

STUDYING THE LEVEL OF ANGIOTENSIN II IN VARIOUS AREAS OF JORDAN WITH DIFFERENT ALTITUDES

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Abstract

Background: angiotensin II is involved in the development of hypertension.

Study objectives: to measure and compare the levels of angiotensin II among normal population in various areas with different ~~attitudes~~altitudes

Methods and subjects:

Study design: cross- sectional study was conducted to collect data from participants at the same time.

Study setting: participants from various areas with different ~~at~~titudes were recruited to participate in this study. A total of 1500 participants were included.

Study procedure: data was collected from participants based on a questionnaire that was constructed for this study.

Blood samples were withdrawn from participants by a well- trained nurse. Angiotensin II was measured using enzyme linked immune sorbent assay (ELIZAEELISA).

Statistical analysis: data was analyzed using SPSS version 20. Data was represented as means, standard deviations, frequencies and percentages. The relationship between variables was tested using independent T-Test. The significance was considered at ~~alpha~~pvalue<0.05.

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Study findings: the level of angiotensin II was 8.84 ± 4.65 pg/ml in Dead Sea, 11.21 ± 6.05 pg/ml in Sea level, and 12.08 ± 5.19 pg/ml in Ajloun. There was a significant difference between the means of angiotensin II between Ajloun and Dead Sea ($p=0.039$). no other significant differences were observed between the study areas.

Conclusion: the angiotensin II varies between the areas according to their altitudes and this consideration should be taken into account when hypertensive drugs are prescribed.

Keywords: angiotensin II, altitudes, the Dead Sea, Ajloun, Sea level.

Introduction

Angiotensin is an oligopeptide in the blood that causes vasoconstriction, increased blood pressure, and release of aldosterone from the adrenal cortex. It is derived from the precursor molecule angiotensinogen, a serum globulin produced in the liver and it plays an important role in the renin-angiotensin-aldosterone system. Angiotensin was independently isolated in Indianapolis and Argentina in the late 1930s (as 'Angiotenin' and 'Hypertensin' respectively) and subsequently characterized and synthesized by groups at the Cleveland Clinic and Ciba laboratories in Basel, Switzerland (Basso and Terragno, 2001).

Precursor of angiotensin

Angiotensinogen

Angiotensinogen is an α -2-globulin that is produced constitutively and released into the circulation mainly by the liver (Skurk [et al., Lee, and Hauner](#), 2001). It is a member of the serpin family (serine protease inhibitor)-family of proteins in blood interacts with and inhibits other enzymes of the blood coagulation system (Devlin, 2006), although it is not known to inhibit other enzymes, unlike most serpins. Plasma angiotensinogen levels are increased by plasma corticosteroid, estrogen, thyroid hormone, and angiotensin II levels. Angiotensinogen is also known as renin substrate. Human angiotensinogen is 452 amino acids long, but other species have angiotensinogen of varying sizes ([reference](#)).

Angiotensin I

Angiotensin I is formed by the action of renin on angiotensinogen. Renin cleaves the peptide bond between the leucine (Leu) and valine (Val) residues on angiotensinogen, creating the ten amino acid peptide, angiotensin I. Angiotensin I appears to have no biological activity and exists solely as a precursor to angiotensin II- ([reference](#)).

Angiotensin II

Angiotensin I is converted to angiotensin II through removal of two terminal residues by the enzyme *Angiotensin-converting enzyme* (ACE), which is found predominantly in the capillaries of the lungs (Skurk, ~~et al~~ Lee, and Hauner, 2001). ACE is actually found all over the body, but it has its highest density in the lung. Angiotensin II acts as an endocrine, autocrine/ paracrine, and intracrine hormone (Lees et al., 1993).

Effects of Angiotensin II

Cardiovascular effects

~~It~~ is a potent direct vasoconstrictor that constricts arteries and veins and increases blood pressure by increasing blood volume and peripheral resistance (Ardaillou, 1997).

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Neural effects:

~~Angiotensin II~~ increases thirst sensation through the subfornical organ of the brain, decreases the response of the baroreceptor reflex, and increases the desire for salt. It increases secretion of ADH in the posterior pituitary and secretion of ACTH in the anterior pituitary. It also potentiates the release of norepinephrine by direct action on postganglionic sympathetic fibers (Berry et al., 2002).

Adrenal effects

Angiotensin II acts on the adrenal cortex, causing it to release aldosterone, a hormone that causes the kidneys to retain sodium and lose potassium (Hall, 2003).

Renal effects

Angiotensin II causes constriction of the efferent renal arterioles, which has two effects on peritubular capillary dynamics that raise sodium and water reabsorption. First, efferent arteriolar constriction reduces peritubular capillary hydrostatic pressure. Second, efferent arteriolar constriction reduces renal blood flow, raises filtration fraction in the glomerulus and increases the concentration of proteins and colloid osmotic pressure in the peritubular capillaries. This leads to an increase in the reabsorptive force at the peritubular capillaries and raises tubular reabsorption of sodium and water. Angiotensin II directly stimulates sodium reabsorption in the proximal tubules, in the loops of Henle, in the distal tubules, and in the collecting tubules (Guyton, Hall, 2006).

The effect of altitude on hypertension

Parati et al (2014) studied the level of angiotensin II and blood pressure in high altitude areas conducted a study taking into consideration that a lot of hypertensive patients usually visit high altitudes, and little information is available about ambulatory blood pressure (ABP) variations and the efficacy of antihypertensive drugs under such

conditions. Moreover, the authors expressed their views that there is a deficiency of information about the efficacy of angiotensin receptor blockers under these condition. Findings of their study showed that both blood pressure and angiotensin II were increased with high altitudes and that the blockage of angiotensin receptor II helped in maintaining blood pressure.

~~Study objectives:~~ **Our study aimed** to measure and compare the levels of angiotensin II among normal population in various areas with different attitudes.

Methods and subjects

Study design

Cross sectional design was conducted.

~~Study setting~~

~~The present study was conducted~~ in three areas: the Dead Sea, the Sea-level area and Ajloun area, Jordan.

Study sample

The study sample included a total of 1500 participants of them 500 participants were included from each area. All participants were males, matched for age grouping, and they were apparently healthy.

Data collection

The data for each participant was collected and tabulated. Data included study variables such as blood pressure, weight, height, waist circumference, heart rate per minute, the level of angiotensin II, and packed cell volume (PCV).

Study procedure

The following measurements were taken: blood pressure for all participants was measured using sphygmomanometer with a stethoscope. Height was measured using 2 metric scaled rulers fixed to the wall of the room. Weight was measured using a well calibrated scale. Waist circumference was measured using a manual metric scale in centimeters. Heart rate was measured through radial pulse from the left hand for full minute, while the subjects were at rest. Angiotensin II was measured using **enzyme immunoassay (EIA)**.

Data analysis

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The analysis of data was carried out using SPSS version 20. All data were included and represented as mean —and standard deviation. The relations between variables were computed using independent T test. Significance was considered at alpha-pvalue <0.05.

Results

General characteristics of participants

As seen in table 1, age was within the similar pattern in study areas in which it was 17.6 years in both Dead sea level and Sea level, and slightly higher in Ajloun (17.83 years). Weight (kg) was also following similar distribution in study areas (67.31 kg-67.69 kg). The height (cm) was also observed within similar patterns and this pattern was observed for the remaining variables included in table 1.

Table 1: General characteristics of participants

variables	Dead sea level	Sea level	Ajloun
Age	17.6	17.6	17.83
Wt/kg	67.31	67.69	67.37
Ht/cm	169.29	170.5	169.51
BMI	23.45	23.26	23.42
Waist/cm	76.37	76.38	75.99
SBP/mmHg	122.42	118.07	125.74
DBP/mmHg	76.31	75.74	79.62
MBP/mmHg	91.64	89.84	94.95
Pulse/min	79.74	79.07	81.71
PCV	42.17	41.50	45.27

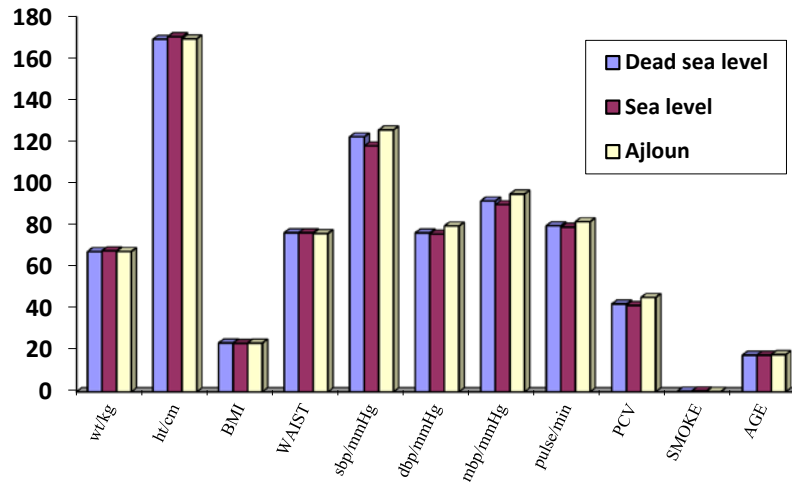


Figure1: Comparison between the means of variables Affecting Blood Pressure.

The level of Angiotensin II in study areas

As it can be seen in from table 2, the level of angiotensin II is 8.84 ± 4.65 pg/ml in Dead Sea, 11.21 ± 6.05 pg/ml in Sea level, and 12.08 ± 5.19 pg/ml in Ajloun. When the significance was tested using independent T test, there was a significant difference between the means of angiotensin II between Ajloun and Dead Sea ($p=0.039$). no other significant differences were observed between the study areas.

Table 2: Comparison between Angiotensin II Concentration (pg/ml) in study areas

Target Area	Mean \pm std	Target Area	Mean \pm std	P value
Dead Sea	8.84 ± 4.65	Sea level	11.21 ± 6.05	NS
Ajloun	12.08 ± 5.19	Dead Sea	8.84 ± 4.65	0.039

Sea level	11.21± 6.05	Ajloun	12.08 ± 5.19	NS
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Discussion

The results of the present study showed that among subject who are within similar patterns of demographic characteristics, there were slight variations in blood pressure parameters.

The concentration of angiotensin II, a hormone which is involved in the long-term regulation of blood pressure, was the highest at high altitude and it declined as we went down to the Dead Sea area (p value ≤ 0.05). This implies the effect of altitude on the level of angiotensin II. The highest level of angiotensin II was in Ajloun 12.08 pg/ml (the area with the highest altitude), and the lowest level was in the Dead sea 8.84 pg/ml. The difference in means among the participants was statistically significant ($p=0.039$). Up to the best knowledge of authors, this is the first study in Jordan that measures the level of angiotensin among population from various areas with different altitudes.

The data of our results agree with the study of Parati et al (2014) who reported increased blood pressure and angiotensin II among participants in high altitude areas and they confirmed their results through blocking of angiotensin receptor to maintain blood pressure.

Conclusions:

The present study reflected changes in the level of angiotensin II with high altitude areas and this factor should be taken into account when anti-hypertensive drugs have to be selected.

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