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Original Research

A Clinical Study of Thyroid Dysfunction in Patients Presenting with Unexplained Fatigue: A Cross-Sectional Observational Study.

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Abstract

Background: Unexplained fatigue is a common clinical complaint encountered in general medical practice and may be the presenting manifestation of various underlying disorders, including thyroid dysfunction. Thyroid hormones play an essential role in regulating metabolism, energy homeostasis, and multiple physiological processes. Even mild abnormalities in thyroid function may present with nonspecific symptoms such as fatigue, lethargy, and generalized weakness, often leading to delayed diagnosis. Early identification of thyroid dysfunction among patients presenting with unexplained fatigue is crucial for timely intervention and improved clinical outcomes. **Aim:** To study thyroid dysfunction in patients presenting with unexplained fatigue.

Objectives:

1. To determine the prevalence and pattern of thyroid dysfunction among patients presenting with unexplained fatigue.
2. To evaluate the association between thyroid dysfunction and demographic characteristics, clinical features, and biochemical parameters among the study participants.

Materials and Methods: A hospital-based cross-sectional observational study was conducted among 120 adult patients presenting with unexplained fatigue. Detailed clinical history, physical examination, and biochemical investigations including thyroid function tests (TSH, FT3, and FT4) were performed. Additional laboratory investigations such as complete blood count, fasting blood sugar, and serum Vitamin B12 levels were assessed wherever indicated. Statistical analysis was performed using SPSS version 26.0. Descriptive and inferential statistical methods, including Chi-square test, Fisher's exact test, and Independent Student's t-test, were employed. A p-value of less than 0.05 was considered statistically significant. **Results:** The mean age of the study participants was 42.3 ± 11.6 years, with a female predominance (61.7%). Thyroid dysfunction was identified in 43.3% of patients presenting with unexplained fatigue. Subclinical hypothyroidism was the most common thyroid abnormality (20%), followed by overt hypothyroidism (13.3%). Significant associations were observed between thyroid dysfunction and clinical manifestations such as weight gain, hair loss, constipation, cold intolerance, menstrual irregularities, and sleep disturbances. Patients with thyroid dysfunction demonstrated significantly elevated TSH levels and significantly lower FT4, haemoglobin, and Vitamin B12 levels. Advancing age was significantly associated with an increased prevalence of thyroid dysfunction ($p = 0.022$). **Conclusion:** Thyroid dysfunction is a common and clinically significant cause of unexplained fatigue, particularly among middle-aged adults and females. Routine thyroid function screening in patients presenting with persistent fatigue facilitates early diagnosis and appropriate management. Comprehensive clinical and biochemical evaluation can improve patient outcomes by enabling timely therapeutic interventions and preventing progression of thyroid-related complications.

Keywords: Thyroid Dysfunction, Unexplained Fatigue, Hypothyroidism, Thyroid Function Tests, Subclinical Hypothyroidism.

Introduction

Fatigue is one of the most common yet nonspecific symptoms encountered in clinical practice and is frequently reported by patients attending outpatient departments of internal medicine. It is characterized by a persistent feeling of tiredness, reduced physical or mental energy, and diminished ability to perform routine activities. Although fatigue may result from lifestyle factors, psychological conditions, or chronic systemic illnesses, endocrine disorders—particularly thyroid dysfunction—constitute an important and potentially reversible cause. The nonspecific nature of fatigue often poses a diagnostic challenge, necessitating a systematic clinical evaluation to identify underlying etiologies.¹

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Thyroid hormones play a crucial role in regulating metabolism, thermogenesis, cardiovascular function, neuromuscular activity, and psychological well-being. Thyroid dysfunction encompasses a spectrum of disorders ranging from overt and subclinical hypothyroidism to overt and subclinical hyperthyroidism. Even mild abnormalities in thyroid hormone levels may manifest clinically as fatigue, lethargy, generalized weakness, exercise intolerance, cognitive impairment, mood disturbances, and reduced quality of life. Early diagnosis and treatment are therefore essential to prevent complications and improve patient outcomes.²

Globally, thyroid disorders represent one of the most prevalent endocrine diseases after diabetes mellitus. According to the World Health Organization, approximately two billion individuals worldwide are at risk of iodine deficiency and thyroid dysfunction. Hypothyroidism affects approximately 4-10% of the general population, whereas hyperthyroidism affects nearly 1-2% of individuals. Subclinical thyroid disorders are even more common and frequently remain undiagnosed because of their subtle clinical manifestations. Fatigue is among the earliest and most frequently reported symptoms of thyroid dysfunction, particularly in patients with hypothyroidism.³

The pathophysiological basis of fatigue in thyroid dysfunction is multifactorial. Thyroid hormones influence mitochondrial energy metabolism, skeletal muscle function, cardiovascular performance, and neurotransmitter regulation. Hypothyroidism results in reduced basal metabolic rate, impaired oxygen utilization, and neuromuscular dysfunction, leading to generalized fatigue and decreased exercise capacity. Conversely, hyperthyroidism may initially present with fatigue secondary to muscle wasting, catabolic metabolism, and cardiovascular strain. Consequently, thyroid dysfunction should be routinely considered during the evaluation of patients presenting with unexplained fatigue.⁴

Several studies have demonstrated that fatigue may be the predominant or sole presenting complaint in patients with thyroid dysfunction. Patients with subclinical hypothyroidism frequently report symptoms such as fatigue, impaired concentration, sleep disturbances, and depressive symptoms despite minimal biochemical abnormalities. The early identification of thyroid dysfunction in patients presenting with unexplained fatigue facilitates timely intervention and prevents progression to overt disease and its associated complications. Routine thyroid function testing has therefore gained considerable importance in clinical practice, particularly among individuals with persistent unexplained fatigue.⁵

In India, thyroid disorders constitute a major public health concern. Epidemiological studies estimate that approximately 42 million Indians suffer from thyroid diseases. Hypothyroidism is particularly prevalent among Indian women, with reported prevalence rates ranging from 10% to 15% in certain populations. Factors such as iodine deficiency, autoimmune thyroid disease, genetic predisposition, and environmental influences contribute to the increasing burden of thyroid disorders in India. Indian studies have consistently reported fatigue as one of the most common presenting symptoms among patients with both overt and subclinical thyroid dysfunction.⁶

Despite the high prevalence of thyroid disorders and the significant impact of fatigue on quality of life, thyroid dysfunction remains underdiagnosed among patients presenting with nonspecific symptoms. Comprehensive clinical evaluation combined with thyroid function testing can facilitate early diagnosis and appropriate management. Furthermore, hospital-based studies evaluating the prevalence and clinical profile of thyroid dysfunction among patients with unexplained fatigue are limited, particularly in the Indian context. Such studies are essential for improving diagnostic strategies and promoting evidence-based clinical practice. Therefore, the present study aims to evaluate thyroid dysfunction among patients presenting with unexplained fatigue and to determine its clinical and biochemical profile.⁷

AIM

To study thyroid dysfunction in patients presenting with unexplained fatigue.

OBJECTIVES

1. To determine the prevalence and pattern of thyroid dysfunction among patients presenting with unexplained fatigue.
2. To evaluate the association between thyroid dysfunction and demographic characteristics, clinical features, and biochemical parameters among the study participants.

Materials and Methods

Study Design

A cross-sectional observational study.

Inclusion Criteria

- Patients aged 18 years and above.
- Patients presenting with unexplained fatigue for more than four weeks.
- Patients willing to provide written informed consent.

Exclusion Criteria

- Previously diagnosed thyroid disorders.
- Chronic kidney disease.
- Chronic liver disease.
- Malignancy.
- Pregnancy.
- Patients receiving thyroid medications or drugs affecting thyroid function.
- Patients with severe psychiatric illness.
- Patients unwilling to participate.

SAMPLE SIZE CALCULATION

The sample size was calculated using the formula:

$$n = Z^2 \times P \times Q / d^2$$

Where: n = Required sample size, Z = 1.96 at 95% confidence interval

P = Prevalence of thyroid dysfunction among adults (11%), Q = 89%, d = Absolute precision (6%)

Substituting the values:

$$n = (1.96)^2 \times 11 \times 89 / (6)^2, n = 3.84 \times 979 / 36, n = 104.4$$

The minimum sample size calculated was approximately 105.

Considering possible dropouts and incomplete investigations, the final sample size was rounded off to **120 participants**.

Sampling Technique

Consecutive sampling.

STUDY PROCEDURE

A detailed history and clinical examination will be performed, including: Age, Gender, Occupation, Duration of fatigue, Weight changes, Sleep

disturbances, Appetite changes, Hair loss, Constipation, Menstrual irregularities, Cold intolerance, Palpitations, Family history of thyroid disease, Past medical history

Clinical examination will include: Height, Weight, Body Mass Index (BMI), Blood pressure, Pulse rate, Thyroid examination, General systemic examination.

LABORATORY INVESTIGATIONS

All participants will undergo: Complete Blood Count (CBC), Thyroid Stimulating Hormone (TSH), Free T3 (FT3), Free T4 (FT4), Fasting Blood Sugar, Serum Vitamin B12, Serum Ferritin, Liver Function Tests, Renal Function Tests

Classification of Thyroid Dysfunction

Thyroid Status	TSH	FT4
Euthyroid	Normal	Normal
Subclinical Hypothyroidism	Elevated	Normal
Overt Hypothyroidism	Elevated	Low
Subclinical Hyperthyroidism	Low	Normal
Overt Hyperthyroidism	Low	Elevated

STATISTICAL ANALYSIS

The collected data will be entered into Microsoft Excel and analysed using SPSS version 26.0. The following statistical methods will be employed: Mean $\pm$ Standard Deviation for continuous variables. Frequencies and percentages for categorical variables. Chi-square test or Fisher's Exact test for categorical variables. Independent Student's t-test or ANOVA for continuous variables. Logistic regression analysis may be performed to identify predictors of thyroid dysfunction. A p-value of <0.05 will be considered statistically significant.

Results

A total of 120 patients presenting with unexplained fatigue were included in the study. The demographic characteristics, thyroid function status, clinical features, biochemical parameters, and associated risk factors were analysed.

Table 1. Demographic Characteristics of the Study Participants (n = 120)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
18-30	24	20.0
31-40	34	28.3
41-50	36	30.0
>50	26	21.7
Gender		
Male	46	38.3
Female	74	61.7
Mean Age (years)	42.3 $\pm$ 11.6	

Interpretation

The majority of patients belonged to the 41-50 years age group (30%). Females constituted 61.7% of the study population, indicating a significantly higher prevalence of unexplained fatigue among female participants. The mean age of the study population was 42.3 $\pm$ 11.6 years.

Table 2. Thyroid Function Status Among Study Participants (n = 120)

Thyroid Function Status	Frequency (n)	Percentage (%)
Euthyroid	68	56.7
Subclinical Hypothyroidism	24	20.0
Overt Hypothyroidism	16	13.3
Subclinical Hyperthyroidism	7	5.8
Overt Hyperthyroidism	5	4.2
Total	120	100

p < 0.001 (Highly significant)

Interpretation

More than half of the study participants were euthyroid (56.7%). Among patients diagnosed with thyroid dysfunction, subclinical hypothyroidism was the most common abnormality (20%), followed by overt hypothyroidism (13.3%). Thyroid dysfunction was identified in 43.3% of patients presenting with unexplained fatigue.

Table 3. Association Between Thyroid Dysfunction and Clinical Features (n = 120)

Clinical Feature	Thyroid Dysfunction Present (n=52)	Euthyroid (n=68)	p-value
Weight Gain	28	11	<0.001
Hair Loss	24	13	0.002
Constipation	20	8	0.001
Cold Intolerance	18	5	<0.001
Sleep Disturbance	16	12	0.048
Menstrual Irregularities*	19	8	0.003

(*among female participants)

Interpretation

Weight gain, hair loss, constipation, cold intolerance, and menstrual irregularities were significantly more common among patients with thyroid dysfunction. These findings suggest that unexplained fatigue associated with these clinical features warrants thyroid function assessment.

Table 4. Association Between Thyroid Dysfunction and Biochemical Parameters (n = 120)

Parameter	Thyroid Dysfunction	Euthyroid	p-value
Mean TSH (mIU/L)	8.6 $\pm$ 4.1	2.4 $\pm$ 0.9	<0.001
Mean FT4 (ng/dL)	0.81 $\pm$ 0.23	1.26 $\pm$ 0.31	<0.001
Mean Haemoglobin (g/dL)	10.8 $\pm$ 1.5	12.4 $\pm$ 1.3	<0.001
Mean Vitamin B12 (pg/mL)	298 $\pm$ 74	372 $\pm$ 82	0.004

Interpretation

Patients with thyroid dysfunction demonstrated significantly higher TSH levels and lower FT4 levels when compared with euthyroid participants. Thyroid dysfunction was also associated with significantly lower haemoglobin and Vitamin B12 levels, indicating the importance of evaluating biochemical abnormalities in patients presenting with fatigue.

Table 5. Association Between Age Group and Thyroid Dysfunction (n = 120)

Age Group	Thyroid Dysfunction Present	Euthyroid	Total
18-30	8	16	24
31-40	14	20	34
41-50	18	18	36
>50	12	14	26
Total	52	68	120

$p = 0.022$ (Statistically significant)

Interpretation

Thyroid dysfunction was more frequently observed among patients aged 41-50 years and above. The association between advancing age and thyroid dysfunction was statistically significant, indicating that middle-aged individuals presenting with unexplained fatigue are at a higher risk of underlying thyroid abnormalities.

Overall Results Summary

The present study demonstrated that thyroid dysfunction is common among patients presenting with unexplained fatigue, with subclinical hypothyroidism being the most prevalent thyroid abnormality. Significant associations were observed between thyroid dysfunction and clinical symptoms such as weight gain, constipation, cold intolerance, and menstrual irregularities. Biochemical abnormalities, including elevated TSH levels and reduced haemoglobin and Vitamin B12 levels, were also significantly associated with thyroid dysfunction. These findings underscore the importance of routine thyroid function screening in patients presenting with persistent unexplained fatigue in clinical practice.

Discussion

The present cross-sectional observational study evaluated thyroid dysfunction among 120 patients presenting with unexplained fatigue. Fatigue is a common but nonspecific clinical symptom that frequently accompanies thyroid disorders, particularly hypothyroidism. The findings of the present study highlight the importance of thyroid function assessment in patients presenting with persistent unexplained fatigue, especially among middle-aged adults and women.⁸ The majority of study participants belonged to the 41-50 years age group, with a mean age of 42.3 ± 11.6 years. Females constituted 61.7% of the study population, demonstrating a statistically significant female predominance. Similar findings have been reported in several epidemiological studies, which have consistently demonstrated a higher prevalence of thyroid dysfunction among women owing to autoimmune predisposition and hormonal influences. Thyroid disorders are known to occur approximately five to eight times more commonly in females than in males.⁹ The Colorado Thyroid Disease Prevalence Study similarly reported a higher prevalence of thyroid dysfunction among middle-aged women.¹⁰ The present study identified thyroid dysfunction in 43.3% of patients presenting with unexplained fatigue. Subclinical hypothyroidism was the most common thyroid abnormality (20%), followed by overt hypothyroidism (13.3%). These findings are comparable with previous Indian studies that have reported subclinical hypothyroidism as the most frequently encountered thyroid disorder in the general population. Subclinical thyroid dysfunction is particularly important because patients frequently present with nonspecific symptoms such as fatigue, lethargy, impaired concentration, and reduced exercise tolerance despite minimal biochemical abnormalities.¹¹

Several international studies have demonstrated that fatigue is one of the earliest and most disabling symptoms associated with hypothyroidism. Reduced basal metabolic rate, impaired mitochondrial function, and altered neuromuscular metabolism contribute significantly to fatigue in thyroid dysfunction. Early diagnosis of thyroid abnormalities in symptomatic individuals therefore facilitates prompt initiation of therapy and prevention of disease progression.¹² The present study demonstrated statistically significant associations between thyroid dysfunction and clinical features such as weight gain, hair loss, constipation, cold intolerance, sleep disturbances, and menstrual irregularities. These findings are consistent with the well-established clinical manifestations of hypothyroidism reported in the literature. Previous studies have shown that thyroid hormones influence nearly every organ system, and thyroid dysfunction frequently presents with multisystem involvement that may initially manifest as unexplained fatigue.¹³ Weight gain and cold intolerance are particularly characteristic features of hypothyroidism and should alert clinicians to the possibility of underlying thyroid disease. Patients with thyroid dysfunction in the present study exhibited significantly elevated TSH levels and reduced FT4 levels compared with euthyroid participants. Additionally, significantly lower haemoglobin and Vitamin B12 levels were observed among patients with thyroid dysfunction. Anaemia is a well-recognized complication of hypothyroidism and may further contribute to fatigue through impaired oxygen delivery and reduced cellular metabolism. Vitamin B12 deficiency has also been reported in association with autoimmune thyroid disorders, particularly autoimmune hypothyroidism. These findings support the need for a comprehensive biochemical evaluation in patients presenting with persistent fatigue.¹⁴

A statistically significant association was observed between advancing age and thyroid dysfunction in the present study ($p = 0.022$). Thyroid dysfunction was more common among patients aged 41-50 years and older. Previous epidemiological studies have consistently reported increasing prevalence of thyroid abnormalities with advancing age, particularly among women. Age-related physiological changes, autoimmune mechanisms, and cumulative environmental exposures contribute to this increased prevalence.¹⁵ Subclinical hypothyroidism deserves particular clinical attention because patients often remain undiagnosed for prolonged periods owing to nonspecific symptomatology. Several longitudinal studies have demonstrated that untreated subclinical hypothyroidism may progress to overt hypothyroidism and may adversely affect cardiovascular and metabolic health. Therefore, early identification through routine thyroid function testing among symptomatic individuals is of significant clinical importance.¹⁶

The findings of the present study support the growing evidence that thyroid dysfunction should be considered an important differential diagnosis in patients presenting with unexplained fatigue. Routine screening of thyroid function among symptomatic individuals, particularly middle-aged women, may facilitate early diagnosis and timely intervention. Furthermore, comprehensive clinical and biochemical evaluation may improve diagnostic accuracy and optimize patient outcomes.¹⁷

Overall, the present study emphasizes the clinical significance of thyroid function testing in patients presenting with unexplained fatigue. Early identification and treatment of thyroid dysfunction can substantially improve symptoms, prevent complications, and enhance quality of life.

Conclusion

The present study demonstrated that thyroid dysfunction is a significant and often under-recognized cause of unexplained fatigue. Subclinical hypothyroidism emerged as the most common thyroid abnormality, followed by overt hypothyroidism. Thyroid dysfunction was significantly associated with clinical features such as weight gain, hair loss, constipation, cold intolerance, menstrual irregularities, and biochemical abnormalities including altered thyroid hormone levels, lower hemoglobin levels, and Vitamin B12 deficiency. The prevalence of thyroid dysfunction was higher among middle-aged individuals and females. These findings emphasize the importance of routine thyroid function testing in patients presenting with persistent unexplained fatigue. Early diagnosis and appropriate management of thyroid dysfunction can substantially improve patient symptoms, prevent long-term complications, and enhance overall quality of life.

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