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Research Article

A comparative study of autonomic functions in in hypothyroid patients and euthyroid subjects

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ABSTRACT

Background: Thyroid hormones exert profound effects on the cardiovascular system and play a crucial role in maintaining autonomic balance. Hypothyroidism can lead to sympathovagal imbalance, predisposing individuals to cardiac autonomic neuropathy (CAN). **Aims and Objectives:** To conduct a comparative evaluation of autonomic functions in hypothyroid patients and euthyroid subjects.**Materials and Methods:** This case-control study included 40 hypothyroid patients and 40 age-matched euthyroid controls who met the inclusion and exclusion criteria. Cardiac autonomic function was assessed using Ewing's and Clarke's criteria. The test battery comprised three parasympathetic function tests (deep breathing test, 30:15 ratio, and Valsalva ratio) and two sympathetic function tests (sustained handgrip test and postural hypotension test). **Results:** Comparative analysis revealed that the Valsalva ratio among parasympathetic tests and both sympathetic function tests showed statistically significant differences between hypothyroid patients and euthyroid controls. **Conclusion:** The findings indicate an increased prevalence of cardiac autonomic neuropathy in hypothyroid patients compared to euthyroid individuals, highlighting the importance of early autonomic function assessment in these patients.

Keywords: Cardiac Autonomic Neuropathy; Deep Breathing Test; Valsalva Ratio; Sustained Handgrip Test; Postural Hypotension Test

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders encountered in clinical practice. It presents with a wide spectrum of clinical manifestations affecting multiple organ systems. A significant proportion of the cardiovascular and neurological manifestations observed in hypothyroidism are attributed to underlying autonomic dysfunction.

The autonomic nervous system, comprising sympathetic and parasympathetic components, plays a vital role in maintaining cardiovascular homeostasis. In hypothyroidism, reduced sympathetic activity typically manifests as bradycardia, decreased cardiac contractility, narrow pulse pressure, ptosis, and reduced thermogenesis. Conversely, altered autonomic balance may also lead to increased sympathetic activity, presenting as tachycardia and diastolic hypertension [1]. Parasympathetic dysfunction is reflected by impaired heart rate variability and orthostatic hypotension [1]. These autonomic alterations contribute to increased cardiovascular morbidity and mortality, including ischemic heart disease and cardiac dysrhythmias in hypothyroid patients [2].

Early identification of autonomic dysfunction and timely initiation of appropriate therapy can significantly reduce the associated morbidity [3]. Serum thyroid-stimulating hormone (TSH) is widely accepted as a sensitive biomarker for the diagnosis and monitoring of thyroid disorders [4]. The American Academy of Neurology recommends simple, non-invasive bedside autonomic function tests for the assessment and follow-up of autonomic dysfunction. These include heart rate response to deep breathing, Valsalva maneuver, sustained handgrip test, and blood pressure and heart rate response to standing [5].

Hypothyroidism results from decreased synthesis and secretion of thyroid hormones—thyroxine (T4) and triiodothyronine (T3) [6]. Approximately 99% of cases are due to primary hypothyroidism, resulting from intrinsic thyroid gland dysfunction, while the remaining 1% are secondary or tertiary (central) hypothyroidism due to pituitary or hypothalamic disorders [7].

Although studies in the Indian population have evaluated autonomic dysfunction in thyroid disorders, there remains limited data specifically addressing cardiovascular autonomic changes in hypothyroid patients. Given the significant influence of thyroid hormones on the cardiovascular system, this study aims to assess cardiac autonomic neuropathy in hypothyroid patients using standardized autonomic function tests (AFTs).

MATERIALS AND METHODS

Study Design and Setting

This case–control study was conducted in the Department of Physiology at Venkateshwara Institute of Medical Science after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to their inclusion in the study. A total of 80 subjects were enrolled, comprising 40 diagnosed hypothyroid patients (cases) and 40 euthyroid individuals (controls).

Inclusion Criteria

- Patients diagnosed with hypothyroidism
- Age ≥20 years

Exclusion Criteria

The following participants were excluded:

- Patients with diabetes mellitus, hypertension, multiple sclerosis, or other demyelinating diseases associated with neuropathy
- History of head injury, cerebrovascular accident, or epilepsy
- Patients with known cardiovascular diseases or established cardiac autonomic neuropathy
- History of smoking, alcoholism, or chronic drug intake

Data Collection Protocol

Participants fulfilling the inclusion criteria and providing informed consent were included in the study. Detailed clinical history was obtained, including personal details, presenting complaints, past medical history, family history, and dietary habits. A comprehensive general, clinical, and neurological examination was performed to exclude other causes of neuropathy.

Anthropometric parameters such as height, weight, and body mass index (BMI) were recorded. A structured questionnaire was used to assess symptoms related to hypothyroidism and autonomic dysfunction.

Baseline Parameters

Baseline measurements of blood pressure (BP) and heart rate (HR) were recorded for all participants. These values were used as reference parameters during autonomic function testing.

Assessment of Autonomic Function

Cardiac autonomic function was evaluated using Ewing's and Clarke's criteria, which include five standardized autonomic function tests (AFTs). These tests assess both parasympathetic and sympathetic components of the autonomic nervous system.

Parasympathetic Function Tests

1. Heart Rate Response to Deep Breathing

The subject was instructed to breathe deeply at a rate of six breaths per minute (5 seconds each for inspiration and expiration). Continuous electrocardiogram (ECG, Lead II) was recorded for six cycles. The difference between the maximum and minimum heart rates was calculated.

- Normal: ≥15 beats/min
- Borderline: 11–14 beats/min
- Abnormal: ≤10 beats/min

2. Valsalva Maneuver

After baseline ECG recording, the subject was asked to exhale forcefully into a mercury sphygmomanometer and maintain a pressure of 40 mmHg for 15 seconds. Continuous ECG recording was obtained during and for 30 seconds after the maneuver. The Valsalva ratio (VR) was calculated as the ratio of the longest R–R interval after the maneuver to the shortest R–R interval during the maneuver.

- Normal: ≥1.21
- Borderline: 1.11–1.20
- Abnormal: ≤1.10

3. Heart Rate Response to Standing (30:15 Ratio)

After resting in the supine position, baseline BP and HR were recorded. The subject was then asked to stand, and ECG (Lead II) was recorded for 1–3 minutes. The 30:15 ratio was calculated as the ratio of the longest R–R interval at beat 30 to the shortest R–R interval at beat 15 after standing.

- Normal: ≥1.04
- Borderline: 1.01–1.03
- Abnormal: ≤1.00

Sympathetic Function Tests

1. Sustained Handgrip Test (HGT)

Using a handgrip dynamometer (INCO), the subject maintained 30% of maximal voluntary contraction with the dominant hand for 4–5 minutes. BP was recorded in the opposite arm during the procedure. The rise in diastolic BP (DBP) was calculated.

- Normal: ≥16 mmHg
- Borderline: 11–15 mmHg
- Abnormal: ≤10 mmHg

2. Blood Pressure Response to Standing (Postural Hypotension Test)

After 10 minutes of rest in the supine position, BP was recorded. Subsequent readings were taken within 30 seconds of standing and at 1st, 2nd, 3rd, and 5th minutes. A fall in systolic BP ≥20 mmHg or diastolic BP ≥10 mmHg was considered indicative of orthostatic hypotension.

- Normal: ≤10 mmHg fall in SBP
- Borderline: 11–20 mmHg
- Abnormal: ≥20 mmHg

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 29. Results were expressed as mean ± standard deviation (SD). Comparison between hypothyroid and euthyroid groups was performed using the Student's *t*-test. A *p*-value <0.05 was considered statistically significant.

RESULTS

Table 1: Age and Sex Distribution in Study Groups

Age (years)	Group Cases Total	(Hypothyroid)	Male	Female	Controls Total	Male	Female
20–30	22		0	22	23	4	19

Age (years)	Group Cases Total	(Hypothyroid)	Male	Female	Controls Total	Male	Female
31–40	13		0	13	9	3	6
41–50	5		1	4	8	3	5
Total	**40**		**1**	**39**	**40**	**10**	**30**

The majority of hypothyroid patients were females (97.5%), whereas the control group also showed female predominance (75%). Most participants in both groups belonged to the 20–30 years age group.

Table 2: Comparison of Thyroid Profile between Cases and Controls

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value
T3 (ng/ml)	1.81 ± 0.16	1.89 ± 0.22	0.067
T4 (µg/dl)	7.5 ± 1.6	9.3 ± 1.1	0.0001*
TSH (µIU/ml)	16.4 ± 1.7	3.5 ± 0.86	0.0001*

*Statistically significant

There was a statistically significant decrease in T4 levels and a significant increase in TSH levels in hypothyroid patients compared to controls ($p < 0.001$). The difference in T3 levels was not statistically significant.

Table 3: Comparison of Cardiac Autonomic Function Tests (AFTs)

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value
E/I Ratio	1.4 ± 0.4	1.5 ± 0.35	0.238
30:15 Ratio	1.26 ± 0.27	1.31 ± 0.40	0.514
Valsalva Ratio (VR)	1.44 ± 0.33	1.60 ± 0.33	0.033*
DBP Rise (mmHg)	18.4 ± 2.7	14.7 ± 2.3	0.0001*
Mean SBP Change (mmHg)	6.9 ± 1.4	4.5 ± 0.7	0.0001*

Among parasympathetic tests, only the Valsalva ratio showed a statistically significant difference between cases and controls ($p = 0.033$). E/I ratio and 30:15 ratio did not show statistically significant differences. Both sympathetic function tests (rise in DBP during handgrip and systolic BP change on standing) showed highly significant differences ($p < 0.001$), indicating impaired sympathetic function in hypothyroid patients.

Overall Interpretation:

The results demonstrate significant impairment of autonomic function in hypothyroid patients, predominantly affecting sympathetic activity along with selective parasympathetic involvement.

DISCUSSION

Cardiac autonomic function tests (AFTs) were employed in the present study to evaluate autonomic neuropathy in hypothyroid patients. The comparison of biochemical and autonomic parameters between hypothyroid and euthyroid subjects revealed several important findings.

With respect to thyroid profile, no statistically significant difference was observed in serum T3 levels between the two groups. However, serum T4 levels were significantly reduced and TSH levels were significantly elevated in hypothyroid patients, which is consistent with the biochemical diagnosis of hypothyroidism. These findings are in agreement with previous studies by Sahin et al. [10], Karthik et al. [11], and Syamsunder et al. [12].

Parasympathetic function was assessed using heart rate response to deep breathing (E/I ratio), 30:15 ratio, and Valsalva ratio (VR). In the present study, the E/I ratio and 30:15 ratio did not show statistically significant differences between hypothyroid and control groups. These findings are consistent with studies by Mahajan et al. [13] and Bhat et al. [14], which also reported no significant differences in these parameters. This may be explained by compensatory mechanisms in hypothyroid patients, where altered sympathetic tone at rest maintains heart rate variability within a near-normal range.

In contrast, the Valsalva ratio showed a statistically significant difference between the two groups, indicating parasympathetic dysfunction. This finding differs from some earlier studies that reported non-significant results for VR, suggesting variability in autonomic involvement depending on disease severity and duration. Sympathetic function was evaluated using the sustained handgrip test and blood pressure response to standing. The rise in diastolic blood pressure during sustained handgrip was significantly reduced in hypothyroid patients compared to controls, indicating impaired sympathetic reactivity. Similar findings have been reported by Lakshmi et al. [18], who also observed improvement in this parameter following thyroxine therapy. Additionally, a significant fall in systolic blood pressure on standing was observed in hypothyroid patients, suggesting impaired sympathetic vasoconstrictor response. This observation is supported by Christensen [19], who proposed that reduced cardiac output in hypothyroidism leads to compensatory neurohumoral changes but inadequate cardiovascular response. The underlying mechanism for autonomic dysfunction in hypothyroidism may involve decreased responsiveness of adrenergic receptors, reduced catecholamine sensitivity, and impaired cardiac contractility. Previous studies by Klein and Ojamaa and Polikar et al. [15–17] have demonstrated reduced catecholamine responsiveness in hypothyroid patients, leading to diminished cardiac performance.

Despite increased circulating catecholamine levels reported in hypothyroid patients, their reduced receptor sensitivity results in an overall decreased adrenergic effect on the heart. This contributes to decreased cardiac output, impaired contractility, and increased systemic vascular resistance, ultimately affecting cardiovascular autonomic regulation. Overall, the findings of the present study indicate the presence of sympathovagal imbalance in hypothyroid patients, with both sympathetic and parasympathetic components being affected. Among parasympathetic parameters, the Valsalva ratio showed significant alteration, while both sympathetic tests demonstrated marked impairment.

Strengths of the Study:

- Well-defined study population
- Use of standardized and validated autonomic function tests
- Comparative case–control design

Limitations of the Study:

- Relatively small sample size
- Lack of follow-up to assess reversibility after treatment
- Absence of stratification based on duration or severity of hypothyroidism

CONCLUSION

The present study concludes that hypothyroidism is associated with a significantly increased prevalence of cardiac autonomic dysfunction. Both sympathetic and parasympathetic autonomic functions are altered in hypothyroid patients compared to euthyroid individuals, indicating the presence of sympathovagal imbalance. These findings highlight the importance of routine assessment of autonomic function in patients with hypothyroidism, in addition to standard clinical and biochemical evaluation. Early detection of cardiac autonomic neuropathy and timely intervention may help improve prognosis and enhance the quality of life in these patients.

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