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Original Article

Euthyroid State in Hashimoto Thyroiditis in Children Seems to Protect Against Subclinical Cardiomyopathy

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Abstract:

Background: Hashimoto thyroiditis (HT) is associated with myocardial dysfunction, it is attributed to the autoimmune chronic inflammation and other endocrine factors.

Aim of the work: Detection of subclinical myocardial dysfunction in children with euthyroid Hashimoto thyroiditis using speckle tracking echocardiography and estimation of carotid intimamedia thickness.

Patients and Methods: We performed a case-control cross-sectional study that involved 15 children with euthyroid HT following up at the Endocrinology Clinic, Ain Shams University Children's Hospital from October 2020 to July 2021 and 15 healthy controls of comparable age and sex. Both groups underwent conventional and speckle tracking echocardiography in addition to estimation of carotid intima-media thickness by high resolution ultrasound machine.

Results: The children with euthyroid HT had a mean \pm SD age of 13.20 ± 3.05 years, while that of the control group was 11.80 ± 3.03 years (p=0.21). Twelve (80%) of the children with HT and 11(73%) of the control group were females (p=0.66). The mean \pm SD for serum-free T3, free T4 and thyroid stimulating hormone (TSH) were 3.57 ± 1.07 , 1.43 ± 0.76 ng/dl, and 4.03 ± 2.27 IU/ml in patients, and were 3.59 ± 9.21 pg/ml, 1.29 ± 0.15 ng/dl and 3.4 ± 0.3 IU/ml in control group (p = 0.474), (p=0.249) and (p=0.316) respectively. The mean (range) left ventricular global longitudinal strain of the cases and control group were within the normal range (-20.44 \pm 1.24) (-23 to -17.4) and (-20.94 \pm 0.59) (-21.8 to -19.5) respectively) (p= 0.159). The mean carotid intimamedia thickness was normal in both cases (0.35 \pm 0.05 cm) and controls (0.33 \pm 0.05 cm) (p = 0.47). **Conclusion:** Euthyroid state seems to protect against subclinical myocardial dysfunction in Hashimoto thyroiditis.

Level of Evidence of Study: IV (1).

Keywords: Hashimoto thyroiditis; speckle tracking echocardiography; carotid intima-media thickness; children

Abbreviations: AITD: Autoimmune thyroid disorder; BMI: body mass index; CIMT: carotid intimal media thickness; EF: ejection fraction; FS: fraction shortening; GLS: global longitudinal strain; HT: Hashimoto thyroiditis; IVST: inter ventricular septum thickness; TSH: Thyroid-stimulating hormone; LVEDd: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; LVESd; left ventricular end-systolic diameter; LVGLS: LV global longitudinal strain; LVPWT: left ventricular posterior wall thickness; SDS: standard deviation score; STE: speckle tracking echocardiography; T3: tri- triiodothyronine; T4: tetraiodothyronine; TSH: thyroid stimulating hormone; TDI: tissue Doppler imaging

Introduction

Hashimoto thyroiditis (HT) is considered the commonest cause of thyroid gland disease in children and adolescents and is the commonest cause of acquired hypothyroidism in iodine-sufficient areas (2, 3). HT is caused by the destruction of the thyroid gland cells by an antibody-mediated autoimmune process, hence it is called chronic autoimmune thyroiditis and chronic lymphocytic thyroiditis. Characteristics of HT include increased volume of the thyroid gland, infiltration of the gland parenchyma by lymphocytes, and the presence of antibodies against the thyroid antigens. HT has increased in frequency during the last decade (3). HT is reported to be complicated by myocardial dysfunction (4) and increases the carotid artery intima-media thickness (CIMT) which is a strong predictor of future cardiovascular disease. It is not known if



this myocardial dysfunction is related to the hypothyroidism/hyperthyroidism associated with HT or to the chronic inflammation or both (5). Left and right ventricular myocardial dysfunction associated with euthyroid HT has been suggested to be attributed to the abnormal state of inflammation associated with autoimmunity (6). This work aimed to study myocardial function in children with euthyroid Hashimoto thyroiditis using speckle tracking echocardiography and estimation of carotid intima-media thickness (CIMT).

Subjects and Methods

This was a cross-sectional case- control study. All the procedures done in the study conformed with the standards of the Institutional Research Committee according to Helsinki Declaration (7) and its later amendments. The study was approved by the Ethics Committee of Ain Shams University (approval number: FMASU MS 880/2020). Written informed consent was obtained from the care givers.

Participants

The study included 15 patients with the confirmed euthyroid HT following up at the Pediatric Endocrinology Clinic, Ain-Shams University Hospital. They were compared to 15 healthy controls of the matched age and sex. The inclusion criteria in our study were: 1) patients whose ages ranged from 1 year to 18 years including patients on levothyroxine replacement therapy, 2) patients confirmed to have Hashimoto thyroiditis based on estimation of free thyroxine (fT4), free triiodothyronine (fT3), thyroid-stimulating hormone (TSH), antithyroid peroxidase antibodies, and positive antithyroglobulin antibodies 3) thyroid parenchymal heterogeneity detected by ultrasonography; and 4) patients who had a normal range of free T3, free T4, and TSH on treatment (euthyroid) at the time of recruitment. During October 2020 till July 2021 all patients fulfilling the inclusion criteria were recruited.

Methods

This study is a case-control cross-sectional study. Data were collected from the patients' files, including age at initial diagnosis, the initial level of antithyroglobulin antibodies, antithyroid peroxidase antibodies, the initial level of thyroid hormones, age at start of levothyroxine treatment, duration of treatment with levothyroxine, and history of thyroid disorders in their family members. They all underwent thorough systematic clinical examination of the chest, heart, and abdomen. It also included the weight and height, body mass index (BMI), weight standard deviation score (SDS), height SDS and BMI SDS according to the norms (ϑ). The body surface area (BSA) was calculated using the formula: (weight (kg) × 4) + 7/(weight (kg) + 90) (ϑ). Systolic, and diastolic blood pressure and heart rate were assessed and compared with age and sexmatched norms (10).

Lab Investigations

The venous blood samples were obtained in the morning by venipuncture after overnight fasting for 6 hours and were used to measure the following:

a) Serum free thyroxine (T4), free triiodothyronine (T3), and thyroid stimulating hormone (TSH). A Cobas analyzer (Cobas e411, Roche Diagnostics, Switzerland) was used for immunoassay tests and compared to the following reference ranges for free T3 (2.5-5.2 pg/ml), free T4 (0.97-1.67 ng/dl) and TSH (0.6-4.8 IU/ml).

b) Antithyroglobulin and antithyroid peroxidase antibodies were assessed using indirect immunohistochemistry. Positive antithyroglobulin was defined as antithyroglobulin above 0.6 U/ml, while positive antithyroid peroxidase antibodies was defined as antithyroid peroxidase antibodies above 100 U/ml.

c) Serum low-density lipoproteins (LDL), high-density lipoprotein (HDL), triglycerides in addition to total cholesterol. They were assessed using Cobas analyzer (Cobas c6000, Roche Diagnostics, Switzerland). In this study, total serum cholesterol normal level was considered if less than 200 mg/dl, while a value of 200 to 239 mg/dl was borderline, and more than 240 mg was considered elevated. Normal serum LDL reference range was defined as normal up to 160 mg/dl. The serum HDL reference was defined as normal up to 60 mg/dl. The serum triglycerides reference range was defined as normal up to 150 mg/dl, with borderline levels between 150 and 199 mg/dl, while more than 200mg/dl was classified as high.

Imaging: All children underwent:

a) Standard transthoracic two-dimensional (2D) echocardiography imaging by an expert pediatric cardiologist blinded to the clinical data of the patients using a Vivid 9, GE Ultrasonography Machine (Norway) with 5 megahertz (MHz) transducer. An electrocardiogram (ECG) cable was used to define the cardiac cycle timing. Examination was performed in the left lateral semi-recumbent or the supine position in a resting quiet breathing condition. The measurements of the M-mode were done at the level of the tips of mitral valve leaflets in the parasternal long-axis view of the left ventricle (LV), as left ventricular end-systolic diameter (LVESd), left ventricular end-diastolic diameter (LVEDd), interventricular septum thickness (IVST) and LV posterior wall thickness (LVPWT), and ejection fraction (EF) (11).

b) 3D speckle tracking echocardiography (STE) that measured average LV global longitudinal strain (LV GLS). Apical long axis, apical four-chamber and apical two chamber images were taken. All 17 segments were presented (*12*).

c) CIMT was done using ultrasonography machine (Vivid 9 GE, Norway) by a linear transducer 5 MHZ probe. The probe was placed over carotid artery. M mode was applied and CIMT was measured in cm. The probe was placed in the anterolateral position over the patients extended neck. Measurements were made in the longitudinal plane of the common carotid artery. The CIMT was identified as the distance from the intima-blood interface to the adventitia-media junction. Three readings were recorded in centimeters and the mean value was used for the statistical purposes. A cut off value above 0.5 cm was considered abnormal. CIMT Z-score was then calculated (*13*).

Statistical Analysis

Data were collected, revised, coded, and entered into the Statistical Package for Social Science (IBM SPSS) version 23 (IBM Corp, Armonk, NY, USA). The quantitative data were presented as mean, standard deviations, ranges and median. Qualitative variables were presented as numbers and percentages. The comparison between groups regarding qualitative data was done by using the chi-square test and/or Fisher exact test when the expected count in any cell found less than five. The comparison between two independent groups with quantitative data and parametric distribution was done by using an independent t-test while in case of non-parametric distribution Mann-Whitney test was used. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p value significance was considered if p value was < 0.05.

Results

The mean age of the children with HT was 13.2 ± 3 years, of them 12 were females (80%) and 3 males (20%). The mean age \pm standard deviation (SD) of the control group (15 healthy children) was of them 11 females (73%) and four males (26%) (p=0.21) and (p=0.66) respectively. Patients group included 5 (33%) newly diagnosed patients (within one month of their diagnosis) and 10 (66%) patients with HT disease duration ranging from 21 to 50 months.

Upon comparing the anthropometric parameters between the two groups, no statistically significant differences were found in the BMI SDS (p=0.83), weight SDS (p=0.059) and body surface area (BSA) (p=0.8). However, height SDS was lower in the patients' group (p value = 0.003) (Table 1).

Regarding the heart rate, blood pressure, echocardiography parameters and CIMT, no significant statistical difference was found between both groups. Also, LV GLS comparison between both groups showed no significant statistical difference (p=0.34). (Tables 2 and 3). CIMT did not correlate with anthropometry, lipid profile, or level of thyroid antibodies in our studied cohort. (Table 4).

The LV GLS mean was not affected by disease duration (p = 0.14) (Table 5 and Figure 1). No statistically significant correlation was noticed between the LV GLS and the duration of the disease (p=0.11) (Table 6).

There was no significant correlation between CIMT and lipid profile, level of thyroid hormones, serum anti-bodies initially or at the time of recruitment in our study. (Table 4). There was no correlation between CIMT z-score with the duration of the disease. (Tables 5 and 6).

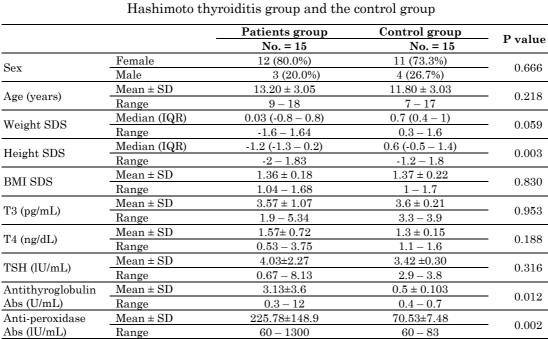


Table 1. Anthropometric measures, thyroid profile, and antibodies the euthyroid
Hashimoto thyroiditis group and the control group

Abs: antibodies; BMI: body mass index; T3: tri- triiodothyronine; T4: tetraiodothyronine; TSH: thyroid stimulating hormone; SDS: standard deviation score

		Patients group	Control group	D 1	
		No. = 15	No. = 15	P value	
Sustalia DD (mmHm)	$Mean \pm SD$	108.67 ± 8.34	112.47 ± 7.96	0.212	
Systolic BP (mmHg)	Range	90 - 120	100 - 125	0.212	
	Below 50th	6 (40.0%)	4 (26.7%)		
CDD 0/ and to am	50th percentile	5 (33.3%)	3 (20.0%)	0.437	
SBP % acc. to age	Above 50th	4 (26.7%)	7 (46.7%)	0.457	
	90th percentile	0 (0.0%)	1 (6.7%)		
Diastalia BD (mmHa)	$Mean \pm SD$	69.67 ± 8.34	67.87 ± 4.64	0.471	
Diastolic BP (mmHg)	Range	60 - 80	60 - 75	0.471	
	Below 50th	4 (26.7%)	3 (20.0%)		
$\mathbf{D}^{*}_{1} = t + 1^{*}_{1} = \mathbf{D} \mathbf{D}^{*}_{1}$	50th percentile	2 (13.3%)	6 (40.0%)		
Diastolic BP %	Above 50th 4 (26.7%) 4 (26.7%)		0.432		
according to age	90th percentile	4 (26.7%)	2 (13.3%)		
	Above 90	1 (6.7%)	0 (0.0%)		
UD (D/min)	Mean \pm SD	80.87 ± 7.64	77.33 ± 5.35	0.154	
HR (B/min)	Range	70 - 90 $68 - 8$		- 0.154	

Table 2. Vital signs of the euthyroid Hashimoto thyroiditis group and the control group

BP: blood pressure; HR: heart rate

Table 4. Correlation of carotid intimal media thickness with anthropometry, lipid profile and thyroid antibodies

	CIMT			
	Patients group		Contro	ol group
	r	P value	r	P value
Weight SDS	-0.139	0.620	-0.263	0.344
BMI (kg/m2)	-0.186	0.507	0.065	0.817
BMI SDS	-0.155	0.582	-0.264	0.343
Fasting Cholesterol (mg/dL)	0.016	0.956	0.443	0.098
HDL (mg/dL)	-0.466	0.080	0.335	0.222
LDL (mg/dL)	-0.108	0.700	0.492	0.062
Triglycerides (mg/dL)	0.031	0.913	0.033	0.906
Antithyroglobulin antibodies (U/mL)	0.248	0.373	-0.423	0.116
Anti-peroxidase antibodies (IU/mL)	0.232	0.405	0.148	0.598

BMI: body mass index; CIMT: carotid intimal media thickness; HDL; high density lipoproteins; LDL: low density lipoproteins; SDS: standard deviation score

M mode data —		Patients group	Control group	- P value	
		No. = 15	No. = 15		
LVEDd	$Mean \pm SD$	4.23 ± 0.39 4.05 ± 0.3		0.190	
LVEDa	Range	3.5 - 5.1	3.2 - 4.5	0.189	
LVEDd z-score	Median (IQR)	-0.3 (-0.9 – 0.8)	-0.5 (-1.6 – 0.2)	0.383	
LVEDu z-score	Range	-1.9 - 1.2	-1.9 - 1.3	0.365	
LVESd	$Mean \pm SD$	2.61 ± 0.36	2.49 ± 0.31	0.335	
LVESU	Range	2 - 3.1	2 - 3	0.555	
LVESd z-score	Median (IQR)	-0.04 (-1.3 – 0.7)	-1 (-1.8 – 0.3)	0.383	
LVES0 Z-score	Range	-2.9 - 1.2	-2.3 - 1.7	0.383	
FS %	$Mean \pm SD$	40.60 ± 3.78	38.20 ± 4.06	0.105	
F5 %	Range	32 - 45	31 - 43	0.105	
LVPWT	$Mean \pm SD$	0.62 ± 0.11	0.58 ± 0.07	0.235	
	Range	0.5 - 0.9	0.5 - 0.7		
LVPWT z-score	Median (IQR)	-0.3 (-1.3 – 0.1)	-0.9 (-1.40.4)	0.109	
LVPW1 z-score	Range	-1.9 - 0.7	-1.9 - 0.75		
EF	$Mean \pm SD$	64.93 ± 5.12	67.20 ± 5.44	0.250	
БГ	Range	57 - 75	59 - 77		
GLS	Median (IQR)	-20.6 (-2119.7)	-21.1 (-21.420.2)	0.340	
	Range	-2317.4	-21.8 - 20.8		
CIMT	$Mean \pm SD$	0.35 ± 0.05	0.33 ± 0.05	0.450	
	Range	0.3 - 0.4	0.3 - 0.4	0.473	
	Below 25 th	8 (53.3%)	8 (53.3%)	- 1.000	
CIMT z-score	25 th	7 (46.7%)	7 (46.7%)		

Table 3. The echo parameters, LV GLS, and CIMT among the euthyroid Hashimoto thyroiditis group and the control group

CIMT: cardiac intimal media thickness; EF: ejection fraction; FS: fraction shortening; GLS: global longitudinal strain; IVST: inter ventricular septum thickness; LVEDd: left ventricular end diastolic diameter; LVESd: left ventricular end systolic diameter; LVPWT: left ventricular posterior wall thickness

Table 4. Comparison between newly diagnosed patients and known patients with euthyroid Hashimoto
thyroiditis regarding M-mode parameters, global longitudinal strain, and carotid intima-media thickness

		Newly diagnosed			
	_	Yes	No	P value	
	_	No. = 5	No. = 10	_	
LVEDd	$Mean \pm SD$	4.26 ± 0.52	4.22 ± 0.34	0.950	
	Range	3.8 - 5.1	3.5 - 4.7	0.859	
LVEDd z-score	Median (IQR)	-0.5 (-0.60.3)	0.3 (-0.9 – 0.8)	0.712	
LVEDu z-score	Range	-0.9 - 1.2	-3.1 - 1.2	- 0.713	
LVESd	$Mean \pm SD$	2.56 ± 0.41	2.64 ± 0.35	0.701	
LVESU	Range	2.2 - 3	2 - 3.1	- 0.701	
LVESd z-score	Median (IQR)	-1.1 (-1.3 – 0.1)	-0.02 (-0.8 – 0.8)	0.901	
LVESU Z-SCORE	Range	-1.8 - 0.4	-2.9 - 1.2	- 0.391	
FS %	$Mean \pm SD$	40.20 ± 5.17	40.80 ± 3.19	- 0.784	
r5 %	Range	32 - 45			
LVPWT	$Mean \pm SD$	0.62 ± 0.16 0.62 ± 0.08		1.000	
	Range	0.5 - 0.9	0.5 - 0.7	- 1.000	
LVPWT z-score	Median (IQR)	-0.3 (-0.550.1)	-0.5 (-1.3 – 0.1)	0.059	
LVPWIZ-score	Range	-1.9 - 0.7	-1.8 - 0.1	0.853	
EF	$Mean \pm SD$	64.60 ± 8.26	65.10 ± 3.21	0.900	
СГ	Range	57 - 75	60 - 70	- 0.866	
ara	$Mean \pm SD$			0.014	
GLS	Range	-2320.6	-2117.4	- 0.014	
CIN/IT	$Mean \pm SD$	0.36 ± 0.05	0.34 ± 0.05	0 500	
CIMT	Range	0.3 - 0.4	0.3 - 0.4	- 0.500	
	Below 25th	3 (60.0%)	5 (50.0%)	0.714	
CIMT z-score	25 th or more	2 (40.0%)	5 (50.0%)	- 0.714	

CIMT: cardiac intimal media thickness; EF: ejection fraction; FS: fraction shortening; GLS: global longitudinal strain; IVST: inter ventricular septum thickness; LVEDd: left ventricular end diastolic diameter; LVESd: left ventricular end systolic diameter; LVPWT: left ventricular posterior wall thickness



Table 5. Correlation between echocardiography parameters and carotid intima-media thickness, with
duration of disease and antibody levels among studied groups

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	Duration of the disease (months) r P value		Antithyroglobulin Abs. (U/mL) r P value		Anti- Peroxidase antibodies (IU/mL)	
-					r P value	
LVEDd	0.305	0.269	-0.069	0.806	-0.132	0.639
LVEDd z-score	0.412	0.127	-0.003	0.992	0.084	0.766
LVESd	0.397	0.143	-0.030	0.916	-0.194	0.489
LVESd z-score	0.586*	0.022	-0.147	0.602	0.005	0.985
FS %	-0.306	0.268	-0.089	0.753	0.198	0.480
LVPWT	0.211	0.451	-0.009	0.973	0.405	0.135
LVPWT z-score	0.103	0.714	0.056	0.844	0.511	0.051
E.F	-0.068	0.810	0.013	0.964	-0.137	0.626
GLS	-0.637	0.011	-0.123	0.661	-0.309	0.262
CIMT	0.079	0.780	0.248	0.373	0.232	0.405

CIMT: cardiac intimal media thickness; EF: ejection fraction; FS: fraction shortening; GLS: global longitudinal strain; IVST: inter ventricular septum thickness; LVEDd: left ventricular end diastolic diameter; LVESd: left ventricular end systolic diameter; LVPWT: left ventricular posterior wall thickness

Discussion

Over the past years, several studies have revealed an association between Hashimoto thyroiditis and cardiovascular disease. They were attributed to autoimmunity associated with chronic thyroiditis, medications and thyroid hormonal level abnormalities (14).

In our study, we focused on the effect of euthyroid Hashimoto thyroiditis on cardiac functions estimated by using conventional echocardiography parameters as well as speckle tracking. Conventional echocardiographic parameters including LVEDD, LVESD, IVST, and LVPWT, and their z-score showed no statistically significant difference between euthyroid Hashimoto cases and controls. The LV function estimated by EF and FS were also within the normal range for both groups suggesting that proper control and maintaining the thyroid hormones within normal is protective against cardiac dysfunction irrespective of duration of disease. This finding is in agreement with other studies conducted on adults with Hashimoto thyroiditis (*15*, *16*). Thyroid hormones was reported to have regulating effects on genes encoding for cardiac proteins (*15*).

In other studies, conventional echocardiography was not sufficient to detect subclinical cardiac dysfunction timely and only tissue Doppler imaging (TDI) in patients with autoimmune euthyroid chronic thyroiditis was able to show earlier functional changes in the heart, even at the euthyroid stage. Myocardial systolic performance assessment in adult heart failure using ejection fraction and STE found that patients with normal ejection fraction showed impaired LV functions by STE which supports the importance of STE in early detection of myocardial dysfunction (17). Hence in our study, we used STE to measure LV GLS for both euthyroid HT patients and control group. LV GLS was within the normal range for age and sex in both groups. This is in disagreement with other studies that found higher LV GLS values in treated subclinical hypothyroidism when compared to untreated cases and lower LV GLS in untreated cases when compared to controls emphasizing the effect of normalizing thyroid hormone levels on LV GLS (18). The LV GLS was not affected by duration of disease or presence of autoantibodies. This is consistent with other studies (19). It seems that strict control of thyroid hormone level in children with HT protects against cardiac dysfunction. This highlights the role of life long stringent follow up of children with HT to guard against life threatening cardiac complications.

The lack of correlation of strain and cardiac dysfunction to auto-antibodies suggests that the cardiac dysfunction is primarily the result of poor thyroid hormone level control, and that autoimmune component is triggered or magnified or permissible by the thyroid hormone level abnormalities.

Cardiovascular disease in Hashimoto thyroiditis includes cardiomyopathy, left ventricular hypertrophy related to systemic hypertension, atherosclerosis and heart failure (20). Thyroid hormones have a significant impact on the cardiovascular system. Many of the clinical manifestations of hyperthyroidism are because of the effect of thyroid hormones on cardiovascular hemodynamic functions (15). Hypothyroidism is also associated with cardiovascular diseases and affects both LV and RV function (21). Alterations in cardiac hemodynamics have been reported even in patients with subclinical hyper- and hypothyroidism (22).



It was suggested that cardiac functional and autonomic changes in HT probably may be related to abnormal thyroid hormone levels or an abnormal cytokines profile, molecular, physiological, or other unseen factors (15). The autoimmune condition associated with HT could be a factor contributing to the cardiovascular changes through endothelial dysfunction and inflammation leading to hypertension, atherosclerosis, and myocardial dysfunction. However, we did not find a correlation between various echocardiography parameters, CIMT, and thyroid autoantibody levels in our studied cases, this could be due to small number of recruited patients or the fact that normalizing thyroid hormone levels with treatment annuls the effect of autoimmunity on cardiac functions (14).

In our study, we found that there was no statistically significant difference between the patients and the control group regarding the CIMT and their Z-score. This may indicate that proper control has an upper hand on the duration of being in a state of chronic inflammation with positive antibodies (14). Both BMI SDS and lipid profile were similar in patients and controls. The normal lipid profile, normal BMI SDS, and the euthyroid state in our cases could explain the lack of abnormal findings in both STE and CIMT results in our studied cases. This contradicts another study that found higher CIMT in euthyroid patients newly diagnosed with HT that correlated with the high BMI SDS and with the higher total and LDL cholesterol levels in their studied patients compared to controls (23).

Our study has limitations. The small number of HT patients not being prospective to study the cardiac functions according to compliance in children with Hashimoto thyroiditis.

Conclusion

Control of thyroid hormone level in children with HT was associated with normal cardiac function as detected by both conventional and speckle tracking echocardiography. Strict control of thyroid hormone levels seems to protect against cardiac dysfunction in children with HT. Prospective large cohort studies are needed to address reproducibility of our results.

Author Contributions:

Elsedfy: formulation of the idea, study design and methodology, revision of paper and results Elsamman: performance of echocardiography, speckle tracking, and CIMT assessment. Nawar: revising the results, data interpretation, manuscript writing, submission and revision. Mahmoud: revising results and data interpretation. Ali: data collection, tabulation, and statistical analysis. All shared and approved the final submitted work.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.

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