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Comparison of serum angiotensin II, sodium and potassium levels between normotensive, prehypertensive and hypertensive young adults of Punjab population, Pakistan

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Abstract

Background and Objectives: Hypertension is one of the most common diseases that is affecting large proportion of population worldwide. Exact pathophysiology of this disease is not known. Most of the studies are conducted in middle aged and older subjects. Young adults are overlooked in our country and not given importance because of misunderstanding that hypertension is disease of middle and old age. The major objective of the study was to compare serum angiotensin II, sodium and potassium levels between normotensive, prehypertensive and hypertensive young adults.

Material and Methods: A total of 589 patients were enrolled in the present study and divided into normotensive, prehypertensive and hypertensive subjects. This study was conducted at different colleges and universities of Lahore, Pakistan. For enrolment, informed written consent was obtained at start of study. Five ml of venous blood sample was obtained taken from subjects for analysis. Serum angiotensin II levels were estimated by ELISA method. Serum sodium and serum potassium were measured by electrochemical method. Statistical Analysis were performed by SPSS. For comparison, one way ANOVA and post-hoc test were used.

Results: No difference of age was observed between the participants. Serum angiotensin II values (1.22 ± 0.09, 1.28 ± 0.07 and 5.31 ± 0.29) in normotensive, prehypertensive and hypertensive young adults showed significant difference (p value < 0.05). The mean level of serum electrolytes; sodium and potassium were also raised in subjects with hypertension compared to normotensive and prehypertensive subjects (p value < 0.05).

Conclusion: Results of the present study revealed that fluid and electrolyte disturbance is implicated in the pathogenesis of hypertension disease and angiotensin II is the key factor. Incidence of hypertension can be controlled/delayed by adopting dietary interventions targeting salty diet in young adults.

Key words: Angiotensin II, Potassium, Sodium, Prehypertension, Hypertension

Introduction

Hypertension is persistent health risk upsetting large population worldwide. It is directly associated with adverse outcome especially cardiovascular and chronic kidney ailments. Mortality due to hypertension associated diseases is increasing every year than any other chronic disease (Fisher and Curfman 2018). Prevalence of high blood pressure is more than billion worldwide but in just 15% of individuals with hypertension, blood pressure is observed within normal limits. The survey conducted in the United States from 2017–2020 reported that about thirty percent young people had either high blood pressure or taking treatment and about 20% are unaware of having hypertension (Heaton et al. 2024).

Different mechanisms linking to hypertension are under investigation in the recent past of which important role of renin-angiotensin system is observed by many investigators in regulation and pathology of blood pressure. Angiotensin II regulates both sodium and balance to maintain blood pressure within normal range and its dysregulation is considered major factor implicated in hypertension disease (Pellegrino et al. 2016).

Angiotensin II function provide intricate blood pressure regulatory mechanism that act efficiently in regulating arterial blood pressure nearly normal (Vargas, Millán, and Bonilla 2022). Angiotensin II and high sodium dietary intake fuel each other to produce increase in blood pressure. Excess sodium consumption and its health implications specifically in relation to hypertension is topic of debate in research circles. High sodium intake is reflected as major factor linked with hypertension. Due to its close relevance with blood pressure, hypertension is classified as salt sensitive and salt resistant type (SA Majid, C Prieto, and Gabriel Navar 2015).

The present study was planned to evaluate the role of angiotensin II and serum electrolytes in prehypertension and hypertension in young adults of Punjab population because such study is non-existent in our population and little data is available globally regarding role of these markers in young adults between 16-21 years of age.

2. Methodology

2.1. Study Aims: The aim of the study was to evaluate the role of angiotensin II and serum electrolytes in the pathogenesis of prehypertension and hypertension to decrease or delay the incidence and progression of prehypertension to hypertension in young adults.

2.2. Study Participants: Informed written consent was attained from the individuals who offered themselves to participate in the present study. Young adults were selected from different institutions of Lahore that belonged to rural and urban areas of Punjab, Pakistan. Five hundred and eighty nine (589) participants were initially enrolled for the study. Information was recorded on a standardized questionnaire. Subjects participating in the study were categorized into normotensive, prehypertensive and hypertensive groups on the basis of blood pressure values.

2.3 Sampling Technique: Under aseptic conditions, five (05) ml of blood was collected from all prehypertensive and hypertensive individuals consented for blood sampling in the second phase. Equal number of normotensive subjects were also selected for blood sampling to compare between three groups. Venous blood was shifted in yellow top vacutainer and were transported under cold conditions to the research laboratory at the Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore.

2.4. Inclusion and Exclusion Criteria

Subjects between 16 and 22 years were included in the study. Both male and female subjects were recruited for the study. Young adults physically fit as per general physical examination. They were divided into three groups; group A (Normotensive), group B (prehypertensive) and group C (hypertensive). Subjects less than 16 years of age and more than 22 years of age were not included. Morbidly obese, pregnant, and taking antihypertensive therapy were excluded from the study. Subjects with history of diabetes mellitus, tuberculosis and chronic kidney disease were also excluded.

2.5 Determination of Blood pressure

Blood pressure was recorded after five minutes of rest using mercury sphygmomanometer in a sitting position. The average of three blood pressure readings were used for to declare subjects as normotensive, prehypertensive and hypertensive (Muntner et al. 2018).

2.6 Determination of Angiotensin II using ELISA Kit Assay

Serum angiotensin II levels were measured by using the enzyme-linked immunosorbent assay (ELISA) method in the study subjects. For this purpose, ELISA kit for measurement of angiotensin II by Glory Biosciences Lot No. 201901 was used. All assay protocol was followed as per user guide and the assay was run at room temperature. The color change was noted and the absorbance was measured at 450 nm within 15 minutes after adding stop solution to record the results.

2.7 Determination of Serum Electrolytes

Serum electrolytes were estimated by electrochemical method using Ion Selective Electrodes. The instructions of manufacturers were followed. Diestro electrolyte solution pack Lot No. 028 IVD, Ref. No. IN0750 was used for estimating levels of serum sodium, potassium and chloride.

2.8 Statistical Analysis

Data was entered using SPSS 24. All data were presented as mean ± SEM. Group means were analyzed and compared by one-way ANOVA and post-hoc test was applied to assess pairwise difference. A *p*-value less than 0.05 was considered statistically significant.

3 Results

A total number of five hundred and eighty nine subjects participated in the present study. Both male and female young subjects participated in the present study. Subjects were divided into normotensive, prehypertensive and hypertensive on the basis of blood pressure. Number of normotensive subjects was 504, prehypertensive 66 and 19 had hypertension. Out of 589 young adult subjects, 320 were male and 264 were female participants (Table 1). Subjects were declared normotensive if had systolic pressure below 120 mmHg and diastolic pressure below 80 mmHg. Declared prehypertensive if systolic BP was >120 and less than 140 mmHg or diastolic pressure >80 and <90 mmHg. Subjects were classified as hypertensive if had systolic BP ≥140 or more and diastolic pressure > 90 mmHg. Frequency of normotensive, prehypertensive and hypertensive subjects on the basis of systolic and diastolic BP is presented in Table 2.

Table 1: Demographic and phenotypic characteristics of the study subjects

Variables		Characteristics
Total Number of Subjects		589
Age		19-21 years
Gender	Male	325 (55.17%)
	Female	264 (44.82%)
Profession		Students of the university and colleges
Region		Lahore and different cities of the Punjab, Pakistan

Family History of Hypertension	Positive in 37.3% subjects Males: 118 (20%) Females: 102 (17.3%)
Normotensive	504 (85.56%)
Prehypertensive	66 (11.2%)
Hypertension	19 (3.2%)

Table 4.2: Distribution and %age of subjects on the basis of systolic and diastolic BP

Variable	Groups		
	Normotensive	**Prehypertensive**	**Hypertensive**
Systolic BP	521 (88.45%)	60 (10.2%)	8 (1.3%)
Diastolic BP	530 (90%)	40 (6.8%)	19 (3.2%)

In the second stage of study, blood samples were drawn from all prehypertensive and hypertensive young adults who consented to be part of the study. Equal number of blood samples were drawn from the normotensive subjects to compare between normotensive (Group A), prehypertensive (Group B) and hypertensive (Group C) subjects. The comparisons are presented in table 3. Table 3 revealed no difference of age between three groups. All subjects had age between 19 to 20 years of age (Fig. 1). Serum angiotensin levels were significantly differed between three groups (p value < 0.05). The post hoc test revealed no difference of angiotensin values (A = B < C) between subjects with normotension (1.22 ± 0.09) and prehypertension (1.28 ± 0.07). The high levels of angiotensin II were found in hypertensive group (5.31 ± 0.29) than normotension and prehypertension group as shown in Figure 2. Similarly, serum levels of sodium revealed significant difference between normotension (136 ± 0.5), prehypertension (140.2 ± 0.46) and hypertension groups (141.66 ± 0.68). Post hoc test shown statistically raised level of sodium (A < B = C) in group B and C to that of normotensive group (Fig. 3) but no difference was observed between prehypertensive and hypertensive group. The subjects in group C (4.55 ± 0.07) had significantly higher potassium levels compared to prehypertension (4.25 ± 0.05) and normotension groups (3.9 ± 0.05) with p value < 0.05 (Table 3; Fig. 4).

Table 3: Comparison and Pair-wise analysis of study variables between normotensive, prehypertensive and hypertensive groups.

Parameter	Normotensive	Prehypertensive	Hypertensive	p-value	Post Hoc Test
	Mean ± S.E.M	Mean ± S.E.M	Mean ± S.E.M		
Age	19.2 ± 0.3	20.1 ± 0.4	19 ± 0.2	0.25	A=B= C
SBP	111.9± 1.4	127.5 ± 0.9	142 ± 0.7	0.001	A<B< C
DBP	75.2 ± 1.1	82.1 ± 0.3	94.3 ± 1	0.001	A<B< C
Angiotensin II	1.22 ± 0.09	1.28 ± 0.07	5.31 ± 0.29	0.001	A=B<C
Sodium	136 ± 0.5	140.2 ± 0.46	141.66 ± 0.68	0.001	A<B=C
Potassium	3.9 ± 0.05	4.25 ± 0.05	4.55 ± 0.07	0.001	A<B<C

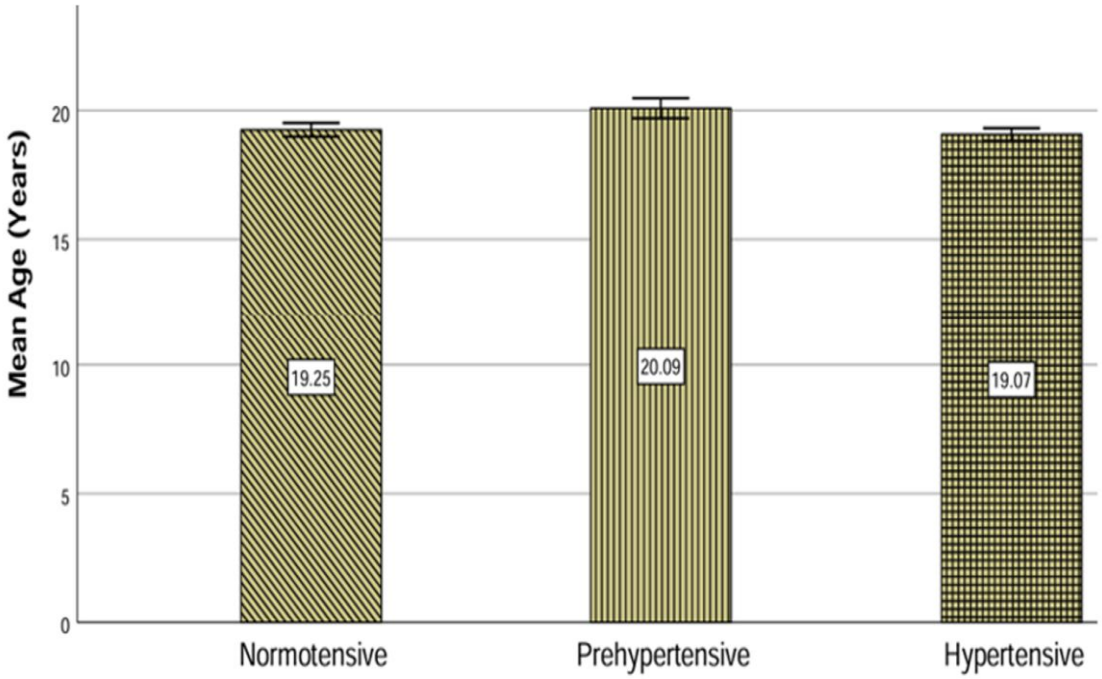

Figure 1: Comparison of age between three groups.

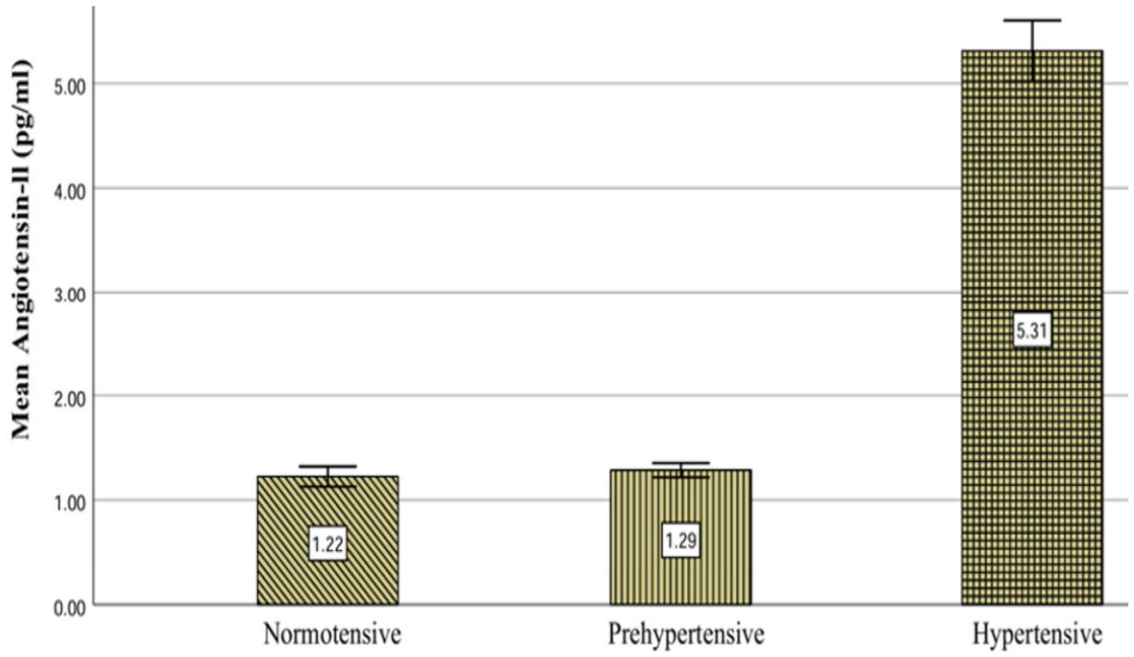

Figure 2: Comparison of serum angiotensin II between three groups.

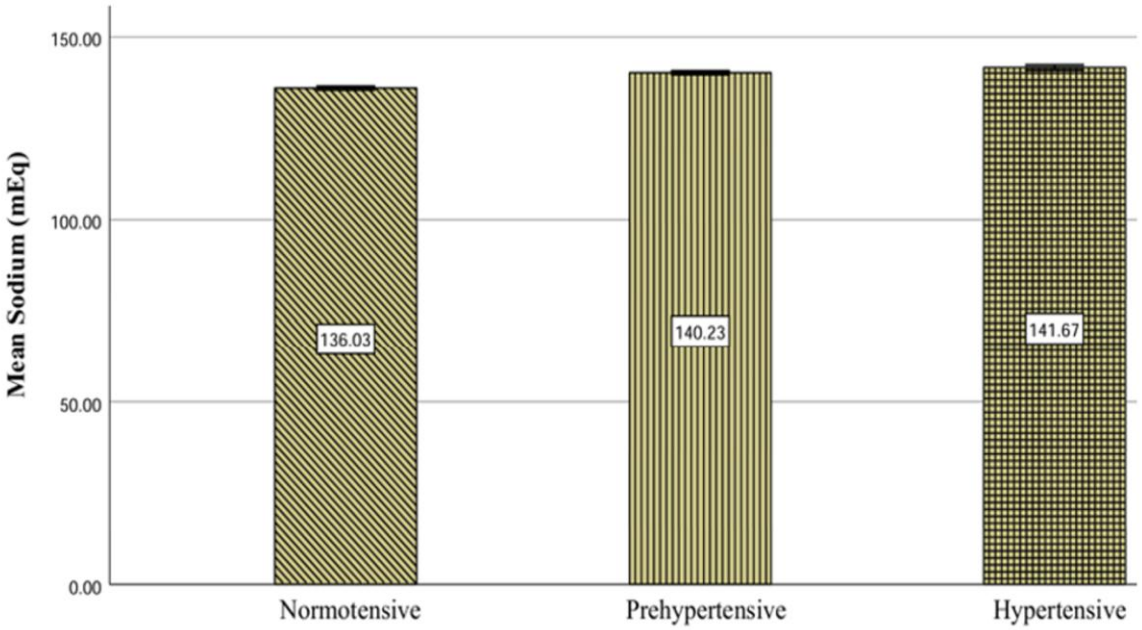

Figure 3: Comparison of serum sodium between three groups.

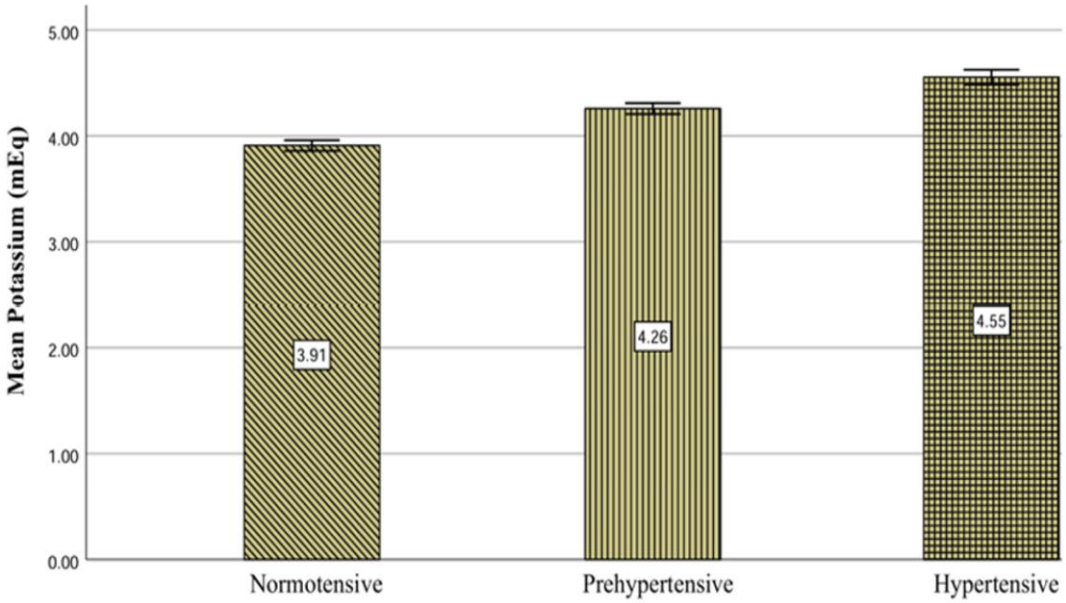

Figure 4: Comparison of serum potassium between three groups.

4 Discussion

Dysregulation of RAAS is described as the main cause of hypertension. Diverse mechanisms link angiotensin II with hypertension. Most notable mechanisms that link include vascular muscle proliferation and growth, impaired salt and water balance and activation of sympathetic system (Forrester et al. 2018). This relation is explored by several investigators in the recent past. Main cause of angiotensin II dysfunction is its prolonged persistence in the blood that impair proper functioning of blood vessels, brain and heart (Wu et al. 2018).

Persistent raised angiotensin II accelerate more aldosterone secretion that fuel up excessive fluid and electrolyte reabsorption. High aldosterone is reported in hypertensive subjects with associated heart failure and heart enlargement (Magill 2011). Persistently elevated angiotensin II also excite sympathetic activity that further weaken cardiovascular and renal dynamics (Konukoglu and Uzun 2017).

Hyperactive angiotensin II system also produce oxidative stress and induce inflammation that dysfunction vascular endothelium (Gorini et al. 2018). Deregulated angiotensin production perturbs nitric oxide/endothelin balance and correlate with increased blood pressure (Mancia and Hall 2019). In addition, enhanced local production of angiotensin II is another mean associated with high blood pressure by some investigators (Goyal et al. 2014). Overproduction of renin, angiotensin II and aldosterone has been associated with harmful effects on organs, genesis of high blood pressure and related vascular abnormalities (Szczepanska-Sadowska, Czarzasta, and Cudnoch-Jedrzejewska 2018).

Results of our study demonstrated significant difference of angiotensin II among three groups. Post hoc test found no difference of angiotensin II between normotensive and prehypertensive subjects. The angiotensin II levels were significantly higher than prehypertensive and normotensive groups. The present study showed strong positive relation of angiotensin II with SBP (r value .560) in prehypertensive subjects and weak positive relation (r value = 0.290) in the hypertensive group. The reason of weak relationship might be small sample size in the hypertensive group. The simple and multivariate linear regression analysis revealed significant impact of angiotensin II on SBP in prehypertensive and hypertensive subjects. The angiotensin II showed weak positive relation with diastolic pressure in the prehypertensive group and fair relation (r value = 0.343) in the hypertensive group.

Study conducted in China found similar results to our study and documented raised angiotensin II in hypertensive patients than normotensive (Han et al. 2022). Significant difference was also observed in day time and 24 hour systolic pressure in subjects with higher angiotensin II than subjects with normal angiotensin II. Difference of systolic BP was not found significant between low renin and aldosterone groups compared to high renin and aldosterone group (Liu et al. 2020). Likewise, angiotensin substrate 1-12 shown significant relation with systolic blood pressure and demonstrated higher level in hypertensive patients than in subjects with normal arterial pressure (Ferrario et al. 2021). Double risk of developing high blood pressure was observed in prehypertensive individuals in five year follow up investigation (Ferrario and Mullick 2017). Similar to present study, angiotensin II revealed direct association with systolic blood pressure in prehypertensive group (Mueller and Nickenig 2008). Another study stressed to use angiotensin II estimation as early marker to predict the occurrence of hypertension in subjects presenting with higher than normal blood pressure (Patten et al. 2016). It is demonstrated that angiotensin II and high sodium consumption are directly associated with each other and both further affect blood pressure dynamics (SA Majid, C Prieto, and Gabriel Navar 2015). Current study found similar results and documented higher sodium values in prehypertensive and hypertensive groups compared to normotensive group. Like our study, a mega survey in sixty 66 countries reported that sodium consumption is low income regions is above critical level and high sodium intake is the cause of death in more than million patients in developing countries (Mozaffarian et al. 2014). Slight decrease in dietary sodium can not only decreased disease risk bur also will lessen health system liability in low income countries (Carey et al. 2018). High sodium consumption is linked with blood pressure and heart dysfunction. Small decrease in sodium use not only lower blood pressure but also decrease mortality due to hypertension related problems (Long et al. 2022).

The present study found strong relation of sodium with SBP in prehypertensive subjects and weak connotation in hypertensive subjects. A study in recent past also evidenced direct relation of high sodium intake with BP rise (Frieden 2016). It was investigated that Even a mild to moderate reduction in dietary sodium created momentous decrease in blood pressure in all individuals irrespective of ethnicity and other risk factors (Hughes 2010). The results of current study also showed significant variation in potassium levels between normotensive, prehypertensive and hypertensive groups. Pairwise comparison established considerably upper potassium value in prehypertensive and hypertensive subjects compared to normotensive. Similarly, significantly inverse relation between potassium and systolic pressure is observed in the prehypertensive group and weak negative relation in the hypertensive group in the present study. Potassium had blood pressure lowering property and is seen closely linked with blood pressure regulation. A high dietary potassium content decreased blood pressure in higher blood pressure group (Binia et al. 2015).
Adequate intake of potassium has been shown to have a beneficial effect on blood pressure. Inverse relation of potassium rich diet was documented by many investigations (Kanbay et al. 2013). Potassium diminishes stress on blood vessels and favors blood flow due to its vasodilatory function (McDonough and Nguyen 2012). Similarly, other studies also reported that diets high in potassium impact on blood pressure (Su, Yang, and Ellison 2020). Experimental studies also established the same relationship and demonstrated decreased risk of cardiovascular diseases in subjects consuming high potassium diet (Jones 2019, Iwahori, Miura, and Ueshima 2017).

4.1 Study Limitations: The study limitation is the cross-sectional design and small sample size.
4.2 Strength of the study: Hypertension being chronic disease is main challenge and burden globally especially for low income countries. The results of the study describe that high sodium and angiotensin II are implicated in the pathogenesis of hypertension.
4.3 Future Recommendations: It is plausible to hypothesize that preventive (low sodium diet) and therapeutic approaches can be looked to reduce and control the occurrence of the hypertension disease.

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Informed Consent Statement: The subjects were informed about the study and consent was attained from the subjects.

Data Availability Statement: All the data is incorporated within the manuscript.

Conflict of Interests: The author declares no conflict of interest.

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