Determination of heart rate and blood pressure responses and hyperlipidemia in clinical hypothyroidism

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ABSTRACT

Objective: To evaluate the correlation between blood pressure, heart rate and lipid profile in Clinical hypothyroidism.
Study Design: Comparative Cross-sectional study.
Place and Duration: Department of Physiology, Islamic International Medical College, Rawalpindi from January 9, 2013 to December 8, 2013.
Methodology: The subjects were selected through non-probability, purposive sampling and divided into 2 groups on the basis of thyroid profile. i.e. control (euthyroids), and case (clinical hypothyroids). Clinical assessment of vital parameters such as heart rate, blood pressure and laboratorial evaluation of blood for lipid profile was analyzed in a systematic way.
Results: A highly statistically significant association was found in serum cholesterol, triglyceride and low density lipoprotein levels (the calculated probability was less than 0.01). Likewise, a statistically significant association was found in heart rate (the calculated probability was equal to 0.02) and maximum heart rate (the calculated probability was equal to 0.03) Additionally, A highly statistically significant association was found in mean arterial blood pressure, systolic and diastolic blood pressure (the calculated probability was less than 0.01) between the two study groups.
Conclusion: Clinical hypothyroid patients have higher risk of hypertension and pro-atherogenic lipid abnormalities.
Keywords: Hypothyroidism, Heart rate, Blood pressure, Hyperlipidemia, Tri-iodothyronin, Thyroid stimulating hormone.

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INTRODUCTION

Endocrine diseases are amongst the most abundant disarrays in the world. They stand next to diabetes mellitus in fatal outcome globally. It has been estimated that 0.2% of death in Asia result from endocrine disorders. The prevalence of clinical and subclinical hypothyroidism is 4.1% and 5.4% respectively and these disorders are higher in females than males in Asia[1-3].

Hypothyroidism, merely like obesity, happens to be one of the pathological disorders, which is most often related with ailments of lipid metabolism. Additionally, dyslipidemia happens to be one of the prime risk factors leading to cardiovascular diseases[4,5]. It is strongly believed that hypothyroidism is one of the most well-known causes of hyperlipidemia. The first change to occur in hypothyroidism is the abnormal lipid pattern and after treatment it disappears lastly. The most frequent lipid abnormality is increased concentration of cholesterol and low density lipoprotein (LDL). An enhanced esterification of fatty acids at hepatic level leads to increased levels of plasma triglycerides. Major mechanism of hyperlipidemia in hypothyroidism is due to reduced binding activity of hepatic LDL receptors[6]. There are clear effects of T_3 on LDL receptor mRNA but they could not be noticeably ascribed to TRα1 or TRβ. The transcription of the LDL receptor genesis is T_3 rapidly regulated, however, no specific TRE (thyroid response element) has so far been found in the LDL receptor gene promoter[7,8].

The most common cardiovascular manifestation of hypothyroidism may include bradycardia, mild hypertension (diastolic), narrowed pulse pressure, cold intolerance, and fatigue. Raised hypercholesterolemia in addition to diastolic hypertension in such patients leads to accelerated atherosclerosis and coronary artery disease. Genomic changes in heart elucidate the physiological variations comprising of the decelerating isovolumic relaxation phase in diastolic function which remain a characteristic feature in hypothyroidism. The decreased cardiac contractility results from variations in the cardiac gene expression precisely reduced expression of the sarcoplasmic reticulum Ca2-ATPase in addition to enhanced expression of inhibitor of it namely phospholamban. Altogether, such proteins work in the ambience of intracellular calcium cycling. Thus they regulate diastolic functions. It is well reported

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in black and white that patients having hypothyroidism are able to develop a protein-embedded pericardial in addition to/or pleural effusion[9,10].

Thyroid hormone functions as principal to lesser SVR (Systemic vascular resistance) that causes reduction in the mean arterial pressure. It is thereby noticed by the juxtaglomerular apparatus that leads to raised renin synthesis as well as secretion. T_3 unswervingly stimulates the synthesis of substrate of renin in the liver too. While, thyroid hormone reduces SVR as well as after load, it raises renin in addition to aldosterone secretion resulting in rise in blood volume as well as preload in addition to contributing in the distinctive rise in cardiac output[11,12]. The current study was designed in the wake of an effort and rationale to assess discrete association not only between heart rate as well as blood pressure responses but also hyperlipidemia in clinical hypothyroidism to help enhance quality of life in the menace of clinical hypothyroidism. We hypothesized that there was a likely unswerving association between heart rate as well as blood pressure responses and hyperlipidemia in clinical hypothyroidism. The objective of this study was to evaluate the correlation between blood pressure, heart rate and lipid profile in Clinical hypothyroidism.

METHODOLOGY

This comparative cross sectional study was carried out in the Department of Physiology, Islamic International Medical College, Rawalpindi from January 9, 2013 to December 8, 2013. The study was approved by the Riphah Institutional Ethical Committee and all subjects gave their informed consent.

A group of 100 adults aged 30-60 years were selected over a period of 12 months who visited the outpatient endocrinology clinic of Railway Hospital Rawalpindi in response to announcement for free examination and biochemical tests having unrecognized symptoms of weight gain, lethargic, easy fatigability and constipation. Thyroid function tests and lipid profile were included in the protocol. Subjects enrolled were equally sub-divided into two groups; namely Control (euthyroid group) and Case (hypothyroid group), respectively. Inclusion criteria consisted of diagnosed cases of hypothyroid and euthyroid subjects of either gender between 30-60 years of age in addition to hyperlipidemia. Exclusion criteria consisted of subjects suffering chronic illnesses like diabetes, tuberculosis etc.; medications like anti thyroid drugs and oral contraceptive pills, etc.; and pregnancy.

5ml of fasting blood (12 to 14 h after the last meal) samples was drawn between 08:00–09:00 a.m from antecubital vein of participants and collected in serum vacutainer and EDTA tubes separately under aseptic condition. Blood was taken for assessment of lipid and thyroid profile (serum fT3, fT4 and TSH). The blood samples were allowed to clot at room temperature and then centrifuged using a remi centrifuge (R-8C) to separate the serum. The serum so obtained was divided into two parts. The samples were analyzed only when the control values were within one standard deviation.

First part of the serum was analyzed for thyroid profile. Serum TSH and free T3, T4 were measured on immuno-analyzer Centaur CP by using an analyzer specific kit.

The subjects were grouped on the basis of their TSH (6 µIU/mL and 10 µIU/mL) into Euthyroid group as controls and Clinical group.

As per WHO guidelines, two readings of Systolic and diastolic blood pressure of all subjects in a sitting position at 5 minutes intervals were taken by using a standard mercury manometer and the mean value of the two readings was calculated.

If high blood pressure (≥140/90 mmHg) was noted, a third reading was taken after 5 minutes. The lowest of the three readings was taken as blood pressure. The measurement of pulse rate was done by palpitating the Radial pulse on the wrist for one minute.

Data Analysis: All analysis were performed by the computerized SPSS version 21.0 (Statistical Package for Social Sciences). Results were expressed as means ± SD. Kolmogorov-Smirnov test was used to test the Normality of the data. Comparisons between Clinical and euthyroid groups were made by using the Student's T-test and the relationship between thyroid hormones and blood pressure parameters were evaluated by Pearson correlation test. The $P<0.05$ was considered to be statistically significant and $P<0.01$ as highly statistically significant.

RESULTS

One hundred euthyroid and hypothyroid subjects were enrolled who were equally sub-divided into two groups; namely control (euthyroid group) and case (hypothyroid group) groups respectively. A highly statistically significant association was found in serum cholesterol, triglyceride and LDL levels ($P<0.01$**) between the study groups, whereas no statistically significant association was found in HDL levels ($P=0.165$) as shown in (Table-I).

Table-I: Comparison of cholesterol, triglyceride, low density lipoprotein and high density lipoprotein levels between control and case groups (N=100)

Parameters	Control Mean+SEM (n=50)	Case Mean+SEM (n=50)	P-value
Cholesterol (mg/dl)	160.95+33.54	312.77+31.26	<0.01**
Triglyceride (mg/dl)	128.36+15.30	354.14+38.70	<0.01**
LDL (mg/dl)	116.15+18.85	227.16+33.92	<0.01**
HDL (mg/dl)	52.45+5.20	41.57+5.79	0.165

Moreover, a statistically significant association was found in heart rate ($P=0.02$*) and maximum heart rate ($P=0.03$*) between the study groups, whereas no statistically significant association was found in minimum heart rate ($P=0.265$) as shown in (Table-II).

Table-II: Comparison of heart rate, minimum heart rate and maximum heart rate between control and case groups (N=100)

Parameters	Control Mean+SEM (n=50)	Case Mean+SEM (n=50)	P-value
Heart Rate (Beats Per Minute)	85.63+9.22	61.04+5.98	0.02*
Minimum Heart Rate (Beats Per Minute)	68.09+8.43	56.35+6.21	0.265
Maximum Heart Rate (Beats Per Minute)	87.35+7.98	65.08+6.56	0.03*

Additionally, A highly statistically significant association was found in mean arterial blood pressure as well as systolic blood and diastolic blood pressure (P<0.01**) as shown in (Table-III).

Table-III: Comparison of mean arterial blood pressure, systolic blood pressure and diastolic blood pressure between control and case groups (N= 100)

Parameters	Control Mean+SEM (n=50)	Case Mean+SEM (n=50)	P-value
Mean Arterial Blood Pressure (mmHg)	113.43+12.35	74.66+6.28	<0.01**
Systolic Blood Pressure (mmHg)	143.16+15.70	93.45+8.52	<0.01**
Diastolic Blood Pressure (mmHg)	98.65+9.11	63.80+5.23	<0.01**

DISCUSSION

Comparison of serum cholesterol, triglyceride LDL and HDL levels was done between control (euthyroid) and case (hypothyroid) groups. The mean total cholesterol levels were comparatively found to be highly statistically significant in clinical hypothyroidism. These findings were comparable to previous studies showing similar results by Lu et al[13] and Singh et al[14]. Moreover, Tuzcu et al[15] found that with higher grades of hypothyroidism there was an increase in total cholesterol levels. This increase could usually be attributed to the decreased activity of lipoprotein lipase and HMG-CoA reductase. The increased serum cholesterol may represent an alteration in a substrate steady state level caused by a transient proportionally greater retardation in degradation than in synthesis. The increase of serum cholesterol was largely accounted for by an increase of LDL-cholesterol, which was cleared less efficiently from the circulation due to a decreased T3-dependent gene expressing of the hepatic LDL-receptor[16].

The mean serum triglyceride levels were comparatively found to be highly significantly in clinical hypothyroidism. Studies conducted by Tuzcu et al[15] and Lu et al[13] also showed similar results. The elevation of triglycerides in clinical hypothyroidism was due to the fact that there was poor clearance of endogenous and exogenous triglycerides from circulation in hypothyroidism. Triglycerides are usually increased in hypothyroid patients because of decreased activity of lipoprotein lipase which in turn results in decreased clearance of triglyceride rich lipoproteins. Al Sayed et al[17] carried out a study in which similar results were shown too.

Additionally, it was reported that patients with clinical hypothyroidism exhibited elevated LDL-C. Study conducted by Al Sayed et al[17] also found that HDL levels were decreased in both clinical hypothyroid cases comparatively. However, these findings were in contrast to the studies by Singh et al[14] which demonstrated that with increasing grades of hypothyroidism there was decrease in serum HDL values. A highly statistically significant association was found in serum cholesterol, triglyceride and LDL levels (P<0.01**) between the study groups. Whereas no statistically significant association was found in HDL levels (P=0.165). Similar results were found by Tuzcu et al[15] and Lu et al[13]. However, the results which were seen by Singh et al[14] stood in disparity. He found that HDL level were significantly lower. The elevation of triglycerides in clinical hypothyroidism was due to the fact that there was poor clearance of endogenous and exogenous triglycerides from circulation in hypothyroidism. The rise in serum cholesterol happened to be principally accounted for by rise in LDL-cholesterol that remained emptied less efficiently through the circulation thanks a reduced T_3-dependent gene expression of hepatic LDL-receptor[18].

Moreover, a statistically significant association was found in heart rate (P=0.02*) and maximum heart rate (P=0.03*) between the study groups, whereas no statistically significant association was found in minimum heart rate (P=0.265). Additionally, A highly statistically significant association was found in mean arterial blood pressure, systolic blood pressure and diastolic blood pressure (P<0.01**). Similar results were found by Syamsunder et al[19]. However, the results which were seen by Yicong et al[20] stood in disparity

The action of Thyroid hormone on the cardiovascular system is exerted mainly via its intra as well as extra nuclear genomic effects[21]. The thyroid hormone has very important ability to change function of Endothelial and vascular smooth muscle cells[22].

In thyroid hormone deficiency, there is reduction of arterial compliance leading to rise in systemic vascular resistance and increase in diastolic blood pressure[23].

In hypothyroidism, a decreased LDL receptor activity is observed due to reduced number of low density lipoprotein (LDL) receptors in the liver which causes diminished LDL clearance[24].

As a result, clinical hypothyroidism is characterized by a marked increase in cholesterol and LDL-C levels in blood [24]. There is also increased LDL-C concentration in blood in subclinical hypothyroidism[25]. However, thyroid hormone replacement therapy can reverse altered lipid profile[26]. The hypothyroid patients are predisposed to accelerated atherosclerosis and CHD mainly due to the dyslipidemia and the diastolic hypertension[24]. Although direct confirmations about the effect of levothyroxine on CHD are deficient, clinical studies have shown have beneficial effects of levothyroxine treatment on early markers of atherosclerosis. like endothelial function [22] and carotid artery intima-media thickness especially in subclinical hypothyroidism[25].

CONCLUSION

Clinical hypothyroid patients have higher risk of hypertension and pro-atherogenic lipid abnormalities.

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