Clinical assessment of cardiovascular dysfunction among hypothyroidism and hyperthyroidism subjects residing at Veligonda hill range of Eastern Ghats

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ABSTRACT
The prevalence of cardiovascular complications is predicted to increase in next two to three decades especially in developing countries with an increasing incidence worldwide, thyroid disorders causing cardiovascular complications will be a leading cause of mortality and morbidity in future. Symptoms like Heart rate, blood pressure, body mass index, total cholesterol, ECG and echocardiographic changes in both hypothyroid and hyperthyroid patients can serve as reliable indicators of incidence of cardiovascular involvement. Heart rate and blood pressure have the advantage of daily monitoring in clinical practice, inexpensive and simple to measure with good reproducibility. However studies showing correlation between these measures and cardiovascular complications are sparse and reveal inconsistent findings

INTRODUCTION:

The thyroid glands produces hormones, which play a key role in various systems of the body. When it is produced either too much or too little, it's called a thyroid disease (1). Various types of thyroid disease has been classified, that includes hyperthyroidism, hypothyroidism, thyroiditis and Hashimoto's thyroiditis (2). Majorly Hypothyroidism, arises due to under active thyroid gland, which doesn't produce enough thyroid hormones to meet body's requirements whereas in Hyperthyroidism there is over production of thyriod hormone (3). In India, recent studies reveal that thyroid disorders are the most common endocrine disorders among the population. The total burden of thyroid disorder in India was 42 million. In India, Iodine deficiency disorders account 27 per 1000 whereas Grave's disease accounts 5 per 10,000, In South India residing in towns (non costal and non hilly regions), 11.5% were estimated to have hypothyroidism whereas only 1.8% had hyperthyroidism. One in every eight women during their life time has risk of thyroid disorder. Its prevalence depends on sex, age, ethnicity, iodine intake environmental, geographical factors and epigenetics (4). Hypothyroidism is more in women when compared to men. Its prevalence is 25% in females

and 0.6% in males of all thyroid disorders. Moreover its prevalence in females may be associated with higher levels of oestrogen and progesterone. Earlier studies reported that Hyperthyroidism in coastal area is about 5% whereas hypothyroidism in 0.6%. Due to leaching of the soil by annual flooding, hilly region people are found to be iodine deficient.

Various researches revealed that hypothyroidism could leads to morbidity from Osteoporosis, Hyperlipidaemia, Hypercholesterolaemia, and as well as Cardiovascular and Neuropsychiatry diseases. Often thyroid disorders are underestimated, sometimes they could lead to death in a significant number of cases were reported (5). Thyroid hormone effects on the heart and peripheral vasculature include decreased SVR (systemic vascular resistance) and increased resting heart rate, left ventricular contractility, and blood volume. In general the thyroid hormone causes decreased resistance in peripheral arterioles, which impacts on VSM (vascular smooth muscle), leads to decline in mean arterial pressure, affect kidneys, to activate renin-angiotensin-aldosterone system, which further elevates renal sodium absorption (6).

T3 enhances erythropoietin synthesis, results in increase in red cell mass, which promotes rise in blood volume levels causing elevated preload. In hyperthyroidism, these combined effects increase cardiac output 50% to 300% higher than in normal individuals. In hypothyroidism, the cardiovascular effects are diametrically opposite and cardiac output may decrease by 30% to 50% (1). The effects of T3 on the heart are well known, since it alters vascular smooth muscle (VSM) and endothelial cell function. Particularly in the VSM due to T3 mediates both genomiec and non-genomic actions (7).

In non-genomic actions, it targets membrane ion channels and endothelial nitric oxide synthase, results in decline of SVR (Systemic Vascular Resistance), further relaxes VSM, causing reduction in arterial resistance and pressure, furthermore enhances cardiac output. Elevated levels of endothelial nitric oxide causes T3-mediated effects on TR (Thyroid receptors) on the protein kinase B pathway either via non genomic or genomic mechanisms. Nitric oxide generated in endothelial cells, acts in a paracrine manner on adjacent VSM cells to enable vascular relaxation (8). In hypothyroidism, arterial compliance is decreased, causing elevation of SVR. Impaired endothelium-dependent vasodilatation leads to reduction in nitric oxide production, is observed in subclinical hypothyroidism. In hyperthyroidism, SVR declines followed by elevation in blood volume and increase in rate of peripheral tissue perfusion. (9).

Adrenomedullin, a polypeptide of 52 amino acids, is a potent vasodilator transcriptionally regulated by thyroid hormone, and serum levels are increased in thyrotoxicosis. Interestingly, SVR is decreased and Adrenomedullin is increased in thyrotoxicosis, restoration of euthyroid normalised SVR but was not correlated with plasma adrenomedullin levels (10).

The above mentioned factors play a significant role in status of thyroid fuction and its effect on the heart. Apart from that few studies also explained the role of Iodine in hyper thyroid and hypothyroid conditions. However, the role of cardiovascular dysfunction among hypothyroidism and hyperthyroidism cases among the hilly regions not studied. Hence the present study is undertaken in an aim to **a**ssess the significance of cardiovascular dysfunction among hypothyroidism and hyperthyroidism subjects residing at Veligonda hill range of Eastern Ghats.

METHODS:

STUDY DESIGN:

A hospital based cross sectional study has been carried out in the outpatient section of the department of general medicine, Narayana medical college and hospital (NMCH), Nellore, Andhra Pradesh, India (11-15)

PERIOD OF STUDY:

18 months (FEB 2021 – JULY 2022)

INCLUSION CRITERIA:
Patients of newly diagnosed & untreated hypothyroidism and hyperthyroidism were included in the study, who are able to give informed consent

EXCLUSION CRITERIA:
1. Diagnosed hypothyroidism and hyperthyroidism on regular medication
2. Comorbidity's like COPD, diabetes, anaemia, CKD which effect cardiovascular function
3. Patients on drugs that alter cardiovascular functions like beta blockers, ammiodron, CCB

SAMPLE SIZE:
80 newly diagnosed patients with thyroid defects

DETAILS OF THE STUDY:
In the present study 80 patients were considered, among which A total of 40 newly diagnosed hypothyroid patients and 40 newly diagnosed hyperthyroidism patients were analysed they were subjected to clinical and laboratory work up including serum TSH, heart rate, blood pressure, BMI, total cholesterol, ECG changes, 2D ECHO the data was then assessed

STATISTICAL ANALYSIS:
The collected data was expressed as Mean ± SD, and the categorical data in %. Differences between the variables were analysed by chi-square test. P- valueless than 0.05 was considered significant. Statistical analysis was performed using SPSS software version 21.0 (SPSS Inc, US)

RESULTS:
As previously discussed, the prevalence of cardiovascular complications is rapidly increasing worldwide, particularly in relation to thyroid disorders, which significantly contribute to mortality and morbidity rates. Various factors influence thyroid dysfunction and its impact on cardiovascular health. Additionally, the relationship between cardiovascular issues and thyroid conditions such as hypothyroidism and hyperthyroidism in hilly regions remains poorly understood. Therefore, this study aims to investigate the significance of cardiovascular dysfunction in individuals with hypothyroidism and hyperthyroidism residing in the Veligonda hill range of the Eastern Ghats and findings documented (see Table 1 and Table 2).

In this study, 80 patients living in the Veligonda range were selected with their informed consent. They were attending the outpatient department of General Medicine at Narayana Medical College and Hospital in Nellore. The research was conducted following approval from the institutional ethics committee. Initially, patients were screened based on their thyroid profiles and categorized into two groups: hypothyroidism and hyperthyroidism, with 40 newly diagnosed subjects in each group. Participants underwent routine clinical and laboratory evaluations, including serum TSH, heart rate, blood pressure, BMI, total cholesterol, ECG changes, and 2D echocardiography, with all data documented.

Results indicated that among the 40 diagnosed hypothyroid patients, 30 (75%) were female and 10 (25%) were male. The most prevalent age group was 40-50 years, accounting for 18 (45%) subjects, followed by those over 50 years (12 or 28%) and 30-40 years (10 or 27%). Of these, 8 (20%) had a TSH level below 20, classified as mild hypothyroidism, while moderate hypothyroidism (TSH 20-50) was present in 20 (50%) subjects, and severe hypothyroidism (TSH over 50) was found in 12 (30%) subjects.

Heart rate assessments showed that 25 patients (62.5%) had a heart rate below 60 bpm, 15 patients were within the normal range, 10 (25%) had rates between 60-80 bpm, and 5 (12.5%) had rates exceeding 80 bpm. Blood pressure evaluations revealed that 17 (42.5%) patients had hypertension, with 15 (37.5%) in stage I and 2 (5%) in stage II hypertension. The remaining 23 (57.5%) exhibited normal blood pressure or pre-hypertension.

Regarding BMI, 18 (45%) subjects were classified as overweight (BMI 25-30), 5 (12.5%) were obese (BMI >30), and 17 (42.5%) had a normal body mass index. Additionally, various ECG abnormalities were noted in hypothyroid subjects, with the most common being sinus bradycardia, observed in 25 (62.5%) patients. Other ECG abnormalities included ST segment depression in 5 (12.5%) subjects and AV block in 10 (25%).

Lipid profile analysis showed that hypercholesterolemia (cholesterol >200 mg/dl) was prevalent, with 10 (25%) subjects having cholesterol levels between 200-239 mg/dl and 30 (75%) exceeding 240 mg/dl. Ejection fraction analysis via 2D echocardiography indicated that 30 patients (75%) had normal ejection fraction (55-60%), 9 (22.5%) had levels over 60%, and only 1 patient (2.5%) had an ejection fraction below 55%. This suggests that systolic function was relatively less affected in hypothyroid patients.

In the group of 40 hyperthyroid subjects, 12 (30%) were male and 28 (70%) were female. The age distribution included 16 (40%) in the 30-40 year range, 6 (15%) in both the 40-50 and >60 year categories, and 5 (12.5%) in the 50-60 year range, with 2 patients (5%) aged 20-30 years. TSH levels revealed that 12 (30%) subjects had TSH levels below 0.009 miu/ml, 20 (50%) had levels between 0.01 and 0.009 miu/ml, and 8 (20%) had TSH levels above 0.1 miu/ml, indicating that 80% of patients presented with moderate to severe hyperthyroidism. Heart rate evaluation showed that 23 (57.5%) subjects had rates between 100-120 bpm, 12 (30%) had rates between 80-100 bpm, and 5 (12.5%) had rates between 60-80 bpm. Blood pressure measurements indicated that 8 (20%) were in stage II hypertension and 16 (40%) were in stage I, while 16 (40%) had normal blood pressure or pre-hypertension, suggesting a strong association of hypertension with hyperthyroidism.

BMI assessment showed that 18 (45%) patients had a normal BMI (18-24.9), 14 (35%) were underweight (BMI < 18), and 8 (20%) were classified as overweight (BMI > 25), with no patients identified as obese (BMI > 30). A total of 30 patients (75%) had cholesterol levels within the normal to high normal range (up to 240 mg/dl), with only 10 patients showing elevated total cholesterol, indicating that most hyperthyroid patients had normal cholesterol levels. ECG analysis showed sinus tachycardia in 25 patients (62.5%), atrial fibrillation in 12 (30%), and left ventricular hypertrophy in 3 (7.5%). Finally, 2D echocardiography findings revealed that diastolic dysfunction was the most common abnormality, present in 18 patients (45%), followed by mitral regurgitation in 10 (25%), left atrial enlargement in 5 (12.5%), left ventricular hypertrophy in 4 (10%), pulmonary hypertension in 2 (5%), and mitral valve prolapse in 1 patient (2.5%).

	DEMOGRAPHIC VARIABLES		**N**	**%**
1	AGE DISTRIBUTION	30-40	10	27
		40-50	18	45
		>50	12	28
2	SEX DISTRIBUTION	FEMALE	30	75
		MALE	10	25
3	SEVERITY OF HYPOTHYROIDISM BASED ON TSH LEVELS	MILD (<20)	8	20
		MODERATE (20-50)	20	50
		SEVERE (>50)	12	30
4		<60	25	62.5
		60-80	10	25

	HEART RATE IN HYPOTHYROIDISM	>80	5	12.5
5	BLOOD PRESSURE IN HYPOTHYROIDISM	<120/80 or upto 140/90 (normotensive/pre HTN)	23	57.5
		140-160/90 (STAGE 1 HTN)	15	37.5
		>160/90 (STAGE 2 HTN)	2	5
6	BODY MASS INDEX	<25	17	42.5
		25-30	18	45
		>30	5	12.5
7	TOTAL CHOLESTEROL	200-239	10	25
		>240	30	75
8	ECG CHANGES IN HYPOTHYROIDISM	SINUS BRADYCARDIA	25	62.5
		1st DEGREE AV BLOCK	10	25
		ST DEPRESSION	5	12.5
9	EJECTION FRACTION IN HYPOTHYROIDISM	<55%	1	2.5
		55-60%	30	75
		60%	9	22.5
10	SYMPTOMS OF HYPOTHYROIDISM	FATIGUE	28	70
		WEIGHT GAIN	30	75
		COLD INTOLERANCE	24	60
		CONSTIPATION	18	45
		MENSTRUAL IRRIGULARITY	14	35

TABLE 1 : characteristics of study subjects in relation to hypothyroidism among 40 patients

	DEMOGRAPHIC VARIABLES		N	%
1	AGE DISTRIBUTION	<20	2	5
		20-30	5	12.5
		30-40	16	40
		40-50	6	15
		50-60	5	12.5
		>60	6	15
2	SEX DISTRIBUTION	MALE	12	30
		FEMALE	28	70
3	SEVERITY OF HYPERTHYROIDISM BASED ON TSH LEVELS	TSH<0.009	12	30
		TSH 0.01-0.009	20	50
		TSH >0.1	8	20
4	HEART RATE IN HYPERTHYROIDISM	60-80	5	12.5
		80-100	12	30
		100-120	23	57.5
5	BP IN HYPERTHYROIDISM	<120/80 OR UPTO 140/90	16	40
		140-160/90	16	40
		>160/90	8	20
6	BODY MASS INDEX	14-17.9	14	35
		18-24.9	18	45
		>25	8	20
7	TOTAL CHOLESTEROL	<200	15	37.5
		200-240	15	37.5
		>240	10	30
8	ECG CHANGES IN HYPER THYROIDISM	SINUS TACHYCARDIA	25	62.5
		ATRIAL FIBRILLATION	12	30
		LVH	3	7.5
9		DIASTOLIC DYSFUNCTION	18	45
		MITRAL REGURGITATION	10	25

	ECHOCARDIOGRAPHIC CHANGES	LEFT ATRIAL ENLARGEMENT	5	12.5
		LVH	4	10
		PULMONARY HYPERTENSION	2	5
		MVP	1	2.5
10	SYMPTOMS	FATIGUE	22	55
		WEIGHT LOSS	28	70
		HEAT INTOLERENCE	16	40
		DIARRHEA	12	30
		MENSTRUAL ABNORMALITIES	14	35

Table 2 : Characteristics of study subjects in relation to hyperthyroidism among 40 patients

DISCUSSION:

Hyperthyroidism and hypothyroidism are frequently observed conditions among adults in the general population. However, the understanding of thyroid disorders within the residents of hilly regions remains limited. This study aims to evaluate and gain deeper insights into the clinical manifestations of hyperthyroidism and hypothyroidism among individuals from the Veligonda hill range of the Eastern Ghats. Participants diagnosed with thyroid disorders who visited the outpatient department of general medicine at Narayana Medical College were included in the study with their consent. A total of 40 patients each with hypothyroidism and hyperthyroidism were randomly selected, and all necessary investigations were conducted to analyze the data.

The findings of this study (see Table 1 and Table 2) indicate that the majority of individuals affected by hypothyroidism and hyperthyroidism were between the ages of 30 and 50 years (16), with a predominance of female subjects. Similar findings are reported in another study (17). In patients with hyperthyroidism, palpitations emerged as the most commonly reported cardiac symptom. Sinus tachycardia was often seen in those with hyperthyroidism, while bradycardia was more prevalent among hypothyroid patients. Atrial fibrillation was also frequently detected in individuals suffering from hyperthyroidism. Our findings are well correlated to other studies (18).

Additionally, obesity and high total cholesterol levels were commonly associated with hypothyroidism which was reported in earlier studies too (19). Many patients in both groups exhibited blood pressure readings classified as borderline hypertension or Grade 1 hypertension (20). Echocardiography, known for being a non-invasive and accurate assessment tool, was effectively used to evaluate cardiac function in those with hypothyroidism. Normal systolic function was observed across both conditions; however, hyperthyroidism was identified as a significant risk factor for diastolic dysfunction. Various valvular abnormalities were recorded, with mitral regurgitation and mitral valve prolapse being the most prevalent cardiac valve issues among patients with hyperthyroidism. Finally results from our studies are well correlated to findings reported by others (16-21).

CONCLUSION:

This study underscores the significant cardiovascular complications associated with thyroid disorders, particularly among individuals residing in the Veligonda hill range of the Eastern Ghats. Our findings indicate that both hypothyroidism and hyperthyroidism contribute to notable cardiac dysfunction, with variations in symptoms and physiological responses between the two conditions. Hypothyroid patients demonstrated higher instances of bradycardia, obesity, and hyperlipidemia, while hyperthyroid patients exhibited tachycardia and a marked prevalence of hypertension. The results reveal a concerning link between thyroid dysfunction and cardiovascular health, emphasizing the need for regular cardiovascular assessments in these populations. The predominance of female patients in both groups highlights the importance of gender-specific considerations in diagnosis and management. Given the high prevalence of thyroid disorders and their potential cardiovascular implications, especially in under-researched hilly regions, further studies are warranted to explore long-term outcomes and develop tailored interventions. Ultimately, integrating cardiovascular monitoring into the management of thyroid disorders could enhance patient care and reduce associated morbidity and mortality, paving the way for improved health outcomes in affected individuals.

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