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A COMPARATIVE STUDY OF LIPID PROFILE BETWEEN CHILDREN WITH SUBCLINICAL HYPOTHYROIDISM VERSUS EUTHYROID CHILDREN

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ABSTRACT

Background: Subclinical hypothyroidism is one of the most prevalent endocrine disorders, affecting 4-15% of adults and about 2% of children. Although thyroid dysfunction is associated with dyslipidemia, the incidence of dyslipidemia in children with subclinical hypothyroidism is still subject to debate, and whether these children should be treated for subclinical hypothyroidism remains unknown. **Objectives:** To determine whether children with subclinical hypothyroidism have a greater incidence of blood lipid disorders than those with normal thyroid function. **Materials and Methods:** An Observational Comparative-Cross Sectional Study included all children (ages 2–18) years diagnosed with subclinical hypothyroidism compared with euthyroid children attending the Pediatric Endocrine Clinic at Tishreen University Hospital during the study period from June 2023 to June 2024. **Results:** A higher percentage of lipid serum disorders was found in the subclinical hypothyroidism (SCH) group in comparison with euthyroid group (higher levels of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL), and lower levels of high-density lipoprotein (HDL) levels), with statistical significance (P-value<: 0.0001, 0.0001, 0.04, 0.0001) respectively, regardless of age, sex, or body mass index (BMI). **Conclusion:** The study revealed a significant difference between the percentages of dyslipidemia in subclinical hypothyroidism and euthyroid children, highlighting the importance of early screening and monitoring blood lipid levels in those children. Further research is necessary to clarify whether mild doses of Levothyroxine can reverse the dyslipidemia induced by SCH in children.

KEYWORDS: children, euthyroid, lipid profile, subclinical hypothyroidism.

INTRODUCTION

Subclinical hypothyroidism (SCH) refers to early-stage diagnosed hypothyroidism when thyroid stimulating hormone (TSH) is above the upper limit of the normal range, but the T3 and T4 levels are normal.[1] It is a common disorder with an underestimated prevalence of 4-15% in adults[2,3] and slightly lower than 2% in paediatrics.[2,4] Each year, 2-5% of SCH patients progress to overt hypothyroidism.[5]

The most common cause of SCH in children and adults is chronic autoimmune thyroiditis (Hashimoto's disease).[6] SCH is a biochemical dysfunction in the absence of clinical signs or symptoms of thyroid failure.[7] It seems that mild thyroid dysfunction in adults could be associated with subtle clinical, biochemical, or functional alterations.[8] Only a few studies have examined the effects of untreated SCH in children, examining its complications on metabolic parameters, cardiovascular risk factors, growth, and neurocognitive development.

Data from adult studies and a few pediatric studies showed that SCH could be associated with dyslipidemia.[13-18-19]

Thyroid hormones play a role in lipid synthesis, metabolism, and mobilization, and lipid abnormalities are well-known with primary hypothyroidism.[9] The association between SCH and dyslipidemia in

children and the effect of compensatory treatment on these disorders remains controversial. Studies have correlated SCH in adults with higher levels of total cholesterol (TC), low-density lipoprotein (LDL), triglycerides (TG), and lower levels of HDL.[10]

To date, there have been multiple studies on children attempting to determine how dyslipidemia correlates with subclinical hypothyroidism.

As there are controversies about the association of dyslipidemia with SCH in children, we designed this comparative cross-sectional study to compare lipid profiles, including TG, TC, LDL, and HDL in children with SCH with the normothyroidism children group.

PATIENTS AND METHODS

Study the population

The study included 160 children aged (2–18) years, divided into two groups (SCH:70 children, EG:90 children), who were referred to the Pediatric Endocrinology Clinic at Tishreen University Hospital, Lattakia City, Syria, between June 2023 - June 2024.

After obtaining informed consent from the guardian, samples were collected from children diagnosed with subclinical hypothyroidism based on age and gender reference values. Information on height, weight, and BMI calculations was obtained. Blood samples were taken in the morning after an 8-12 hour fast to measure TC, LDL, HDL, and TG.

The diagnosis of SCH was based on an elevated TSH level along with normal FT4 levels based on age and gender reference values measured in two morning fasting blood samples obtained at an interval of 2 to 6 weeks.

Abnormal lipid levels were defined according to the National Cholesterol Education Program (NCEP) Expert Panel on cholesterol levels in children (taking borderline values as disorders), measured in morning fasting blood samples.[12]

For the precise calculation of body mass index (BMI), body mass index standard deviation score (BMI-SDS) and BMI percentile, which are based on the growth charts of the Centre for Disease Control (CDC)(11), was used. Obesity levels were determined according to the Centres for Disease Control and Prevention, where children are classified as overweight when 85 >BMI> 95 percentile, while obesity when BMI is greater than 95 percentile.[20]

Children with glandular disorders, metabolic syndrome, chronic renal diseases, and a history of receiving medication that could affect their lipid profil,[21] were excluded from the study.

STATISTICAL ANALYSIS

The statistical analysis was conducted utilising IBM SPSS version 20. Basic descriptive statistics include means, standard deviations (SD), medians, frequencies, and percentages. In order to examine the difference between the percentages of the two groups, a Z-test was used. The results were considered statistically significant with p-value ≤ 5%.

RESULTS

In this study, as shown in Table 1, of 160 children, 70 participants had elevated TSH levels with normal FT4. They were classified as the subclinical hypothyroidism group (SCH), and 90 participants had normal TSH and FT4 levels and were considered as the euthyroid group (EG). 60% of the SCH group and 53.3% of the EG were females. 30% of the SCH group was in the (6-9 years old) subgroup, whilst 45.6% of EG were in the (10-13 years old) subgroup. Depending on the BMI score and BMI percentile, children were divided into subgroups according to weight categories.

The severe obesity subgroup constituted 30% of the SCH sample and 22.2% of the EG sample, whilst the overweight subgroup constituted 17.1% of the SCH sample and 30% of the EG sample.

There was no statistically significant difference in age (or BMI) between the two groups. However, there were statistically significant differences between age groups, as 27.1% of subclinical hypothyroidism cases were in the age group 2-5 years (p-value=0.009).

Table 1: Distribution of study sample by gender, age and BMI.

	Total 160		
	SCH (70)	EG (90)	P
Gender			
Male	28 (40%)	42 (46.7%)	0.3
Female	42 (60%)	48 (53.3%)	
Age			
(2-5) y.o	19 (27.1%)	8 (8.9%)	0.009
(6-9) y.o	21 (30%)	29 (32.2%)	
(10-13) y.o	19 (27.1%)	41 (45.6%)	
14-18	11 (15.7%)	12 (13.3%)	
BMI			
Low weight	5 (7.1%)	4 (4.4%)	0.3
Normal	27 (38.6%)	33 (36.7%)	
Overweight	12 (17.1%)	27 (30%)	
Obesity	5 (7.1%)	6 (6.7%)	
Severe obesity	21 (30%)	20 (22.2%)	

BMI body mass index, Y.O years old.

Table 2 shows the prevalence of dyslipidemia in each (TG, TC, LDL, HDL) in the SCH and EG groups.

The SCH group was associated with a higher prevalence of dyslipidemia compared to EG. Elevated levels were observed in 54.3% of total cholesterol (TC), 38.6% for triglycerides (TG), 24.3% for low-density lipoprotein (LDL), and low values of 61.4% for high-density lipoprotein (HDL), in the SCH group, with statistical significance of 0.0001, 0.0001, 0.04, and 0.0001 respectively.

To detect if the association between SCH and dyslipidemia is affected by age, gender, or different BMI levels, we examined lipids between these different groups and no differences in lipid parameters were observed.

Table 2: Distribution of study sample by prevalence of lipid disorders.

Total 160			
	SCH (70)	EG (90)	P-value
↑TG	38 (54.3%)	9 (10%)	0.0001
↑TC	27 (38.6%)	5 (5.6%)	0.0001
↑LDL	17 (24.3%)	11 (12.2%)	0.04
↓HDL	43 (61.4%)	25 (27.8%)	0.0001

TG triglycerides; TC total cholesterol; LDL-c low-density lipoprotein cholesterol; HDL-c high-density lipoprotein cholesterol.

DISCUSSION

In the current study, a significant prevalence of lipid disorders (higher levels of triglycerides, total cholesterol, and LDL, and lower levels of HDL) in children with subclinical hypothyroidism was indicated in comparison with euthyroid children.

Thyroid hormones regulate a wide range of metabolic processes, especially lipoprotein metabolism, as well as many cardiovascular risk (CVR) factors.[6]

Elevated TSH leads to increased hepatic HMGR gene expression and increased hepatic cholesterol synthesis.[13] TSH also plays a role in inhibiting the production of bile acids in the liver, thus reducing the biliary excretion of cholesterol.[15] These abnormalities of lipid metabolism caused by thyroid dysfunction in children are considered as very important risk factors for the development of atherosclerosis, which is known to start in childhood, leading to cardiovascular diseases at an early age in adults.[22]

Numerous studies in the medical literature on the association of subclinical hypothyroidism with lipid disorders in children have shown different and conflicting results.

Similar to our findings, Witte and co-workers from Germany found a positive correlation between SCH and dyslipidemia (higher TG, TC, and LDL, and lower HDL levels) in children compared to controls. The 0differences were more pronounced in the overweight and obese groups, whilst we did not find such differences across BMI scores in our study. In the adolescent group, no correlation between SCH and lipids was found (14). In a study by Dahl and colleagues in the USA on children with SCH compared with EG, mild SCH led to increased TC levels, with no alteration in HDL levels.[15] By contrast, no difference in lipids was found in the Habib study conducted in Iran on SCH children compared to controls.[16] Whilst Marwaha and others did not find any significant difference in lipid profile between mild SCH children and the euthyroid group, HDL levels were significantly lower in severe SCH compared to controls.[17]

The differences between our results and those of these studies can be explained by variations in sample size, fasting status, reference values used to determine dyslipidemia, and the method and duration of the statistical study conducted, but none of these explanations can confirm the reason for these differences. The limitations of the study included the limited sample size, and the design of the study which is not sufficient to determine association, causality, or patient follow-up, in addition to the limited financial resources to study other types of lipids.

CONCLUSION

The study indicates significant differences in the percentages of lipid disorders of the four parameters (TG, TC, LDL, HDL) between subclinical hypothyroidism (SCH) and euthyroid children, suggesting a prospected association between subclinical hypothyroidism (SCH) and dyslipidemia in children, which reveals the potential risk of atherosclerosis and cardiovascular complications in those patients. This highlights the importance of early screening and monitoring blood lipid levels in those children. Further research with extended follow-up periods is needed to affirm the subsistence of the association and the effectiveness of Levothyroxine treatment in reversing the dyslipidemia induced by SCH in children.

DECLARATIONS

Ethical approval and consent to participate

Ethical approval to study was obtained from the Scientific Research Ethics Committee at Tishreen University in June 2023 by the Declaration of Helsinki.

COMPETING INTERESTS

None.

FUNDING
None.

AUTHOR CONTRIBUTION
Fatima Kher bek, collected the data, checked the quality of the data collection, analyzed and interpreted the data, designed and coordinated the study, undertook and checked the quality assessment, produced the first draft of the manuscript, wrote and edited the manuscript, and approved the final manuscript before submission.

Ahmad Chreitah and Faisal Radwan were the supervisors of the project; undertook and checked the quality assessment, checked the quality of the collected data; analyzed and interpreted the data; checked the quality assessment; edited the manuscript, and approved the final manuscript before submission.

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