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ESTIMATION OF THYROID PROFILE AND SERUM FASTING INSULIN IN NEWLY DETECTED HYPOTHYROID ADULTS: A CASE CONTROL STUDY

Biochemistry

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ABSTRACT

Background: Thyroid hormone influences glucose homeostasis by modifications of the circulating insulin levels and peripheral tissues uptake of glucose. Thyroid function has been associated with insulin resistance. There is infrequent information about thyroid function in relation with glucose homeostasis in young adults.

Objective: To evaluate the thyroid profile, fasting serum insulin, HOMA-IR, Fasting blood sugar among newly detected hypothyroid adults (cases) in comparison with normal healthy adults (controls).

Methodology: A case control study of 164 subjects was carried out on hypothyroid adults (n=82) and controls (n=82), general medicine OPD, RRMC & hospital, Bengaluru. Fasting blood samples were taken. Thyroid profile, serum fasting insulin was done with CLIA. HOMA-IR was employed to assess the level of insulin resistance.

Results: The study subjects with mean age of 35 years and female predominance. TSH levels were higher in cases as compared to controls ($p<0.01$). However, the value of both T3 and T4 levels were found to be lower in cases as compared to controls and the difference of T3 between the groups was statistically significant ($p=0.03$) while that of T4 was not significant ($p=0.07$). FT3 & FT4 levels were within the reference range. Serum fasting insulin levels and HOMA-IR levels were higher in cases than controls ($p=0.007$) and ($p<0.01$) respectively. A strong positive correlation was found between TSH and insulin ($r=.528$, $p<.01$), TSH and HOMA-IR ($r=.462$, $p<.01$), insulin and HOMA-IR ($r=.962$, $p<.01$).

Conclusion: Our study shows that hypothyroidism is common among females and associated with mild degree of insulin resistance as reflected by HOMA-IR.

KEYWORDS

Hypothyroid adults, Insulin, Thyroid profile, Cases & Controls.

INTRODUCTION

Thyroid diseases are common in our population. Hypothyroidism is a common disorder encountered in clinical practice. In India thyroid disorders are the second most glandular disorder of the endocrine system and are increasing predominantly among women. According to a survey done by the Indian Government the prevalence of hypothyroidism is about 11%.[1] Hypothyroidism is characterized by deficient thyroid hormone production which can be severe or moderate. The most common cause of hypothyroidism is a lack of dietary iodine, termed iodine deficiency disorders by the World Health Organisation. In iodine sufficient areas, Hashimoto's thyroiditis, an auto-immune disease is the most frequent cause of hypothyroidism. Thyroid hormones are the primary determinants of glucose homeostasis.[2] The effect of the thyroid hormones can be insulin agonistic as demonstrated in muscles or antagonistic as demonstrated in the liver. However this occurs in a fine balance necessary for normal glucose metabolism. Deficit or excess of thyroid hormones can break this equilibrium leading to alterations in insulin sensitivity and glucose metabolism. Insulin resistance (IR), which is defined as decreased responsiveness of the peripheral tissue to the insulin action has been reported in hypothyroidism. The possible explanations hypothesised for this phenomena range from dysregulation of mitochondrial oxidative metabolism to reduction of blood flow in muscles and adipose tissue under hypothyroid conditions. [3-4]. Reduced glucose absorption from gastrointestinal tract accompanied by prolonged peripheral glucose accumulation; gluconeogenesis, diminished hepatic glucose output and reduced disposal of glucose are hallmarks of hypothyroidism. Thyroid function has been associated with insulin resistance [5]. There is infrequent information about thyroid function in relation with glucose homeostasis in young adults. In this study we hypothesized that insulin resistance is associated with hypothyroidism.

OBJECTIVE

The study aimed to evaluate the Fasting Serum Insulin, HOMA-IR, Thyroid profile, Fasting blood sugar among newly detected hypothyroid adults (cases) in comparison with normal healthy adults (controls).

MATERIAL AND METHOD

This study comprised of a total of 164 subjects who satisfied inclusion and exclusion criteria who present to the Department of General Medicine OPD in RRMCH, Bengaluru and three years of study period (2014-2017). The study was approved by the ethical Committee, RRMCH Bengaluru. An informed consent was taken from all the study groups. Blood sample were collected for the analysis in the vacuum evacuated tubes. Flouride-EDTA vacuum evacuated tubes was used for the estimation of blood glucose, insulin. Clot activator containing vacuum evacuated tubes was used for the estimation of serum TSH, T3, T4, FT3, FT4. Thyroid Profile and serum fasting insulin was done by Chemiluminescence Immunoassay (CLIA). HOMA-IR was calculated by HOMA index=fasting serum insulin (μU/ mL) × fasting blood sugar (mmol/L) /22.5 fasting blood glucose by glucose oxidase enzymatic method .

Inclusion Criteria

· Newly detected hypothyroid cases between age group of 18-55 years attending General Medicine OPD, RRMCH and Bengaluru.

Exclusion Criteria

·Subjects who were not given written informed verbal consent.
·Subjects with history of any Medical/ Surgical illness like cardiovascular disorders, Diabetes Mellitus, Renal failure, Liver disorders and other chronic illness.
·Hypothyroid adults on any other medications.
·Recording of Blood Pressure (BP) was recorded in lying down position using sphygmomanometer.
·All blood samples were taken between 8-10 am after 12 hours of fasting period. After collection, serum samples were stored at -20° until assayed.

RESULTS

In The study was a hospital based cross sectional study conducted in the Department of Biochemistry, RRMCH Bengaluru, India. A total of 164 subjects were included in the study. The whole study population was divided into two groups i.e. cases (newly detected hypothyroid subjects) n=82 and control (normal healthy subjects) n=82. The study subjects in the study were in the age group of 18-55 years in both the groups. The data were anlaysed using Microsoft Excel, SAS 9.2 and SPSS 21. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two groups. Pearson correlation coefficient was used analyse the correlation between thyroid values.

Figure 1 shows the pie chart depicting gender distribution of study groups: About 91% (n=75) subjects in cases and 79% (n=65) in controls were females.

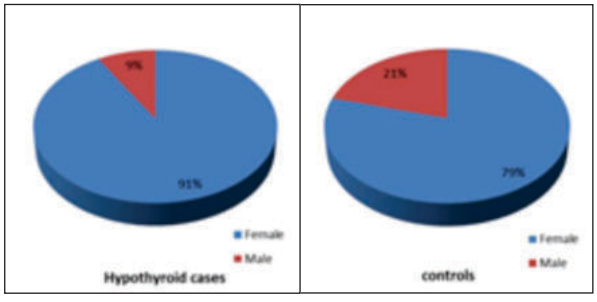

Figure 1: Gender Distribution Of Study Groups

Sources: Researchers' Calculation

Figure 2 depicts the bar diagram showing age distribution of study groups (18-55years). In this study, mean age of cases was 35.43 ± 11.47 years and controls was 34.93±10.22 years

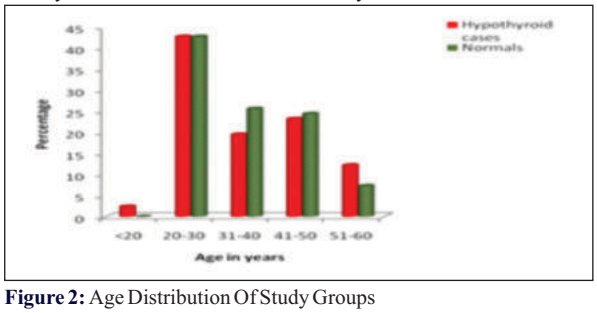

Figure 2: Age Distribution Of Study Groups

Sources: Researchers' Calculation

Table 1 shows the FBS, SBP and DBP levels comparison between cases and controls. The mean FBS levels in cases was higher (91±14 ng/dl) than in controls (80 ±11mg/dl) and was statistically significant (p<0.01). The mean SBP and DBP levels in cases were slightly increased than in controls and was statistically significant (p=0.01).

Table – 1 Comparison Of Cases And Controls According To Fasting Blood Glucose (FBS) & Blood Pressure (BP)

	Cases n=82	Controls n=82	p value
FBS (mg/dl)	91 ±14	80 ±11	< 0.001**
SBP (mmHg)	122.8±14.3	118.1±11.0	= 0.017*
DBP(mmHg)	81.9 ±10	78.4 ± 7.5	= 0.012*

Source: Researchers' Calculation

Table 2 shows the distribution of cases and controls according to TSH, T3, T4, FT3 and FT4. All the subjects in the controls group were in the normal reference range of TSH 0.3-4.4 µIU/L. The mean TSH levels (14.26 ± 8.9 µIU/mL) of cases were high compared to controls and was statistically significant (p<0.01). Total T3 (121.1±33.7 vs 140.7 ±32.4ng/dl), T4 (7.8 vs 8.4 ± 2.3 µg/dl) levels were low in cases and T3 was statistically significant (p=0.03) whereas T4 was not significant (p=0.07). FT3 (1.9 ± 0.8 vs 2.1 ± 0.8 pg/ml, p=0.42) and FT4 (0.8 ± 0.4 vs 0.8 ±0.08 ng/dl, respectively, p=1.00) levels in cases were found to be lower than controls and the difference was not statistically significant when compared to controls.

Table–2 Comparison Of Cases And Controls According To Thyroid Profile

	Cases n=82	Controls n=82	p value
TSH µIU/ml	14.26 ± 8.9	2.4 ± 0.96	<0.01*
T3 ng/dl	121.1± 33.7	140.7 ± 32.4	= 0.03*
T4 µg/dl	7.8 ± 1.9	8.4 ± 2.3	= 0.07
FT3 pg/ml	1.9 ± 0.8	2.1± 0.8	= 0.42
FT4 ng/ml	0.8 ± 0.4	0.8 ± 0.09	= 1.00

Source: Researchers' Calculation

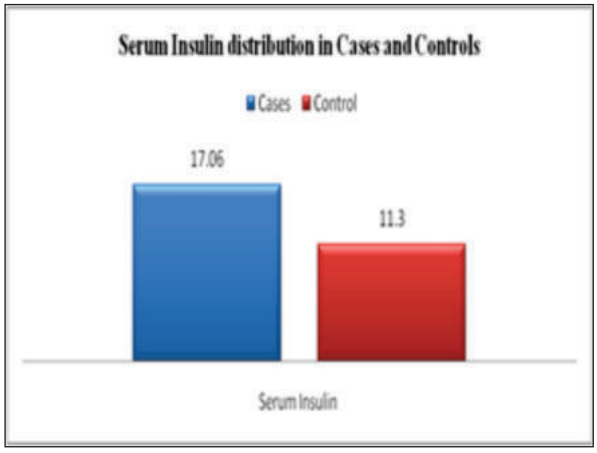

Figure 3: Serum Fasting Insulin Levels Among Study Groups
Sources: Researchers' Calculation

Figure 3 shows a bar diagram depicting serum fasting insulin levels among study subjects.

Table 3 shows a comparison of cases & controls according to Fasting Insulin Levels & HOMA-IR. The mean serum insulin values were 17.06 ± 13.4 µIU/mL in cases and 11.3 ± 6.8 µIU/mL in controls and the difference was statistically significant (p<0.07). The mean HOMA-IR values were 3.8 ± 2.5 in cases and 2.4 ± 1.5 in controls and the difference was statistically significant (p<0.01).

Table – 3 Comparison Of Cases And Controls According To Fasting Insulin & HOMA-IR

	Cases n=82	Controls n=82	p Value
INSULIN µIU/ml	17.06 ± 13.4	11.3 ± 6.8	= 0.007*
HOMA	3.8 ± 2.5	2.4 ± 1.5	< 0.001*

Source: Researchers' Calculation

In Table 4, the Pearson's correlation coefficient for the relationships between different parameters like serum TSH, Insulin, HOMA-IR is shown. The serum TSH levels had significant positive correlation with insulin, HOMA-IR and insulin vs HOMA-IR.

Table – 4 Pearson's Correlation Between Different Parameters In Hypothyroidism

Parameters	R value	P value
TSH vs INSULIN	.528**	<.001
TSH vs HOMA-IR	.462**	<.001
INSULIN vs HOMA	.962**	<.001

Source: Researchers' Calculation

DISCUSSION

Thyroid disorders are one of the commonest disorders of the adult population with its prevalence increasing with age. It is more familiar in women and usually autoimmune in origin presenting either as primary atrophic hypothyroidism or Hashimoto's thyroiditis. Biochemically, it is characterised by elevated TSH levels (reference range 0.3-4.5 µIU/ml) and normal or reduced levels of peripheral thyroid hormones [6]. Hypothyroidism has been associated with glucose and insulin metabolism disorders that affect insulin secretion in response to glucose, hyperinsulinemia, altered peripheral glucose disposal, and insulin resistance [7]. The present study has investigated the possible association of hypothyroidism with insulin resistance which reportedly associated with the risk of cardiovascular disease. A total of 164 subjects participated in this study. 82 subjects were newly

detected hypothyroid subjects (cases) and 82 were normal healthy Controls. About 91% of cases and 79% of controls were females showing female preponderance (Figure 1). Hypothyroidism is known to inflict females more than the males. Figure no 2 shows that the maximum number of cases and controls were in age group of 20-30 years 35(42.7%) and 35(42.7%) respectively. Bipin Sethi et al (2017) in their study also observed a similar female preponderance with female to male ratio 7:3 (1061 females and 438 males). A redox imbalance elicited by estrogens could be responsible for the increased prevalence in females [8]. In our study, Fasting Blood Sugar (FBS) was within the normal range both in cases (91±14 mg/dl) and controls (80±11 mg/dl) but the difference was found to be statistically significant (p<0.01). This was supported by Maram Sushma et al (2014) who also found similar results in cases (99.5±9.8) and controls (83±10mg/dl, p <0.01). The study of mean systolic and diastolic blood pressure was within normal limits both in cases and controls but the difference (SBP p=.017) & (DBP p=.012) was statistically significant [9] (Table 1).

Thyroid Profile In Hypothyroid Subjects

Hypothyroidism occurs when the thyroid gland fails to produce sufficient quantities of two hormones, T4 and its more active form, called T3. Initially this condition is asymptomatic with a slight rise in TSH and normal levels of peripheral thyroid hormones and is called Sub Clinical Hypothyroidism (SCH). Later, unbound T4 levels fall and TSH levels rise further; symptoms become more readily apparent at this stage, of peripheral thyroid hormones [10] Participants in our study were newly detected hypothyroid cases. In our study, the mean level of serum TSH was significantly higher in cases compared to controls (14.26±8.9 vs 2.4±0.96 µIU/mL) respectively and was statistically significant (p<0.01). The mean serum FT3 levels (1.9±0.8 vs 2.1±0.8 pg/ml, p=0.42) and serum FT4 levels (0.8±0.4 vs 0.8 ± 0.09 ng/dl, p=1.0) in both cases and controls respectively were within the reference range (Table 2). Several studies have shown an association between Thyroid Function and Insulin Resistance. Kiran Dahiya et al (2016) reported on newly diagnosed hypothyroid patients have found that the mean TSH levels were higher in cases compared to controls (32.68 ± 12.91, µIU/mL vs 1.89±0.69) and was statistically significant (p<0.01). The FT4 levels were low in cases as against controls (0.89±0.06 vs 1.34±0.32ng/dL) and was statistically significant (p<0.01). The FT3 levels were higher in controls as compared to cases (3.14±0.63 vs 2.39±0.73) and was also statistically significant (p<0.01) [11].

Serum Insulin And Insulin Resistance In Hypothyroid Subjects

Generally, a fine balance exists between the insulin agonistic and antagonistic action of thyroid hormones in the muscle and liver respectively but this equilibrium is altered in hypothyroidism leading to altered insulin levels [4]. Hypothyroidism is associated with insulin resistance and is defined as the subnormal response of the target tissues to the effects of insulin and is calculated by HOMA-IR index. The possible explanations hypothesised for this phenomenon range from dysregulation of mitochondrial oxidative metabolism to reduction of blood flow in muscles and adipose tissue under hypothyroid condition [5]. Insulin resistance leads to an increases production of hepatic cholesterol and very low density lipoprotein (VLDL), an increased high density lipoprotein cholesterol (HDL-C) clearance. Insulin resistance augments the deleterious effects of hypothyroidism on the lipid profile as suggested by Bakker et al. [12].

In our study, fasting serum insulin levels in cases and controls (17±13 vs 11±7µIU/mL) were within the reference range but the difference was statistically significant (p=0.007) .We have found that there was a significant increase in insulin resistance as reflected by HOMA-IR index. The mean HOMA-IR value in cases was 3.8±2.5 and about 33% of the cases in our study had a HOMA-IR index of ≥3. The mean HOMA-IR value in controls was 2.4±1.5 and about 23% in the control group had an index of ≥ 3and the difference in HOMA-IR was statistically significant (p<0.01) (Table 3).

We found a significant positive correlation between TSH and fasting serum insulin (r=.528, p<.001) and also between serum TSH levels and HOMA-IR in the hypothyroid group (r=.46, p <0.01). Serum insulin was also positively correlated with HOMA-IR (r=.962, p<.01) (Table 4)

Hyperinsulinemia and insulin resistance observed in cases, in the presence of normal blood glucose levels might be due to the influence of glycemic status by insulin which is known to modulate TSH levels and also due to oxidative stress in these subjects [13-14]. The observation in this study was consistent with the findings of various other researchers. Purvi Purohit et al (2014) in their study observed that fasting serum insulin levels were elevated in hypothyroid patients (41.78 ± 2327µIU/mL) compared to the healthy euthyroid controls (16.73±4.24 µIU/mL, p<.001) and also observed that HOMA-IR in cases 17.29 ±15.61 were higher compared to healthy controls 3.33±0.78 and statistically significant (p<0.001) [15]. Kunal B.K. et al (2013) found significant increase in HOMA-IR in hypothyroid (1.90±0.21) compared to normal healthy subjects (0.43±0.02) and found positive correlation between TSH vs Insulin (r=0.62, p=0.02), TSH vs HOMA-IR (R=0.54, P=0.16) which is consistent with results of our study [16].

CONCLUSION

Our study shows that Hypothyroidism is common among female and associated with mild degree of insulin resistance. There is no significant change in blood pressure and fasting blood sugar levels in cases. The hypothyroid subjects should be investigated for insulin resistance as they are predictive of cardiovascular risk. It is necessary to closely monitor and re-evaluate patients diagnosed with hypothyroidism to assess whether it is persistent so that the course of the treatment may be decided accordingly.

REFERENCES

[1] Abilash Nair, CP Jayakumaria nd PK (2018), "Jabbar. Prevalence and Asssociations of hypothyroidism in Indian patients with type 2 Diabetes Mellitus". Journal of thyroid research. 10, 1-7.

[2] L. Chiovato, Flavia magri and Allan Carle (2019), Advance in therapy, SPRINGER.,36 (supp; 12) 47-58.

[3] Gabriela, B.(2011), "Why Insulin Resistance be a natural consequence of Thyroid Dysfunction?". Journal of Thyroid Research,10,4061.

[4] Sapna Vyakaranam, swati Vanaparthy, Srinivas Nori et al. (2014), "Study of Insulin Resistance in Subclinical Hypothyroidism". International Journal of Health Science Research. Sep 4(9),147-153.

[5] Leonidas H Duntas, Jacques Orgiazzi and Georg Brabant. "The interface between thyroid and Diabetes Mellitus". Clinical Endocrinology, Feb. 75(1).

[6] Luca Chiovato, Flavia Magri and Allan Carle (2019), "Hypothyroidism in Context: where we've been and where we're going". Advance in Therapy. 2019:36 (suppl 2),47-58.

[7] Ujwal Upadaya B, Suma Mn and Srinath Km (2011), "Effect of Insulin Resistance in Assessing the Clinical Outcome of Clinical and Subclinical Hypothyroid Patients". Journal of Clinical and Diagnostic Research, 9(2), 1-4.

[8] Bipin Sethi, Sumitav Barua, M.S. Raghavendra et al. (2017), "The Thyroid Registry: Clinical and Hormonal characteristics of Adult Indian Patients with Hypothyroidism". Indian Journal of Endocrinology Metabolism, 20,302-307.

[9] Sushma M, Ramalingam K, Naidu N Jupalli et al. (2014), "Lipid profile alterations and fasting blood glucose levels in primary hypothyroidism". International journal of research in medical sciences, 4,1694-1698.

[10] Longo, Fauci, Kasper et al. (2018), Harrison's Principles of Internal Medicine. 20th edition, Mc Graw-Hill Medical Publications.

[11] Kiran Dahiya, Monica Verma, Rakesh Dhankar et al.(2016), "Thyroid profile and iron metabolism: mutual relationship in hypothyroidism". Biomedical Research, 27(4),212-1215.

[12] Bernadette Biondi, George J Kahaly and R Paul Robertson (2019), "Thyroid Dysfunction and Diabetes Mellitus: Two closely Associated Disorders". Endocrine Society endocrine reviews, 40(3),789-824.

[13] Ujwal Upadya B, Suma MN, Srinath KM et al. (2015), "Effect of Insulin Resistance in Assessing the Clinical Outcome of Clinical and Subclinical Hypothyroid Patients". Journal of Clinical and Diagnostic Research, 9(2), 754.

[14] Antonio Mancini, Chantal D Segni and Sebastiano Raimondo et al. (2016), "Thyroid Hormones, Oxidative stress, and inflammation". Mediators of Inflammation,Mar 8: 675

[15] Purohit P (2014), "Estimation Of Serum Insulin, Homeostasis Model Assessment Insulin Resistance And C-Peptide Can Help Identify Possible Cardiovascular Disease Risk In Thyroid Disorder Patients". Indian Journal Of Endocrinology And Metabolism,16, 97-103.

[16] Kapadia B Kunal, Bhatt A Parloop and Shah S J (2013), "Association between altered thyroid state and insulin resistance". Journal of Pharmacology and Pharmacotherapeutics, 3(2), 156-160.