



HYPOTHYROIDISM INDUCED HYPERTENSION, AN OBSERVATIONAL STUDY

Kamlesh Taori

Junior Resident , MD Medicine, Rohilkhand Medical College , Barielly .

Seema Seth*

Associate Prof, MD Medicine, Rohilkhand Medical College , Barielly *Corresponding Author

ABSTRACT

Introduction/ Background: In hypothyroidism, hypertension is not a usual sign but hypothyroidism is one of major however often ignored cause of hypertension, which can be easily treated with thyroxine therapy most of the times. This study was undertaken to find the relationship of thyroid function with blood pressure and compare the age-related increase in blood pressure in euthyroid patients with that of hypothyroid patients and to assess the effect of thyroid hormone replacement therapy on blood pressure in hypertensive hypothyroid patients.

Objective: To study the association between hypertension and hypothyroidism and to assess the response of adequate thyroid hormone replacement therapy on blood pressure in hypothyroid hypertensive subjects.

Material and Method: Prospective observational study was undertaken in Rohilkhand Medical College and Hospital, Bareilly. This study included 241 female patients aged 19-69 years admitted in the medical wards from 1st Jan to 31st Dec 2018. Detailed clinical examination including measurement of blood pressure and routine investigations including thyroid profile were done. The data was expressed as means \pm SEM and was statistically analyzed.

Results: On the basis of thyroid profile out of 241 cases, 87 were hypothyroid and 154 were euthyroid. Adiposity, age and sex related factor that could influence blood pressure were excluded. Diastolic, rather than systolic blood pressure was significantly higher in hypothyroid patients over 50 years than in euthyroid patients of corresponding age groups. 9 hypertensive hypothyroid patients who received adequate thyroid replacement therapy for 6 ± 2 months had reduction in blood pressure. In rest of 5 patients who did not receive adequate thyroid replacement therapy due to poor compliance, blood pressure and thyroid function tests remained unchanged.

Conclusion: In patients over 50 years, we encountered hypertension more in hypothyroid patients than in euthyroid cases. Hypothyroid patients had significantly higher diastolic blood pressure than euthyroid patients. Hypertension that was associated with hypothyroidism often reduces in response to adequate thyroid hormone replacement therapy.

KEYWORDS :

INTRODUCTION

Hypothyroidism is recognized as a cause for hypertension since long period, however is often over looked or ignored.

Previous studies on the prevalence of hypertension in subjects with hypothyroidism have demonstrated that prevalence widely varied as shown in Table 1.

Table 1 : Previous studies on the prevalence of hypertension in subjects with hypothyroidism.

Survey	Date	Country	n	Prevalence of hypertension or hypothyroidism	Notes
Endo et al ¹	1979	Japan	81	0-60% ^a	Age 30-60yrs
Saito et al ²	1983	Japan	477	30% ^b	Age over 50yrs
Streeten et al ³	1988	USA	688	3.6% ^c	Age 20-69yrs
Anderson et al ⁴	1994	USA	1061	3.0% ^d	

These differences may possibly be because of the different criteria employed for diagnosis of hypertension and hypothyroidism both, differing degrees of hypothyroidism and varying ages of patients.

In present study, the age-related increase in blood pressure in euthyroid patients was compared with that of hypothyroid patients and assessment of the effect of thyroid hormone replacement therapy on blood pressure in hypertensive hypothyroid patients was done.

MATERIAL AND METHOD

In present study 241 patients who visited to Rohilkhand Medical College And Hospital between 1st Jan 2018 to 31st Dec 2018 were included. Only female patients (to avoid sex-related factor that could influence blood pressure) were include in this study between age group of 19-69 years.

It was ensured that none of patients was previously treated for hypertension or hypothyroidism. Hypertension was defined as Blood pressure 140/90mmHg (ESC guidelines). Blood pressure was measured after 10min of rest in a quiet room with sphygmomanometer (Brachial arterial pressure). Serum T3, T4 and TSH was determined by ELISA techniques. Values are expressed as means \pm SEM. Statistical

analysis was done by Student's t test for paired and unpaired data as appropriate and chi square test. Correlations were calculated by the method of least squares.

RESULTS

Clinical profiles of patients are shown in table 2. Weight, height and body mass indexes (BMI) were similar in both groups. 11 out of 154 patients (7.14%) in euthyroid patients and 14 of 87 (16.09%) in hypothyroid patients had hypertension.

The number of patients and prevalence of hypertension by age was shown in table 3.

Blood pressure increased with age in both euthyroid and hypothyroid patients. (fig.1)

Table 2 : Clinical profile of euthyroid and hypothyroid groups.

	Euthyroid n=154	Hypothyroid n=87	Significance
Weight (kg)	49.1 \pm 1.2	51.9 \pm 1.0	Ns
Height (cm)	151.1 \pm 0.8	152 \pm 0.9	Ns
BMI	21.8 \pm 0.5	22.4 \pm 0.4	Ns
T4 ng/dL	1.25 \pm 0.4	0.35 \pm 0.3	<0.001
T3 pg/mL	2.45 \pm 0.95	0.85 \pm 0.5	<0.001
TSH mIU/mL	2.60 \pm 1.05	95.1 \pm 7.8	<0.001

Hypothyroid patients had significantly higher diastolic blood pressure than euthyroid patients in the 5th and 6th decades. Heart rate in euthyroid patients was higher than in hypothyroid patients; however, the difference did not reach statistical significance in the 40- to 49-year and 60- to 69-year groups.

14 out of 87 hypertensive hypothyroid patients aged 29 to 69 years were reviewed after 6 ± 2 months. In 9 patients (Group 1) who received sodium-L-thyroxine, 75 to 150mg/daily (depending on requirement), treatment suppressed TSH and increased serum T3 and T4 into normal range and was therefore considered adequate. All except one exhibited significant reductions of blood pressure.

Table 3: Number of patients and prevalence of hypertension in euthyroid and hypothyroid patients

Age in years	Patients with Hypertension		Significance
	Euthyroid	Hypothyroid	
20-29	0/28	0/17	Ns
30-39	1/25	1/16	Ns
40-49	3/37	3/19	Ns
50-59	4/44	6/21	<0.01
60-69	3/20	4/12	<0.01
Total	11/154 (7.14%)	14/87 (16.09%)	<0.01

In rest of 5 patients (Group 2) who did not receive adequate amount of sodium-L-thyroxine due to poor compliance, blood pressure and thyroid function tests remained unchanged.

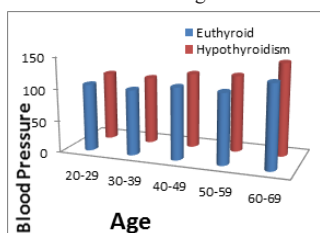


fig 1. Blood pressure in euthyroid (blue bar) and hypothyroid (red bar) patients by age. Hypothyroid patients had significantly higher blood pressure than euthyroid patients in the 5th and 6th decades.

DISCUSSION

Hypothyroidism is common, recent study has shown that the lifetime incidence of spontaneous hypothyroidism in female to be 4.1 per thousand survivors per year, and 0.6 per thousand male survivors per year.⁵ In the present study, only female cases were studied to avoid sex-related factors that may influence blood pressure. Adiposity could also influence blood pressure⁶⁷ that was excluded as there were no major difference in weight, height, and body mass index between euthyroid and hypothyroid cases in our study.

In case above 50 years old, diastolic blood pressure of hypothyroid cases were significantly higher than that of euthyroid patients whose age-related change in blood pressure was similar to that of general population. This finding suggested that the hypothyroidism is a state that accelerates the age-related increases in blood pressure. The prevalence of hypertension in the subjects over 50 years old is approximately 30% in our study.

The mechanism of increased blood pressure in hypothyroidism is not known; various mechanisms proposed are described below:

1. Structural change of vascular tissue is promoted in thyroid hormone deficiency could be a local factor in causing an increase in total peripheral resistance which may lead to hypertension.⁸
2. Autonomic nervous function modification by thyroid hormone deficiency can cause hemodynamic changes. Rise in norepinephrine level in plasma, mostly due to increase in secretion rate, rather than decrease in metabolism of norepinephrine have been observed in hypothyroid cases.⁹ In addition to this further evidence to support the role of noradrenaline is described in a report that concluded that plasma noradrenaline concentration return to normal after euthyroidism (and normotension) has been restored by thyroxine therapy.¹⁰
3. For synthesis and regulation of adrenergic receptors, thyroid hormone plays a major role¹¹ and alteration in the distribution of these receptors may lead to the development of hypertension in hypothyroid cases. A rat experiment confirmed that, the rise in α -adrenergic receptor responsiveness can lead to the increase in peripheral vascular resistance which may account for hypertension.¹²
4. The correlation between hypothyroidism and low plasma aldosterone and renin activity levels is well established and is reported in several studies.¹³⁻¹⁵ Restoration of euthyroidism in hypothyroid accounts for normalisation of aldosterone level and renin activity in plasma.¹⁴
5. Although total body water percentage rises in hypothyroidism, there is a relative fall in intravascular volume and hyponatraemia in encountered frequently (however the total body sodium rises). There is suppression of ADH by a central mechanism probably due to a receptor or post-receptor defect under thyroid hormone

influence of thyroid hormone.¹⁶

6. A reduced dopaminergic activity in central nervous system is encountered in hypothyroidism probably because of high serum prolactin and TSH concentration^{17,18} which may contribute to the development of hypertension by increase in norepinephrine release.¹⁹
7. Alter red blood cell sodium level and transport is influenced by thyroid hormone.²⁰ This is achieved partly by altering the lithium-sodium (Li-Na) counter transport mechanism, which also has functional importance in regulating sodium transport in vascular smooth muscle and in the kidney. Essential hypertension is associated with increased red blood cell Li-Na counter transport.²¹
8. The brain is an essential site of thyroxine and triiodothyronine metabolism.²² The exact mechanism by which thyroid hormones could cause hypertension centrally is not clear but on giving thyroxine intrathecally in rats has confirmed that thyroid hormones in the brain are play a important role in the regulation of peripheral autonomic nervous system.²³

To summarize, hypertension that accompanies hypothyroidism is likely to have a multifactorial etiology, like alteration of autonomic nervous function, acceleration of structural change of vascular tissue, low plasma aldosterone and renin activity levels, changes in total body water and sodium transport and central nervous system effects, all playing a part.

In a study by Bjorn O Asvold, Trine Bjorn, Tom I.L. Nilsen and Laras J. Vtten in 1995-97 in Norway on 30,728 subjects found that within a reference range of TSH there was a linear positive association between TSH and blood pressure that may long term implicate for cardiovascular health.²⁴ In one other study, the number of patient under the age of 40 years required no additional anti-hypertensive therapy once euthyroidism had been restored, in contrast to 50% in the age group 40-49 years, to 75% in 50-59 year and to 100% in 60-69 year patients.

CONCLUSION

In our prospective observational study, we observed that hypertension was more prevalent in hypothyroid patients than in euthyroids, in cases over 50 years of age. Hypothyroid patients had significantly higher diastolic blood pressure than euthyroid patients. Hypertension that was associated with hypothyroidism often reduces in response to adequate thyroid hormone replacement therapy.

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