Original Article

Cardiovascular Risk Factors in Children and Adolescents with Subclinical Hypothyroidism

Yogesh Yadav, Uma Kaimal Saikia, Dipti Sarma, Manoj Hazarika[1]

Department of Endocrinology, Gauhati Medical College, Guwahati, [1]Department of Radiology, Assam Medical College, Dibrugarh, Assam, India

Abstract

Background: Subclinical hypothyroidism (SCH) is a commonly encountered entity in day-to-day clinical practice and has been associated with adverse cardiovascular risk profile in adults and children. Data on children and adolescents with SCH, from India, are limited. **Materials and Methods:** This study was a cross-sectional case–control study, conducted at a tertiary care center in Northeast India. Twenty-seven children and adolescents aged 11 ± 2.4 years with SCH and thyroid-stimulating hormone >7.5 mIU/L were included in the study along with 20 age-, gender-, and height-matched controls. Multiple clinical, biochemical, and radiological cardiovascular risk factors were assessed and compared between the two groups. **Results:** Body mass index (BMI) ($P = 0.048$), waist circumference ($P = 0.008$), waist to height ratio ($P = 0.007$), low-density lipoprotein cholesterol ($P = 0.04$), triglycerides (TGs) ($P = 0.038$), TGs to high-density lipoprotein (HDL) cholesterol ratio ($P = 0.005$), non-HDL cholesterol ($P = 0.019$), fasting insulin ($P = 0.006$), and homeostasis model assessment of insulin resistance ($P = 0.007$) were found to be significantly higher while free T4 ($P = 0.002$) and HDL cholesterol ($P = 0.019$) were found to be significantly lower in SCH subjects compared to controls. On multiple regression analysis, BMI was found to have significant association with multiple cardiovascular risk factors. **Conclusion:** Children and adolescents with SCH were found to have adverse cardiovascular risk profile. Long-term follow-up studies are required to assess the clinical significance of these findings and requirement for therapy.

Keywords: Carotid intima-media thickness, high-sensitivity C-reactive protein, homeostasis model assessment of insulin resistance, insulin, waist to height ratio

Introduction

Subclinical hypothyroidism (SCH) is a common endocrine problem with an estimated prevalence of 4%–10% in adults and <2% in children and adolescents.[1,2] SCH has been defined as a state of increased serum thyroid-stimulating hormone (TSH) level with normal serum free thyroxine (FT4) level. SCH is considered as a state of early, mild thyroid failure, and this condition seems to be benign and remitting in children with lower risk of progression to overt hypothyroidism compared to adults.[3-5]

Thyroid hormones play an important role on cardiovascular system and in modulation of several atherogenic factors. Although overt hypothyroidism has been found to be associated with dyslipidemia, inducing an increase in total cholesterol and in low-density lipoprotein (LDL) cholesterol and predisposing to atherosclerotic cardiovascular disease, this relation is controversial in patients with SCH.[6,7] Early atherosclerotic lesions in children have been found to correlate with body mass index (BMI), systolic and diastolic blood pressure (BP), triglycerides (TGs), total cholesterol, LDL cholesterol, and high-density lipoprotein (HDL) cholesterol.[8]

High-sensitivity C-reactive protein (hsCRP) is a well-known cardiovascular risk marker, but data on hsCRP in patients with SCH are conflicting.[9,10] Hyperinsulinemia and insulin resistance have been suggested as independent risk factors for atherosclerosis. No consistent data are available regarding insulin sensitivity in patients with SCH, with a few studies reporting increased insulin levels and impaired insulin sensitivity in patients with SCH compared to controls, while other studies failed to find such difference.[11-13]

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Address for correspondence: Dr. Yogesh Yadav, Department of Endocrinology, Gauhati Medical College, Guwahati - 781 032, Assam, India.
E-mail: yogeshyadav44@rediffmail.com

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Increased carotid intima-media thickness (CIMT) in SCH patients has been reported, and a recent meta-analysis has indicated that SCH is associated with an increased CIMT, which may be due to elevated TSH, dyslipidemia, and hypertension.[14] Adults with SCH have also been found to have both left ventricular systolic and diastolic dysfunction.[1]

Most of the studies have been done in adults, and data on cardiovascular risk factors in children with SCH are scarce. Limited data are available from India on cardiovascular risk factors in children and adolescents with SCH. Considering the scarcity of data, the present study was carried out to find out the effects of SCH on markers of cardiovascular risk.

Materials and Methods

Subjects and controls

The present study was a cross-sectional case–control study, conducted at a tertiary care center in Northeast India. Children and adolescents, more than 7 years of age with SCH and TSH >7.5 mIU/L, attending the endocrinology clinic were included in the study. A TSH cutoff value of 7.5 mIU/L was taken based on a large retrospective multicenter study by Lazar *et al*., in which they reported that predictive factors for a sustained highly elevated TSH (>10 mIU/L) were an initial TSH >7.5 mIU/L and female gender.[15] Patients with chronic diseases, severe acute illness, diabetes mellitus, previous or current treatment with levothyroxine replacement therapy, genetic syndromes, previous thyroid diseases, usage of drugs interfering with thyroid function, or previous neck irradiation/surgery were excluded from the study.

Twenty-seven children and adolescents, with a mean age of 11.0 ± 2.4 years, fulfilling the inclusion criteria were included in the study. Twenty healthy euthyroid children and adolescents, matched for age, gender, and height, were included in the study as controls. The cases and controls were from the same geographical region.

Participants and their parents/guardians were informed regarding the study, and informed consent was taken before enrollment in the study. The study was approved by the Institutional Ethics Committee.

Height standard deviation score (SDS), BMI SDS, and obesity were determined using recently published standards for Indian children.[16] Waist to height ratio was calculated as an indicator of abdominal adiposity.[17]

Biochemical tests

After an overnight fast, blood sample was collected from enrolled subjects. TSH, FT4, thyroid peroxidase (TPO) antibody, plasma glucose, total cholesterol, TGs, HDL cholesterol, insulin, and hsCRP were measured in the collected samples. The degree of insulin resistance was evaluated using the homeostasis model assessment of insulin resistance (HOMA-IR).

Fasting plasma glucose (FPG) was measured using glucose oxidase method, and lipid profile was measured by enzymatic colorimetry, using Vitros 5600 autoanalyzer. TSH, FT4, TPO antibody, fasting serum insulin, and hsCRP were measured by chemiluminescence immunoassay on IMMULITE 1000, using commercial kits (Siemens Healthcare Diagnostics). Analytical sensitivity of hsCRP assay was 0.1 mg/L, with a reportable range of 0.3–100 mg/L and intra-assay coefficient of variation of 5.0%. For statistical purpose, value of hsCRP <0.3 mg/L was taken as 0.3 mg/L. Analytical sensitivity of insulin assay was 2 μIU/ml, with a reportable range of 2–300 μIU/mL and intra-assay coefficient of variation of 6.4%.

Imaging tests

CIMT was measured by B-mode ultrasound using a 10-MHz linear transducer (Siemens). Two-dimensional echocardiogram and Doppler analysis were performed in all subjects by means of available apparatus (Siemens) using appropriate transducer. Isovolumetric relaxation time (IVRT) was measured as a parameter of left ventricular diastolic function, and preejection period (PEP)/left ventricular ejection time (LVET) ratio was determined as measure of systolic function.

Statistical analysis

Statistical analysis was done using SAS® University Edition software. The continuous data were expressed as mean ± standard deviation. Student's unpaired *t*-test was used to compare the two groups. The correlation of TSH, FT4, BMI, and waist to height ratio with other clinical, biochemical, and radiological variables was estimated by Pearson's correlation method. Multiple linear regression analysis was used to determine the association between various dependent and independent variables. Tests were considered statistically significant at $P < 0.05$.

Results

Table 1 shows the clinical and hormonal characteristics of cases and controls. Age and height were similar in the two groups. TSH levels were significantly higher in SCH children and adolescents compared to controls (9.63 ± 2.33 vs. 2.50 ± 0.95 mIU/L; $P < 0.001$), while FT4 levels were significantly lower in SCH subjects than in controls (1.15 ± 0.14 vs. 1.28 ± 0.13 ng/dL; $P = 0.002$). TPO antibody was found to be positive in 4 (14.8%) SCH cases and in 1 (5%) control.

The clinical, biochemical, and radiological cardiovascular risk factors in children and adolescents with SCH as compared to those in healthy euthyroid controls are presented in Table 2.

BMI SDS was higher in children and adolescents with SCH though it failed to reach statistical significance ($P = 0.069$). Both waist circumference and waist to height ratio were significantly higher in SCH subjects compared to controls ($P = 0.008$ and $P = 0.007$, respectively). Systolic and diastolic BP was normal in both groups, without any significant difference.

Total cholesterol levels were higher in SCH subjects but without any significant difference. HDL cholesterol levels were significantly lower ($P = 0.019$), whereas LDL cholesterol ($P = 0.04$) and TG levels ($P = 0.038$) were

significantly higher in children and adolescents with SCH compared to controls. Both non-HDL cholesterol ($P = 0.019$) and TGs to HDL cholesterol ratio ($P = 0.005$) were also found to be significantly higher in SCH subjects.

FPG and hsCRP levels were comparable between SCH subjects and controls, while fasting insulin levels were found to be significantly higher in SCH subjects compared to their euthyroid counterparts ($P = 0.006$). Consequently, the calculated HOMA-IR was also found to be significantly higher in children and adolescents with SCH compared to controls ($P = 0.007$).

Table 1: Baseline characteristics of children and adolescents with subclinical hypothyroidism compared to healthy euthyroid controls

	SCH subjects ($n=27$) Male:female=13:14	Controls ($n=20$) Male:female=10:10	*P*
Age (years)	10.98±2.36	10.85±2.44	0.853
Height (cm)	137.78±13.18	136.30±11.11	0.687
Height SDS	−0.603±0.833	−0.602±0.807	0.995
TSH (mIU/L)	9.63±2.33	2.50±0.95	<0.001
FT4 (ng/dL)	1.15±0.14	1.28±0.13	0.002

SDS: Standard deviation score, TSH: Thyroid-stimulating hormone, FT4: Free thyroxine, SCH: Subclinical hypothyroidism

Table 2: Cardiovascular risk factors in children and adolescents with subclinical hypothyroidism compared to euthyroid controls

	SCH subjects ($n=27$)	Controls ($n=20$)	*P*
Weight (kg)	34.17±10.50	30.00±6.46	0.124
BMI (kg/m^2)	17.79±4.11	15.99±1.69	0.048
BMI SDS	0.218±1.388	−0.347±0.629	0.069
Waist circumference (cm)	63±10.863	56.35±5.071	0.008
Waist to height ratio	0.459±0.071	0.417±0.020	0.007
Systolic BP (mm Hg)	102.96±8.12	99.20±8.50	0.131
Diastolic BP (mm Hg)	66.07±6.01	64.90±5.21	0.488
Total cholesterol (mg/dL)	146.74±26.95	136.55±15.60	0.110
HDL (mg/dL)	45.00±6.80	49.60±5.80	0.019
LDL (mg/dL)	78.48±20.71	66.60±16.53	0.040
TG (mg/dL)	116.81±31.96	102.35±11.94	0.038
Non-HDL cholesterol (mg/dL)	101.74±24.693	86.95±17.092	0.019
TG/HDL	2.647±0.811	2.102±0.417	0.005
hsCRP (mg/L)	6.080±18.930	5.658±20.627	0.942
FPG (mg/dL)	77.93±9.26	78.10±6.10	0.942
Fasting insulin (μIU/mL)	6.82±6.25	3.20±1.18	0.006
HOMA-IR	1.33±1.25	0.62±0.25	0.007
CIMT (mm)	0.483±0.075	0.475±0.087	0.725
IVRT (ms)	71.78±9.02	68.40±8.43	0.199
PEP/LVET	0.314±0.014	0.312±0.012	0.486

hsCRP: High sensitivity C-reactive protein, HOMA-IR: Homeostasis model assessment of insulin resistance, CIMT: Carotid intima-media thickness, IVRT: Isovolumetric relaxation time, PEP: Preejection period, LVET: Left ventricular ejection time, BMI: Body mass index, SDS: Standard deviation score, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, FPG: Fasting plasma glucose, SCH: Subclinical hypothyroidism, BP: Blood pressure

Mean CIMT, IVRT, and PEP to LVET ratio were comparable between children and adolescents with SCH and euthyroid controls.

To assess effect of insulin resistance on lipid parameters and hsCRP, we compared groups based on HOMA-IR (≥2 vs. <2) and the results are presented in Table 3.

The correlation of TSH, FT4, BMI, and waist to height ratio with other clinical, biochemical, and radiological variables was estimated by Pearson's correlation method. TSH was not found to have any significant correlation with other parameters, expect for a significant negative correlation with CIMT ($r = -0.421$; $P = 0.029$). No significant correlation of FT4 was observed with other parameters.

BMI was found to have significant positive correlation with waist circumference, waist to height ratio, systolic BP, diastolic BP, TG levels, and TG/HDL cholesterol ratio as presented in Table 4. No significant correlation of BMI was found with rest of the parameters.

Waist to height ratio was observed to have significant positive correlation with weight, BMI, total cholesterol, TG levels, non-HDL cholesterol, TG/HDL cholesterol ratio, and hsCRP as presented in Table 5. Other parameters were not found to have any significant correlation with waist to height ratio.

Table 3: Comparison of lipid parameters and high sensitivity C-reactive protein in two groups based on homeostasis model assessment of insulin resistance, in subjects with subclinical hypothyroidism ($n=27$)

Parameter	Group I (HOMA-IR <2; $n=21$)	Group II (HOMA-IR ≥2; $n=6$)	*P*
Total cholesterol (mg/dL)	146.0±26.6	149.2±30.5	0.808
HDL (mg/dL)	45.0±7.2	44.8±5.7	0.947
LDL (mg/dL)	78.4±20.5	78.7±23.4	0.981
TG (mg/dL)	113.4±32.2	128.7±30.8	0.312
Non-HDL cholesterol (mg/dL)	101.0±24.1	104.3±28.8	0.777
TG/HDL	2.57±0.83	2.91±0.75	0.381
hsCRP (mg/L)	2.52±5.01	18.53±39.04	0.362

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, hsCRP: High sensitivity C-reactive protein, HOMA-IR: Homeostasis model assessment of insulin resistance

Table 4: Correlation of body mass index with cardiovascular risk parameters in subjects with subclinical hypothyroidism

Parameter	Correlation coefficient *r*	*P*
Waist circumference (cm)	0.891	<0.001
Waist/height	0.922	<0.001
Systolic BP (mm Hg)	0.460	0.016
Diastolic BP (mm Hg)	0.451	0.018
TG (mg/dL)	0.492	0.009
TG/HDL	0.494	0.009

TG: Triglyceride, HDL: High-density lipoprotein, BP: Blood pressure

Multiple linear regression analysis was performed to assess the effects of age, BMI, height, TSH, and FT4 on the different cardiovascular risk factors in the SCH subjects [Table 6]. Only BMI was found to have a significant association with waist circumference, waist to height ratio, TGs, and TGs to HDL cholesterol ratio. TSH and FT4 were not found to have a significant association with cardiovascular risk factors.

Only TGs (P = 0.03) and TGs to HDL cholesterol ratio (P = 0.017) were found to be significantly higher in obese compared to nonobese SCH subjects [Table 7].

Discussion

SCH is a commonly encountered entity in day-to-day clinical practice. The optimal treatment strategy in children with SCH is still a matter of debate. Although multiple studies have evaluated the effect of hypothyroidism on cardiovascular risk factors, limited data are available regarding the effects of SCH on cardiovascular risk factors in children and adolescents.

The present study was aimed at evaluating cardiovascular risk factors in children and adolescents with SCH which was done by assessing three broad indices affecting and reflecting the status of the cardiovascular system – clinical, biochemical, and radiological parameters. Results of this study suggest that children and adolescents with SCH may develop various metabolic derangements such as increased abdominal obesity, dyslipidemia, and insulin resistance, resulting in adverse cardiovascular risk profile.

Table 5: Correlation of waist to height ratio with cardiovascular risk parameters in children and adolescents with subclinical hypothyroidism

Parameter	Correlation coefficient *r*	*P*
Weight (kg)	0.611	0.001
BMI (kg/m^2)	0.922	<0.001
Total cholesterol (mg/dL)	0.393	0.043
TG (mg/dL)	0.578	0.002
Non-HDL cholesterol (mg/dL)	0.412	0.033
TG/HDL	0.492	0.009
hsCRP (mg/L)	0.497	0.008

TG: Triglyceride, HDL: High-density lipoprotein, hsCRP: High sensitivity C-reactive protein, BMI: Body mass index

In our study, BMI was found to be significantly higher in SCH subjects compared to euthyroid controls and also found to have a significant positive association with waist circumference, waist to height ratio, TGs, and TGs to HDL cholesterol ratio. The association of SCH with BMI has been inconsistent among different studies. Denzer *et al*., in a large cohort study of 22,747 children and adolescents with type 1 diabetes, found 7.2% of the subjects to have SCH and these children had significantly higher BMI as compared to euthyroid children.[18] In a large community-based study in the Indian population, Marwaha *et al*. found a significantly higher prevalence of SCH in obese children compared to nonobese children.[19] In contrast, few other studies have failed to confirm the association between SCH and obesity.[3,4] Furthermore, as the TSH level in obese children tends to decrease with weight loss, it is controversial whether the mildly elevated TSH is the consequence of obesity or the cause.[20]

Multiple studies have identified waist to height ratio as a useful parameter in detecting abdominal adiposity and related cardiometabolic risk also among normal-weight children.[12,17] In the present study, we also found that waist circumference and waist to height ratio were significantly higher among children and adolescents with SCH compared to euthyroid controls. Furthermore, waist to height ratio was found to have positive correlation with weight, BMI, multiple lipid parameters, and hsCRP in our study. Similar to our results, Cerbone *et al*. had reported that waist circumference and waist to height ratio were higher among children with mild SCH compared to healthy euthyroid children matched for age, sex, height, and pubertal status.[13]

Although few studies have found higher systolic and diastolic BP in children and adolescents with higher TSH, we did not find any such relationship.[21,22] Indeed, systolic and diastolic BP was found to be normal in SCH subjects and was comparable to controls in our study. Similar to our results, Cerbone *et al*. also did not find any significant difference in systolic and diastolic BP in children with long-standing SCH compared to euthyroid children.[13]

Hyperinsulinemia and insulin resistance have been suggested as risk factors for atherosclerosis and adverse cardiovascular risk. In our study, we found fasting insulin levels and HOMA-IR to be significantly higher in subjects with SCH compared to euthyroid controls with comparable fasting glucose levels. Data

Table 6: Association between cardiovascular risk factors, thyroid function, and body mass index

	TSH		FT4		BMI	
	Parameter estimate	*P*	Parameter estimate	*P*	Parameter estimate	*P*
Waist circumference	−0.482	0.137	−5.040	0.338	2.296	<0.0001
Waist to height ratio	−0.004	0.118	−0.041	0.266	0.016	<0.0001
TGs	−2.111	0.450	−18.752	0.682	4.024	0.0098
TG/HDL ratio	−0.043	0.532	−1.123	0.328	0.102	0.0085
HOMA-IR	−0.106	0.401	0.260	0.899	0.027	0.676

HOMA-IR: Homeostasis model assessment of insulin resistance, TGs: Triglycerides, HDL: High-density lipoprotein, TSH: Thyroid-stimulating hormone, FT4: Free thyroxine, BMI: Body mass index

Table 7: Comparison of various parameters between obese and nonobese subjects with subclinical hypothyroidism

	SCH subjects obese ($n=6$)	SCH subjects nonobese ($n=21$)	*P*
TSH (mIU/L)	9.38±1.13	9.70±2.59	0.669
FT4 (ng/dL)	1.09±0.22	1.17±0.11	0.458
Systolic BP (mm Hg)	108.0±8.5	101.5±7.6	0.085
Diastolic BP (mm Hg)	69.7±8.1	65.0±5.0	0.098
Total cholesterol (mg/dL)	155.7±33.5	144.2±25.2	0.368
HDL (mg/dL)	42.5±4.2	45.7±7.3	0.316
LDL (mg/dL)	85.0±27.8	76.6±18.7	0.392
TG (mg/dL)	141.3±26.1	109.8±30.4	0.030
Non-HDL cholesterol (mg/dL)	113.2±32.3	98.5±22.0	0.205
TG/HDL	3.32±0.50	2.45±0.78	0.017
hsCRP (mg/L)	19.89±38.31	2.14±5.04	0.308
FPG (mg/dL)	79.7±3.0	77.4±10.4	0.394
Fasting insulin (μIU/mL)	8.54±5.84	6.33±6.41	0.455
HOMA-IR	1.67±1.12	1.24±1.29	0.465
CIMT (mm)	0.50±0.05	0.48±0.08	0.546
IVRT (ms)	66.67±8.36	73.24±8.84	0.117
PEP/LVET	0.320±0.005	0.312±0.015	0.054

FPG: Fasting plasma glucose, TSH: Thyroid-stimulating hormone, FT4: Free thyroxine, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, hsCRP: High sensitivity C-reactive protein, HOMA-IR: Homeostasis model assessment of insulin resistance, CIMT: Carotid intima media thickness, IVRT: Isovolumetric relaxation time, PEP: Preejection period, LVET: Left ventricular ejection time, SCH: Subclinical hypothyroidism, BP: Blood pressure

on insulin sensitivity in subjects with SCH are inconsistent.[11-13] Maratou *et al*. found HOMA to be increased in hypothyroid and SCH patients compared to euthyroid adults.[11] Nader *et al*., in a retrospective study among pediatric population, found significantly higher fasting insulin and HOMA index in individuals with TSH levels between 2.5 and 5.0 mIU/L compared to individuals with TSH levels between 0.30 and 2.4 mIU/L without any significant difference between fasting glucose levels between the two groups.[12] Our findings are in concordance with the results of these studies. In another study done in children with long-standing SCH, no significant difference was found between SCH children and controls in glucose, insulin levels, and HOMA index.[13]

Hypothyroidism has been associated with dyslipidemia, especially increased total and LDL cholesterol.[6] Although the relation between overt hypothyroidism and serum lipids is well documented, this relation is still controversial in patients with SCH. In our study, multiple lipid parameters were found to be significantly different between individuals with SCH and euthyroid controls. Similar to our results, Marwaha *et al*., in a study done in children and adolescents, found HDL cholesterol to be significantly lower and LDL cholesterol and TGs to be significantly higher in subjects with SCH having TSH >10 mIU/L.[23] They also observed serum TSH to be positively and FT3 and FT4 to be negatively correlated with total cholesterol and LDL cholesterol.[23] Another recent study, done in South India, reported significantly higher levels of total cholesterol and TGs and significantly lower levels of HDL cholesterol in children with SCH.[21] Yet, another study on cardiovascular risk factors in children with long-standing SCH reported significantly higher TG to HDL cholesterol ratio and significantly lower HDL cholesterol in SCH children compared with controls, without any significant difference in other lipid parameters.[13]

Several studies in adults with SCH have found variable and somewhat inconsistent changes in lipid profile. Bakker *et al*., in a group of healthy euthyroid subjects, reported a strong, positive relationship between TSH and LDL in insulin-resistant subjects but not in insulin-sensitive subjects.[24] In the Busselton study, serum total cholesterol was significantly higher in subjects with SCH than in euthyroid subjects, but the difference was barely significant after adjustment for age and sex.[25] Moreover, LDL was significantly increased in subjects with mild SCH and TSH levels of at least 10 mIU/L.[25] In a study by Kvetny *et al*., SCH was associated with a higher concentration of TGs and CRP.[26]

The conflicting results of lipid pattern and SCH might reflect differences in the population studied (e.g., cause of SCH, duration of thyroid dysfunction, TSH levels), as well as differences in age, gender, and ethnicity of the subjects tested. In addition, insulin resistance may play a role in mediating the effects of mild hypothyroidism on serum lipids.[24]

Low-grade inflammation has been implicated in atherogenesis and its progression. Increased hsCRP levels have long been regarded as cardiovascular risk as it denotes ongoing low-grade inflammatory process. In this study, we failed to find any significant difference in hsCRP levels between children and adolescents with SCH and euthyroid controls. Similar findings have been reported in children with long-standing untreated SCH and in adults[9,13] though few other studies in adults have reported significantly higher levels of CRP in SCH patients.[26,27]

We did not find any significant difference in lipid parameters and hsCRP between the two groups based on HOMA-IR (≥2 vs. <2), suggesting these parameters are independent of insulin resistance.

Increased CIMT is a measure of early atherosclerosis and is used as a predictor of cardiovascular events. We did not find any significant difference in mean CIMT between SCH subjects and euthyroid subjects in our study. Similar to our results, Cerbone *et al*. also failed to find any significant difference in CIMT among children with mild but long-lasting idiopathic SCH versus healthy euthyroid children matched for age, sex, height, and pubertal status.[28] A recent meta-analysis indicated SCH to be associated with an increased CIMT and also found increased CIMT to be present in patients with serum TSH values <10 mIU/L although with significant heterogeneity.[14]

Multiple studies have been carried out in adults to evaluate systolic and diastolic function in SCH subjects, with limited data being available in children and adolescents. Both left

ventricular systolic function, as defined by an increased PEP/LVET ratio, and diastolic function, defined as prolonged IVRT, have been found to be impaired in adults with SCH.[1]

No significant difference was observed in systolic and diastolic function between SCH subjects and healthy controls in our study. Similar to our results, Toscano *et al*. in a case–control study enrolling children with both Down syndrome and SCH did not document any abnormalities in systolic and diastolic function.[29] In a study done in South India enrolling children with SCH, left ventricular function was found to be normal.[21] In contrast, in a small case–control study, obese children and adolescents with SCH were found to have significant impairment of diastolic and longitudinal systolic cardiac function on echocardiography as compared to obese euthyroid children although no significant difference was observed with respect to IVRT.[30]

Conclusion

SCH in children and adolescents is characterized by adiposity, dyslipidemia, and insulin resistance. Adiposity is evident from increased BMI, waist circumference, and waist to height ratio in cases with SCH. Dyslipidemia in children and adolescents with SCH is characterized by higher TG, LDL cholesterol, non-HDL cholesterol, and TG to HDL cholesterol ratio and lower HDL cholesterol. These subjects also manifest fasting hyperinsulinemia with normal FPG and higher HOMA-IR indicative of a state of insulin resistance. Significant positive correlations of BMI and waist to height ratio with multiple lipid parameters and hsCRP suggest a role of obesity in dyslipidemia and low-grade inflammation, leading to an adverse cardiovascular risk profile.

In view of the small sample size and cross-sectional design, it is difficult to establish the clinical significance of the subtle abnormalities noticed in this study. Further prospective studies are needed to verify these findings and their long-term effect on cardiovascular outcomes and to address the issue of need for therapy in children and adolescents with SCH.

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Conflicts of interest

There are no conflicts of interest.

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