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Correlation of Arginine Vasopressin coding gene and Human High Blood Pressure

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Abstract

Arginine vasopressin (AVP) is a Peptide synthesized in the hypothalamus and transported via axons to the posterior part of the pituitary gland that regulates the arteries' High blood pressure, Then released to the blood when needed. A study design data were collected from the Al-Salam teaching hospital and the Ibn-Sena teaching hospital in Mosul as blood samples during the period 1/2/2022 to 1/9/2022. To perform a hormonal study and molecular study, (5ml) of blood was taken. The number of purposive samples is (160) samples taken from males only; aged less than 20 years to 50 years and above had been utilized in this study. The control group included 60 healthy individuals, the unhealthy group was divided into (40) patients without treatment, and (60) patients which have treatment. The serum concentration of this hormone had been measured and it was between (20.7-34.2 ng), Significantly decreased at ($p< 0.05$) in all groups except in those aged 50 years and above compared with the control group had been determined. Besides the Amplicon copy numbers of AVP coding genes were very low in all patient groups compared with the control is considered an important indicator of gene activities utilizing Real-time-PCR technique. These results concluded that this hormone had an important correlation with hypertension.

Keywords
Hypertension, Arginine vasopressin, Amplicon, AVP coding gene.

Hypothalamus made pre-pro-hormone are that first expressed by AVP coding gene transported to the pituitary gland then cleaved and altered to create the active form that stored until it is needed. Activation of either (V1R or V2R) receptors rise the AVP which causes vasoconstriction and water retention , with both participate in the blood pressure increase [1,2]

Chronic elevation of arterial blood pressure (BP) consistently higher than 140/90 mmHg is called hypertension[3] which is regulated by five mechanisms including the sympathetic nervous system(SNS), natriuretic peptides(ANP), renin-angiotensin system(RAS), vascuature, and the immune system[4,5] AVP-hormone released into the blood stream when the plasma osmolality increased by 1-2%, that had a vasoconstrictor and antidiuretic effects [6,7] Beside it has a vital role in blood pressure regulation, sodium homeostasis, and kidney function. AVP primarily affects the ability of the kidney to reabsorb water by induce the expression of water transport proteins in distal tubule and collecting duct that increase water reabsorption. Number of illness cases had been developed when the body is unable to regulate AVP production and its existence. AVP role is crucial at times of thirst bleeding, and other situations where there is a reduction in the effective arterial blood flow. It works to

keep blood pressure and volume status stable so that appropriate tissue perfusion can continue [8,9] Consuming excessive amounts of salt over time encourages aberrant plasticity in the circuit that regulates vasopressin secretion [10].

Material and methods

A study design deals with two axis, hormonal and molecular studies. Fasting venous blood samples containing samples were kept at -20 °C.

(5 ml) from healthy individuals and patients were collected from the Al-Salam teaching hospital and the Ibn-Sena teaching hospital in Mosul during the period 1/2/2022 to 1/9/2022.

Samples were placed inside free anti-clotting gel test tubes, left in room temperature, A total of (2 ml) was added to an EDTA tube for use in a genetic study, , and gel tube were placed (3 ml) centrifuged after 2 hours to obtain serum, and transferred to an Eppendorf tube. Both the EDTA tube and the Eppendorf tube

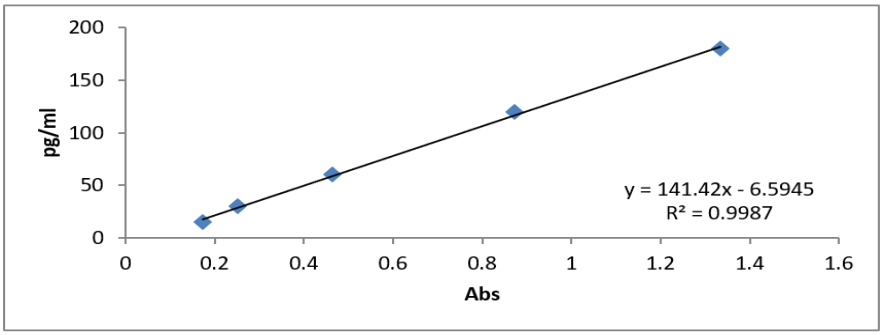

Fig (1) shows the direct relationship between concentration and optical absorbance in the ELISA device.

Concentration of AVP in blood serum was estimated using a ready-made assay kit from (Sun long-biotech company Chinese origin) using Enzyme −Linked Immunosorbent Assay technique (ELISA). Referring to the standard curve of the ready-made assay kit used to estimate the concentration of the hormone.

Extraction of DNA

Extracted DNA the blood of hypertensive and healthy patients had been made by the method of utilizing the assay kit (AddPrep) processed by the Korean company Addbio [11]

Determination of Deoxyribonucleic acid Concentration and purity

The concentration and purity of DNA (Deoxyribonucleic acid) were quantitatively and qualitatively estimated using a device Implen Nanodrop Photometer Spectrophotometer.

Primers Design

Designed Primers by (NCBI) the National Center for Biotechnology Information, Primer Blast website, as shown in the table (1).

Table (1): Primers Design

Gene	Primers Sequence	primers Length	GC %
VAP Forward	5'- GAGACTGAGACAGACGCGAG-3'	20 mer	60
VAP Revers	5'- GCTGTCACCGAGAGGTCATC-3'	20 mer	60

Q – PCR amplification for DNA

Previously prepared, extracted DNA (25 microliters) had been utilized In the process of amplification using the primers for specific genes prepared by the American company "Promega," catalog no. 72050. As show in table (2).

Table (2) PCR amplification for DNA process.

Constituent	Volume	Final Conc.
Master Mix PCR 2X	12.5 µl	1X
Upstream primer, 10 µM	0.25-2.5 µM	0.1-1.0µM
Downstream primer, 10 µM	0.25-2.5 µM	0.1-1.0µM
Template DNA	1-5 µM	< 250ng
Free Water- Nuclease	25 µM	N.A

The Eco Real Time PCR System uses heat-map to complete the reaction that shown in table (3).

Table (3) the heat map of Eco Real Time PCR System.

Stage	Step	Temperature (C°)	Duration	Cycles
Polymerase Activation	Step1	95	00:02:15	1
PCR Cycling	Step1	95	00:00:15	40
PCR Cycling	Step2	60	00:01:00	40
PCR Cycling	Step3	60	00:01:00	40
Total Program Length	1 Hour 51 Minutes 37 Seconds			
Total Cycle Count	40			

Statistical Analysis

Determination of any differences between control and patients (treatment and no treatment) groups had been made by Complete randomized design (C.R.D.) and Duncan's Multiple Range Test. Means and standard errors and the Significant difference at ($p \leq 0.05$) probability level for each group had been estimated.

Results and discussions

Serum vasopressin concentration :

Significant decrease had been showed in the vasopressin concentration at ($p \leq 0.05$) between study groups (control, untreated patients, and treated patients). As in table (4) and Fig-2 revealed. These results elucidate that hypertension decreases the firing of baroreceptors in the arteries which leads to sympathetic activity repressed that decrease the AVP release [12,13] determined in their results that hypovolemia causes a decrease in the arterial pressure that specialized receptors stretch. They also confirmed that hypertension was affected by many factors such as Hypovolemia that occurs during hemorrhage and dehydration cause a decrease in atrial pressure and large veins due to the decrease of atria firing of cardiopulmonary baroreceptors which give rise to the fall in atrial pressure. The afferent nerve fibers from these receptors synapse within the nucleus tractus solitaries of the medulla sends fibers to the hypothalamus that regulate the release of AVP from the posterior pituitary gland that had been inhibited by normal firing of the atrial receptor (type A). Hypovolemia or decreased central venous pressure decrease firing of atrial stretch receptors that cause an increase in AVP release. Also Angiotensin II receptors in hypothalamus regulate AVP release[14].

The results also revealed that AVP concentration had been increased in the serum of aging group (50 years and above) compared with control and younger groups. This result was accepted with Plasencia et al. (2019) which concluded in their results that aging patients had higher plasma AVP than young ones[15].

Also Al Ghorani et al. (2022) results revealed that aging reduced the kidney sensitivity of to AVP and this accepted with the results of this study that the concentration of AVP was increased in the aging group [16].

Table 4. Comparison of vasopressin concentration between healthy, untreated and treated hypertension patients

Age of groups	No of control	Mean ± Standard Deviation	No. Untreated patients	M (S.D)	No. Treated patients	M (S.D)
< 20	3	33.275 d ±6.84	3	26.735 bc ±5.96	3	20.729 a ±0.001
20-29	3	34.227 d ±0.98	6	30.637 cd ±3.09	6	32.867d ±0.12
30-39	3	30.011cd ±2.83	6	28.383bcd ±5.97	6	26.621bc ±5.82
40-49	3	29.683cd ±5.24	6	24.95 abc ±3.77	6	25.019abc ±5.06
50 and above	3	26.479bc ±5.78	6	29.223bcd ±6.28	6	23.418ab ±5.85

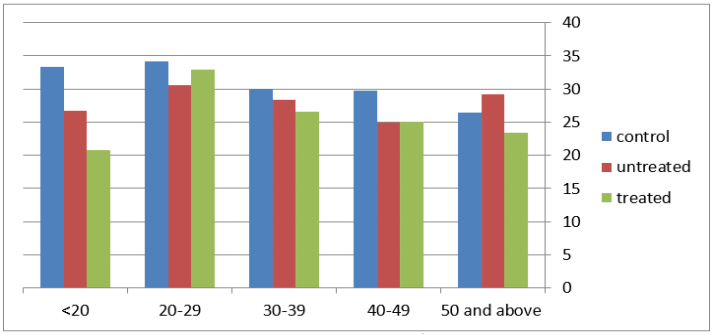

Fig 2. Comparison of vasopressin concentration between control and hypertension patients

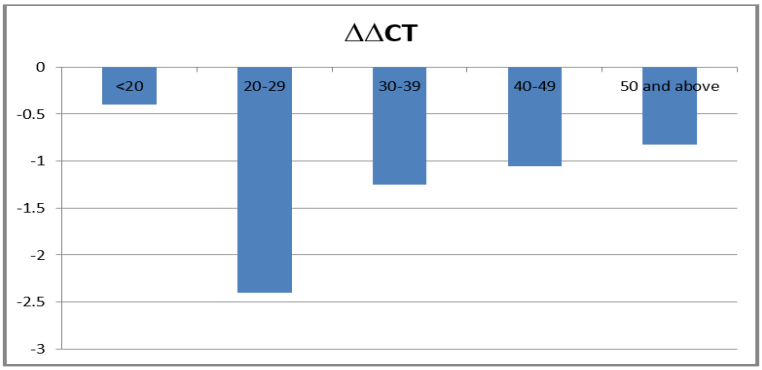

Fig. (3) Comparison of Amplicon copy numbers of Vasopressin coding gene between Healthy control and hypertension patients groups.

Molecular results in this research elucidated differences in the DNA concentration between different groups ranged between (18-68 ng) and the purity was ranged between (1.8-2)which indicated the high purity of DNA samples of all groups. Besides the results revealed that amplicon copy numbers of AVP coding gene had been decreased in patient's groups compared with control and housekeeping gene, as shown in (Fig. 2) and this gives an indirect indication about the expression of this hormone which was very low in all patients groups compared with control perhaps due to many mutations that occurred in this gene or the contributions of other factors that affected the expression of this gene, such as a mutation in the AVP receptors in these patients, and this was accepted by Rauf et al., (2022) results that revealed in their conclusion that the hypertension patients had a novel mutation in to two genes of AVP synthesis pathway[17,18] Kohava et al. (2008) revealed in their conducted association study between 758 cases and 726 controls utilizing 307 Single Nucleotide Polymorphisms (SNPs) in genes encoding components of signal transduction pathway that may be connected to blood pressure management , such as receptors, enzymes ; channels protein ; soluble carrier, and G-proteins and discovered that multiple candidate genes mutation in the hypertension-susceptibility pathways can be occurred[19].

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Conclusion

This study concluded that Amplicon copy numbers of AVP coding gene were very low in all patient groups compared with the control considered an important indicator of gene activities utilizing Real-time-PCR technique, and this accepted the low concentration of this hormone in patient's serum compared with control .These results concluded that this hormone had an important correlation with hypertension .

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