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Research Article

Assessing Diastolic Hypertension in Patients of Primary Hypothyroidism among Adults Visiting a Tertiary Care Hospital in North India

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Abstract

Background: Elevation of diastolic BP has been shown in few studies among patients with hypothyroidism. However, the evidence is still obsolete when it comes to Indian settings. This study intends to evaluate association between hypertension and primary hypothyroidism in North Indian population.

Methodology: One hundred primary hypothyroid patients (TSH level >5.5) were subjected to a cross-sectional comparative study in a tertiary care hospital in North India from August 2015 to June 2017. Patients had no thyroid complications and were unknown of their blood pressure status. Sociodemographic profile and clinical and laboratory status was evaluated which included blood pressure measurements; lipid profile, kidney function tests, and other vitals were recorded.

Results: Individuals with diastolic and overall hypertension had significantly less serum T3 values and high TSH and serum creatinine values as compared to non-hypertensive individuals. Pearson test showed a significant correlation between serum TSH levels with both systolic and diastolic BP.

Conclusion: This study showed that both systolic and diastolic blood pressure increased linearly with increasing TSH. Despite the differing estimated prevalence of hypertension in hypothyroidism, there seems to be a positive association of thyroid with BP.

Keywords: Thyroid, Blood pressure, Hypothyroidism, Lipid profile

Introduction

Hypertension (HTN), or elevated blood pressure (BP), is a well-documented risk factor for cardiovascular morbidity and mortality,[1] affecting all groups regardless of race, origin, ethnicity or socioeconomic status.[2] HTN is defined as a BP index of greater than 135/85 mmHg for automated office/home/ambulatory day-time BP readings, or more than 130/80 mmHg for 24 hour ambulatory BP readings.[3]

The prevalence of HTN in Indian settings presents a grim picture. The 2005 worldwide analysis of data available for the global burden of hypertension, the prevalence of hypertension amongst Indian men and women were 20.6% and 20.9%, respectively.[4] These rates amongst Indian men and women are expected to go up to 22.9% and 23.6% by 2025, respectively.[5] A 2008 WHO (World Health Organization) report says that HTN prevalence in Indians is 32.5% (33.2% in men and 31.7% in women).[6]

Thyroid gland is an endocrine organ involved in metabolic and energy production through its hormones thyroxine (T4) and triiodothyronine (T3). The synthesis of thyroid hormone is dependent on factors like the nutritional availability of

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iodine, and is predominantly regulated by thyrotropin (thyroid stimulating hormone, TSH), a hormone secreted by the pituitary gland.[7]

Thyroid diseases are frequently observed in clinical practice. Primary hypothyroidism is defined as an elevated TSH concentration in combination with a decreased FT4 concentration, is a commonly occurring disorder, most prevalent in women and most often caused by autoimmune thyroiditis, in which the immune system produces antibodies against normal thyroid tissue.[8,9] Evidence suggests that primary hypothyroidism is associated with increased risk of cardiovascular disease and leads to an increase of the levels of plasma total, LDL-cholesterol and BP.[10-13]

Elevation of diastolic BP has been shown in few studies among patients with hypothyroidism[14] and has been reported in small groups of patients with myxoedema by some investigators,[15,16] who have found a fall in diastolic BP when the hypothyroidism was corrected with thyroid replacement therapy. However, the evidence is still obsolete when it comes to Indian settings. With this background, we aim to evaluate whether there is an association between diastolic hypertension and primary hypothyroidism by measurements of BP and thyroid function in Indian population.

Methodology

The present cross-sectional comparative study was done in a tertiary care hospital in North India from August 2015 to June 2017 among 100 adult patients (>18 years of age), diagnosed with primary hypothyroidism with no further severe complications (such as cancer) and unknown of their blood pressure status. A cutoff level of TSH was taken to be more than 5.5. However, patients with congenital malformations of thyroid, other comorbidities such as diabetes mellitus, cancer or suspicion of malignancy, patients with known hypertension history, any family history or other factors causing hypertension were excluded.

Ethical approval was taken from the Institutional Ethical Committee after explaining the aims and objectives of the study. A written informed consent was obtained from each patient for the study. The involvement of the subject was voluntary and deliberate.

All patients underwent a clinical and laboratory evaluation. The demographic data were obtained from a questionnaire survey. Following variables were assessed: gender, age (years), ethnicity, occupation, education, income, socioeconomic status (calculated with combination of occupation, income and education in accordance with modified Kuppuswamy scale, 2016.[17] Data on comorbidities such as, dyslipidemia, previous TD (hyperthyroidism, hypothyroidism, nodules, cancer), were also noted.

The reference values for thyroid biochemical assessment were:

- Hypothyroidism: if TSH levels were greater than 5.5 µUL/mL
- Sub-clinical hyperthyroidism: if TSH levels were lower than 0.27 µUL/mL

(Individuals with detected subclinical hyperthyroidism were excluded).

Study Factors

- Vitals of the individual: Pulse, Weight, Temperature
- Lipid profile: Total Cholesterol, LDL and Triglyceride levels
- Serum Creatinine and Blood Urea Nitrogen (BUN) levels
- Thyroid biochemical assessment
- Systolic and Diastolic Blood Pressure

Specimen Collection

Five mL of venous blood was drawn from each subject. It was dispensed into fluoride oxalate bottles for plasma glucose estimation. One EDTA vial containing 0.5 mL of it was used for estimation of glycosylated hemoglobin and the rest of the blood sample was discharged into a plain sample bottle and allowed to clot. The serum was separated from the red blood cells, divided it into three aliquots and stored them frozen at −20°C. TSH, T4 and T3 estimation was done by enzyme immunoassay (EIA) kit method using commercial kits within 2 weeks of collection.

Statistical Analysis

Statistical analysis was performed using SPSS v17.0. Differences between parametric groups were compared by the student-t test; correlation was done by Pearson's correlational analysis. Non-parametric variables were evaluated using chi-square test for statistical comparisons.

Results

Majority of study participants were in the 31-50 year age group, with a mean of 45.1±13.1 years and range 21–73 years. Majority were males (87%) and 13% females. Most of the study participants were married (92%), 6% were unmarried and 2% divorced. More than half of the subjects (55%) belonged to middle class, followed by 26% in lower-middle class, 11% in upper middle and 8% in upper class (Table 1).

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Table 1.Sociodemographic Characteristics

Sociodemographic Characteristics		Frequency	Percent (%)	p-value
Age group (years)	18–30	11	11.0	0.342
	31–40	32	32.0	
	41–50	30	30.0	
	51–60	12	12.0	
	>60	15	15.0	
Gender	Males	87	87.0	0.884
	Females	13	13.0	
Marital status	Married	92	92.0	0.719
	Unmarried	6	6.0	
	Divorced	2	2.0	
Socioeconomic status	Lower Middle	26	26.0	0.092
	Middle	55	55.0	
	Upper Middle	11	11.0	
	Upper	8	8.0	

The mean pulse rate of study participants was 78.06±9.71 (range 64–94). The mean weight of study participants was 88.9±9.9 kg (range 75–111 kg). Mean body temperature of study participants was 97.8±0.9 (range 96–100). Systolic BP had a mean value of 135.8±9.9 (range: 122–158); Diastolic BP mean was 90.8±7.1 (range: 78–106). The Thyroid hormone levels are depicted in Table 2.

Table 2.Descriptive Statistics of Study Parameters

	Systolic BP	Diastolic BP	Serum T3	Serum T4	Serum TSH
N	100	100	100	100	100
Mean	135.84	90.82	68.57	3.333	8.977
Median	136.00	90.00	68.00	3.300	8.900
Mode	136	86	55	4.2	8.2
SD	9.981	7.079	11.382	.6225	1.8712
Range	36	28	43	2.0	6.4
Minimum	122	78	48	2.2	5.9
Maximum	158	106	91	4.2	12.3

Lipid profile was assessed using three basic parameters: total cholesterol, estimation of low-density lipoprotein (LDL), and triglyceride levels. Most of the parameters were under acceptable ranges. The mean value of serum creatinine was 2.3±0.6 (range: 1.0–3.2); mean blood urea nitrogen (BUN) was 46.05±14.4 (range: 25–81).

Pearson correlations of BP levels with thyroid hormone levels showed a significant correlation between serum TSH levels with both systolic and diastolic BP in all subjects (Table 3). Since all subjects recruited in the study had a TSH level >5.5, i.e., all subjects had primary hypothyroidism, it was observed that 54% of study subjects had diastolic hypertension as per the objective of the study. A significant association (performed using unpaired t-test) was seen among few study parameters and hypertension (Table 4). It was noticed that individuals with diastolic and overall hypertension had significantly less serum T3 values and high TSH and serum creatinine values as compared to non-hypertensive individuals.

Table 3.Pearson Correlation among Thyroid Levels and BP

		Systolic BP	Diastolic BP
Serum TSH	Pearson Correlation	0.844	0.733
	p-value	0.040*	0.033*
Serum T3	Pearson Correlation	0.070	0.053
	p-value	0.489	0.602
Serum T4	Pearson Correlation	0.088	0.126
	p-value	0.383	0.212

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Table 4.Association of Hypertension with Study Parameters

	Diastolic Hypertension (n=54)				Overall Hypertension (n=68)			
	No. of Subjects	Mean	SD	p-value	No. of Subjects	Mean	SD	p-value
Serum T3	Yes	67.28	10.154	0.022*	Yes	68.06	10.876	0.041*
	No	70.09	12.617		No	69.66	12.499	
Serum T4	Yes	3.302	.6332	0.051	Yes	3.357	.6363	0.069
	No	3.370	.6146		No	3.281	.5986	
Serum TSH	Yes	9.117	1.8079	0.038*	Yes	9.904	1.8258	0.002*
	No	8.813	1.9500		No	9.131	1.9852	
Blood Urea	Yes	47.39	15.857	0.622	Yes	50.24	15.645	0.271
	No	46.83	12.625		No	49.78	11.373	
Serum Creat	Yes	2.339	.6629	0.006*	Yes	2.357	.6347	0.002*
	No	2.293	.5670		No	2.278	.5912	
Total Cholesterol	Yes	251.06	37.755	0.196	Yes	254.54	39.725	0.836
	No	240.83	40.755		No	250.19	38.717	
LDL	Yes	156.56	30.019	0.452	Yes	144.21	29.976	0.391
	No	143.41	31.926		No	142.91	33.170	
Triglyceride	Yes	202.07	28.153	0.547	Yes	202.60	27.969	0.274
	No	197.91	27.366		No	194.97	26.915	

Discussion

Hypothyroidism has been recognized as a cause of secondary hypertension. Previous studies on the prevalence of hypertension in subjects with hypothyroidism have demonstrated elevated systolic or diastolic BP values, whereas one study has reported no association between hypertension and hypothyroidism. However, due to limited evidence from India, the present study was envisaged.

In our study, the proportion of individuals diagnosed to have diastolic hypertension was as high as 54%. Even the overall hypertension in current study was as high as 68%. Several studies have demonstrated that prevalence of hypertension amongst hypothyroid patients varies widely from 0% to 50% (18–20). These differences reflect different criteria employed for diagnosis of hypertension and hypothyroidism, differing degrees of hypothyroidism and varying ages of patients and places surveyed.

Evidence suggests that prevalence of hypertension in hypothyroid patients is approximately three times that of euthyroid patients. Further, the most profound changes tend to be confined to diastolic hypertension.[18] The mean value of systolic BP was 135.8 and that of diastolic BP it was 90.8 in the current study. The findings are comparable with study by Kotsis et al. in 2007, wherein mean systolic BP in hypothyroid individuals was found to be 139.0±9.7 mm Hg.[21] In another study, TSH in the upper part of the reference range was associated with arterial stiffness and high mean blood pressure.[22] In another study, clinic blood pressures taken at the beginning of the 24-hour period were 138.4±21.1 systolic for hypothyroid subjects and 121.3±10.3 in control subjects, 87.2±12.9 diastolic for hypothyroid subjects and 77.9±6.9 diastolic for control subjects.[21]

Further, our study also showed that both systolic and diastolic BP increased linearly with increasing TSH. Asvold et al. have depicted such relationship as well in 2007.[23] Underlying mechanisms that may explain these findings are not fully understood, but increased systemic vascular resistance,[24,25] blood vessel vasoconstriction and arterial stiffness[24-26] may accompany low thyroid function.

The vasoconstriction may be due to the absence of vasodilator thyroid hormone effects on the vascular smooth muscle, or may be the result of circulating norepinephrine levels with a decrease in the number of vascular beta-adrenergic receptors. The increases in blood pressure in hypothyroid individuals may also be related to obesity. It has also been shown that thyroid hormones may have direct vasodilatory effects on vascular muscle cells and that endothelial dysfunction may be more prevalent in hypothyroid patients.[24]

Thus, despite the differing estimated prevalence of hypertension in hypothyroidism, there seems to be positive association of thyroid with BP and the effects of thyroxin supplementation further strengthen this. Another mechanism suggested for hypertension in hypothyroid patients is hypothyroidism is a low-renin hypertensive state.[24] The renin–angiotensin–aldosterone system is important for medium- and long-term BP regulation. The hypothyroid population is characterized by significant volume changes, initiating a volume-dependent, low-plasma renin activity (PRA) mechanism of BP elevation.

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Thyroid and renal functions are interrelated. Thyroid hormone insufficiency has been associated with deterioration of renal function. The renal disorders that follow hypothyroidism are attributed to the cardiovascular consequences of T3 deficiency. As was evident in the current study, serum creatinine levels were significantly higher in patients comorbid with diastolic hypertension. Similarly, blood urea levels were relatively higher in same cohort of patients. Evidence suggests that creatinine clearance in patients with hypothyroidism is generally low.[27] However, all the aforementioned changes are reversible with hormonal substitution.

Overall, hypertensive patients and those diagnosed with diastolic hypertension showed higher concentrations of unfavorable lipids within them (with LDL being significantly higher than those who were normotensive). Similar linear association between TSH and serum lipids has been reported in the past also.[23] Dyslipidemia is a common finding in patients with clinical hypothyroidism, consisting of high levels of total and LDL cholesterol.[28]

Further, hypothyroid patients have increased arterial stiffness. Patients with hypothyroidism have been reported to have greater radial wall thickness and compliance than euthyroid healthy age- and sex-matched controls.[29] It has been seen normalization of thyroid function by hormone replacement was associated with reduced levels of LDL-cholesterol and improvement in the total/HDL-cholesterol ratio. Uptil now, it is known that cardiovascular complications are some of the most profound and reproducible clinical findings associated with thyroid disease. The dysfunction ranges from functional systolic/diastolic dysfunction to overt failure and coronary artery disease.[30]

Limitations of the Study

- A research group of 100 individuals may not be diagnostically sufficient for concluding such evidences. A larger sample size with preferably a cohort-based periodical evaluation would be more helpful.
- Other parameters, particularly related to cardiovascular abnormalities and thyroid function would also have been helpful in judging the status of the chronic comorbidity.
- Most of the clinical parameters are a superficial estimate of the condition; however, a detailed analysis of the parameters should be done for proper assessment.

Conclusion

Hypothyroidism has been recognized as a cause of secondary hypertension. Several studies have demonstrated that prevalence of hypertension amongst hypothyroid patients varies widely. This study showed that both systolic and diastolic blood pressure increased linearly with increasing TSH. Despite the differing estimated prevalence of hypertension in hypothyroidism, there seems to be positive association of thyroid with BP, and the effects of thyroxin supplementation further strengthen this. Similarly, blood urea levels were relatively higher in same cohort of patients. However, all the aforementioned changes are reversible with hormonal substitution.

Conflict of Interest: None

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