ISSN Print: 2664-6188
ISSN Online: 2664-6196
Impact Factor: RJIF 5.35
IJCBB 2023; 5(1): 85-89
www.biochemistryjournal.net
Received: 01-11-2022
Accepted: 14-12-2022

Manal B Haffd
Department of Chemistry, College of Sciences, University of Basrah, Basrah, Iraq

Usama H Ramadhan
Department of Clinical Laboratory Sciences, College of Pharmacy, University of Basrah, Basrah, Iraq

Khaldon A Zaydan
Al Fayhaa Teaching Hospital, Basrah, Iraq

Corresponding Author:
Usama H Ramadhan
Department of Clinical Laboratory Sciences, College of Pharmacy, University of Basrah, Basrah, Iraq

Apelin and lipid profile in hypertensive patients a correlation data

Manal B Haffd, Usama H Ramadhan and Khaldon A Zaydan

DOI: https://doi.org/10.33545/26646188.2023.v5.i1b.41

Abstract
High blood pressure is directly related to the rise in non-HDL-c harmful fats in the body, as it narrows the arteries and thus increases blood pressure. However, blood pressure decreases significantly with high UHDL-c, so it is considered good fat. Volunteers have divided into two groups the control group included healthy people and the patients' group involved hypertension. Lipid profile and Apelin were measured for both groups, and apelin was measured using an ELISA kit. As a result, apelin was decreased significantly in hypertension patients'. Also, lipid parameters like TG, LDL-c, and non-HDL-c were elevated. Apelin level in the control group was higher than in the patients' group, which was a good indicator of normal blood pressure. A low level of apelin in the patients' group was a bad sign for hypertension, a decrease in apelin concentration in connection with an increase in non-HDL-c levels. So, this maybe increases the risk of hypertension and dyslipidaemia.

Keywords: Lipid profile, apelin, hypertension

Introduction
Hypertension affects millions of patients and is recognised as a risk factor for cardiovascular events and cardiovascular mortality. Hypertension results from a complex interaction between environmental factors, genetic influences, unhealthy lifestyle and abnormalities in the control mechanisms of the cardiovascular system. Consequently, identifying a specific cause for this condition is impossible in many patients, which explains the use of the terms essential or primary hypertension [1].

Many theories offer to explain the hypertension phenomenon. The incidence of blood pressure (BP) increases anomalies in salt and water levels in a person handled by the kidneys. Especially through the intrarenal route of the renin-angiotensin-aldosterone system in the body. Also, deregulation of neuronal autonomic modulation of the circulatory system. These mechanisms are not mutually exclusive, and they could all have a role in the rise in blood pressure seen in many people with essential hypertension. Endothelial dysfunction and inflammation linked to heart disease in recent studies of the emergence of a hypertensive state [2].

Cardiovascular diseases (CVDs) are the leading cause of death worldwide, accounting for nearly 4 million fatalities (45 percent of all deaths) in Europe each year [1]. Important risk considerations are lipoprotein changes are responsible for around half of all CVDs. Include high levels of total cholesterol (TC), low levels of low-density lipoprotein cholesterol (LDL-c) and low levels of high-density lipoprotein cholesterol (HDL-c) concentrations. LDL-cholesterol, intermediate-density lipoproteins, VLDLs, and non-HDL-c cholesterol show the total cholesterol carried by all potentially atherogenic particles and lipoprotein remnants. European guidelines propose lowering TC and LDL-c levels as primary targets in treatment approaches because it includes remnant cholesterol and is unaffected by triglyceride fluctuation. Non-HDL-c considers a better measure [3].

Apelin is an adipokine discovered by Tatemoto *et al.* in 1998. Apelin is expressed and secreted by both mouse and human adipocytes. In adipocytes, insulin can upregulate apelin expression. The expression of apelin in adipose tissue of humans swiftly cleaved from circulation with a half-life of <5 minutes. Furthermore, apelin and its receptor, the orphan G protein-coupled receptor (OGPR) and APJ receptor are expressed in pancreatic islet cells [4]. Apelin has a regulator effect of glucose stimulation on insulin production [5].

The peripheral physiological effects of apelin have also been investigated, and apelin has been proven to reduce blood pressure after intravenous administration in rats. In 2000, this effect was eliminated by the presence of an inhibitor of nitric oxide synthase, implying that apelin reduces blood pressure by releasing nitric oxide [6, 7]. Furthermore, apelin's restricted distribution within blood artery endothelial cells supports a role in blood vessel endothelial cells' job as a paracrine blood vessel contractility mediator. We now show that preproapelin occurs in a dimeric form in native tissues. On the other hand, apelin-13 has better blood pressure-lowering effects in spontaneously hypertensive rats than in normal Wistar rats [8].

Materials and Method

Study Design and Site

The project was a classic sectional study done at the University of Basrah and Al Faiha Teaching Hospital over four months, between April and August 2021 in Basrah, South Iraq. The hospital is a major referral centre for private, primary and secondary healthcare facilities in this Governorate. Eighty-nine people were recruited (56 females and 33 males) and divided into two groups: the control group included 25 healthy people and the patients' group included 64 hypertensive patients.

Eligibility Criteria

In this study, all patients were diagnosed as hypertensive and attending Internal medicine consultants. Patients with high blood pressure accompanied by one of the following diseases are excluded: diabetes, kidney failure, and thyroid disease.

Measurements

The pressure was measured electronically with a device from the Beurer company in a sitting position after 5 min of rest. Body mass index (BMI) was calculated after measuring weight and height. Five ml of blood was collected the next day after an overnight fast (10–12 h) to assess the fasting serum lipid profile. The lipid profile includes: total cholesterol (TC), triglyceride TG, Ultra high-density lipoprotein-cholesterol (UHDL-c), low-density lipoprotein-cholesterol (LDL-c) both Direct LDL-c (DLDL-c) and calculated (LDL-c cal.). They were analysed using an enzymatic method on an automated chemistry analyser, Selectra Pro M (ARCHITECT c4000). Non-HDL-c was calculated as TC minus UHDL-c. LDL-c cal. was calculated using the Friedewald formula as following:

$$\text{LDL-c cal.} = (\text{Total Cholesterol}) - (\text{UHDL-c}) - (\text{TGs}/5)$$

Definition of Terms

According to the National Cholesterol Education Program (NCEP), dyslipidaemia occurred at an elevated TG level of 1.7 mmol/L, reduced HDL-c to 1.04 mmol/L, LDL-c level >3.37 mmol/L, and/or a TC level of 5.2 mmol/L [9].

Hypertension is systolic blood pressure (SBP) of 140 mm Hg and/or diastolic blood pressure (DBP) of 90 mm Hg on the report of the Joint National Committee [10]. Blood pressure is controlled within an SBP <140 mm Hg and a DBP < 90 mm Hg by antihypertensive drug(s) and/or no pharmacological methods. Uncontrolled or poorly controlled BP is an SBP ≥140 mm Hg and/or DBP ≥90 mm Hg.

Results

The current study included (89) participants, with a group of patients (n=64) compared to the control group of healthy adults (n=25).

Table 1 shows the characteristics of patients and control groups. Table 2 shows the parameters levels of the hypertension patients group compared to the control group. There are statistically significant differences between the patients and the control group in all biochemical variables ($p \leq 0.01$). There was a significant increase in hypertension. On the other hand, there was a significant decrease in apelin and UHDL-c.

Table 1: Variables and characteristics of patients and control groups.

Group	n	n %	M/F	M/F%	Age (year)	BMI (Kg/m^2)
Control	25	29.1	11/14	44.8/55.2	34.4±12.18	30.61±7.73
Patients	61	70.9	32/29	52.4/47.5	52.13±12.56	28.93±7.23

Table 2: Lipid profile, blood pressure and Apelin of patients and control groups.

Biochemical	Control	Patients
Stolic. mmHg	117.4±14.53	154.8±18.6**
Diastolic. mmHg	71.92±11.72	91.73±16.6**
LDL-c cal. mmol/L	1.267±0.611	1.792±0.872**
DLDL-c. mmol/L	1.336±0.607	1.973±0.703**
Cholesterol. mmol/L	1.094±0.471	1.622±0.473**
Triglycerides. mmol/L	1.097±0.638	2.311±0.559**
Non-HDL-c. mmol/L	1.773±0.773	2.808±0.891*
UHDL-c. mmol/L	0.791±0.375	0.949±0.246*
Apelin. ng/L	73.60±20.75	43.30±53.1**

Values are expressed as mean ± stander deviation in each group.
* = significant at $p < 0.01$; ** = significant at $p < 0.001$

General Comparison for all Studied Parameters

Serum Apelin

In Table 2, an inverse relationship was observed in DLDL-c (LDL-c cal.) and cholesterol in both patients and control, while with systolic and diastolic pressure an inverse relationship appeared with the control group only whereas a direct relationship with patients. The same table also showed that apelin was nonsignificant with LDL-c cal. in patients ($p<0.430$), while systolic and diastolic were shown as nonsignificant ($p<0.295$) and ($p<0.146$) respectively, but inverse relationship as shown in figure 1.

Table 2: The relationship of Apelin with other parameters of patients and control groups in terms of probability (P) and correlation coefficient (R).

Biochemical Parameter	Apelin			
	Control		Patients	
	R	P	R	P
Stolic	-0.223	0.295	0.19	0.885
Diastolic	-0.306	0.146	0.022	0.866
LDL-c cal.	-0.035	0.872	-0.103	0.430
DLDL-c	-0.028	0.89	-0.087	0.507
Cholesterol	-0.033	0.878	-0.010	0.941
Triglyceride	0.158	0.460	0.065	0.617
Non-HDL-c	0.032	0.883	0.034	0.796
UHDL-c	-0.094	0.663	0.003	0.985

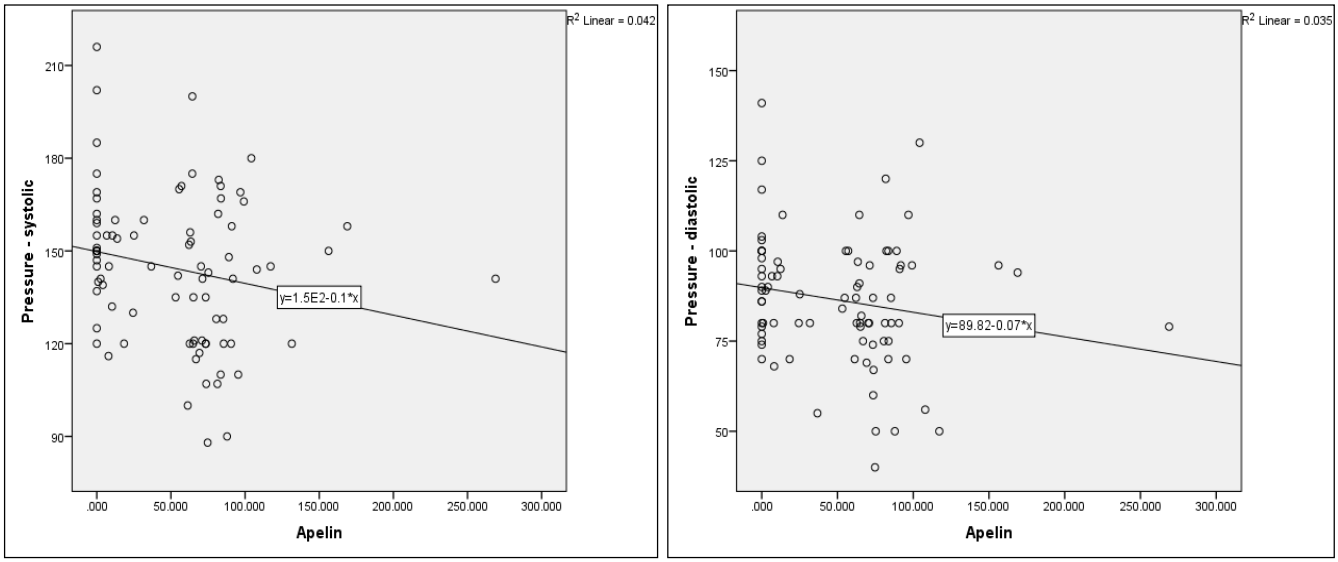

Fig 1: The correlation between apelin and blood pressure.

Serum Ultra-High-Density Lipoprotein-Cholesterol (UHDL-c)

Table 3 shows the direct association of UHDL-c with DLDL-c, LDL-c cal., cholesterol and Non-HDL-c in control and patients' groups. The same table shows an inverse relationship with the apelin in the control group only. Moreover, an inverse relationship between patients and control groups in the systolic and diastolic. On the other hand, DLDL-c, LDL-c cal. and cholesterol are significant (p<0.001) changes with UHDL-c and triglyceride for the control group only. The non-HDL-c change is significant (p<0.001) in the control group but in the patients' group nonsignificant (p<0.054) with UHDL-c. The UHDL-c and Non-HDL-c were in positive correlation in the control group significant (p<0.000) and patients group nonsignificant (p<0.054)

Table 3: The relationship of UHDL-c with other parameters of patients and control groups in terms of probability (P) and correlation coefficient (R)

Biochemical Parameter	UHDL-c			
	Control		Patients	
	R	P	R	P
Stolic	-0.065	0.759	-0.084	0.519
Diastolic	-0.098	0.640	-0.067	0.607
LDL-c cal.	0.729	0.000	0.501	0.000
DLDL-c	0.710	0.0001	0.456	0.000
Cholesterol	0.737	0.000	0.446	0.000
Triglyceride	0.549	0.004	-0.011	0.932
Non-HDL-c	0.698	0.000	0.248	0.054

Serum Non-High Density Lipoprotein-Cholesterol (Non-HDL-c)

Table 4 shows the direct relationship of Non-HDL-c with each of DLDL-c, LDL-c cal., UHDL-c, triglycerides, cholesterol, and apelin in patients and control groups. Table 4 shows an inverse relationship between systolic and diastolic in the control group only. In the same table, Non-HDL-c appears direct correlation with DLDL-c, as well as triglycerides and cholesterol (p<0.001) in both patients and control groups. Also, the systolic for the control group was significant with non-HDL-c (p<0.027), but the Diastolic was nonsignificant with non-HDL-c (p<0.143). Figure 2 shows the correlation of apelin with UHDL-c and non-HDL-c.

Table 4: The relationship of non-HDL-c with other parameters of patients and control groups in terms of probability (P) and correlation coefficient (R).

Biochemical Parameter	Non-HDL-c			
	Control		Patients	
	R	P	R	P
Stolic	-0.443	0.027	0.178	0.169
Diastolic	-0.192	0.358	0.143	0.272
LDL-c cal.	0.954	0.000	0.524	0.000
DLDL-c	0.965	0.000	0.849	0.000
Cholesterol	0.967	0.000	0.965	0.000
Triglyceride	0.788	0.000	0.602	0.000

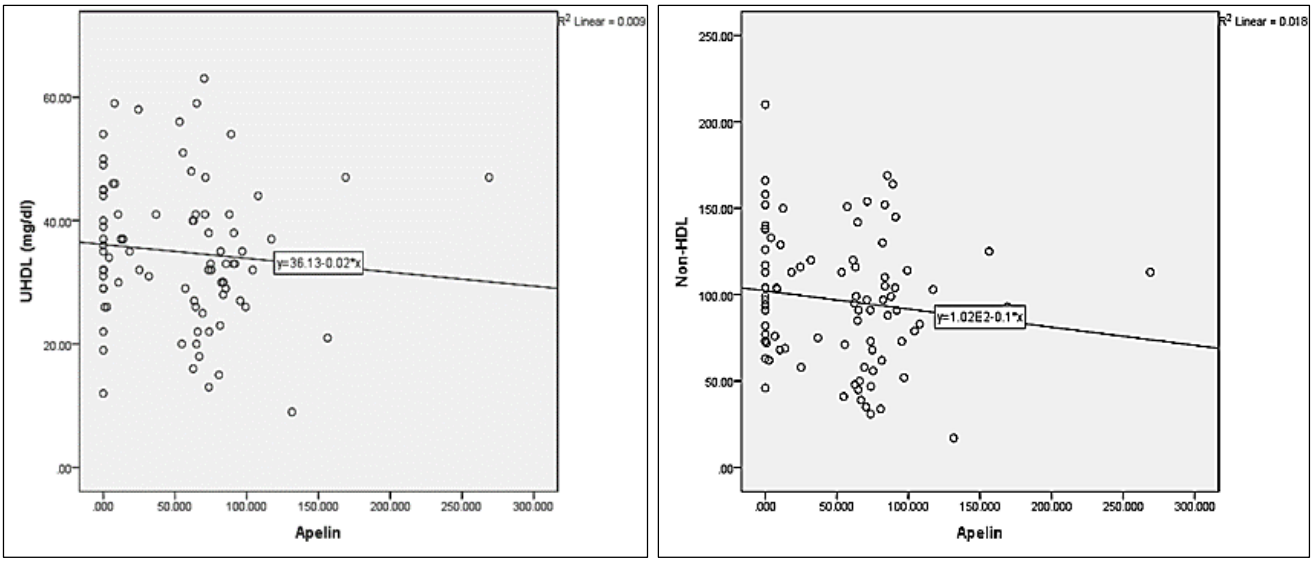

Fig 2: The correlation of apelin with UHDL-c and non-HDL-c.

Discussion

Hypertension is recognized as a risk factor for cardiovascular disease, stroke, diabetes and kidney disease. Obesity, glucose intolerance and abnormalities in lipid metabolism are among the comorbidities that affect about 80% of hypertensive people. High serum TC, TG and LDL-c were reported in a study comparing hypertension patients' lipid profile status to healthy normotensive people [11]. Our findings of elevated TC levels in hypertension patients are consistent with other researches [12]. However, few researchers have investigated the primary link between high blood pressure and dyslipidaemia [13].

The current study aims to investigate patients with high blood pressure and the causes that lead to high pressure. High pressure comes from the narrowing of the arteries due to the deposition of LDL-c particles. That leads to an increase in non-HDL-c levels, which is all the harmful cholesterol found inside the human body. The results indicate there is a correlation between high blood pressure and an increase in non-HDL-c concentration, it is a direct relationship where R is positive. Also, there is a positive correlation between women and men with Non-HDL-c. It is no secret to everyone that the cause of high blood pressure is excess body fat [14, 15]. However, high blood pressure has an inverse correlation with UHDL-c, and high UHDL-c is considered beneficial to health [16].

We have also measured the value of the serum apelin and found its reverse relation with hypertension where R is negative in the control group, but in the patients' group, the relationship becomes positive. Also, the apelin concentration in the control group is so high and becomes low in the patients' group.

The natriuretic peptide system is an endocrine system that controls salt and water balance and arterial blood pressure (BP). The natriuretic peptide precursor gene (NPPA) encodes the atrial natriuretic peptide (ANP), which is produced from atrial myocardium cells and helps to reduce cardiac stress by promoting bedwetting, vasoconstriction and other physiological actions mediated by natriuretic peptide receptors [17]. Since the action of apelin is to stimulate the ANP (apelin is a part of the natriuretic peptide system with ANP), Apelin works to inhibit the Angstein II hormone by competing with him to bind with receptors in the arteries to relax and expand the arteries [18].

Conclusion

We concluded from this research that high blood pressure is associated with increased harmful fats (Non-HDL-c) in the body, which are deposited on the walls of the arteries causing them to narrow, which leads to high blood pressure. Also, an increase in apelin peptide concentration in blood is a good indicator. On the other hand, a deficiency of apelin combined with high blood pressure. Furthermore, a decrease in apelin levels is associated with increased non-HDL-c levels in the blood, which increase hypertension risk factors.

Conflict of interest: The authors have no conflicts of interest to declare.

References

1. Lowry EA, Sanders DS. Hypertension Management and Glaucoma: Hypothesizing Causes in Correlational Data. Ophthalmology. 2021;128(3):401-402.

2. Calvillo L, Gironacci MM, Crotti L, Meroni PL, Parati G. Neuroimmune crosstalk in the pathophysiology of hypertension. Nature Reviews Cardiology. 2019;16(8):476-490.
3. Pinart M, Jeran S, Boeing H, Stelmach-Mardas M, Standl M, Schulz H, *et al*. Dietary macronutrient composition in relation to circulating HDL and non-HDL cholesterol: A federated individual-level analysis of cross-sectional data from adolescents and adults in 8 European studies. The Journal of nutrition. 2021 Aug 7;151(8):2317-2329.
4. Estienne A, Bongrani A, Froment P, Dupont J. Apelin and chemerin receptors are G protein-coupled receptors involved in metabolic as well as reproductive functions: Potential therapeutic implications?. Current Opinion in Endocrine and Metabolic Research. 2021 Feb 1;16:86-95.
5. Ma WY, Yu TY, Wei JN, Hung CS, Lin MS, Liao YJ, *et al*. Plasma apelin: a novel biomarker for predicting diabetes. Clinica chimica acta. 2014 Aug 5;435:18-23.
6. Sonmez A, Celebi G, Erdem G, Tapan S, Genc H, Tasci I, *et al*. Plasma apelin and ADMA Levels in patients with essential hypertension. Clinical and Experimental Hypertension. 2010 May 1;32(3):179-183.
7. Zhang H, Mo X, Zhou Z, Zhu Z, HuangFu X, Xu T, *et al*. Associations among NPPA gene polymorphisms, serum ANP levels, and hypertension in the Chinese Han population. Journal of Human Hypertension. 2019 Sep;33(9):641-647.
8. Lee DK, Saldivia VR, Nguyen T, Cheng R, George SR, O'Dowd BF. Modification of the terminal residue of apelin-13 antagonizes its hypotensive action. Endocrinology. 2005 Jan 1;146(1):231-236.
9. Than A, He HL, Chua SH, Xu D, Sun L, Leow MK, Chen P. Apelin enhances brown adipogenesis and browning of white adipocytes. Journal of Biological Chemistry. 2015 Jun 5;290(23):14679-14691.
10. Ayoade OG, Umoh I, Amadi C. Dyslipidemia and associated risk factors among Nigerians with hypertension. Dubai Medical Journal. 2020;3(44):155-161.
11. Choudhury KN, Mainuddin AK, Wahiduzzaman M, Islam SM. Serum lipid profile and its association with hypertension in Bangladesh. Vascular health and risk management. 2014 Jun 30:327-332.
12. Bertrand C, Pradère JP, Geoffre N, Deleruyelle S, Masri B, Personnaz J, *et al*. Chronic apelin treatment improves hepatic lipid metabolism in obese and insulin-resistant mice by an indirect mechanism. Endocrine. 2018 Apr;60:112-121.
13. Chua NK, Coates HW, Brown AJ. Squalene monooxygenase: a journey to the heart of cholesterol synthesis. Progress in Lipid Research. 2020 Jul 1;79:101033.
14. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, *et al*. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension. 2003;42(6):1206-1252.
15. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA. 2001;285:2486-2497. 10.1001/jama.285.19.2486.
16. Flahault A, Couvineau P, Alvear-Perez R, Iturrioz X, Llorens-Cortes C. Role of the vasopressin/apelin balance and potential use of metabolically stable apelin analogs in water metabolism disorders. Frontiers in Endocrinology. 2017 May 31;8:120.
17. Ahamad A. Hypertension and Lipid Profile of Patients of DG Khan District. Clin Med Biochem. 2018;4(142):2471-663.
18. Izgut-Uysal VN, Acar N, Birsen I, Ozcan F, Ozbey O, Soylu H, *et al*. Apelin-APJ system is responsible for stress-induced increase in atrial natriuretic peptide expression in rat heart. Tissue and Cell. 2018 Apr 1;51:91-96.