

EVALUATING THE LEVEL OF ANGIOGENIN, ENDOTHELIN-1, AND SOME BIOCHEMICAL VARIABLES IN PEOPLE WITH HYPERTENSION

Muhammad Abdullah Hassan Al-Jubouri 1,

Muhammad Khattab Omar Al-Samarrai 2,

Omar Thaer Jawad Al-Samarrai 3

1,2- Department of Pathological Analysis, College of Applied Science,
University of Samarra, Samarra, Iraq

3- Department of Biotechnology, College of Applied Science,
University of Samarra, Samarra, Iraq

*E. Mail: Usach23015@uosamarra.edu.iq

Abstract

The study's objectives included assessing the levels of endothelin-1 and angiogenin in hypertensive individuals as well as certain biochemical markers. Ninety blood samples were used in this investigation; sixty samples were from hypertension patients and thirty samples were from healthy individuals. The patient's age ranged from 25 to 70 years old, and both sexes received the same diagnosis from a specialist physician. Between January 10, 2023, and December 20, 2023, samples were taken from hypertension patients at the cardiovascular centers of Al-Dhuluiya and Balid General Hospital in Salah Al-Din. The level of endothelin-1 and angiogenin was assessed, along with a few physiological indicators such as blood electrolytes (potassium and sodium ions), aspartate aminotransferase activity, and body mass index computation.

According to the findings, potassium and angiogenin were significantly low in the hypertensive patients specimens compared with normotensive persons. But the level of Endothelin-1, Sodium, Aspartate aminotransferase activity, and calculation of Body Mass Index show significant elevated in the hypertensive patients compared with normotensive persons. So this study can conduct that the angiogenin, endothelin-1, Na, K, and body mass index may effect on the hypertension and increase the blood pressure, but Aspartate aminotransferase activity is affect by hypertension.

Keywords: Hypertension disease, Angiogenin, Endothelin-1, Sodium, Potassium, Aspartate amino transferase, and Body mass index.

Introduction

Blood Pressure (BP) represents one of the forces resulting from the pumping rate of the heart muscle Cardiac Out Put and the resistance of the peripheral blood vessels (Hurst, 1978). Blood pressure is considered one of the most important vital signs of life in general, and blood pressure is described as arterial pressure, the rate, volume, and viscosity of the blood and the resistance of the peripheral of the blood vessels, high blood pressure is one of the diseases of the blood vessels that is subject to genetic transmission or has environmental causes such as high salt

consumption, it may have effects on the integrity of blood vessels (Squeri, 2012). In order for tissues to remain alive and be able to perform their biological functions, they need oxygen-rich blood, The pressure produced in the blood vessels is the work of the heart, and it is also caused by the movement of blood through them when the heart beats (Benjamin *et al.*, 2017). The Pressure is result from two forces: systolic blood pressure, systolic pressure occurs at its highest level when the left ventricle contracts forcing blood through the arteries and is called (high pressure), and diastolic blood pressure occurs at its lowest level when the left ventricle relaxes, and is measured when the muscle of heart is relaxes (Keoni & ND., 2016; Hassan & Humaish., 2022).

Hypertension is one of the most common disorder in the world, as it is the main contributor to early death and in 2015 the number of people infected with it was estimated at about 900 million people (Forouzanfar *et al.*, 2017). This disease has been given attention by global health organizations because it is closely linked to cardiovascular disease and kidney damage (Gabb *et al.*, 2016), as high blood pressure increases significantly in prevalence with age, affecting about 6% of the population. 18 to 34 years, and this percentage increases significantly to 75% of adults aged 75 years and over (Hussein *et al.*, 2019). Hypertension is defined as increased blood flow from the heart through the blood vessels, when the heart works stronger than normal, This makes it a major risk factor for heart disease, stroke and other serious problems (Mancia *et al.*, 2013). The amount of pressure is determined by The amount of blood expelled by the heart and the amount of resistance of the arteries to the flow of blood through them. High blood pressure is usually a disease that develops over the years. Despite what was mentioned previously, high blood pressure can be identified early to control or reduce it, and high systolic blood pressure is usually more dangerous. of diastolic pressure. As the effect of its height is directly related to the performance of the aorta (Rivera *et al.*, 2019). high blood pressure is a major health problem all over the world, especially in developing countries as it has become a global health concern (Guo, 2016; Jadoo, 2016). High blood pressure is classified into: First; essential hypertension, This type is known as cardiovascular disease and constitutes about 90% to 95% of cases in which blood pressure is high among people who are classified as essential hypertension, which may be One of the reasons for its occurrence is genetic factors in people who have a family history of high blood pressure or early death from heart disease (Muntner *et al.*, 2018). Second; Secondary hypertension, This type represents 10% of cases of high blood pressure, and its causes may be genetic or congenital (Bundy *et al.*, 2017).

Besides the risks of stroke and coronary heart disease, high blood pressure is a risk factor for cardiovascular disease coronary heart disease and stroke usually occur early in the life of patients with high blood pressure, which determines Elderly individuals are still more vulnerable, at risk of these events, but other consequences are also seen at this age, such as hypertensive cardiomyopathy (with its consequences heart failure and atrial fibrillation) and heart valve disease. (Kage & Murashima, 2019).(ANG) Angiogenin: Also referred to as RNase 5, it is a small protein consisting of 123 amino acids, which was first discovered at Harvard University in 1985 (Fett *et al.*, 1985). ANG is a member of the ribonuclease family. The name angiogenin indicates that it was first identified as a factor that stimulates the formation of blood

vessels, a process known as angiogenesis, Angiogenin also interacts with endothelial and smooth muscle cells, leading to cell migration, invasion, proliferation, and the formation of tubular structures (Xu Z *et al.* ,2003). (ET-1) Endothelin-1 is a polypeptide consisting of 21 amino acids, it is produced from Endothelium, it stimulates vasoconstriction directly or indirectly, it acts as a vasoconstrictor and has functions such as controlling the transport of ions in the digestive system and recruiting immune cells in inflammation (Inoue *et al.*, 1989; Davenport *et al.*, 2016).

Materials & Methods

Design of the study and Subjects: Ninety samples of the serum were collected from the Cardiovascular center in Al-Duluiya and Balid General Hospital in Salah Al-Din city, this collected from ninety person (sixty serum sample for hypertensive patients and thirty sample for normotensive persons). The time for collecting is from 1/10/2023 to 20/12/2023, and the ages of individual between (25-70) years. Spacmens were collected without tourniquet due to sample need to measurement of electrolyte.

This study includes assessing the levels of of serum Angiogenin and Endothelin-1 concentration, Electrolyte such as Sodium(Na) (Burtis *et al.*, 2018) and Potassium(K)(Hillmann *et al.*, 1987), and Aspartate aminotransferase (AST) activity (Ruhi & Everhart, 2012) and calculation of Body Mass Index in according to standard methods.

Statistical work:

In this study, we used the SPSS statistical program to analyze the results obtained, and this was done by using a random design for the results using of Duncan test to identify of the variance to identify the differences between the study results at probability levels $p \leq 0.05$, $p \leq 0.01$.

Results:

Serum Angiogenin(Ang) and Endothelin-1(ET-1) Levels:

The results of **Angiogenin and Endothelin-1** obtained from the current study were summarized in **Table 1**.

Table -1 appears that the **Angiogenin** rates significantly low at probability $p \leq 0.01$ in hypertensive patients group as compared to the control group, but significantly elevated in **Endothelin-1** levels in the probability $p \leq 0.01$ in hypertensive patients group as compared to the control group.

Table -1: Mean \pm SD levels of the **Angiogenin and Endothelin-1** at the studying group

Groups Parameters	Mean \pm SD		t-value	P-value
	Control	Patients		
Angiogenin	255.028 \pm 68.678	196.854 \pm 38.154	4.318	0.0001**
Endothelin-1	7.464 \pm 3.282	82.081 \pm 27.676	20.595	0.0001**

Levels of sera Electrolyte(Sodium and Potassium):

This study also evaluated the levels of serum Electrolyte(Sodium and Potassium) in serum of specimens of hypertensive patients and normotensive group, the results obtained from this study are recorded in the table -2.

significant elevated at the level of Sodium ion at probability $p \leq 0.01$ was noted in Table -2 between hypertensive and normotensive group, and significantly low in the level of Potassium ion at probability $p \leq 0.01$ was noted in Table -2 between hypertensive and normotensive group.

Table -2: Mean \pm SD of serum Electrolyte(Sodium and Potassium) level at the studying group

Groups Parameters	Mean \pm SD		t-value	P-value
	Control	Patients		
Na	137.93 \pm 4.719	155.18 \pm 11.086	10.326	0.0001**
K	4.399 \pm 0.524	3.533 \pm 0.727	5.803	0.0001**

Serum Levels of Aspartate aminotransferase (AST) activity and Body mass index:

The study also evaluated the serum level of Aspartate aminotransferase activity and calculation of Body mass index in serum of samples of hypertensive patients and normotensive group, the results obtained from this study are recorded in the table -3.

significantly increase in the Serum Aspartate aminotransferase activity in the probability $p \leq 0.01$ was noted in Table -3 between hypertensive and normotensive group, also significant increase in the level of Body mass index at probability $p \leq 0.05$ was noted in the table -3 between hypertensive and normotensive group.

Table -3: Mean \pm SD of serum Aspartate aminotransferase (AST) activity and Body mass index level at the studying group.

Groups Parameters	Mean \pm SD		t-value	P-value
	Control	Patients		
AST	23.27 \pm 5.583	27.95 \pm 7.247	3.106	0.003**
BMI	25.679 \pm 2.909	27.086 \pm 2.560	2.348	0.021*

DISCUSSION

The results of the study that were conducted indicated some variables, namely: Angiogenin is show significantly decrease in the serum of persons who diagnostic as hypertensive patients compared with control group, Previous studies included (Bush *et al.*, 2019; Marek *et al.*, 2015) indicated an Significantly low in the angiogenin level with hypertensive patients a cases report for the type of this study. The current study find The significantly elevated in endothelin-1 in the patient with hypertension compared with normal group, agreeing with the finding of

(Kostov *et al.*, 2021; Kaze *et al.*, 2022) that indicate that an endothelin-1 increased in patient with hypertension, But this study disagree with (Putri *et al.*, 2022) study who refer to decrease in an endothelin-1 level in the hypertensive patients.

The level of serum electrolyte was also measured in this study, which revealed many results and differences in hypertensive patients compared with normotensive, include significantly elevated of the sodium ion in the sera of hypertensive patients compared to control group that agree with (Stocker, 2023), That indicate significantly elevated in the sodium ion, so this result are associated with hypertension and increase the hypertension level. The significantly low in the potassium in the curent study may be a marker for hypertension, this result agreeing with the result of (Mehklef, & Al-Hamdany, 2018: Ndong *et al.*, 2022) Which indicated that the potassium decrease in hypertensive patients compared to control group.

The results of this study noted a significantly raise in the Aspartate aminotransferase activity in the hypertensive patients compared to control group which agree with the study of (Katzke *et al.*, 2020), which indicated significantly increase in the Aspartate aminotransferase activity, but disagree with (Wu *et al.*, 2017) that refer to no change in the Aspartate aminotransferase activity with hypertensive patients. The body mass index show significantly elevated in the serum of hypertensive patients compared to control group that agree with (Hammed *et al.*, 2019), which indicated significantly elevated in the body mass index.

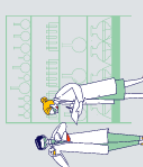
Conclusion:

Based on the results of this study conducted on blood pressure patients, it can be discussed that the angiogenin, endothelin-1, Na, K, and body mass index may effect on the hypertension and increase the blood pressure, but Aspartate aminotransferase activity is affect by hypertension.

References:

1. Gabb, G. M., Mangoni, A. A., Anderson, C. S., Cowley, D., Dowden, J. S., Golledge, J., ... & Arnolda, L. (2016). Guideline for the diagnosis and management of hypertension in adults—2016. *Medical Journal of Australia*, 205(2), 85-89.
2. Benjamin, E. J., Blaha, M. J., Chiuve, S. E., Cushman, M., Das, S. R., Deo, R., ... & Muntner, P. (2017). Heart disease and stroke statistics—2017 update: a report from the American Heart Association. *circulation*, 135(10), e146-e603.
3. Bundy, J. D., Mills, K. T., Chen, J., Li, C., Greenland, P., & He, J. (2018). Estimating the association of the 2017 and 2014 hypertension guidelines with cardiovascular events and deaths in US adults: an analysis of national data. *JAMA cardiology*, 3(7), 572-581.
4. Burtis, E.R. Ashwood, W.B. Saundersp.Ti.W .(2018). Text book of clinical chemistry, 7rd Ed. C.A. 1031-1044, 1104.
5. Davenport, A. P., Hyndman, K. A., Dhaun, N., Southan, C., Kohan, D. E., Pollock, J. S., ... & Maguire, J. J. (2016). Endothelin. *Pharmacological reviews*, 68(2), 357-418.
6. Fett, J. W., Strydom, D. J., Lobb, R. R., Alderman, E. M., Bethune, J. L., Riordan, J. F., & Vallee, B. L. (1985). Isolation and characterization of angiogenin, an angiogenic protein from human carcinoma cells. *Biochemistry*, 24(20), 5480-5486.

7. Forouzanfar, M. H., Liu, P., Roth, G. A., Ng, M., Biryukov, S., Marczak, L., ... & Murray, C. J. (2017). Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990-2015. *Jama*, *317*(2), 165-182.
8. Guo, Y. (2016). *DASH Intervention Effects on Home Food Environment and Diet Quality among Adolescents with Pre-hypertension and Hypertension* (Doctoral dissertation, University of Cincinnati).
9. Hammed, A. D., Jawad, A. H., & Ali, N. M. (2019). 4-Hydroxy-2-nonenal, Induced Nitric Oxide Synthase Status in Hypertension with Kidney Disease Patients. *Iraqi Journal of Medical Sciences*, *17*(2).
10. Hassan, S. S., & Humaish, H. H. (2022). Study of hematological parameters in patients with renal failure. *Wasit Journal for Pure Sciences*, *1*(2).
11. Hillmann, G; Beyer, G; Z.(1987). *Klin. Chem.. Klin. Biochem.* *4*, 91-98.
12. Hurst, J.W. (1978). "Normal physiology of cardiovascular system " 4th ed., Meogram Hill , London : p88- 93.
13. Hussein, M. A., Noaman, A. A., & Aboud, A. A.(2019). Risk Factors Associated with Hypertensive Patients at Baquba Teaching Hospital. *Diyala Journal of Medicine*; *16*(1), 30-36.
14. Inoue, A., Yanagisawa, M., Kimura, S., Kasuya, Y., Miyachi, T., Goto, K., & Masaki, T. (1989). The human endothelin family: three structurally and pharmacologically distinct isopeptides predicted by three separate genes. *Proceedings of the national academy of sciences*, *86*(8), 2863-2867.
15. Jadooa, H. (2016). Study of Adiponectin and Lipid Profile Levels in Normotensive and Hypertensive Type 2 Diabetic Patients. *Donnish Journal of Medicine and Medical Sciences*, *3*(6), 23-26.
16. Kage, M., & Murashima, N. (2019). *Clinical investigation of portal hypertension*. K. Obara (Ed.). Springer Singapore.
17. Katzke, V., Johnson, T., Sookthai, D., Hüsing, A., Kühn, T., & Kaaks, R. (2020). Circulating liver enzymes and risks of chronic diseases and mortality in the prospective EPIC-Heidelberg case-cohort study. *BMJ open*, *10*(3), e033532.
18. Kaze, A. D., Gao, X., Musani, S. K., Bidulescu, A., Bertoni, A. G., Abdalla, M., & Echouffo-Tcheugui, J. B. (2022). Association of plasma endothelin-1 with blood pressure progression among Blacks: The Jackson Heart Study. *American heart journal*, *246*, 144-151.
19. Keoni, Teta, ND.(2016). Hypertension Interventions (Dealing with High Blood Pressure) , Natural Triad ; PP: 30 .
20. Kostov, K., & Blazhev, A. (2021). Circulating levels of endothelin-1 and big endothelin-1 in patients with essential hypertension. *Pathophysiology*, *28*(4), 489-495.
21. Mancia, G., Fagard, R., Narkiewicz, K., Redon, J., Zanchetti, A., Bohm, M., ... & Wood, D. A. (2013). 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of



Hypertension (ESH) and of the European Society of Cardiology (ESC). *European heart journal*, 34(28), 2159-2219.

22. Marek-Trzonkowska, N., Kwieczyńska, A., Reiwer-Gostomska, M., Koliński, T., Molisz, A., & Siebert, J. (2015). Arterial hypertension is characterized by imbalance of pro-angiogenic versus anti-angiogenic factors. *PLoS One*, 10(5), e0126190.
23. Mehklef, E. H., & Al-Hamdany, W. A. S. (2018). Study of the Physiological effects of heart Atherosclerosis on concentrations of some electrolytes, lipid component, sex hormones in Tikrit city and its Governorate. *Tikrit Journal of Pure Science*, 23(7), 12-17.
24. Muntner, P., Carey, R. M., Gidding, S., Jones, D. W., Taler, S. J., Wright Jr, J. T., & Whelton, P. K. (2018). Potential US population impact of the 2017 ACC/AHA high blood pressure guideline. *Circulation*, 137(2), 109-118.
25. Ndong, A., K. EvaL., vander Linden Erik J.A.J. et al.(2022). Serum potassium concentration and its association with hypertension among Ghanaian migrants and nonmigrants: The RODAM study. *Atherosclerosis* Volume 342, Pages 36-43. 121
26. Putri, M., Hartopo, A. B., Inggriani, M. P., Fachiroh, J., & Dewi, F. S. T. (2022). 29 ENDOTHELIN-1 LEVEL IN HYPERTENSIVE SUBJECTS BETWEEN CORONARY ARTERY DISEASE AND HEALTHY POPULATIONS. *Journal of Hypertension*, 40(Suppl 2), e7-e8.
27. Rivera, S. L., Martin, J., & Landry, J. (2019). Acute and chronic hypertension: What clinicians need to know for diagnosis and management. *Critical Care Nursing Clinics*, 31(1), 97-108.
28. Ruhl, C. E., Everhart, J. E. (2012). Upper limits of normal for alanine aminotransferase activity in the United States population. *Hepatology*; 55 : 447 – 54.
29. Squeri, A. (Ed.). (2012). *Coronary Artery Disease: New Insights and Novel Approaches*. BoD–Books on Demand.
30. Stocker, S. D. (2023). Altered Neuronal Discharge in the Organum Vasculosum of the Lamina Terminalis Contributes to Dahl Salt-Sensitive Hypertension. *Hypertension*, 80(4), 872-881.
31. Wu, L., He, Y., Jiang, B., Liu, M., Yang, S., Wang, Y., ... & Wang, J. (2017). Gender difference in the association between aminotransferase levels and hypertension in a Chinese elderly population. *Medicine*, 96(21).
32. Xu, Z. P., Tsuji, T., Riordan, J. F., & Hu, G. F. (2003). Identification and characterization of an angiogenin-binding DNA sequence that stimulates luciferase reporter gene expression. *Biochemistry*, 42(1), 121-128.

