A survey-based analysis of symptoms in patients with postural orthostatic tachycardia syndrome

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Postural orthostatic tachycardia syndrome (POTS) is a type of dysautonomia seen most commonly in young women and children. It is defined as an increase in heart rate of 30 beats per minute (bpm) or more within 10 minutes of standing in adults, or by 40 bpm or more in children in the absence of orthostatic hypotension. In addition to typical autonomic symptoms, POTS patients report a wide range of subjective complaints in multiple organ systems, though the exact frequencies are unclear. To address the symptom frequency, we had 39 patients with POTS at our institution complete an intake form consisting of a list of 37 symptoms. The most frequently reported symptoms included palpitations, lightheadedness, and headache, although sleep disturbances, gastrointestinal complaints, sensitivity to temperature, and rash were also common.

Postural orthostatic tachycardia syndrome (POTS) is one of the most prevalent presentations of orthostatic intolerance (1, 2) and is defined as an increase in heart rate of 30 beats per minute (bpm) or more within 10 minutes of standing in adults, or 40 bpm or more in children (3), typically with associated symptoms of orthostatic intolerance, and in the absence of orthostatic hypotension, prolonged bed rest, medications that impair autonomic regulation, and any debilitating disorder causing tachycardia (i.e., dehydration, anemia, or hyperthyroidism). POTS predominantly affects women (female: male ratio 4.5:1 [4]) who are relatively young (5, 6), with ages ranging from 15 to 50 years (1). The symptoms of POTS vary widely. Cerebral hypoperfusion may present with lightheadedness, blurred vision, or cognitive deterioration, while autonomic dysfunction may present as palpitations, chest pain, or neuropathy (3). Additional chronic symptoms include pain, sleep disturbances, and gastrointestinal dysfunction, which can be severe and often compromise quality of life. While some studies have reported subjective complaints in POTS patients, the extent of these comorbid symptoms remains unclear. Here, we present frequencies of symptoms involving various organ systems as reported by a cohort of POTS patients. There are multiple syndromes of orthostatic intolerance in which patients develop symptoms upon standing, but not all fulfill the diagnostic criteria of POTS (7). This heterogeneity contributes to the diagnostic and management challenges faced by patients and providers.

METHODS

Intake forms were given to 39 patients with POTS seen in the Boston Medical Center Autonomic Clinic. All patients had been diagnosed with POTS by a documented increase in heart rate of ≥30 bpm occurring within the first 10 minutes of standing or head-up tilt in the absence of orthostatic hypotension. The forms were completed from 2006 to 2014 and comprised 37 questions describing various symptoms. Patients were asked to answer "yes" or "no" according to the symptoms they experienced often. Data analysis was performed using StatPlus.

RESULTS

Baseline characteristics of 38 of the 39 patients are listed in *Table 1* (no demographic data were available for one patient). Autonomic symptoms were among the most common complaints in our population *(Table 2).* Palpitations were reported by 92% of patients. Other commonly experienced autonomic symptoms included lightheadedness with standing (87%) and worsening of symptoms in the morning (69%).

Headaches were common in POTS patients (87%). Patients reported memory problems and word-finding difficulties at a rate of 54% and 59%, respectively. About half the patients complained of tremor. Disturbances of sleep and alertness were also common, with 90% reporting fatigue; 51%, early morning awakenings; 46%, nocturnal awakenings; and 39%, insomnia. Forty-one percent of patients reported having difficulty swallowing, and 46% reported irritable bowels. Additional symptoms reported at high frequencies included sensitivity to temperature, breathing difficulties, joint pain, and loose joints.

DISCUSSION

POTS is characterized by a variety of associated symptoms. In this study, 92% of patients experienced palpitations and 77% had facial flushing or rash, supporting the theory of an increase in circulating catecholamines and a hyperadrenergic pathophysiology in these patients. The high frequency

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Table 1. Baseline characteristics of POTS patients (n = 38)*

Variable	Result
Age, mean ± SD (years)	35 ± 12
Females	34 (89%)
Body mass index, mean ± SD (kg/m^2), n = 22	25 ± 6
Age at symptom onset (years), n = 34	
<18	12 (35%)
18–25	8 (24%)
26–35	10 (29%)
>35	4 (12%)
Time to diagnosis (years), n = 26	
<1	6 (23%)
1–10	10 (38%)
>10	10 (38%)
Highest education level, n = 30	
High school	8 (27%)
Associate's degree	4 (13%)
Undergraduate degree	9 (30%)
Graduate degree	9 (30%)
Hypermobility disorders	
Ehlers-Danlos syndrome	6 (15%)
Joint hypermobility syndrome	1 (2.6%)

*n = 38 unless otherwise stated (no demographic data available for one patient).

Table 2. Symptoms reported by POTS patients (n = 39)

Symptom	Frequency
Autonomic	
Palpitations	92%
Lightheadedness	87%
Lightheadedness with standing	87%
Morning exacerbation of symptoms	69%
Lightheadedness with sitting	64%
Fainting	54%
Lightheadedness with laying	36%
Neurological	
Headache	87%
Concentration difficulty	77%
Blurry vision	69%
Word-finding difficulty	59%
Memory difficulty	54%
Tremor	49%
Sleep	
Fatigue	90%
Early morning awakenings	51%
Nighttime awakenings	46%
Insomnia	39%
Gastrointestinal	
Irritable bowel symptoms	46%
Swallowing difficulty	41%
Respiratory	
Breathing difficulty	64%
Autoimmune	
Sensitivity to hot or cold temperature	87%
Hands change color in the cold	74%
Medication sensitivity	56%
>2 medication allergies	33%
Connective tissue	
Loose joints/double-jointed	44%
Dermatological	
Facial flushing or rash	77%
Pain symptoms	
Pain	69%
Muscle cramping	69%
Joint pain	62%
Leg pain	56%
Miscellaneous	
Susceptibility to cold or infections	44%
Iron deficiency anemia	39%
Hearing loss	28%
Family history of low blood pressure	28%

of tremor further suggests sympathoexcitation. Headaches of various types, including migraine and orthostatic headaches, have been reported in POTS (5, 8–10). In this study, 87% of patients suffered from headaches.

Patients with POTS have sleep abnormalities and fatigue (11–13). Bagai et al showed that POTS patients report poor sleep quality, more daytime sleepiness, and more fatigue than healthy controls (14). Similarly, about half of our patients reported insomnia, nocturnal awakenings, and early morning awakenings, and nearly all (90%) reported fatigue. Recent studies using wrist actigraphy and polysomnography have confirmed that POTS patients have decreased sleep efficiency, increased nocturnal awakenings, and increased REM latency compared to controls (11, 15). The hyperadrenergic state present in POTS patients may account for differences in autonomic functioning during sleep, resulting in less restful sleep and subjective tiredness, but additional mechanisms such as hypovolemia and increased energy expenditure from a hyperadrenergic state may also contribute.

POTS patients often experience chronic gastrointestinal symptoms. Electrical activity of the stomach has been shown to change during upright position in children with POTS, and both increased and decreased gastric emptying has been noted as well (16, 17). Functional gastrointestinal disorders, such as irritable bowel syndrome and functional dyspepsia, are also associated with POTS, suggesting the possibility that increased variability of the gastric pacemaker rhythm and sympathetic

nervous system dysfunction in POTS can directly disturb gastrointestinal function (18).

There is still limited data on respiratory symptoms in POTS. In a study of 152 patients with POTS, 42% reported dyspnea as a common symptom (5), and 64% of our patients endorsed difficulty breathing. Del Pozzi et al showed that POTS patients have an initial increase in respiratory rate and a significant increase in minute ventilation during head-up tilt table testing compared to normal controls (19). It is thought that reduction of central blood volume secondary to peripheral pooling in POTS patients may stimulate the carotid body, resulting in sympathetic activation and hyperpnea (19).

POTS has been associated with multiple connective tissue disorders, primarily joint hypermobility syndrome and Ehlers-Danlos syndrome (EDS). Wallman et al showed the prevalence of EDS in patients with POTS (18%) is significantly higher than the suggested prevalence of EDS in the general population (0.02%) and in those with dysautonomia not meeting criteria for POTS (4%) (20). In our cohort, 15% of patients carried a diagnosis of EDS. EDS patients are also significantly more likely to be diagnosed with POTS by tilt-table testing compared to healthy controls (21). Although no cohesive mechanism exists to explain comorbid dysautonomia in hypermobility syndromes, current evidence points to multiple mechanisms, including adrenoreceptor hyperresponsiveness, molecular defects in blood vessel connective tissue, and peripheral neuropathy as likely contributors (22).

Dermatologic changes are common but rarely reported in POTS patients. A recent case report described multiple dermatologic findings in a patient with POTS, including hyperemia of the trunk and extremities and Raynaud's phenomenon (23). The author speculated that these findings can be explained by excessive vasoconstriction and hypoxia in the cutaneous vasculature secondary to imbalances in local mediators, especially increased angiotensin II and decreased nitrous oxide (23). In our study, 77% of patients reported facial flushing or rashes, likely representing hyperemia, and 74% endorsed symptoms consistent with Raynaud's phenomenon.

POTS, a common form of orthostatic intolerance seen in young females, remains poorly understood. This analysis of 39 patients at a large medical center was conducted in an attempt to better understand the heterogeneous presentations of POTS patients. Limitations of our study include a small sample size and lack of comparison to a control group. With more patients, it will be easier to differentiate between high-frequency and low-frequency symptoms. Comparison of frequency of symptoms between POTS and healthy controls would eliminate a bias towards symptoms that occur in both. The intake survey format limited interpretation of symptoms with yes-no questions and was not validated. Additional information on each symptom would be useful in terms of symptomatic treatment but also in elucidating pathophysiology. In the future, a survey with more detailed questions regarding each symptom, specifically relating to frequency and severity, would be useful.

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