PREVALENCE OF SUB CLINICAL HYPOTHYROIDISM IN SCHOOL CHILDREN (6-11 YEARS) OF DERA ISMAIL KHAN

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ABSTRACT

Objective: *To determine the prevalence of sub clinical hypothyroidism (hyperthyrotropinemia) in obese school children.*

Methodology: *This cross-sectional study was carried out in Department of Chemistry, Gomal University, Dera Ismail Khan, from June 2007 to August 2010 including eight primary schools of Dera Ismail Khan having mixed population with some of the wards belonging to high socioeconomic group. Thorough clinical examination excluded those suffering from chronic health problems. Height and weight of each child was taken according to standard anthropometric procedures. Body mass index and body mass status of each study subject was calculated according to Quetelet's Index and WHO criteria respectively. A total of 83 school children (6-11 years) were randomly selected among 1336 children. The sample included 23 (27.71%) normal weight children and 60 (72.28%) obese. Gender wise distribution of the sample was 48 (57.83%) boys and 35 (42.16%) girls. Free Thyroxin (FT_4) and Thyroid Stimulating Hormone (TSH) were measured using radioimmunoassay.*

Results *Hyperthyrotropinemia was the most commonly observed thyroid hormone dysfunction (8.43%) in the whole sample (n=83) and 8.33% in obese children compared with 3-8% in general population of the United States.*

Conclusion: *Sub clinical hypothyroidism is the most common finding in the childhood obesity. The prevalence of sub clinical hypothyroidism in the present study is 8.43% in the whole sample (n=83) compared with 3-8% in general population of the United States. It is suggested that all the obese children expressing minimum organ abnormalities be investigated to prevent the irreversible problems over the course of many years.*

Keywords: *Sub Clinical Hypothyroidism, Childhood Obesity, Cardiovascular risk factor.*

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INTRODUCTION

Obese patients frequently show alterations of thyroid function that are now considered to be consequence rather than a cause of overweight/ obesity. Thyroid hormones and thyroid stimulating hormone concentration have been variously described as normal, elevated or even low in obese patients when compared with normal weight control individuals[1,2]. Elevated serum TSH and thyroid hormone concentrations have also been reported in obese children[1,3,4]. A satisfactory explanation of these findings is not yet available; though several mechanisms leading to hyperthyrotropinemia have been hypothesized, including increased leptin-mediated production of prothyrotropin–releasing hormone[5], impaired feedback due to lowered number of T_3 receptors in the hypothalamus and variations in peripheral deiodinase activity[6].

Recently, it has been demonstrated that thyroid structure can be altered to different degrees in a group of overweight/obese children[4]. The structural changes observed by Ultrasound resembled those of typical Hashimoto's thyroiditis, which was excluded on the basis of the absence of anti thyroid antibodies. A completely normal cytological pattern was also observed by needle biopsy. The cause of these findings is still unknown.

The major concern with compensated hypothyroidism is that minimal end organ abnormalities may be present which are undetectable because of lack of sensitive peripheral indicators such as serum TSH for the pituitary. Such minimal abnormalities may lead to important irreversible problems over the course of many years. Lipid metabolism, myocardial function, linear growth and cognitive ability are some of the functions that may be adversely affected by Sub Clinical Hypothyroidism (SCH)[7,8]. Even mild impairment of cognitive functions may have negative consequences for the developing child, and even school achievements with in the normal range does not prove that the child would not have performed better if treated with L-thyroxin (L-T_4). The issue of treatment is still a matter of debate[9,10].

METHODOLOGY

The present study assesses the prevalence of thyroid hormones dysfunction in the primary school children of Dera Ismail Khan as assessed by Free Thyroxin (FT_4) and Thyroid Stimulating Hormone (TSH) in randomly selected 83 children: normal weight = 23 (27.71%) and obese = 60 (72.28%). There were 48 boys (57.83%) and 35 girls (42.16%). Subjects were randomly selected among children from 08 primary schools of the study area. Thorough clinical examination excluded those suffering from chronic health ailments. Written permission was obtained from the parents and the principals of the institutions. Participation was voluntary. Weight and height of each child was taken according to standard anthropometric methods without foot wear and wearing minimum clothing. Body mass index of each study subject was determined according to Quetelet's Index. BMI number was plotted on Center for Disease Control and Prevention (CDC) gender specific growth charts 2-20 years to determine BMI-for-age-percentile. Body mass status of each child was determined according to WHO criteria. Children having BMI-for-age-percentile $\geq 95^{th}$ percentiles were considered obese. Normal or healthy weight children were having BMI-for-age between 5^{th} and 85^{th} percentile and those between 85^{th} to 95^{th} percentile were overweight[11].

Determination of the Free Thyroxin (FT_4) and Thyroid Stimulating Hormone (TSH) was the criteria for the assessment of thyroid function. Radioimmunoassay was used for the assessment of peripheral and central thyroid hormones at the Institute of Radiotherapy and Nuclear Medicine (IRNUM) at Peshawar, Pakistan. For FT_4, RIA kit and TSH IRMA kit for TSH determination (IMMUNOTECH Czech Republic) were used. Normal serum concentration of FT_4 was taken as 11.5-23ρmol/L and TSH = 0.5-5μIU/L[12].

Descriptive statistics of lipid and thyroid hormone profile were calculated using the procedures given by Ott (1984)[13] and Bhatti (2006)[14].

RESULTS

The present study investigated the prevalence of thyroid dysfunction with sub clinical hypothyroidism in the primary school children of Dera Ismail Khan as assessed by Free Thyroxin (FT_4) and Thyroid Stimulating Hormone (TSH) in randomly selected 83 children: normal weight = 23 (27.71%) and obese = 60 (72.28%). There were 48 boys (57.83%) and 35 girls (42.16%). Distribution of the sample according to body mass status and gender is given in Table 1.

Table 2 summarizes the concentration of thyroid hormones in normal weight children. Mean, for the FT_4 was centered at 15.31ρmol/L and 13.260ρmol/L in normal weight boys and girls respectively. Mean serum concentration of FT_4 for the normal weight boys was observed higher than normal weight girls. Opposite to what was observed in normal weight boys for FT_4, mean TSH serum concentration was measured higher in normal weight girls (3.48μIU/L) as compared to normal weight boys (2.70μIU/L). Thyroid dysfunction (SCH) was observed in 2 (8.6%) normal weight children (boys=2 and girls=0.00).

Table 3 describes the serum levels for FT_4 and TSH in obese children of the present study. Mean, for the FT_4 in obese children was noted 13.20ρmol/L in boys and 13.74ρmol/L in girls reflecting no significant gender difference compared to normal weight children. The mean serum level for the TSH in obese girls was noted higher (4.06μIU/L) as compared to obese boys (2.45μIU/L). The gender difference for TSH was similar to what was observed in normal weight children. Thyroid dysfunction (SCH) was observed in 5 (8.33%) obese children (boys=3 and girls=2). Earlier, 3 children (normal weight = 2 and obese = 1) were detected to be having Hyperthyroidism and hypothyroidism and were excluded from the study.

Table 1: Sample Distribution of the School Children for the Biochemical and Hormonal Profile (n = 83)

Body Mass Status	Normal Weight				Obese			
Gender	Boys		Girls		Boys		Girls	
	N	%	N	%	N	%	N	%
No. of Children	14	16.86	9	10.84	34	40.96	26	31.32
Total	23 (27.71%)				60 (72.28%)			

Table 2: Hormonal Profiles (FT_4 and TSH) of Normal Weight School Children (n = 23)

Serial Number	Normal Weight Boys (n = 14)		Normal Weight Girls (n = 9)	
	Free T_4 (ρmol/L)	TSH (μIU/L)	Free T_4 (ρmol/L)	TSH (μIU/L)
1	15.1	1.5	14.5	2.3
2	10.4	1.1	13.5	4.9
3	14.2	4.0	11.4	3.7
4	11.8	2.1	14.3	2.7
5	13.0	3.0	15.5	2.5
6	14.6	2.6	12.9	2.6
7	12.4	3.4	11.4	2.0
8	14.1	0.9	13.3	1.7
9	13.6	6.6	14.0	1.8
10	14.8	5.3	---	---
11	14.4	2.1	---	---
12	11.8	3.7	---	---
13	11.6	1.9	---	---
14	9.0	1.7	---	---

Descriptive Statistics for Hormonal Profile of Normal Weight School Boys (n = 14)

Variable	*Mean*	*S.D*	*SE Mean*	*Range*	*p-Value*
Free T_4	15.31	9.46	2.44	9.00-48.90	0.011 (11)
TSH	2.707	1.666	0.430	0.70-6.60	0.014 (1.5)

Descriptive Statistics for Hormonal Profile of Normal Weight School Girls (n = 9)

Variable	*Mean*	*S.D*	*SE Mean*	*Range*	*p-Value*
Free T_4	13.260	1.391	0.440	11.40-15.50	0.019 (12)
TSH	3.480	2.681	0.848	1.70-10.60	0.044 (1.5)

Table 3: Hormonal Profiles (FT_4 and TSH) of Obese School Children (n = 60)

Serial Number	Obese Boys (n = 34)		Obese Girls (n = 26)	
	Free T_4 (ρmol/L)	TSH (μIU/L)	Free T_4 (ρmol/L)	TSH (μIU/L)
1	16.7	1.6	12.5	5.2
2	13.1	2.1	12.6	1.8
3	11.9	2.2	14.6	3.1
4	11.5	0.7	13.7	2.7
5	15.7	6.9	14.7	3.4
6	14.6	1.9	13.1	2.4
7	10.7	2.4	12.2	2.2
8	12.1	7.3	15.4	3.2
9	13.3	3.0	13.5	2.6
10	14.1	2.6	20.0	1.7
11	12.9	1.0	13.3	2.5
12	11.7	1.6	13.9	1.0
13	13.1	1.9	13.9	1.1
14	12.3	1.7	14.3	1.6
15	11.0	0.6	15.4	2.4
16	11.6	1.8	14.8	6.1
17	16.6	1.4	15.8	0.06
18	11.2	1.7	11.1	3.1
19	13.4	1.6	20.8	0.08
20	13.7	1.6	12.9	2.6
21	12.7	2.0	18.6	0.07
22	12.4	5.0	11.7	3.4
23	15.5	0.7	12.8	1.1
24	14.8	1.9	16.6	1.9
25	23.6	0.5	9.1	2.3
26	12.4	1.5	11.9	2.1
27	10.8	1.2	----	----
28	9.8	2.6	----	----
29	10.7	6.3	----	----
30	12.8	1.6	----	----
31	14.5	3.7	----	----
32	11.5	3.5	----	----
33	12.4	2.6	----	----
34	13.9	4.9	----	----

Descriptive Statistics for Hormonal Profiles of Obese School Boys (n = 34)

Variable	*Mean*	*S.D*	*SE Mean*	*Range*	*p-Value*
Free T_4	13.206	2.50	0.43	9.80-23.60	0.0083
TSH	2.459	1.73	0.30	0.50-7.30	0.0028

Descriptive Statistics for Hormonal Profiles of Obese School Girls (n = 26)

Variable	*Mean*	*S.D*	*SE Mean*	*Range*	*p-Value*
Free T_4	13.74	3.49	0.67	1.90-20.80	0.015
TSH	4.06	9.28	1.79	0.06-50.00	0.16

Table 4: Descriptive Statistics of Obese Children (n = 61)

Gender	Boys (n = 34)		Girls (n = 27)	
Variable	**Mean ± SD**	**Range**	**Mean ± SD**	**Range**
WC (cm)	75.29 ± 8.25	60-93	75.52 ± 7.15	63-88
TG (mg/dl)	204.15 ± 55.48	109-375	238.10 ± 95.2	125-475
TC (mg/dl)	161.03 ± 21.19	119-230	172.37 ± 25.04	129-234
HDL-C (mg/dl)	33.79 ± 5.151	25-47	42.63 ±7.33	29-60
LDL-C (mg/dl)	88.44 ± 17.69	62-146	102.70 ± 16.29	67-140

Abbreviations: WC = Waist Circumference, TG = Triglycerides, TC = Total Cholesterol, HDL-C = High Density Lipoprotein Cholesterol, LDL-C = Low Density Lipoprotein Cholesterol

DISCUSSION

Obesity commonly coexists with hypothyroidism as a consequence or cause of it. Obesity affects hypothalamic-pituitary-thyroid axis directly or indirectly leading to alteration in thyroid function tests. The commonest observed change is alteration in thyroid stimulating hormone (TSH), Triiodothyronine (T_3) and also of thyroxin (T_4) hormones.

The present study was undertaken to assess the frequency of thyroid dysfunction (SCH) in school children of the study area. It included 83 children: normal weight = 23 and obese = 60 (Table 1). Both, normal as well as obese children were having thyroid dysfunction (normal weight = 2 and obese = 5). The prevalence of SCH was observed to be 8.69% and 8.33% in normal weight and obese children respectively (Table 2,3).

Sub Clinical Hypothyroidism, a mild thyroid failure, is diagnosed when peripheral thyroid levels (T_4, T_3) are within normal reference laboratory range, 11.5-23.5ρmol/L[12], but TSH is mildly elevated[15]. Ours findings can be compared with the findings reported by Hollowell et al, 2002[16], Karmisholt et al, 2008[17], that SCH generally occurs 3-8% in general population of the United States. Herrick, 2008[18] had reported the prevalence of SCH (4-8%) in the general population of the United States. Our rates for SCH are in agreement with the similar ones by Villar et al, 2007[19] in Brazil where prevalence of SCH was 4-8% in general population. Much higher rates (30%) for SCH have been reported by Hari Kumar et al, 2008[20] in India. 50 overweight and obese children aged 2-18 years (overweight 20, obese 30) were evaluated for relationship between body mass index and TSH in euthyroid and SCH obese children and compared the serum TSH levels among obese and overweight children aged 6.4-18 years. SCH was found to be 30% in 9/30 obese children.

The major concern in children with compensated hypothyroidism is, that minimum end organ abnormalities may be present, which are undetectable because of lack of sensitive peripheral indicators such as TSH from the pituitary. Such minimal abnormalities may lead to important irreversible problems over the course of many years. Lipid metabolism, myocardial infarction, linear growth and cognitive ability are some of the functions that may be adversely affected by SCH[21, 8].

Longitudinal studies suggest that 20-50% of individuals with SCH develop overt hypothyroidism with in 4-8 years[7]. The views expressed by the Surks and Ocampo, 1996[7], have been shared by the Vander pump et al, 1995[22] that the likelihood of progression of SCH to clinical hypothyroidism is 2.6-4.3% each year, if thyroperoxidase (TPO) antibodies are absent or present respectively.

Obese children with SCH (5/60) in the present study had more risk factors for cardiovascular disease (CVD) than those obese (as well as normal weight) without SCH. 4/5 (80%) among obese children with SCH had >3 CVD risk factors and altered lipid levels (Table 4). Altered lipid metabolism and development into overt hypothyroidism had also been reported by Surks and Ocampo, 1996[7]. Ours study is in agreement with the Hack et al, 2000[8], that SCH adversely affects the lipid metabolism; myocardial infarction, linear growth and cognitive ability. Azad Reza et al, 2008[23], had expressed the similar views that SCH is associated with higher cholesterol, LDL-C compared with euthyroid controls.

Razvi et al, 2008[24], reported the increased incidence of ischemic heart disease (IHD), both in prevalence and incidence and cardiovascular mortality only in young subjects (less than 65 years) with SCH. However, Fatourechi, 2009[25], considers it a matter of debate and that it (SCH) is

a cardiovascular risk factor. Primary prevention and intervention through risk factor modification can be effective in children and will reduce the morbidity and mortality from this disease in future.

CONCLUSION

Childhood obesity may coexist with sub clinical hypothyroidism and may develop in to hypothyroidism with irreversible organ damage. The present study revealed the prevalence of sub clinical hypothyroidism as 8.43% in the whole sample (n=83). It is suggested that obese children with minimum organ damage may be investigated to prevent the permanent organ damage in future.

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CONTRIBUTORS

MR conceived the idea. IA supervised the study. FR helped in designing of tables and had done the statistical analysis. FR & MHR helped in typing the manuscript and collection of literature for the discussion of manuscript.