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Evaluation of BMI in Hypothyroid patients and its response to Thyroxin Therapy

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Abstract:
Introduction: Hypothyroidism is associated with decreased thermogenesis, decreased metabolic rate, and has also been shown to correlate with a higher body mass index (BMI) and a higher prevalence of obesity. There is clinical evidence suggesting that even mild thyroid dysfunction in the form of subclinical hypothyroidism is linked to significant changes in body weight and represents a risk factor for overweight and obesity. It has been further noted that small variations in serum TSH caused by minimal changes in Thyroxin dosage during replacement therapy are associated with significantly altered resting energy expenditure in hypothyroid patients. ***Methods:*** This is a prospective study conducted in the Department of General Medicine, Shadan Institute of Medical Sciences Teaching Hospital and Research Centre over a period of 1 year among 60 subjects. The variables collected were gender, age, thyroid dysfunction etiology, TSH levels, free levothyroxine (FT4) levels, presence of thyroid autoimmunity (considered as detection of anti-thyroperoxidase antibodies and/or TSH receptor antibodies), BMI and weight at the time of referral to the Department and after normalization of thyroid hormone levels after treatment. ***Result:*** T3 and TSH of control group (2.32±0.21, 83.54±8.35) respectively. In the mean of them in the second visit (1.35±0.11, 36.23±16.24) respectively in comparison with control group. The correlation between T3 and T4 in the first visit which revealed that there was strong positive correlation (r=0.432) with a highly significant difference (P=0.00). Correlation between T3 and TSH in this table showed that there was a weak negative relationship (r =-0.103) with a non-significant difference (P=0.325). In correlation between T4 and TSH there was a weak negative correlation (r= -0.024) with a highly significant difference (P= 0.542). Between T4 and BMI there was a weakly negative correlation (r = -0.019) with a non-significant difference (P=0.431). ***Conclusion:*** The number of patients with an elevated BMI (obese) differs significantly from the others. Thyroxin played a part in a lower BMI. Finding hypothyroid patients as soon as feasible is crucial.
Keywords: Endocrine abnormalities, Hypothyroidism, BMI,

Introduction:

The thyroid hormone (TH) controls dietary intake as well as energy expenditure, both resting and total, and consequently, obesity and different metabolic diseases can appear in patients with altered thyroid function. Furthermore, altered thyroid function is characterized by the presence of changes in total body weight and total body composition, body temperature, and metabolic expenditure [1].

Thyroid function studies are frequently indicated in the evaluation of obesity etiology [2]. It is common to find slightly increased values of thyrotropin (TSH) in obesity [3]. It is unclear whether the altered thyroid function present in obesity is due to the excess adiposity or, alternatively, the decreased thyroid function is the cause of the excess adiposity. The thyroid axis regulates the adipose tissue and the adipose tissue affects the activity of the thyroid axis[4].

The most prevalent endocrine disease in obesity is subclinical primary hypothyroidism. It is suggested to test all patients with obesity for the presence of altered thyroid function [5,6]. Hypothyroidism, defined as an increased circulating TSH value, affects up to 10% of the adults, affecting more women than men [7]. Obesity is accompanied with endocrine alterations, including a decreased growth hormone (GH) response to different stimuli and altered thyroid function [8]. Thyroxine values have been found to be normal, increased, and decreased in obesity; these

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different results are likely due to the fact that the patients were examined at various time periods, have different sexes and ages, and may differ in the severity and kind of obesity as well as in the presence of obesity comorbidities [9].

The disturbance of thyroid function in Hypothyroid patients and the role of Thyroxin treatment on thyroid function change is unclear at the present time. There are different studies showing various results in connection with the change of thyrotropin after BMI changes and the influence of weight decrement. The free thyroxine (FT4) results in Hypothyroid patients and the influence of BS are even more controversial.

MATERIALS AND METHODS

This is a prospective study conducted in the General Medicine, Shadan Institute of Medical Sciences Teaching Hospital and Research over a period of 1 year among 60 subjects.

The variables collected were gender, age, thyroid dysfunction etiology, TSH levels, free levothyroxine (FT4) levels, presence of thyroid autoimmunity (considered as detection of anti-thyroperoxidase antibodies and/or TSH receptor antibodies), BMI and weight at the time of referral to the Department and after normalization of thyroid hormone levels after treatment.

Inclusion criteria

Patients over 18 years of age were referred to the Department of Medicine for thyroid dysfunction evaluation.

Exclusion criteria

We excluded for the analysis patients with any variable that for any reason could influence on BMI: Hypocalorific diets, tobacco use, recent quit smoking or recreational drug use, severe psychiatric illness, pregnancy and postpartum stages, diabetes mellitus treated with insulin therapy, sulfonylureas, GLP-1 analogues or SGLT-2 inhibitors, prescription of drugs affecting body weight (corticosteroids, antipsychotics, mirtazapine, anticonvulsants, antineoplastic hormone therapy, fluoxetine or topiramate) and other comorbidities such as advanced congestive heart failure, chronic obstructive pulmonary disease, end-stage renal disease or active neoplasm.

Thyroid function was assessed in all patients at first presentation and at every follow-up visit. The definition of subclinical hypothyroidism was based on TSH levels >5.5 to 10 mcUI/ml with normal FT3 (free triiodothyronine) and FT4 (free thyroxine) levels. The diagnosis of overt hypothyroidism was made when TSH values were higher than 5mcUI/ml and FT3 (free triiodothyronine) and FT4 (free thyroxine) levels were below the normal range. During the clinical follow-up patients exhibiting subclinical/overt hypothyroidism or with positive TPO and/or Tg antibodies underwent thyroid ultrasound. Diffuse low echogenicity was considered an indicator of thyroid autoimmune disease.

Sera of each patient were assessed for autoantibodies in parallel to thyroid function at first presentation and at every follow-up visit. Patients' sera were tested for Abs to Tg) and TPO by chemiluminescence method; parietal cells, adrenal cortex and islet cell by indirect immunofluorescence; steroid 21-hydroxylase (21-OH), glutamic acid decarboxylase (isoform 65) (GADA), protein tyrosine phosphatase IA2 (insulinoma-associated antigen 2) and insulin by RIA. Total IgA, IgA anti-gliadin and anti-transglutaminase were also measured for celiac screening.

Statistical analysis

Qualitative variables were described as numbers and percentages. A $\chi 2$-test was used to compare frequency of qualitative variables among the different groups. A Fisher's exact test was computed for 2x2 tables. Results were analyzed using the Graph Pad Prism software version number 5. A result with $p < 0.05$ was considered statistically significant.

RESULTS

Table 1: Distribution of gender

Gender	Number	Percentage	P-value
Male	13	21.6	<0.0001
Female	47	78.3	

All forms of thyroid disease were four to five times more common in females than in males in table 1.

Table 2: Distribution of Age group

Age groups (Year)	Number	Percentage	P-value
10-30	9	15	<0.0001
31-50	28	46.6	
51-70	23	38.3	

In table 2, shows that the majority of patients were between [31-50] years (46.6%), also the age's frequency of patients at [51-70] years was (38.3%) and moreover, the table showed that the number of hypothyroid patients [10-30] years

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was (15.0%) only. The data analysis revealed a highly significant difference between the number of patients in the different age groups with (P<0. 0001).

Table 3: Characteristics of studied samples according to BMI

BMI (Kg/m^2)	**Number**	**Percentage**	**P-value**
<24.9	13	21.6	<0.0001
25-29.9	19	31.6	
>30	28	46.6	

Table 4: Mean distribution of serum thyroid hormone levels among studied groups

Thyroid hormone	**Studiedgroups**	**Mean**	**Std. Deviation**
T3 ng/ ml	Control	2.32	0.21
	1st visit	0.84	0.15
	2nd visit	1.35	0.11
T4 nmol/L	Control	83.54	8.35
	1st visit	36.23	16.24
	2nd visit	52.43	5.35
TSH µIu/mL	Control	3.24	0.43
	1st visit	18.22	2.94
	2nd visit	8.54	1.63

In table 4, T3 and TSH of control group (2.32±0.21, 83.54±8.35) respectively. In the mean of them in the second visit (1.35±0.11, 36.23±16.24) respectively in comparison with control group.

Table 5: - Correlation between serum chemicals in 1st visit patients

Thyroid hormone	**Pearson Correlation**	**T 4 nmol/L**	**TSH µIu/mL**	**BMI Kg/m^2**
T3 ng/ml	r	0.432	-0.103	-0.103
	P-value	0.00**	0.325	0.122
T4 nmol/L	r	-	-0.024	-0.019
	P-value	-	0.542	0.431
TSH µIu/mL	r	-	-	-0.014
	P-value	-	-	0.642
BMI Kg/m^2	r	-	-	-
	P-value	-	-	-

In table 5, showed the correlation between T3 and T4 in the first visit which revealed that there was strong positive correlation (r=0.432) with a highly significant difference (P=0.00). Correlation between T3 and TSH in this table showed that there was a weak negative relationship (r =-0.103) with a non-significant difference (P=0.325).

In correlation between T4 and TSH there was a weak negative correlation (r= -0.024) with a highly significant difference (P= 0.542). Between T4 and BMI there was a weakly negative correlation (r = -0.019) with a non-significant difference (P=0.431). The relationship between TSH and BMI revealed that there was a weakly Negative correlation (r= - 0.014) with a non-significant difference (P=0.642).

DISCUSSION

Thyroid hormones regulate basal metabolism, thermogenesis and play an important role in lipid and glucose metabolism, food intake and fat oxidation. [10] Thyroid dysfunction is associated with changes in body weight and composition, body temperature and total and resting energy expenditure (REE) independent of physical activity. [11] Hypothyroidism is associated with decreased thermogenesis, decreased metabolic rate, and has also been shown to correlate with a higher body mass index (BMI) and a higher prevalence of obesity. [12] There is clinical evidence suggesting that even mild thyroid dysfunction in the form of subclinical hypothyroidism is linked to significant changes in body weight and represents a risk factor for overweight and obesity; [13] however, this remains a gray area. It has been further noted that small variations in serum TSH caused by minimal changes in L-T4 dosage during replacement therapy are associated with significantly altered REE in hypothyroid patients. [14]

In addition, after analyzing the two different types of thyroid function disorder (hyper- and hypothyroidism) separately, we observed statistically significant differences between baseline and post-treatment body weight and BMI. Hypothyroid patients experienced a mean weight loss of 2.25±2.01 kg, which is much less than the weight loss described in classic series. [15] However, we are unaware of the existence of any recent series that had addressed this topic. Our results may have been influenced by the fact that seven of the hypothyroid patients showed a subclinical hormone alteration (TSH <10 µU/mL). However, it is noteworthy that patients with a greater degree of

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hypothyroidism (TSH 18.22 μU/mL on first visit and 8.54 μU/mL on second visit) experienced a weight loss of less than 2 kg when they reached euthyroid status.

Some authors suggest that weight gain is greater in post-surgical hypothyroidism than in autoimmune hypothyroidism. [16] In our study, there was only one case of post-surgical hypothyroidism; this might account for the non-significant weight loss experienced by these patients.

The relationship between hypothyroidism and obesity has historically been based on studies with a baseline population selected from obese patients whose thyroid hormone levels were assessed. In several of these studies, higher incidences of hypothyroidism were found in obese patients than in the general population. [17] Based on these findings, some authors have suggested that minor thyroid dysfunction might contribute to significant changes in body weight that could represent a risk factor for overweight and obesity. [18] However, these studies are inconclusive in establishing a cause–effect relationship, as the demonstration of a higher incidence of hypothyroidism in obese patients does not necessarily mean that the obesity is caused by the disorder. The relationship between hypothyroidism and obesity seems to be weaker than previously thought, even more in subjects with treated hypothyroidism.

In the hyperthyroidism patients group, weight gain was observed on completion of treatment when the results of the thyroid function test returned to normal. This is a common finding in the literature and there are several theories regarding it. Hyperthyroidism induces an increased basal energy expenditure that leads to weight loss as a result of a decrease in the body's lean and fat mass. When euthyroidism is regained, weight gain occurs at the expense of both compartments. [19] Another possible explanation for the tendency of hyperthyroid patients to gain weight after achieving euthyroidism could be related to an increase in post-treatment TSH levels over baseline levels. Hence, this would indicate the presence of relative hypothyroidism within the limits of analytic normality. [26] In our study, we were unable to test this hypothesis because of unavailability of patients' TSH levels prior to the onset of hyperthyroidism. [20]

Hypothyroidism induces a decreased basal metabolism and thermogenesis, an accumulation of hyaluronic acid and a decreased renal flow, all factors leading to water retention. Severe hypothyroidism states lead to a clinical picture known as myxoedema in which hyperkeratosis of the skin and facial edema could give the patient a false appearance of overweight. [21] Patients with hypothyroidism have also slow peristalsis causing chronic constipation that may result in weight gain. This weight gain is mainly due to water retention and is not related to an increase in fat mass. [22] In addition, some studies have found a higher prevalence of subclinical hypothyroidism among obese patients. [23] Altogether, these factors have probably contributed to a general belief of a direct association of hypothyroidism with obesity.

CONCLUSION

Thyroxin played a part in a lower BMI. The prevalence of hypothyroidism is higher in females than in males. When compared to other age groups, patients aged (31–50) years displayed a high prevalence of hypothyroidism. The number of patients with an elevated BMI (obese) differs significantly from the others. TSH has been acknowledged as a reliable marker for the laboratory diagnosis and monitoring of hypothyroid individuals. Thyroxin played a part in a lower BMI. Finding hypothyroid patients as soon as feasible is crucial.

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