Original Article

Utility of Epicardial Fat Thickness in Subclinical Hypothyroid Children to Determine Existence of Subclinical Atherosclerosis in Them

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Abstract

Context: Adult studies have shown the association of subclinical hypothyroid (SCH) with various cardiovascular dysfunction, which indicates SCH may be a potentially modifiable risk factor of CV disease and mortality. However, there is still controversy about the association of cardiovascular dysfunction in children with SCH. Epicardial fat thickness (EFT) is a reliable and sensitive marker of cardiovascular risk and has become an emerging modality to predict CV risks. **Aims:** To measure the EFT in children with subclinical hypothyroidism and compare with healthy children. To find its correlation with subclinical atherosclerosis. To compare EFT between TPO positive and TPO negative subclinical hypothyroid patients. **Materials and Methods:** Children of subclinical hypothyroidism (TSH >5 μIU/ml with normal FT3, FT4, and age and sex matched control were included as per inclusion and exclusion criteria. Clinical data was collected from all study subjects. Thyroid function tests including FT3, FT4 and TSH, TPO antibody, fasting insulin, hsCRP, Lp(a), USG neck for carotid intima media thickness (CIMT), USG brachial artery for flow mediated dilation (FMD) and echocardiography for epicardial fat thickness (EFT) were done in all patients. **Results:** A total 42 number of SCH and 50 age and sex matched controls were recruited and screened for various parameters of subclinical atherosclerosis. EFT was significantly higher in the cases than in the controls (6.27 mm vs 4.54 mm) with *P* value < 0.001. Brachial FMD was significantly lower in cases than the cohort (4.5% vs 8.93%, *P* < 0.001). Difference in CIMT was not significant amongst the cases and controls. EFT failed to correlate with the level of TSH though it had significant positive correlation with hsCRP. The patients who were TPO positive, had higher fasting insulin, HOMAIR, hsCRP, Lp(a) than those who were TPO negative. **Conclusion:** Results of this study show the presence of subclinical atherosclerosis in children with SCH regardless of the aetiologies. The patients of Hashimoto thyroiditis had significantly high insulin resistance and inflammation than the SCH patients of other aetiologies.

Keywords: CIMT, EFT, FMD, hsCRP, Lp(a), SCH

Introduction

Subclinical hypothyroidism (SCH) is a biochemical condition where the serum level of thyroid stimulating hormone (TSH) is above the upper limit of the reference range for the assay, with free thyroid hormone (FT4 and FT3) values within the reference interval of the assay.[1] Adult studies have shown the association of SCH with various cardiovascular dysfunction such as hypertension, dyslipidaemia and atherosclerosis, metabolic syndrome and heart failure, which indicates SCH may be a potentially modifiable risk factor of CV disease and mortality.[2,3] However, there is still controversy about the association of cardiovascular dysfunction in children with SCH.[4,5]

Various studies have demonstrated the origin of atherosclerosis starts from childhood. This increases the importance of understanding cardiac affection in children in various diseases such as SCH.

Epicardial fat thickness (EFT), which is a layer of adipose tissue surrounding the heart and coronary vessels has emerged

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to be a reliable and sensitive marker of cardiovascular risk. It is simple yet non-invasive procedure.[6,7] Recently it has been reported that EFT is significantly correlated with the severity of coronary artery disease and can be easily obtained as an indicator in patients with high cardiovascular risk.[6,8,9]

In recent years, few studies have evaluated EFT in adults with SCH.[10,11] There are only few studies determining EFT in children with SCH. To our knowledge, there is no published data about EFT in children with SCH in India. This study aims to evaluate EFT in children with SCH and to find its correlation with subclinical atherosclerosis.

Materials and Methods

Study design and population

This was a cross sectional study conducted in Department of Endocrinology, where children with SCH meeting the inclusion and exclusion criteria were enrolled.

Inclusion criteria

Cases

1. Drug naïve children (<18 years) of subclinical hypothyroidism (TSH >5 mIU/ml, FT4, FT3 within normal limit).

Control

1. Children <18 years age with normal TFT and Anti TPO ab level,
2. No h/o any form of thyroid disease.

Exclusion criteria

1. Presence of comorbidities, such as heart disease (congenital/acquired), cardiac arrhythmias, acute respiratory failure, or severe respiratory disease at the time of enrolment syndromic cases,
2. Thyroid malignancies,
3. Hypertension,
4. Liver disease,
5. Renal diseases and nephrotic syndrome,
6. Primary lipid disorders and
7. Any h/o Thyroid hormone replacement

Informed consent was taken from the patients parents or guardian. The ethical clearance for the study was obtained from our institute ethical committee. A total 42 number of cases with a confirmed diagnosis of SCH and 50 number of age and sex matched controls were recruited. Controls chosen, were the healthy siblings accompanying the patient. In a small study group, where the number of case is less than 50, as many as 2, 3 even 4 control can be selected for each study subject. Due to unfortunate covid pandemic, the controls recruited were 50 but the number was still higher than the number of cases. Diagnosis of AIT was done by detection of elevated serum level of antithyroid peroxidase antibodies (TPOAb). In all SCH patients repeat TFT was done, 8 weeks apart from the first one. The ones who had persistent of elevated TSH were taken in the study. Patients with serum TSH >10 mIU/L were also taken in this study where the baseline measurements were done without waiting for the second measurement and levothyroxine treatment was started for this group if required.

All participants were subjected to full medical history and examination as per the preformed proforma.

Investigations

Blood samples were drawn after an overnight fast for at least 12 hours at 8:00 –10:00 a.m. for assessment of the serum levels of total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), glucose, and insulin. TSH, FT4, FT3, anti TPO ab, serum Insulin were measured by Roche Cobas e 411 ECLIA method. TPOAb concentrations >34 IU/mL, was considered positive. IR was calculated using the homeostasis model assessment (HOMA-IR) equation formula: HOMA-IR = fasting insulin (μU/mL) multiplied by fasting glucose (mg/dl) divided by 405. Patients were considered to have IR if HOMA-IR ≥2.6.[12] hsCRP, lipoprotein A were measured by Beckman Coulter AU480 by particle enhanced immunoturbidimetric test.

Radiological assessment

USG neck to see carotid intima media thickness (cIMT)

All participants underwent an ultrasound scan to measure carotid intima-media thickness (cIMT). Examination of cIMT was manually performed using a colour duplex flow imaging system by SAMSUNG HS 70 A USG machine with 7 MHz probe. All studies were done according to a predetermined, standardized scanning protocol for children and both right and left carotid arteries were scanned.[13]

USG brachial artery to see flow mediated dilation (FMD)

The brachial artery was scanned above the antecubital fossa, and its diameter was measured from B-mode ultrasound images with the patient at rest (baseline brachial artery diameter). Reactive hyperaemia was induced by inflation of a pneumatic tourniquet placed around the forearm to a pressure of 50 mm Hg above the systolic blood pressure for 5 mins, followed by release. A second scan of vessel diameter was performed at a fixed distance manually using ultrasonic calipers (maximal brachial artery diameter) after 90 seconds.[14] FMD was calculated according to the formula, FMD = % mean diameter of the hyperaemic flow-baseline diameter/baseline.[15]

Echocardiography to see epicardial fat thickness (EFT)

All participants underwent echocardiographic examination by an experienced cardiologist using a PHILLIPS HD 7 machine with the patient in the left lateral decubitus position. EFT was identified as the echolucent region between the external wall of the myocardium and the visceral layer of the pericardium and was measured perpendicularly on the free wall of the right ventricle at the end of systole over 3 cardiac cycles, using a parasternal long and short axis. The average value of the 3 cardiac cycles from each echocardiographic view was used for the statistical analysis.[6]

Statistical analysis

The data obtained was entered into Microsoft Excel Worksheet and analysed using Statistical Package for Social Sciences (SPSS, IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp.). All the figures were generated using Microsoft Excel Worksheet. The normal distribution of data was confirmed using Shapiro-Wilk's Test and appropriate Parametric statistics was employed. Mean and Standard deviations including Standard error were computed for continuous variables. Frequencies and Proportions were calculated for categorical variables. Comparison of continuous variables between Cases and Controls, Within-group Comparisons were done using Unpaired Student's Paired *t*-test. Categorical variables were compared using Chi-Square statistics. Pearson's correlation coefficient was applied for correlation among continuous variables. A value of $P < 0.05$ was considered significant for all statistical inferences.

Results

A total 42 number of cases and 50 number of age and sex matched control were recruited. The mean age of patients in cases and in control was comparable. About 61.91% of the cases were female, while in the control group, female constituted 56%. The mean weight, height of cases were comparable to that of control children, though the BMI of cases (20.39 ± 2.51 kg/m^2) was significantly higher than the control (18.81 ± 3.13 kg/m^2) ($P = 0.01$) [Table 1]. However, the correlation of BMI with various biochemical parameters and parameters for atherosclerosis was nonsignificant. So, it was not considered a confounding factor. The subclinical hypothyroid had comparable systolic Blood Pressure, diastolic blood pressure to the control children [Table 1]. Amongst the cases, majority of the patients were TPO positive (61.91%, n = 26). The mean TSH of the healthy control was 3.28 ± 1.04 mIU/l while in cases, 9.52 ± 3.96 mIU/l [Table 2].

The TC was significantly higher in cases (174.52 ± 30.91 mg/dl) vs. the controls (159.06 ± 35.17 mg/dl) ($P = 0.03$) [Table 3]. Similarly, the LDL level was significantly higher in cases (104.45 ± 29.95 mg/dl) vs. the control (87.12 ± 32.08 mg/dl) ($P = 0.009$). There was no difference between the groups for TG and the HDL level [Table 3]. The fasting blood glucose, fasting insulin did not differ across the two groups. The HOMAIR in cases was slightly higher than the control but did not show any statistical significance ($P = 0.23$). Both hsCRP and Lip A were significantly higher in cases than the control group ($P < 0.001$). The EFT was significantly higher and the brachial FMD was significantly lower in the cases than in the controls with ($P < 0.001$) [Table 4]. However, the CIMT value was not significantly different between the groups [Table 4].

The children in cases were categorized into TPO positive and negative groups. There was no difference between the anthropometry and clinical characteristics between the TPO positive and TPO negative groups. The level of TSH was higher in the TPO positive groups, however, the difference was not statistically significant [Table 5]. There was no difference between the lipid parameter between the TPO+ and TPO– cases. The fasting insulin and the HOMA IR were significantly higher in TPO positive cases than the TPO negative cases ($P = 0.002$ and 0.007, respectively) [Table 5]. The hsCRP and the Lip A level are significantly higher ($P = 0.001$) in the TPO positive patients vs. the TPO negative cases [Table 5]. There was no significant difference in the CIMT, EFT or FMD across both the groups [Table 6].

In our study, the EFT level positively correlated with hsCRP level significantly ($P = 0.008$) [Table 7]. We also found a significant negative correlation of EFT with the level of fT4 level ($P = 0.005$) [Table 7]. However, the EFT neither correlate with any anthropometric parameters nor the level of TSH, any lipid parameters, HOMAIR, Lip A, FMD or CIMT value [Table 7]. The EFT in TPO positive vs TPO negative subgroups of cases, also had significant positive correlation with hsCRP ($P = 0.02$) and a significant negative correlation with FT4 level ($P = 0.002$) [Table 8].There was no correlation of EFT with any other markers of subclinical atherosclerosis [Table 8].

We further compared all the parameters for the group with TSH <10 mIU/ml with the control. We found that the hsCRP, Lp(a), EFT were significantly higher ($P < 0.001$)

Table 1: Baseline characteristics of cases vs control

Variable	Category	Cases ($n=42$) *n* (%)	Controls ($n=50$) *n* (%)	*P*
Age (in years) (Mean±SD)		10.36±3.75	10.11±3.11	0.7
Gender	Male	16 (38.09)	22 (44)	0.4
	Female	26 (61.91)	28 (56)	
Puberty	Pre-Puberty	19 (45.24)	19 (38)	0.6
	Puberty	23 (54.76)	31 (62)	
Height (cm) (Mean±SD)		134.81±19.02	131.96±16.34	0.44
Weight (Kg) (Mean±SD)		38.17±13.02	33.76±11.86	0.09
BMI (kg/m^2) (Mean±SD)		20.39±2.51	18.81±3.13	0.01
SBP (mmHg)		104.86±4.38	103.52±6.02	0.5
DBP (mmHg)		67.57±5.14	66.48±6.73	0.39

Values mentioned in mean±SD

Table 2: Subcategorization of cases on the basis of TSH and anti-TPO

Variable	Category	Cases (*n*=42) *n* (%)	Controls (*n*=50) *n* (%)
ANTI-TPO (U/ml)	0	16 (38.09)	-
	1	26 (61.91)	
TSH (mIU/l)	<10	29 (69.04)	-
	10 or above	13 (30.96)	

Table 3: Comparison of biochemical parameters between case and control

Variable	Group	Mean	SD	*P*
FT3 (pmol/l)	Cases	4.61	0.88	0.14
	Controls	4.28	1.16	
FT4 (pmol/l)	Cases	16.19	2.46	0.43
	Controls	15.79	2.32	
TSH (mIU/l)	Cases	9.52	3.96	<0.001
	Controls	3.28	1.04	
TC (mg/dl)	Cases	174.52	30.91	0.03
	Controls	159.06	35.17	
TG (mg/dl)	Cases	108.86	53.88	0.24
	Controls	121.52	50.6	
HDL (mg/dl)	Cases	49.33	8.75	0.08
	Controls	45.66	10.85	
LDL (mg/dl)	Cases	104.45	29.95	0.009
	Controls	87.12	32.08	
VLDL (mg/dl)	Cases	19.98	10.65	0.04
	Controls	24.92	11.78	
FBG (mg/dl)	Cases	77.86	4.43	0.3
	Controls	78.78	3.84	
F Insulin (µU/ml)	Cases	5.17	0.38	0.1
	Controls	4.94	0.83	
HOMA IR	Cases	0.99	0.09	0.23
	Controls	0.96	0.16	
hsCRP (mg/l)	Cases	1.97	0.33	<0.001
	Controls	0.87	0.28	
Lp (a) (mg/dl)	Cases	14.02	2.67	<0.001
	Controls	9.24	2.41	

Table 4: Comparison of markers of subclinical atherosclerosis between case and control

Variable	Group	Mean	SD	Mean difference	*P*
EFT (mm)	Cases	6.27	0.91	1.73	<0.001
	Controls	4.54	0.66		
CIMT (mm)	Cases	0.52	0.12	0.03	0.12
	Controls	0.49	0.08		
FMD (%)	Cases	4.5	1.34	−4.43	<0.001
	Controls	8.93	1.36		

and the FMD was significantly lower in cases than the control ($P < 0.001$) [Table 9] The CIMT difference between the group was nonsignificant ($P = 0.66$) [Table 9]. However, in this group also, the EFT did not correlate with the level of TSH.

Discussion

In children, SCH is often a benign and remitting condition. The long-term clinical consequences of persistent SCH in children are still debated. Consequent to this, data regarding the prevalence of SCH in children and adolescents are scanty. Therefore, in children the need for L-T4 supplementation remains controversial.

In the current study, there was a significant difference in serum total cholesterol, and LDL level between the two groups with both being statistically higher in the cases [Table 3]. There was no difference between the groups in TG and the HDL level [Table 3]. This is in concordance with previous studies done, where similar results were found.[16] Contrary to this, some authors have reported no differences in parameters of lipid profile between children with subclinical hypothyroidism and healthy children.[16] The studies evaluating children, adolescents and adults with subclinical hypothyroidism suggested that abnormalities in lipid profile are more pronounced in adult patients, and those with severe form of the disease. In contrast to firm scientific and clinical evidence which consistently points to elevated LDL-C concentrations in patients with hypothyroidism, data regarding HDL-C are not homogenous.[16] In some studies HDL-C levels were found to be decreased.[17,18] however, some studies did not find any change in HDL level in patients of SCH,[19] which was similar to our study. A recent study found that subclinical hypothyroid children of AIT (autoimmune thyroiditis) had lower HDL than the healthy control, while TC and LDL levels were not significantly different between the two groups.[20] Their studies analysing HDL-C concentration in children with hypothyroidism were conducted in smaller cohorts, which might affect the reliability of the obtained results. Therefore, larger studies with prospective design may resolve this issue in future.

It has been reported that SCH results in low-grade chronic inflammation, that causes endothelial dysfunction, which in turn is a promoter of atherosclerosis. In our study, both the inflammatory markers, hsCRP and Lp(a) were significantly higher in cases than the control group [Table 3]. This is in concordance with the study in SCH children, where hsCRP was significantly high in cases[20] The increase in Lp(a) has also been demonstrated by a study in Chinese subjects with asymptomatic subclinical hypothyroidism.[21]

In our study, EFT was significantly higher in the cases than in the controls, with $P < 0.05$ [Table 4]. This is in concordance with previous studies in adult SCH patients.[22,23] The same has also been observed in children with SCH, where the EFT was significantly higher in cases.[20]

In the current study, the brachial FMD was significantly lower in cases than the cohort. However, CIMT was not different amongst the cases and controls [Table 4]. cIMT is measure of structural changes and FMD is a dynamic measure of endothelial function.[24] It is difficult to estimate the duration of

Table 5: Biochemical parameters of TPO+ vs. TPO− cases

Variable	Group	Mean	SD	Mean difference	*P*
FT3 (pmol/l)	Anti TPO −ve	4.70	0.7	0.15	0.6
	Anti TPO +ve	4.55	0.98		
FT4 (pmol/l)	Anti TPO −ve	16.52	2.36	0.54	0.49
	Anti TPO +ve	15.98	2.55		
TSH (mIU/l)	Anti TPO −ve	8.11	2.5	−2.28	0.06
	Anti TPO +ve	10.39	4.46		
TC (mg/dl)	Anti TPO −ve	166.75	25.91	−12.55	0.2
	Anti TPO +ve	179.31	33.19		
TG (mg/dl)	Anti TPO −ve	107.5	33.27	−2.19	0.9
	Anti TPO +ve	109.69	63.99		
HDL (mg/dl)	Anti TPO −ve	48.81	8.52	−0.84	0.7
	Anti TPO +ve	49.65	9.03		
LDL (mg/dl)	Anti TPO −ve	97.25	23.09	−11.63	0.2
	Anti TPO +ve	108.88	33.14		
VLDL (mg/dl)	Anti TPO −ve	18.38	6.33	−2.58	0.4
	Anti TPO +ve	20.96	12.62		
FBG (mg/dl)	Anti TPO −ve	77.44	5.36	-0.67	0.6
	Anti TPO +ve	78.12	3.84		
F Insulin (μU/ml)	Anti TPO −ve	4.95	0.44	−0.36	0.002
	Anti TPO +ve	5.31	0.26		
HOMA IR	Anti TPO −ve	0.95	0.1	-0.07	0.007
	Anti TPO +ve	1.02	0.07		
HSCRP (mg/l)	Anti TPO −ve	1.77	0.17	−0.32	0.001
	Anti TPO +ve	2.09	0.35		
Lp (a) (mg/dl)	Anti TPO −ve	12.31	1.82	−2.74	0.001
	Anti TPO +ve	15.06	2.6		

Table 6: Markers of subclinical atherosclerosis in TPO+ vs TPO− cases

Variable	Group	Mean	SD	Mean difference	*P*
EFT (mm)	Anti TPO −ve	6.08	1.01	−0.32	0.27
	Anti TPO +ve	6.4	0.85		
CIMT (mm)	Anti TPO −ve	0.5	0.11	−0.04	0.3
	Anti TPO +ve	0.54	0.12		
FMD (%)	Anti TPO −ve	4.98	1.45	0.77	0.06
	Anti TPO +ve	4.21	1.21		

the SCH state, which may be itself be directly related to gradual structural changes in the arterial wall. Functional changes like impaired FMD can be the preceding changes before change in cIMT occurs in these patients. Since our study was a cross sectional one it was not possible to ascertain the duration of the disease.

In our study, the EFT failed to correlate with the level of TSH [Table 7]. We also did not find any correlation of EFT with any anthropometric parameters, lipid parameters, Lipoprotein A, CIMT or brachial FMD [Table 7]. The only significant positive correlation of the EFT was with hsCRP level and significant negative correlation with the level of fT4 level [Table 7]. There was no correlation of EFT with

Table 7: Correlation with EFT with various parameters in cases

Variable		Mean±SD	*r*	*P*
EFT (mm) 6.27±0.91	Age	10.36±3.75	−0.09	0.5
	Weight	38.17±13.02	−0.12	0.4
	BMI	20.39±2.5	−0.06	0.7
	SBP	104.38±4.86	0.03	0.8
	DBP	67.57±5.14	−0.1	0.5
EFT (mm) 6.27±0.91	TSH	9.52±3.96	0.01	0.9
	FT3	4.61±0.88	−0.17	0.3
	FT4	16.19±2.46	−0.4	0.005
EFT (mm) 6.27±0.91	TC	174.52±30.91	−0.07	0.6
	TG	109.86±53.88	−0.05	0.7
	HDL	49.33±8.75	0.09	0.5
	LDL	104.45±29.95	−0.12	0.4
	VLDL	19.98±10.65	0.05	0.7
EFT (mm) 6.27±0.91	HOMAIR	0.99±0.09	0.04	0.7
	hsCRP	1.96±0.33	0.4	0.008
	Lp (a)	14.02±2.67	−0.06	0.7
EFT (mm) 6.27±0.91	CIMT	0.52±0.12	0.07	0.6
	FMD	4.5±1.34	0.15	0.3
	POST	3.19±0.21	0.03	0.8
	PRE	3.05±0.17	0.001	0.9

Values mentioned in mean±SD

Table 8: Correlation ewith EFT with various parameters in TPO positive cases

Variable		Mean±SD	*r*	*P*
EFT 6.4±0.85	Age	10.24±3.69	−0.04	0.8
	Weight	37.74±12.99	−0.08	0.6
	BMI	20.07±2.5	−0.12	0.5
	SBP	104.62±4.07	0.01	0.9
	DBP	67.08±4.64	−0.02	0.9
EFT 6.4±0.85	TSH	10.39±4.47	−0.21	0.29
	FT3	4.55±0.98	−0.24	0.2
	FT4	15.98±2.55	−0.6	0.002
EFT 6.4±0.85	TC	179.31±33.19	0.02	0.9
	TG	109.69±63.99	−0.01	0.9
	HDL	49.65±9.03	0.07	0.7
	LDL	108.88±33.14	−0.03	0.8
	VLDL	20.96±12.62	0.08	0.6
EFT 6.4±0.85	HOMAIR	1.02±0.07	0.14	0.5
	hsCRP	2.09±0.34	0.4	0.02
	Lp (a)	15.06±2.6	−0.23	0.2
EFT 6.4±0.85	CIMT	0.53±0.12	−0.03	0.8
	FMD	4.21±1.2	0.11	0.5
	POST	3.18±0.19	0.04	0.8
	PRE	3.05±0.16	0.02	0.8

FT3 level. The minimum level of FT4 below which EFT rises could not be found from our study due to small sample size. Our results were discordant with that of by Farghaly *et al.*,[20] where a strong positive correlation of EFT with the TSH level and FMD. This discrepancy might be due to the population included in their study, where all the subclinical

Table 9: Comparison of various parameters between the patients with TSH <10 mIU/ml with control

Variable	Group	Mean	SD	*P*
TSH (mIU/l)	Cases	7.32	1.10	<0.001
	Controls	3.28	1.04	
F insulin (μU/ml)	Cases	5.072	0.34	0.43
	controls	4.94	0.82	
HOMAIR	Cases	0.97	0.09	0.57
	Controls	0.96	0.16	
hsCRP (mg/l)	Cases	1.96	0.31	<0.001
	Controls	0.87	0.28	
Lp (a) (mg/dl)	Cases	14.16	2.94	<0.001
	Controls	9.24	2.41	
EFT (mm)	Cases	6.16	0.94	<0.001
	Controls	4.54	0.66	
FMD (%)	Cases	4.53	1.35	<0.001
	Controls	8.93	1.36	
CIMT (mm)	Cases	0.50	0.11	0.66
	Controls	0.49	0.08	

hypothyroidism were of autoimmune aetiology. Considering the autoimmune group of SCH children in our study, the EFT still did not correlate with the TSH level which may be due to small sample size of TPO positive cases.

TPO positive and negative cases were studied separately to see whether the parameters of atherosclerosis are different for the two groups despite having SCH. TPO antibodies have been linked to atherosclerosis although the data has been inconsistent. Though exact mechanism how TPO Ab leads to chronic inflammation is still unknown, yet various studies have led to the findings that suggest the association of TPO Ab with inflammation. A study in 66 euthyroid girls with TPO positive, showed significantly high hs-CRP, TC, LDL and CIMT levels compared to TPO negative control.[25] Another study concluded that the presence of normal TPO-Ab titer, though not associated with autoimmune thyroid disease, it could still influence endothelial remodelling including atherosclerosis.[26] However, some other studies conducted did not support the association of TPO antibodies with cardiovascular disease risk in patients with subclinical hypothyroidism.[27]

In the current study, we observed that the TPO positive patients (10.39 ± 4.46 mIU/l) had higher TSH than the TPO negative (8.11 ± 2.5 mIU/l) patients, though it was not statistically significant (P = 0.06). The patients who were TPO positive SCH, had higher fasting insulin, HOMAIR, hsCRP, Lp(a) than those who were TPO negative [Table 5]. The radiological parameters like EFT, brachial FMD, CIMT, were not different between the TPO positive and TPO negative groups [Table 5]. The explanation of this seemingly discrepancy in the results of biochemical versus radiological parameters, might be due to the longer time period for functional and structural vascular changes to appear. So, if these patients will be followed up for a longer time, the changes could probably be documented. The findings in this study suggests the association of TPO antibody to various markers of chronic inflammation though the direct causation could not be proven.

There are several limitations of the current study. The study was a cross-sectional type of study and no follow up of the patients could be done. The sample size was small and the disease duration was not known which can have a huge influence on results.

Conclusion

Though proven data of occurrence of subclinical atherosclerosis in adult SCH exist beyond doubt, data children is scarce. Children with persistent SCH may be at risk of having subclinical atherosclerosis. Our study does support this as we found a positive correlation of EFT with hsCRP in SCH children. We found the patients of Hashimoto thyroiditis having high insulin resistance and markers of inflammation than the SCH patients of other aetiologies.

To summarize, we demonstrated the presence of subclinical atherosclerosis in children with SCH regardless of the aetiologies. These children are at greater risk of early cardiovascular disease during adulthood, which is a matter of concern. So, we suggest to further lower the threshold of TSH and consider treatment in children of persistent SCH regardless of the aetiology. However further large-scale studies with longitudinal follow up including larger number of participants of SCH would probably substantiate our findings.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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