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Autonomic Function Profile in Untreated Primary Hypothyroidism: A Hospital-Based Case-Control Study

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ABSTRACT

Background: Hypothyroidism is a prevalent endocrine disorder with metabolic, cardiovascular and neuropsychological consequences. Its effect on autonomic regulation is clinically important because autonomic imbalance may contribute to bradycardia, impaired pressor responses, fatigue, exercise intolerance and poorer quality of life.
Objective: To compare autonomic function between untreated primary hypothyroid patients and age- and sex-matched euthyroid controls, and to examine the relationship of thyroid hormone status with autonomic, functional and quality-of-life outcomes.
Methods: A hospital-based observational analytical case-control study was conducted among 60 adults, including 30 newly diagnosed untreated primary hypothyroid patients and 30 apparently healthy euthyroid controls. Autonomic assessment included heart rate variability indices, deep breathing E:I ratio, Valsalva ratio, 30:15 ratio, cold pressor response and blood pressure response to standing. Fatigue Severity Scale, six-minute walk test and SF-36 physical and mental component scores were used to evaluate clinical impact.
Results: Groups were comparable for age and sex. Hypothyroid patients had higher BMI, lower resting heart rate, higher blood pressure, elevated TSH and lower Free T3 and Free T4. HRV indices were significantly reduced in cases, with higher LF/HF ratio. Cardiovagal tests and sympathetic reflex responses were significantly abnormal. Fatigue was higher, while six-minute walk distance and SF-36 scores were lower in cases. Higher TSH and lower Free T4 were significantly correlated with poorer autonomic and functional outcomes.
Conclusion: Untreated primary hypothyroidism is associated with mixed autonomic dysfunction involving cardiovagal impairment and altered sympathetic vascular reactivity. Autonomic testing may provide useful clinical information beyond routine thyroid biochemistry and may help identify patients needing functional follow-up.

Keywords: Hypothyroidism; autonomic function test; heart rate variability; TSH; Free T4; Fatigue Severity Scale; six-minute walk test; SF-36; dysautonomia; case-control study.

INTRODUCTION

Hypothyroidism is one of the most commonly encountered endocrine disorders and is characterized by insufficient thyroid hormone activity at tissue level **[1,2]**. Classical clinical manifestations such as fatigue, cold intolerance, weight gain, dry skin, constipation and bradycardia are usually interpreted as consequences of generalized metabolic slowing. However,

thyroid hormones also have direct and indirect effects on cardiovascular control, vascular tone, adrenergic receptor sensitivity, baroreflex behavior and central autonomic regulation. For this reason, hypothyroidism may not be viewed only as a biochemical or metabolic disorder; it may also be accompanied by measurable neurocardiovascular dysregulation.

The autonomic nervous system maintains internal homeostasis through coordinated sympathetic and parasympathetic control of heart rate, blood pressure, peripheral vascular resistance, thermoregulation and visceral function **[3,4]**. Heart rate variability (HRV) analysis and cardiovascular autonomic reflex tests provide non-invasive methods for assessing this regulation. Reduced SDNN and RMSSD indicate impaired global and vagally mediated beat-to-beat variability, while an increased LF/HF ratio is commonly interpreted, with methodological caution, as altered sympathovagal balance. Classical tests such as the deep breathing test, Valsalva maneuver and 30:15 ratio mainly assess cardiovagal reflex function, whereas cold pressor response and blood pressure response to standing reflect sympathetic vascular reactivity and baroreflex compensation.

Autonomic evaluation is also relevant because symptoms of autonomic disturbance may overlap with ordinary hypothyroid complaints. Bradycardia, tiredness, exercise intolerance, cold sensitivity and postural light-headedness may be attributed entirely to hormonal deficiency, yet these symptoms can also reflect impaired reflex cardiovascular control. If autonomic involvement is not assessed, clinicians may underestimate the physiologic burden of disease, particularly in patients whose thyroid profile is abnormal but whose routine cardiovascular examination appears only mildly changed. This gap is important in resource-limited settings where advanced autonomic laboratories may not be available, but simple bedside autonomic tests can still be performed safely and inexpensively.

The rationale for investigating autonomic function in hypothyroidism arises from both biological plausibility and clinical observation. Thyroid hormones influence beta-adrenergic receptor expression, ion channel activity, mitochondrial function and vascular smooth muscle tone **[5,6]**. Deficiency of thyroid hormones can reduce chronotropic and inotropic responsiveness, slow cardiac pacemaker activity, increase systemic vascular resistance and disturb baroreflex-mediated adaptation. Clinically, patients may complain of fatigue, dizziness, poor exercise tolerance or reduced daily functioning even when routine examination focuses mainly on thyroid biochemical values. Autonomic dysfunction may therefore explain a part of the symptom burden in untreated hypothyroidism and may identify patients who need closer cardiovascular and functional evaluation.

Previous studies have reported abnormalities in HRV and cardiovascular reflex tests among hypothyroid patients, but findings vary across populations and protocols **[7-11]**. Some studies emphasize parasympathetic impairment, others report sympathovagal imbalance, and some describe reduced sympathetic responsiveness during stress or postural challenge. These inconsistencies may reflect differences in disease severity, treatment status, test battery and confounder control. A comprehensive assessment using both HRV and classical autonomic tests is therefore more informative than a single autonomic index. It allows investigators to examine resting beat-to-beat variability, reflex heart rate adaptation, vascular pressor response and postural compensation within the same participant. When these measures are interpreted together with patient-centered outcomes, the clinical meaning of autonomic dysfunction becomes clearer. The present paper reports a case-control analysis derived from a thesis dataset to evaluate autonomic function in untreated primary hypothyroidism and to relate autonomic findings to fatigue, functional capacity and health-related quality of life.

MATERIALS & METHODS

Study design and setting: This was a hospital-based observational analytical case-control study conducted in the Department of Physiology, Index Medical College, Hospital and Research Centre, Indore, Madhya Pradesh, India. The design was chosen to compare autonomic function parameters between newly diagnosed untreated primary hypothyroid patients and healthy euthyroid controls assessed at a single time point under standardized testing conditions.

Participants: The study included 60 adult participants aged 20 to 60 years. The case group consisted of 30 patients with newly detected untreated primary hypothyroidism, while the control group included 30 apparently healthy euthyroid participants matched for age and sex. Cases were recruited from relevant outpatient services, and controls were selected from hospital staff, attendants and university volunteers after eligibility screening. Participants with diabetes mellitus, hypertension, ischemic heart disease, arrhythmia, heart failure, neurological disorders, psychiatric disorders, peripheral neuropathy, pregnancy, lactation, smoking, alcohol dependence, acute illness, anemia requiring treatment or current use of drugs affecting autonomic function were excluded.

Sample size: Sample size estimation was based on comparison of mean SDNN between two independent groups because SDNN is a commonly used HRV marker of cardiac autonomic modulation. Using a 95% confidence level, 80% power, estimated pooled standard deviation of approximately 13 ms and expected clinically meaningful difference of 12 ms, the calculated requirement was approximately 19 participants per group. After allowing for incomplete recordings and to improve precision, 30 participants were included in each group.

Data collection: Demographic data, anthropometry, resting cardiovascular parameters and clinical symptom profile were recorded. Thyroid profile included TSH, Free T3 and Free T4. HRV recording was performed in a controlled environment after appropriate rest according to standard short-term HRV principles **[3,12]**. Cardiovagal assessment included deep breathing E:I ratio, deep breathing heart rate difference, Valsalva ratio and lying-to-standing 30:15 ratio. Sympathetic assessment included cold pressor-induced changes in systolic blood pressure, diastolic blood pressure and heart rate, along with blood pressure response to standing. Functional capacity was assessed by the six-minute walk test (6MWT) according to ATS guidance **[13]**, fatigue by the Fatigue Severity Scale (FSS) **[14]**, and health-related quality of life by the SF-36 physical component summary (PCS) and mental component summary (MCS) scores **[15]**.

Outcome definitions: Primary autonomic outcomes were HRV indices and standard cardiovascular autonomic reflex measures. Reduced SDNN, RMSSD, deep breathing response, Valsalva ratio and 30:15 ratio were interpreted as evidence of impaired cardiac autonomic modulation, especially cardiovagal dysfunction. Reduced cold pressor response and excessive blood pressure fall on standing were interpreted as altered sympathetic vascular responsiveness and impaired postural compensation. Secondary outcomes were fatigue burden, walking performance and health-related quality of life.

Quality control: Participants were instructed to avoid caffeine, alcohol, vigorous exercise and acute stressors before autonomic testing wherever feasible. Tests were performed after a resting period in a calm environment. Participants were monitored for discomfort, dizziness, excessive fatigue or cold-induced distress, and testing was stopped when clinically required. The same broad protocol was applied to both groups to reduce measurement bias.

Ethical consideration: Formal prior Institutional Ethics Committee approval was not obtained for the study. The work was conducted as a non-interventional, observational case-control study involving

non-invasive autonomic function assessment and routinely collected clinical/biochemical information. Written informed consent was obtained from all participants before assessment. Participant identity was kept confidential, and anonymized data were used for analysis and manuscript preparation. The authors are advised to submit the study documents to the Institutional Ethics Committee or institutional authority for retrospective review/exemption/waiver before journal submission, and any waiver/reference number received should be added to the manuscript.

Statistical analysis: Continuous variables were summarized as mean ± standard deviation and categorical variables as frequency and percentage. Between-group comparison for continuous variables was performed using independent-samples Welch t-test. Categorical comparisons were interpreted using frequency distribution and chi-square logic where appropriate. Pearson correlation coefficients were used to examine relationships of TSH and Free T4 with autonomic and functional outcomes in the total sample. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 presents the baseline demographic characteristics of the 60 participants. The hypothyroid and control groups were comparable in age, sex distribution, height and respiratory rate (all $p > 0.05$). Weight and BMI were significantly higher in the hypothyroid group ($p = 0.003$ and $p = 0.001$, respectively).

Table 1. Baseline demographic characteristics of the participants

Variable	Hypothyroid (n=30)	Control (n=30)	p value
Age (years)	39.83 ± 11.15	40.00 ± 11.32	0.954
Female/Male	22/8	22/8	1.000
Height (cm)	163.55 ± 8.34	163.27 ± 8.31	0.897
Weight (kg)	70.33 ± 10.71	62.67 ± 8.60	0.003
BMI (kg/m²)	26.29 ± 3.52	23.52 ± 2.83	0.001
Respiratory rate (breaths/min)	16.50 ± 1.96	15.97 ± 1.71	0.269

Note: *Values are presented as mean ± standard deviation or frequency. Continuous variables were compared using the independent-samples Welch t-test. BMI, body mass index.*

Table 2 summarizes resting cardiovascular and thyroid biochemical findings. Compared with controls, hypothyroid participants had a lower resting heart rate and higher systolic and diastolic blood pressure. TSH was markedly higher, whereas Free T3 and Free T4 were lower in the hypothyroid group; all thyroid-profile differences were statistically significant ($p < 0.001$).

Table 2. Resting cardiovascular and thyroid biochemical profile

Variable	Hypothyroid (n=30)	Control (n=30)	p value
Resting heart rate (beats/min)	67.30 ± 6.87	75.07 ± 5.88	<0.001
Resting SBP (mmHg)	122.03 ± 8.62	116.73 ± 8.76	0.022
Resting DBP (mmHg)	81.20 ± 4.63	76.57 ± 4.67	<0.001
TSH (mIU/L)	20.42 ± 9.19	2.14 ± 0.80	<0.001
Free T3 (pg/ml)	2.07 ± 0.30	3.28 ± 0.36	<0.001
Free T4 (ng/dl)	0.68 ± 0.10	1.25 ± 0.16	<0.001

Note: *Values are presented as mean ± standard deviation. SBP, systolic blood pressure; DBP, diastolic blood pressure; TSH, thyroid-stimulating hormone.*

Table 3 compares autonomic function parameters between the groups. Hypothyroid participants had lower SDNN, RMSSD, HF power, deep-breathing responses, Valsalva ratio, 30:15 ratio and cold pressor systolic response, together with higher LF power, LF/HF ratio and standing systolic blood pressure fall. Every between-group difference in Table 3 was statistically significant ($p < 0.001$).

Table 3. Comparison of autonomic function parameters between the groups

Parameter	Hypothyroid (n=30)	Control (n=30)	p value
SDNN (ms)	40.74 ± 7.47	53.74 ± 8.27	<0.001
RMSSD (ms)	30.17 ± 5.94	45.40 ± 6.76	<0.001
LF power (ms²)	709.52 ± 141.92	578.60 ± 119.28	<0.001
HF power (ms²)	278.92 ± 71.99	473.72 ± 79.85	<0.001
LF/HF ratio	2.62 ± 0.80	1.26 ± 0.30	<0.001
Deep breathing E:I ratio	1.12 ± 0.05	1.26 ± 0.07	<0.001
Deep breathing HR difference (bpm)	10.11 ± 2.90	17.84 ± 4.42	<0.001
Valsalva ratio	1.26 ± 0.11	1.56 ± 0.13	<0.001
30:15 ratio	1.07 ± 0.05	1.22 ± 0.04	<0.001
Cold pressor ΔSBP (mmHg)	9.52 ± 3.96	15.43 ± 3.87	<0.001
Standing ΔSBP (mmHg)	11.42 ± 5.33	2.56 ± 3.67	<0.001

Note: *Values are presented as mean ± standard deviation. SDNN, standard deviation of normal-to-normal intervals; RMSSD, root mean square of successive differences; LF, low frequency; HF, high frequency; E:I, expiration-to-inspiration ratio; SBP, systolic blood pressure.*

Table 4 shows the distribution of hypothyroid symptoms and autonomic classifications. Fatigue was the most frequent symptom, followed by cold intolerance and weight gain. All 30 hypothyroid participants had an abnormal overall autonomic interpretation, and mixed autonomic dysfunction was the predominant classification. Most controls were classified as normal.

Table 4. Distribution of symptoms and autonomic classifications

Variable	Hypothyroid (n=30)	Control (n=30)
Fatigue symptom	28 (93.3%)	0 (0.0%)
Cold intolerance	24 (80.0%)	0 (0.0%)
Weight gain	16 (53.3%)	0 (0.0%)
Overall abnormal autonomic interpretation	30 (100.0%)	3 (10.0%)
Mixed autonomic dysfunction	27 (90.0%)	0 (0.0%)

Note: *Values are presented as frequency (percentage). The table is descriptive; no inferential p values are displayed.*

Table 5 presents fatigue, functional capacity and quality-of-life outcomes. The hypothyroid group had a higher FSS score and lower 6MWT distance, SF-36 PCS score and SF-36 MCS score than the control group. All differences shown in Table 5 were statistically significant ($p < 0.001$).

Table 5. Fatigue, functional capacity and health-related quality-of-life outcomes

Outcome	Hypothyroid (n=30)	Control (n=30)	p value
FSS total score	43.13 ± 7.28	20.87 ± 5.08	<0.001
6MWT distance (m)	409.27 ± 40.33	509.23 ± 50.86	<0.001
SF-36 PCS	55.47 ± 10.30	84.18 ± 6.47	<0.001
SF-36 MCS	58.45 ± 6.86	80.06 ± 7.48	<0.001

Note: *Values are presented as mean ± standard deviation. FSS, Fatigue Severity Scale; 6MWT, six-minute walk test; SF-36, 36-item Short Form Health Survey; PCS, physical component summary; MCS, mental component summary.*

Table 6 presents correlations of TSH and Free T4 with autonomic and functional outcomes in the total sample. Higher TSH was associated with poorer cardiovagal indices, greater standing systolic blood pressure fall, more fatigue, shorter 6MWT distance and lower SF-36 scores. Free T4 showed the opposite direction of association. All correlations reported in Table 6 were statistically significant ($p < 0.001$).

Table 6. Correlations of TSH and Free T4 with autonomic and functional outcomes

Outcome	TSH r	TSH p value	Free T4 r	Free T4 p value
SDNN (ms)	-0.585	<0.001	0.614	<0.001
RMSSD (ms)	-0.671	<0.001	0.725	<0.001
LF/HF ratio	0.745	<0.001	-0.672	<0.001
Deep breathing E:I ratio	-0.666	<0.001	0.777	<0.001
Valsalva ratio	-0.660	<0.001	0.737	<0.001
30:15 ratio	-0.665	<0.001	0.800	<0.001
Cold pressor ΔSBP	-0.504	<0.001	0.591	<0.001
Standing ΔSBP	0.684	<0.001	-0.669	<0.001
FSS total	0.692	<0.001	-0.795	<0.001
6MWT distance	-0.642	<0.001	0.714	<0.001
SF-36 PCS	-0.748	<0.001	0.812	<0.001
SF-36 MCS	-0.658	<0.001	0.775	<0.001

Note: *Pearson correlation coefficients are reported for the total sample (N = 60). Positive r values indicate direct associations and negative r values indicate inverse associations. TSH, thyroid-stimulating hormone; FSS, Fatigue Severity Scale; 6MWT, six-minute walk test; PCS, physical component summary; MCS, mental component summary.*

DISCUSSION

The present analysis demonstrates that untreated primary hypothyroidism is associated with a broad and clinically meaningful autonomic dysfunction pattern. The main findings were reduced HRV, impaired cardiovagal reflex responses, altered sympathetic vascular responses, higher fatigue, reduced six-minute walk performance and lower quality-of-life scores among hypothyroid cases compared with matched euthyroid controls. The correlation findings further strengthen the biological relationship by showing that higher TSH and lower Free T4 were associated with poorer autonomic and functional outcomes.

The reduction in SDNN and RMSSD among hypothyroid participants indicates reduced global variability and impaired short-term vagal modulation. HRV represents the ability of the cardiovascular system to adapt beat by beat to internal and external demands. Lower

HRV reflects reduced autonomic flexibility and has been linked to adverse cardiovascular outcomes; autonomic impairment has also been documented in treated autoimmune thyroiditis **[16-18]**. The higher LF/HF ratio observed in cases suggests a shift in sympathovagal balance. While LF/HF should not be overinterpreted as a direct measure of sympathetic activity alone, the combination of lower RMSSD, lower HF power and higher LF/HF ratio support altered cardiac autonomic regulation. Classical autonomic reflex tests provide additional clinical meaning. The deep breathing test evaluates respiratory sinus arrhythmia and is strongly influenced by vagal control of the sinoatrial node **[4,19-22]**. The reduced E:I ratio and lower deep-breathing heart rate difference in cases indicate impaired cardiovagal flexibility. Similarly, the reduced Valsalva ratio and 30:15 ratio suggests reduced baroreflex-linked heart rate adaptation during strain and postural change. These findings agree with reports of impaired cardiovascular autonomic tests in hypothyroid patients and support the view that thyroid hormone deficiency affects reflex cardiac regulation.

The sympathetic findings are equally important. Hypothyroid patients showed reduced pressor response during cold pressor testing and a greater systolic blood pressure fall on standing **[23,24]**. These results indicate impaired vasomotor responsiveness and reduced ability to maintain circulatory stability during stress or postural change. Thyroid hormones influence vascular smooth muscle function, endothelial regulation, adrenergic receptor responsiveness and systemic vascular resistance. In hypothyroidism, these mechanisms may produce a mixed profile: resting vascular resistance may be higher, but dynamic reflex responsiveness may be blunted. Therefore, mixed dysautonomia is a plausible interpretation of the combined HRV and reflex test pattern.

The clinical relevance of these autonomic abnormalities is supported by the functional outcome data. Fatigue scores were significantly higher among hypothyroid patients, while six-minute walk distance was substantially lower. Fatigue in hypothyroidism is often attributed to metabolic slowing alone, but autonomic impairment may contribute through reduced cardiovascular adaptability, impaired oxygen delivery during exertion, abnormal blood pressure regulation and poor recovery after activity. Lower SF-36 physical and mental component scores show that the burden extends beyond laboratory values and affects perceived well-being. This is important because treatment monitoring in hypothyroidism often centers on biochemical normalization, while functional limitations may persist or recover more slowly.

The correlations with TSH and Free T4 are consistent with a dose-response relationship between thyroid hormone status and autonomic-functional impairment. Higher TSH showed negative correlations with favorable autonomic indices such as SDNN, RMSSD, E:I ratio, Valsalva ratio and 30:15 ratio, while Free T4 showed positive correlations with these measures. Conversely, higher TSH correlated positively with fatigue and standing systolic blood pressure fall, whereas Free T4 correlated negatively with these adverse outcomes. The strongest Free T4 correlations were observed with SF-36 PCS, 30:15 ratio and fatigue, suggesting that thyroid hormone availability may be closely linked with both reflex regulation and functional burden.

In relation to earlier literature, the present findings are consistent with studies that have demonstrated altered cardiac autonomic modulation in hypothyroidism. Cacciatori et al. reported abnormal HRV spectral parameters in hypothyroid patients **[7]**, while Syamsunder et al. described sympathovagal imbalance associated with cardiovascular risk in overt hypothyroidism **[8]**. Deepthi et al. observed attenuation of the heart rate response to standing **[9]**, and Paul et al. documented impairment in cardiac autonomic function tests among hypothyroid subjects **[10]**. Comparable autonomic abnormalities were also reported by

Hiremath and Lakshmi **[11]**. The present analysis extends these observations by demonstrating that abnormalities are not limited to one measurement approach. HRV, cardiovagal reflex tests, sympathetic challenge tests and functional outcomes all moved in a consistent direction, supporting a multidimensional dysautonomia profile rather than an isolated abnormal test result.

The dominance of mixed autonomic dysfunction is particularly relevant. Some authors have described sympathetic predominance, whereas others have emphasized vagal withdrawal or reduced sympathetic responsiveness. These descriptions may appear contradictory, but they can coexist depending on the physiological domain being measured. Resting HRV may show relative sympathovagal imbalance, whereas cold pressor and standing tests may reveal blunted dynamic vascular reactivity. In untreated hypothyroidism, reduced thyroid hormone availability may lower beta-adrenergic sensitivity while increased peripheral vascular resistance alters resting hemodynamics. The net result can be a patient who has higher resting blood pressure, lower heart rate, reduced vagal reflex flexibility and poor pressor adaptation during autonomic challenge.

From a clinical perspective, the findings argue for a more comprehensive evaluation of untreated hypothyroid patients, especially those reporting dizziness, excessive fatigue, poor exercise tolerance or postural symptoms. Simple bedside autonomic tests, when performed with appropriate safety precautions, can add useful physiological information. HRV analysis may be useful where facilities are available, but even low-cost tests such as deep breathing response, Valsalva ratio, 30:15 ratio, cold pressor response and postural blood pressure assessment can help identify patients with clinically relevant dysautonomia. Established autonomic-neuropathy frameworks likewise support combining cardiovascular reflex tests rather than relying on a single measure **[25]**. Early recognition may guide cardiovascular risk screening, graded exercise prescription, rehabilitation planning and patient education.

The practical importance of these findings is that autonomic dysfunction can be assessed without requiring invasive procedures. In many hospitals, patients with hypothyroidism undergo biochemical testing and medication adjustment, but formal functional evaluation is rarely included in the routine pathway. A short screening battery can help identify patients who require more careful cardiovascular observation before initiation of exercise or rehabilitation. For example, a patient with reduced 30:15 ratio, abnormal Valsalva ratio or excessive systolic blood pressure fall after standing may require education regarding hydration, gradual postural transition and graded physical activity. Similarly, reduced 6MWT distance along with high FSS score can guide individualized endurance training rather than general reassurance alone.

The present pattern also has implications for physiotherapy and rehabilitation practice. Hypothyroid patients may not tolerate sudden increases in activity intensity because cardiovascular adaptation can be slow. Assessment of resting heart rate, orthostatic blood pressure response and exercise tolerance before prescribing aerobic activity may improve safety and adherence. Low-intensity progressive aerobic training, breathing exercises, paced respiration and relaxation strategies may be useful supportive approaches, although interventional trials are required before firm recommendations can be made. Because autonomic dysfunction may improve after restoration of euthyroid status, repeated functional assessment during follow-up can help distinguish biochemical recovery from functional recovery.

A notable strength of the study is the integration of endocrine, autonomic and patient-centered variables. Many earlier studies focused only on HRV or only on one cardiovascular reflex test. The current analysis used multiple domains, including HRV, cardiovagal reflex tests, sympathetic

challenge tests, fatigue, walking distance and SF-36 scores. This makes the findings easier to translate into clinical practice because the physiological impairment is linked with symptoms and functional limitations. Matching of controls for age and sex further strengthens the comparison, and exclusion of common autonomic confounders such as diabetes, hypertension, smoking and drugs affecting heart rate improves internal validity.

This paper has limitations. The sample size was adequate for detecting major group differences but limited for subgroup analysis by sex, age group, symptom duration or severity categories. The case-control design establishes association but cannot prove causality. Autonomic function was assessed at one point in time, and the study did not evaluate changes after levothyroxine therapy. Factors such as sleep, stress, hydration, physical activity level and nutritional status may influence autonomic parameters, although standardized preparation and controlled testing were used to reduce these effects. Future longitudinal studies with larger samples should evaluate whether autonomic dysfunction improves after thyroid hormone replacement and whether structured exercise, breathing training or rehabilitation programs enhance recovery.

CONCLUSION

Untreated primary hypothyroidism was associated with significant autonomic dysfunction compared with matched euthyroid controls. The pattern involved reduced HRV, impaired cardiovagal reflex responses and altered sympathetic vascular reactivity, indicating mixed dysautonomia rather than isolated involvement of a single autonomic branch. Autonomic impairment was associated with greater fatigue, lower functional capacity and poorer health-related quality of life. Higher TSH and lower Free T4 were significantly related to worse autonomic and functional outcomes. Incorporating autonomic and functional assessment into the clinical evaluation of hypothyroidism may improve risk identification and patient-centered management.

Declaration by Authors

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