ISSN: 0975-1556

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 13(6); 840-846

Original Research Article

A Case-Control Study to Evaluate Electrocardiogram (ECG) Changes in A Group of Newly Diagnosed Subclinical Hypothyroid Females

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Received: 01-10-2021 / Revised: 23-11-2021 / Accepted: 20-12-2021
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Conflict of interest: Nil

Abstract

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: This study was conducted in the Department of Physiology, Department of Physiology, Patna Medical College & Hospital, Patna, Bihar for 1 year. We studied 50 patients with newly diagnosed and untreated primary SCH who presented to KIMS, outpatient department 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. Clinical and biochemical parameters and ECG were studied. Statistical software, "GraphPad QuickCalcs," was used for the statistical analysis.

Results: A total of 100 subjects (50 in the study group and 50 in the control group) were included in the study. 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 fT4 and fT3 were comparable.

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.

Keywords: Subclinical Hypothyroidism; Thyroid Hormones; Electrocardiogram; QTc Interval

Introduction

There are multiple systems on which thyroid hormone acts or contributes to their function but heart and the vessels are the major target organs. Marked changes in these organs occur in patients with thyroid dysfunction. [1]Many symptoms and signs recognized in patients with overt hyperthyroidism and hypothyroidism are due to increased or reduced action of thyroid hormones on heart and vascular system.[2]

Thyroid dysfunction has been widely demonstrated to be associated with various cardiovascular disorders and is associated with increased all-cause mortality, increased cardiovascular mortality as well as morbidity.[3-5] Subclinical thyroid dysfunction is defined as abnormal thyroid-stimulating hormone (TSH) values with thyroxine (T4) and triiodothyronine (T3) levels within the normal range. Even these minor changes in the thyroid function in subclinical thyroid dysfunction are associated with various kinds of cardiovascular disorders, such as heart failure,[6] atrial fibrillation[3-7]and coronary artery disease.[8]

The clinical presentation of SCH is non-specific, and the symptoms are usually subtle as compared with those of over thypothyroidism, probably in relation to the intensity and the duration of thyroid hormone deficiency and the age of the patients.[9]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.[10]

Common ECG changes in hypothyroidism are bradycardia, low voltage complex, ST segment depression, QT interval lengthening and increased QT dispersion, flattening or inversion of T wave, which reflects the prolonged cardiac action potential. In addition, these patients are more prone to ventricular arrhythmias particularly in presence of ischemic heart disease, due to increased electrical depression in myocardium.[11-13]

Similarly, hyperthyroidism is associated with increased incidence of atrial arrhythmias and changes in the QT interval.[14-16]

Hence, we aim 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:

This study was conducted in the Department of Physiology, Department of Physiology, Patna Medical College & Hospital, Patna, Bihar for 1 year.

Inclusion and exclusion criteria

All the participants were in the age group of 20–40 years and body mass index (BMI) was below 30 kg/m2. 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.

Methodology

We studied 50 patients with newly diagnosed and untreated primary SCH who presented to KIMS, outpatient department 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 fT3 and fT4 were included in the study group. Thirty age- and sex-matched healthy volunteers from staff and friends formed the control group.

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, fT3, and fT4 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. [22]

Statistical analysis

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 100 subjects (50 in the study group and 50 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 fT4 and fT3 were comparable.

Mean QTc interval [Table 3] of the study group was significantly longer than those of the control group ($P = 0.028$). 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/m2)	20.81±2.91	21.82±1.10
TSH (mIU/L)	2.01±1.6	8.21±1.91
T3 (ng/ml)	0.61±0.04	0.32±0.03
T4 (µg/dl)	9.91±1.89	8.71±1.51

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)	79.29±5.21	75.91±7.1
Systolic Blood Pressure (SBP) (mmHg)	108.21±4.11	129.1±4.01
Diastolic Blood Pressure (DBP) (mmHg)	72.81±3.32	72.91±4.89

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)	136.8±29.2	128.20±30.2	0.51	0.681	NS
QRS interval (ms)	87.21±15.91	91.23±7.82	1.71	0.133	NS
QTc interval (ms)	329.25±36.80	404.51±14.63	2.01	0.028	S
QRS axis (°)	63.81±27.28	66.72±26.28	0.44	0.861	NS

NS: Not Significant, S: Significant

Discussion:

In 1900, Von Noorden from Vienna, stated that thyroid played a key role in causation of 'fatty disease'.[17]In 1918, scientists ascertained correlation of blood cholesterol to the secretion of adrenals and thyroid. In 1930s the connection of cholesterol with thyroid function and disease was observed.[18]On Christmas day of 1930, a landmark article was published by Mason and colleagues in the New England Journal of Medicine which showed the significance of cholesterol values in hypothyroidism and hyperthyroidism.[19] In a multicenter study of prevalence of hypothyroidism in 752 hyperchloremic patients, primary hypothyroidism occurred in 3.7%.[20]In contrast, in thyrotoxicosis, cholesterol synthesis in increased, but this is simultaneously counter‑balanced by an increased rate of degradation and excretion.[21]

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.[22]

Most of the previous studies have investigated the relationship of thyroid dysfunction with QTc interval as both prolonged and shorter QTc interval have been associated with sudden cardiac death and complex ventricular arrhythmias.[23]

The lipid profile in hypothyroidism in characterized by increased total and LDL cholesterol with increased or normal HDL levels involving HDL2 sub fraction.[24, 25]TG levels are not affected or are slightly elevated.[26]

Further research on the physiology behind this interaction will enrich our knowledge on the impact of thyroid dysfunction in cardiovascular morbidity and mortality. Moreover, the present study establishes that subclinical thyroid dysfunctions are also associated with important ECG changes that are known to be of prognostic importance.[27-30]

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*.[31]and Galetta *et al*.[32]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.[33,34]

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. Kahaly GJ, Dillmann WH. Thyroid hormone action in the heart. Endocr Rev 2005;26:704‑28.
2. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med 2001;344:501‑9.
3. Selmer C, Olesen JB, Hansen ML, et al. The spectrum of thyroiddisease and risk of new onset atrial fibrillation: a large population cohort study. BMJ 2012;345:e7895.
4. Selmer C, Olesen JB, Hansen ML, et al. Subclinical and overt thyroid dysfunction and risk of all-cause mortality and cardiovascular events: a large population study. J Clin Endocrinol Metab 2014;99:2372–82.
5. Parle JV, Maisonneuve P, Sheppard MC, et al. Prediction of allcause and cardiovascular mortality in elderly people from one low serum thyrotropin result: a 10-year cohort study. Lancet 2001;358:861–5.
6. Rodondi N, Bauer DC, Cappola AR, et al. Subclinical thyroid dysfunction, cardiac function, and the risk of heart failure. The Cardiovascular Health study. J Am Coll Cardiol 2008;52:1152–9.
7. Cappola AR, Fried LP, Arnold AM, et al. Thyroid status, cardiovascular risk, and mortality in older adults. JAMA 2006;295:1033–41.
8. Dorr M, Empen K, Robinson DM, et al. The association of thyroid function with carotid artery plaque burden and strokes in a population-based sample from a previously iodine-deficient area. Eur J Endocrinol 2008;159:145–52.
9. 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.
10. 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.
11. Fazio S, Palmieri EA, Lombardi G, Biondi B. Effects of thyroid hormone on the cardiovascular system. Recent Prog Horm Res 2004;59:31‑50.
12. Fredlund BO, Olsson SB. Long QT interval and ventricular tachycardia of torsade de pointe type in hypothyroidism. Acta Med Scand 1983;213:231‑5.
13. Ojamaa K, Klein I, Sabet A, Steinberg SF. Changes in adenylyl cyclase isoforms as a mechanism for thyroid hormone modulation of cardiac beta‑adrenergic receptor responsiveness.Metabolism 2000;49:275‑9.
14. Wahid, R. ., & Rathinasamy, E. V. . L. .(2022). Explore and Develop a Culturally Adopted Behavioral Psycho Educational Family Intervention for Caregivers of Schizophrenic Patients in Egyptian Context. Journal of Medical Research and Health Sciences, 5(2), 1779–1785. https://doi.org/10.52845/JMRHS/2022-5-2-3
15. Tribulova N, Knezl V, Shainberg A, et al. Thyroid hormones and cardiac arrhythmias. Vascul Pharmacol 2010;52(3-4):102–12.
16. Colzani RM, Emdin M, Conforti F, et al. Hyperthyroidism is associated with lengthening of ventricular repolarization. Clin Endocrinol 2001;55:27–32.

17. Dorr M, Ruppert J, Robinson DM, et al. The relation of thyroid function and ventricular repolarization: decreased serum thyrotropin levels are associated with short rate-adjusted QT intervals. J Clin Endocrinol Metab 2006;91:4938–42.
18. Noorden Cv. Die Fettsucht. In Nothnagel: Handbuch der speziellen Pathologie und Therapie, Bd 7/4. Wien: Hölder; 1900.
19. Luden G. Collected papers of Mayo Clinic. Mayo Clinic Proc 1918;10:483‑7.
20. Mason RL, Hunt HM, Hurxthal L. Blood Cholesterol values in hyperthyroidism and hypothyroidism their significance. N Engl J Med 1930;203:1273‑8.
21. Tagami T, Kimura H, Ohtani S, Tanaka T, Tanaka T, Hata S, et al. Multi‑center study on the prevalence of hypothyroidism in patients with hypercholesterolemia. Endocr J 2011;58:449‑57.
22. Walton KW, Scott PJ, Dykes PW, Davies JW. The significance of alterations in serum lipids in thyroid dysfunction. II. Alterations of the metabolism and turnover of 131‑I‑low ‑density lipoproteins in hypothyroidism and thyrotoxicosis. Clin Sci 1965;29:217‑38.
23. Al-Khatib SM, LaPointe N, Kramer JM, Califf RM. What clinicians should know about the QT interval. JAMA 2003;289:2120-7.
24. Straus SM, Kors JA, De Bruin ML, et al. Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. J Am Coll Cardiol 2006;47:362–7.
25. Verdugo C, Perrot L, Ponsin G, Valentin C, Berthezene F. Time‑course of alterations of high density lipoproteins (HDL) during thyroxine administration to hypothyroid women. Eur J Clin Invest 1987;17:313‑6.
26. Leonidas HD, Gabriela B. The effect of thyroid disorders on lipid levels and metabolism. Med Clin North Am 2012;96:269‑81.
27. O'Brien T, Dinneen SF, O'Brien PC, Palumbo PJ. Hyperlipidemia in patients with primary and secondary hypothyroidism. MayoClin Proc1 993;68:860‑6.
28. Nielsen JB, Graff C, Rasmussen PV, et al. Risk prediction of cardiovascular death based on the QTc interval: evaluating age and gender differences in a large primary care population. Eur Heart J 2014;35:1335–44.
29. Nielsen JB, Pietersen A, Graff C, et al. Risk of atrial fibrillation as a function of the electrocardiographic PR interval: results from the Copenhagen ECG Study. Heart Rhythm 2013;10:1249–56.
30. Srivastava, D. M. ., Chowdhury, D. S. .,& Vishal, D. G. . (2022). Giant Mucocele of Maxillary Sinus, Scarce Occurrence: Case Report. Journal of Medical Research and Health Sciences, 5(2), 1774–1778. https://doi .org/10.52845/JMRHS/2022-5-2-2
31. Usoro AO, Bradford N, Shah AJ, et al. Risk of mortality in individuals with low QRS voltage and free of cardiovascular disease. Am J Cardiol 2014;113:1514–7.
32. Nielsen JB, Kuhl JT, Pietersen A, et al. P-wave duration and the risk of atrial fibrillation: Results from the Copenhagen ECG Study. Heart Rhythm 2015;12:1887–95.
33. 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.
34. 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.