Original Research Article

A study of autonomic status in hypothyroid

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Abstract

Background and objective: The cardiovascular system is one of the most important targets of thyroid hormone affecting which may be due to changes at the autonomic nervous system level. Hence hypothyroidism is associated with changes not only in cardiac and vascular function but is also believed to alter the autonomic regulation of heart., it is possible to prevent the development of various complications related to autonomic dysfunction by early diagnosis and treatment. Therefore the present study was undertaken to assess the autonomic status in newly detected hypothyroid female patients and to note the autonomic status of hypothyroid patients **Methods:** 30 newly detected cases of hypothyroid female patients between the age group of 20-50years were selected from SDM College of Medical Science and Hospital, Sattur, Dharwad. Height, weight and body mass index were recorded. Pulse rate, blood pressure and corrected QT interval were recorded in a resting condition. Cardiovascular autonomic function was studied by testing the sympathetic activity (Blood pressure response to immediate standing, cold pressor test, and sustained handgrip exercise) and parasympathetic activity (Heart rate variation at rest, during deep breathing and during Valsalva manoeuvre). **Result:** Result were analyzed. In hypothyroid patients the BMI was significantly high. In the resting condition, the heart rate was significantly decreased, diastolic blood pressure was increased, and QT interval was normal. When tested for the sympathetic activity, Blood pressure response to immediate standing and cold pressure test did not show any significant difference. Sustained handgrip test showed significant change in the diastolic blood pressure. Test reflecting the parasympathetic activity that is, heart rate variability (HRV) at rest showed significant smaller HF(MS2) values, higher LF (n.u) values and higher values of LF/HF ratio. Whereas the heart rate response to deep breathing and valsalva manuovre did not show any significant changes. **Conclusion:** The findings of the present study show that the autonomic status in hypothyroid patient is altered, and there is increased sympathetic activity and decreased parasympathetic activity.

Keywords: Hypothyroidism, cardiovascular system, Sympathetic activity, Parasympathetic activity, sympatho vagal balance.

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INTRODUCTION

99% of hypothyroidism cases are due to primary hypothyroidism, which may be caused by an abnormality in the thyroid gland itself and 1% of the cases are due to secondary and tertiary or central hypothyroidism, which may result from pituitary or hypothalamicdiseases.[2] Though the studies done in Indian population have assessed the autonomic status in thyroid dysfunction, but very less data is available on the changes in autonomic functions affecting cardiovascular system. Hence the present study was undertaken to assess the autonomic status in newly detected hypothyroid female patients attending SDM medical college, Sattur, Dharwad during the period, December 2010 to November 2011.

AIMS AND OBJECTIVES

1. To study the autonomic status of cardiovascular system in newly diagnosed hypothyroid patients (Cases).

METHODOLOGY

The study was conducted in the laboratory set up of department of Physiology, SDM College of Medical

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Sciences and Hospital, Dharwar from December 2010 to November 2011.

Source of data:

Newly detected cases of hypothyroidism were taken from out patient department (OPD) of medicine, SDM College of Medical Sciences And Hospital, Sattur,Dharwad.

Method of collection of data:

30 newly detected cases of hypothyroid female patients between the age group of 20- 50 years, diagnosed on the basis of general history, clinical examination and by serum levels of FT3, FT4, and TSH were selected.

Informed written consent for the conduction of study was obtained from hypothyroid patients and healthy after the detailed procedure and purpose of the study was explained to them.

Institutional Ethical committee approval for the study was obtained. The subjects were categorized into two groups.

Group I - Newly detected case of hypothyroidism, with serum thyroid hormone level47 FT3 < 1.4 pg/ml. FT4 < 0.8 ng /dl TSH >5.6µIu/ml

INCLUSION CRITERIA:

-Newly detected hypothyroid patients.

-Female patients with age group of 20-50 years.

EXCLUSION CRITERIA:

-Previously diagnosed case of hypothyroidism and who are on treatment

-Persons with a history of diseases which are known to affect autonomic functions for example diabetes mellitus, renal diseases, psychiatric disease, electrolyte imbalance, cardiovascular diseases, central and peripheral nervous system diseases, anemia and pregnancy.

-History of acute / chronic infections.

Investigations: Cases of hypothyroidism were selected based on the estimations of serum FT3, FT4 and TSH levels in the hospital laboratory of biochemistry department.

Estimations of serum FT3, FT4 and TSH levels were done by Acculite CLIA Microwellschemiluminesce Immunoassay manufactured by Monobind INC.U.S.A.

Methods of assessment of cardiovascular autonomic function tests

The following Six established autonomic functions tests were performed .Results of the tests were expressed as ratios and differences which have been accepted by Ewing and Clarke.

Test for sympathetic activity or (sympathetic function tests)

1. Blood pressure response to immediatestanding
2. Blood pressure response to Cold pressortest
3. Blood pressure response to sustained hand gripexercise

Test for parasympathetic activity or (parasympathetic function tests)

4. Heart rate variation during deepbreathing
5. Heart rate response during Valsalvamanoeuvre
6. Heart rate variability by power spectral analysis (PSA) at rest.

RESULTS

Mean and standard deviation (SD) values were evaluated for all measured parameters. The significance of difference in the mean value was analyzed.

TABLE 4: MEAN AND SD OF AGE AND BMI BY STUDY CASES

Parameter	CasesMean ± SD	„p" value	Significance
Age (yrs)	36.43±8.51	1.00	NS
BMI(kg/m²)	26.49±5.48	<0.05	S

*p<0.05

The mean and SD of age of study samples in cases (36.43±8.51) are (p=1.00). A significant difference is observed BMI scores (p<0.05). The cases (26.49±5.48) have significantly higher BMI scores.

Table 5: Mean and SD scores of thyroid profiles (FT3pg/ml, FT4 ng/dl and TSH µIU/ml) in cases

Thyroid profiles	Mean	SD
FT_3pg/ml	1.72	0.71
FT_4 ng/dl	0.66	0.36
TSHµIU/ml	31.67	21.89

Results of the above table present the Mean and SD scores of thyroid profiles (FT3pg/ml, FT4 ng/dl and TSH µIU/ml) in cases.

Table 6: cases with respect to pulse scores, systolic, and diastolic blood pressure (SBP and DBP)

Parameter	CasesMean ± SD	„p" value	Significance
Pulse rate (bpm)	71.50±5.86	<0.05	S
SBP (mm Hg)	126.13±21.19	>0.05	NS
DBP (mm Hg)	81.73±12.21	<0.05	S

*p<0.05

A significant difference is observed in cases with respect to pulse scores (t=-2.22, p<0.05). The cases (71.50±5.86) have significant smaller pulse scores (75.30±7.29).
A non-significant difference is observed in cases with respect to Systolic BP scores (, p>0.05). The cases (126.13±21.19) Systolic BP scores.
A significant difference is observed in cases with respect to Diastolic BP (mm /Hg) scores (p<0.05). The cases (81.73±12.21) have significant higher Diastolic BP (mm /Hg) scores Corrected QT interval (QTC).

TABLE 7: CASES WITH RESPECT TO QTC SCORES.

Parameter	Cases Mean ± SD	„p" value	Significance
QT_C	400.20±68.68	>0.05	NS

A non-significant difference is observed between cases s with respect to QTC scores (t=1.45, p>0.05). The cases (400.20±68.68) QTC scores.

1. BP response to immediate standing

Table 8: cases with respect to Systolic and Diastolic BP (SBP andDBP) during immediate standing (mm /Hg)

Parameter	Cases Mean ± SD	„p" value	Significance
SBP (mmHg) during immediate standing	117.87±20.45	>0.05	NS
DBP(mm Hg)during immediate standing	78.07±12.35	>0.05	NS

A non-significant difference is observed between cases with respect to Systolic BP on immediate standing (mm /Hg) scores (p>0.05).The cases (117.87±20.45) Systolic BP scores on immediate standing (mm/Hg).
A non-significant difference is observed between cases with respect to diastolic BP on immediate standing (mm /Hg) scores (p>0.05).The cases (78.07±12.35) diastolic BP scores on immediate standing (mm/Hg).

2. BP response to cold pressor test

Table 9: cases with respect to Systolic and diastolic BP (SBPandDBP) during Cold pressor test (mm /Hg)

Parameter	Cases Mean ± SD	„p" value	Significance
SBP (mmHg) during cold pressor test	129.73±20.75	>0.05	NS
DBP (mm Hg) during cold pressor test	82.40±10.70	>0.05	NS

A non-significant difference is observed between cases with respect to Systolic BP on Cold pressor test (mm /Hg) scores (, p>0.05).The cases (129.73±20.75) have similar Systolic BP scores on Cold pressor test (mm/Hg).
A non-significant difference is observed between cases with respect to diastolic BP on Cold pressor test (mm /Hg) scores (p>0.05). The cases (82.40±10.70) have similar diastolic BP scores on Cold pressor test (mm /Hg).

3. BP response to sustained hand grip test

Table 10: cases with respect to Systolic and diastolic BP (SBPandDBP) during Handgrip test (mm /Hg)

Parameter	Cases Mean ± SD	„p" value	Significance
SBP (mm Hg) during hand grip test	138.60±19.12	>0.05	NS
DBP (mm Hg) during hand grip test	90.53±9.58	<0.05	S

*p<0.05

A non-significant difference is observed between cases respect to Systolic BP on Handgrip test (mm /Hg) scores , p>0.05). The cases (138.60±19.12) have similar Systolic BP scores on Handgrip test (mm /Hg).
A significant difference is observed between cases with respect to diastolic BP on Handgrip test (mm /Hg) scores (, p<0.05). The cases (90.53±9.58) have significant higher diastolic BP on Handgrip test (mm /Hg) scores.

Parasympathetic tests

1. **Heart rate response to deep breathing**

TABLE 11: CASES WITH RESPECT TO HEART RATE (HR) VARIATION DURING DEEP BREATHING

Parameter	Cases Mean ± SD	„p" value	Significance
HR (bpm) variation during deep breathing	27.17±8.60	>0.05	NS

A non-significant difference is observed between cases with respect to HRV during deep breathing (Beats /min) scores (p>0.05). It means that, the cases (27.17±8.60) have similar HRV during deep breathing (Beats /min).

2. **Heart rate response to ValsalvaManoeuvre**

Table 12: cases with respect to Heart rate response during Valsava manoeuvre (Valsalva Ratio)

Parameter	Cases Mean ± SD	„p" value	Significance
HR (bpm) Response during Valsalva manoeuvre (valsalva ratio)	1.42±0.26	>0.05	NS

A non-significant difference is observed between cases with respect to HRV during Valsava manoeuvre (Valsalva Ratio) scores (t=-1.16, p>0.05). The cases (1.42±0.26) have similar HRV during Valsava manoeuvre (Valsalva Ratio).

Heart rate variability by Power spectral analysis at rest

Table 13: cases with respect to LF (ms2) and HF (ms2) scores in HRV during rest

Parameter	Cases Mean ± SD	„p" value	Significance
LF(ms^2) (HRV by PSA at rest)	268.93±204.29	>0.05	NS
HF(ms^2) (HRV by PSA at rest)	262.67±197.62	<0.05	S

*p<0.05

A non-significant difference is observed cases with respect to LF (ms2) scores (p>0.05). The cases (268.93±204.29) have similar LF (ms2) scores. A significant difference is observed between cases with respect to HF (ms2) scores (t=-3.34, p<0.05). The cases (262.67±197.62) have significant smaller HF (ms2) scores.

Table 14: cases with respect to LF (n.u), HF (n.u) scores in HRV during rest

Parameter	Cases Mean ± SD	„p" value	Significance
LF(n.u) (HRV by PSA at rest)	51.42±13.65	<0.05	S
HF(n.u) (HRV by PSA at rest)	48.19±13.58	>0.05	NS

*p<0.05

A significant difference is observed cases with respect to LF (n.u) scores (p<0.05). The cases (51.42±13.65) have significant higher LF (n.u) scores. A non-significant difference is observed cases respect to HF(n.u) scores (t=1.43, p>0.05). The cases (48.19±13.58) LF (n.u) scores.

Table 15: cases with respect to LF/HF ratio scores in HRV during rest

Parameter	Cases Mean ± SD	„p‟ value	Significance
LF/HF ratio (HRV by PSA at rest)	1.25±0.72	<0.05	S

*p<0.05

A significant difference is observed between cases with respect to LF/HF scores (t=2.85, p<0.05). The cases (1.25±0.72) have significant higher LF/HF scores.

DISCUSSION

The autonomic nervous system maintains the internal physiological homeostasis. Any abnormalities in the autonomic function results in diverse clinical manifestations. The assessment of autonomic functions is an important part of the evaluation of peripheral and central nervous system. A number of autonomic function tests are considered reliable, noninvasive, reproducible, simple and quick to carryout. The autonomic functions in hypothyroidism mainly affecting **the cardiovascular system are discussed as below:**

Since age and sex of cases and were matched, age and sex related differences in autonomic tests were avoided.

Body mass index: In our study, the cases have statistically significant higher BMI scores as compared to . Karthik *et al*, also recorded similar results in hypothyroid subjects. According to them, Obesity in hypothyroidism is not a pure increase in adiposity as increase in body weight, in thyroid deficiency is mostly due to accumulation of water and mucopolysaccharides in subcutaneous tissues.[24]

Resting pulse rate: Our study shows that, the cases have significant smaller pulse scores as compared to . The study is similar to R.Poliker, A.G. Burger *et al*. Decreased HR is one of the important features of hypothyroidism. In hypothyroidism decreased thyroid hormone decreases the direct chronotropic effect on S.A node and heart, which is attributed to decreased β adrenergic receptor density sensitivity and also due to cardiac chronotropic response to adrenergic stimulation despite evidence of sympathetic over activity. It has also been suggested that decreased binding of catecholamines with β receptors in cardiac myocytes might be responsible for cardiovascular changes in Hypothyroids. Several investigators suggested that though plasma catecholamines are increased in hypothyroidism but overall depression of adrenergic responses at cardiac and peripheral level indicates desensitization both at the receptor or post receptorsite.[12] Resting blood pressure: Statistically a significant difference is observed between cases and with respect to Diastolic BP scores in our study, which shows that, the cases have significant higher Diastolic BP scores as compared to . Bhat *et al*, recorded similar readings. 20 -40% of patients with hypothyroidism have hypertension. Diastolic pressure is increased more than the systolic blood pressure. Normally the thyroid hormone decreases the systemic vascular resistance, maintains the blood volume and smooth muscle relaxation of arterioles. In hypothyroidism the increase in diastolic blood pressure is due to increase in systemic vascular resistance, low blood volume and constriction ofarterioles.[21].

Corrected QT interval (QTc): In our study, the recording of QT interval did not show any significant change in hypothyroid patients. But Galetta *et al*. recorded the prolonged QT interval in overt hypothyroidism. Experimental evidence suggests that thyroid hormones may selectively prevent the induction of fibrosis, by the inhibition of collagen type 1 synthesis and maintain the ventricular repolarization (QTinterval). Prolonged QT interval is considered to be one of the risk factors for developing arrhythmias. Contradictory findings in our study may be explained on the basis of duration of hypothyroidism.[22]

Autonomic function tests

Sympathetic tests

Blood pressure on immediate standing

Statistically the difference observed in Systolic and diastolic blood pressure on immediate standing between the two groups is not significant.Bhat *et al*. recorded the similar results. The maintenance of an adequate upright blood pressure on immediate standing from lying down position requires a normal baroreceptor mediated feedback loop and an intact sympathetic nervous system. The result of our study may indicate the intact baroreflex function with stress and intact sympathetic nervoussystem.2[1]

Cold pressor test

Our study result is similar to Sushil kumar *et al*.In hypothyroidism there is altered response to β adrenergic receptor. The Nor- adrenaline has more action on α receptors than that on β adrenergic receptor. Due to decreased β adrenergic receptor density and sensitivity there is less stimulation of β adrenergic receptor and less change in heart rate and force of contraction. The test lacks sensitivity because many normal subjects do not have a significant rise of blood pressure on coldimmersion.[26]

Sustained Handgrip test

The result of our study result is similar to Sushil kumar *et al*. The result can be explained as follows. In hypothyroidism decreased thyroid hormone decreases the direct chronotopic effect on S.A node and heart leading to bradycardia and decreased myocardial contractility, which is attributed to decreased β adrenergic receptor density and sensitivity. Even though there is increased sympathetic stimulation, there is less effect on β adrenergic receptor and less change in heart rate and force of contraction.[26] Sympathetic stimulation liberates Nor-adrenaline, which has more action on α receptors than that of β adrenergic receptor. In hypothyroidism direct stimulation of VMC lead to release of Nor-Adrenaline at the sympathetic nerve endings, which stimulates α receptors. This in turn increases systemic vascular resistance, aortic stiffness hence the diastolic blood pressure.

Parasympathetic tests

Heart rate response to deep breathing

In our study, non-significant difference is observed between cases and with respect to HRV during deep breathing, which is similar to Inkui et.al. Sinus arrhythmia consists of a variation in the heart rate with an increase heart rate during inspiration and decrease heart rate during expiration. It is a normal phenomenon and is due to fluctuation in the parasympathetic outflow to the heart rate. Hence the above result shows that the efferent parasympathetic or vagal (tone) activity is unaffected.[11]

Heart rate response during Valsalva manoeuvre (valsalvaratio)

A non-significant difference observed between cases and with respect to HRV during Valsavamanuovre (Valsalva Ratio) is similar to the results recorded by Bhat *et al.* [21] Valsalva manoeuvre reflects the changes in heart rate and blood pressure secondary to changes in intrathoracic pressure. These reflex changes are mediated through the baroreceptor of aortic arch and carotid sinus. The reflex pathway includes both parasympathetic and sympathetic fibres. Hence our study results show that the baroreflex function mediated via the parasympathetic activity is unaltered.

Heart rate variability by power spectral analysis at rest

Our study result is similar to Ahmed *et al*.Two major components of spectral band, HF Power and HF norm reflect the parasympathetic activity where as LF Power and LF norm reflect sympathetic activity on heart. LF/HF ratio is considered as a marker of sympathovagal balance. In our study Lower values of HF power (ms2) indicate their reduced vagal modulation of heart. Higher values of LF norm (n.u) in cases indicate increased sympathetic activity. Increased LF/HF ratio shows altered sympathovagal balance. So over all there is reduced parasympathetic and increased sympathetic activity. The site of action for thyroid hormone is also likely to be in the central nervous system for reducing the vagal tone, as the iodothyronine compounds have been isolated from various parts of nervous system including hypothalamus and medulla. Increase in sympathetic activity may be due to TRH which directly stimulate sympathetic outflow within the central nervoussystem.[25]

CONCLUSION

The conclusion is that the autonomic status in hypothyroidism is altered; there is increased sympathetic activity and decreased parasympathetic activity. Power Spectral Analysis of HRV was more sensitive than conventional autonomic function tests in assessing autonomic dysfunction.

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