

## Original Research Article

# Is the clinic pathological profile of hypothyroidism gradually changing: a comparative study from North India

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### ABSTRACT

**Background:** Thyroid dysfunction has been subject of academical and therapeutically interest not only to the endocrinologist but also to the disciplines of medicine. Statistical data and studies on hypothyroidism are scanty, clinical picture is varied, investigations are usually not available at all levels and therefore to enlarge clinical profile of hypothyroidism minimal base line investigation, clinical approach and effects of replacement therapy and complications are to be studied.

**Methods:** Observational cross-sectional study conducted among patients with hypothyroidism registered at the Air Force Central Medical Establishment (AFCME) New Delhi.

**Results:** Among 50 patients with hypothyroidism were enrolled in this study during the study period. Idiopathic hypothyroidism was present in 98% patients while only one patient (2%) had Hashimoto's thyroiditis. Generalized weakness was the commonest presenting symptom followed by lethargy and anorexia. Thyroid swelling was diffuse in nature with no predilection to right or left lobe enlargement. Hypertension (40%) and ischemic heart diseases (36%) were the most common comorbid condition. Mean serum TSH was elevated while serum T3 and T4 values were reduced. Antithyroid antibody titre was positive in more than seventy percentage of patients. X-ray among patients revealed cardiomegaly in ten patients (20%), pulmonary Koch's in (4%) of patient and in rest of patients x-ray chest PA view was normal. ECG changes showed low voltage on electrocardiogram in (20%) of patients and sinus bradycardia in (24%) of patients. Most of the patients were put on replacement therapy (L. thyroxine) in dose of 1.6 - 1.7 mcg/kg/day.

**Conclusions:** Hypothyroidism as a clinical entity is common between 4<sup>th</sup> and 6<sup>th</sup> decade of life and seen more among females. Though etiology remained unknown in majority of the patients, weakness, and lethargy were the common clinical presentation.

**Keywords:** Antithyroid antibody, Hypothyroidism, India, Triiodothyronine, Thyroxine, Serum thyroid-stimulating hormone

### INTRODUCTION

Thyroid gland is one of the most important endocrinal glands governing numerous physiological processes. Although its physiology is not completely understood, it

has created great interest in many investigations.<sup>1</sup> The derangement in its physiology leads to hyper or hypofunction of the gland.<sup>1</sup> In the past, diagnosis of thyroid disease was possible only by indirect methods like BMR, Serum cholesterol, delayed relaxation of ankle

jerk, ECG etc. But changing trends in investigation in medicine and endocrinology is attributed to early diagnosis and management in thyroid disorders.

The use of T3, T4, and TSH assays some more diagnostic methods like PBI, THIST, free thyroxine index, TRH estimation, I131 uptake studies, TC99 Thyroid scan, ant thyroglobulin antibodies, ATS and TSH binding inhibitors are some of the further progressive measures in the field of thyroid disease.<sup>2</sup> With introduction of cellular histochemistry, molecular biology, fluorescent techniques, radio-immune assays, ELISA, CT scan, MRI and digital subtraction angiography, the entire picture of clinical endocrinology has been revolutionized.<sup>2</sup> With further knowledge of genetic engineering, gene therapy and introduction of biotechnology with pharmacology, the theocentric aspects of endocrinal dysfunction has been updated.

Thyroid dysfunction has been subject of academical and therapeutically interest not only to the endocrinologist but also to the disciplines of medicine. Statistical data and studies on hypothyroidism are scanty, clinical picture is varied, investigations are usually not available at all levels and therefore to enlarge clinical profile of hypothyroidism minimal base line investigation, clinical approach and effects of replacement therapy and complications are to be studied. This has resulted interest in the development of this study with the aim to evaluate clinicopathological profile of patients with hypothyroidism and study any changing trends and to study the effect and complication during follow up of patients.

## METHODS

### Design and study center

The present study was an observational cross-sectional study conducted among patients with hypothyroidism registered at the Air Force Central Medical Establishment (AFCME) New Delhi. This is a prestigious defense establishment and cater to a large population of serving defense personnel's, their families, dependents and retired armed forces personnel's in Delhi, National Capital Region (NCR) and North India. It is also one of the two centers in India approved by NABH for conducting medical examinations for civil pilots prior to their civil pilot license testing and its periodic renewals. The aim of the study was to collect original Indian data of hypothyroidism and also analyze any change in the trend of the disease. Study duration was the study was conducted over a period of 2 year (April 2014 to March 2016). Ethics committee approval was taken before the start of study.

### Selection criteria

The criteria selected for diagnosis of hypothyroidism was presence of clinical symptoms like edema feet, Weight

gain, Loss of appetite, Easy fatigue with the generalized weakness, Deceased sweating with the dry and course skin and hoarseness of voice along with clinical signs like delayed relaxation of the ankle jerk, loss of the outer one third of the eyebrow, Sinus bradycardia or low voltage complexes on electrocardiogram.

### Inclusion and exclusion criteria

Adult patients with confirmed diagnosis of hypothyroidism with high TSH value with normal or decreased level of T3 or T4. All pediatric patients or patients with post ablative hypothyroidism or those on thyroid replacement therapy or those with drug induced hypothyroidism were excluded from the study. Patients who fulfilled the inclusion and exclusion criteria were enrolled in the study after obtaining written informed consent from them.

### Study procedure

All patients underwent hematological evaluation (including hemoglobin, total and differential leukocyte count, platelet count), biochemical (thyroid function test like T3, T4 and TSH, liver function tests, renal function test). Data was presented as percentages for categorical variables and mean (SD) for normally distributed continuous variables.

## RESULTS

Among 50 patients with hypothyroidism were enrolled in our study during the study period. Majority of the patients were in the age group of 31-50 years (range 18 to 74 years). Clinical hypothyroidism was more common in females (72%) as compared to those seen in males (28%) (Table1). Idiopathic hypothyroidism was present in 98% patients while only one patient (2%) had Hashimoto's thyroiditis.

**Table 1: Age and gender wise distribution of patients.**

Age group	No. of patients		
	Male no. pts. (%)	Female no. pts. (%)	Total no. pts. (%)
Below 20 years	0(0)	1(3.84)	1(2)
21-30 years	1(7.143)	6(23.08)	7(14)
31-40 years	3(21.42)	11(42.30)	14(28)
41-50 years	7(50)	12(46.15)	19(38)
51-60 years	2(14.28)	4(15.38)	6(12)
61 onwards	1(7.143)	2(7.7)	3(6)
Total	14(28)	26(72)	50(100)

Generalized weakness was the commonest presenting symptom followed by lethargy and anorexia. Other common symptoms were breathlessness, weight gain, and change in voice, sensation of cold, palpitations, precordial pain, menorrhagia and impairment of memory

(Table 2). Bilateral non-pitting edema was seen in 72% patients while puffiness of face and delayed relaxation of ankle jerk was present in 68% patients each. Skin changes varied from 60%-75 % (Table 3).

**Table 2: Symptomatology of hypothyroidism in fifty patients (n=50).**

Symptoms	No. of patient	Percentage
Gen. Weakness	49	98
Lethargy	46	92
Breathlessness	35	70
Weight gain	35	70
Hoarseness of voice	39	78
Anorexia	45	90
Constipation	29	58
Decreased sweating	43	86
Sensation of cold	35	70
Palpitation	16	32
Precordial pain	15	30
Menorrhagia	8	16
Impairment of memory	10	20

Nervousness, bradycardia, thick tongue and thyroid swelling were present only in 10%-30% patients. Thyroid swelling was diffuse in nature with no predilection to right or left lobe enlargement. Hypertension (40%) and ischemic heart diseases (36%) were the most common comorbid condition (Table 4). Erythrocyte sedimentation rate was higher in patients of Hashimoto's thyroiditis and in patients with associated pulmonary tuberculosis while in others it was within normal limits (Table 5). Mean serum TSH was elevated while serum T3 and T4 values were reduced. Antithyroid antibody titre was

positive in more than seventy percentage of patients (Table 6).

**Table 3: Clinical signs of hypothyroidism in fifty patients (n=50).**

Symptoms	No. of patients	Percentage
Bilateral peripheral non-pitting edema	36	72
Puffiness of face	34	68
Delayed relaxation of ankle jerk	30	60
Pallor of skin	28	56
Cold skin	30	60
Boggy eyelids	28	56
Slow speech	16	32
Loss of hairs	14	28
Pallor of lips	14	28
Dry skin	36	72
Coarse skin	36	72
Coarse hairs	14	28
Thick tongue	06	12
Nervousness	10	20
Sinus bradycardia	18	36
Thyroid swelling	4	8

**Table 4: Comorbid condition among enrolled patients.**

Co-existing disease	No. of patient	Percentage
Hypertension	12	24
Ischemic heart disease	11	22
Pulmonary tuberculosis	2	4
Bronchial asthma	5	10

**Table 5: Blood parameters in hypothyroid patient (n=50).**

Indices	Mean value		No. of patients	%
	Male	Female		
Hemoglobin (GM %)	10.0 %	9.6%	50	100%
Total count (CMM)	8012	6021	50	100%
Differential count	P64 L30 E4 M2 BO	P64 L30 E4M2 B0	50	100%
ESR (MM/1 <sup>st</sup> HR.)	12.00	16.34	50	100%

**Table 6: Serum thyroid parameter among enrolled patients.**

Tests	Observed mean value	Normal value
Serum T3	0.473 nmol/l	1.1-2.9 nmol/l
Serum T4	2.05 mcg/dl	5-11 mcg/dl
Serum TSH	43.72 mu/l	0.5-5 mu/l
Antithyroid antibody titre	++ (>70%)	-

Thyroid swelling was observed only in three patients (8%). All these 4 patients were submitted for FNAC. Out of these, one patient had classical changes of Hashimoto's thyroiditis (2%). X-ray among patients revealed cardiomegaly in ten patients (20%), pulmonary Koch's in (4%) of patient and in rest of patients x-ray chest PA view was normal. ECG changes showed low voltage on electrocardiogram in (20%) of patients and sinus bradycardia in (24%) of patients (Table 7). Twelve patients (24%) had ST-T changes while fifteen patients

(30%) had normal electrocardiogram. ECHO findings revealed seven patients (14%) had pericardial effusion, while CCF and Hypertensive heart disease was seen in four (8%) patients and five (10%) patients respectively. Otherwise all patients had normal echocardiography (Table 8).

**Table 7: ECG changes among enrolled patients.**

ECG changes	No. of patients (n=50)	%
ST-T changes	12	24%
Within normal limit	15	30%
Low voltage	10	20%
Sinus bradycardia	12	24%
Chamber hypertrophy	1	2%
Disturbance of rhythm	-	-
Av dissociation	-	-
Complete heart block	-	-
Atrial/ventricular premature beats	-	-

Management among enrolled patients revealed, most of the patients were put on replacement therapy (L. thyroxine) in dose of 1.6-1.7 mcg/kg/day. Patient of Hashimoto's thyroiditis who also treated with prednisolone 40-60 mg/day, there was decrease in levels

of thyroid hormones in initial phase of disease, followed by state of hypofunction of gland, at that time replacement therapy was added.

**Table 8: Echo findings among enrolled patients.**

Echo findings	No. of patients	Percentage
Normal study	34	68%
Pericardial effusion	7	14%
CCF	4	8%
Hypertensive heart disease	5	10%

Co-existing conditions like hypertension with hypothyroidism were treated by L-thyroxine + calcium channel blocker in two patients and L- thyroxine + ACE-inhibitors in two patients. Ischemic heart disease with hypothyroidism was treated with L-thyroxine + Nitrates + Antiplatelet agent + tranquilizer. Pulmonary tuberculosis with hypothyroidism was treated with L-thyroxine + AKT containing HERZ regime. Bronchial Asthma with hypothyroidism was treated with L-thyroxine + bronchodilators. Iron-preparation, vitamins, calcium, zinc were given as a supportive therapy. There was no mortality among study patients during the study period (Table 9).

**Table 9: Side effect profile among enrolled patients.**

Disease	Drugs used	Side effect	No. of patients	Percentage
Hypothyroidism	LT	Chest pain,	5	10%
		Palpitation	3	6%
Hashimoto's thyroiditis	LT with steroids	None	NIL	NIL
Hypertension	LT with (1) calcium channel blockers (2) ace inhibitors	Constipation,	1	2%
		Dry cough	2	4%
Ischemic heart disease	LT with (1) nitrates (2) anti-platelet agent	Headache,	4	8%
		None	NIL	NIL
Pulmonary tuberculosis	LT with AKT	None	NIL	NIL
Bronchial asthma	LT with bronchodilators	Gastritis,	2	4%
		Rhythm disturbance	1	2%

**DISCUSSION**

Hypothyroidism is the most common disorder of thyroid gland. The clinical syndrome of hypothyroidism is the result of deficient production of thyroid hormone or very rarely the defect in its receptor. In hypothyroidism, virtually every tissue, every organ and every in the body is affected to a greater or lesser extent.

**Table 10: Comparing age distribution in the hypothyroid patients.**

Age groups (years)	Vairamanikandan et al <sup>3</sup>	Present study
0-40	28	22
41-60	17	25
>60	5	3
Total	50	50

**Table 11: Gender distribution of hypothyroid patients.**

Studies	Gender		Total no. of patients	(%)	
	M	F		M	F
Vairamanikandan et al <sup>3</sup>	17	33	50	34	66
Sinha and bhattachar <sup>4</sup>	12	44	56	21.42	78.57
Present series	14	36	50	28	72
V.c. matthew <sup>5</sup>	7	21	28	25	75
Rakesh dhadhal <sup>6</sup>	25	3	28	10.72	89.28
Arindam bose <sup>7</sup>	515	1614	2129	31.90	68.10

The clinical picture that emerges, however, depends on a variety of factors particularly age of the patient, rate of onset of deficiency and the severity or degree of deficiency. In this study, an attempt has been made to study this varied clinical profile of hypothyroidism (Table 10). In table 10 comparison confirms hypothyroid state is more common after third decade of life, especially 5th decade similar to 50% in present series.

Hypothyroidism was more common amongst female patients in all series (66-89.28%) and clinical hypothyroidism is 3 times more common in female compare to males in present study and also in other studies (Table 11). Most of patients were having primary (idiopathic) hypothyroidism, while secondary hypothyroidism due to Hashimoto’s thyroiditis varied from 3-11% (Table 12).

**Table 12: Etiology of hypothyroidism.**

Studies	Etiology		No. of patients	Percentage (%)	
	Idiopathic	Hashimoto’s		Idiopathic	Hashimoto’s
Kikuchi et al <sup>8</sup>	16	2	18	88.8	11.2
Present studies	49	1	50	98	2

**Table 13: Symptomatology of hypothyroid in patients (n=50).**

Symptom	Larson et al <sup>9</sup>	Present study (%)
Generalized weakness	99	98
Lethargy	91	92
Decreased sweating	89	56
Cold sensation	89	70
Memory impairment	66	20
Constipation	61	58
Weight gain	59	70
Breathlessness	55	70
Hoarseness	52	78
Anorexia	45	90
Menorrhagia	32	16
Palpitation	31	32
Precordial pain	26	30

Generalized weakness and lethargy were predominant symptoms with patients presented. Other symptoms were anorexia, weight gain, change of voice (hoarseness of voice) and breathlessness. Decreased sweating, sensation of cold, impairment of memory, were not common in present series (Table 13).

**Table 14: clinical signs of hypothyroid patients.**

Clinical sign	Larsen et al <sup>9</sup>	Present study (%)
Dry skin	97	72
Coarse skin	97	72
Coarse hair	95	14
Slow speech	91	32
Boggy eyelids	90	56
Cold skin	83	60
Thick tongue	82	12
Puffiness of face	79	68
Pallor of skin	67	60
Loss of hairs	57	32
Pallor of lips	57	28
Bilateral non pitting edema	55	72
Nervousness	35	20

Patients presenting with bilateral non-pitting edema and puffiness of face, skin changes and changes in hair were common in Lippincott study. Most patients were having overt hypothyroidism in Lippincott study while they were less common in our study because subclinical signs like S. bradycardia, thyroid swelling and delayed relaxation of



ankle jerk were not taken into consideration in their study. Dr. A. M. Somalwal has noticed patients having gradual onset of progressive cerebellar syndrome without involvement of cranial nerves or pyramidal tract involvement.<sup>10</sup> This study had none (Table 14).

**Table 15: Cholesterol level in hypothyroid patients**

Studies	Normal value	Hyper-cholesterolemia	Mean value
Vairamanikand an et al <sup>3</sup>	57.14%	42.8%	233.18
Present study (n=30)	42%	58%	215.22

**Table 16: Thyroid function test of hypothyroid patients.**

Tests	Sinha and bhattacharya <sup>4</sup> (n=56)	Present series (n=50)
Serum T3	0.51 +/- 0.05 nmol/l	0.473 nmol/l
Serum T4	20.31 +/- 2.4 ng/ml	2.05 ng/ml
Serum TSH	52.61 mu/l	43.72 mu/l

Hypercholesterolemia was seen in about 58% of patients in this study. In hypothyroid state, LDL fraction and triglyceride were mostly affected, and HDL fraction was decreased. This was mostly because of both lipid synthesis and degradation of lipid were at slower rate. Caraccio N. Ferrannin, concluded in his study that only serum LDL levels are increased specifically and reversibly in association with subclinical hypothyroidism.<sup>11</sup> Altered Lipoprotein (a) values reflect a

genetic influence rather than a reduced thyroid hormone action (Table 15).

In hypothyroidism, there is decreased amount of circulating levels of serum T3 and T4, that leads to stimulation of pituitary gland and hypothalamic region both of which leads to increase level of serum TSH which result in increased synthesis of thyroid hormone in blood.

Serum TSH is most sensitive parameter for diagnosis of hypothyroid state. Ditta A and Tauyab M proposed from their study that estimation of TSH in the patients with type-1 diabetes may be useful in the early identification of thyroid dysfunction. It is observed that mean value of S. TSH increased in both of series while S. T3 and S. T4 levels were reduce in both the series (Table 16).

**Table 17: Changes in X-ray chest PA view in hypothyroid patients**

Studies	Cardiomegaly	No. of patients	%
V.C. Mathew Roy <sup>5</sup>	22	28	78.75%
Present study	12	50	24%

Cardiomegaly was considered when cardiothoracic ratio was more than 0.5. They could be due to peri-cardinal effusion, cardiomyopathy, CCF, anemia etc. There were differences in patients having cardiomegaly in present series and V.C. Mathew Roy study group, it may be due to the fact that most of the patients were having full blown picture of myxedema and study was targeted for study of pericardial effusion in latter series (Table 17).<sup>5</sup>

**Table 18: Electrocardiographic changes in hypothyroid patients.**

ECG changes	V.C. Mathew Roy series <sup>5</sup> (N=28)		Present series (N=50)	
	No. of patient	Percentage	No. of patient	Percentage
ST-T changes	13	46.42	12	24
Low voltage complex	2	7.15	10	20
Sinus bradycardia	7	25	12	24

**Table 19: Echocardiographic findings in hypothyroid patients.**

Pericardial effusion	V.c. Mathew Roy series <sup>5</sup> (n=16)		Present series (n=50)	
	No. of patients	%	No. of patients	%
Mild	6	37.5	4	8
Moderate	8	50	3	6

The findings were similar in both V.C. Mathew Roy series and in present series.<sup>5</sup> Common ECG findings in

study groups were sinus bradycardia, low voltage ECG and ST-T changes which are 24%, 20%, and 24% respectively (Table 18).

Moderate amount of pericardial effusion was seen in 50% of patients in V.C. Mathew Roy series and it could be mainly due to most of patients having overt hypothyroidism. In present series 8% of patients were having mild pericardial effusion while 6% of patients had moderate pericardial effusion (Table 19).<sup>5</sup>

All the patients after confirmation of hypothyroidism by clinical data and supported laboratory investigations,

were put-on lowest dosage of Levo-thyroxine (0.1 mg). Then dosage of replacement therapy was increased in subsequent follow-up visits at interval of 6-8 weeks. Reviewing patient's symptoms, particularly paying attention to development of new symptoms, like angina pain, palpitation and by keeping watch on patient wellbeing, dosage of Levo-thyroxine had been adjusted individually. Thyroid function tests, particularly TSH estimation were done after six weeks of starting therapy. Then it was repeated annually or when required. Side effects of L-thyroxine were chest pain and palpitation. Chest pain was in 10% patients and it was non-specific, non-cardiac and not due to coronary artery disease. No definite explanation can be offered for this and therefore it was assumed to attribute as side effect of L-thyroxine. Palpitation is a well-known side effect of L-thyroxine and was observed in 6% patients. This was commonest amongst the patients of Ischemic Heart Disease and anaemia. Palpitation appeared to be related with dosage L-thyroxine as increase in the dosage resulted in palpitation. However, it was tolerated well. Conditions co-existing with hypothyroidism like hypertension, Ischemic Heart Disease, pulmonary Koch's, Bronchial asthma were treated accordingly with addition of L-thyroxine. On follow-up examination at three weeks, none of the patients were having side effects due to treatment regime used for co-existing medical disease. None of the complications were observed during follow-up examination and there was no mortality.

## CONCLUSION

This study thus concludes, hypothyroidism as a clinical entity is common between 4<sup>th</sup> and 6<sup>th</sup> decade of life and seen more among females. Though etiology remained unknown in majority of the patients, weakness, and lethargy were the common clinical presentation and pedal edema with puffiness of face being the common clinical findings. Hypertension and heart disease were the commonest comorbidities in this study.

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