Original Article

Hypothyroidism in Obese Diabetics

Subclinical Hypothyroidism is More Common in Hyperglycemic Adult Overweight and Obese Individuals as Compared to Normoglycemics

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ABSTRACT

Objective: To know the significance of subclinical hypothyroidism in un-controlled diabetic adult overweight and obese individuals in district Peshawar.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Chemical Section of the Department of Pathology in Khyber Medical College Peshawar from April, 2015 to September, 2015

Materials and Methods: Two hundreds samples were collected by convenient sampling technique from general population of Peshawar district. The selected subjects were obese and overweight(BMI $\geq$ 24.9 kg/m^2) and of the age 18-50 years. Out of 200 subjects, 40 were female and 160 were male. Minimum age of the patient was 18 years and maximum age was 50 years. On the basis of age three groups were made, 18-28 years which included 40 patients 10 were female and 30 were male, age group between 29-40 years included 120 patients out of which 20 were female and 100 were male, age group 41-50 years included total number of 40 patients with 10 females and 30 males. 33 patients out of 200 had uncontrolled diabetes (DM-II). This included 26 male (13%) and 7 (3.5%) were female.

Results: The results are summarized in table 1 and 2. Whether plasma TSH levels were correlated with adiposity, we calculated Spearman Rank correlation of plasma TSH and BMI.In the results an inclination towards the association of plasma TSH level and body mass index was noted (r= 0.125, p= 0.078), while there is a substantial correlation between random blood sugar level and plasma TSH (r= 0.14, p= 0.046).Results showed that TSH level was elevated particularly in hyperglycemic overweight and obese subjects.This observation supports the view that SCH may be the result rather than an etiological factor for obesity and overweight.

Conclusion: The calculations of Spearman Rank correlation of plasma TSH and BMI show an inclination towards the association of plsma TSH level and body mass index (r= 0.125, p= 0.078), while there is a substantial correlation between random blood sugar level and plasma TSH (r= 0.14, p= 0.046).

Key Words: Subclinical hypothyroidism (SCH), Body mass index (BMI), thyroid stimulating hormone (TSH).

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INTRODUCTION

Hypothyroidism is frequently associated with weight gain but whether changes occur in weight in SCH has been observed in a limited number of studies that show slightly elevated TSH (within normal range) relating to an increase in BMI. SCH is diagnosed on biochemical levels in otherwise normal patients free of symptoms who show persistent elevation of TSH with normal free thyroxin level. Whether SCH should be treated is still a controversial issue and has to be solved by further evaluation.

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On medical basis owerweight and obesity is the situation of excess fat deposition in the body to the extent that it damages the health and reduce expectancy of life by increasing health related problems[1]. Obesity has got doubled in the past few decades and it is quite alarming. WHO has reported that globally 1.5 million people are either overweight or obese by the age 20[2]. This exagerrated increase in obesity prevalence threats the health of general population by multiplying the chances for the development of non-communicable diseases.

Obesity may follow certain conditions I-e iatrogenic, administration of insulin, medicines like anti-epileptics, anti-psychotics, and anti-depressants and medical conditions like hypothyroidism and hypercortisolism (Cushing syndrome)[3]. High calorie diets, lacking physical activity and decreased rate of metabolism individually or combined can induce obesity particularly in genetically predisposed population[4]. The

most routinely used method for the diagnosis of overweight and obesity is calculating BMI that is the ratio of weight and height. Genetic and epigenetic influences, behavior of the individual, lacking activity, positive energy balance, socioeconomic status, food and cultural taboos all influence the BMI of a person[5]. Association of hypertension, heart disease, type-2 diabetes, cerebrovascular accident, certain cancer types, osteoarthritis and sleep apnea with high BMI is well established[6]. Strong correlation between obesity, diabetes mellitus type-II and glucose tolerance test impairment has been proved by certain studies[7]. The adipose tissue in obese individuals release high amounts of pro-inflammatory cytokines, glycerol and non-esterified fatty acids. All these products are important players in inducing resistance to insulin causing overstimulation of the beta-pancreatic cells to secrete excess insulin along with causing a decrease in insulin receptors[8].

Abnormalities of lipid metabolism are very common in obese and overweight patients. Adiposity is characterized by high triglycerides, decreased level of HDL, elevated total cholesterol and LDL[9]. LDL molecules generated by hepatic lipases are well known for their atherogenic capability[10]. Energy metabolism of the body is strongly controlled by thyroid hormones having a critical role in the modification of weight. Energy metabolism in young type-1 diabetics and children may be affected by SCH, as SCH is associated with an increased chance of symptomatic hypoglycemia. Auto-immune thyroid disorders are more common in young diabetic girls particularly in the teenage and may have association with elevated TSH levels indicating the importance of SCH in such patients. There is a link between nephropathy, cardiovascular disease and SCH especially in type-2 diabetics, however retinopathy is excluded[11]. The available data suggests that increased rate of cardiovascular disease in type-2 diabetics with SCH may be secondary to nephropathy. Diabetic patients must be checked for thyroid function each year to look for a symptomless thyroid dysfunction that is more common in these patients[12].

MATERIALS AND METHODS

This was a cross-sectional type of study performed from April, 2015 to September, 2015 in the chemical section of the department of pathology in Khyber Medical College Peshawar. Two hundred samples were collected by convenient sampling technique from general population of Peshawar district. The selected subjects were obese and overweight (BMI $\geq$ 24.9 kg/m^2) and of the age 18-50 years. Out of 200 subjects, 40 were female and 160 were male. Minimum age of the patient was 18 years and maximum age was 50 years. On the basis of age three groups were made, 18-28 years which included 40 patients 10 were female and 30 were male, age group between 29-40 years included 120 patients out of which 20 were female and 100 were male, age group 41-50 years included total number of 40 patients with 10 females and 30 males. 33 patients out of 200 had uncontrolled diabetes (DM-II). This included 26 male (13%) and 7 (3.5%) were female.

RESULTS

200 patients including 40 (20%) females and 160 (80%) males. Participated in this study Median age of all patients was 34 years (interquartile range; 10 years). There was no significant difference in the median age between male and female patients (p=0.628, Mann-Whitney U test) (table 1). Minimum and maximum age of the patients was 18 years and 50 years. Total number of patients age between 18-28 years were 40 (female; 10, male; 30), between 29-40 years were 120 patients (female; 20, male; 100), and between 41-50 years were 40 patients (female; 10, males; 30).

The results are summarized in Table 1, and Table 2.

Table No.1: Descriptive statistics of study participants

Variable	Female (n=40)		Male (n=160)		p-value*
	Median	IQR	Median	IQR	
Age (years)	34.00	12.50	34.000	9.750	0.628
SBP (mmHg)	150.00	48.75	130.00	45.00	0.004
DBP(mmHg)	97.50	27.50	85.00	20.00	0.008
RBS (mg/dl)	125.50	30.00	121.00	25.75	0.344
Ht. (inches)	64.000	2.000	64.000	1.000	0.058
Wt. (Pounds)	188.00	16.00	180.00	30.00	0.0002
BMI (kg/m^2)	32.800	2.150	31.200	5.600	0.002
TSH (mIU/L)	2.880	4.017	1.695	1.488	0.0004
T4 (pmol/L)	119.30	34.52	115.05	31.99	0.455

*Mann-Whitney U test, SBP; systolic blood pressure, DBP; Diastolic blood pressure, RBS, Random blood sugar, Ht. height, Wt.; Weight, BMI; Body mass index, TSH; Thyroid stimulating hormone, T4;

The Correlation Of Plasma TSH with Adiposity was calculated according to Spearman Rank correlation of plasma TSH and BMI. There was a tendency towards a relationship between the levels of TSH and BMI (r= 0.125, p= 0.078) (figure 6). However there was a significant positive correltaion between TSH and plasma random blood sugar (r= 0.14, p= 0.046) (figure 7). Levels of TSH were not significanlty correlated with age (p=0.236), systolic blood presure (p=0.144), and diastolic blood pressure (p=0.981). Binary logistic regression analysis was used to determine the association of plasma TSH with BMI and other variables (random blood sugar, systolic blood pressure, diastolic blood pressure, age and gender).There was a tendency towards a significant association of plasma TSH with BMI when no other variable was considered in the model (odds ratio; 1.056 CI; 0.992, 1.124, p-value; 0.086). However significant association was

observed between plasma TSH and BMI (Odds ratio; 1.0935, CI; 1.0088, 1.1853, p=0.028) when plasma random blood sugar, systolic and diastolic blood pressure, age and gender were included in the model (table-2). Body mass index, random blood sugar, age, and gender were significantly associated with plasma levels of TSH (table 2).

Table No.2: Binary logistic regression analysis of subclinical hypothyroidism with BMI, RBS, blood pressure, age and gender.

Variable	Odds Ratio	95% CI	P - value
BMI (kg/m^2)	1.0935	(1.0088, 1.1853)	0.028
RBS (mg/dl)	1.0164	(1.0089, 1.0239)	0.000
SBP (mmHg)	1.0077	(0.9874, 1.0284)	0.460
DBP (mmHg)	0.9848	(0.9531, 1.0176)	0.359
Age (Years)	0.9379	(0.9058, 0.9712)	0.000
Sex	0.5019	(0.3140, 0.8021)	0.004

BMI; Body mass index, SBP; systolic blood pressure, DBP; Diastolic blood pressure, RBS, Random blood sugar

DISCUSSION

Subclinical means the presence of a disorder in a person who is otherwise symptoms free.

Compared to the prevalence of SCH in general population (5.4%), in our study 16% of the overweight and obese participants had SCH (raised TSH level in the face of normal T4)[13]. These findings indicate high prevalence of SCH in the persons with BMI > 24.9 when compared to general public. In our study the female to male ratio for BMI is significantly higher. This observation can be partially explained by the cultural setting in Peshawar where females are very minimally facilitated for exercise. High literacy and least interest in media information leading to unawareness results in carelessness about adiposity and its complications.

Females participating in our study showed significantly elevated levels of TSH in comparison to males and SCH was more prevalent in females (30%) versus males (13%). Our study showed a tendency towards the correlation of BMI and plasma TSH levels. In a study from Italy 13.7% of the overweight and obese individuals were recorded to have SCH[14]. In a study from India 46% participants of overt hypothyroidism and 34% of SCH were overweight or obese[15].

In our study type-II diabetes was present in 17% of the participants (total 33), 7 were females and 26 were males.

Diabetes is a chronic metabolic disorder due to insulin lack (type-1) or insulin resistance (type-II). Although the two types have different etiological and pathogenical pathways i.e., inflammation is common to both. In our study high prevalence of Type-2 diabetes mellitus was observed in patients of SCH. There is possibility that the two diseases (SCH and diabetes) may share the immunity related mechanisms at some points during their course. These findings go in favor of the idea that SCH may be a consequence rather than an etiological component for obesity and its related comorbidities.

Dyslipidemias like high cholesterol and triglyceride levels are well known to occur in overt hypothyroidism but their association to SCH needs further evaluation. In Brazil a study was conducted and it was observed that participants with hypercholesterolemia had a three to four times more chance of having SCH[16]. In a study in Switzerland sixty six females with diagnosed SCH having hypercholesterolemia were treated with thyroid hormone and a significant decrease in total cholesterol, LDL-cholesterol and an increase in HDL-cholesterol was observed[17].

Hyper lipidemia is a well-known risk factor for cardiac disease by accelerating atherosclerosis. Thyroxin administration can lower the cholesterol level by 8% and so the risk of ischemic heart disease[18]. In our study evidenced by ultrasonography fatty liver was observed in 48 participants (20 men and 28 women). The high prevalence of fatty liver in female participants in this area can also be partially explained by their sedentary life when compared to male gender. A functional level of thyroid hormones is essential for normally functioning liver hepatocytes. In India in a study elevated levels of transaminases and total protein was observed in patients of SCH[19]. Conducted in Korea in a study a range dependent correlation between SCH and non-alcoholic fatty liver disease was observed[20]. In an another study in Italy it was observed that SCH in obese persons was significantly associated with abnormal carbohydrate and fat metabolism leading to hepatic steatosis[21]. Whether SCH is an etiological factor for hepatic steatosis or an outcome needs more evaluation.

Treatment of subclinical hypothyroidism with thyroid hormone replacement therapy is controversial till date. Treatment of subclinical hypothyroidism is limited only to certain conditions like high risk of overt hypothyroidism, presence of thyroid antibodies, young age and pregnancy

CONCLUSION

The calculations of Spearman Rank correlation of plasma TSH and BMI show an inclination towards the association of plsma TSH level and body mass index (r= 0.125, p= 0.078), while there is a substantial correlation between random blood sugar level and plasma TSH (r= 0.14, p= 0.046).

Author's Contribution:

Concept & Design of Study:	Pervez Mohammad
Drafting:	Mohammad Javed
Data Analysis:	Mohammad Javed & Aurangzeb
Revisiting Critically:	Aurangzeb & Pervez Mohammad
Final Approval of version:	Pervez Mohammad & Mohammad Javed

Conflict of Interest: The study has no conflict of interest to declare by any author.

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