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Research Article

Study of insulin levels in hypothyroidism patients

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ABSTRACT

Background: Overt hypothyroidism is an established risk factor for insulin resistance. In this study we find out whether this association exists between insulin resistance and subclinical hypothyroidism.
Methods: Serum Insulin, Fasting blood sugar, Cholesterol were estimated in 60 clinically diagnosed patients of hypothyroidism these patients were divided in to two groups as group I, 30 overt hypothyroidism and group II, 30 subclinical hypothyroidism. Results were compared with a group of 30 normal subjects. To measure the level of insulin resistance using HOMA IR software.
Results: In our study total cholesterol were significantly high in both overt hypothyroidism and sub clinical hypothyroidism as compared to euthyroid control group and serum TSH and serum insulin levels were positively correlated with total cholesterol levels in hypothyroidism patients. We also found that TSH levels were positively correlated with insulin and HOMA IR in patients with subclinical hypothyroidism.
Conclusions: Hence it will be good practice to screen people for presence of subclinical hypothyroidism and insulin resistance for early detection and prolong the appearance of various fatal complications associated with insulin resistance in hypothyroidism.

Keywords: Subclinical hypothyroidism, Overt hypothyroidism, HOMA-IR, Insulin resistance

INTRODUCTION

Hypothyroidism is a clinical syndrome due to deficiency of thyroid hormones which results in a generalized slowing down of metabolic[1] process. It is a common disorder that occurs in mild to severe forms in 2% to 15% of the population. Women are affected more often than men and both sexes are affected more frequently with increasing age. Clinical symptoms can range from the obvious and easy to recognise lethargy, fatigue and cold intolerance to more subtle, subclinical disease with general symptoms that escape detection. Prevalence of subclinical hypothyroidism is 6-8% in women and 3% in men. Myxoedema is a severe form of hypothyroidism in which there is accumulation of mucopolysaccharides in skin and other tissues, leading to thickening of facial features and a doughy induration of skin. On the basis of severity of clinical signs and symptoms, hypothyroidism is classified into 1 overt hypothyroidism (OH) patient has high TSH but low T3 and low T4 levels in serum as compared to normal reference levels & distinct signs and symptoms of hypothyroidism. 2 Subclinical hypothyroidism patient has high TSH but normal T3 and T4 levels as compared to normal reference levels. These patients have very few or no clinical signs and symptoms.

Overt hypothyroidism is an established risk factor for insulin resistance[2] and hyperlipidemia. Several studies have shown an association between insulin resistance and hypothyroidism for overt hypothyroidism, but there is controversy as to whether this association is also present in subclinical hypothyroidism. Our study is being carried out to find whether an association exists between insulin resistance and subclinical hypothyroidism in adult males and females.

Insulin resistance will be calculated by using values of fasting serum insulin level and fasting plasma glucose level in Homeostasis Model Assessment for insulin resistance (HOMA–IR) calculator developed by diabetes trial unit endocrinology department, University of oxford.

Thyroid dysfunction leads to altered glucose and lipid metabolism[3] leading to insulin resistance, which is an important risk factor for cardio vascular diseases. Early detection of insulin resistance and prompt intervention for it in hypothyroid patients will be helpful to decrease cardiovascular morbidity and mortality.

In case of type 2 diabetes mellitus hypothyroidism may also contribute to insulin resistance.[4,5] Only treatment of diabetes will not be that effective to resolve insulin resistance completely. Along with diabetes treatment, if we check and treat hypothyroidism even in subclinical stage then it will take care of its contribution to total insulin resistance.

METHODS

This study was carried out in the department of Biochemistry Rangaraya Medical College, Kakinada in collaboration with Department of Medicine & Surgery. 60 clinically diagnosed patients of hypothyroidism were selected as cases from out patients of medicine and surgery and diagnosed by the physician and confirmed by thyroid function test. These were divided in to two groups group-I 30 overt hypothyroidism and group-II 30 subclinical hypothyroidism and control group 30 all are above the age 15 yrs.

Estimation of serum TSH,T3,T4 and fasting serum insulin were done by Sandwich ELISA method, (Elisa reader and washer-Erba Lisa Scan 2) plasma glucose by GOD-POD end point method. Estimation of insulin resistance by using HOMA-IR[6,7] (Homeostasis model assessment for insulin resistance) software on HOMA calculator select proper units enter plasma glucose (mmol/L)and serum insulin[8] values (pmol/L) then click on calculate then we got the value of insulin resistance. Estimation serum total cholesterol includes HDL, LDL, and VLDL cholesterol by CHOD-PAP end point method. All the above parameters were analysed in both control and cases including both OH and SCH.[9] All statistical data was analysed by ANOVA (one way analysis of variance) correlation between different parameters in SCH by using Pearson's formula. P value <0.05 was considered to be statistically significant.

RESULTS

In this study, Serum TSH levels are increased in SCH (12.3±5.2) and further increased in Overt Hypothyroidism (18.4±6.4) when compared to controls (3.1±1.32) and serum T3 and T4 significantly decreased in SCH and OH when compared to controls.

Table 1: Comparison of serum TSH, T3 & T4 levels in all groups.

Parameter	Control (Mean + SD)	SCH (Mean + SD)	OH (Mean+ SD)	P value
Serum TSH (µIu/ml)	3.1 ± 1.32	12.3± 5.2	18.4 ± 6.4	< 0.001 (HS)
Serum T3(ng/dl)	111± 32	108 ± 31	58 ± 11	< 0.001 (HS)
Serum T4 (µg/dl)	8.8 ± 1.6	7.7 ± 2.2	3.1 ± 1.5	<0.001 (HS)
Cholesterol (mg/dl)	134± 14	176 ± 47	222 ± 53	<0.001 (HS)

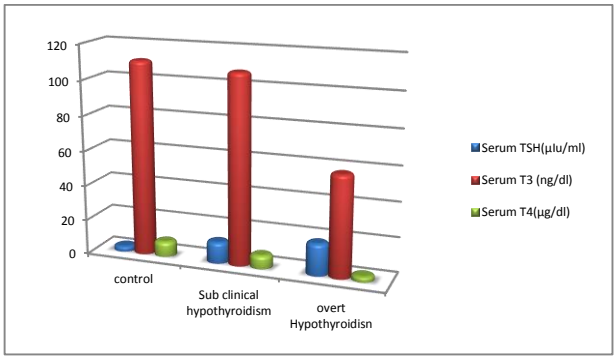

Figure 1: Figure showing comparison of serum TSH, T3, T4 levels in controls, subclinical hypothyroidism, overt hypothyroidism.

In present study, Total Cholesterol are highly significantly elevated in OH (222±53mg/dl) as compared to control (134±14mg/dl) and SCH (176±47mg/dl), and significantly increased in SCH as compared to control(p value <0.001).

In this, HOMA-IR is significantly increased in SCH (1.7±0.71, p<0.001) and further highly increased in OH (2.2±0.91, p<0.001) as compared to controls (0.76±0.36) and fasting serum insulin levels increased in SCH (13±5.8) and OH (17±7.1) as compared to controls (5.9±2.7).

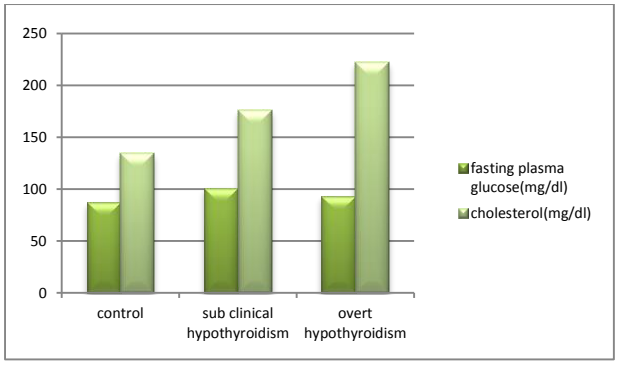

Figure 2. Showing comparison of fasting plasma glucose and cholesterol levels in controls, subclinical hypothyroidism and overt hypothyroidism.

Table 2: Comparison of fasting plasma glucose, fasting insulin and insulin resistance levels in all groups.

Parameter	Control	SCH	OH
Fasting plasma glucose(mg/dl)	87± 8.7	101±11	93 ± 12
F serum Insulin (µIU/ml)	5.9 ± 2.7	13 ±5.8	17 ± 7.1
Insulin Resistance	0.76±0.36	1.7±0.71	2.2±0.91

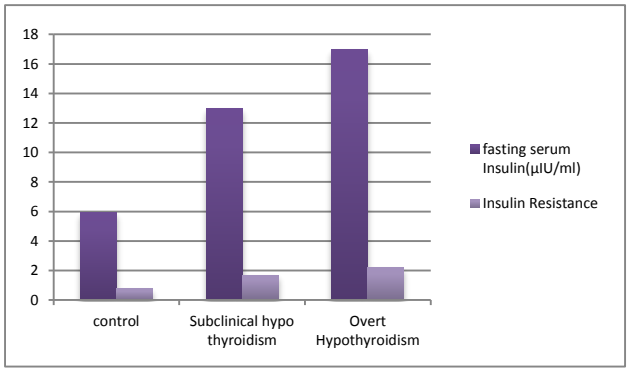

Figure 3: Figure showing comparison of fasting serum insulin and insulin resistance levels in controls, subclinical hypothyroidism, overt hypothyroidism.

Table 3: Significance of fasting plasma glucose, fasting insulin, and insulin resistance levels in all groups.

Parameter	Control Vs SCH	Control vs OH	SCH Vs OH
Fasting plasma glucose (mg/dl)	<0.001 (HS)	>0.05 (NS)	<0.05 (S)
Fasting serum insulin (µIu/ml)	<0.001 (HS)	<0.001 (HS)	<0.05(S)
Insulin resistance	<0.001 (HS)	<0.001(HS)	<0.05(S)

Pearson's correlations between different parameters in SCH

Parameter	Coefficient of correlation	P value
TSH Vs HOMA-IR	0.712	<0.001
TSH Vs Insulin	0.693	<0.001
TSH Vs TC	0.602	<0.001
HOMA-IR Vs TC	0.560	<0.05
Insulin Vs TC	0.553	<0.05

DISCUSSION

Insulin resistance is a cardinal feature of type 2 diabetes mellitus[10] and is relatively frequently found in mild thyroid dysfunction[11] with increased risk of dyslipidemia. In recent times tremendous interest has been raised in the influence of thyroid hormone action on insulin levels. The development of insulin resistance leads to many metabolic abnormalities. Hypothyroidism can increase the risk of cardiovascular disease, infertility and osteoporosis. In the present study we have explored the possible linkage among TSH, insulin resistance[12,13] and serum total cholesterol in subclinical hypothyroidism patients. In this study total cholesterol are highly significantly elevated in OH (222±53mg/dl) as compared to control (134±14mg/dl)and SCH (176±47mg/dl), and significantly increased in SCH as compared to control(p value <0.001). The serum TSH levels and levels are positively correlated with total cholesterol in subclinical hypothyroidism patients (r=0.602, p<0.001) (r=0.553, p<0.05) correspondingly. This indicates along with OH, patients of SCH also develop hypercholesterolemia.

Thyroxine increases the activity of HMG CoA reductase leading to increased synthesis of cholesterol. So hypothyroidism should manifest with low cholesterol levels, but levels of serum total cholesterol increase in hypothyroidism. This is due to that even though decrease production of cholesterol in hypothyroidism but there is significant decrease in clearance of cholesterol by liver due to decrease in cholesterol receptors on liver cells in hypothyroidism. So net effect is the accumulation of cholesterol leading to hypercholesterolemia.

Thyroid hormones exert profound effects in the regulation of glucose homeostasis. These effects include modifications of circulating insulin levels, counter regulatory hormones, intestinal absorption, hepatic production and uptake of glucose by peripheral tissues, all these changes produce insulin resistance which is the culprit for many complications mainly cardiovascular diseases. In this study HOMA-IR[14] is highly significantly increased in SCH (1.7±0.71,p<0.001) and further highly increased in OH(2.2±0.91,p<0.001) as compared to controls(0.76±0.36). In our study showed that TSH levels were positively correlated with insulin and HOMA-IR in patients with SCH(r=0.693, p<0.001), (r=0.712, p<0.001) respectively. And HOMA-IR values were positively correlated with TC (r=0.560 and p<0.05). The serum insulin levels were significantly correlated with total

cholesterol (r=0.553, P<0.05). This indicates that insulin resistance is present not only in overt hypothyroidism but it is significantly present in subclinical hypothyroidism patients also. It indicates that levels of insulin resistance directly correlate with levels of TSH and cholesterol.

Presence of insulin resistance in SCH and OH can be explained by that the thyroid hormones act differently on liver, skeletal muscles and adipose tissue – the main target of insulin action. Thyroid hormones up regulate the expression of genes for GLUT-4 and phosphoglycerate kinase, involved in glucose transport[15] and glycolysis respectively, thus acting synergistically with insulin in facilitating glucose disposal and utilization in peripheral tissue.

In hypothyroidism because of altered metabolism of lipid and insulin,[16] binding of insulin to insulin receptor decreases. Impaired translocation of GLUT-4 glucose transporters on plasma membrane occurs, resulting in decreased glucose uptake in muscles and adipose tissue occurs.

It was postulated that elevated total cholesterol levels and dyslipidemia may act as one of the main culprit for development of insulin resistance in hypothyroidism. Our study combined with previous studies provides an evidence of presence of insulin resistance in SCH patients.

CONCLUSIONS

Our study confirms that hypercholesterolemia and insulin resistance correlate positively with hypothyroidism status.

Hence it will be good practice to screen people for presence of Sub Clinical Hypothyroidism and insulin resistance, so that early detection and prompt intervention can prevent or prolong the appearance of various fatal complications associated with insulin resistance in hypothyroidism.

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