AUTONOMIC DYSFUNCTION IN CHILDREN AND ADOLESCENTS: NEUROCARDIAC MECHANISMS, CLINICAL MANIFESTATIONS, AND MODERN APPROACHES TO DIAGNOSIS AND MANAGEMENT

Oramova Sevinch
sevinchoromova57@gmail.com

Solijonova Ruxshonabonu
Ruxshonasolijonova05@gmail.com

Payziyeva Nilufar
payzievanilufar1@gmail.com

Scientific supervisor: **Talipov Rustam**
PhD, Associate professor Tashkent State Medical University,
Tashkent, Republic of Uzbekistan
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Abstract

Autonomic dysfunction in children and adolescents comprises a heterogeneous group of disorders in which impaired regulation of heart rate, vascular tone, blood pressure, venous return, and cerebral perfusion produces orthostatic symptoms and functional impairment. Postural orthostatic tachycardia syndrome (POTS), vasovagal syncope, orthostatic hypotension, and other forms of orthostatic intolerance may present with dizziness, palpitations, headache, fatigue, exercise intolerance, presyncope, or syncope. Because these manifestations overlap with cardiac, neurological, hematological, endocrine, metabolic, and functional disorders, diagnosis requires a structured clinical approach. This review examines pediatric autonomic dysfunction from a neurocardiac perspective, focusing on the interaction between the autonomic nervous system, cardiovascular regulation, and cerebral hemodynamics. Current evidence concerning pediatric-specific physiology, POTS, neurally mediated syncope, orthostatic hypotension, cerebral autoregulation, possible small-fiber involvement, and post-infectious autonomic symptoms is summarized. Diagnostic strategies include detailed history and examination, supine and standing heart-rate and blood-pressure measurements, active standing testing, head-up tilt testing when indicated, electrocardiography, ambulatory monitoring, and targeted laboratory or imaging investigations. Contemporary management is centered on education, adequate fluid intake, individualized salt strategies, graded exercise and reconditioning, sleep optimization, trigger avoidance, compression measures, and treatment of relevant comorbidities. Pharmacological treatment may be considered in selected patients with persistent, functionally significant symptoms. A multidisciplinary model involving pediatrics, cardiology, neurology, rehabilitation, and psychological support can improve continuity of care. Future research should prioritize age-specific diagnostic criteria, cerebral hemodynamics, post-infectious autonomic syndromes, small-fiber neuropathy, and individualized treatment pathways.

Keywords: autonomic dysfunction; children; adolescents; postural orthostatic tachycardia syndrome; orthostatic intolerance; syncope; neurocardiac interaction; pediatric cardiology; autonomic nervous system; cerebral perfusion

1. Introduction

Autonomic regulation is essential for maintaining cardiovascular stability during standing, exercise, emotional stress, sleep, and changes in circulating volume. In childhood and adolescence, cardiovascular autonomic control develops alongside growth and pubertal maturation. Consequently, pediatric patients cannot always be evaluated using adult physiological assumptions. Recent pediatric research has demonstrated age-related differences in vascular and autonomic responses to orthostatic stress, supporting the use of pediatric-specific diagnostic frameworks [1].

Orthostatic intolerance refers to symptoms that occur or worsen in the upright position and improve after recumbency. Common manifestations include dizziness, weakness, headache, visual disturbance, palpitations, tremulousness, fatigue, nausea, cognitive difficulties, exercise intolerance, presyncope, and syncope. POTS, vasovagal syncope, and orthostatic hypotension represent clinically important phenotypes [2,3]. A 2025 review from pediatric cardiology emphasized that orthostatic intolerance and POTS are increasingly recognized during adolescence and that management should begin with careful history taking, patient education, and non-pharmacological measures [2].

The diagnostic challenge is intensified by overlap with other conditions. Tachycardia may be secondary to dehydration, anemia, infection, endocrine disease, medications, or deconditioning. Transient loss of consciousness may reflect neurally mediated syncope, but cardiac arrhythmia and structural heart disease must be considered, while seizures and metabolic disorders may mimic syncope. The 2024 revised pediatric guideline provides a structured approach incorporating history, examination, orthostatic measurements, ECG, active standing testing, head-up tilt testing, and targeted investigations [3].

The neurocardiac perspective integrates these apparently different manifestations. The brain, autonomic nervous system, heart, blood vessels, and cerebral circulation form a continuously interacting regulatory system. Failure to maintain adequate vascular resistance, cardiac output, or cerebral perfusion during upright posture may therefore produce both cardiovascular and neurological symptoms. This review summarizes current evidence on pediatric autonomic dysfunction and discusses its mechanisms, clinical phenotypes, diagnostic strategy, differential diagnosis, and multidisciplinary management.

2. Neurocardiac Regulation in the Developing Child

When a child stands, gravity causes redistribution of blood toward dependent vascular beds. A healthy response involves baroreceptor activation, increased sympathetic activity, relative parasympathetic withdrawal, peripheral vasoconstriction, and a modest increase in heart rate. These responses preserve venous return, cardiac output, arterial pressure, and cerebral perfusion.

The arterial baroreflex links changes in blood pressure to autonomic output. Stretch receptors in the carotid sinus and aortic arch transmit signals to brainstem cardiovascular centers, which regulate sympathetic and parasympathetic efferent activity. During development, autonomic responses change with age, body size, puberty, and physical conditioning. A 2025 study of children and adolescents with orthostatic syncope or presyncope found differences in orthostatic cardiovascular and cerebral autoregulatory responses compared with pediatric controls, emphasizing that children should not simply be treated as smaller adults [1].

The heart is only one component of the response. A rise in heart rate can compensate for reduced stroke volume, but excessive tachycardia may become symptomatic. Conversely, inadequate vasoconstriction or insufficient chronotropic compensation may reduce effective cerebral perfusion. This explains why patients can experience palpitations together with dizziness, visual changes, headache, or cognitive slowing.

Cerebral autoregulation is particularly relevant to the neurocardiac concept. Cerebral blood flow depends on arterial pressure, vascular resistance, carbon dioxide, and local regulatory mechanisms. A 2025 pediatric neurology review highlighted impaired cerebral autoregulation as an important physiological phenomenon in children with several neurological and systemic conditions [4]. In pediatric orthostatic disorders, earlier studies have demonstrated changes in cerebral blood-flow velocity and oxygenation during active standing [5], while newer work is examining clinically useful relationships between cardiovascular responses and cerebral oxygenation in POTS [6].

3. Major Clinical Phenotypes

1. Postural Orthostatic Tachycardia Syndrome

POTS is a chronic form of orthostatic intolerance characterized by excessive heart-rate elevation during upright posture together with compatible symptoms and without another condition that adequately explains the response. Pediatric criteria differ from adult criteria because normal heart-rate responses vary with age. The 2024 pediatric guideline defines age-specific positive orthostatic responses and requires exclusion of significant blood-pressure reduction and alternative diagnoses [3].

Symptoms include palpitations, dizziness, headache, fatigue, blurred vision, chest discomfort, tremulousness, exercise intolerance, nausea, and presyncope. Symptoms may worsen with prolonged

standing, heat, dehydration, insufficient sleep, acute illness, or physical deconditioning. Pediatric POTS is heterogeneous. Hypovolemia, impaired peripheral vasoconstriction, excessive sympathetic activation, reduced skeletal-muscle pump activity, and other mechanisms may coexist [2,7].

2. Vasovagal Syncope

Vasovagal syncope is a common neurally mediated cause of transient loss of consciousness. A reflex response leads to vasodilation, bradycardia, or both, causing transient cerebral hypoperfusion. Typical triggers include prolonged standing, emotional stress, pain, heat, crowded environments, and sudden postural changes. The 2024 guideline recognizes vasodepressor, cardioinhibitory, and mixed responses and emphasizes exclusion of cardiac and neurological mimics [3].

Although generally associated with a favorable prognosis, recurrent syncope can affect school attendance, physical activity, confidence, and quality of life. Recognition of prodromal symptoms, trigger avoidance, physical counter-pressure maneuvers, and individualized education are therefore clinically important.

3. Orthostatic Hypotension and Broader Orthostatic Intolerance

Orthostatic hypotension is characterized by a significant blood-pressure decrease after standing. It can accompany dehydration, medication effects, autonomic neuropathy, endocrine disorders, acute illness, or other systemic conditions. Orthostatic intolerance is broader and may occur without meeting blood-pressure criteria for orthostatic hypotension.

Phenotypes can overlap or change over time. Symptoms may vary with hydration, illness, sleep, conditioning, and developmental stage. Consequently, one abnormal heart-rate or blood-pressure measurement should be interpreted in the context of symptoms and repeated clinical assessment.

4. Pathophysiological Mechanisms

Current evidence supports a multifactorial model rather than a single mechanism. Relative hypovolemia may reduce stroke volume and increase compensatory tachycardia. Inadequate peripheral vasoconstriction can promote venous pooling and reduce effective venous return. Excessive sympathetic activation may contribute to tachycardia, sweating, tremulousness, and palpitations. Reduced physical conditioning can further impair the skeletal-muscle pump and cardiovascular tolerance [2,7].

Cerebral hemodynamics may provide an additional explanation for neurological symptoms. During orthostatic stress, cerebral blood-flow velocity and oxygenation can change even when systemic blood pressure appears relatively preserved. Pediatric studies have reported altered cerebral oxygenation in POTS and neurally mediated syncope [5], and a recent cross-sectional study specifically investigated cardiovascular and cerebral oxygenation predictors of visual darkening in pediatric POTS [6]. These findings support a model in which symptoms are not caused by heart-rate elevation alone.

Small-fiber dysfunction is another emerging area. A 2024 retrospective study of children, adolescents, and young adults with chronic orthostatic intolerance or POTS and neuropathic symptoms investigated epidermal nerve-fiber density and inflammatory or autoimmune markers [8]. Such findings are hypothesis-generating rather than proof of a universal mechanism, but they may help explain heterogeneity and identify future therapeutic targets.

Post-infectious autonomic disturbance has also attracted increasing attention. Pediatric long COVID studies have identified orthostatic intolerance as a clinically relevant phenotype. In one 2025 study of 92 children with long COVID who underwent a passive standing test, 71% met criteria for an orthostatic condition, including POTS, orthostatic tachycardia, orthostatic hypotension, delayed hypotension, or orthostatic hypertension [9]. These data support clinical screening in appropriately selected patients but do not establish that infection is the cause of every pediatric autonomic disorder.

5. Clinical Manifestations and Comorbidities

The symptom spectrum is multisystemic. Cardiovascular manifestations include palpitations, tachycardia, chest discomfort, presyncope, and syncope. Neurological manifestations include dizziness, headache, visual disturbance, cognitive difficulties, and subjective brain fog. General symptoms include fatigue, weakness, reduced exercise tolerance, and sleep disturbance.

Gastrointestinal symptoms may include nausea, abdominal discomfort, altered bowel habits, and reduced oral intake. These symptoms can worsen volume depletion and make dietary management more difficult. The 2024 pediatric syncope guideline also notes associations with migraine, sleep disorders,

mental-health conditions, chronic fatigue, joint hypermobility, and gastrointestinal disorders [3]. Such associations should be interpreted clinically and should not be assumed to prove a common cause.

Functional impairment deserves explicit attention. Adolescents with POTS or chronic orthostatic intolerance may experience limitations in school participation, exercise, and social activities. Therefore, outcome assessment should include functional status and quality of life rather than relying only on heart-rate criteria.

6. Differential Diagnosis

The differential diagnosis of dizziness, palpitations, presyncope, and syncope should be systematic. Cardiac causes include arrhythmias and structural heart disease. Warning features include exertional syncope, syncope without prodrome, abnormal ECG, concerning family history, or symptoms strongly suggestive of cardiac disease.

Neurological causes include epileptic seizures and selected disorders associated with altered consciousness. Other mimics include anemia or iron deficiency, dehydration, hypoglycemia, thyroid disease, electrolyte abnormalities, medication effects, and functional neurological or psychological conditions.

The 2024 guideline stresses that cardiac syncope is less common than neurally mediated syncope but can carry a high risk of adverse outcomes. It also emphasizes differentiation from epilepsy, metabolic disorders, and psychological pseudosyncope [3]. A diagnosis of autonomic dysfunction should therefore follow appropriate clinical assessment rather than be used as a default explanation for unexplained symptoms.

7. Diagnostic Approach

Diagnosis begins with a detailed history. The clinician should document posture at onset, duration, triggers, prodrome, recovery, hydration, sleep, physical activity, recent infections, medication and substance exposure, menstrual factors when relevant, and family history of arrhythmia or sudden cardiac death. Physical examination should include supine and upright heart rate and blood pressure and an assessment for cardiac or neurological abnormalities.

Active standing testing is a practical tool for assessing orthostatic responses. The 2024 pediatric guideline recommends standardized supine measurements followed by upright monitoring, generally for 10 minutes, while observing symptoms and changes in heart rate, blood pressure, and ECG [3]. Head-up tilt testing may be useful in selected cases when the diagnosis remains uncertain or formal autonomic evaluation is required.

Electrocardiography is important when syncope or palpitations raise concern for cardiac disease. Ambulatory ECG monitoring can be considered when intermittent arrhythmia is suspected. Echocardiography and exercise testing are targeted to patients with findings that suggest structural or exertional cardiac disease rather than performed indiscriminately in every patient with orthostatic symptoms [3].

Laboratory testing should be individualized. Depending on the presentation, clinicians may consider complete blood count, ferritin or iron studies, glucose, electrolytes, renal function, or thyroid testing. Neurological investigations are indicated when the history suggests seizure or another neurological disorder. This targeted approach helps avoid both under-investigation of important disease and excessive testing of benign orthostatic syndromes.

8. Modern Management

Contemporary pediatric reviews consistently place education and non-pharmacological management at the center of care [2,7]. Families should receive a clear explanation of the condition, expected triggers, warning symptoms, and the rationale for daily management. Adequate fluid intake is important when low intake or relative hypovolemia contributes to symptoms. Increased dietary sodium may be appropriate for selected patients after consideration of blood pressure, renal status, and other contraindications [3,7].

Physical reconditioning is a major component of treatment. A gradual exercise program may begin with recumbent or semi-recumbent activity and progress toward upright endurance and resistance exercise as tolerated. The aim is to improve cardiovascular conditioning and orthostatic tolerance rather than simply suppress the heart-rate response. Sleep regularity, adequate nutrition, avoidance of prolonged inactivity, and trigger management are also important.

Compression garments can reduce venous pooling in selected patients. Counter-pressure maneuvers, such as leg crossing and muscle tensing, may be useful when prodromal symptoms occur. School accommodations may include access to fluids, permission to change position, reduced prolonged standing, and a gradual return to physical activity when symptoms are severe.

Pharmacological treatment may be considered when symptoms remain functionally significant despite appropriate

non-pharmacological measures. Pediatric evidence remains more limited than adult evidence. A 2024 clinical review describes studied options including ivabradine, beta-blockers, midodrine, pyridostigmine, fludrocortisone, and intravenous fluids, while emphasizing that non-pharmacological interventions should be attempted first [7]. Medication selection should be individualized and supervised by clinicians experienced in pediatric autonomic disorders.

9. Multidisciplinary Care and Rehabilitation

The multisystem nature of autonomic dysfunction supports coordinated care. Pediatricians can provide initial assessment and longitudinal follow-up. Pediatric cardiology is particularly important when syncope, palpitations, abnormal ECG findings, exertional symptoms, or suspected structural or electrical disease are present. Neurology may be involved when seizure, focal neurological symptoms, severe headache syndromes, or other neurological diagnoses are suspected. Rehabilitation specialists can design graded exercise programs, while psychological support can address coping, sleep, anxiety, school reintegration, and functional impairment when clinically relevant.

A multidisciplinary approach should not imply that symptoms are primarily psychological. Contemporary pediatric literature emphasizes that anxiety and depressed mood may exacerbate symptom burden without being the central cause of orthostatic physiology [2]. Appropriate psychological support should therefore complement, rather than replace, medical assessment and rehabilitation.

10. Emerging Research Directions

Future research is likely to focus on four interconnected areas. First, pediatric-specific autonomic and cerebral hemodynamic markers may improve phenotyping and explain why similar heart-rate responses produce different symptoms. Second, post-infectious autonomic syndromes, including long COVID, may clarify relationships among inflammation, vascular function, and autonomic regulation [9]. Third, small-fiber neuropathy and immune mechanisms may identify subgroups of patients with distinct pathophysiology [8]. Fourth, patient-reported outcomes and functional measures should be integrated into clinical trials so that treatment success is assessed by participation and quality of life as well as physiological parameters.

Standardization is particularly important. Children undergo major physiological changes during growth and puberty, and diagnostic thresholds may need to account for age, sex, height, developmental stage, and baseline cardiovascular status. Large prospective pediatric studies are needed to validate diagnostic criteria, compare interventions, and establish long-term outcomes.

11. Discussion

The available evidence supports viewing pediatric autonomic dysfunction as a disorder of integrated physiological regulation rather than as an isolated cardiovascular problem. The interaction among autonomic neural pathways, vascular tone, venous return, cardiac output, and cerebral perfusion explains why a child may simultaneously experience tachycardia, dizziness, headache, fatigue, gastrointestinal symptoms, and exercise intolerance.

However, a broad neurocardiac framework must not lead to overdiagnosis. The diagnosis should remain clinically disciplined: important cardiac, neurological, hematological, endocrine, metabolic, and medication-related causes must be considered when indicated. The 2024 pediatric guideline provides a practical structure for this process and emphasizes age-specific orthostatic testing and individualized treatment [3].

The evidence base still has limitations. Many pediatric studies are observational, sample sizes are modest, and treatment studies are less numerous than adult studies. Nevertheless, recent publications from pediatric cardiology, neurology, rehabilitation, and autonomic medicine are increasingly converging on a multidisciplinary model. This convergence is particularly relevant for adolescents whose symptoms cross traditional specialty boundaries.

12. Conclusion

Autonomic dysfunction in children and adolescents represents a heterogeneous group of conditions involving the interaction of the autonomic nervous system, cardiovascular regulation, vascular tone, and cerebral perfusion.

POTS, vasovagal syncope, orthostatic hypotension, and broader orthostatic intolerance can produce overlapping cardiovascular and neurological symptoms and may substantially affect school participation, physical activity, and quality of life.

A neurocardiac perspective provides a useful framework for integrating pediatric, cardiological, neurological, and rehabilitative care. Diagnosis should be based on careful history and examination, appropriate orthostatic assessment, ECG when indicated, and targeted investigation of alternative diagnoses. Current management emphasizes education, individualized hydration and sodium strategies, graded physical reconditioning, sleep optimization, trigger avoidance, compression measures, and treatment of comorbidities, with pharmacological therapy reserved for selected patients.

Future research should prioritize standardized pediatric diagnostic criteria, cerebral hemodynamics, post-infectious autonomic syndromes, small-fiber neuropathy, gastrointestinal comorbidity, and individualized treatment pathways. Better integration of these fields may improve recognition of pediatric autonomic disorders and reduce fragmented care.

References

1. Lucci V-E M, Protheroe C-L, Albaro C-A, et al. Autonomic responses in children and adolescents with orthostatic syncope and presyncope: children are not small adults. Autonomic Neuroscience. 2025;262:103340. doi:10.1016/j.autneu.2025.103340.
2. Hebson C, Harberg M, Borasino P. Pediatric orthostatic intolerance—A review with focus on recent research. Current Opinion in Pediatrics. 2025;37(4):342-349. doi:10.1097/MOP.0000000000001469.
3. Wang C, Li Y, Liao Y, et al. Guidelines for the diagnosis and treatment of neurally mediated syncope in children and adolescents (revised 2024). World Journal of Pediatrics. 2024;20(10):983-1002. doi:10.1007/s12519-024-00819-w.
4. Castillo-Pinto C, Yu P, Wainwright MS, Kirschen MP. Impaired Cerebral Autoregulation in Children. Pediatric Neurology. 2025;167:9-16. doi:10.1016/j.pediatrneurol.2025.03.003.
5. Changes in cerebral blood oxygenation induced by active standing test in children with POTS and NMS. PubMed-indexed pediatric study. 2014.
6. Hemodynamic and cerebral oxygenation predictors of visual darkening in pediatric POTS: a cross-sectional study. Journal of Clinical Monitoring and Computing. 2025. doi:10.1007/s10286-025-01169-x.
7. Huynh P, Brown A, Campisi L, et al. Management of Postural Orthostatic Tachycardia Syndrome in Pediatric Patients: A Clinical Review. Journal of Pediatric Pharmacology and Therapeutics. 2024;29(5):456-467. doi:10.5863/1551-6776-29.5.456.
8. Moak JP, Ramwell CB, Gordish-Dressman H, et al. Small fiber neuropathy in children, adolescents, and young adults with chronic orthostatic intolerance and postural orthostatic tachycardia syndrome: A retrospective study. Autonomic Neuroscience. 2024;253:103163. doi:10.1016/j.autneu.2024.103163.
9. Morrow AK, Villatoro C, Kokorelis C, Rowe PC, Malone LA. Orthostatic Intolerance in Children With Long COVID Utilizing a 10-Minute Passive Standing Test. Clinical Pediatrics. 2025;64(3):416-424. doi:10.1177/00099228241272053.
10. Kakavand M, et al. Association Between COVID-19 and Orthostatic Intolerance in Children: A Retrospective Study. Cureus. 2024. PMID:39741599.