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RESEARCH PAPER

CARDIAC DYSFUNCTION IN PATIENTS WITH HYPOTHYROIDISM IN ADULTS

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ABSTRACT

BACKGROUND: Hypothyroidism is a graded disorder and its cardiovascular effects need further exploration.
METHODS: In this prospective case control study, we evaluated, 50 newly diagnosed hypothyroid patients and 25 age and sex matched controls, attending a tertiary care centre of North India for cardiac dysfunction. Statistical analysis was done using SPSS (statistical package for social sciences) software.
RESULTS: Hypothyroid patients had significant dyslipidaemia than controls. Though, the in-group difference for 10-year ASCVD risk score was statistically insignificant (4.81 ± 5.75 vs 3.66 ± 3.50; p = 0.36). On echocardiography, Interventricular septal wall thickness and Left ventricular posterior wall thickness and LVEDD were significantly increased. Also, significant number of patients had Diastolic Dysfunction, mean E/A ratio (0.90 ± 0.16 vs 1.02 ± 0.10; p = 0.001). No significant LV Dysfunction or RWMA was noted.
CONCLUSION: The cardiovascular changes and dyslipidaemia were more marked in hypothyroidism compared to controls.

KEY WORDS : Hypothyroidism, Cardiovascular, Echocardiography, ASCVD-risk

INTRODUCTION

The most common functional disorder of the thyroid gland is hypothyroidism. Hypothyroidism is a cluster of clinical manifestations, including its effect on cardiovascular system and lipid metabolism [2,3,4]. Because, there are many risk factors like hypertension, obesity, hypercholesterolemia and, hypothyroid patients are prone to coronary artery disease. There is a risk of atherosclerosis and myocardial infarction even in subclinical hypothyroidism [6,7]. Since Hypothyroidism is a graded disorder affecting cardiovascular status along with its other effects, there arises the need to explore cardiac manifestations of hypothyroidism and association with dyslipidaemia, metabolic syndrome, and increased risk for atherosclerotic cardiovascular disease.

MATERIALS AND METHOD

This prospective case control study was undertaken to assess the cardiovascular changes in 50 newly diagnosed hypothyroid patients and 25 age and sex matched controls, attending a tertiary care centre of northern India over the duration one year and six months. After approval from the ethical committee, consenting individuals were enrolled and evaluated for cardiac dysfunction by analysing electrocardiographic and echocardiographic profile, 10-year ASCVD risk score (using official ACC-online ASCVD risk calculator) and other variables like Blood pressure, BMI, HBA1C, RBS, Lipid Profile etc. Statistical analysis was done using SPSS (Statistical package for social sciences) software and applying Student's t-test for mean of continuous variables and Chi-square test for proportions for statistical significance. Hypothyroidism in this study was diagnosed in patients with TSH values elevated above normal. Patients with TSH > 4.68 IU/ml with low FT4 or FT3 would be said to have hypothyroidism (Chemiluminescence Immunoassay technique). Patients with TSH elevated above normal and normal FT3 or FT4 would be said to have Subclinical hypothyroidism. All documented patients suffering from hypothyroidism above 18 years were included in the study. While, patients above 60 years and on medicines that could alter cardiac functions like amiodarone, beta blockers, calcium channel blockers, Antihypertensives, Statins, Antiplatelets, Antidiabetic drugs, Insulin therapy, Dialysis, Bronchodilators, L-thyroxine etc or having past history of Primary cardiac disease, chronic kidney disease, diabetes, hypertension, COPD, Severe Anaemia and having Drug induced hypothyroidism or pregnancy were excluded.

RESULTS

Group A: Untreated cases of hypothyroidism (n=50)

Group B: Hypothyroidism patients having subclinical hypothyroidism [13(26%), n=50]

Group C: Control cases - (n=25).

A total of 75 patients were analysed, 50 newly diagnosed hypothyroid Patients (GROUP A) and 25 age and sex matched controls (GROUP C). Of the 50 Hypothyroid patients 66% were females and 34% males. The mean age of presentation and mean TSH was 48.73 years and 31.85 IU/L, respectively. 26.5% patients were said to have subclinical hypothyroidism (GROUP B). In Group A, 62% patients had hypertension as per ACC and AHA 2017 guidelines. The mean systolic Blood Pressure was 123.43mm Hg and mean diastolic Blood Pressure was 76.12 mmHg. Though no significant in group difference was present. The mean BMI, RBS and HBA1C noted in Group A was 24.86, 166.61mg/dl and (6.5), respectively. Hypothyroid patients had significantly higher Total Cholesterol (197.12 ± 38.65 vs 163.24 ± 23.96; p = 0.001); LDL (115.53 ± 23.77 vs 97.64 ± 15.84; p = 0.001); VLDL (24.19 ± 3.07 vs 22.03 ± 2.09; p = 0.002) and lower HDL levels than controls. Though, the in-group difference for 10-year ASCVD risk score was statistically insignificant (4.81 ± 5.75 vs 3.66 ± 3.50; p = 0.36). Commonest ECG

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abnormality noted was sinus bradycardia in 18% patients of Group A followed by Sinus Arrhythmia. No significant QT interval prolongation seen. In echocardiographic study, Interventricular septal wall thickness and Left ventricular posterior wall thickness and LVEDD were significantly increased in hypothyroid patients. Also, significant number of patients had Diastolic Dysfunction, mean E/A ratio (0.90 ± 0.16 vs 1.02 ± 0.10; p = 0.001) in controls. The mean LVEF in Group A was (54.65 ± 5.10 vs 55.76 ± 1.09; p = 0.29) in controls, while LV Dysfunction was present in 8% hypothyroid population. Our study population in Group A had Mild LV systolic Dysfunction in 2 (4%) patients, Moderate LV Dysfunction in 1(2%), Severe LV Dysfunction in 1 (2%) population. RWMA was present in 18% in Group A vs 8% patients in control group; (p = 0.32). Pericardial effusion occurred in 8 % hypothyroid patients.

TABLE 1-Baseline characteristics of the patients with hypothyroidism and control group.

Characteristics		GROUP-A No.	%	GROUP C No.	%
Age Group	18 – 40yrs	9	18	5	20.0
	>40yrs	41	82	20	80.0
Sex	Female	33	66	17	68.0
	Male	17	34	8	32.0
Smoker	No	37	74	19	76.0
	Yes	13	26	6	24.0
Blood Pressure	Normal	14	28	9	36.0
	Elevated	5	10	3	12.0
	Stage I HTN	22	44	11	44.0
	Stage II HTN	9	18	2	8.0
RBS	Normal	40	80	21	84.0
	Elevated	10	20	4	16.0
Pallor	Absent	46	92	23	92.0
	Present	4	8	2	8.0
Pedal Edema	Absent	45	90	25	100.0
	Present	5	10	0	0.0
Cyanosis	Absent	50	100.0	25	100.0
	Present	0	0.0	0	0.0
JVP	Raised	2	4	00	0.0
	Not Raised	48	96	25	100.0
ASCVD Risk Score	No Risk	38	76	20	80.0
	Risk Present	12	24	5	20.0

TABLE 2- Comparison of Baseline characteristic among cases and control

Characteristics		Group A No.	%	Group C No.	%	Total	p Value
Age Group	18 – 40yrs	9	64.3	5	35.7	14	1.00
	>40yrs	41	67.2	20	32.8	61	
Sex	Female	33	66	17	34	50	0.86
	Male	17	68.0	8	32.0	25	
Smoker	No	37	66.1	19	33.9	56	0.85
	Yes	13	68.4	6	31.6	19	
Blood Pressure	Normal	14	60.9	9	39.1	23	0.67
	Elevated	5	62.5	3	37.5	8	
	Stage I HTN	22	66.7	11	33.3	33	
	Stage II HTN	9	81.8	2	18.2	11	
RBS	Normal	40	65.6	21	34.4	61	0.76
	Elevated	10	71.4	4	28.6	14	
Pallor	Absent	46	66.7	23	33.3	69	1.00
	Present	4	66.7	2	33.3	6	
Pedal Edema	Absent	45	64.3	25	35.7	70	-----
	Present	5	100.0	0	0.0	5	
Cyanosis	Absent	50	66.7	25	33.3	75	-----
	Present	0	0.0	0	0.0	00	
JVP	Raised	2	100.0	00	0.0	2	-----
	Not Raised	48	65.8	25	34.2	73	
Risk Score	No Risk	38	65.5	20	34.5	58	0.69
	Risk Present	12	70.6	5	29.4	17	

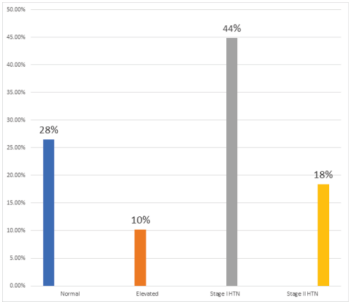

TABLE-1-Figure 1: - PREVALENCE OF HYPERTENSION IN GROUP A – HYPOTHYROIDISM AS PER ACC/AHA 2017 GUIDELINES

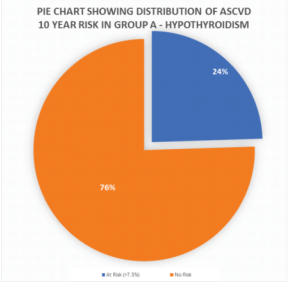

TABLE 1 -Figure 2

TABLE 3- Comparison of Mean of various characteristics among cases and controls

Characteristic	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	p Value A vs C	p Value B vs C
Age	48.73 ± 10.24	48.62 ± 6.60	50.04 ± 10.51	0.61	0.66
BMI	24.86 ± 2.61	24.53 ± 1.96	24.33 ± 1.95	0.34	0.76
Pulse Rate	71.29 ± 8.99	74.0 ± 9.73	77.36 ± 11.36	0.01	0.37
SBP	123.43 ± 14.24	122.77 ± 13.98	120 ± 11.36	0.36	0.57
DBP	76.12 ± 7.09	75.23 ± 6.50	73.92 ± 6.39	0.19	0.55
RBS	166.61 ± 63.36	179.46 ± 89.71	145.00 ± 60.82	0.16	0.17
Hb	11.90 ± 1.30	12.76 ± 1.75	11.90 ± 1.52	0.99	0.13
Total Cholesterol	197.12 ± 38.65	194.54± 40.76	163.24 ± 23.96	0.001	0.005
HDL	37.94 ± 4.40	36.38 ± 3.28	40.56 ± 3.98	0.01	0.003
LDL	115.53 ± 23.77	109.69 ± 18.81	97.64 ± 15.84	0.001	0.04
TG	152.57 ± 25.23	135.69 ± 18.48	154.64 ± 20.42	0.72	0.008
VLDL	24.19 ± 3.07	23.46 ± 1.66	22.03 ± 2.09	0.002	0.03
ASCVD 10-year Risk Score	4.81 ± 5.75	5.39 ± 6.10	3.66 ± 3.50	0.36	0.27
QT Interval	0.42 ± 0.05	0.41 ± 0.60	0.41 ± 0.03	0.34	0.59

TABLE 4- Comparison of ECHO findings among cases and controls

Echo Finding		Group A No.	%	Group C No.	%	Total	p Value
RWMA	Absent	41	64.1	23	35.9	64	0.32
	Present	9	81.8	2	18.2	11	
LV Systolic Dysfunction	Absent	43	64.2	24	35.8	67	0.26
	Present	7	87.5	1	12.5	8	
Pericardial Effusion	Absent	46	64.8	25	35.2	71	---
	Present	4	100.0	0	0.0	4	

TR/TS	Absent	43	65.2	23	34.8	66	0.71
	Present	7	77.8	2	22.2	9	
PR/PS	Absent	50	66.7	25	33.3	75	
	Present	00	0.0	00	0.0	00	
AS/AR	Absent	49	66.2	25	33.8	74	--
	Present	1	100.0	00	0.0	1	
MS/MR	Absent	42	64.6	23	35.4	65	0.48
	Present	8	80.0	2	20.0	10	

TABLE 5- Comparison of Mean of ECHO findings among cases and controls

Characteristic	Group A	Group B	Group C	p Value	p Value
	Mean ± SD	Mean ± SD	Mean ± SD	A vs C	B vs C
LVEF	54.65 ± 5.10	56.23 ± 1.30	55.76 ± 1.09	0.29	0.24
E Wave	0.69 ± 0.08	0.71 ± 0.08	0.79 ± 0.07	0.001	0.01
A Wave	0.77 ± 0.07	0.76 ± 0.06	0.76 ± 0.07	0.60	0.69
E/A Ratio	0.90 ± 0.16	0.93 ± 0.13	1.02 ± 0.10	0.001	0.02
Deceleration Time	195.49 ± 9.31	194.62 ± 5.18	189.60 ± 7.35	0.007	0.03
LVEDD	4.29 ± 0.44	4.24 ± 0.29	4.04 ± 0.24	0.009	0.02
IVS(D)	1.20 ± 0.15	1.14 ± 0.14	1.06 ± 0.07	0.001	0.01
LVPW (D)	1.20 ± 0.15	1.22 ± 0.19	1.06 ± 0.12	0.001	0.003

DISCUSSION

There is a growing body of evidence suggesting numerous cardiac manifestations of hypothyroidism and association with dyslipidaemia, metabolic syndrome, increased 10-year risk for atherosclerotic cardiovascular disease (ASCVD) and response to treatment. Hence this study assumes significance as it would lead on to assess various cardiovascular manifestations of hypothyroidism. Thus, giving insights on how to effectively manage such patients by starting appropriate therapy and secondary prophylaxis as per current guidelines and ASCVD 10 years risk estimation.

In our study Group A, 31 (62%) patients had hypertension of which 22(44%) had stage I hypertension and 9 (18%) had stage II hypertension. 14(28%) had normal blood pressure and 5 (10%) had Elevated Blood Pressure as per ACC and AHA 2017 guidelines. The mean systolic Blood Pressure was 123.43mm Hg with standard deviation of 14.24 vs [120.11 ± 11.36, p = 0.36] in controls and mean diastolic Blood Pressure was 76.12 mmHg with standard deviation of 7.09 vs [73.92 ± 6.39, p = 0.19]. Similar results were seen in the study by Biondi et al that reported a mean systolic Blood Pressure of 120mm Hg and mean diastolic pressure of 78mm Hg [16]. Though a greater number of patients in Group A had Hypertension 62 % vs 52%, the difference was statistically insignificant. Bergus et al also reported no correlation between hypertension and TSH levels [25]. While, Danzi S et al reported a 20 % diastolic hypertension in hypothyroidism [8]. In our study it was observed that there was no significant rise in BMI in hypothyroidism. This is in contrast to studies done by Marina A et al, as they observed an incidence of 11% of hypothyroidism in obese individuals [22]. and DH Streeten et al as they observed a prevalence of 3.6% of hypothyroidism in a population of obesity [24].

Group A had 10 (20%) patients having RBS > 200 mg/dl, with a mean of 166.61 having standard deviation of 63.36 vs [145 ± 60.82, p = 0.16] in controls. While the mean HBA1C noted was 6.5 in these patients, in Group A, 7 (14%) patients had HBA1C above 6.5. This is in agreement with study done by Ashrafuzzaman et al and Joffe et al in which newly detected diabetes among the subjects diagnosed as hypothyroidism is significantly higher 4.8 vs. 7.01% (p<0.01) and the prevalence of pre-diabetic state Impaired Glucose Tolerance (IGT) is also higher (11% vs. 12.6%) among hypothyroid subjects [22,23].

Our findings show significant dyslipidaemia in hypothyroidism which are in agreement with various studies by Biondi et al, KCR et al, Kim et al, Moon et al implying association of hypothyroidism with dyslipidaemia and metabolic syndrome and increased risk of developing atherosclerotic vascular disease including coronary artery disease though we did not find statistically significant difference in 10-year ASCVD risk score between the study groups [16], [20], [21].

Most common ECG abnormality was sinus bradycardia, which was noted in 9(18%) patients. T inversions were also seen in 9 (18%) patients, followed by sinus arrhythmia in 7 (14%) patients, Left Axis Deviation in 7 (14%) patients, First degree AV block in 6 (12%), RBBB in 5 (10%), QT interval was prolonged in 5 (10%) patients, ST Depression in 4 (8%), Low voltage complexes in 4 (8%). Poor R wave Progression was present in 2 (4%) patients, LBBB in 1(2%) patients, Atrial fibrillation in 1 (2%) patients. No patient had ST elevation or pathological Q waves. These findings are consistent with findings of others like Biondi et al, Rawat et al, Klein et al which report similar incidence of above findings [13], [16], [18].

This study highlights the role of echocardiography in assessing the cardiovascular changes that occur in hypothyroidism. The most common abnormality observed was septal and LV posterior wall hypertrophy. Diastolic dysfunction and occurrence of pericardial effusion were noted in a significant number of patients. There was no significant systolic dysfunction. Though, the frequency of RWMA was more in our study group as compared to controls which is indicative of high likelihood of Coronary artery disease, the ingroup differences were insignificant. Implying the need of a larger study to evaluate the association of CAD with hypothyroidism. Perk et al also found greater progression of coronary angiographic lesions in hypothyroid patients with increased TSH levels compared with patients whose TSH levels were assiduously maintained in the normal range [19]. Other studies done by Rawat et al, Biondi et al, Grossman et al and Varma et al have shown similar results [12], [16-18].

CONCLUSION

Our findings support a growing body of evidence suggesting a need of a larger study to evaluate the outcomes, emphasising need of timely screening and starting appropriate thyroxine therapy and secondary prophylaxis for ASCVD risk, as per need.

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