Study of Clinicobiochemical Spectrum of Hypothyroidism

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Abstract

Background: The aim of this study was to assess the clinico biochemical spectrum of hypothyroidism and the relative importance of thyroid function tests, clinical symptoms and signs in thyroid dysfunction.

Methods: A retrospective study was done and 1702 requisitions for screening of hypothyroidism were analysed. The clinical presentation of cases was correlated with the results of thyroid profile tests.

Results: 31.5% of the 1702 cases referred had thyroid dysfunction in the form of subclinical or overt hypothyroidism. In the hypothyroid group generalized weakness, weight gain and myxoedema was common. In cases of primary infertility and depression, subclinical and overt hypothyroidism was high (40% and 45.8% respectively). The average age of females with subclinical hypothyroidism was 30.8 years, 5.4 years less than females with overt hypothyroidism.

Conclusion: We conclude that hypothyroidism is common and often under-diagnosed. Therefore routine evaluation of female patients with weight gain, generalized weakness, infertility, depression and mood changes should include thyroid profile.

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Key Words : Hypothyroidism; Thyroid profile; Screening; Infertility; Depression

Introduction

Hypothyroidism in adults has an insidious onset with a range of non-specific symptoms resulting in delayed diagnosis. Many of the common signs and symptoms of hypothyroidism occur frequently in euthyroid patients. Common symptoms such as fatigue, lethargy and constipation have limited diagnostic value, while weakness, insomnia and loss of memory are usually attributed to old age [1].

This downgrading of clinical aspects of hypothyroidism has paralleled the increase in demand for thyroid function tests over the past 20 years. Few authors believe that a diagnosis of clinical hypothyroidism can be made on the basis of biochemical measurements alone and that signs and symptoms are not important [2]. Others challenge this statement and maintain that biochemical tests can be misleading and that diagnosis can be made on clinical grounds alone [3]. Therefore an attempt was made to study the clinico-biochemical spectrum of hypothyroidism and the relative importance of thyroid function tests.

Material and Methods

A hospital based retrospective study was done. During the study period 2560 requisitions were received from which 289 known cases of hypothyroidism, 64 cases of hyperthyroidism and 505 cases referred with clinical suspicion of hyperthyroidism were excluded. Remaining 1702

requisitions were studied. These cases were referred for screening or confirmation of clinical suspicion of hypothyroidism. All these cases were clinically analysed on a preset proforma and arranged into two groups. Group -1 included cases referred with high index of suspicion, having two or more of the signs or symptoms of hypothyroidism (Table 1), and the remaining cases were included in Group- 2. This group included cases referred with vague or non-specific signs and symptoms on routine screening. The two groups were further graded as subclinical, overt hypothyroidism and normal cases (Table 2) based on the results of T3, T4 and thyroid stimulating hormone (TSH) [2].

Serum T3, T4 and TSH was determined by radioimmuno assay (RIA) method using kits from BARC, Mumbai. Normal ranges of T3, T4 and TSH were 0.7-2.0 ng/ml, 5.5-13.5µg/dl and 0.17-4µIU/ml, respectively. The sensitivity of assay for TSH was 0.025µIU/ml.

Results

Analysis of the 1702 cases revealed that 946 cases were referred with high index of clinical suspicion (Group-1) and 756 were referred with vague symptoms or occasional signs and symptoms of hypothyroidism (Group-2). The distribution of subclinical hypothyroidism, overt hypothyroidism and normal biochemical profile as per T3, T4 and TSH values in the above groups is given in Table 3.

Of 1702 cases, 31.5% had thyroid dysfunction in the form of subclinical or overt hypothyroidism (Table 3). In Group-1, 380 (40%) had subclinical hypothyroidism and 24 (3%) were

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Table 1**Signs and symptoms of hypothyroidism**

Symptoms	Signs
1. Diminished sweating	1. Slow movements
2. Hoarseness	2. Delayed ankle reflex
3. Paraesthesia	3. Coarse skin
4. Dry skin	4. Periorbital puffiness
5. Constipation	5. Myxoedema
6. Hearing impairment	6. Cold skin
7. Weight gain	7. Bradycardia
8. Cold intolerance	
9. Depression	

Table 2**Definitions of hypothyroidism**

Diagnosis	TSH	Thyroxine levels
Subclinical hypothyroidism		
Grade-1	Above upper limit (4 - 10 mU/L)	Normal
Grade-2	10.1-20mU/L	Normal
Grade-3	>20mU/L	Normal
Overt hypothyroidism	Raised	Low

Table 3**Distribution of cases in Group-1 and Group -2**

	Subclinical hypothyroidism	Overt hypothyroidism	Normal
Group-1 (946)	380 (40%)	24 (3%)	542 (57%)
Group-2 (756)	119 (16%)	13 (2%)	624 (82%)
Total (n=1702)	499	37	1166

overtly hypothyroid while 57% cases were incorrectly clinically classified as hypothyroidism and they had normal biochemical thyroid profile. 119 (16%) cases had subclinical hypothyroidism, 13 (2%) had overt hypothyroidism and 82% had normal thyroid profile in Group-2. Chi-square test was done on the above data and there was a significant difference in distribution of cases in Group-1 and 2 (p value <0.001).

There were 37 cases of overt primary hypothyroidism. Out of 499 cases of subclinical hypothyroidism, 283 were Grade-1, 105 Grade-2 and 111 Grade-3 while 1176 cases had normal parameters. The details of thyroid profile values are given in Table 4. There was no significance difference in the TSH values between Group-1 and Group- 2 in subclinical and overt

Table 4**Levels of T3, T4 and TSH in subclinical, overt hypothyroidism and normal cases**

		n	TSH (mIU/L)				T3(ng/ml)				T4(µg/ml)			
			Mean	Min	Max	SD	Mean	Min	Max	SD	Mean	Min	Max	SD
Subclinical hypothyroidism	Gp 1	380	11.2	4.3	34.3	12.0	1.06	0.7	2	0.27	9.62	5.5	13.2	1.8
	Gp 2	119	10.9	4	30.2	12.3	1.89	0.92	1.9	0.32	9.9	5.5	13.5	1.7
Overt hypothyroidism	Gp 1	24	56.9	9.4	92.9	26.3	0.44	0.01	1.09	0.19	1.71	0.01	5.30	1.52
	Gp 2	13	56.4	7.5	90.1	25.7	0.61	0.42	1.6	0.27	1.89	0.93	4.98	1.32
Normal	Gp 1	542	1.7	0.18	4	1.05	1.4	0.8	2	0.3	8.36	5.01	11.67	2.1
	Gp 2	624	1.9	0.36	4	1.2	0.9	0.93	2	0.41	10.9	5.6	12.99	1.97

cases. In our study, seven (18.9%) hypothyroid cases had low T4 and normal T3 while rest of the 30 cases had low T3 and T4 levels. No case had low T3 and normal T4 levels. Out of 37 hypothyroid cases, 32 (86.9%) were females and five males. The average age was 36.2 years in females and 46.8 years in males. In 499 cases of subclinical hypothyroidism, 440 were females and 59 were males. The average age in this group was 30.8 years in females and 45.3 years in males. In this group, the mean age in the females was 14.5 years less than in the males, which was statistically significant (p<0.001). It is also seen that the average age in females with subclinical hypothyroidism is 5.4 years less than those with overt hypothyroidism and this difference was statistically significant (p<0.001).

The analysis of the clinical presentation of the hypothyroid cases is given in Table 5. Weight gain was a common symptom in both the groups (62.5% and 53.8% in Group-1 and 2 respectively). Myxoedema was the commonest sign in both groups accounting for 37.5% of cases in Group- I and 15.3% in Group-2. Generalized weakness (66.6%) and weight gain (62.5%) were the commonest symptoms in Group-1 followed by mood changes and dry skin. Cold intolerance was present in 33.3% and change of voice in 4.16% cases. However in Group-2 weight gain was the most common symptom (53.8 %) followed by mood changes (46.1%). In Group-1 dry skin and myxoedema was commonest, pedal oedema was seen in 25%, bradycardia in 4.16% and delayed ankle jerks in 12.5% cases. In Group-2, myxoedema and coarse skin was seen in 15.3 % cases. None had bradycardia, delayed ankle jerks, slow movement or cold skin.

Out of 1702 cases reviewed, 306 cases were referred from gynaecology out patient department (OPD) and primary infertility (105 cases, 34.3 %) was the commonest cause (Table 6). Three patients of primary infertility were hypothyroid and 39 (37.1%) patients had subclinical hypothyroidism (total of 40% had thyroid dysfunction in the form of subclinical or overt hypothyroidism). Of the 28 cases referred with dysfunctional uterine bleeding (DUB), two were hypothyroid and 12 (42%) had subclinical hypothyroidism. Other causes of subclinical hypothyroidism were secondary infertility (15.25%) and recurrent abortions (10.25%).

Most of the patients referred by the surgeons were cases of goitre. A total of 153 patients had goitre of which two were detected to have subclinical hypothyroidism and none had overt hypothyroidism.

A large number of cases (n=194) were referred from

Table 5**Clinical presentation of hypothyroid cases**

Symptom	% Occurrence		Sign	% Occurrence	
	Group-1 (n=24)	Group-2 (n=13)		Group-1 (n=24)	Group-2 (n=13)
Generalised weakness	66.6	30.7	Myxoedema (puffiness of face, hands and feet)	37.5	15.3
Weight gain	62.5	53.8	Coarse skin	33.3	15.3
Mood changes	54.16	46.1	Pedal oedema	25.1	7.6
Dry skin	45.8	15.3	Delayed ankle jerks	12.5	Nil
Constipation	41.6	7.6	Slow movements	8.3	Nil
Menorrhagia	37.5	23.07	Cold skin	8.3	Nil
Cold intolerance	33.3	Nil	Bradycardia	4.16	Nil
Poor mentation	16.6	Nil			
Headache	12.5	23.07			
Increased hair fall	8.3	30.7			
Hoarseness of voice	4.16	Nil			
Palpitations	Nil	15.3			
Impaired hearing	Nil	Nil			
Giddiness	Nil	7.6			

Table 6**Details of the cases referred from gynaecology OPD**

Diagnosis	Normal (%)	Hypothyroidism (%)	Subclinical hypothyroidism (%)	Total
Primary infertility	63 (60)	3 (2.8)	39 (37.1)	105
Secondary infertility	50 (84.8)	-	9 (15.2)	59
Dysfunctional uterine bleeding (DUB)	14 (50)	2 (7.2)	12 (42.8)	28
Bad obstetric history (BOH)	35 (89.8)		4 (10.2)	39
Fibroid uterus	8 (80)		2 (20)	10
Antenatal cases	19 (95)		1 (5)	20
Post partum cases	19 (86.4)		3 (13.6)	22
Endometriosis	3 (100)		-	3
Uterovaginal prolapse	6 (100)		-	6
Pelvic inflammatory disease (PID)	14 (100)		-	14
Total	231 (75.6)	5 (1.6)	70 (22.8)	306

psychiatric OPD and depression was the commonest cause (n=109). Of them four had hypothyroidism and 46 (42.2%) subclinical hypothyroidism. A total of 45.8% had thyroid dysfunction in the form of subclinical or overt hypothyroidism.

Discussion

Hypothyroidism is often under diagnosed. In our study 31.5% of the 1702 cases referred had thyroid dysfunction in the form of subclinical or overt hypothyroidism. In Group - 2, 16% patients referred with vague symptoms had elevated TSH levels while 2% had overt hypothyroidism. In comparison 40% of patients with typical clinical signs and symptoms (Group-1) had subclinical hypothyroidism and 3% overt hypothyroidism. 57% cases in this group had a normal biochemical profile and were incorrectly classified clinically as hypothyroid. Bajaj et al [4] concluded that clinical parameters alone are insufficient in establishing a diagnosis of hypothyroidism and biochemical tests should be a routine criterion for establishing the diagnosis of hypothyroidism.

In community surveys 8-17% of people older than 55 years may have subclinical hypothyroidism [5] and 3-7% will have TSH values >10mU/L. The Whickham study suggested that in a population survey all the cases with a TSH concentration >6mU/L should be diagnosed as being hypothyroid irrespective of their clinical status[6].

In our study 18.9% of the hypothyroid cases had low T4 and normal T3 and rest of the cases had low T3 and T4 levels. Serum T3 concentrations are usually low in patients of hypothyroidism. However about 20- 30% have normal serum T3 due to TSH induced stimulation and extra thyroidal conversion of T4.

The most specific and discriminating features of hypothyroidism are decreased sweating, hoarseness of voice, paraesthesias, cold intolerance, delayed reflexes and periorbital oedema [7]. However in our study, we found that the symptoms of weight gain, generalized weakness and mood changes were common. The commonest sign in both the groups was myxoedema,

which accounted for 37.5% of cases in Group-1 and 15.3% in Group-2. Cold intolerance was present in 33.33%, change of voice in 4.16% and delayed reflexes in 12.5% cases.

This study also shows that in certain subgroups of patients e.g primary infertility, subclinical hypothyroidism was prevalent (37.1%). In hypothyroidism the FSH and LH secretions are usually in the normal range for the follicular phase of menstrual cycle but there is no ovulatory surge. The women therefore have irregular anovulatory cycles, excessive menstrual bleeding and tend to be infertile. On conception these patients may have normal outcome of pregnancy or an increased likelihood of abortion, stillbirth and premature delivery [7]. In our study four (10.2%) cases referred with bad obstetric history had subclinical hypothyroidism. Menorrhagia was seen in 32.4 % of hypothyroid cases. Therefore screening for hypothyroidism in these cases is of great significance. Patients with depression also had high (42.2%) incidence of thyroid dysfunction This highlights the importance of evaluating all cases of depression and mood changes for hypothyroidism.

This study suggests that the problem of hypothyroidism is prevalent significantly and is commonly under diagnosed. It is also evident that clinical parameters alone are insufficient in establishing a diagnosis of hypothyroidism and are often misleading, thus biochemical confirmation is a must. This is in accordance with the American Academy of Clinical Endocrinologists guidelines which state that appropriate laboratory

evaluation with a sensitive TSH test should always be used as the standard criterion for confirming the diagnosis [8]. The study shows that the average age of females with subclinical hypothyroidism is 30.8 years, 5.4 years less than those with overt hypothyroidism. Therefore routine screening of female patients with symptoms of weight gain, generalized weakness, mood changes, infertility and depression should be carried out so that these cases can be diagnosed and managed earlier.

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