

## ORIGINAL ARTICLE

## A RETROSPECTIVE CHART REVIEW OF THE HEAD-UP TILT TABLE TEST AT A TERTIARY CARE UNIVERSITY HOSPITAL

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**Objectives:** Syncope is a non-traumatic and self-limiting transient loss of consciousness (TLOC) caused by momentary cerebral hypo-perfusion. It can be classified into orthostatic, cardiac, and vasovagal etiologies, distinguished using the up-tilt table test (HUTT). Our objective was to determine the characteristics of patients undergoing HUTT for TLOC.

**Methodology:** We conducted a single-center retrospective chart review of patients aged > 16 years who underwent HUTT from January 2010 to March 2020 at the cardiology and neurology departments of Shifa International Hospital, Islamabad, Pakistan. Charts were reviewed for basic demographic data and indications and outcomes of HUTT.

**Results:** Our study included 496 patients with 72.2% males and a mean age of  $51.1 \pm 19.08$  years. Vasovagal syncope was the most common etiology (79.8%, 158), followed by orthostatic syncope (11.6%, 23), autonomic syncope (6.1%, 12) and postural orthostatic tachycardia syndrome (2.5%, 5). Vasovagal syncope was divided into three subtypes, with the most common being mixed type (82.3%, 130), followed by pure vasodepressor (14.6%, 23) and cardio-inhibitory (3.2%, 5). The two most common prodromal symptoms were loss of consciousness (45.8%, 227) with or without preceding dizziness, followed by dizziness alone (34.5%, 171). Both symptoms had a statistical significance when compared to the diagnostic yield of HUTT testing ( $p < 0.05$ ). No significant correlation ( $p > 0.05$ ) was found between presenting symptoms, age, gender, and HUTT outcomes.

**Conclusion:** The most common etiology of syncope is vasovagal, predominantly the mixed type. LOC and dizziness were significantly associated with the HUTT yield.

**Keywords:** Syncope; head-up tilt table test; transient loss of consciousness; vasovagal syncope; POTS

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## INTRODUCTION

Transient loss of consciousness (TLOC) occurs due to a momentary global cerebral hypoperfusion characterized by a rapid onset, short duration, and spontaneous complete recovery.<sup>1</sup> These events are very common in the general population. According to the Framingham study, the cumulative incidence of syncope was 11% for both men and women aged 70 to 79 years and 17% and 19% for men and women aged >80 years, respectively.<sup>2</sup>

Syncope is classified according to the etiology into reflex (vasovagal), orthostatic hypotension, and cardiogenic.<sup>3</sup> Population-based studies have

demonstrated that almost three-fourths of patients with syncope have vasovagal syncope, making it by far the most frequent etiology of syncope.<sup>4</sup> The pathophysiology behind vasovagal syncope involves a surge in the parasympathetic tone alongside inhibition of the sympathetic vascular tone. Depending on the severity, it can either cause presyncope or syncope. Furthermore, syncope can be classified into pure vasodepressor, cardio-inhibitory, and mixed types.<sup>5</sup> Pure vasodepressor type involves a drop in blood pressure (BP) without a drop in heart rate (HR), cardio-inhibitory type involves a drop in HR and/or asystole, and the mixed type in which a simultaneous drop in both HR and BP is seen.<sup>5</sup>

European Society of Cardiology (ESC) has outlined evidence-based guidelines for the workup to aid in the definitive diagnosis of the underlying cause and management of syncope to treat it efficiently.<sup>3</sup> ESC defines syncope as “a transient loss of consciousness due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery.”<sup>3</sup> An essential component of this workup is the head-up tilt table (HUTT) test, which is valuable in distinguishing the diverse etiologies of syncope, including vasovagal, orthostatic, and autonomic diseases. The HUTT test consists of two stages: passive and active.<sup>6-9</sup> In the passive stage, the patient is observed for symptoms and hemodynamic changes with sequential tilt. If no changes are observed, the passive phase is perceived to be negative. In the active phase, the patient is administered sublingual nitroglycerine (NG), and the tilt is repeated to increase the diagnostic yield and sensitivity of the test.<sup>7</sup> However, the use of sublingual NG may raise the false positive rate.<sup>10</sup>

**METHODOLOGY**

This single-center retrospective chart review was conducted in the Department of Cardiology at Shifa International Hospital, Pakistan. Approval was obtained from the institutional review board and ethics committee. The committee waived participants' need for informed consent given the retrospective study design. Patients who had undergone HUTT testing from January 2010 to March 2020 were identified from the hospital's computerized database. Charts of these patients were reviewed for basic demographic data, indication for the HUTT test, and outcome of the test. Patients younger than 16 years of age or with a prior history of permanent pacemaker placement were excluded from the study.

HUTT was performed in a relaxed environment with the light off according to the nitroglycerin protocol,<sup>11</sup> in which the patient was tilted at 70° for 40 minutes, followed by a single sublingual spray (0.4 mg) of nitroglycerin and subsequently tilted for 15 additional minutes. The blood pressure, pulse, ECG, and symptoms were monitored during this time.

For this study, postural orthostatic tachycardia syndrome (POTS) was defined as an increase in the heart rate of 30 or more beats/minute or to at least 120 beats/minute within the first 10 minutes of orthostasis associated with symptoms of orthostatic intolerance but without significant orthostatic hypotension<sup>12</sup>.

Data were collected by the investigators and maintained in a safe environment, which only the investigators could access. All data were anonymized

to maintain patient confidentiality. SPSS version 21 was used for statistical analysis. Mean and standard deviation were calculated for age and quantitative variables; frequencies were calculated for categorical variables. The patients were categorized into groups based on syncope types, and their characteristics were compared. Crosstabs were performed to compare different variables, and the chi-square test was used to calculate the p values. P values less than 0.05 were taken as statistically significant.

**RESULTS**

A total of 520 patients were identified to have undergone HUTT testing. However, 24 patients were excluded from the analysis. Eight patients were below the age of 16, four had permanent pacemakers placed, and twelve had incomplete records, so they were excluded from the study. After excluding these patients, 496 patients were included in the analysis. The mean age of these patients was 51.1 years, with an SD of 19.08. The patients were divided into three groups according to their ages: 156 patients (31.5%) were between 16-40 years of age, 189 patients (38.1%) were between 41-65 years of age, and 151 patients (30.4%) were older than 65 years of age. The study participants had a majority of male patients, with 358 (72.2%) males and 138 (27.8%) female patients.

**Table 1: Diagnostic yield of HUTT. This table presents the total number of patients with the indicated symptoms and the number of patients with these preceding symptoms who demonstrated positive HUTT results. A comparison is presented for the age group and gender**

	Number (percentage)	HUTT positive (diagnostic yield)	P-value
<b>Symptom</b>			
Loss of consciousness	174 (45.8%)	114 (57.6%)	<0.01
Dizziness	171 (34.5%)	54 (27.3%)	<0.01
Visual symptoms	48 (9.7%)	25 (12.6%)	0.05
Fall	40 (8.1%)	15 (7.6%)	0.44
Palpitations	37 (7.5%)	14 (7.1%)	0.47
Diaphoresis	25 (5.0%)	8 (4%)	0.27
Vertigo	56 (11.3%)	16 (8.1%)	0.04
Nausea	27 (5.4%)	10 (5.1%)	0.46
Weakness	16 (3.2%)	5 (2.5%)	0.33
<b>Age Group</b>			
16-40 years	156 (31.5%)	63 (31.8%)	0.2
41-65 years	189 (38.1%)	87 (43.9%)	
>65 years	151 (30.4%)	48 (24.2%)	
<b>Gender</b>			
Male	358 (72.2%)	85 (39.35%)	0.73
Female	138 (27.8%)	32 (37.2%)	

HUTT=head-up tilt table

The patients presented with a wide range of symptoms: transient LOC (227; 45.8%), dizziness (171; 34.5%), vertigo (56; 11.3%), blackouts (graying of vision) (48; 9.7%), falls (40; 8.1%), palpitations (37; 7.5%), nausea and vomiting (27; 5.4%), diaphoresis (25; 5%), and generalized weakness (16; 3.2%). The HUTT test was positive in 298 patients (60.1%). The most common diagnosis based on the HUTT test result was vasovagal syncope (158; 79.8%), orthostatic hypotension (23; 11.6%), autonomic dysfunction (12; 6.1%) and POTS (5; 2.5%). Patients with vasovagal syncope were divided

into mixed type (130; 82.3%), vasodepressor type (23; 14.6%), and cardioinhibitory type (5; 3.2%). The correlation between age, gender, and presenting symptoms with HUTT results is shown in Tables 1 and 2. It is imperative to mention here that only vertigo, dizziness, blackouts, and LOC were statistically significant when compared to the diagnostic yield of HUTT testing. No significant correlation (p-value>0.05) was found between the presenting symptoms, age, gender, and specific diagnosis on HUTT testing.

**Table 2: Distribution of symptoms, gender and age across results of HUTT. This table describes the number of patients diagnosed with various types of syncope according to their presenting symptoms, age group, and gender**

	Orthostatic	Postural Orthostatic Tachycardia Syndrome (POTS)	Autonomic Dysfunction	Vasovagal
<b>Symptoms</b>				
Loss of consciousness	8 (34.8%)	1 (20%)	5 (41.7%)	40 (25.3%)
Dizziness	14 (60.9%)	3 (60%)	6 (50%)	91 (57.6%)
Visual symptoms	3 (13%)	0	0	22 (13.9%)
Fall	1 (4.3%)	1 (20%)	2 (16.7%)	11 (7%)
Palpitations	2 (8.7%)	1 (20%)	1 (8.3%)	10 (6.3%)
Diaphoresis	2 (8.7%)	0	0	6 (3.8%)
Vertigo	1 (4.3%)	0	2 (16.7%)	13 (8.2%)
Nausea	1 (4.3%)	0	0	9 (5.7%)
Weakness	1 (4.3%)	0	1 (8.3%)	3 (1.9%)
<b>Age Group</b>				
16-40 years	3 (13%)	4 (80%)	0	56 (35.4%)
41-65 years	10 (43.5%)	1 (20%)	3 (25%)	73 (46.2%)
>65 years	10 (43.5%)	0	9 (75%)	29 (18.4%)
<b>Gender</b>				
Male	17 (73.9%)	3 (60%)	9 (75%)	117 (74.1%)
Female	6 (26.1%)	2 (40%)	3 (25%)	41 (25.9%)

**DISCUSSION**

A greater male-to-female proportion was seen undergoing HUTT, possibly due to the higher healthcare-seeking behavior of males compared with females in South Asia. Such gender disparities have also been seen in a previous similar study.<sup>13</sup> The most common indications for HUTT in our study were reported to be LOC and dizziness. In a previous study, similar results were found, with dizziness being the most common indication for undergoing HUTT.<sup>14</sup>

According to our study, apart from dizziness, we did not find any significant correlation between presenting symptoms, age, sex, and outcomes of HUTT. This is synchronous with the reported findings of other investigators who performed similar studies.<sup>9,15,16</sup> However, a previous study found that patients with vasovagal syncope were more likely to be men. Among the prodromal symptoms, only dizziness

significantly correlated with HUTT results. Many patients complaining of dizziness were found to have positive HUTT results. Additionally, another study<sup>15</sup> contended that specific symptoms do not predict the cause of syncope; instead, the number of prodromal signs and symptoms can indicate a definitive diagnosis.

In patients greater than 60 years of age with unexplained syncope, HUTT has a positive predictive value of 93% and specificity as high as 100%. Since the negative predictive value is only 43% in patients with negative HUTT, a diagnosis of vasovagal syncope can still be made based on clinical suspicion.<sup>7</sup> As vasovagal syncope is the predominant cause of syncope in both western and south Asian populations.<sup>4,13</sup> Among the vasovagal syncope, the mixed type was reported to be the most common (62%), followed by pure vasodepressor and cardio-inhibitory.<sup>17</sup> Our study revealed similar findings.

We found that the diagnostic yield of the HUTT was 38%. Although some patients had symptoms during the test, results were still negative; importantly, none developed paradoxical bradycardia. One might consider performing the test again in these symptomatic patients with negative HUTT results. However, evidence reveals that repeating HUTT will not increase the diagnostic yield.<sup>18</sup>

In developing countries like Pakistan, socioeconomic burden limits physicians from performing definitive diagnostic testing in conditions that may be clinically obvious. Such is the case for orthostatic hypotension. It is more often clinically diagnosed rather than using diagnostic testing.<sup>19</sup> However, AST is often performed to confirm the suspicion of orthostatic hypotension.

HUTT can be an unpleasant experience, especially for elderly and anxious patients, as it is time-consuming and since most patients are not very keen on re-experiencing their symptoms. Efforts are being made to address this issue and spread awareness regarding this test's importance and benefit. A short HUTT test using new protocols is being implemented now. The passive phase of HUTT is bypassed by administering low-dose provocative doses of isosorbide dinitrate before the test. This reduces the study response time compared to conventional protocol without decreasing the diagnostic yield of the test.<sup>20,21</sup> This may help in decreasing the anxiety of the patients and increasing their compliance with the test. Investigators have also debated whether assessing the serum level of mid-regional-fragment of pro-atrial-natriuretic-peptide (MR-pro-ANP) at rest is possibly diagnostic for vasovagal syncope, but it remains experimental.<sup>22</sup> Regardless of the method used to evaluate patients presenting with syncope, prompt evaluation, and management remain essential given its substantial impact on the quality of life of patients.<sup>19</sup>

Our study had several limitations that should be considered when interpreting our results. First, this study was conducted at a single institution. Second, the sample size was small. Therefore, our results need more generalizability. Third, data were collected retrospectively, possibly introducing bias into our results. Fourth, we used a single HUTT protocol for testing. Therefore, future studies should perform HUTT using various protocols to verify our results. Finally, given that this was a retrospective study, we could not collect several variables of interest, e.g., raw data regarding heart rate at baseline, 3 minutes, prodrome or positive test, ECG findings, and vagal symptoms.

## CONCLUSION

We conclude that neurogenic syncope (vasovagal), particularly the mixed type, is the most common underlying etiology in patients undergoing HUTT tests due to complaints of unexplained presyncope or TLOC. Moreover, other than the symptoms of vertigo, dizziness, and LOC, no other symptoms were predictive of a positive HUTT test in our study.

## AUTHORS' CONTRIBUTION

RZ and AAS: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. RZ, AAS, AKN, AA, AN, and DHK: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

**Conflict of interest:** Authors declared no conflict of interest.

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