

CLINICAL PROFILE OF PATIENTS HAVING SUBCLINICAL AND CLINICAL HYPOTHYROIDISM ATTENDING GENERAL MEDICINE OPD OF A TERTIARY CARE MEDICAL CENTER

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ABSTRACT

Objective: The objective of this study was to analyze and compare the clinical profile of patients having clinical and subclinical hypothyroidism.

Methods: This was a comparative observational study in which adult patients with clinically overt and subclinical hypothyroidism were included on the basis of predefined inclusion and exclusion criteria. Written and informed consent was obtained from all the patients. Demographic details such as age gender and occupation were noted. The normal reference values of T3, T4, and TSH for diagnosis of subclinical and clinical hypothyroidism were taken to be 0.8–2 ng/mL, 5.5–12.2 µg/dL, and 0.3–4.5 µIU/mL. The cases were divided into two groups, namely, Group C (clinical hypothyroidism) and Group SC (Subclinical hypothyroidism). Mean T3, T4, and TSH levels and clinical signs and symptoms were compared in both the groups. SSPS 21.0 software was used for statistical analysis and $p < 0.05$ was taken as statistically significant.

Results: In cases of clinical hypothyroidism out, there were 42 (70%) females and 18 (30%) males, whereas in cases of subclinical hypothyroidism, there were 38 (63.33%) females and 22 (36.67%) males. There was an overall female preponderance in both the groups. The mean age of patients in group C was found to be 39.48±12.36 whereas the mean of patients in SC group was found to be 42.82±13.46. The mean T3 and T4 were low in clinical hypothyroidism and mean TSH levels were high and the difference was statistically highly significant ($p < 0.0001$). In cases with clinical as well as subclinical hypothyroidism, the most common clinical features were dry skin, fatigue, and cold intolerance. The prevalence of fatigue, weight gain, cold intolerance, dry skin, pedal edema, and thyroid swelling was more in patients with clinical hypothyroidism as compared to the patients with subclinical hypothyroidism and the difference was found to be statistically significant.

Conclusion: The clinical presentation of clinical as well as subclinical hypothyroidism varies and a high index of suspicion is necessary for the diagnosis particularly in cases of subclinical hypothyroidism so that appropriate interventions can be undertaken.

Keywords: Hypothyroidism, Clinical features, Thyroid function test, Gender distribution.

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INTRODUCTION

Hypothyroidism, a condition where there is reduced levels of thyroid hormone secondary to insufficient production of thyroid hormones, primarily thyroxine (T4) and triiodothyronine (T3), by the thyroid gland. This condition profoundly influences various physiological processes, including metabolism, energy expenditure, and thermoregulation [1].

The pathophysiology of hypothyroidism is rooted in dysfunction at various levels of the hypothalamic-pituitary-thyroid axis. TSH stimulates the thyroid gland to produce and release T4 and T3 [2]. In hypothyroidism, this harmonious sequence is disrupted in conditions such as autoimmune thyroiditis (Hashimoto's disease), iodine deficiency, or congenital abnormalities. These etiological factors contribute to a deficiency in thyroid hormones, leading systemic effects that define the clinical profile of hypothyroidism [3].

Hypothyroidism is divided into clinical and subclinical forms on the basis of severity of thyroid hormone deficiency and the presence of clinical symptoms. Clinical hypothyroidism is characterized by elevated TSH levels accompanied by reduced free T4 and T3, along with overt clinical manifestations [4]. The usual symptoms in cases of clinical hypothyroidism are fatigue, weight gain, cold intolerance, and in neglected cases cognitive impairment may also develop. In contrast, subclinical hypothyroidism is defined by elevated TSH levels with normal free T4 and T3 concentrations and an absence of overt clinical symptoms. This subtle presentation often makes the detection of subclinical hypothyroidism challenging without routine thyroid

function tests [5]. Distinguishing between clinical and subclinical hypothyroidism is crucial, as it impacts patient management and therapeutic interventions. Clinical hypothyroidism demands prompt initiation of thyroid hormone replacement therapy to alleviate symptoms and prevent long-term complications. Whereas in cases of subclinical hypothyroidism, the management strategy is not straightforward and considerable controversies exist regarding its management [6].

Hypothyroidism affects multiple organ systems. Classical symptoms include cold intolerance fatigue, weight gain, constipation, dry skin, and in some cases cognitive impairment. However, the severity and prevalence of these symptoms vary between clinical and subclinical hypothyroidism [7]. Patients with clinical hypothyroidism often present with more pronounced symptoms. Subclinical hypothyroidism, on the other hand, may exhibit milder or even absent symptoms, posing a diagnostic challenge. Subtle manifestations, such as elevated cholesterol levels and impaired diastolic function, may be early indicators of subclinical hypothyroidism, necessitating a comprehensive understanding of its clinical spectrum [8].

Despite the extensive body of literature on hypothyroidism, there exists a noticeable knowledge gap in clinical profiles of patients with subclinical and clinical hypothyroidism. There are many studies which have analyzed the clinical profile of patients with clinical and subclinical hypothyroidism separately, but very few studies have systematically compared the distinct features of these two entities [9]. This knowledge gap poses a significant challenge for treating physician as it affects their ability to undertake interventions based on the severity of thyroid dysfunction and the presence of clinical symptoms. Addressing this

gap is crucial for refining diagnostic criteria, optimizing treatment strategies, as well as improving patient outcomes [10].

With this background, we undertook this cross-sectional study to analyze and compare the clinical profile of patients having clinical and subclinical hypothyroidism.

METHODS

This was a comparative observational study in which adult patients with clinically overt and subclinical hypothyroidism were included on the basis of predefined inclusion and exclusion criteria. The study was conducted in the Outpatient Department of General Medicine, Basaweshwar Teaching and General Hospital, Kalaburagi, India. The sample size was calculated on the basis of pilot studies done on the subject of hypothyroidism. Assuming 90% power and 95% confidence interval, the sample size required was 55 patients. Based on central limit theorem, sample size was calculated to be sufficient if it was more than 55 thus, 60 patients were included in our study in each group. Demographic details such as age, gender, occupation, and socioeconomic status were noted. Height, weight, as well as body mass index were also noted in all the cases. The detailed history with respect to duration of symptoms were asked and noted. Presence of any comorbid condition such as hypertension, diabetes mellitus, arthritis, or chronic obstructive airway disease was asked and noted. History of any drugs known to affect thyroid hormones (metformin, lithium, amiodarone, tricyclic antidepressants, and rifampicin) was asked for and noted. A thorough clinical examination was done with respect to any local signs such as enlarged thyroid gland (thyroid goiter or multinodular goiter) or altered consistency. A thorough systemic examination was also done in all the cases. Blood investigations such as complete blood count, CRP, ESR, and thyroid function tests were done in all the cases. Ultrasound of thyroid gland was done in selected cases. The blood samples for thyroid function tests were collected in the morning before breakfast. The normal reference values of T3, T4, and TSH for diagnosis of subclinical and clinical hypothyroidism were taken to be 0.8–2 ng/mL, 5.5–12.2 µg/dL, and 0.3–4.5 µIU/ml. Depending on the results thyroid function test and clinical features patients were labeled to be having either subclinical hypothyroidism (raised TSH and normal T3 and T4) or clinical hypothyroidism (Raised TSH and reduced T3 and T4). Patients were analyzed on the basis of thyroid function test as well as clinical features. Patients were divided into two groups as following:

- Group C: Cases with overt clinical features and raised TSH and reduced T3 and T4.
- Group SC: Cases with subtle clinical features and raised TSH with normal T3 and T4.

Mean age and gender distribution, clinical features, and thyroid function tests were compared in both the groups. The statistical analysis was done using SPSS version 21.0 software. To compare groups, independent sample t-tests were used for continuous data, while Chi-square tests were utilized for categorical data. For repeated observations, paired t-tests or repeated measures ANOVA were applied, depending on the suitability of the method. $p < 0.05$ was considered as indicative of statistical significance.

Inclusion criteria

The following criteria were included in the study:

1. Patients of either gender diagnosis to be having subclinical or overt hypothyroidism on the basis of clinical features and thyroid function test
2. Age above 18 years
3. Those who gave written and informed consent to be part of study.

Exclusion criteria

The following criteria were excluded from the study:

1. Age <18 years
2. Those patients who refused consent to be part of the study
3. Pregnant females

4. Those taking drugs known to affect thyroid hormone levels such as metformin, lithium, amiodarone, tricyclic antidepressants, and rifampicin
5. Patients with psychiatric illnesses.

RESULTS

The analysis of the patients on the basis of gender distribution showed that in cases of clinical hypothyroidism out of 60 cases, there were 42 (70%) females and 18 (30%) males, whereas in cases of subclinical hypothyroidism, there were 38 (63.33%) females and 22 (36.67%) males. There was an overall female preponderance in both groups. The gender distribution was found to be comparable in both the groups with no statistically significant difference ($p = 0.5616$) (Table 1).

The analysis of the patients on the basis of age distribution showed that in cases of patients in group C, the most common age group was 31–40 years (61.67%), whereas in group SC, most common age group was 41–50 years (38.33%). The mean age of patients in group C was found to be 39.48±12.36 whereas the mean of patients in SC group was found to be 42.82±13.46. The mean age of patients in group C and group SC was found to be comparable with no statistically significant difference ($p = 0.1595$) (Table 2).

Thyroid function tests of both the groups were compared. The mean T3, T4, and TSH levels were analyzed. The mean T3, T4, and TSH level in cases of subclinical hypothyroidism was found to be 2.3±0.31 ng/mL, 7.98±1.98 µg/dL, and 9.12±3.1 µIU/mL, whereas mean T3, T4, and TSH level in cases of clinical hypothyroidism was found to be 0.3±0.24 ng/mL, 3.7±2.64 µg/dL, and 27.98±9.12 µIU/mL. The mean T3 and T4 were low in clinical hypothyroidism and mean TSH levels were high and the difference was statistically highly significant ($p < 0.0001$) (Table 3).

Table 1: Comparison of gender distribution of the studied cases

Gender distribution	Group C		Group SC	
	Cases	Percentage	Cases	Percentage
Males	18	30.00	22	36.67
Females	42	70.00	38	63.33
Total	60	100.00	60	100.00

$p = 0.5616$ (Not Significant)

Table 2: Comparison of age groups in the studied cases

Age Group	Group C		Group SC	
	No of Patients	Percentage	No of Patients	Percentage
18–30 years	2	3.33	1	1.67
31–40 years	37	61.67	19	31.67
41–50 years	11	18.33	23	38.33
51–60 years	6	10.00	12	20.00
>60 years	4	6.67	5	8.33
Total	60	100.00	60	100.00
	Mean age: 39.48±12.36		Mean age: 42.82±13.46	

$p = 0.1595$ (Not significant)

Table 3: Comparison of thyroid function test in subclinical and clinical hypothyroidism

Comparison of thyroid function test in both the groups	Mean T3 (ng/mL)	Mean T4 µg/dL	Mean TSH µIU/mL
Subclinical hypothyroidism	2.3±0.31	7.98±1.98	9.12±3.1
Clinical Hypothyroidism	0.3±0.24	3.7±2.64	27.98±9.12
P-value	<0.0001	<0.0001	<0.0001

The analysis of clinical presentation showed that in cases with clinical hypothyroidism, the most common clinical features were dry skin (86.7%), fatigue (71.7%), and cold intolerance (61.7%). The other clinical features included weight gain (48.3%), constipation (41.7%), menstrual irregularities (35.0%), pedal edema (35%), and hair loss (30.0%) (Table 4).

In cases of subclinical hypothyroidism, also the most common clinical features were dry skin (70.0%), fatigue (50.0%), and cold intolerance (38.3%). The other clinical features included weight gain (23.3%), constipation (30.0%), menstrual irregularities (21.7%), and hair loss (18.3%) (Table 5).

The clinical features of both the groups were compared. The prevalence of fatigue, weight gain, cold intolerance, dry skin, pedal edema, and thyroid swelling was more in patients with clinical hypothyroidism as compared to the patients with subclinical hypothyroidism and the difference was found to be statistically significant ($p < 0.05$), whereas the clinical features such as constipation, hair loss, cognitive impairment, depression, menstrual irregularities, bradycardia, pallor, and hypertension though more common in patients with clinical hypothyroidism were found to be comparable in both the groups with no statistically significant difference (Table 6).

DISCUSSION

In this study of patients of clinical and subclinical hypothyroidism, the analysis of gender distribution in both the groups showed a uniform female preponderance. Many studies have reported that the hypothyroidism exhibits a notably higher prevalence in females compared to males [11]. Female preponderance in cases of hypothyroidism is attributed to factors such as autoimmune diseases (Hashimoto's thyroiditis) which are generally more common in females. Hormonal influences, particularly estrogen, have also been implicated in modulating the immune response and may contribute to the increased susceptibility of females to autoimmune thyroid disorders. In addition, the higher prevalence of goitrous hypothyroidism in women could be associated with hormonal fluctuations during puberty, pregnancy, and menopause. Unnikrishnan *et al.* conducted a study to analyze the prevalence of hypothyroidism among adult population [12]. Thyroid abnormalities were diagnosed on the basis of laboratory results). A total of 5376 adult male or non-pregnant female participants ≥ 18 years of age were enrolled, of which 5360 were evaluated. The overall prevalence of hypothyroidism was 10.95% of which 7.48% patients self-reported the condition, whereas 3.47% ($n=186$) were previously undetected. Inland cities showed a higher prevalence of hypothyroidism as compared to coastal cities. A significantly higher proportion of females versus males (15.86% vs. 5.02%) and older versus younger, adults were diagnosed with hypothyroidism. In addition, 8.02% patients were diagnosed to have subclinical hypothyroidism that anti-TPO antibodies suggesting autoimmunity were detected in 21.85% patients. The female preponderance in this study was similar to our study. The similar female preponderance in cases of hypothyroidism was also reported by the authors such as Meng *et al.* [13] and Wiersinga [14].

In our study, the mean age of patients in group C was found to be 39.48 ± 12.36 whereas the mean of patients in SC group was found to be 42.82 ± 13.46 . Kumar *et al.* conducted an observational cross-sectional study to analyze prevalence of hypothyroidism amongst adults [15]. In this study, two-fifty consecutive primary hypothyroidism participants, aged ≥ 18 years, who were on treatment for at least 3 months responded to a structured questionnaire, to assess their knowledge about the disease and adherence to treatment. The mean age of patients in this study was found to be 43.24 ± 10.80 years. The mean age of patients with clinical as well subclinical hypothyroidism was similar to this study. Similar mean age of the cases with hypothyroidism was also reported by the authors such as Gul *et al.* [16] and Lo *et al.* [17].

The analysis of clinical presentation showed that in cases with clinical as well subclinical hypothyroidism, the most common clinical

Table 4: Signs and symptoms of patients with clinical hypothyroidism

Signs and symptoms in cases of clinical hypothyroidism	Number of Patients	Percentage
Fatigue	43	71.7
Weight gain	29	48.3
Cold intolerance	37	61.7
Constipation	25	41.7
dry skin	52	86.7
Hair loss	18	30.0
Cognitive impairment	9	15.0
Depression	14	23.3
Menstrual irregularities	21	35.0
Bradycardia	9	15.0
Pallor	15	25.00
Pedal edema	21	35.00
Hypertension	13	21.67
Thyroid swelling	6	10.00

Table 5: Signs and symptoms of patients with clinical hypothyroidism

Signs and symptoms in cases of subclinical hypothyroidism	Number of patients	Percentage
Fatigue	30	50.0
Weight gain	14	23.3
Cold intolerance	23	38.3
Constipation	18	30.0
Dry skin	42	70.0
Hair loss	11	18.3
Cognitive impairment	3	5.0
Depression	8	13.3
Menstrual irregularities	13	21.7
Bradycardia	7	11.7
Pallor	11	18.33
Pedal edema	4	6.67
Hypertension	10	16.67
Thyroid swelling	0	0

Table 6: Comparison of signs and symptoms in clinical and subclinical hypothyroidism cases

Clinical feature	P value	Significance
Fatigue	0.02	Significant
Weight gain	0.007	Significant
Cold intolerance	0.0173	Significant
Constipation	0.2532	Not Significant
Dry skin	0.04	Significant
Hair loss	0.2003	Not Significant
Cognitive impairment	0.1254	Not Significant
Depression	0.2378	Not Significant
Menstrual irregularities	0.1556	Not Significant
Bradycardia	1.00	Not Significant
Pallor	0.50	Not significant
Pedal edema	0.0002	Significant
Hypertension	0.64	Not significant
Thyroid swelling	0.0274	Significant

features were dry skin, fatigue, and cold intolerance. The prevalence of fatigue, weight gain, cold intolerance, dry skin, pedal edema, and thyroid swelling was more in patients with clinical hypothyroidism as compared to the patients with subclinical hypothyroidism and the difference was found to be statistically significant. Mishra and Gupta conducted a study of patients with subclinical hypothyroidism. In this study, patients were aged 15–50 years old [18]. The most common manifestation was generalized weakness, lethargy and tiredness (60%) followed by generalized body ache (52.5%). About 46.7% of the patients had complaints of weight gain. Triglyceride levels and serum

cholesterol levels were deranged in 28.3% of all cases. Body mass index was increased in 28.3% of all patients with obesity in only two patients. Fifteen patients (11.7%) were found to be anemic with increased MCV and MCH/MCHC, attributable to hypothyroidism. Similarly, in another study on the topic of clinical hypothyroidism conducted by Jain *et al.*, the authors reported that most common symptoms in studied cases were weakness, weight gain, facial puffiness, irritability, hair loss, and menstrual irregularities. On general examination, most common findings are weight gain, pallor, dry skin, pedal edema, and goiter. Type 2 diabetes mellitus, dyslipidemia, obesity, and hypertension were commonly associated with the hypothyroidism. Similar clinical presentation in cases of hypothyroidism was also reported by the authors such as El-Shafie [19] and Khurram *et al.* [20].

CONCLUSION

The signs and symptoms of clinical as well as subclinical hypothyroidism vary and, in many cases, diagnosis is delayed due to non-specific symptomatology particularly in cases of subclinical hypothyroidism. A high index of suspicion and confirmation of diagnosis by thyroid function test at an early stage will help confirm the diagnosis and help in appropriate management of these cases.

CONFLICTS OF INTEREST

None.

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