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RESEARCH ARTICLE

THYROID DYSFUNCTION IN OBESE CHILDREN AND ADOLESCENTS

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ABSTRACT

Aim: to reveal the effects of obesity on thyroid function in obese children and adolescents.
Material and methods: we conducted a retrospective cohort study on a total of 183 participants. Patient group included pre-obese and obese children and adolescents (102 patient). While control group included normal individuals within the age-range that of patients' group (81 participants). Relation of TSH and fT4 with BMI was investigated.
Result: There was a significant difference in the mean and median levels of TSH as obese children showed higher mean levels of TSH compared to the control group (95% C.I of the mean difference= 0.8 to 2.1). When data was stratified by gender, mean TSH were higher in males and female obese children (P <0.001 and 0.017 respectively). Moreover, mean TSH levels was compared between obese and non-obese children and it's found to be higher in children younger than 10 years old (P < 0.001).
Conclusion: Obesity is associated with an elevation of TSH serum levels with normal fT4 serum levels.

INTRODUCTION

Obesity is one of the major problems in both developing and developed countries and it's considered as an epidemic disease world wild.(1) Pathophysiology of obesity is still under investigation because of its deprival understanding. It has multifactorial causes including hereditary, environmental, behavioral, and psychological influences. Previous studies on different families showed that heredity may reached up to 67% of the population variance in BMI.(2) Prevalence of children and adolescents overweight, obesity and severe obesity in Saudi Arabia (KSA) has been estimated as 23.1%, 9.3% and 2%, respectively, with boys having significant prevalence rate of obesity (10.1% vs 8.4%) and severe obesity (2.3% vs 1.6%) than girls, respectively.(3) In general, complications that is related to obesity is: coronary heart disease, type 2 diabetes, hypertension, dyslipidemia, stroke, sleep apnea, respiratory problems, osteoarthritis, and of endocrine issues.(1)

In the past decade, several studies assessed the significance of hormonal changes associated with obesity.(4) Body configuration and thyroid hormones seem to be closely related. Fat accumulation result in failure of the hypothalamic-pituitary-thyroid axis and eventually affect thyroid function.(5) Thyroid hormones control basal metabolism, heat production and show a significance role in lipid and glucose metabolism, food intake and fat oxidation. Thyroid dysfunction is associated with alterations in the weight of the body and its composition, body temperature and whole resting energy expenditure (REE) independent of physical activity. Hypothyroidism is associated with decreased thermogenesis, reduced metabolic rate, and has also been approved to associate with a greater body mass index (BMI) and a higher prevalence of obesity.(5) There is a clinical evidence proposing that even mild reduction in thyroid gland function in the form of subclinical hypothyroidism is linked to significant changes in body weight and reflect a risk factor for overweight and obesity; however, this remains a dark area and need more clarifications.(6)Presence of the disease with no notable symptoms, is the definition of the "subclinical" word.(9) Subclinical hypothyroidism (SH), is defined as increased TSH

serum levels and normal serum fT4 concentrations. Subclinical hypothyroidism can be mild (serum TSH concentrations of 4·5–9 mU/L) or severe (TSH ≥10 mU/L).(9) Although our problem is thought as a "subclinical" issue, there're complications associated with it. Nneuromuscular symptoms (e.g., weakness, cramps and paresthesia),(7) increased likelihood of having common bile duct stones,(8) cardiovascular complications such as: depressed systolic function at rest, and left ventricular diastolic dysfunction at rest and during exercise (10), and hypercholesterolemia.(11) Many studies has linked obesity with elevated TSH without significant change in fT4 levels.(14,15 and 16) Obesity has many complications. Such as: cardiovascular, hepatobiliary, hematologic and endocrine.(12) However, we are going to focus in this study on association of obesity and endocrine complications. Particularly, thyroid complications, is our target in this study. TSH levels has been recorded to be elevated in obese individuals.(13) We implemented a retrospective cohort study to assess TSH and fT4 levels among obese Saudi children and adolescents.

METHODS AND MATERIAL

The study was conducted in retrospective cohort fashion with patients being selected from Security Forces Hospital information system. The total number of patients included in the study was 183, where they were allocated into two groups: obese/pre-obese group (102) and control group (81). Inclusion criteria for obese/pre-obese were done on the basis of BMI: equal or more than 85 percentile less than 95 percentile were pre-obese and equal or more than 95 percentile were obese, while patients with BMI less than 85 percentile were put in the control group. Patients with hypothyroidism, history of chronic use of steroid medications, comorbidity conditions, or Down syndrome cases all were excluded; TSH readings were not recorded for a number of patients- those patients were excluded as well. The study parameters were MRN, gender, age, BMI, TSH, and fT4. A team of 3 data collectors were put in charge for retrieving the data from SFH and it was done in a two week period. Data entry was a done in a Microsoft Excel. Data interpretation and analysis were then performed by a biostatistician to generate the study results.

RESULTS

Table 1 shows the demographic data for both groups included in the current study. The study included 101 males and 82 females.

Table 1. Demographic data for children included in the current study

	Cases	Controls	P- value
Age	10.31 (2.78)	9.7 (2.3)	0.1
BMI (Kg/m^2)	31.57 (10.14)	15.1 (2.04)	<0.001**
BMI percentile	98.03 (3.15)	27.1 (25.02)	<0.001**
Gender			
Males	55 (53.9%)	46 (56.8%)	0.81
Females	47 (46.1%)	35 (43.2%)	

Data is shown as mean [standard deviation] for continuous variables and as count (percentage) for categorical variables

There was no significant difference in age and gender between controls and cases. Body mass index and BMI percentile was significantly higher in the obese group as expected. One hundred and eight children were older than 10 years old and 75 children were younger than 10 years old. Regarding TSH and fT4 levels, mean TSH and fT4 levels did not differ significantly between males and females.

When TSH and fT4 were compared among obese and non-obese children (Table 2.), There was a significant difference in the mean and median levels of TSH as obese children showed higher mean levels of TSH compared to the control group (95% C.I of the mean difference= 0.8 to 2.1). However, there was no significant difference in the fT4 levels between groups. When data was stratified by gender, mean TSH were higher in males and female obese children (P <0.001 and 0.017 respectively) and there was no significant difference in fT4 levels in either groups (Table 2).

When TSH levels were examined across different age categories (less than and greater than 10 years old as this was the median age value), the difference in mean TSH levels between obese and non-obese children was higher in children younger than 10 years old (P < 0.001). Gender did not affect this association (Figure 1.)

Table 2 TSH levels and free T4 levels in cases and controls

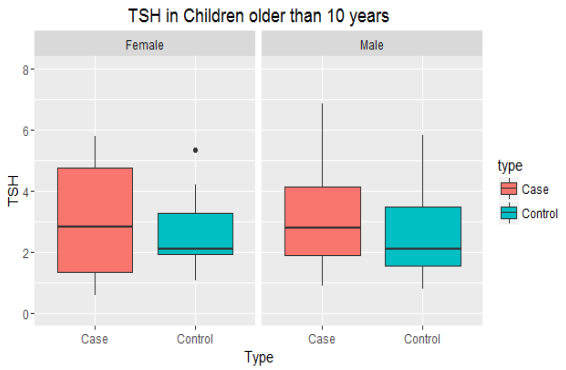
	Cases	Controls	P- value
Total (n=183)			
TSH	4.11 (2.7)	2.7 (1.8)	< 0.001**
Free T4 (pg/L)	17.2 (2.9)	17.2 (2.6)	0.96
Females (n=82)			
TSH	4.5 (3.3)	2.6 (1.2)	0.001**
Free T4	17.1 (3.2)	17.6 (2.7)	0.4
Males (n=101)			
TSH	3.8 (2.1)	2.7 (2.2)	0.017*
Free T4	17.3 (2.8)	16.9 (2.5)	0.45
Younger than 10 years (n=75)			
TSH	4.5 (1.9)	2.5 (1.3)	< 0.001*
Free T4	18.6 (2.7)	17.3 (3.1)	0.06
Older than 10 years (n=108)			
TSH	3.9 (3.1)	2.9 (2.1)	0.05*
Free T4	16.3 (2.8)	17.1 (2.7)	0.08

Data is shown as mean [standard deviation] for continuous variables and as count (percentage) for categorical variables.

Table 3 Correlations between BMI and TSH FT4 in obese children

	FT4		TSH	
	r	P	R	P
Total (n=183)				
BMI	-0.16	0.027*	0.25	< 0.001*
Age	-0.2	0.005*	-0.03	0.74
Cases (n=101)				
BMI	-0.28	0.003*	0.08	0.432
Age	-0.35	0.003*	-0.14	0.16
Control (n=82)				
BMI	-0.08	0.47	-0.08	0.48
Age	0.05	0.65	0.12	0.29

Data is shown as mean [standard deviation] for continuous variables and as count (percentage) for categorical variables



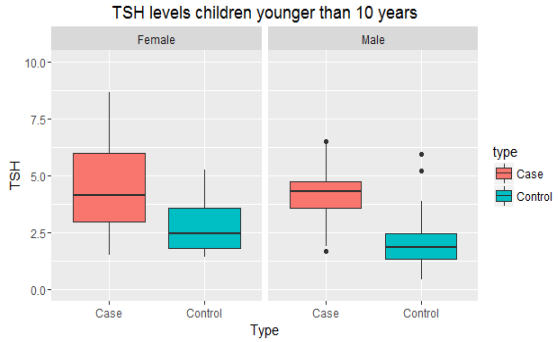


Figure 1 TSH levels stratified by age in children older and younger than 10 years

Body mass index showed a weak positive correlation with TSH levels (r=0.25, P < 0.001) as TSH levels increased with increasing body mass index while age and did not show any association with TSH levels. However, when the association between body mass index and TSH levels was investigated among both groups (obese and non-obese children), no correlation was found between body mass index and TSH levels in the individual groups (Figure 2).

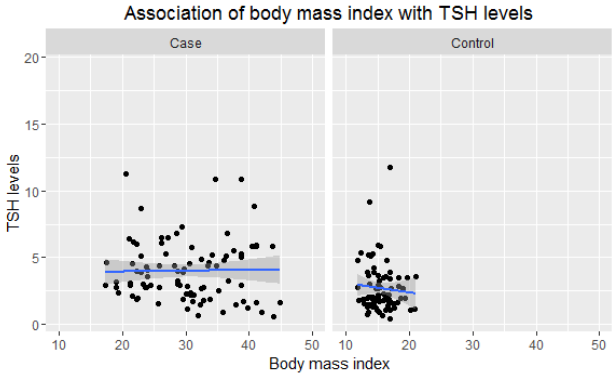
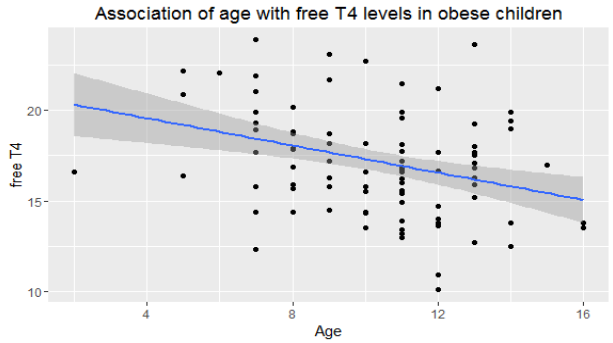


Figure 2 Association between TSH levels and body mass index

Age and body mass ındex (tested as contınuous varıables thıs time) on the other hand were associated with fT4 levels (P = 0.005 and 0.027, respectively) where T4 levels seemed to decrease with increasing age and body mass index (Table 3).

When this was further investigated, there was a significant correlation between age, body mass index and the levels of fT4 in obese children only (P = 0.03 for both associations, Figure 3.). Such a relationship was not observed in the normal weight children (P = 0.65 and 0.45 for age and BMI, respectively).



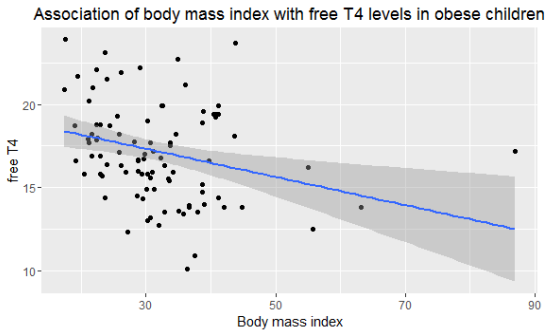


Figure 3 Association of age and body mass index with free T4 levels in obese children

DISCUSSION

The main finding of this study represents a significant relationship between obese and TSH level in euthyroid obese children. The normal serum level of TSH is derived exclusively from its relationship with thyroid hormones in euthyroid children. There are many different scales in which the interaction between TSH and adipose tissue can occur, other than that involved in thyroid regulation. Recent studies in man and other mammalian species have found that adipocytes and preadipocytes contain thyrotropin receptors. (17,18) Adipogenesis is mediated by the action of thyrotropin that induces differentiation of preadipocytes into adipocytes, and expansion of adipose tissue.(17) However , mean serum T4 levels were within the normal range and very similar among lean and obese subjects. There is no statistical relationship between serum T4 and obesity. Due to the lack of a correlation between T4 and obesity, and high coincident with a positive correlation between serum TSH and adiposity would be consistent with a direct interaction of thyrotropin and adipose tissue. Our study was not designed to prove or disprove a direct role of thyrotropin in adipogenesis. It was at best investigating the relationship between TSH, T4 serum levels and obesity. It is still unknown whether increased TSH levels lead to the deposition of fat or, in contrast, whether excessive accumulation fatty tissue increases TSH secretion, therefore, no cause-effect relationship can be built based on these findings. Moreover, when correlation was performed between BMI and fT4 levels, an inverse correlation was found between body mass index andfT4 levels. An inverse relationship was also found between age and fT4 levels.

CONCLUSION

TSH levels are significantly higher in obese than non-obese children although it did not correlate with the body mass index in the individual groups.fT4 levels were not significantly different in obese and non-obese children (unpaired t-test). However, when correlation was performed between BMI and fT4 levels, an inverse correlation was found between body mass index and fT4 levels. An inverse relationship was also found between age and fT4 levels.fT4 levels were correlated with body mass index and age in the obese children only were T4 levels decreased as body mass index or age decreased. This was not observed in the non-obese children.

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