

CARDIOVASCULAR MANIFESTATIONS OF PRIMARY HYPOTHYROIDISM

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Date of Submission : Apr 29, 2021
Date of Acceptance : Jan 20, 2022
Date of Publication : Feb 15, 2022

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Citation:

Shrestha S, Sharma KL, Shrestha B, Bajracharya S. Cardiovascular Manifestations of Primary Hypothyroidism. Medphoenix. 2021;6(2):44-48

DOI: 10.3126/medphoenix.v6i2.36794

Conflict of interest: None, **Funding:** None

Publisher: National Medical College Pvt. Ltd.
MedPhoenix - Journal of National Medical College (JNMC); 2021,6(2), available at www.jnmc.com.np

ISSN:2631-1992 (Online); ISSN:2392-425X (Print)



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**ABSTRACT**

Introduction: Hypothyroidism is a clinical syndrome that results from decreased secretion of thyroid hormone from thyroid gland. Primary hypothyroidism accounts for 90-95% of all cases of hypothyroidism. Hypothyroidism has various cardiovascular manifestations. This study was conducted with an aim to identify cardiovascular manifestations of hypothyroidism for an early prevention and management.

Methods: A cross sectional observational study was conducted in Department of Medicine in Bir Hospital. Ethical clearance was taken from Institutional Review Board National Academy of Medical Sciences. A total of 70 patients with untreated primary hypothyroidism without any prior known comorbidities or under any medication were randomly selected. Data were collected and entered in Microsoft Excel to tabulate data and analyze results.

Results: Out of 70 enrolled participants, 41 cases had sub-clinical hypothyroidism and 29 overt/clinical hypothyroidism with male to female ratio of 1:4. Most common presenting cardiovascular symptoms was peripheral edema (60%) followed by easy fatigability (47.14%). Body mass index (BMI) and blood pressure was elevated in 70% and 60% of participants respectively. Dyslipidemia was present in 48.57% of cases among which majority changes were in triglyceride and total cholesterol level. Abnormality in ECG was seen in only 22.85% of cases with T wave abnormality (18.57%) being most common followed by sinus bradycardia (14.28%). Echocardiography was abnormal in 7.14% of cases with 2.86% showing pericardial effusion.

Conclusions: Cardiovascular manifestations were present in majority of patients of primary hypothyroidism especially High BMI, Hypertension and Dyslipidemia. The newly diagnosed primary hypothyroidism patients should be screened routinely for cardiovascular manifestations.

Keywords: body mass index; cardiovascular manifestations; dyslipidemia; hypertension; primary hypothyroidism.

INTRODUCTION

Hypothyroidism is a clinical syndrome that results from decreased secretion of thyroid hormone from thyroid glands.¹ Thyroid disorders are the most abundant endocrine disorder in the world after diabetes mellitus.² Hypothyroidism can be classified into primary hypothyroidism, in which the defect is intra thyroid and secondary hypothyroidism, in which other pathologies cause indirect decrease of circulating hormone.³

Primary hypothyroidism is the permanent loss or destruction of the thyroid, through processes as autoimmune destruction or irradiation injury.⁴ Overt hypothyroidism is elevated serum thyroid stimulating hormone (TSH) concentration and reduced free thyroxine concentration (fT4) while subclinical hypothyroidism is elevated serum TSH level with normal serum fT4 concentration.⁴ TSH levels increases with age and age specific TSH should be considered to prevent unnecessary treatment.⁵

The mean annual incidence rate of autoimmune hypothyroidism is up to 4 per 1000 women and 1 per 1000 men.⁶ Thyroid disorders may be due to iodine deficiency or in form of thyroiditis, hypothyroidism or autoimmune dysfunction. Nepal is an endemic area for iodine deficiency in Himalayan, sub-himalayan and terai regions.²

Hypothyroidism affects all organ systems independent of the underlying disorders.⁴ Thyroid hormone increases sympathetic system activity, angiotensinogen and atrial natriuretic peptide levels and decrease vasopressin levels.⁷ Hypothyroidism is associated with decreased cardiac output due to impaired relaxation of vascular smooth muscle and decreased availability of endothelial nitric oxide producing increased arterial stiffness and hence increased vascular resistance.⁸

This study was performed in an attempt to find out the cardiovascular manifestations in primary hypothyroidism

in our setup.

MATERIALS AND METHODS

A descriptive cross sectional observational study was conducted from July 2017 to December 2018 in outpatient department of medicine at Bir Hospital. Ethical clearance was taken from Institutional Review Board of National Academy of Medical Sciences. (Reference no. 1300 075/76)

The study included any patient presenting in Department of Medicine OPD above 18 years of age and excluded those with underlying known comorbidities, under medications and pregnancy. Sample size was calculated using formula with 95% confidence interval, 16% prevalence of primary hypothyroidism⁹ and 10% margin of error. In this study, total of 70 cases were taken by simple randomization.

A written consent was taken from each participant for the study. Data were collected using structured proforma with details on cardiovascular sign and symptoms, laboratory and imaging data. The collected data were tabulated and analysed using Microsoft Excel.

RESULTS

Out of 70 cases enrolled in study, 14 (20%) cases were male and 56 (80%) cases were female.

Among 14 male cases, 8 cases had subclinical and 6 had overt/clinical hypothyroidism while among 56 female cases, 33 had subclinical hypothyroidism and 23 had clinical hypothyroidism Thus there were a total of 41 subclinical hypothyroidism and 29 overt hypothyroidism patients.

Table 1– Presenting signs and symptoms of Hypothyroidism

Symptoms	No. of cases (%)
Easy fatigability	33 (47.1%)
Exertional dyspnea	19 (27.1%)
Weight gain	30 (42.3%)
Peripheral edema	42 (60%)
Orthopnea/Paroxysmal Nocturnal Dyspnoea	3 (4.3%)
Palpitation	17 (24.3%)

BMI of all the cases were measured which showed majority of the cases i.e. 70% (49/70) had high BMI (≥ 23). Among those cases 85.57% (12/14) of Male and 66.07% (37/56) of female had high BMI.¹⁰

Table 2- Body Mass Index in Primary Hypothyroidism

Body Mass Index	Primary Hypothyroidism Cases				Total No. (%)
	Subclinical		Overt / Clinical		
	Male (N)	Female (N)	Male (N)	Female (N)	
High (≥ 23)	7	23	5	14	49 (70%)
Normal (18.5-22.9)	1	9	1	9	20 (28.6%)
Low (<18.5)	0	1	0	0	1 (1.4%)

Out of 70 cases enrolled in this study, 42 patients (60%) had high blood pressure recorded while rest of them had normal range blood pressure but no record of low blood pressure was seen.¹¹

Table 3- Pattern of blood pressure in primary hypothyroidism

Blood Pressure	Primary Hypothyroidism Cases				Total No. (%)
	Subclinical		Overt / Clinical		
	Male (N)	Female (N)	Male (N)	Female (N)	
High ($\geq 140/90$)	6	15	5	16	42 (60%)
Normal(18.5-22.9)	2	18	1	7	28 (40%)
Low (<90/60)	0	0	0	0	0

Comparing subclinical and clinical hypothyroidism with blood pressure, majority of patients with overt hypothyroidism 72.41% (21 cases) had high blood pressure while only 51.21% (21 cases) of subclinical hypothyroidism patients had high blood pressure.

Lipid abnormalities was seen in 34 cases (48.57%) among study group. Out of this, 34 patients, 16 cases (39.02%) were of subclinical hypothyroidism while 18 patients (62.06%) were of overt hypothyroidism.

Table 4– Pattern of lipid profile in primary hypothyroidism

Abnormal Lipid Levels	Subclinical Hypothyroidism		Overt Hypothyroidism		Total (%)
	Male	Female	Male	Female	
Cholesterol	2	10	4	5	21 (30%)
Low Density Lipoprotein	0	0	0	1	1 (1.42%)
High Density Lipoprotein	2	2	0	2	6 (8.57%)
Triglyceride	3	10	6	13	32 (45.71%)

Overall 16 cases out of 70 (22.85%) of primary hypothyroidism under study were found to have abnormal electrocardiography (ECG). Among overt hypothyroidism 9 of 29 (31.03%) patients showed ECG abnormalities in any form whereas 7 of 41 (17.07%) cases of subclinical hypothyroidism had ECG changes.

Table 5- Pattern of ECG changes in cases of primary hypothyroidism

ECG Changes	Primary Hypothyroidism Cases		
	Male (N)	Female (N)	Total (%)
Sinus Bradycardia	3	7	10 (14.2%)
Flat or inverted T - Waves	3	10	13 (18.57%)
Low QRS Complex	0	1	1 (1.42%)
Conduction Blockage	0	0	0
QT _c Interval Prolongation	0	1	1 (1.42%)

Echocardiographic findings of the cases revealed only 7.14% (5 cases) had abnormal echo reading of which 2 cases were subclinical and 3 cases were clinical hypothyroidism.

Table 6- Echocardiographic changes in cases of primary hypothyroidism

Echocardiographic changes	Primary hypothyroidism cases		
	Male (N)	Female (N)	Total (%)
Ejection Fraction Changes (<40%)	0	1	1 (1.42%)
Increased inter ventricular septum thickness changes (IVS)	1	1	2 (2.85%)
Increased left ventricular posterior wall thickness changes (LVPW)	1	2	3 (4.28%)
Increased IVS / LVPW	0	3	3 (4.28%)
Pericardial Effusion	1	1	2 (2.85%)

DISCUSSION

Hypothyroidism is a clinical state of reduced production of thyroid hormones.⁴ Cardiovascular risk is increased in patients with overt hypothyroidism and several potential cardiovascular risk factors were similarly reported in patients with subclinical hypothyroidism.¹²

In our study of randomly selected 70 cases, 14 cases (20%) were males and 56 cases (80%) female which was similar to other studies. In a study by Jagota G et al in 2021 in Punjab showed majority of cases were female (72.6%) in 150 participants.¹³ Similarly in a study by Baral N et al in 2002 in Dharan, out of 185 participants majority of cases were females (83.2) ¹⁴ Our study had 58.57% subclinical hypothyroidism and 41.43% overt/clinical hypothyroidism which was comparable to study by Mahato RV et al. in 2015 in tribhuvan university teaching hospital, Kathmandu which showed 69.15% (885 cases) cases of Subclinical hypothyroidism and 30.85% (395 cases) of overt hypothyroidism among 1280 cases of Primary hypothyroidism.¹⁵ Aryal M et al.in 2010 studied prevalence of thyroid dysfunction in Dhulikhel Hospital, Dhulikhel, Nepal which showed equal number of cases of subclinical and clinical/overt hypothyroidism.⁹

While a study by Jagota G et al showed 41.3% of overt hypothyroidism among 150 randomly sampled participants.¹³

In our study, the most common cardiovascular symptom was peripheral edema (60%) followed by easy fatigability (47.17%), weight gain (42.86%), exertional dyspnea (27.14%) and palpitation (24.29%). In a study done by Al-Farttoosi A.J.M et al in 2010 in Iraq showed easy fatigability (88.9%) as the most common cardiac manifestation followed by exertional dyspnea (75%), weight gain (66.7%) and peripheral edema (11.11%).¹ In a study by Dangi V and Meena R.S in 2018 in Bhopal showed the most common cardiovascular symptoms being weight gain (73%) followed by lethargy (65%).¹⁶

Among 70 cases enrolled in our study, 49 cases had high BMI while 20 cases had normal BMI and 1 case had below normal BMI. Different studies showed significant variation in TSH with increasing BMI.^{17, 18}

In our study, 42 (70%) cases had high blood pressure while 28 cases (30%) had blood pressure within normal range. 72.42% (21 of 29) of overt hypothyroidism developed hypertension while only 51.21% of cases (21 of 41) in subclinical hypothyroidism developed hypertension. In a study by Fommei E and Iervasi G in year 2002 and Duan Y et al in 2009, showed that during hypothyroid state, day time arterial systolic and diastolic blood pressure level increased slightly but significantly.^{19,20} However with higher level of subclinical hypothyroidism hypertension was not seen.²⁰ In another study by Hofstetter L et al published on 2018 revealed that systolic blood pressure was marginally elevated compared to euthyroid individuals however diastolic blood pressure was not significantly different.²¹

In this study, 34 cases (48.57%) had abnormal lipid profile of which 39.02% (16 cases) and 62.06% (18 cases) were with subclinical hypothyroidism and overt hypothyroidism respectively. Most of the patients in our study had high triglyceride level which was comparable to study by Al-Farttoosi et al in 2010 and Rizos C.V et al, which found statistically significant higher total serum cholesterol, triglyceride level ^{1,22} and LDL- C ²² respectively. In another study done in Rawalpindi, Pakistan by Malik A et al., found significant changes in total cholesterol, HDL, triglyceride and LDL compared to control.²³ Also in a study by Sucharita G et al showed altered lipid profile with high cholesterol level in 26.7% and triglyceride in 53.4%.²⁴

In our study ECG abnormality was seen in 22.86% (16 cases) which included 31% of overt hypothyroidism and 17.07% of subclinical hypothyroidism cases. The most common ECG abnormality was flat or inverted T waves

(18.57%) followed by sinus bradycardia (14.28%). In contrast to our study, different studies showed low voltage complex as the most common finding in 34%¹³, 40%²⁵, 22.38%²⁶ and sinus bradycardia as the most common finding in 47.2%¹, 22.38%²⁶ while T wave changes were seen in 27.8%¹, 23.3%²⁵, 14.98%²⁶ of cases. There has been case reports of Torsades de pointes, a rare event which was not seen in our study.²⁷

In our study, only 7.14% cases had abnormal echocardiographic changes with 4.28% having abnormal IVS/LVPW ratio, 2.86 % cases pericardial effusion and 1.43% cases abnormal ejection fraction. In contrast to our study, various studies showed pericardial effusion present in 32.7%¹³, 32%¹⁶, 20%²⁴ of cases and diastolic dysfunction and pericardial effusion in 26.6% of cases²⁴ while diastolic dysfunction was seen in 20%¹³, 18%¹⁶, 26.6% of cases.²⁵ In a study by Al-Farttoosi A.J.M et al., significant changes in ejection fraction, fractional shortening and changes IVS thickness, IVS and LVPW ratio were found.¹ In contrast to our study, Behera B.K et al in Eastern India found 67% had abnormal echocardiography findings.²⁵

There were several limitations in our study. Our study had small sample size as many potential association could have been properly demonstrated and interpreted had the sample size been larger. No controls were taken in our study so proper interpretation could not be made whether the findings were incidental or not. This study being a hospital based study, enrolled patients would be more symptomatic which has caught their attention to seek healthcare facility.

CONCLUSION

Cardiovascular manifestations are common in cases of primary hypothyroidism. Our study showed high prevalence of increased BMI, hypertension and dyslipidemia and they mostly present with peripheral edema and easy fatigability. The study insights the need for routine screening of primary hypothyroidism for cardiovascular manifestations so that early intervention can be performed. However further study is needed with more number of study subjects and control cases to validate and establish these recommendations.

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