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Research Article

Correlation between anthropometry measurements, adipokines, lipid profile and blood pressure parameters in hypertensive patients treated with enalapril

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Background: Hypertension and obesity are major risk factors for health problems and cardiovascular diseases in developing and developed countries. There is limited evidence available on the correlation between high blood pressure and obesity despite their close association.

Methods: The current study aimed to find the correlation between anthropometric measurements, lipid profile, visfatin, apelin, and blood pressure parameters in 31 newly diagnosed hypertensive patients and 32 enalapril-treated hypertensive patients.

Results: In enalapril treated patients, a significant negative relationship between visfatin and triglyceride (TG). Conversely, there is a positive correlation between visfatin and HDL. Moreover, visfatin expressed a negative correlation with VLDL. Concerning the newly diagnosed hypertensive group, a non-significant correlation was found between serum visfatin and lipid profile parameters. Additionally, a significant negative correlation between apelin and DBP in enalapril treated patients. Moreover, significant negative correlation between apelin and SBP in enalapril treated patients. On the other hand, a non-significant correlation between apelin and blood pressure parameters in the newly diagnosed hypertensive group was found. Moreover, there was a significant positive relationship between BMI and visfatin by comparing these two variables in all studied group participants.

Conclusion: We concluded that anthropometric measurements, adipokines, and lipid profiles most closely relate to high blood pressure in hypertensive patients.

Keywords: *enalapril, adipokine, lipid, hypertension*

Introduction

Hypertension is a significant negative health characteristic that can have severe health consequences if not properly managed. Unhealthy lifestyle habits and lack of health assessments often occur simultaneously, forming complicated and challenging-to-treat patterns. Obesity-related hypertension often occurs alongside other cardiovascular risk factors, creating a group of conditions known as metabolic syndrome. The metabolic syndrome is characterized by four essential components: central obesity, insulin resistance, hypertension, and an underlying dyslipidemia marked by high TG and low levels of HDL(Katsimardou et al., 2020). Visfatin is a pro-inflammatory adipokine that plays a significant role in endothelial dysfunction by increasing inflammatory and adhesion molecule expression (Engin, 2017; Romacho et al., 2020). While apelin can be considered as an anti-inflammatory adipokine has a beneficial role in endothelial dysfunction associated with hypertension (Zhou et al., 2016). Angiotensin converting enzyme inhibitors are the first-line anti-

hypertensive medications that may affect the circulating apelin and visfatin that may have an expected role in hypertension. The objective of this study is to evaluate the presence of correlations between these adipokines and lipid profiles, body mass index (BMI), systolic blood pressure (SBP), and diastolic blood pressure (DBP).

Materials and Methods

Study design, inclusion and exclusion criteria

A total of 63 overweight hypertensive patients were enrolled in this comparative case-control study. the study was conducted between October 2023 and March 2024. The inclusion criteria determined that the participants should be hypertensive patients with a duration of hypertension of not less than 5 weeks. Patients with hypertension were being treated with enalapril and patients who were newly diagnosed hypertensives were without any antihypertension medication. Exclusion criteria involved pregnant and lactating women, pregnant and lactating women, individuals unable to comply with study procedures or visits, patients on any other drugs, alcoholism and patients with hypertension complications or other clinical conditions were ineligible. This study was approved by the Research Ethics Committee of College of Pharmacy/University of Mosul (approval number: 186 on 1/11/2023).

Study participants

The study involved 63 participants divided into two groups, 31 newly diagnosed hypertensive group and 32 enalapril-treated hypertensive patients. 31 participants were retrieved, consisting of 13 females and eighteen males, who had recently received a diagnosis of hypertension and were not currently using any anti-hypertensive medication. The average age of this group was 28.87±7.1 years. The second group included 32 hypertensive patients who were treated with enalapril equally divided between males and females. The mean age of the studied group was 50± 6.5 years.

Biochemical measurement

Five milliliters of blood samples were obtained from all participants and tubes were gently inverted many times to ensure proper mixing with the clotting factor and allowed to stand for 15 minutes. Then, tubes were centrifuged at 2500 RPM for 20 minutes to obtain the sera. The obtained serum from each blood samples were divided into 4 eppendorf tubes of 0.5 ml, then stored at -20°C for estimation of apelin, visfatin, TC, LDL, TG, VLDL and HDL. Concentrations of apelin and visfatin were demonstrated by application of the ELISA technique using the device BioTek ELx800 Absorbance Microplate Reader. The kits used were provided by Bioassay Technology Laboratory BT LAB (Shanghai Korain Biotech Co.).Serum levels of TC and TG are determined by enzymatic colorimetric method using BIOLABO kit, while VLDL and LDL levels were determined using Friedewald's equation.

Statistical analysis

All data are expressed as an average value ± standard deviation (SD). Data were analyzed using non parametric (kruskal-wallis) test followed by a comparison of all group's data using Dunn's multiple comparison tests to determine the significance of variations between the means of the groups. Spearman's correlation was utilized to determine the presence of correlation between the parameters under study. Using GraphPad Prism version 10.0 (San Diego, California, USA). Data values $p < 0.05$ were represented as statistically significant. All groups had undergone normality and lognormality tests and passed by shapiro-wilk test.

Results

Demographic characteristics of the study population

Table 1. Demographical and clinical characteristics in patient groups

Parameters	Newly diagnosed hypertensive (n=31)*	Enalapril (n=32)
Age (years)	50.40±7.347	51.50±6.546
BMI (kg/M^2)	28.87±7.065	27.34±3.945
SBP mmHg	149.9±13.40	123.4±4.96****
DBP mmHg	98.79±7.75	83.59±3.95

The demographic characteristics of the study population at baseline were matched between control and patient groups and no significant variations were found. However, analysis of clinical characteristics that include systolic and diastolic blood pressure are considered significantly higher in patient groups compared to the control group Table 1.

Results are expressed as mean ± standard deviation and are significantly different where indicated (****p<0.0001; in comparison to the newly diagnosed hypertensive group). Using Kruskal Wallis test followed by Dunn's multiple comparison test. N: number of participants. HT: hypertension, BMI: body mass index, M; male, F: female, SBP; systolic blood pressure, DBP; diastolic blood pressure. Mean and standard deviation were obtained by descriptive statistics/prism.

Correlation between visfatin and lipid profile

In enalapril treated patients, correlation analysis between visfatin and lipid profile parameters determined a significant negative relationship between visfatin and TG (p-value = 0.034). Conversely, there is a positive correlation between visfatin and HDL (p-value = 0.022). Moreover, visfatin expressed a negative correlation with VLDL (p-value = 0.031). Concerning the newly diagnosed hypertensive group, non-significant correlation was found between serum visfatin and lipid profile parameters.

Table 2. Visfatin and lipid profile in patients groups

Parameters	Enalapril Visfatin	
	r	P value
TG	-0.3503	0.034*
HDL	0.3842	0.022*
VLDL	-0.3574	0.031*
TC	0.004926	0.490
LDL	0.2069	0.145

Results are computed using non-parametric Spearman correlation where (*p < 0.05: is statistically significant.)

Correlation between apelin and blood pressure parameters

Statistical analysis exhibited a strong significant negative correlation between apelin and DBP in enalapril treated patients (p-value=0.0065). Moreover, significant negative correlation between apelin and SBP in enalapril treated patients (p-value=0.0251). On the other hand, non-significant correlation between apelin and blood pressure parameters in the newly diagnosed hypertensive group. Data were analyzed using Spearman correlation matrix with one tailed p-value and 95% confidence interval.

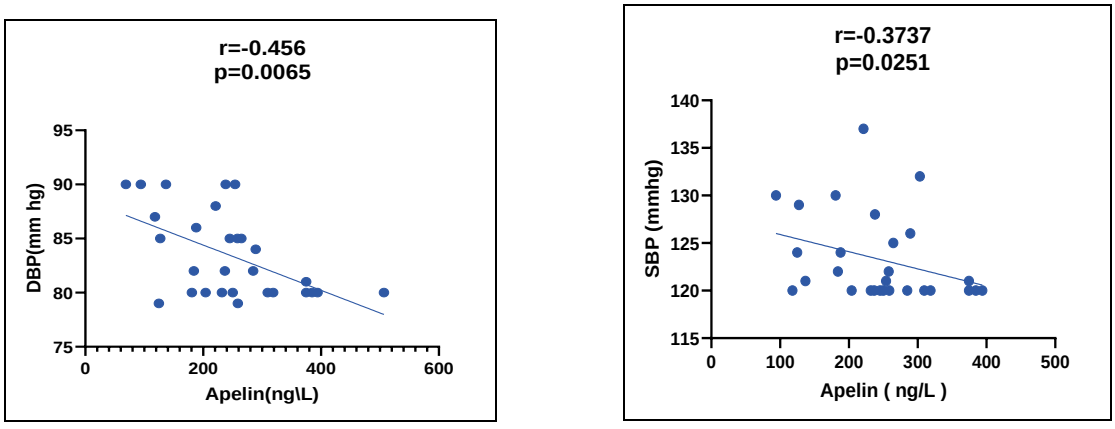

Figure 1 Correlation between apelin and systolic blood pressure, diastolic blood pressure in enalapril group.

Effect of body mass index on visfatin

Results of correlation analysis showed a significant positive relationship between BMI and visfatin (p value=0.0439) by comparing these two variables in all studied groups participants. Data were analyzed by using non-parametric Spearman correlation with one tailed p value as illustrated in Figure 2.

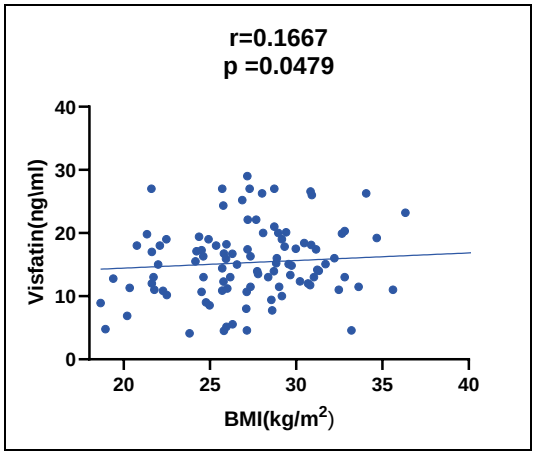

Figure 2. Correlation between visfatin and body mass index in hypertensive patients.

Discussion

ACEis are considered as the cornerstones for the management of hypertension. Despite extensive research on the role of those drugs in the management of hypertension, the impact of ACEis on the adipokines that may have a distinct role in the pathogenesis of hypertension has not been extensively investigated. In order to fill that gap, the present study aimed to provide valuable information concerning the impact of enalapril on the serum levels of apelin and visfatin among hypertensive patients. Furthermore, our study investigated the correlation between those parameters and lipid profile parameters, blood pressure parameters and BMI. The baseline characteristics were matched in the two study groups in terms of age, BMI and gender. The primary significant variation was conducted in our study which exhibits that visfatin is significantly reduced in the patient group using enalapril in comparison with the newly diagnosed hypertensive group. Our findings agreed with Hung et al, (Hung et al., 2011), which revealed that RAS blockers captopril, peridinopril and losartan exhibited reduction in the mRNA expressions of visfatin in 3T3 L1 adipocyte, captopril expressed the highest inhibition of visfatin mRNA expression followed by peridinopril and the ARB losartan.

Hypertensive patients using enalapril expressed a significant elevation in apelin in comparison with newly diagnosed hypertensive patients. Our finding is in line with the study conducted by Hongxian Wu et al (2014). This study demonstrated a significant reduction in plasma apelin, apelin mRNA and APJ mRNA in perirenal adipocytes of OH-rats (obesity-induced hypertension) and they were restored by perindopril treatment (Wu et al., 2014). Our study conducted a significant positive correlation between visfatin and HDLc and a negative correlation between visfatin and TG in patients treated with enalapril. This finding agreed with Jin et al., 2008. This study demonstrated a positive correlation between visfatin and HDLc in obese adolescents. Furthermore, wang et al. found a correlation between plasma NAMPT concentration and HDL-cholesterol levels, as well as low triglyceride levels, in non-diabetic Caucasian patients. Additionally, obese people with a lower plasma NAMPT content had lower HDL-cholesterol levels and greater triglyceride levels in comparison to lean individuals. This study elucidated the association between visfatin and lipid profile by considering the cytosolic role of visfatin as a nicotinamide phosphoribosyltransferase (NAMPT) (Wang et al., 2007). Another study has indicated a potential association between visfatin and the alteration of HDL-c levels via NAD (nicotinamide dinucleotide) metabolism. This connection is attributed to visfatin's role as an intracellular enzyme that act as the rate limiting step in NAD pathway, which has been linked to the metabolism of HDL-c (Archer, 2005). A meta-analysis conducted on clinical trials utilizing NAD+ precursors revealed that the administration of NAD+ precursors led to decrease in TG, TC, LDLc, and an increase in HDLc levels in human subjects. However, it was observed that this supplementation also resulted in hyperglycemia when compared to the use of a placebo or no treatment (Zhong et al., 2022). The expected mechanism for this correlation can be explained in the light of cytosolic NAMPT. NAD+ is obtained from various sources (Yamaguchi et al., 2019; Yamaguchi & Yoshino, 2017), including external dietary intake, endogenous de novo production, and the NAD+ salvage route. Nicotinamide mononucleotide (NMN) is one of the most proximal NAD+ precursors (Garten et al., 2015). Sirtuins, also known as silent information regulator 2 proteins (SIRT), are a group of protein deacetylases and ADP-ribosyltransferases that are extremely conserved. Their main characteristic is their dependence on the oxidized form of NAD+ for their action, which connects sirtuin function to the metabolic condition of the cell. Deacetylation and subsequent activation of LXR (liver x receptor) enhance the expression of ATP-binding cassette (ABC) sub-family A member (ABCA) 1 and ABC sub-family G member (ABCG) 1. This contributes to the process of reverse cholesterol transport and helps suppress the formation of foam cells and the accumulation of

cholesterol in macrophages (Sosnowska et al., 2017). Activation of LXR enhances the production of HDL through the basolateral ABCA1 pathway (Wang & Tontonoz, 2018). In addition, SIRT1 interacts with various transcription factors such as peroxisome proliferator-activated receptor gamma (PPARg), nuclear receptor co-repressor (N-CoR), and peroxisome proliferator-activated receptor gamma co-activator 1-alpha (PGC-1a). Furthermore, it may also play a role in activating LXR in cells through the NF-kB pathways (Sosnowska et al., 2017).

Regarding the impact of BMI on visfatin, the current investigation revealed a positive correlation between BMI and visfatin. Our finding agreed with YH Chang et al.(Chang et al., 2011). The study revealed that plasma visfatin concentrations were elevated in individuals diagnosed with overweight/obesity, type 2 diabetes mellitus, metabolic syndrome, and cardiovascular illnesses. Furthermore, The current investigation is also supported by the clinical study conducted by Sylwia Rotkegel et al.(Rotkegel et al., 2013). The study suggested a positive correlation between BMI and visfatin in all study groups (hypertensives and normotensives). In contrast to our findings, the study has demonstrated low plasma visfatin levels in patients with increased BMI (Pagano et al., 2006). Although there is conflicting data on the relationship between visfatin and overweight/obesity, certain researchers have suggested that visfatin may have a role in obesity-related damage. The activation of the inflammasome has been demonstrated to be a key factor in the development of inflammation in adipose tissue, insulin resistance, and metabolic disorders associated with obesity. More importantly, inflammasome activation was shown in many instances to be adipokine-driven.(Pham & Park, 2020). Additionally, it has been demonstrated that visfatin has the capacity to facilitate podocyte injury caused by obesity by activating the NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3)-inflammasome (Koka et al., 2019). Moreover, it has been demonstrated that visfatin has a role in the initiation of arterial inflammation and impairment of endothelial function in the initial phases of obesity, through the development of an endothelial inflammatory response that relies on the NLRP3 inflammasome (Xia et al., 2014). Similarly, it was demonstrated that vascular dysfunction in mice caused by visfatin is associated with the activation of NLRP3-inflammasome and the release of IL-1ß through a mechanism that depends on NAMPT and involves the Toll-like receptor 4 (TLR4) (Romacho et al., 2020). An additional investigation discovered that the activation of endothelial NLRP3-inflammasomes by visfatin can lead to the synthesis of high mobility group box protein 1 (HMGB1). As a result, HMGB1 has the ability to disturb the connections between endothelial cells and increase the permeability of the endothelium by paracrine and autocrine signaling. This leads to early-stage damage to the endothelial cells during metabolic disorders (Chen et al., 2015).

This study also expressed a significant negative correlation in enalapril treated patients between apelin and SBP, DBP. This association reflects the impact of enhanced apelin levels after treatment with enalapril. Our findings agreed with Zhu et al., 2013. This study is a cross-sectional analysis with 1031 participants who were randomly chosen from the coastal regions of China. The objective of the study is to investigate the correlation between plasma apelin levels and blood pressure, as well as cardiovascular risk factors. As mentioned above, individuals with essential hypertension have a notably decreased plasma apelin level compared to those who are considered normal (Papadopoulos et al., 2013).

Conclusion

In enalapril-treated group, visfatin provide a positive correlation with HDL, and a negative correlation with TG and VLDL. Additionally, visfatin was proportionally changed with BMI, demonstrating a positive correlation of BMI with visfatin levels. Moreover, apelin provided a significant positive correlation with SBP and DBP. These findings suggest that apelin could potentially serve as a therapeutic target for the treatment of hypertension.

Author contributions

Zainab H. Fathi was involved in study design and development of research articles including data collection.
Mina K. Mohammed, Zainab H. Fathi, Jehan A. Mohammad helped in writing the entire manuscript including data analysis and interpretation.
Mina K. Mohammed and Jehan A. Mohammad helped in data collection.

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Conflict of interest

The author declares no conflict of interest. The manuscript has not been submitted for publication in other journal.

Ethics approval

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Consent to participate

Not applicable

Consent to publish

Not applicable

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