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ORIGINAL ARTICLE

Study of Lung Function Tests and ECG Changes in Subclinical Hypothyroid Female Subjects

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ABSTRACT

Objectives: To study changes in electrocardiogram AND pulmonary function tests in a group of women with newly diagnosed subclinical hypothyroidism.

Methodology: The study was conducted on 30 women between the ages of 20 and 40 with subclinical hypothyroidism and compared to 30 age and gender-matched controls. The student's test was used to do statistical analysis in SPSS version 23.

Results: A total of 30 women who had subclinical hypothyroidism and 30 healthy, age- and sex-matched controls were included. The mean±SD height of the controls was 152.9 ± 3.7 cm and that of SCH patients was 153.1 ± 4.08 cm. Height differences between the two groups were insignificant. The mean±SD weight of the controls was 51.9 ± 4.5 kg and that of SCH subjects was 53.2 ± 4.3 kg. Weight differences between the two groups were insignificant. The mean±SD BMI of the controls was 22.16 ± 1.64 kg/m2 and that of SCH subjects was 22.71 ± 1.99 kg/m2. BMI differences between the two groups were insignificant.

Conclusion: Results have suggested that the changes will occur in spirometry and electrocardiogram, even in the subclinical state of hypothyroidism. Precautions can be taken at this stage to prevent progression to overt hypothyroidism.

Keywords: Subclinical hypothyroidism; TSH; spirometry; ECG; muscle strength; QTc; females; early treatment

INTRODUCTION

In today's environment, endocrine dysfunction is one of the most common disorders. Thyroid problems are one of them. The thyroid gland ensures tissues are functioning at their optimum potential by regulating the body's metabolism. Most cells in the body consume more oxygen when thyroid hormones are present.

Metabolic processes in the body, which are essential for growth and development. Mental and physical slowness, poor resistance to the cold, and dwarfism in youngsters are all symptoms of a thyroid gland deficiency. Thyroid secretion that is too prime causes wasting of the body, agitation, tremor, and excessive heat production.[1]

Thyroid hormones affect nearly every organ system and regulate a wide range of metabolic parameters1. Both hypothyroidism and hyperthyroidism are characterized by a deficiency or overproduction of thyroid hormone, respectively.[2] More people suffer from hypothyroidism than hyperthyroidism.[3] 3.47% of previously undiagnosed cases and 7.48 self-reported cases make up 10.95% of the total prevalence of hypothyroidism, according to the CDC. The prevalence of thyroid dysfunction in women is consistent with reports from around the world, particularly those aged 46 to 54.[4]

When hypothyroidism develops, the severity of the condition can range from modest subclinical symptoms to full-blown myxedema. It is more prevalent than overt hypothyroidism and occurs in 3% to 8% of the general population, it is more common in women than men, and its frequency rises with age as it does with overt hypothyroidism.[5]

SCH Slightly elevated levels of the thyroid hormone thyrotropin (TSH), along with normal levels of serum-free T3 (FT3) and free T4 (FT4) hormones, constitute subclinical hypothyroidism (SCH).[6]

Some other synonyms for subclinical hypothyroidism include mild hypothyroidism, preclinical hypothyroidism, biochemical hypothyroidism, and a decrease in the thyroid's reserve of hormones.[6]

TSH levels have long been seen as compensatory for subclinical hypothyroidism, and the pituitary adaptation to maintain these levels has long been assumed. Thyroid failure or tissue hypothyroidism may be the cause of the increased TSH in SCH, as more and more research shows.[7]

The heart and vascular system, as well as the respiratory system, are all impacted by thyroid hormones. It has been established that hypothyroidism is linked to problems with the respiratory and cardiovascular systems. In SCH, the question of whether or not there are similar issues is open to debate. As a result, similar dysfunctions, albeit milder, are expected in SCH. Hypothyroidism may influence the cardiovascular system in both subclinical and overt hypothyroidism, according to the same pattern of cardiovascular abnormalities.[7] The 'dosage effect' phenomenon occurs when the serum TSH level rises.[8] Also, investigations have shown that TSH and spirometric parameters are negatively correlated.[9]

Several metabolic and organ function markers will reveal relatively small changes in subclinical hypothyroidism because of the minor thyroid hormone secretion impairment. Such changes may, however, have a clinical impact if they damage specific organs over time.

any time in the past.[10]

Subclinical hypothyroidism has received only a little research in Sindh Pakistan. Aside from the fact that research on subclinical hypothyroidism has been inconsistent and that approximately half of SCH patients may eventually develop full-blown hypothyroidism, further study is needed in this area.[8]

Subclinical hypothyroidism patients' circulatory and pulmonary abnormalities haven't been researched in the same participants to provide a complete picture of the disease's effects. Because of this, we have made an effort. We included PFT and ECG tests in our study since they are straightforward screening procedures for SCH, which is frequent among young females. Detection and treatment of these girls may help them live better lives.

MATERIALS AND METHODS

We carried out this research at Peoples University of Medical and Health Sciences for Women Shaheed Benazir Abad, Sindh Pakistan. Thyroid hormones were measured, spirometry was recorded, and ECG was recorded for controls and study subjects

in and around Sindh Pakistan. The study group included 30 non-pregnant subclinical hypothyroid female subjects, while the control group included 30 non-pregnant normal healthy people. They were chosen based on criteria for inclusion and exclusion. We recruited 30 healthy females between the ages of 21 and 40 years old who were not pregnant and saw doctors at OBG, Dermatology, and Medicine OPDs. Medically healthy, non-pregnant women of the same age and gender were used as controls. In this investigation, only newly diagnosed cases with TSH levels between 5 and 10 mIU/L were considered while females below 20 years and above 40 years, pregnant females, any known illnesses, any obesity, overt hypothyroidism, family history of thyroid diseases, smoking and alcohol history, under any medication or therapy were not included in this research.

Patients newly diagnosed with subclinical hypothyroidism who meet the study's inclusion criteria were included. This study was conducted with written informed permission from all of its participants. Patients enrolled in the study were evaluated using a proforma that comprised taking complete medical histories, performing physical exams, and ordering tests. During meetings and testing, both study subjects and controls were handled with respect. Before the test, they were instructed to fast for at least two hours and to drink only water. When they had questions, they were patiently handled and made sure they had all of their questions answered before, during, or after the testing. Participants and controls were given instructions in their native language. This is a non-invasive test, and the findings will be kept private from us. They will be referred to an endocrinologist at Peoples University of Medical and Health Sciences for Women Shaheed Benazir Abad, Sindh Pakistan if the need arises. The study comprised thirty people with newly diagnosed and untreated primary subclinical hypothyroidism. LUMHS, OPD (Dermatology, Medicine, and OBG) staff performed a thyroid hormone assay on 30 patients who came to the OPD with nonspecific complaints of fatigue, minor weight gain, and depression. Subjects who had TSH levels above normal (5–10 mIU/L) with FT3 and FT4 levels that were normal were diagnosed with subclinical hypothyroidism (SCH). Thirty medical professionals, including undergraduate and graduate students, faculty, and non-faculty members, were included in the study. Thyroid hormone assays were performed on healthy individuals who had no symptoms, and these individuals were used as a control group since their levels of thyroid hormone were normal. To assess thyroid hormones, the Roche Cobas E411 Immunology Analyzer detects glow-based chemiluminescent reactions. Conventional colorimetric methods are slower and less sensitive, but this method is more flexible and gives a wider dynamic range. Each person's measurements, including height and weight, were taken. Using the formula BMI in kg/m2 = weight kg / (height m) 2, the BMI was computed. All of one's critical bodily functions, such as heart rate and blood pressure, were tracked. There was a thorough examination of the lungs, heart, abdomen, and brain.

Lung function tests: This is where we took measurements of both static and dynamic lung function tests. The ndd EasyOn Spirometer (ndd Medical Technologies, Zurich, Switzerland) was used to gather data on lung function[11] because of its portability and precision. Analyzed spirometric parameters were recorded.

1 Forced vital capacity (FVC),
2 Forced expiratory volume in 1st second (FEV1),
3 FEV1/FVC
4 FEV1/FVC, Peak expiratory flow (PEF),
5 Forced expiratory flow 25%-75% (FEF 25%-75%).

Soft nose clips were used to keep air from escaping during the experiment. Using Filter Mouthpieces prevented the spread of disease. For reproducibility, we performed the test at least three times to show patient cooperation and effort were critical to the maneuver's success. A patient's two FVC readings should be within 5% and 100ml of each other (to show consistency).

Electrocardiogram: Using an electrocardiogram, the heart's electrical activity was measured. The individual was made to lie down on a couch for the duration of the experiment. Wearing clothing in a way that does not interfere with ECG recordings was requested from the subjects, who were informed there was no danger or suffering involved. At the time of recording ECG, a female attendant was requested. During connecting the leads, the gel was given to both wrists and the left ankle joint, as well as to the chest. The ECG was so recorded in all 12 leads.

Spirometer: If you're going to examine lung function, you need to perform a spirometry test, which is a fundamental test.[12]

In 1846, a surgeon the name of John Hutchinson invented the water spirometer to gauge a patient's vital capacity. To measure the amount of air exhaled by a person, he developed a water-based calibrated bell. To describe his findings on the association between vital capacity and height and age, Hutchinson wrote an article about his water-spirometer and his measurements of over 4,000 people. At any height, vital capacity is not related to weight.[13]

Statistical analysis: The data were entered SPSS version 23 and analyzed. All the participants had their thyroid function, spirometry, and an electrocardiogram tested. The data was entered a master chart and analyzed. The mean and standard deviation were determined for each of the variables.

Students were used to determining the importance of the mean difference in value between the cases and controls. An unpaired 't-test. QuickCals (GraphPad) was used for the statistical analysis of the data. For all parameters, an unpaired "t" test is performed between the control and the subject. A probability “p" value of < 0.05 is significant(S).

RESULTS

Thirty women who had subclinical hypothyroidism and 30 healthy, age- and sex-matched controls were included in this study. The anthropometric data, viral parameters, and thyroid function tests are between the controls and subclinical hypothyroid females are shown in Tables 1 and 2. The mean [±SD] height of the controls was 152.9 ± 3.7 cm and that of SCH patients was 153.1 ± 4.08 cm. Height differences between the two groups were insignificant.

The mean [±SD] weight of the controls was 51.9 ± 4.5 kg and that of SCH subjects was 53.2 ± 4.3 kg. Weight differences between the two groups were insignificant.

The mean [±SD] BMI of the controls was 22.16 ± 1.64 kg/m2 and that of SCH subjects was 22.71 ± 1.99 kg/m2. BMI differences between the two groups were insignificant.

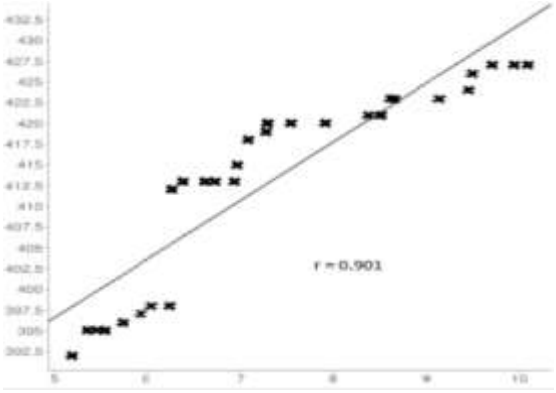
Table 1: Anthropometric data, viral parameters, and thyroid function tests between controls and study subjects:

Parameters	Controls (Mean ± SD)	Subjects (Mean ± SD)	t - Value	P-value	Significance
Height(cm)	152.9±3.7	153.1±4.08	0.198	0.843	NS
Weight (kg)	51.9±4.51	53.2±4.26	1.148	0.255	NS
BMI(kg/m2)	22.16±1.64	22.71±1.99	1.168	0.247	NS
Vital parameters					
Heart Rate (bpm)	75.1±5.11	74.03±6.4	1.384	0.171	NS
SBP (mmHg)	117±3.79	118.26±3.88	1.676	0.099	NS
DBP (mmHg)	74.6±3.24	75.93±4.01	0.712	0.479	NS
Thyroid function tests					
TSH (mg/L)	2.5±0.7	7.39±1.49	16.26	0.0001	ES
T3 (µg/dl)	0.13±0.03	0.12±0.03	1.29	0.202	NS
T4 (µg/dl)	7.05±1.9	7.63±1.78	0.883	0.3806	NS

Table 2: Comparison of ECG changes and lung function tests in controls and study subjects

Comparison of ECG changes	Controls (Mean ± SD)	Subjects (Mean ± SD)	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 (degrees)	60.03±24.5	59.53±23.8	0.08	0.936	NS
Lung function tests					
FVC (L)	2.74±0.49	2.42±0.37	2.887	0.005	HS
FEV1 (L)	2.28±0.43	1.93±0.34	3.467	0.001	HS
FEV1/FVC %	82.76±4.25	80.29±6.11	1.822	0.0736	NS
FEF 25-75%	2.76±0.32	2.24±0.39	5.612	0.0001	ES
PEF (L/sec)	5.75±1.05	5.06±0.64	3.074	0.0032	HS



Graph 1: Correlation between serum TSH levels and QTc for all SCH subjects (n = 30, r = 0.90, p = 0.037).

DISCUSSION

The initial stage of thyroid dysfunction is subclinical hypothyroidism. Subclinical hypothyroidism may be caused by chronic autoimmune thyroiditis, subacute thyroiditis, thyroid surgery, radioactive iodine treatment, or inadequate thyroid hormone replacement therapy.[14] Current use of the term "subclinical hypothyroidism" refers to persons with minimal or no symptoms of hypothyroidism, but who have normal blood-free t4, t3 concentrations, and increased serum TSH levels.[15]

Lung functions in SCH: Hypothyroid individuals are more likely to be obese, complicating the evaluation of changes in pulmonary function.[16] According to NIH/WHO recommendations, the average BMI of the participants in the current study was 22.71±1.99, which is within the healthy range for their age, gender, and sexual orientation. And there is no significant change in BMI between the SCH participants and the control group. " This means that spirometric parameters cannot be affected by obesity in combination.

FVC (Forced Vital Capacity): The mean FVC level (L) in our study was 2.742 ± 0.49 L in controls and 2.42 ± 0.36 L in subjects. The difference between the two groups was statistically significant ('a value less than 0.01). Gulfidan Cakmak et al. reported similar observations. Compared to controls, FVC values in subclinical hypothyroid patients were considerably lower.[14] Spirometric values were greater in the control group, lower in SCH participants, and lowest in clinical hypothyroidism patients, according to the researchers.[17]

FEV1 (Forced Expiratory Volume in the first second): Controls had a mean FEV1 (L) of 2.28±0.43 L, whereas subjects had a mean FEV1 (L) of 1.934 ± 0.34 L. The difference between the two groups was statistically significant ('a value less than 0.01). Gulfidan Cakmak et al. reported similar observations. Compared to controls, FEV1 levels in subclinical hypothyroid patients were considerably lower.[14]

FEV1/FVC %: The mean FEV1/FVC % in Controls was 82.76%, ± 4.25 %, and 80.29 %, ± 6.11 % in Subjects. There was no significant difference between the two groups ('P-value 0.05).

Gulfidan Cakmak et al. reported similar observations. Compared to controls, FEV1/FVC levels in subclinical hypothyroid patients were not substantially lower.[14] Lokman Koral et al. also made similar observations. FEV1/FVC values in SCH participants did not differ substantially before and after therapy with L-thyroxine. [15]

FEF 25-75% (Forced Expiratory Flow at 25–75%): Mean FEF 25-75% in Controls was 2.76 ±0.32% and in Subjects was 2.24 ± 0.39 %. The difference between the two groups was extremely significant (p-value < 0.0001) Similar observations were made by Gulfidan Cakmak et al. The values of FEF 25-75% in subclinical hypothyroid subjects were significantly reduced in comparison with the controls.[14]

PEF (Peak Expiratory Flow): In Controls, the mean PEF (L/sec) was 5.75 ± 1.05 L/sec, whereas, in Subjects, it was 5.06 ± 0.64 L/sec. There was a significant difference between the two groups ('p' value 0.05). Similar findings were not found in any other investigations. The individual effort has a big impact on peak expiratory flow. FEV1 has nearly twice the intersubject and intra-subject variability.

The impact of subclinical hypothyroidism on various organ systems is well established, however, the impact on the respiratory system is not. Although subclinical hypothyroidism can proceed to overt hypothyroidism, the decrease in respiratory function may start in the subclinical stage.[18] In individuals with clinical hypothyroidism, studies have showed a considerable reduction in the strength of the inspiratory and expiratory muscles. The weakening of these muscles might cause a considerable drop in spirometric parameters. SCH individuals also experience weariness, weakness, and somnolence, according to studies.[15,17] Reduced physical activity ability has also been noted in SCH patients,[7] which might contribute to poor spirometry performance. We attribute this decline to subclinical hypothyroidism since no systemic or respiratory illnesses could explain the difference between the individuals (controls and patients). Some experts believe that levothyroxine medication should be started in these patients, while others believe it had no meaningful effect on their spirometric data. As a result, there is still a need for more research on this subject. As with clinical hypothyroidism, respiratory functions may be compromised in patients with SCH, according to Cakmak et al. They also advocate community screening for anyone who may be at risk of SCH because of their respiratory function.

ECG CHANGES IN SUBCLINICAL HYPOTHYROIDISM: Different authors, such as Sureshbabu KP et al[19], Goyal V et al[20], and K. Ramesh et al[21], have well-established ECG alterations in clinical hypothyroidism, which include bradycardia, ST-T shifts, and low voltage complexes. There were ST-T alterations, such as T wave inversion or ST-segment depression and flattening. Hypothyroidism causes the QT interval to lengthen, which is a well-known risk factor for the development of ventricular arrhythmias.

The ECG did not show any significant alterations in the current investigation. In subclinical hypothyroid patients, only the QTc interval was substantially longer than in controls.

('p' value < 0.05). The mean QTc interval in subjects was 413.46 ± 11.7 and in controls was

400.1 ± 32.27.

The association between TSH levels and QTc intervals in the participants was positive, which agrees with a previous study.[22]

Many formulas have been presented to account because the QT interval is longer at slower heart rates and shorter at higher heart rates. The QT interval can be corrected for heart rate using the Bazett formula, which divides the QT interval by the square

root of the R-R interval.[23] As a result, we included QT intervals that were adjusted for heart rate in the current investigation (QTc).

ventricular depolarization and repolarization times are included in the QTc interval in the ECG, and the QTc interval changes inversely with heart rate. The link between an exceptionally high number of occurrences.

There is therefore an association between a prolonged QTc and disruption of long axis lengthening that occurs simultaneously in both the mechanical domains. O. Bakiner et findings .'s are in line with our findings. For the study group, the mean QTc interval was substantially longer than that of its control group. TSH levels and QTc intervals had a positive relationship as well. In patients with prolonged QT intervals, this shows that their hearts are repolarizing slowly.[22] A study by Galetta et al. found SCH can change the autonomic control of heart rate, resulting in higher ventricular recovery times that are less consistent. That study's findings matched ours. We also found considerable QTc interval prolongation in SCH patients.[6]

Factors that increase the risk of QT prolongation include older age, female sex, low left ventricular Ejection Fraction, left ventricular hypertrophy, ischemia, and slow heart rate. QT prolongation can also be caused by some medications.[23] The pre- and post-treatment groups, as well as the pretreatment and control groups, all had a significantly different diastolic function at rest, according to another study by Gabriela Brenta et al. Myocardial relaxation is compromised, as can be seen by the LV function. Hypophosphorylation of phospholamban, the protein that controls SERCA2's negative regulation, and decreased levels of SERCA2 in the sarcoplasmic reticulum could explain the existence of left ventricular diastolic failure in subclinical hypothyroidism.[24]

CONCLUSION

The results, which are significant for preventing the development of overt hypothyroidism and raising public awareness of this condition, are as follows. All the spirometry's values, including the FVC, FEV1, and FEV1/FVC, were found to be within the normal range. Subclinical hypothyroidism was associated with a decrease in FEF25-75 percent and PEF relative to the control group. In subclinical hypothyroidism, muscles in the inspiratory and expiratory tracts may become dysfunctional, which might explain why the pulmonary function is decreased. It was observed that electrocardiogram changes in subclinical hypothyroidism causes include an increase in the QTc interval as compared to controls. Also, there was a positive correlation between TSH level and mean QTc interval. However, the other parameters of ECG like QRS duration, PR interval, and QRS axis were like the controls. Because of subclinical hypothyroidism, patients are more susceptible to potentially fatal ventricular arrhythmias. In this way, it might be an effective tool for keeping track of cardiovascular risk. Hence, SCH subjects at risk and who had clinical signs and symptoms may be screened with simple procedures like spirometry and ECG. These simple screening tests may be more helpful in a community in knowing the effects of subclinical hypothyroidism on the cardio-respiratory system.

Subclinical hypothyroidism has been shown to affect the cardiovascular and pulmonary systems in its early stages. Preventing the development of overt hypothyroidism can be accomplished by recognizing and addressing these early signs of thyroid malfunction. Starting L-thyroxine therapy when hypothyroidism is just mild raises questions, so more research is needed. Prescription of LT4 medication should be done on a case-by-case basis, considering the possibility of both progressive thyroid failure and cardiovascular problems.

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