ASSOCIATION OF ANGIOTENSIN II LEVELS IN PATIENTS OF VASOVAGAL SYNCOPE AND POSTURAL TACHYCARDIA SYNDROME.

Hammad Raziq¹, Humaira Fayyaz Khan², Noman Sadiq³, Muhammad Athar Abdullah Baig⁴, Azmat Hayyat⁵

ABSTRACT... Syncope occurs as a result of cerebral hypoperfusion. Various neuroendocrine hormones have some role in the pathogenesis of Syncope. Current study was conducted to determine the role of Angiotensin II in pathophysiology of vasovagal syncope (VVS) and Postural tachycardia syndrome (POTS).

Study Design: Cross sectional analytical study. Setting: Islamic International Medical College, Rawalpindi and in Electrophysiology department (AFIC). Period: April 2017 to April 2018. Material and Methods: Sample size of this study was comprises of 80 subjects, having 35 cases of VVS and POTS each and 10 controls were also taken. Cases were collected on the basis of Head up tilt test (HUT) result and on their previous history of syncope, then their blood samples were collected and stored. Hormonal analysis of Angiotensin II was performed by ELISA technique. SPSS statistics 21 was used to evaluate result by applying ANOVA test. p value of < 0.05 was considered significant. Result: Analysis of Angiotensin II concentration in Postural tachycardia syndrome, Vasovagal and control group was found 170.93 ± 118.59 pg/ml, 152.16 ± 91.40 pg/ml and 136.93 ± 43.18 pg/ml respectively. In statistical analysis p value was 0.570 which is insignificant. Conclusion: It is concluded that Angiotensin II exerts role in the pathophysiology of VVS and POTS as shown by the difference in the value of Angiotensin II in VVS, POTS and in control group.

Key words: Angiotensin II, Head up Tilt Test, Postural Tachycardia Syndrome, Syncope, Vasovagal Syncope.

INTRODUCTION

Orthostasis is the intolerance of the body to the upright position that results in cerebral hypoperfusion which manifests itself as syncope or presyncope like condition. 3% of population visits in emergency is due to syncope and 6.2 out of 1000 admissions in hospital occurs due to syncope.¹

In orthostatic intolerance person is unable to compensate the effect of gravity on circulation. Gravitational stress on circulation leads to accumulation of venous blood in vascular beds of abdomen, buttocks and limbs. Accumulation of venous blood in lower extremities causes attenuation of venous return, cardiac output and stroke volume. Physiologically, there is increased vascular tone of legs and abdomen vessels to compensate it and prevents the body from syncope.²

Head up tilt test (HUT) is used to unveil the symptoms of syncope by positioning the patient at the angle of 70° for 45 minutes until the symptoms appears in susceptible patients. In this test we can determine the Neuro-cardio vascular responses in orthostasis.³ On head up tilt test pronounced variation in blood pressure and heart rate is observed due to orthostatic intolerance and autonomic dysfunctions.⁴ Syncope can be classified into neurocardiogenic (reflex) syncope, cardiac and orthostatic syncope.⁵ Vasovagal syncope (neurocardiogenic syncope) is the most frequent in origin that occurs due to bradycardia and vasodilation. Patients of vasovagal syncope usually encountered with sweating, dizziness, nausea, blurry vision and multiple episodes of syncope.⁶
Postural tachycardia syndrome (POTS) is also caused by orthostatic intolerance in which tachycardia occurs with normotension. In POTS there is rise in 30 beats/minute or heart rate reaches up to 120 beats/ minute during head up tilt or in standing position. Blood pressure is within normal limits. There are different etiologies of POTS, which could be due to autonomic dysfunctions, hypovolemia, disturbance in Renin-Angiotensin and Aldosterone secretion, autoimmunity and increased level of catecholamines in blood.7

It has been found that there are certain hormones like catecholamine, serotonin and Renin – Angiotensin hormones which play their important role in regulation of vessels tone, blood pressure, heart rate and circulation.8 Literature shows that these neuroendocrine hormones have some role in pathogenesis of Syncope i.e. VVS and POTS.

Angiotensin II hormone is released in response to low blood pressure and volume by Renin – Angiotensin system thus it leads to constriction of blood vessels, release of Aldosterone and regulates blood volume to normalize blood pressure. Angiotensin II hormone mediates its action through two types of receptors which are Angiotensin II receptor 1 (AT1R) or Angiotensin II receptor 2 (AT2R). These receptors are seven trans membrane G protein coupled receptors. In addition to peripheral receptors central receptors are also present which regulates cardio vascular system functioning.

Syncope occurs due to impaired regulation of blood pressure control and Angiotensin II has an important role in regulation of cardio vascular system. Review of literature shows inadequate data regarding Angiotensin II concentration in cases of syncope i.e. VVS and POTS. Evaluation of Angiotensin II in these cases of syncope may help us in future to explore the causes of disease and to evaluate and treat them effectively.

**METHODOLOGY**
A cross sectional Analytical study was conducted from April 2017 to March 2018 in Islamic International Medical college and in Armed forces Institute of Cardiology (AFIC) Rawalpindi. Sample size of this study was comprises of 80 subjects, which were 35 cases of VVS and POTS each and 10 controls were also taken. Cases were collected on the basis of Head up tilt test (HUT) result and on their previous history of syncope. In head up tilt test patients were tilted at 70° under the monitoring of blood pressure and heart rate. Blood samples of the subjects were collected, centrifuged and stored. Hormonal analysis of Angiotensin II was performed by Enzyme linked Immunosorbent Assay (ELISA) technique. SPSS statistics 21 was used to evaluate result by applying ANOVA test. *p* value of < 0.05 was considered significant.

**RESULTS**
In Table-I there is the comparison of Angiotensin II concentration between vasovagal, postural tachycardia and control group. Analysis of Angiotensin II concentration shows that in Postural tachycardia syndrome patients it was 170.93 ± 118.59 pg/ml, in Vasovagal group the mean concentration was 152.16 ± 91.40 pg/ml whereas in control group the mean concentration of Angiotensin II was found as 136.93 ± 43.18 pg/ml. It is apparent in results that the concentration of Angiotensin II is higher in POTS group as compared to VVS and control group. Although in statistical analysis *p* value was 0.570 which is insignificant.

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<th>N</th>
<th>X</th>
<th>X±SD</th>
<th>P-Value</th>
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<tr>
<td>Vasovagal Syncope</td>
<td>35</td>
<td>152.16</td>
<td>152.16±91.40</td>
<td>.570</td>
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<td>Postural Tachycardia Syndrome</td>
<td>35</td>
<td>170.93</td>
<td>170.93±118.59</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>10</td>
<td>136.93</td>
<td>136.93±43.18</td>
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Table-I. Comparison of angiotenism II (Pg/m) levels in VVS, POTS and control subjects
DISCUSSION
In our study we hypothesized that the Angiotensin II hormone will vary in concentration in VVS, POTS and in control group because it is vasoactive polypeptide that can play its role in pathogenesis of syncope. We collected blood samples and then Angiotensin II concentration was analyzed, our results showed that Angiotensin II concentration was higher in Postural Tachycardia group then Vasovagal and control group. Waldréus et al conducted similar type of study but they analyzed Angiotensin II in Vasovagal syncope patients with thirst by radio-immunological method and found higher levels of Angiotensin II in VVS group then in control group so our study supports this study. Gajek, J., Zyśko, D., & Mazurek performed a study, in which they assessed the Renin and Aldosterone activity during head up tilt (HUT) test, and they found increased concentration of Renin and Aldosterone and both these hormones are linked with Angiotensin II activity so our study also supports that study.

In another study, Angiotensin II was estimated in POTS patients relative to the status of blood volume which was conducted by Stewart, Glover, Medow et al, they found that Angiotensin II level was high in those patients who had decreased blood volume as compared to those who had normal blood volume. The results of that study were not statistically significant which are in aligned with our study results. Another study conducted by Mitro et al in which Angiotensin II receptors were studied in syncope patients and they found Angiotensin II type 1 receptor polymorphism that causes decreases in sympathetic activity and hypotension during head up tilt test. In previously discussed studies it has been found that Angiotensin II plays some role in Pathophysiology of syncope and in our study we also found variation among three groups of our study.

CONCLUSION
After the analysis and evaluation of the results, we made the conclusion that Angiotensin II hormone plays some role in pathophysiology of syncope that might be Postural tachycardia syndrome and vasovagal syncope as directed by increased Angiotensin II concentration in POTS and VVS groups as compared to normal control group. In future it is recommended to increase the sample size of the study and to study the effects of these hormones on its receptors. Further study on hormones and on its receptors in patients of syncope could help in improvement of diagnosis and prognosis of syncope.

REFERENCES


### AUTHORSHIP AND CONTRIBUTION DECLARATION

<table>
<thead>
<tr>
<th>Sr. #</th>
<th>Author-s Full Name</th>
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<td>1</td>
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