

## AGE AND GENDER RELATED OUTCOMES IN PATIENTS UNDERGOING HEAD UP TILT TEST FOR VASOVAGAL SYNCOPE

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### ABSTRACT

**Objective:** To evaluate different types of vasovagal syncope among the study group and assess the various outcomes in relation to age and gender in patients.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** Electrophysiology department, Rawalpindi Institute of Cardiology, Rawalpindi Pakistan, from July to Dec 2020.

**Methodology:** We analyzed prospectively 260 patients after excluding patients not meeting inclusion criteria to undergo HUTT. One hundred and two patients who were finally diagnosed vasovagal were included. Italian protocol was used and nitroglycerin was given for induction. Different responses were noted and outcome and hemodynamic parameters were compared according to age and gender. The collected data was analyzed by using SPSS-23.

**Results:** Out of 102 patients, 57 (55.9%) were males and 45 (44.1%) were females with the mean age of  $41.95 \pm 18.91$  years. Common prodromal symptoms were dizziness 27 (26.5%), vertigo 27 (26.5%), blackout 25 (24.5%) and apprehension 16 (15.7%). Mixed response was common in males while for females it was vasodepressor. Distribution of different responses and hemodynamic parameters were not statistically significant among age groups.

**Conclusion:** Dizziness and vertigo are the important prodromal symptoms. Older age group and females are more likely to have vasodepressor response but there is no difference in the SBP, DBP and HR parameters among both genders. Nitroglycerin is a useful drug for reaching to the diagnosis.

**Keywords:** Age, Gender, Head up tilt test, Vasovagal syncope.

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### INTRODUCTION

Syncope is a relatively common symptom experienced by around 3.3% patients presenting to outpatient department<sup>1</sup>. One of the commonest cause of syncope is vasovagal syncope (VVS) and it is reported to be around 66% of the total cases who present in Emergency department for syncope<sup>2</sup>. The pathophysiological basis for this disorder is poorly contemplated. One dictum is that it occurs due to pooling of the blood in the peripheral veins which results in decreased venous return to the heart and loss of consciousness occurs due to decrease perfusion to the brain<sup>3</sup>. It is mostly associated with prodromal symptoms which include dizziness, fatigue, feeling lightheaded, sweating, pallor, nausea<sup>4</sup>.

Initially VVS was considered to occur only in the younger population and was assumed to be rare in elderly but now it is being picked up more commonly<sup>5</sup>. Study by chen *et al*<sup>6</sup>, on 1,180 patients showed that VVS occurred in 49% of patients <65 years and 31% of age >65 years had positive result. In addition study by

Alboni *et al*<sup>7</sup>, showed that VVS had bimodal age distribution with first peak seen in age group 20-29 years while 2<sup>nd</sup> peak was among individuals aged >70 years.

HUTT is very useful test nowadays to diagnose the cause of syncope, especially VVS but also helps in identifying the prodromal symptoms<sup>8</sup>. This is further augmented by the fact that elderly group usually don't present with classical features and do not show common prodromal symptoms<sup>9</sup>. Study by kou *et al*<sup>10</sup>. Showed that HUTT findings were reproducible in 98% of elderly study group which makes it an excellent to test to perform when syncope evaluation is mandated.

In this study, we evaluated the various outcomes among the study group and observed the hemodynamic responses in relation to age and gender.

### METHODOLOGY

This cross sectional study was carried out in Rawalpindi Institute of Cardiology, Rawalpindi, from July to December 2020. Approval was taken from institutions ethical review committee. 340 consecutive patients presenting in EP opd for head up tilt test were taken into account. All patients undergo targeted history and physical examination followed by 12 lead

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electrocardiograms (ECG). Following patients were excluded from the study: patients with structural heart disease, diagnosed coronary artery disease, sick sinus disease, Av block, anemia, thyrotoxicosis, on b blockers or ca channel blockers. After exclusion 260 patients were finally included in the study. These patients underwent HUTT. Those patients with negative tilt test or diagnosis other than VVS were also excluded from the study. After a fasting period of at least 4 hours procedure was done in a quiet and temperature controlled room (22-26 C) with lights dimmed. Italian protocol was used to perform the tilt test. After 5 mins of rest in supine position patient head was tilted to around 60° and patient was observed for any symptoms. This position was kept for 20 mins in the absence of any symptoms. Following this in the provocation phase 0.4 mg of nitroglycerin (NTG) was given sublingually and observed for any response for an additional 15 mins. Systolic BP, diastolic BP and heart rate were continuously measured non invasively. The test was terminated when either of the following was present: negative for VVS, orthostatic hypotension, type 1 (mixed), type-2A (cardio inhibitory without asystole), type 2B (cardio inhibitory with asystole), or type 3 (vasodepressive). Those patients who were negative for any response or had orthostatic hypotension were also excluded from the study. The study was carried out in accordance with the Declaration of Helsinki (2000) and has been approved by the Medical Ethics Committee.

Statistical analysis was performed by using SPSS-23. Categorical variables were presented as frequencies and percentages and they were compared using chi square or Fischer exact test. The continuous variables were expressed as mean ± standard deviation and they were compared by using the Student t-test in case of normal distributed data and for non-normal distribution Mann-Whitney U test was used. Normality was assessed by Shapiro Wilk test. A *p* value ≤0.05 was considered statistically significant.

**RESULTS**

A total of 260 consecutive patients were studied. 40 patients did not undergo testing due to either being unfit or were unable to tolerate tilt testing, 220 patients completed the protocol. Out of these 102 were positive for vasovagal syncope while rest were either negative or having different responses. There were 57 (55.9%) males and 45 (44.1%) females in the study population. Mean age was 41.95 ± 18.91 years. Patients were further stratified according to the age groups. The comm-

on prodromal symptoms seen among the study group were dizziness 27 (26.5 %), vertigo 27 (26.5%), blackout 25 (24.5%) and apprehension 16 (15.7%). The distribution of different types of VVS were as mixed response VVS 140 (24%), vasodepressor type VVS 76 (13%) and cardio inhibitory type VVS 41 (7%). Average time for the patients to show positive response was 23.2 ± 5.7 mins. Overall 79 (77.5%) patients tested positive after nitroglycerin while 23 (22.5%) became positive in

**Table-I: Baseline characteristics of patients with vasovagal syncope.**

Variable	No. of Patients	Mean / n(%)
Age (years)	102	41.95 ± 18.91
<b>Gender</b>		
Male	57	55.9
Female	45	44.1
<b>Presenting Symptom</b>		
Blackout	25	24.5
Dizziness	27	26.5
Apprehension	16	15.7
Vertigo	27	26.5
Chest pain	1	1
Headache	1	1
Palpitations	2	2
Sweating	1	1
Nausea	1	1
Asymptomatic	1	1
<b>VVS Responses</b>		
Vasodepressor	52	51
Cardioinhibitory type 2A	8	7.8
Cardioinhibitory type 2B	4	3.9
Mixed	38	37.3
<b>Phase of Test</b>		
Passive	23	22.5
Active	79	77.5

passive phase as shown in table-I.

Taking into account gender differences overall male patients had a significantly higher number of vasovagal responses (n=57, *p*-value=02). Male patients predominantly showed mixed response (n=27) followed by vasodepressor response (n=23) while females depicted vasodepressor (n=29) as the most common result. Males had a significantly lower mean values for all the hemodynamic parameters i.e. SBP and DBP and HR at the time of positive response compared to females (*p*=0.061),(*p*=0.095) and (*p*=0.096), respectively as shown in table-II.

The distribution of different responses were not statistically significant among different age groups

( $p=0.444$ ). Vasodepressor VVS was commonly seen in age group >50 individuals while younger patients showed predominance of cardio inhibitory type 1 response. There was no statistical significance in mean values of hemodynamic parameters in the age groups

can result in the prevention of injury associated with syncope.

Taking into account gender differences we observed that there was a mixed result with female statistically having more vasodepressor responses compa-

**Table-II: Distribution of diagnosis and hemodynamic correlates according to gender**

Variable Gender				
	Male (n%, mean)	Female (n%, mean)	Total	p-value
Vasodepressor response	23 (44.23%)	29 (55.76%)		
Cardioinhibitory	7 (58.33%)	5 (41.66%)	12	1.00
Mixed	27 (71.05%)	11 (28.94%)	38	0.023
HR at event	62.93 ± 23.20	71.56 ± 28.66		0.096
SBP at event	48.01 ± 25.59	57.40 ± 28.96		0.061
DBP at event	23.59 ± 19.17	29.88 ± 21.41		0.095

**Table-III: Comparison of age groups with types of responses and hemodynamic parameters.**

Variable Age Groups				
	<30 (n%, mean)	30- 50 (n% ,mean)	>50(n%, mean)	p-value
<b>Type of Response</b>				0.444
Vasodepressor response	17/52 (32.6%)	16/52 (30.76%)	19/52 (36.53%)	
Cardioinhibitory type 1	4/8 (50%)	1/8 (12.5%)	3/8 (37.5%)	
Cardioinhibitory type 2	1/4 (25%)	3/4 (75%)	0/4	
Mixed	11/38 (28.9%)	14/38 (36.8%)	13/38 (34.2%)	
HR at event	72.36 ± 30.27	64.59 ± 24.11	63.51 ± 23.07	0.317
SBP at event	56.48 ± 28.6	47.76 ± 26.52	52.34 ± 27.18	0.432
DBP at event	27.42 ± 19.03	23.05 ± 19.58	28.60 ± 22.30	0.498

as shown in table-III.

**DISCUSSION**

HUTT is considered an important tool in the diagnosis of patients with unexplained syncope and use of nitroglycerin for provocation makes it stronger in evaluation of suspected VVS<sup>11</sup>. Our study showed that male was predominantly found to have tested positive for vasovagal syncope. Ghariq *et al*<sup>12</sup>. Also reported 23% men showing positive response compared to 14% female. Although the exact mechanisms are not clear but large muscle mass in males leads to more pooling of blood in the circulation owing to having larger compliant properties.

The most common prodromal symptoms reported by the patients were dizziness and vertigo followed by blackout. There have been inconsistencies in finding the specific prodromal symptom related to neurocardiogenic syncope to date however symptoms of blurred vision, sweating, nausea, chest pain and vertigo are considered to be linked to the involvement of autonomic symptoms which form the pathophysiological basis of this disorder<sup>13</sup>. The might have a therapeutic implication in which patients who experience increase number of prodromal symptoms can be educated that

red to males while males had significantly higher mixed type response. Cardio inhibitory response was only numerically higher in males. Studies have shown conflicting results with Roome *et al*<sup>14</sup>, showed that women tend to have higher incidence of different types of vasovagal syncope while Yalcin *et al*<sup>8</sup>, observed no differences in the type of response among gender. Since women show a larger reduction in the amount of thoracic blood volume compared to men when they stand up this results in resulting in lower orthostatic tolerance leading to decreased cardiac filling hence resulting in vasodepressor response<sup>15</sup>. More studies are needed in future before any conclusions are drawn in terms of gender variability to responses.

Among age groups we found that there was no statistically significant difference in the type of response among different age groups but vasodepressor response was overall more in older patients especially females. Study by Noormand *et al*<sup>16</sup>, also reported the similar finding. This can be explained by the fact that owing to the aging of the nervous system there is blunted heart rate response to the orthostatic stress. These is further supported by the higher baseline epinephrine levels and significantly lower high and low frequency HRV in elderly and failure of sinus node to fire

appropriately due to degenerative sinus node dysfunction<sup>17</sup> Cardioinhibitory response was seen the least (11.7%) in our study. It happened mostly in Younger age group (<30 years) while mixed response had a predilection for middle age group (30-50). The underlying mechanism for younger individuals developing both bradycardia and hypotension is still debatable but may be related to inappropriately overactive cardiac and autonomic responses<sup>18</sup> Mixed response in age group 30-50 can be associated with blunted baroreceptor reflexes<sup>19</sup>.

Various hemodynamic responses to tilt test in our study showed that there was no statistical significance in terms of SBP, DBP and HR among different age groups but male patients showed significant reduction in all these parameters. This can be explained partly by the orthostatic increase in blood pressure is larger in women and interaction of female sex hormones with nitroglycerin<sup>20</sup>. However, future studies are required to investigate these observations objectively.

## CONCLUSION

HUTT is an important tool when vasovagal syncope is suspected and it should be performed irrespective to the age and gender of the patient. Dizziness and vertigo are the important prodromal symptoms. Older age group and females are more likely to have vaso-depressor response but there is no difference in the SBP, DBP and HR parameters among both genders. Nitroglycerin is a useful drug for reaching to the diagnosis.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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