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RESEARCH ARTICLE

Electrocardiographic changes in subclinical hypothyroidism

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) is an apparently asymptomatic condition defined by increased serum thyrotropin (thyroid-stimulating hormone) concentrations, but normal serum free T3 and free T4 hormone levels. Thyroid hormones are known to affect the heart and vasculature. The effect of SCH on cardiovascular system is not much studied. **Aims and Objectives:** The objectives of this study were to study the electrocardiogram (ECG) changes in a group of newly diagnosed subclinical hypothyroid females and to compare the ECG changes in subclinical hypothyroid females with normal healthy euthyroid individuals. **Materials and Methods:** We studied 30 non-pregnant females with primary SCH in the age group of 20–40 years, who were newly diagnosed and untreated. Thirty age- and body mass index-matched healthy individuals were taken as controls. Clinical and biochemical parameters and ECG were studied. Statistical software, "GraphPad QuickCalcs," was used for the statistical analysis. **Results:** Mean QTc interval of the study group was significantly longer than those of the control group (P = 0.037). Other parameters of ECG were comparable in both the groups. **Conclusion:** ECG changes in SCH showed increase in the QTc interval as compared to controls, which predisposes to the potentially life-threatening ventricular arrhythmias. However, the other parameters of ECG such as QRS interval, PR interval, and QRS axis were similar to the controls.

KEY WORDS: Subclinical Hypothyroidism; Thyroid Hormones; Electrocardiogram; QTc Interval

INTRODUCTION

Subclinical hypothyroidism (SCH) is an apparently asymptomatic condition defined as thyroid state associated with an elevated serum thyroid-stimulating hormone (TSH) concentration (TSH between 5.5 and 10 mIU/L) and normal serum free T_4 (fT_4) and free T_3 (fT_3) levels.[1] SCH is a risk factor which has higher chances of progressing to clinical state.[2]

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The concentration of TSH in 70–80% of apparently healthy persons is between 0.3 and 2.0 mIU/L. If individuals with thyroid autoantibodies, goiter, and strong family history are excluded, the reference range decreases to between 2.5 and 3.0 mIU/L.[3] As there is lack of evidence for benefit of treatment on individuals with TSH levels 3 and 5 mIU/L, keeping the upper limit of 5.0 mIU/L is reasonable.[4]

The overall prevalence of hypothyroidism is 10.95%, of which 3.47% previously undetected and 7.48% self-reported cases. There was a predominance of thyroid dysfunction in women and was consistent with the worldwide reports, especially those in midlife, i.e., between 46 and 54 years.[5]

The clinical presentation of SCH is non-specific, and the symptoms are usually subtle as compared with those of overt

hypothyroidism, probably in relation to the intensity and the duration of thyroid hormone deficiency and the age of the patients.[6] In SCH, several metabolic and organ function indices will show only marginal alterations in view of minor thyroid hormone secretion impairment. Nonetheless, such changes may become clinically relevant when they affect target organs over a period of several years.[7]

Although SCH is milder form of thyroid dysfunction, risk of cardiovascular abnormalities is high as compared to normal population.[8]

Till date, very few studies are there on effect of SCH on electrocardiogram (ECG) changes. Hence, we have made an effort to know whether newly diagnosed subclinical hypothyroid young females are going to manifest dysfunctions in the cardiovascular parameters as compared to their healthy counterparts.

MATERIALS AND METHODS

This study was conducted in the Department of Physiology, Karnataka Institute of Medical Sciences (KIMS), Hubballi, with the assistance of Sumukh Pathology Laboratory, Vidyanagar. The Institutional Ethics Committee approved our study. We studied 30 patients with newly diagnosed and untreated primary SCH who presented to KIMS, outpatient department (Dermatology, Medicine, and Obstetrician-Gynecologist) with non-specific complaints such as fatigue, mild weight gain, dry skin, and depressive feelings but without overt symptoms and signs of thyroid hormone deficiency. They underwent routine investigations including thyroid profile. Subjects with TSH levels above 5 mIU/L and below 10 mIU/L with normal fT_3 and fT_4 were included in the study group. Thirty age- and sex-matched healthy volunteers from staff and friends formed the control group.

All the participants were in the age group of 20–40 years and body mass index (BMI) was below 30 kg/m^2. None of them were suffering from any known illness or on medication. They were non-smokers and non-alcoholics. Subjects with any physiologic or pathologic condition which affects respiration were excluded from the study.

They underwent detailed clinical history and physical examination. Blood samples were collected for thyroid hormone assay and electrocardiography was done.

All cases underwent anthropometric investigation. Body weight was measured in light clothing and BMI was calculated by dividing the weight in kilograms by height in meter squared. Blood pressure was measured with a standard mercury manometer after a 15 min rest in a sitting position. Pulse rate was obtained from the radial artery.

Serum TSH, fT_3, and fT_4 levels were measured by chemiluminescence microparticle immunoassay method using Roche Cobas E411 Immunology Analyzer, which is designed to detect glow-based chemiluminescent reactions.

ECG was done to determine the electrical changes in functioning of the heart using 12-lead ECG machine. Then, reports were examined manually using magnifier. PR interval, QRS interval, QT interval, and QRS axis were recorded and tabulated.

In the present study, we have included QTc interval as QT interval varies with heart rate, i.e., prolonged at slower heart rate and shortened at faster heart rate. QTc interval is QT interval corrected for heart rate which is calculated by dividing QT interval by the square root of the RR interval – Bazett formula. QTc interval in the ECG includes both ventricular depolarization and repolarization.[9]

Statistical software, "GraphPad QuickCalcs," was used for the statistical analysis. Data were presented as means ± standard deviation, $P < 0.05$ was considered statistically significant.

RESULTS

A total of 60 subjects (30 in the study group and 30 in the control group) were included in the study. The clinical and biochemical parameters are tabulated in Tables 1 and 2. Both groups were well matched with regard to age and BMI. Heart rate and blood pressure were comparable in both the groups. TSH levels were significantly higher in SCH patients than controls, but fT_4 and fT_3 were comparable.

Mean QTc interval [Table 3] of the study group was significantly longer than those of the control group ($P = 0.037$). Other parameters in ECG were comparable in both the groups.

Table 1: Biochemical data of the controls and study subjects

Parameters	Controls (Mean±SD)	Subjects (Mean±SD)
BMI (kg/m^2)	22.16±1.64	22.71±1.99
TSH (mIU/L)	2.5±0.7	7.39±1.49
T3 (ng/ml)	0.13±0.03	0.12±0.03
T4 (µg/dl)	8.05±1.9	7.63±1.78

BMI: Body mass index, TSH: Thyroid-stimulating hormone, SD: Standard deviation

Table 2: Hemodynamic parameters

Parameters	Controls (Mean±SD)	Subjects (Mean±SD)
Heart rate (bpm)	76.1±5.11	74.03±6.4
SBP (mmHg)	116±3.79	118.26±3.88
DBP (mmHg)	76.6±3.24	75.93±4.01

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation

Table 3: Comparison of ECG parameters

Parameters	Controls (Mean±SD) (*n*=30)	Subjects (Mean±SD) (*n*=30)	*t*-value	*P*-value	Significance
PR interval (ms)	122.23±25.1	125.33±28.1	0.45	0.654	NS
QRS interval (ms)	85.83±12.67	89.3±5.44	1.58	0.120	NS
QTc interval (ms)	400.1±32.27	413.46±11.7	2.13	0.037	S
QRS axis (°)	60.03±24.5	59.53±23.8	0.08	0.936	NS

NS: Non-significant, S: Significant

DISCUSSION

SCH can be considered as milder form of or early stage of thyroid dysfunction. The cause of SCH may be same as its clinical counterpart such as chronic autoimmune thyroiditis, subacute thyroiditis, thyroidectomy, overtreatment with radioactive iodine, or inadequate hormone replacement therapy.[10]

ECG changes are well established in clinical hypothyroidism, which include bradycardia, ST-T changes, and low voltage complexes. ST-T changes in the form of T wave inversion or ST segment depression and flattening are seen. QT interval may be prolonged in patients of hypothyroidism which is a well-known risk factor for the development of ventricular arrhythmias.[11-14]

In the present study, we observed, QTc interval was significantly prolonged in subclinical hypothyroid subjects compared to controls ($P< 0.05$) and these results were compatible with observations made by Bakiner *et al*.[15] and Galetta *et al*.[16] who have also showed that the mean QTc interval was significantly prolonged in SCH patients compared to the control group. Other parameters in ECG did not show much significant changes.

The limitation of this study was that it had lower number of cases ($n = 30$ in the study group and n = 30 in the controls).

CONCLUSION

The present study concludes with the following important finding that patients of SCH have prolonged QTc interval, which predisposes to the potentially life-threatening ventricular arrhythmias. Therefore, it may present as a useful tool in monitoring the cardiovascular risk.

REFERENCES

1. Duggal J, Singh S, Barsano CP, Arora R. Cardiovascular risk with subclinical hyperthyroidism and hypothyroidism: Pathophysiology and management. J Cardiometab Syndr 2007;2:198-206.
2. Kek PC, Ho SC, Khoo DH. Subclinical thyroid disease. Singapore Med J 2003;44:595-600.
3. Fatourechi V. Subclinical Hypothyroidism: An Update for Primary Care Physicians. Mayo Clinic Proceedings. Amsterdam: Elsevier; 2009.
4. Fatourechi V, Klee GG, Grebe SK, Bahn RS, Brennan MD, Hay ID, *et al*. Effects of reducing the upper limit of normal TSH values. JAMA 2003;290:3195-6.
5. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian J Endocrinol Metab 2013;17:647-52.
6. Biondi B, Fazio S, Palmieri EA, Carella C, Panza N, Cittadini A, *et al*. Left ventricular diastolic dysfunction in patients with subclinical hypothyroidism. J Clin Endocrinol Metab 1999;84:2064-7.
7. Mishra TK, Routray SN, Das S, Behera M. Left ventricular dysfunction in patients with subclinical hypothyroidism and its reversibility after hormone therapy. J Assoc Physicians India 2005;53:943-6.
8. Hak L, Pols H, Visser T, Drexhage H, Witteman J, Hofman A. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The Rotterdam study. Ann Intern Med 2000;132:270-8.
9. Al-Khatib SM, LaPointe N, Kramer JM, Califf RM. What clinicians should know about the QT interval. JAMA 2003;289:2120-7.
10. Cakmak G, Saler T, Saglam ZA, Yenigun M, Ataoglu E, Demir T, *et al*. Pulmonary functions in patients with subclinical hypothyroidism. J Pak Med Assoc 2011;61:951-3.
11. Sureshbabu KP, Oswal A. Cardiac manifestations in hypothyroidism-a cross sectional study. Res J Pharm Biol Chem Sci 2014;5:966-75.
12. Shashi BM. A Study Of Cardiovascular Changes in Newly Detected Hypothyroid Patients, Dissertation. Banglore: Rajiv Gandhi University of Health Sciences; 2006.
13. Goyal S, Goyal V. A study of electrocardiographic changes in thyroid disorders. Int J Med Res Rev 2016;4:486-90.
14. Ramesh K, Nayak BP. A study of cardiovascular involvement in Hypothyroidism. Int Arch Integr Med 2016;3:74-80.
15. Bakiner O, Ertorer ME, Haydardedeoglu FE, Bozkirli E, Tutuncu NB, Demirag NG. Subclinical hypothyroidism is characterized by increased QT interval dispersion among women. Med Princ Pract 2008;17:390-4.
16. Galetta F, Franzoni F, Fallahi P, Rossi M, Carpi A, Rubello D, *et al*. Heart rate variability and QT dispersion in patients with subclinical hypothyroidism. Biomed Pharmacother 2006;60:425-30.

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