

CARDIOVASCULAR MANIFESTATIONS IN PATIENTS OF HYPOTHYROIDISM- RESULTS OF A SINGLE CENTRE STUDY

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ABSTRACT

BACKGROUND

Objective- To examine cardiovascular manifestations in patients with hypothyroidism.

MATERIALS AND METHODS

In this observational study, adult hypothyroid patients were screened for cardiovascular disease. Symptoms of hypothyroidism, cardiovascular system related symptoms, T3, T4 and Thyroid Stimulating Hormone (TSH) were compared between male and female patients. Association between thyroid stimulating hormone and heart disease was also evaluated.

RESULTS

Hundred patients (male 32% and female 68%) with mean age of 39.2 + 9.28 years were enrolled. More number of females showed weight gain over a period of two years as compared to males (p= 0.0217). Dry skin was more common in females as compared to males (p= 0.0336). More females reported breathlessness and chest pain as compared to males (breathlessness p= 0.0187; chest pain p= 0.0008). Pulse rate of female patients was significantly lower than male patients (p= 0.0081). More number of females had raised jugular venous pressure as compared to males (41% vs 19%, p= 0.0475). Diastolic blood pressure was higher in females than in males (p= 0.023). There was no difference in the mean T3 (52.43 ± 14.35 pg/mL vs 46.53 ± 14.19 pg/mL; p= 0.1776), T4 level (4.48 ± 0.97 vs 4.06 ± 0.97; p= 0.1630) or TSH level (31.19 ± 11.9 vs 42.21 ± 26.98; p= 0.1260) between males and females. Number of females with cardiomegaly was higher compared to males [26 (38%) vs 2 (6%); p < 0.0001]. Significant association was observed between higher TSH and presence of breathlessness, chest discomfort and palpitations (p < 0.05). Significantly, more patients with higher TSH showed significantly more heart rate, raised jugular venous pressure and diastolic blood pressure (p < 0.05). Higher TSH was associated with pericardial effusion in more proportion of patients (p= 0.007).

CONCLUSION

Cardiac dysfunction is common in patients with hypothyroidism. Screening and treatment of cardiovascular disease in hypothyroidism may help to reduce morbidity and mortality in hypothyroidism.

KEYWORDS

Cardiovascular Manifestations, Hypothyroidism, Thyroid Stimulating Hormone.

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BACKGROUND

Hypothyroidism is a common endocrinological problem in clinical practice. The reported incidences of clinical hypothyroidism range from 0.5 to 1.9% in women and less than 1% in men. Subclinical hypothyroidism is more common than clinical hypothyroidism, both in females and males.¹ The prevalence of subclinical hypothyroidism is about 4 - 10.5%.² Both clinical and subclinical hypothyroidism are shown to be associated with cardiovascular manifestations. As heart is

the major target organ for action of thyroid hormones, changes can occur in cardiac structure and function in patients with hypothyroidism.³⁻⁵ Diastolic hypertension and sinus bradycardia are the common cardiac manifestations of hypothyroidism. The other reported cardiovascular problems reported include heart block, cardiomyopathy, pericarditis and pericardial effusion.³

The effect of subclinical hypothyroidism on the cardiovascular system is an important topic of research. Link between subclinical hypothyroidism and several cardiovascular risk factors such as blood pressure, atherosclerosis and metabolic syndrome has been suggested.⁶ In Indian patients, subclinical hypothyroidism has been shown to be associated with dyslipidaemia more commonly as compared to control group.² Timely identification of cardiac abnormalities and its management in hypothyroid patients may help to reduce morbidity and mortality. There are very limited studies in Indian population suggesting relationship between hypothyroidism and cardiac disorders.

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Objective

The objectives of the study were to find out prevalence and compare the cardiovascular manifestations of hypothyroidism in males and females and to study the relationship between Thyroid Stimulating Hormone (TSH) levels and cardiovascular manifestations.

MATERIALS AND METHODS

In this observational study, adult (> 18 years of age) hypothyroid patients from a tertiary care hospital in Mumbai were included by convenience sampling. Patients with history of cardiac disease, diabetes mellitus or those taking medications that alter the thyroid function (e.g. beta blockers, lithium, oral contraceptive pills, alcohol, amiodarone, etc.) were excluded. After detailed history, physical examination, systemic examination and laboratory investigations (complete blood count, serum T3, T4 and TSH, serum electrolytes, renal function test, liver function test, serum lipid profile, electrocardiography, echocardiography), enrolled patients were screened for cardiovascular disease based on symptomatology, physical examination, chest x-ray, Electrocardiography (ECG) and echocardiography. Symptoms of hypothyroidism, cardiovascular system related symptoms,

T3, T4 and TSH were compared between male and female patients. Association between thyroid stimulating hormone and heart disease was also evaluated. The study was initiated after obtaining the permission from the Institutional Ethics Committee.

Statistical Analysis

The quantitative data is presented as mean and standard deviation, whereas categorical data is expressed in percentage. The t-test was used for analysing quantitative data. Non-parametric data was analysed by using Mann-Whitney test and categorical data was analysed by chi-square test. P value less than 0.05 was considered statistically significant. Statistical analysis was carried out using SPSS software version 21.

RESULTS

A total of 100 hypothyroid patients (male 32% and female 68%) with mean age of 39.2 + 9.28 years were enrolled in the study. The mean age of males and females was 39.43 ± 10.53 years and 39.12 ± 8.81 years respectively (p= 0.9109). Number of females were more compared to male patients (p < 0.015).

	Weight Gain		Generalised Weakness and Fatigability		Cold Intolerance		Dry Skin		Hair loss	
	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)
< 6 months	--	--	--	--	--	--	2 (6%)	0	2 (6%)	0
6 months	2 (3.12%)	6 (8.82%)	6 (19%)	18 (26%)	0	16 (24%)	2 (6%)	16 (24%)	2 (6%)	10 (15%)
1 year	0	12 (17.64%)	2 (6%)	12 (18%)	0	4 (6%)	4 (13%)	12 (18%)	0	2 (3%)
2 years	0	4 (5.88%)	0	4(6%)	0	0	0	2 (3%)	0	0
Absent	30 (93.75%)	46 (67.64%)	24 (75%)	34 (50%)	32 (100%)	48 (71%)	24 (75%)	38 (56%)	28 (88%)	56 (82%)
P value using Chi Square Test	0.0217		0.0790		---		0.0336		---	

Table 1. Main Symptoms of Hypothyroidism

Significantly more number of females showed weight gain over a period of two years as compared to males (Table 1; P= 0.0217). There was no difference in number of males and females having generalised weakness and fatigue over a period of two years (Table 1; P= 0.0790). Cold tolerance was reported in only females; 16 (24%) since 6 months and 4 (6%) since 1 year (Table 1). Dry skin was significantly more common in females as compared to males (p= 0.0336). Hair loss was reported by 2 (6%), males since less than 6 months and 6 months each. A total of 10 (15%) females reported hair loss since 6 months and 2 (3%) since one year. A total of 8 (12%) females reported menorrhagia since 6 months. Menorrhagia was absent in 60 (88%) females.

	Depression		Constipation		Muscle and Joint Pain		Slowness of Speech	
	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)
< 6 months	2 (6%)	2 (3%)	0	4 (6%)	--	--	0	2 (3%)
6 months	2 (6%)	0	0	0	0	6 (9%)	2 (6%)	4 (6%)
1 year	0	0	0	0	0	0	0	4 (6%)
2 years	4 (13%)	2 (3%)	0	0	0	0	0	0
Absent	24 (75%)	64 (94%)	32 (100%)	64 (94%)	32 (100%)	62 (91%)	30 (94%)	58 (85%)
P value	-----		----		-----		---	

Table 2. Other Symptoms

Depression was presented by 2 (6%) males and 2 (3%) females since less than 6 months and in 2 (6%) males since 6 months. In 4 (13%) male patients and 2 (3%) females, depression was present since 2 years. Constipation since less than 6 months was reported by 4 (6%) females. Muscle and joint pain was present in 6 (9%) females since 6 months. Slowness of speech was reported by 2 (6%) male patients since 6 months, whereas 2 (3%), 4 (6%) and 4 (6%) females reported it since less than 6 months, 6 months and 1 year respectively (Table 2).

	Breathlessness		Chest Pain		Palpitation	
	Male N (%)	Female N (%)	Male N (%)	Female N (%)	Male N (%)	Female N (%)
< 6 months	4 (13%)	6 (9%)	2 (6%)	14 (21%)	--	--
6 months	2 (6%)	14 (21%)	0	8 (12%)	0	6 (9%)
1 year	0	10 (15%)	0	10 (15%)	0	6 (9%)
Absent	26 (81%)	38 (56%)	30 (94%)	36 (53%)	32 (100%)	56 (82%)
P value using Chi Square Test	0.0187		0.0008		-----	

Table 3. Cardiovascular Symptoms of Hypothyroidism

Significantly, more number of females reported breathlessness and chest pain over a period of 2 years as compared to males (breathlessness p= 0.0187; chest pain p= 0.0008). Palpitation was reported by 6 (9%) females, each since 6 months and one year (Table 3).

Parameter Mean ± SD	Males (n=16)	Females (n=34)	P-value (Comparison between Males and Females)
Pulse rate (beats per min)	80.37 ± 6.24	74.35 ± 6.24	0.0081
Raised JVP n (%)	6 (19%)	28 (41%)	0.0475
Systolic BP	132.5 ± 9.84	130.18 ± 8.63	0.4001
Diastolic BP	89.13 ± 5.80	93.06 ± 2.88	0.0023

Table 4. Comparison of Physical Examination between Males and Females

The mean pulse rate of males and females was 80.37 ± 6.24 beats/min and 74.35 ± 6.24 beats/min respectively. Pulse rate of female patients was significantly lower than male patients (p= 0.0081). Significantly, more proportion of females had raised jugular venous pressure as compared to males (41% vs 19%, p= 0.0475; Table 4). There was no significant difference in systolic blood pressure between males and females (p= 0.4001), whereas diastolic blood pressure was significantly higher in females than in males (Table 4; p= 0.023). Muffled heart sound was observed in 2 (6%) males and 30 (44%) females. Significantly, more number of females had abnormal heart sound as compared to males (p < 0.0001).

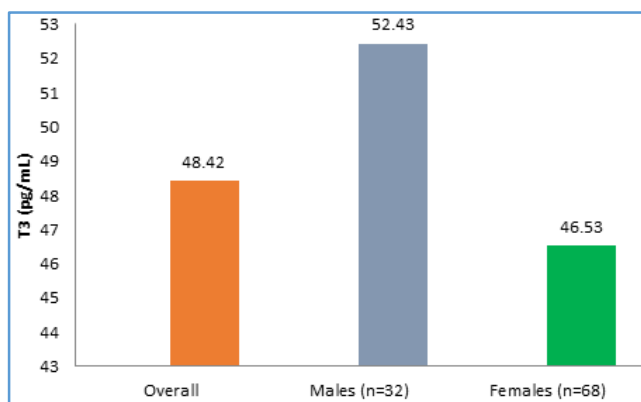


Figure 1. Level of T3 in Males and Females

Overall, mean T3 was 48.42 ± 14.37 pg/mL. There was no difference in the mean T3 of males and females (52.43 ± 14.35 pg/mL vs 46.53 ± 14.19 pg/mL; p= 0.1776; Figure 1).

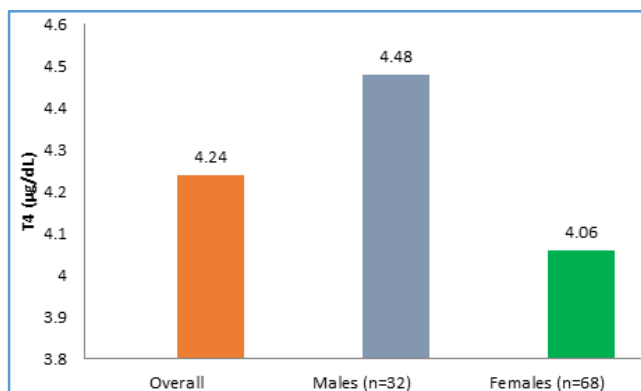


Figure 2. Level of T4 in Males and Females

Overall, mean T4 was 4.24 ± 0.94 mcg/dL. There was no difference in the mean T4 level of males and females (4.48 ± 0.97 vs 4.06 ± 0.97; p= 0.1630; Figure 2).

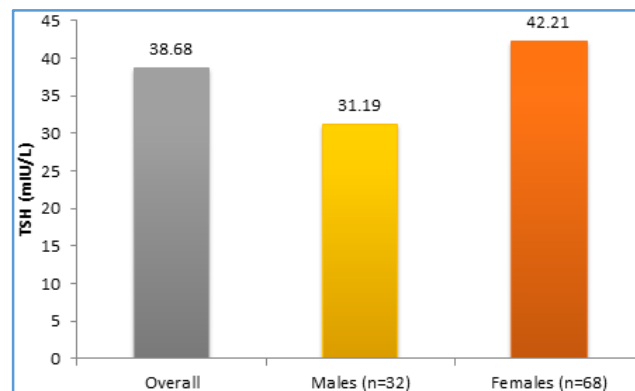


Figure 3. Level of TSH in Males and Females

Overall, mean TSH level was 38.68 ± 23.68. There was no significant difference in mean TSH level in males and females (31.19 ± 11.9 vs 42.21 ± 26.98; p= 0.1260; Figure 3).

Significantly, more number of females showed cardiomegaly on chest x-ray compared to males [26 (38%) vs 2 (6%); p < 0.0001].

Overall, ECG was normal in 52 (52%) patients, whereas some abnormality was observed in 48 (48%) patients. There was no abnormality in ECG in 75% (24/32) males and 29.41% (20/68) females. Low voltage in ECG was observed in 18.75% (6/32) males and 35.29% (24/68) females. A total of 6.25% (2/32) male and 23.53% (16/68) females had left ventricular hypertrophy, whereas 8.82% and 2.94% females showed atrial fibrillation and first degree heart block respectively.

The echocardiogram was normal in 46 (46%) patients. No abnormality in Echo was found in 81.25% (26/32) males and 47.06% (32/68) females. Diastolic dysfunction was observed in 18.75% (6/32) males and 58.82% (46/68) females ($p=0.0139$). Pericardial effusion was seen in 18.75% (6/32) males and 44.12% (30/68) females, ($p=0.1171$).

Association between TSH Levels and Cardiovascular Manifestations

Association between TSH and Cardiovascular Symptoms

In 10 - 39 years of age group there were 16 (16%) patients with breathlessness, 14 (14%) patients complained of chest discomfort and 4 (4%) had palpitation. In 40 - 79 years of age group there were 14 (14%) patients with breathlessness, 10 (10%) patients complained of chest discomfort and 2 (2%) patients had palpitations. In above 80 years of age group, 6 (6%) patients had breathlessness and 6 (6%) each had chest discomfort and palpitations. Significant association was observed between higher TSH and presence of breathlessness, chest discomfort and palpitations ($p < 0.05$).

Association between TSH and Cardiovascular Signs

In 10 - 39 years' age group the mean heart rate was 78.54 ± 10.96 beats/min, 16 (16%) patients had raised jugular venous pressure, whereas 48 (48%) patients had a diastolic BP of more than 90 mmHg. In the 40 - 79 years' age group the mean heart rate was 75.71 ± 8.40 beats/min, 12 (12%) patients had raised jugular venous pressure and 24 (24%) patients had a diastolic BP more than 90 mmHg. In the above 80 years' age group, the mean heart rate was 134.66 ± 4.50 beats/min, 6 (6%) patients had raised jugular venous pressure, while 10 (10%) patients had a diastolic BP more than 90 mmHg. Significantly, more patients with higher TSH showed significantly more heart rate, raised jugular venous pressure and diastolic blood pressure ($p < 0.05$).

Association between TSH and ECG Findings

Low voltage complexes ($p=0.0476$) and left ventricular hypertrophy ($p=0.0492$) were present in significantly greater proportion of patients in 10 - 39 years' age group, while atrial fibrillation was present in significantly greater proportion of patients in patients above 80 years of age ($p < 0.0001$).

Association between TSH and Echocardiography Findings

There was no difference in proportion of patients with and without diastolic dysfunction with different TSH levels ($p=0.1775$). Higher TSH was associated with pericardial effusion in more proportion of patients ($p=0.007$).

DISCUSSION

Hypothyroidism is known to be associated with several cardiac disorders. However, there are limited data from India suggesting the correlation between these two disorders and difference in cardiovascular disease pattern between male and female patients with hypothyroidism. In this study, we evaluated the prevalence and compared pattern of cardiovascular manifestations in patients diagnosed with hypothyroidism. The mean age of 39.22 years in this study suggests common occurrence of hypothyroidism in Indian adult patients. Number of female patients was significantly more compared to males in our study. Our observation of

mean age and gender difference is similar to a study from India.⁷

Clinical features of hypothyroidism include fatigue, dry skin, cold intolerance, hoarseness of voice, bradycardia, constipation and weight gain.¹ We observed weight gain and generalised weakness and fatigability in more number of females. In our study, cold intolerance was reported in only females. Overall, the number of patients reporting cold intolerance and women with menorrhagia were less compared to another study. However, the number of patients with dry skin was similar.⁸ Significantly, more number of females reported breathlessness over a period of two years as compared to males ($p=0.0187$). Total number of patients with breathlessness was less compared to a study by Sureshababu KP and Colleagues.⁸

We also found significantly more number of females complaining chest discomfort over a period of 2 years as compared to males. Similarly, significantly more number of females showed raised jugular venous pressure as compared to males ($p=0.0475$). In a study by Dhawale S et al (2015),⁹ reported 19% patients exhibiting cardiovascular symptoms. There was not a significant difference in the cardiovascular symptoms between males and females. The mean pulse rate of our study population was comparable to another study from India.⁷ In our study, there was no significant difference in systolic blood pressure between males and females. Diastolic hypertension is a known cardiac abnormality in patients with hypothyroidism.³ Diastolic blood pressure was significantly higher in females than in males in our study. Other studies have not shown significant difference in systolic and diastolic blood pressure between males and females.^{9,10}

Significantly, more number of females had abnormal heart sound as compared to males ($p < 0.0001$) in our study. We did not find other studies comparing heart sounds between male and female patients of hypothyroidism. We also did not find difference in male and female population in T3, T4 or TSH levels.

The number of patients with normal chest x-ray findings in our study are in accordance to the reported observations by others.¹¹ In our study, significantly more number of females showed cardiomegaly on chest x-ray as compared to males ($p < 0.0001$).

A study from South India has shown pericardial effusion, diastolic dysfunction, bradycardia and low voltage complexes in ECG.¹² Low voltage complexes, left ventricular hypertrophy, atrial fibrillation and first degree heart block were reported in ECGs of hypothyroid patients in our study. More number of females had diastolic dysfunction in our study.

Overt hypothyroidism is known to be associated with cardiovascular disease. Results of the Rotterdam Study have showed that even subclinical hypothyroidism is a risk factor for atherosclerosis and myocardial infarction in elderly women.¹³

Increased involvement of cardiovascular system has been reported with raising levels of TSH.¹²

Results of the Cardiovascular Health study have shown high risk of heart failure in older patients with elevated TSH level.¹⁴ In our study also, higher TSH level was significantly associated with abnormal cardiovascular problems as compared to lower TSH levels ($p < 0.0001$).

There are no studies found on the parameters such as depression, hair loss, constipation, slowness of speech, palpitations, raised jugular venous pressure, cardiovascular manifestation, chest x-ray findings and correlation between the different levels of TSH and cardiovascular manifestation.

There are some limitations in our study. Considering convenience sampling, single centre study and limited patient population, results of our study should be carefully extrapolated.

CONCLUSION

Hypothyroidism is associated with several cardiac abnormalities. The cardiovascular disease in hypothyroidism is treatable and potentially preventable. Mass education, screening and treatment of cardiovascular disease in hypothyroidism may help to reduce cardiovascular morbidity and mortality in hypothyroidism.

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