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Original Research Article

A study of serum thyroid stimulating hormone levels, and its correlation with clinical features and delayed diagnosis of hypothyroidism in central India

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ABSTRACT

Background: The clinical manifestations of hypothyroidism are variable, depending upon its cause, duration and severity. The spectrum extends from subclinical to overt hypothyroidism to myxedema coma. A high degree of suspicion is thus required in order to appreciate the clinical manifestation of the disorder to reach a diagnosis. Purpose of this study was to correlate serum TSH level with severity of clinical manifestations and evaluate possible cause of delay in the diagnosis.
Methods: A cross section observational and descriptive study for the assessment of severity of primary hypothyroidism at presentation and evaluation of the causes of delay in diagnosis in 86 patients was done from December 2012 to November 2013 in the Department of Medicine, MGM Medical College, Indore, MP, India.
Results: Illiterate patients had significantly (p value 0.002) higher TSH values at presentation. 34.8% of patients presented as severe hypothyroidism with TSH value >100 mIU/L. Delay of as much as 7 years was noted. Majority of patients had a delay of around 1 to 3 years in diagnosis. Only 4.6% patients were diagnosed without any delay due to high level of suspicion at presentation.
Conclusions: Due to non-specific symptomatology of hypothyroidism diagnosis is often delayed. Therefore, high index of suspicion is required at the physician's level and test of thyroid function is available at subsided cost therefore it should be offered to all such patients.

Keywords: Hypothyroidism, Myxoedema coma, Overt hypothyroidism, Primary hypothyroidism, Subclinical hypothyroidism, Thyroid stimulating hormone

INTRODUCTION

There are multiple systems on which thyroid hormone acts or hormone is Supplementary to their functions. Consequently, thyroid abnormalities manifest as varied presentations, ranging from routine complaints like fatigue to painful neuropathies.

Hypothyroidism is a clinical state resulting from an insufficient amount of circulating thyroid hormone to support normal body function. It may exist in utero or develop in infancy, childhood or even in adult life. The prevalence of unsuspected overt hypothyroidism, defined as the combination of biochemical and clinical findings of hypothyroidism, ranges from 1-18 cases per thousand persons.

The female to male ratio in hypothyroidism ranges from 2:1 to 8:1 in various epidemiological survey.[1] Recent surveys indicate hypothyroidism to be more prevalent in elderly population, reaching as high as 20%. The incidence of congenital hypothyroidism was reported to

be 1 in 2640 in a study from this country.[2] A study of the Framingham population showed that 59% of the women and 2.4% of men above the age of sixty had serum TSH levels more than 10 mU/ml.[3] In a survey of 2779 persons carried out in in Durham, England hypothyroidism was detected in 1.9% of women and was overt in 1.4%. The prevalence in men was less than 0.1 percent.[4]

In iodine-replete areas, autoimmune thyroid disease and thyroid ablative therapy is the major reasons of hypothyroidism. Even in children and adolescents, autoimmune thyroiditis is the commonest cause of non-endemic thyromegaly and acquired hypothyroidism.[5] However, worldwide, iodine deficiency is the leading cause.[6]

The clinical manifestations of hypothyroidism are variable, depending upon its cause, duration and severity. The spectrum extends from subclinical to overt hypothyroidism to myxedema coma. The classic change is the slowing of physical and mental activities and of all the body systems. The characteristic pathological finding in a hypothyroid patient is the accumulation of hyaluronic acid and other glycosaminoglycan in the interstitial tissue.[7] Some clinical manifestations of hypothyroidism, such as chronic skin changes may take up to 3-6 months despite of proper therapy.[8]

A high degree of suspicion is thus required in order to appreciate the clinical manifestation of the disorder to reach a diagnosis. Unfortunately, there is very little information available on this subject from this part of the world. One of the objectives of this study was to look at the presenting clinical features of hypothyroidism in the population and then comparing it to the already available results from other parts of the world. Hypothyroidism is highly prevalent in India with an estimated 42 million people suffering from thyroid disorders.

Hypothyroidism is a common endocrinological disorder. Its clinical presentation is variable but well established. However, clinical features vary significantly among different populations owing to their climate, education status and awareness about the disease. This study is designed to evaluate the difference in clinical presentation of the population from already available literature. Despite the easy availability of thyroid function tests and effective therapy for hypothyroidism there is a delay in the diagnosis of hypothyroidism leading to picking up of disease at a later stage, thereby increasing morbidity at presentation. There is an urgent need to find the causes of delay and find measures to rectify the shortcomings.

METHODS

It was a cross section observational and descriptive study for the assessment of severity of primary hypothyroidism at presentation and evaluation of the causes of delay in diagnosis. Study started from December 2012 to November 2013.

In this study, a total of 86 patients were selected from endocrinology and general medicine OPD, M.Y Hospital, Indore, MP, India, over a period of 1 year. There was no age bar for inclusion in the study. Complete evaluation was done of each patient according to the Performa prepared Investigation like T3, T4, TSH, CBC, RBS/RFT, ECG, CXR, USG thyroid were done to facilitate a systematic study.

Inclusion criteria

- Age: Patients from all age groups were included in this study
- Sex Patients of both sexes were studied
- Therapy: Newly diagnosed patients and on therapy patients were included
- Population: Indian patients from all a socioeconomic class, casts and from Rural and urban areas were included in the study.

Exclusion criteria

- Seriously ill patients
- Patients with multi system diseases or cancer.
- Drug induced thyroid disorder.
- Patients with sick euthyroid syndrome
- Patients who were suffering from active renal and liver diseases.
- Patients suffering from acute psychiatric illness

Biodata of the particulars including age, sex, locality etc. were recorded. The particular undergoing any therapy regarding thyroid surgery, antipsychotic treatment and previous treatment for hyper or hypothyroidism was noted. Symptoms were recorded to aid systematic study of thyroid dysfunction.

Patients were defined diabetic if,

- Previously diagnosed and received treatment for DM
- Random blood glucose level ≥200 mg/dl with diabetic symptoms based on the ADA diagnostic criteria OR
- Fasting blood glucose level of ≥126 mg/dl.

Statistical analysis

Total 87 cases attending endocrine and general OPD in M Y Hospital, Indore with informed consent and who met the inclusion criteria were recruited.

The Statistical software namely SPSS 15.0, Stata 8.0 and Graph Pad were used for the analysis of the data. Microsoft Word and Excel software have been used to generate graphs, tables etc.

Descriptive statistical analysis has been carried out the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%).

Student t-test (two tailed, Independent) has been used to find the significance of study parameters on continuous scale between two groups. Chi-square test and fisher exact test is used for qualitative data by 2x2 contingency table, p values are two tailed, p value <0.05 is taken as statistically significant.

Significant figures

+ Suggestive significance (p value: 0.05<p<0.10)
*Moderately significant (p value: 0.01<p <0.05)
**Strongly significant (p value: p<0.01).

RESULTS

Mean age of patients of hypothyroidism that presented to the OPD was 37 years. Maximum patients belonged to the age group of 21 to 30 years followed by 31 to 40 years (Table 1).

Table 1: Age distribution of patients of hypothyroidism.

Age distribution	No. of patients (%)
11 to 20	5(5.8)
21 to 30	25(29)
31 to 40	23(26.7)
41 to 50	16(18.6)
51 to 60	11(12.8)
61 to 70	5(5.8)
Mean Age = 37 years	

There was statistically significant (p value=0.002) correlation between literacy and TSH levels. It means illiterate patients had significantly higher TSH values at presentation (Table 2).

Table 2: Association between TSH levels and literacy.

TSH level (mIU/L)	Literate	Illiterate
<10	17	5
11-100	13	20
>100	8	18

X^2=12.5, df=2, p value=0.002

Mild, moderate and severe hypothyroidism was present in 27.9%, 37.7% and 34.8% patients respectively. Years delayed in diagnosis of mild, moderate, and severe hypothyroidism was 1.2 years, 2.1 years and 4.3 years respectively. There was a rise in the TSH level found at presentation. It suggests that with active screening at earlier stages, hypothyroidism might have been picked up at an earlier stage (Table 3).

Table 3: Level of hypothyroidism at presentation and years delayed in diagnosis.

TSH (in mIU/L)	Patients (%)	Years delayed in diagnosis
5 to 9.9	24(27.9)	1.2years
10 to 100	32(37.2)	2.1years
>100	30(34.8%)	4.3years

In this study delay of as much as 7 years was noted. Majority of patients had a delay of around 1 to 3 years in diagnosis in diagnosis. Only 4 patients out of 86 were diagnosed without any delay due to high level of suspicion at presentation (Table 4).

Table 4: Delay in diagnosis of hypothyroidism.

Delay in diagnosis	No. of patients
None	4
<1 year	13
1 to 2 years	18
2 to 3 years	19
3 to 4 years	8
4 to 5 years	5
5 to 6 years	13
>6 years	6

Patient ignorance was the commonest cause of delay in diagnosis. Significantly 20% of cases had a diagnostic delay due to lack of strong clinical suspicion due to nonspecific symptomatology in hypothyroid patients (Table 5).

Table 5: Causes of delay in the diagnosis of hypothyroidism.

Causes of delay	No of patients
Patient ignorance	61
Lack of suspicion	20
Both	1
Incidentally detected	1
No Delay	3

Tiredness (79%), weight gain (67%), hair loss (46%) and inappropriate cold (38%) were most common symptoms observed in this study. Puffy hands and feet (60%) were most common signs observed. As most of the patients were on treatment, bradycardia and delayed tendon reflexes were probably not detected at presentation as expected (Table 6).

DISCUSSION

Hypothyroidism was predominantly seen in females. 87% patients were females, Female: Male ratio being 7:1. In a survey of 2,779 persons carried out in Country Durham, England, hypothyroidism was detected in 1.9% of females and was overt in 1.4%. The prevalence in males was less than 0.1%. A study of the Framingham population showed

that 5.9% of the women and 2.4% of men above the age of sixty had serum TSH levels more than 10 mU/L[3]. Watanakunakorn C et al, reported female to male ratio of 4.79:1 in their series of 400 cases of myxedema.[9] Grave's disease, Hashimoto's disease and primary myxedema are considered as closely related autoimmune thyroid diseases. It has been postulated that amongst the factors influencing the pathogenesis of these autoimmune diseases, sex hormones influences are significant. In general estrogen enhances and testosterone reduces antibody responses. This is probably the reason for the female preponderance seen in all the autoimmune disorders.

Table 6: Symptoms distribution in patients of hypothyroidism.

Symptoms	Present	Absent
Tiredness	68(79%)	17(21%)
Dry Skin	24(28%)	61(72%)
Feeling Cold	35(40.7%)	50(59.3%)
Hair Loss	40(46.5%)	45(53.5%)
Difficulty in concentrating	19(22%)	66(78%)
Constipation	25(29%)	60(71%)
Weight gain	57(66.2%)	28(33.8%)
Dyspnoea	34(39.5%)	51(60.5%)
Hoarse voice	19(22%)	66(78%)
Menorrhagia	16(18.6%)	69(81.4%)
Amenorrhea	12(14%)	73(86%)
Paresthesia	33(38.3%)	51(61.7%)
Signs	**Present**	**Absent**
Dry coarse Skin	19(22%)	67(78%)
Cool peripheral extremities	16(18.6%)	70(81.4%)
Puffy hands, feet	52(60.4%)	34(39.6%)
Diffuse alopecia	16(18.6%)	70(81.4%)
Bradycardia	7(8%)	79(92%)
Peripheral edema	39(45.3%)	47(54.7%)
Delayed tendon reflexes	6(7%)	80(93%)
Carpel tunnel syndrome	0(0%)	86(100%)
Serous cavity effusion	6(7%)	80(93%)

Mean age of patients of hypothyroidism that presented to the OPD was 37 years. Maximum patients belonged to the age group of 21 to 30 years followed by 31 to 40 years. 56% of the patients presented in the age group of 20 to 40 years. 16% presented above the age of 50 years.

In this study 53% patients diagnosed as hypothyroid were illiterate. It was an important association in evaluating the cause in delay in diagnosis. Most of the patients coming to the tertiary care centre belonged to lower socio economic group. Probably because of illiteracy there was ignorance on the part of patients in coming to health care facilities for early diagnosis.

The p value (0.002) in the comparison between TSH values and illiteracy suggests that correlation between TSH values and illiteracy is significant. It means illiterate patients had significantly higher TSH values at presentation.

Statistically 28% cases presented with TSH value 5 to 10 mIU/L, 40% presented with TSH value of 10 to 100 mIU/L. Significantly high (32%) patients in this study presented with severe hypothyroidism with TSH value >100. There are some studies suggesting that a certain subgroup of subclinical hypothyroid patients progress to overt hypothyroidism over years. There is a possibility that delay in picking up these patients at earlier stage because of lack of suspicion might be causing such a high percentage presenting with severe disease. It was found that as there was delay in diagnosis of hypothyroidism, there was a rise in the TSH level found at presentation. It suggests that with active screening at earlier stages hypothyroidism might have been picked up at an earlier stage. Mean delay in diagnosis was 1.2 yr. for TSH range of 5 to 10 at presentation. For a TSH level of 11 to 100 at presentation the Mean delay was 2.1 years. While for a TSH level of >100 at presentation the mean delay was 4.3 years. Only 3 patients out of 86 were diagnosed without any delay from development of symptoms. All 3 of them were young literate females, with two presenting with a TSH in range of 5 to 10 mIU/L. In a study by Rosario PW et al, 117 patients with TSH levels ranging from 5 to 10 mIU/L and normal free T4, without a previously known history of thyroid disease, were followed for a period of 3 years and had two consecutive assessments. 27.3% required replacement therapy with levothyroxine (L-T4) because of progression to overt hypothyroidism or persistence of serum TSH >10 mIU/L over the next 3 years.[10]

It was noticed that delay in diagnosis is related to illiteracy, ignorance of patients, and lack of strong clinical suspicion due to nonspecific symptomatology.

- In the group of patients presenting with a TSH level of 5 to 10 mIU/L, delay from symptom onset was seen in 60% cases due to patient ignorance.
- In the group of patients presenting with a TSH level of 10 to 100 mIU/L, delay from symptom onset was seen in 75% cases due to patient ignorance.
- In the group of patients presenting with a TSH level of >100 mIU/L, delay from symptom onset was seen in 85 % cases due to patient ignorance.

Thus, as the delay in diagnosis of hypothyroidism occurs, percentage of cases delayed due to patient ignorance goes on increasing. Lack of suspicion was seen in 40% of patients presenting with 5 to 10 mIU/L of TSH at presentation.

- In this study 22 % of patients presenting with a TSH level of 5 to 10 mIU/L were illiterate.
- 60% of patients presenting with a TSH level of 10 to 100mIU/L were illiterate
- 70% patients presenting with a TSH level of >100 mIU/L were illiterate.

Thus, percentage of illiteracy goes on increasing as delay is noticed in the diagnosis.

CONCLUSION

Due to non-specific symptomatology of hypothyroidism diagnosis is often delayed. Therefore, high index of suspicion is required at the physicians level and test of thyroid function is available at subsided cost therefore it should be offered to all such patients.

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