1.88	0.431
Total cholesterol (mg/dL)	210.63±7.74	5.27±0.15	0.919
TG (mg/dL)	94.81±6.26	138.76±16.36	**0.001**
HDL (mg/dL)	65.38±5.94	52.48±3.87	**<0.001**
VAİ	3.32±0.32	5.76±0.94	**<0.001**
PAİ	0.16±0.04	0.37±0.04	**<0.001**

Abbreviations: BMI, Body Mass Index; TG, Triglycerides; HDL, High-Density Lipoprotein Cholesterol; VAI, Visceral Adiposity Index; PAI, Plasma Atherogenic Index.

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Table 2 Comparison of VAI, Anthropometric Measurements, Thyroid Hormones, and Blood Lipids Across PAI Risk Groups

	Low Risk PAİ (Group1) (n=29)	Medium Risk PAİ (Group 2) (n=27)	High Risk PAİ (Group3) (n=78)	p	Group (1–2) p1	Group (1–3) p2	Group (2–3) p3
Age(year)	33.345±2.390	38.222±2.396	42.513±1.426	**0.002**	0.102	***<0.001**	0.153
Height (cm)	162.000±1.193	161.630±1.356	163.346±0.853	0.476	0.799	0.274	0.255
Weight (kg)	63.755±3.100	71.556±3.834	80.346±1.874	**<0.001**	0.206	***<0.001**	***0.007**
BMI (kg/m^2)	24.228±1.084	27.337±1.369	30.168±0.686	**<0.001**	0.093	***<0.001**	***0.012**
Waist circumference (cm)	85.586±2.731	89.963±2.812	102.006±1.947	**<0.001**	0.394	***<0.001**	***0.001**
Systolic BP (mmHg)	106.786±3.173	111.400±3.103	121.333±2.680	**0.002**	0.074	***0.001**	0.059
Diastolic BP (mmHg)	68.214±2.061	71.800±2.464	77.733±1.572	**0.003**	0.205	***<0.001**	0.065
TSH (mIU/L)	5.036±1.349	9.750±2.358	12.154±2.311	**0.003**	0.302	0.160	0.268
T4	1.106±0.039	1.065±0.049	1.017±0.029	0.364	0.479	***0.015**	0.588
TC (mg/dL)	194.690±10.648	201.704±9.680	217.882±6.047	**0.032**	0.294	***0.015**	0.142
TG (mg/dL)	60.931±5.149	84.556±3.255	170.295±15.708	**<0.001**	***<0.001**	***<0.001**	***<0.001**
HDL (mg/dL)	83.414±10.662	56.481±2.230	45.735±1.110	**<0.001**	***0.008**	***<0.001**	***<0.001**
VAİ	1.63±0.11	2.80±.08	7.36±0.79	**<0.001**	***<0.001**	***<0.001**	***<0.001**
PAİ	−0.107±0.045	0.176±.008	0.517±0.029	**<0.001**	***<0.001**	***<0.001**	***<0.001**

Notes: Comparisons were made using Bonferroni-corrected values for α=0.05. *p-value <0.166 was considered significant. p1: (p-value for comparison between Group 1 and Group 2), p2: (p-value for comparison between Group 1 and Group 3), p3: (p-value for comparison between Group 2 and Group 3). The bolded data represent statistically significant results ($p < 0.05$).

Abbreviations: BMI, Body Mass Index; BP, Blood Pressure; TSH, Thyroid-Stimulating Hormone; TC, Total Cholesterol; TG, Triglycerides; HDL, High-Density Lipoprotein Cholesterol; VAI, Visceral Adiposity Index; PAI, Plasma Atherogenic Index.

Table 3 Correlation Between VAI; PAI, Anthropometric Measurements, and Blood Lipids

	1	2	3	4	5	6	7	8	9	10	11	12
1. PAİ	1											
2. Age p	**0.001**	1										
r	0.296											
3. Weight p	**<0.001**	**0.001**	1									
r	0.443	0.286										
4. WC p	**<0.001**	**<0.001**	**<0.001**	1								
r	0.446	0.321	0.321									
5. SBP p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	1							
r	0.312	0.467	0.339	0.329								
6. DBP p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	1						
r	0.307	0.431	0.403	0.424	0.833							

(*Continued*)

Table 3 (Continued).

	1	2	3	4	5	6	7	8	9	10	11	12
7. TG												
p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	1					
r	0.901	0.372	0.420	0.445	0.326	0.321						
8. TK												
p	**0.006**	**<0.001**	**0.005**	**0.001**	**0.008**	**0.009**	**<0.001**	1				
r	0.238	0.533	0.245	0.285	0.235	0.231	0.474					
9. BMI												
p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.002	1			
r	0.400	0.349	0.928	0.911	0.377	0.451	0.393	0.269				
10. VAI												
p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.004**	**<0.001**	1		
r	0.963	0.309	0.419	0.487	0.299	0.307	0.884	0.250	0.410			
11. TSH												
p	**<0.001**	0.847	0.012	0.065	0.577	0.498	**<0.001**	0.477	**0.005**	**0.001**	1	
r	0.351	–0.017	0.215	0.160	0.050	0.060	0.297	0.0623	0.243	0.333		
12. T4												
p	0.143	0.971	0.719	0.864	0.262	0.833	0.629	0.344	0.284	0.087	**<0.001**	1
r	0.130	0.003	0.032	0.015	0.102	0.019	–0.043	0.085	0.095	0.151	–0.618	

Notes: The bolded data represent statistically significant results ($p < 0.05$).
Abbreviations: BMI, Body Mass Index; WC, Waist Circumference; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; TSH, Thyroid-Stimulating Hormone; TC, Total Cholesterol; TG, Triglycerides; VAI, Visceral Adiposity Index; PAI, Plasma Atherogenic Index.

Discussion

In this study, patients were stratified into three cardiovascular risk groups based on PAI values, using the thresholds proposed by Dobiásová et al which have been validated in previous population-based studies. A PAI value < 0.11 indicates low atherogenic risk, values between 0.11 and 0.24 indicate moderate risk, and values > 0.24 suggest high cardiovascular risk.[23] These cutoffs are clinically relevant as they reflect increased atherogenic burden even in individuals with normal lipid profiles, allowing for early identification of individuals at higher cardiovascular risk. Incorporating these thresholds into primary care may improve preventive strategies, especially in populations with endocrine disorders such as hypothyroidism. In this study, levels of cardiovascular risk markers VAI and PAI, which can be calculated in primary care using simple anthropometric measurements and blood lipid profiles, were found to be higher in hypothyroid patients compared to the control group. Based on our literature review, we did not identify any prior studies specifically examining these markers in hypothyroid patients. Consistent with the literature, hypothyroid patients were observed to have higher weight, BMI, waist circumference, and atherogenic lipid levels compared to healthy controls. Among patients categorized by PAI levels, those in the high-risk group showed elevated weight, BMI, waist circumference, and atherogenic lipid levels, as well as higher VAI and PAI. Furthermore, a positive correlation was identified between cardiovascular risk markers PAI and VAI and parameters such as weight, BMI, waist circumference, systolic and diastolic blood pressure, total cholesterol, and triglycerides.

The relationship between hypothyroidism and increased cardiovascular risk has been demonstrated in previous studies. Factors such as BMI, waist circumference, blood pressure, atherogenic lipid profiles, hyperhomocysteinemia, and elevated C-reactive protein levels have been used to predict this increased risk.[4,24] While the VAI incorporates anthropometric measurements in addition to triglycerides (TG) and high-density lipoprotein (HDL), the PAI is calculated using HDL and low-density lipoprotein (LDL) levels. Although their formulas differ in structure, various studies have demonstrated that both indices yield favorable results in the assessment of cardiovascular risk.[25–27] It has been suggested that VAI, which incorporates BMI and waist circumference along with blood lipid levels, can be effectively used to

predict cardiometabolic risk.[28,29] A study conducted in Brazil showed that VAI is superior to traditional adiposity measurement methods in detecting metabolic disorders, independent of nutritional status and gender.[29] While there are a few studies evaluating VAI and PAI separately in hypothyroid patients, we did not find any studies in the literature that assessed and compared both markers simultaneously.[30–33] PAI has been shown in many studies to be directly associated with the risk of atherosclerosis, with patients who have higher PAI levels being at greater risk for coronary heart disease compared to those with lower PAI levels.[18,32,33] In this study, we assessed and compared PAI and VAI levels in hypothyroid patients. We found that hypothyroid patients had higher weight, BMI, waist circumference, TG, VAI, and PAI levels, and lower HDL levels compared to the control group. In hypothyroidism, reduced lipoprotein lipase enzyme activity leads to increased TG and LDL levels and decreased HDL cholesterol levels. Similarly, in our study, TG and total cholesterol levels were higher and HDL cholesterol levels were lower in the hypothyroid group compared to healthy controls. Additionally, we identified a positive correlation between PAI and TSH levels. A study involving 95 patients with subclinical hypothyroidism and 65 controls found similar results, reporting higher TG and PAI levels in hypothyroid patients compared to the control group.[16]

In our study, we found that VAI and PAI levels showed a positive correlation with metabolic syndrome parameters reflecting cardiovascular disease risk, such as waist circumference, systolic and diastolic blood pressure, and triglycerides, while a negative correlation was observed with HDL. A study evaluating the relationship between anthropometric measurements and PAI in non-obese sedentary men reported findings similar to ours, demonstrating significant correlations between PAI and waist circumference, BMI, waist-to-hip ratio, waist-to-height ratio, abdominal volume index, and body fat percentage values.[34]

Patients were divided into three groups based on PAI levels: low, moderate, and high risk. In the high-risk group, PAI levels were associated with higher weight, BMI, waist circumference, TG, and VAI. Systolic and diastolic blood pressure levels were significantly higher in the high-risk group compared to the low-risk group but were similar between the high- and moderate-risk groups. Additionally, our study identified a strong positive correlation between VAI and PAI levels. We did not encounter any other studies in the literature that directly compared these two parameters.

Elevated TG and low HDL levels are common lipid abnormalities observed in patients with hypothyroidism. Due to the nature of the formula used for their calculation, a positive correlation between VAI and PAI is logically expected. However, unlike PAI, the VAI formula incorporates BMI and waist circumference in addition to lipid parameters. A study conducted on healthy, normal-weight but sedentary adults investigating the effects of anthropometric measurements on PAI found that even with normal anthropometric measurements and lipid levels, sedentary individuals had a higher risk of atherogenicity. Furthermore, BMI, body fat index, and body fat percentage were shown to have a significant effect on PAI levels.[35] In a study involving 1,000 patients, PAI levels were found to correlate positively with waist circumference and negatively with physical activity status. The study also reported that even with normal lipid levels, elevated PAI could be a useful tool in daily practice for the early detection of cardiovascular diseases.[36]

The present study has certain limitations. Since it was conducted retrospectively, the number of participants in the control group was smaller compared to the patient group. This was primarily due to the study being conducted in a tertiary hospital, where the number of healthy individuals seeking medical attention is relatively low. Another limitation was the insufficient number of male patients and the inability to assess additional cardiovascular risk markers.

Conclusion

Utilizing easily applicable indices instead of more complex, costly, and less accessible methods for determining cardiovascular risk may significantly contribute to the diagnostic and therapeutic processes for both physicians and patients. We aimed to investigate how the VAI and PAI indices—which have shown favorable results and proven reliability in assessing cardiovascular risk in numerous studies—perform in patients with hypothyroidism. In conclusion, this study demonstrated that cardiovascular risk is increased in hypothyroid patients, and VAI and PAI can be reliably used to determine cardiovascular disease risk. Physicians should be vigilant about the increased cardiovascular risk in hypothyroid patients, a condition commonly encountered in primary care. The anthropometric measurements and lipid parameters used in the calculation of VAI and PAI are readily obtainable in all healthcare settings, including primary care. Due to their low cost and ease of assessment, the use of these indices may be promoted for cardiovascular risk

screening and evaluation. VAI and PAI offer simple and cost-effective methods for early identification of cardiovascular disease risk before symptoms appear. By using these tools, it may be possible to take preventive measures and initiate early treatment in hypothyroid patients with a high cardiovascular risk.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the authors on request.

Informed Consent Statement

Written informed consent has been obtained from the patients to publish this paper. The Ethics Committee of Selcuk University Faculty of Medicine did not require separate consent for the review of patients' medical records, as the written informed consent obtained from the patients already included explicit permission for the review of their medical data. All patient data were anonymized and handled in accordance with relevant data protection regulations to ensure confidentiality.

Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Selcuk University Faculty of Medicine (2020/80 and 19.02.2020).

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Disclosure

The authors declare no conflict of interest.

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