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Frequency Of Postural Orthostatic Tachycardia Syndrome In Young Adults With Chronic Fatigue

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Abstract

Background: Chronic fatigue is a frequent presenting complaint in young adults and is often multifactorial. Postural orthostatic tachycardia syndrome (POTS) is an important but under-recognized cause of orthostatic intolerance and fatigue. Local data on the frequency of POTS among young adults with chronic fatigue are limited. **Methodology**: This cross-sectional study was conducted at the Punjab Institute of Cardiology, Lahore, from July 10, 2024 to January 10, 2025. A total of 190 consecutive adults aged 20–40 years presenting with chronic fatigue and fulfilling predefined inclusion and exclusion criteria were enrolled. Demographic and clinical data, including age, sex, body mass index (BMI), smoking status, diabetes mellitus, hypertension, and symptom duration, were recorded. All participants underwent tilt table testing, and POTS was diagnosed based on a ≥30 beats/min increase in heart rate or a heart rate ≥120 beats/min within 10 minutes of tilting,

in the absence of significant orthostatic hypotension. Continuous variables were summarized as mean ± standard deviation (SD), and categorical variables as frequency and percentage N(%). Associations between POTS and clinical variables were assessed using the chi-square test, with $p \leq 0.05$ considered statistically significant.
Results: Among 190 participants, 68(35.8%) were male and 122(64.2%) were female, with a mean age of 32.32 ± 6.16 years. The mean BMI was 25.45 ± 2.16 kg/m²; obesity was present in 32(16.8%) patients. Diabetes mellitus was documented in 30(15.8%), hypertension in 54(28.4%), and current smoking in 33(17.4%) participants. The mean duration of illness was 19.23 ± 11.27 months, and 113(59.5%) had symptoms for >1 year. POTS was diagnosed in 71/190 patients, yielding a frequency of 37.4%. POTS was more frequent in females than males (54/122 [44.2%] vs 17/68 [25.0%]; p = 0.008) and in patients aged ≤30 years compared with >30 years (47/76 [61.8%] vs 24/114 [21.1%]; p = 0.001). Diabetes mellitus was strongly associated with POTS (24/30 [80.0%] vs 47/160 [29.3%] in non-diabetics; p = 0.001). In contrast, POTS was less common among hypertensive patients (6/54 [11.1%]) than among those without hypertension (65/136 [47.7%]; p = 0.002). Obesity and symptom duration showed no statistically significant association with POTS (p = 0.235 and p = 0.543, respectively).
Conclusion: In this single-centre cohort of young adults with chronic fatigue, more than one-third had concomitant POTS on tilt table testing. POTS was particularly frequent among females, younger patients, and those with diabetes, while it was less common in individuals with hypertension. Clinicians evaluating young adults with chronic fatigue should maintain a high index of suspicion for POTS, especially in these higher-risk subgroups, to enable timely diagnosis and appropriate management.

Introduction

Chronic fatigue is a common and often disabling complaint in young adults, with a broad differential diagnosis that spans primary sleep disturbances, endocrine and inflammatory conditions, mood disorders, and autonomic dysfunction. Among autonomic causes, postural orthostatic tachycardia syndrome (POTS) has emerged as a key but frequently under-recognized contributor to orthostatic intolerance, exercise limitation, and reduced quality of life in otherwise healthy individuals. POTS is characterized by an exaggerated increase in heart rate on standing or during head-up tilt testing, in the absence of significant orthostatic hypotension, together with typical symptoms such as lightheadedness, palpitations, weakness, and "brain fog" that improve with recumbency. [1,2]

Epidemiologic data suggest that POTS is one of the most common forms of chronic orthostatic intolerance in specialist autonomic clinics, with an estimated prevalence of about 0.2–1.0% in developed countries.[2,3] The syndrome typically affects adolescents and young adults, with a clear female predominance and peak onset between 15 and 45 years of age.[1–3] Although mortality is not increased, the functional burden is substantial: many patients experience marked limitations in education, employment, and daily activities, and health-related quality of life can be comparable to that seen in heart failure or chronic obstructive pulmonary disease.[2,3]

A substantial clinical and pathophysiological overlap has been described between POTS and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), with fatigue, post-exertional symptom exacerbation, unrefreshing sleep, cognitive impairment, and orthostatic intolerance frequently co-occurring.[4,5] In case–control and cohort studies, POTS has been reported in roughly one quarter of patients with ME/CFS, a proportion substantially higher than in matched control groups.[4,6] At the same time, not all cohorts have found POTS to be a reliable diagnostic marker for chronic fatigue conditions, suggesting that autonomic dysfunction may represent one important, but not universal, path to disabling fatigue in this population.[5] Collectively,

these observations underscore that POTS can both mimic and coexist with chronic fatigue states, making careful autonomic assessment highly relevant when evaluating young adults with persistent fatigue.

Despite growing international interest, data from South Asian settings remain sparse. Most of the published literature originates from North American and European centres, where diagnostic pathways, referral patterns, and background comorbidities may differ from those in low- and middle-income countries.[1–3,6] In Pakistan, young adults frequently present to cardiology clinics with chronic fatigue, palpitations, and non-specific dizziness, but the contribution of POTS to this symptom burden has not been systematically quantified, and clinicians may have limited familiarity with tilt table–based diagnostic criteria. Local data on the frequency of POTS and its clinical correlates in this context could help refine diagnostic suspicion, reduce diagnostic delay, and guide rational use of autonomic testing.

Accordingly, the present study aimed to determine the frequency of POTS among young adults presenting with chronic fatigue to a tertiary cardiac centre in Lahore and to examine its association with demographic and clinical characteristics, including age, sex, body mass index, diabetes, hypertension, smoking, and symptom duration. By focusing on a well-defined outpatient cohort and applying standardized tilt table testing criteria, we sought to provide context-specific evidence that may inform clinical evaluation strategies for chronic fatigue in similar settings.

Materials and Methods

Study Design and Setting

This was an observational, cross-sectional study conducted in the outpatient department of the Punjab Institute of Cardiology (PIC), Lahore, Pakistan, a tertiary care cardiac centre. The study was carried out over six months, from July 10, 204, to January 10, 2025. During this period, all eligible patients presenting with chronic fatigue were screened for inclusion.

Study Population and Eligibility Criteria

The target population comprised young adults with chronic fatigue attending the cardiology outpatient clinics. Consecutive patients aged 20–40 years of either sex were invited to participate.

Chronic fatigue was defined as persistent fatigue interfering with usual daily activities, accompanied by at least two of the following symptoms: light-headedness, difficulty in thinking or concentrating (“brain fog”), exercise intolerance, headache, blurred vision, palpitations, tremors, or nausea. Patients were included if these symptoms were present for several months and no acute medical explanation was evident on clinical assessment.

Patients were excluded if they had any of the following:

Profound hypotension at rest (systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg)

Clinical evidence of acute dehydration

Abnormal coagulation profile (prothrombin time >20 seconds or activated partial thromboplastin time >15 seconds)

Known significant renal dysfunction (serum creatinine markedly elevated as documented in the medical record)

History of chronic asthma or chronic obstructive pulmonary disease

Any acute systemic illness, pregnancy, or inability to undergo tilt-table testing

Sample Size and Sampling Technique

A non-probability consecutive sampling approach was used; all patients meeting the eligibility criteria during the study period were invited to participate until the required sample size was reached.
The sample size was estimated for a single-proportion cross-sectional study, using an expected prevalence of postural orthostatic tachycardia syndrome (POTS) of 40% among patients with chronic fatigue. This assumption was based on prior work in chronic fatigue and related populations showing that roughly one-third to one-half of patients demonstrate orthostatic intolerance or fulfil criteria for POTS on formal testing.[1–5] The calculation assumed a 95% confidence level and an absolute precision (margin of error) of 7%. Using the standard single-proportion formula for prevalence studies ($n \approx Z^2 \cdot p \cdot [1-p]/d^2$), as recommended in contemporary methodological guidance and implemented in dedicated sample size calculators for prevalence studies,[8] the minimum required sample size was approximately 188 participants. To ensure adequate power and allow for minor data loss, 190 consecutive eligible patients with complete data were ultimately included in the analysis.

Data Collection Procedures and Study Variables
After obtaining informed consent, each participant was interviewed and examined by the investigator using a structured case-record form. The form captured:

Sociodemographic data: age (years), sex

Anthropometric data: height (cm), weight (kg), and body mass index (BMI, kg/m²), categorized for descriptive purposes (obese vs non-obese) according to standard thresholds

Clinical history: duration of fatigue symptoms (months), categorized as ≤1 year or >1 year; past medical history of diabetes mellitus and hypertension; smoking status

Comorbidities and risk factors:
Diabetes mellitus: documented diagnosis in the medical record or random plasma glucose >200 mg/dL on presentation
Hypertension: documented diagnosis or blood pressure ≥140/90 mmHg on repeated measurements during the visit
Smoking: current or former smoker with cumulative exposure >5 pack-years
Baseline seated and supine vital signs were recorded, and a focused cardiovascular and respiratory examination was performed to exclude acute illness or conditions that would preclude safe tilt-table testing.

Tilt-Table Testing and Definition of POTS
All included participants underwent standardized head-up tilt-table testing in the PIC non-invasive laboratory under the supervision of the principal investigator and experienced technical staff. After at least 10 minutes of quiet rest in the supine position, heart rate and blood pressure were recorded. The table was then tilted to an upright position (approximately 60–70 degrees), and heart rate and blood pressure were recorded again at 5 minutes and 10 minutes of standing.
POTS was diagnosed according to contemporary international consensus criteria:
An increase in heart rate of at least 30 beats per minute from the supine baseline **or** an absolute heart rate ≥120 beats per minute within 10 minutes of tilting,
Presence of orthostatic symptoms consistent with intolerance (e.g., light-headedness, palpitations, weakness, or presyncope) during tilt, and

Absence of classical orthostatic hypotension (sustained drop in systolic blood pressure ≥20 mmHg or diastolic blood pressure ≥10 mmHg).[7]
These criteria mirror those endorsed by the Heart Rhythm Society and collaborating societies for the diagnosis of POTS in clinical and research settings.[7]
Patients were observed throughout the procedure, and the test was terminated early if they experienced severe symptoms, marked hypotension, or presyncope, in accordance with institutional safety protocols. After testing, all patients received routine clinical advice and follow-up as per departmental practice.
The **primary outcome** was the frequency (proportion) of POTS among young adults with chronic fatigue. **Secondary outcomes** included the association of POTS with sex, age group (≤30 vs >30 years), BMI and obesity status, smoking status, diabetes, hypertension, and duration of symptoms (≤1 year vs >1 year).

Statistical Analysis
Data were entered and analyzed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables (age, BMI, duration of symptoms) were summarized as mean ± standard deviation (SD); ranges were inspected where informative. Categorical variables (sex, age group, obesity, smoking status, diabetes, hypertension, duration category, and presence of POTS) were summarized as counts and percentages, reported in N(%) format.
The prevalence of POTS in the overall cohort was calculated as the proportion of participants meeting diagnostic criteria out of the total sample (n = 190). To explore associations between POTS and categorical predictors (sex, age group, obesity, smoking status, diabetes, hypertension, duration of disease), cross-tabulations were constructed and compared using the chi-square (χ^2) test. Results were reported as N(%) across POTS strata, with corresponding p-values. A two-sided p-value ≤0.05 was considered statistically significant. No advanced modelling or multivariable regression was performed, in keeping with the descriptive and exploratory nature of this single-centre cross-sectional study.

Ethical Considerations
The study protocol was reviewed and approved by the institutional ethics review committee of the Punjab Institute of Cardiology, Lahore, and was conducted in accordance with the Declaration of Helsinki and local regulatory requirements. All participants were informed about the study objectives and procedures, assured of confidentiality and anonymity of their data, and provided informed consent prior to enrolment and tilt-table testing.

Results
A total of 190 patients with chronic fatigue were enrolled during the study period. Of these, 68/190 (35.8%) were male and 122/190 (64.2%) were female. The mean age of the cohort was 32.32 ± 6.16 years (range: 21–40 years), and 114/190 (60.0%) were older than 30 years. The mean BMI was 25.45 ± 2.16 kg/m²; 32/190 (16.8%) participants were classified as obese, while 158/190 (83.2%) were non-obese. Diabetes mellitus was present in 30/190 (15.8%) patients, hypertension in 54/190 (28.4%), and current smoking in 33/190 (17.4%). The mean duration of fatigue symptoms was 19.23 ± 11.27 months, and 113/190 (59.5%) reported symptom duration of more than one year. Baseline characteristics of the study population are summarized in **Table 1**.

Table 1. Baseline characteristics of young adults with chronic fatigue (N = 190)

Variable	Category	N (%)	Mean ± SD / Range

Age (years)	≤30	76 (40.0%)	
	>30	114 (60.0%)	32.32 ± 6.16 (21–40)
Sex	Male	68 (35.8%)	
	Female	122 (64.2%)	
Body mass index (kg/m²)	Non-obese	158 (83.2%)	25.45 ± 2.16
	Obese	32 (16.8%)	
Diabetes mellitus	Yes	30 (15.8%)	
	No	160 (84.2%)	
Hypertension	Yes	54 (28.4%)	
	No	136 (71.6%)	
Smoking status	Smoker	33 (17.4%)	
	Non-smoker	157 (82.6%)	
Symptom duration (months)	≤1 year	77 (40.5%)	19.23 ± 11.27
	>1 year	113 (59.5%)	
POTS on tilt-table testing	Present	71 (37.4%)	
	Absent	119 (62.6%)	

POTS was diagnosed on tilt-table testing in 71/190 patients, corresponding to an overall frequency of 37.4%, while 119/190 (62.6%) did not meet diagnostic criteria for POTS (Table 1). Thus, approximately one in three young adults with chronic fatigue in this cohort had concomitant POTS.

When stratified by sex and age, POTS was more frequent among females and younger participants. Among females, 54/122 (44.2%) had POTS compared with 17/68 (25.0%) males ($p = 0.008$). Among patients aged ≤30 years, 47/76 (61.8%) had POTS, whereas among those >30 years, 24/114 (21.1%) had POTS ($p = 0.001$). These distributions, along with other clinical correlates, are detailed in **Table 2**.

Table 2. Distribution of POTS according to demographic and clinical variables (N = 190)

Variable	**Category**	**POTS Present, N (%)**	**POTS Absent, N (%)**	**p-value**
Sex	Male	17 (25.0%)	51 (75.0%)	0.008
	Female	54 (44.2%)	68 (55.8%)	
Age group (years)	≤30	47 (61.8%)	29 (38.2%)	0.001
	>30	24 (21.1%)	90 (78.9%)	
Diabetes mellitus	Yes	24 (80.0%)	6 (20.0%)	0.001
	No	47 (29.3%)	113 (70.7%)	
Hypertension	Yes	6 (11.1%)	48 (88.9%)	0.002
	No	65 (47.7%)	71 (52.3%)	
Obesity	Obese	15 (46.8%)	17 (53.2%)	0.235
	Non-obese	56 (35.4%)	102 (64.6%)	
Symptom duration	≤1 year	31 (40.2%)	46 (59.8%)	0.543
	>1 year	40 (35.3%)	73 (64.7%)	

Diabetes mellitus showed a strong positive association with POTS: 24/30 (80.0%) diabetic patients had POTS, compared with 47/160 (29.3%) non-diabetic patients ($p = 0.001$). In contrast, POTS was less frequent among hypertensive patients; only 6/54 (11.1%) hypertensive participants had POTS versus 65/136 (47.7%) among those

without hypertension (p = 0.002). Obesity did not show a statistically significant relationship with POTS, with POTS present in 15/32 (46.8%) obese patients and 56/158 (35.4%) non-obese patients (p = 0.235). Symptom duration also was not significantly associated with POTS: 31/77 (40.2%) patients with symptom duration ≤1 year had POTS compared with 40/113 (35.3%) with symptoms >1 year (p = 0.543) (Table 2).
No serious complications related to tilt-table testing were observed. All patients completed the procedure without syncope requiring resuscitation or other major adverse events, and no test had to be terminated prematurely for safety reasons.

Discussion

In this cross-sectional study of young adults with chronic fatigue attending a tertiary cardiac centre, more than one-third of participants met diagnostic criteria for postural orthostatic tachycardia syndrome (POTS) (37.4%; 71/190). This proportion is considerably higher than estimates of POTS prevalence in the general population—commonly cited around 0.1–1.0%—and higher than that reported in most unselected cardiology cohorts, underscoring the strong link between chronic fatigue and orthostatic intolerance. [1–3] The high frequency in our symptomatic, referred sample is therefore likely to reflect both referral bias and true clustering of POTS in patients with disabling fatigue.

Our findings are broadly consistent with prior work in chronic fatigue and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) clinics, where 20–30% of patients show POTS or marked orthostatic tachycardia on formal testing. [4,5] Lewis et al. reported that approximately one quarter of CFS patients met criteria for POTS, with a similar female predominance and substantial symptom burden. [4] Roerink et al. observed frequent autonomic symptoms and orthostatic abnormalities in a CFS referral cohort, though they concluded that POTS alone was an imperfect discriminator between CFS and other fatigue states. [5] The somewhat higher prevalence in our cohort may reflect enrichment for patients with cardiovascular symptoms in addition to fatigue, as our recruitment was from a cardiology-based setting rather than a general fatigue or internal medicine clinic.

The demographic profile of POTS in our sample—predominantly female and relatively young—is in line with large series from autonomic and cardiology centres, where 70–90% of patients are women in their teens through early middle age. [1–3,6] In our data, patients aged ≤30 years were substantially more likely to have POTS than those >30 years, and women had a higher proportion of POTS than men. These patterns echo observations from Raj and colleagues, as well as contemporary reviews, which highlight sex-linked susceptibility and a peak incidence in adolescence and young adulthood. [1–3] Hormonal factors, differences in autonomic responsiveness, and health-care–seeking behaviour have all been proposed as contributors to this age- and sex-specific risk profile. [2,3,6]

We found a strong positive association between POTS and diabetes mellitus: 80.0% (24/30) of participants with diabetes had POTS compared with 29.3% (47/160) of those without diabetes. Although most POTS cohorts report relatively low rates of classical cardiometabolic risk factors, [6,7] diabetic autonomic neuropathy is a well-recognized complication of diabetes and can involve the cardiovascular autonomic nervous system. [11] It is therefore plausible that subclinical autonomic neuropathy—unmeasured in our protocol—may partially explain the clustering of POTS among diabetic participants. At the same time, this association should be interpreted cautiously: our sample contained relatively few patients with diabetes, confidence intervals around the effect estimate are likely wide, and we cannot exclude residual confounding by medication use, comorbidity burden, or referral patterns. Future studies that include formal autonomic reflex testing and stratification by glycaemic control and diabetes duration

are needed to clarify whether diabetes is a true risk factor for POTS or a marker of more complex multisystem disease.

Conversely, a history of hypertension was inversely associated with POTS in this chronic-fatigue cohort. Only 11.1% (6/54) of participants with hypertension met POTS criteria compared with 47.7% (65/136) of those without hypertension. One explanation is pharmacologic: beta-blockers and some other antihypertensive agents can blunt orthostatic tachycardia and may mask POTS on a single tilt-table assessment. [2,7] Alternatively, clinicians may be more likely to attribute fatigue in hypertensive patients to cardiovascular risk and less likely to refer them for formal autonomic testing, leading to selection effects. Existing POTS series typically report low prevalence of hypertension and other conventional cardiovascular risk factors, [6,9] so our inverse association may reflect both medication effects and the specific referral profile of our centre rather than a protective role of hypertension per se.

Obesity and duration of fatigue were not significantly associated with POTS in our dataset. Patients with and without POTS had similar BMI distributions, and symptom duration (>1 year vs ≤1 year) did not meaningfully change the probability of a POTS diagnosis. While deconditioning and weight gain are frequently discussed in the context of POTS, prior observational studies have reported a wide BMI range and inconsistent associations between body habitus, symptom duration, and autonomic findings. [3,6,9] Hutt et al. noted that younger POTS patients often have reduced functional capacity relative to age- and sex-matched norms despite modest or normal BMI, suggesting that deconditioning and impaired exercise tolerance may be more relevant than absolute body weight. [9] Our null findings for obesity and disease duration therefore fit within an emerging picture in which POTS is not simply a consequence of inactivity or weight but a distinct autonomic disorder that may coexist with, but is not determined solely by, these factors.

Our results add to a growing body of evidence that POTS substantially impairs quality of life and psychosocial functioning, particularly in young adults. [1–3,9,10] In the Cleveland Clinic cohort described by Hutt et al., nearly half of POTS patients demonstrated below-average functional capacity on exercise testing, and those with reduced functional capacity had significantly lower SF-36 physical component scores compared with POTS patients with preserved exercise tolerance. [9] Moon et al. showed that orthostatic intolerance symptoms, rather than the magnitude of heart-rate increment alone, were strongly correlated with depressive symptoms and both physical and mental components of health-related quality of life. [10] Our finding that more than one-third of young adults with chronic fatigue have POTS suggests that unrecognized autonomic dysfunction may be an important contributor to symptom persistence, activity limitation, and reduced quality of life in this group, which is already known to experience significant functional impairment. [4,5]

These observations have direct clinical implications. Current consensus statements emphasize the importance of standardized orthostatic vital signs and, where available, head-up tilt testing in patients with suspected POTS or orthostatic intolerance. [2,7] Our data support incorporating such assessments systematically into the evaluation of young adults with chronic fatigue, particularly women and those with coexisting diabetes. Early recognition of POTS allows clinicians to implement structured non-pharmacologic measures—such as volume expansion, compression garments, graded exercise, and avoidance of triggers—and to consider pharmacologic therapies where appropriate. [2,6,10] In addition, the strong link between orthostatic symptoms, depressive features, and diminished quality of life highlighted in prior work suggests that integrated management pathways, involving cardiology, neurology, rehabilitation, and mental health professionals, may be especially valuable for this population. [9,10]

Our study has several strengths. We recruited a relatively homogeneous age group (20–40 years) of patients with chronic fatigue, used a standardized tilt-table protocol aligned with international diagnostic criteria, and collected detailed data on key cardiometabolic comorbidities. [2,7,8] The sample size was determined a priori using contemporary guidance for prevalence studies, [8] which helps ensure that the precision of our prevalence estimate is acceptable for clinical and research interpretation. The resulting confidence intervals around the 37.4% prevalence of POTS in this setting are therefore likely to reflect the underlying uncertainty rather than artefacts of underpowered sampling.

Limitations

Several limitations should also be acknowledged. First, the cross-sectional design precludes inference about causality or temporal relationships between POTS, diabetes, hypertension, obesity, and chronic fatigue. Second, because recruitment occurred in a single tertiary cardiac centre, our findings may not generalize to primary care or general community populations with fatigue, in whom the prevalence of POTS is probably lower. [1,4,6] Third, we did not systematically measure autonomic neuropathy, small fibre neuropathy, or autoantibodies, so mechanistic inferences about the association with diabetes or other comorbidities remain speculative. [3,11] Finally, we used clinical criteria for chronic fatigue rather than formal ME/CFS case definitions, which may have introduced some heterogeneity in the underlying fatigue syndromes. Nonetheless, many of these constraints are shared with prior clinic-based POTS and CFS studies, allowing reasonably direct comparison of prevalence and demographic patterns. [4,5,9,10]

Conclusion

Taken together, our data suggest that POTS is common among young adults with chronic fatigue in a cardiology referral setting and is particularly frequent in women, younger individuals, and those with diabetes. In contrast, obesity and the duration of fatigue do not appear to meaningfully alter risk. These findings reinforce the need for clinicians evaluating chronic fatigue to maintain a high index of suspicion for POTS, to perform structured orthostatic assessment, and to consider multimodal management strategies that address both autonomic symptoms and psychosocial sequelae. Future research should focus on multicentre, longitudinal cohorts that track the natural history of POTS within chronic-fatigue populations, explore mechanistic links with metabolic and autonomic neuropathies, and test targeted interventions aimed at improving both functional capacity and quality of life.

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