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Research Article

Relationship between atherogenic index of plasma, asprosin, and metrnl levels in hemodialysis patients

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Abstract

Objectives: This study aimed to evaluate the relationship between the atherogenic index of plasma (AIP) and plasma asprosin and metrnl levels in hemodialysis (HD) patients.

Methods: Forty-eight patients receiving HD treatment with a diagnosis of end-stage renal disease (ESRD) were included. The control group comprised 34 age-, sex-, and body mass index-matched healthy volunteers without a history of renal disease. ESRD patients were divided into two groups: high-risk (AIP≥0.24) and low-moderate risk (AIP<0.24). Asprosin and metrnl levels in the plasma of blood samples taken just before dialysis were studied by enzyme-linked immunosorbent assay.

Results: A significant difference was found between the control group [23.3(19.9-27.7 ng/mL)], the low-moderate risk group [39.3(34.9-40.8 ng/mL)], and the high-risk group [48.1(44.5-49.9 ng/mL)] in terms of asprosin levels (for each p<0.001). Asprosin values of both low-moderate risk and high-risk groups were significantly higher than the controls. In the high-risk group, plasma asprosin levels were higher than in the low-moderate risk group (p=0.012). Metrnl levels of the high-risk group were found to be lower than both the control and low-risk groups (p<0.001 and p=0.003, respectively). AIP showed a positive relation to asprosin and a negative relation to metrnl.

Conclusion: Logistic regression analysis has revealed important insights into the independent relationships between metrnl, asprosin, and high AIP values in HD patients. These findings support the anti-atherogenic potential of metrnl and suggest the potential atherogenic effects of asprosin, highlighting the complex interplay between adipokines and cardiovascular risk in this patient population.

Keywords: Adipokine, asprosin, atherogenic index of plasma, hemodialysis, meteorin-like protein

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Hemodialysis (HD) patients are more vulnerable to the risk of cardiovascular and metabolic disorders, depending on the underlying disease causing chronic kidney disease and the adverse effects of HD. In HD patients, changes in the visceral and subcutaneous fat tissue, first in the form of adiposity and then in the form of lipodystrophy, may lead to insulin metabolism disorders, which in turn may lead to changes in adipokine synthesis and release [1]. Fat cells try to control the risk of cardio-metabolic diseases by reregulating the synthesis of many different adipokines to prevent adiposity-related adverse effects. Meteorin-like protein (metrnl) and asprosin are two important adipokines involved in insulin resistance, hepatic glucose release, and inflammation regulation [2, 3].

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Stimulation of appetite during fasting and the release of hepatic glucose into the circulation are vital and evolutionary processes regulated by the coordination of the brain and peripheral organs. Metrnl, a peptide homologous to neurotrophin, is an adipokine involved in lipid and glucose metabolism, energy expenditure, insulin sensitivity, and browning of white adipose tissue [4, 5]. In experimental models, metrnl has been shown to reverse hyperglycemia-induced cardiac and renal fibrosis, apoptosis, and oxidative stress [2]. Asprosin is a protein of ~30 kDa and 140 amino acids encoded by fibrillin-1, secreted from adipose tissue during fasting, increasing appetite and stimulating hepatic glucose release [3, 6]. Asprosin, whose circulating levels increase during fasting, decreases to normal levels again with refeeding. In fibrillin gene mutations, decreased circulating levels of asprosin cause loss of fat mass and a lipodystrophic appearance of the individual, while allowing the continuation of insulin sensitivity and the cell's survival [3, 6]. It is known that circulating asprosin levels are increased in type 2 diabetes mellitus (T2DM) and diabetic kidney diseases [7, 8]. Reducing lipid accumulation in macrophages is evidence of the possible protective role of asprosin in atherosclerosis and cardiovascular diseases (CVD) [9].

There are no sufficient clinical studies investigating serum metrnl and asprosin levels and their relationship with metabolic and cardiovascular risk factors in hemodialysis patients. In end-stage renal disease (ESRD) patients at risk of CVD, adipose tissue attempts to balance cardiometabolic risk factors by reregulating the production of adipokines such as asprosin [8]. Metrnl may play a role in contributing to cardiac function and providing protection by exerting anti-inflammatory effects and influencing processes such as vascular function and cardiac remodeling. Metrnl is expressed intensely, especially in the left ventricle and myeloid cells. In experimental infarct models, it has been reported that macrophage-derived metrnl prevents the growth of the infarct area by stimulating post-infarction angiogenesis. Metrnl also acts as a ligand for stem cells to stimulate receptor tyrosine kinase in heart muscle. In metrnl deficiency, the risk of heart failure increases because tyrosine kinase activation cannot be achieved [10]. The atherogenic index of plasma (AIP) has been identified as a predictive biomarker for cardiovascular illnesses, particularly in the context of atherosclerosis and coronary artery disease [11]. Since AIP is a valuable marker in evaluating cardiovascular risk and atherogenicity in various diseases, it is preferred as a cost-effective, fast, and reliable method to reveal early-stage CVD risk [12].

We aimed to assess the association between AIP and plasma asprosin and metrnl levels in HD patients. In addition, we aimed to analyze plasma metrnl and asprosin level changes according to the AIP index and the relationship between these two adipokines and metabolic and demographic parameters.

Materials and Methods

This study was carried out from July 2023 to October 2023, after the permission of Fırat University Non-Invasive Research Ethics Committee (Date and Number: 08.06.2023-2023/08-31). Forty-eight patients receiving HD treatment with a diagnosis of ESRD in Yerköy State Hospital Hemodialysis Unit were included. The control group comprised 34 age-, sex-, and body mass index (BMI)-matched healthy volunteers without a history of T2DM, hypertension, or cardiovascular disease. The study adhered to the principles outlined in the Declaration of Helsinki. All participants were informed, and their consent was obtained.

Patients with active local or systemic infection, malignancy, neurodegenerative disease, or chronic anti-inflammatory and steroid therapy were excluded from this study. ESRD patients were categorized into two groups: high-risk (AIP value ≥0.24) and low-moderate risk (AIP value <0.24). The age, gender, height, and weight of the individuals included in the study were recorded. Lipid parameters and other routine biochemical tests of the participants were performed on 12-hour fasting blood. Fasting plasma glucose, total cholesterol, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), Hemoglobin A1c (HbA1c), serum sodium, potassium, calcium (Ca), phosphorus (P), uric acid, urea, total protein, albumin, creatinine, alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels were measured with an AU680 (Beckman Coulter, Inc., Brea, CA, USA) device. AIP was obtained by taking the logarithm of the ratio of plasma TG to HDL-C level [log10 (TG/HDL-C)]. An AIP≥0.24 was considered high-risk [13]. Fasting insulin, parathyroid hormone (PTH), and ferritin levels were measured by the chemiluminescence method with the Snibe Maglumi 4000 Plus (Snibe Diagnostics, Shenzhen, CHINA) immunoassay analyzer. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) = Fasting glucose (mg/dL) × Fasting insulin (uIU/mL) / 405 [14].

Asprosin and metrnl levels in the plasma of blood samples taken just before dialysis were studied. After the blood samples in the aprotinin tubes were centrifuged at 4000 rpm for 10 minutes, the obtained plasma was transferred to Eppendorf tubes and stored at −20°C until analyzed. Asprosin and metrnl were measured with Human ELISA (Catalog no: E4095Hu, E3941Hu, Bioassay Technology Laboratory, Shanghai, CHINA) kits. The concentration values of the samples were calculated in ng/mL according to the standard curve. The measurement range for asprosin was 0.5–100 ng/mL, and the minimum measurable level (sensitivity) was 0.23 ng/mL. The measurement range for metrnl was 0.05–15 ng/mL, and the minimum measurable level (sensitivity) was 0.023 ng/mL. The intra-assay CV values for both were <8%, and the inter-assay CV values were <10%.

Statistical analysis

Statistical analyses were carried out via SPSS v. 26 (IBM Corp., Armonk, NY). Graphs were created using Graphpad Prism 8.0 (GraphPad Software, San Diego, California, USA). The normality of the data was assessed using the Shapiro-Wilk test. Normally distributed data were presented as mean±standard deviation. Comparisons between groups were made with the one-way ANOVA test. Data that were not normally distributed were pre-

Table 1. Comparison of demographic and laboratory findings among controls and hemodialysis patients with AIP<0.24 and hemodialysis patients with AIP≥0.24

Parameter	Control group (n=34)	Low-moderate risk (n=24)	High-risk (n=24)	p
Age (years)	58 (46–65)	55 (52–67)	59 (47–67)	0.750**
Gender (n, %)				0.905***
Male	15 (44)	12 (50)	11 (46)	
Female	19 (56)	12 (50)	13 (54)	
Body mass index (kg/m^2)	24.2 (22.6–25.9)	24.1 (23.4–25.5)	24.9 (24.0–29.0)	0.063**
Metrnl (ng/mL)	6.80 (5.86–7.71)	3.00 (2.88–3.67)[a1]	1.88 (1.50–2.26)[a1, b2]	**<0.001****
Asprosin (ng/mL)	23.3 (19.9–27.7)	39.3 (34.9–40.8)[a1]	48.1 (44.5–49.9)[a1,b2]	**<0.001****
Urea (mg/dL)	26.4±6.30	140±35.9[a1]	117±25.1[a1]	**<0.001***
Creatinine (mg/dL)	0.68±0.15	7.21±1.77[a1]	7.52±2.16[a1]	**<0.001***
Total protein (g/L)	74.71±3.99	64.0±3.21[a1]	67.58±5.87[a1]	**<0.001***
Albumin (g/L)	43.9 (42.3–46.6)	35.7 (32.8–36.4)[a1]	38.1 (33.9–38.8)[a1]	**<0.001****
Insulin (mIU/L)	9.9 (7.7–11.8)	18.1(11.6–22.2)[a1]	26.6 (22.4–42.9)[a1, b2]	**<0.001****
Glucose (mg/dL)	89.5 (85–92.3)	99.5 (84–136)	143.5 (100.5–201.3)[a1]	**<0.001****
HOMA-IR	2.10 (1.70–2.50)	4.30 (2.45–7.50)[a1]	11.4 (5.75–18.8)[a1, b2]	**<0.001****
HbA1c (%)	5.30 (5.14–5.51)	5.55 (5.44–5.88)[a2]	6.37 (5.68–8.85)[a1]	**<0.001****
AST (U/L)	20.0 (15.8–23.0)	14.0 (11.0–16.8)[a1]	11.0 (7.00–14.0)[a1]	**<0.001****
ALT (U/L)	16.0 (13.0–19.0)	11.0 (10.0–15.5)[a1]	9.00 (5.00–11.0)[a1]	**<0.001****
ALP (U/L)	71.0 (64.0–78.0)	102 (74.5–147)[a1]	147 (106–193)[a1]	**<0.001****
AIP (U/L)	–0.03 (–0.20–0.07)	–0.06 (–0.19–0.11)	0.44 (0.35–0.52)[a1, b1]	**<0.001****
TC (mg/dL)	174 (154–191)	160 (125–176)	150 (121–186)	0.047**
HDL-C (mg/dL)	51.5 (43.0–60.0)	49.5 (39.0–59.0)	30.0 (28.0–33.0)[a1, b1]	**<0.001****
LDL-C (mg/dL)	104 (82.0–112)	92.0 (63.0–98.0)	85.0 (55.0–120)	0.112**
Triglyceride (mg/dL)	112 (73.0–138)	100 (63.0–122)	193 (153–228)[a1,b1]	**<0.001****
Uric acid (mg/dL)	4.45 (4.10–5.20)	5.95 (5.20–7.00)[a1]	6.10 (5.40–6.40)[a1]	**<0.001****
Ca (mg/dL)	9.88±0.39	8.43±0.94[a1]	8.60±1.04[a1]	**<0.001***
P (mg/dL)	3.55±0.44	4.56±1.22[a2]	4.92±5.40[a1]	**<0.001***
Ferritin (µg/L)	62.6 (34.8–105)	454 (89.0–777)[a1]	420 (167–561)[a1]	**<0.001****
PTH (ng/L)	48.5 (32.4–57.8)	602 (453–1376)[a1]	697 (286–1115)[a1]	**<0.001****

*: One-way ANOVA test; **: Kruskal-Wallis test; ***: Chi-Square test. [a]: Comparison with control, [a1]: <0.001; [a2]: <0.017; [b]: Comparison with low-moderate risk group, [b1]: <0.001; [b2]: <0.017. AIP: Atherogenic index of plasma; Metrnl: Meteorin-like protein; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; HbA1c: Hemoglobin A1c; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; TC: total cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-density Lipoprotein Cholesterol; Ca: Calcium; P: Phosphorus; PTH: parathyroid hormone.

sented as median (1st-3rd quartile), and comparisons were analyzed with the Kruskal-Wallis test. Pairwise comparisons were made with the Bonferroni correction. The statistical significance level for Bonferroni correction was accepted as <0.017. *Post-hoc* Bonferroni or Tamhane T2 tests were used for pairwise comparisons of groups in the one-way ANOVA test. Categorical variables were expressed as numbers and percentages, and comparisons between groups were analyzed with the Chi-Square test. Spearman correlation analysis was employed to examine relationships between variables. Binary logistic regression analysis was performed to assess the association between asprosin or metrnl and high-risk (AIP ≥0.24) in HD patients. A p-value <0.05 was considered statistically significant.

Results

A total of 82 patients, including 48 hemodialysis patients with a mean age of 58±11 and 34 healthy controls with a mean age of 55±12, were included in the study. The hemodialysis group consisted of 25 women (52.8%) and 23 men (47.2%), and the control group consisted of 19 women (56%) and 15 men (44%). HD patients with AIP <0.24 were defined as the low-moderate risk group (n=24), and HD patients with AIP ≥0.24 were defined as the high-risk group (n=24). There was no significant difference between the groups regarding age, gender, BMI, total cholesterol, and LDL-C. In the low-moderate and high-risk groups, urea, creatinine, insulin, HOMA-IR, HbA1c, ALP, uric acid, P, ferritin, and PTH levels were significantly higher than those in the control group. Nevertheless, no significant difference was observed between the high-risk and low-moderate risk groups for these parameters, except for insulin and HOMA-IR. Total protein, albumin, AST, ALT, and Ca levels in both low-moderate and high-risk groups were significantly lower compared to the control group (p<0.001); these parameters were similar in the low-moderate and high-

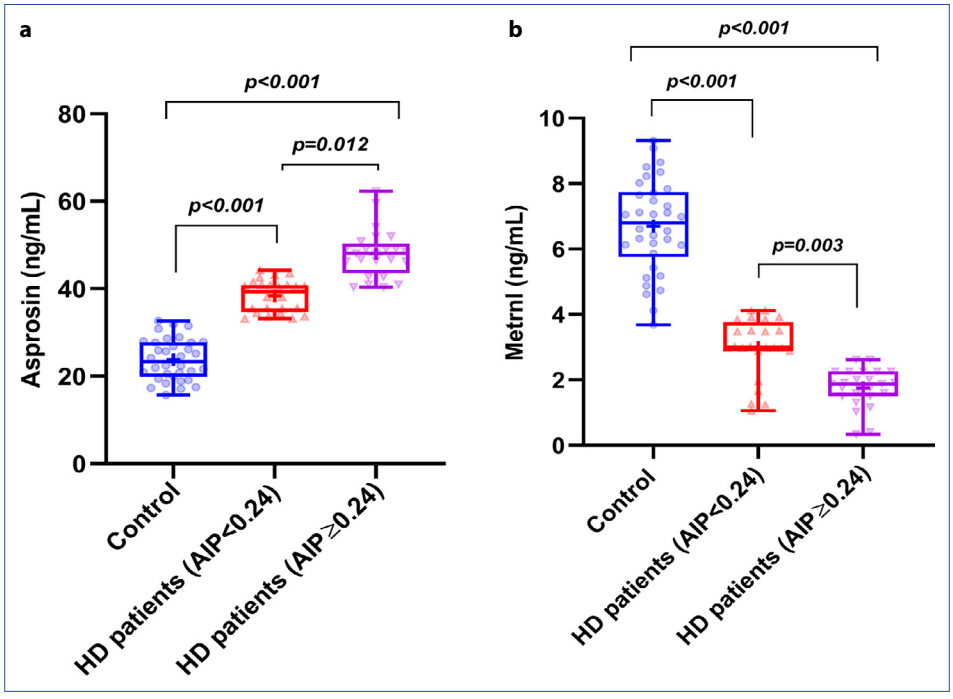

Figure 1. Graphical representation of plasma asprosin (a) and metrnl levels (b) according to AIP values of HD patients.

HD: Hemodialysis; AIP: Atherogenic index of plasma.

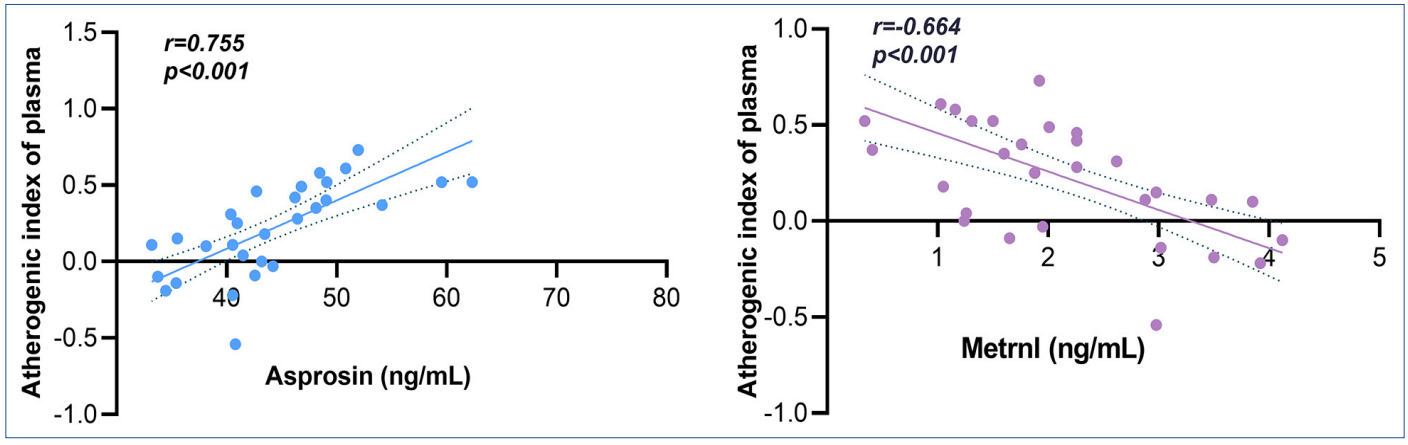

Figure 2. Graphical representation of the relationship between asprosin, metrnl and AIP index in HD patients.

-risk groups. Glucose values were significantly higher in the high-risk group than in the control group (p<0.001) (Table 1).

A significant difference was found between the control group [23.3 (19.9–27.7 ng/mL)], the low-moderate risk group [39.3 (34.9–40.8 ng/mL)] and the high-risk group [48.1 (44.5–49.9)] in terms of asprosin levels (for each p<0.001), (Fig. 1a). Asprosin values of both low- moderate risk and high-risk groups were significantly higher than the controls. Plasma asprosin levels were significantly higher in the high-risk group than in the low-moderate risk group (p=0.012). Metrnl level of the high-risk group was found to be lower than both the control and low-risk groups (p<0.001 and p=0.003, respectively), (Fig. 1b).

AIP showed a positive association with asprosin and a negative association with metrnl (Fig. 2). Metrnl demonstrated a negative correlation with BMI, glucose, TG, HbA1c, HOMA-IR, insulin, and a positive correlation with HDL-C and ferritin (Table 2). Although there was a positive correlation between asprosin and BMI, glucose, TG, P, HbA1c, HOMA-IR, and insulin, a negative correlation was found between asprosin and HDL-C, ferritin, and metrnl (Table 3).

It was observed that asprosin had an independent positive predictive value for high-risk AIP in HD patients when independent variables such as age, BMI, DM, and hypertension were included in the model (OR: 4.662, 95% CI: 1.272 to 17.09; p=0.020). It was observed that metrnl had an independent negative predictive value for high-risk AIP in HD patients

Table 2. Significant correlations between metrnl and the other variables in hemodialysis patients

Parameter	Meteorin-like protein (ng/mL)	
	r	p
AIP	–0.664	**<0.001**
Body mass index (kg/m²)	–0.457	**0.001**
Asprosin (ng/mL)	–0.845	**<0.001**
TG (mg/dL)	–0.568	**<0.001**
HDL-C (mg/dL)	0.575	**<0.001**
HOMA-IR	–0.638	**<0.001**
HbA1c (%)	–0.569	**<0.001**
Glucose (mg/dL)	–0.528	**<0.001**
Insulin (mIU/L)	–0.568	**<0.001**
Ferritin (µg/L)	0.315	**0.029**

r: Spearman correlation coefficient; AIP: Atherogenic index of plasma; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; HbA1c: Hemoglobin A1c.

Table 3. Significant correlations between asprosin and the other variables in hemodialysis patients

Parameter	Asprosin (ng/mL)	
	r	p
AIP	0.755	**<0.001**
Body Mass Index (kg/m²)	0.517	**<0.001**
TG (mg/dL)	0.666	**<0.001**
HDL-C (mg/dL)	–0.676	**<0.001**
HOMA-IR	0.752	**<0.001**
HbA1c (%)	0.672	**<0.001**
Ferritin (µg/L)	–0.403	**0.004**
P (mg/dL)	0.334	**0.020**
Glucose (mg/dL)	0.633	**<0.001**
Insulin (mIU/L)	0.661	**<0.001**

r: Spearman correlation coefficient; AIP: Atherogenic index of plasma; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; HbA1c: Hemoglobin A1c; P: Phosphorus.

Table 4. Binary logistic regression analysis for the association between asprosin or metrnl and high-risk (AIP≥ 0.24)

Univariate regression				Multivariate Regression			
Parameter	**OR**	**95% CI**	**p**	**Parameter**	**OR[a]**	**95% CI**	**p**
Metrnl (ng/mL)	0.143	0.049–0.414	**<0.001**	Metrnl (ng/mL)	0.112	0.028–0.441	**0.002**
Asprosin (ng/mL)	1.818	1.265–2.613	**0.001**	Asprosin (ng/mL)	4.662	1.272–17.09	**0.020**

[a]: Odds ratio adjusted for age, body mass index, diabetes mellitus and hypertension. AIP: Atherogenic index of plasma; OR: Odds ratio; CI: Confidence interval; Metrnl: Meteorin-like protein.

when independent variables such as age, BMI, DM, and hypertension were included in the model (OR: 0.112, 95% CI: 0.028 to 0.441; p=0.002), (Table 4).

Discussion

In this study, for the first time to our knowledge, we analyzed the levels of asprosin and metrnl, two important adipokines, in the plasma of HD patients who were divided into two groups as high (AIP≥0.24) and low-moderate risk (AIP<0.24) according to their AIP values. Plasma asprosin values in both low and high-risk groups in terms of AIP were higher than the controls. Moreover, plasma asprosin levels were significantly higher in the high-risk compared to the low-moderate risk. Since there is no difference between high and low-risk groups in terms of serum urea and creatine values, accompanying metabolic disease and CVD, we can suggest that hemodynamic and metabolic changes due to the HD process may be responsible for the increase in asprosin levels. The positive correlation between asprosin and AIP, BMI, HOMA-IR, HbA1c suggests that the patient's nutritional status and HD-related metabolic disorders could increase asprosin synthesis and release. The fact that plasma metrnl levels of patients in the high-risk group are lower than those in the low-risk group and the inverse correlation between metrnl and AIP values suggests that this adipokine may be anti-atherogenic.

Approximately one-third of patients undergoing hemodialysis for ESRD face increased morbidity and mortality due to non-renal pathologies such as nutritional, metabolic, or atherosclerotic coronary artery disease [15]. Sometimes, as a combined effect of more than one pathology, deterioration in the patient's general condition and even sudden cardiac death may occur [16]. Lipodystrophic changes occur due to fluid-electrolyte imbalance, vascular bed volume changes, and nutritional problems in HD patients who are in the risk group for cardiovascular disease [17]. Adipokines play a role in regulating metabolic pathologies and cardiac risk factors [6, 8, 10]. The reported L- or H-shaped relationship between type 2 diabetes, insulin resistance, and AIP supports a gradual association of AIP with underlying ESRD or other metabolic diseases [18].

Consistent with our results, higher asprosin levels have been reported in diabetic nephropathy. The same study reported a positive correlation between asprosin, BMI, and insulin, while glomerular filtration showed an inverse correlation with asprosin [8]. Zou et al. [19] reported that HD patients with metabolic syndrome had higher plasma asprosin levels than those without. However, we did not classify HD patients according to whether they had metabolic syndrome or not. On the other hand, most of our patients exhibited all or some of the metabolic syndrome criteria. Metabolic syndrome criteria were less

frequent in participants in the control group. When our findings and literature data are evaluated together, increased asprosin levels in HD patients can potentiate cardio-metabolic risks.

The inverse correlation between asprosin and HDL-C is critical as it indicates the atherogenic potential of asprosin. The positive correlation between plasma asprosin and API value is important evidence of our concern that high asprosin levels stimulate atherogenic risk factors in HD patients. In logistic regression analysis, there is an independent association between asprosin and high AIP values, which is a finding indicating the atherogenic potential of asprosin in HD patients. The increase in AIP value by asprosin in HD patients, even after adjustment for age, BMI, diabetes, and history of hypertension, supports that this adipokine is an atherogenic molecule independent of other parameters. Clinical approaches to the regulation of asprosin metabolism may be promising in the treatment of HD-related nutritional pathologies and lipodystrophy [7, 8]. On the other hand, the results of studies analyzing the relationships between asprosin levels and CVD are controversial. In addition to studies reporting that asprosin is cardioprotective, it has also been reported that it is ineffective in cardiac pathologies. The fact that asprosin ameliorates cardiac endothelial damage and corrects dilated cardiomyopathy in diabetic mice supports its cardioprotective nature [20–22]. However, we observed that, paradoxically, asprosin levels increased at a high AIP value.

It has been shown that metrnl is directly associated with obesity in experimental obesity models and in individuals with high BMI. Consistent with this, it has been reported that metrnl levels of mice fed a fat-rich diet are up-regulated [23]. Similarly, it has been shown that children with low BMI have lower Metrnl expression than those with high BMI [24]. The fact that metrnl has a negative correlation with BMI, HOMA-IR, and insulin, and a positive correlation with HDL-C suggests that metrnl is released into the systemic circulation from adipose tissue to prevent cardiac and metabolic pathologies in HD patients. In experimental models, metrnl administration reverses cardiac and renal fibrosis by regulating apoptosis and oxidative stress, which indicates this adipokine's cardioprotective effect [2]. Reporting that circulating and myocardial metrnl levels are downregulated in streptozotocin-induced diabetic mice supports that decreased levels of this protein in metabolic pathologies increase the risk of CVD. Increased expression of metrnl in heart muscle suggests that it could be protective against diabetes-related cardiac damage. Metrnl plays a significant role in improving complications caused by insulin resistance, diabetes, and metabolic syndrome [25]. The logistic regression analysis revealed a negative independent relationship between high AIP values and metrnl, supporting the anti-atherogenic potential of this adipokine. This finding indicated that metrnl could protect against CVD, independent of other confounders. When our results and literature data are evaluated together [25], we can clearly argue that the critical role of metrnl in cardiovascular diseases, obesity, and diabetes is also demonstrated in hemodialysis patients.

The study has several limitations, including a low sample size, a single-center cross-sectional study design, and the inclusion of only end-stage patients with chronic renal failure. Although asprosin and metrnl were recommended as potential metabolic syndrome biomarkers, the grouping of HD patients was not made according to metabolic syndrome criteria [25, 26]. Since all HD patients have ESRD and more than one metabolic risk factor, we thought it would be more appropriate to classify the patients according to AIPs. Not grouping patients according to metabolic syndrome criteria is also a limitation.

Conclusion

Our study is of clinical importance as it shows that adipose tissue-derived metrnl and asprosin secretion changes in HD patients and the relationships between these two adipokines and atherogenic potential. Logistic regression analysis has revealed important insights into the independent relationships between metrnl, asprosin, and high AIP values in HD patients. These findings support the anti-atherogenic potential of metrnl and suggest the potential atherogenic effects of asprosin, highlighting the complex interplay between adipokines and cardiovascular risk in this patient population. It will be possible to reach a more precise conclusion regarding the effects of adipokines on cardiovascular events with prospective cohort studies involving more HD patients.

Ethics Committee Approval: The study was approved by The Fırat University Non-Invasive Research Ethics Committee (No: 2023/08-31, Date: 08/06/2023).

Authorship Contributions: Concept – M.Y., L.D.; Design – M.Y., T.K.; Supervision – M.Y.; Funding – M.Y.; Materials – M.Y., M.A.S.; Data collection &/or processing – M.A.S., M.Y.; Analysis and/or interpretation – M.Y., D.K.; Literature search – M.Y., R.F.A.; Writing – M.Y.; Critical review – M.Y.

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