

## Psychopathology and Cognitiveimpairment in Patients with Hypothyroidism

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### Abstract

**Background and Objectives:** Hypothyroidism is a chronic illness that affects the thyroid gland and is more common in women and the elderly. Patients with hypothyroidism are at a higher risk for psychiatric morbidity and cognitive impairment than the general population. No published Indian study in this precise topic has been identified by the current investigator to date. According to several findings, persons with hypothyroidism are more likely to have major psychiatric illnesses, psychiatric symptoms, or cognitive impairment. Among individuals with hypothyroidism, the researchers hope to determine the prevalence of psychiatric diseases, the frequency and character of psychiatric symptoms, and the presence of cognitive impairment. **Methodology:** It was decided to include 200 patients for the purpose of this investigation. A total of 100 patients with hypothyroidism and 100 patients with hypertension were assessed. The Mini International Neuropsychiatric Interview Plus (MINI Plus) was used to assess psychiatric disorders, the Comprehensive Psychopathological Rating Scale (CPRS) was used to assess psychiatric symptoms, and the Standardized Mini-Mental Status Examination (SMMSE) and the Brief Cognitive Rating Scale (BCRS) were used to assess cognitive functions in the study. **Results:** When compared to controls, patients with hypothyroidism experienced a higher rate of psychological morbidity. The frequency of psychiatric illnesses was found to be 52 percent in patients with hypothyroidism and 12 percent in individuals in the control group, with the difference being statistically significant in both cases. All patients suffering from Hypothyroidism was associated with psychiatric symptoms that did not fulfil the criteria for psychiatric illnesses, according to the study. In the domains of direction, language, and the building of SMMSE, patients with hypothyroidism demonstrated significantly substantial cognitive deficiencies compared to controls. In addition, they demonstrated highly severe cognitive deficits on the BCRS in the aggregate. Psychosomatic diseases, psychiatric symptoms, and cognitive impairment were all found to have a significant relationship with serum TSH concentrations. Additionally, there was a strong link between psychiatric diseases and serum FT4 levels. **Conclusion:** When comparing patients with hypothyroidism to those with hypertension, the prevalence of psychiatric disorders, psychiatric symptoms, and cognitive impairment is much higher in the hypothyroidism group.

**Keywords:** Hypothyroidism, Psychiatric morbidity, Psychopathology, Psychiatric disorders, Psychiatric symptoms, Cognitive Impairment.

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### Introduction

Hypothyroidism is a chronic illness that affects both men and women, but is more common in women and the elderly (1). The illness causes the metabolism to slow down, resulting in the usual symptoms of sluggishness, fatigue, low energy, changes in look and voice, weight gain, cold intolerance, reduced libido, and constipation, among others. It is normal to experience neuromuscular symptoms such as muscle stiffness, cramping, and quick fatigability. [1]

It is critical to establish that any spike in TSH has been sustained over a 3-month period before starting treatment with a thyroid hormone replacement therapy. The danger of correcting a modestly elevated TSH is minimal as long as aggressive medication is avoided. Furthermore, when the TSH level is elevated and TPO antibodies are present, there is a danger that patients will proceed to overt hypothyroidism. Treatment is initiated with a modest dose of levothyroxine (25–50 micro g/d) with the goal of bringing the thyroid stimulating hormone (TSH) back to normal. If thyroxine is not administered, thyroid function should be checked at least once a year. [2] Psychological problems such as poor memory, concentration deficiencies, difficulty with computations, and delayed reaction times can occur in patients suffering from hypothyroidism. There have been several studies that show that hypothyroidism is connected with high rates of mental health morbidity, including depression and paranoid

cavity effusions are some of the physical indications of hypothyroidism.

Severe hypothyroidism is extremely rare, although milder hypothyroidism is quite prevalent in the general population. Hypothyroidism can have a negative impact on memory functions. [3] The difficulty to concentrate is one example of a cognitive disorder. Concentration problems, poor concentration, bradyphrenia, math problems, and difficulty understanding complex questions are all symptoms of ADHD. Memory is frequently impaired from an early stage, with failure to register experiences and amnesia for everyday activities being common occurrences. [4] Whether this impairment is restricted to memory or whether it extends to other cognitive processes such as the blocking of irrelevant information and task switching is not well understood at this time. [5] In the early stages of the disease, the patient is subjectively aware of the changes taking place and may complain of poor memory or concentration difficulties. It is possible that the severe lack of interest and initiative will result in the postponement of medical attention. It is possible that the diagnosis of schizophrenia will be confused with that of depression as a result of these changes in attention and focus, slowing of thought and activity, and lessened receptivity to others. [5] According to one theory, cognitive inefficiency associated with hypothyroidism is the outcome of secondary depression. [5]

The change of the endocrine system, namely thyroid dysfunction, has been related to the aetiology of Alzheimer's disease (AD) and other dementias, according to growing data. Thyroid stimulating hormone (TSH) measurement has therefore become the standard screening test for patients who present with cognitive deterioration.

Hypothyroidism continues to be a significant issue in psychiatric practise today. Concentration and focus problems, as well as bradyphrenia, mathematic difficulties and difficulty comprehending complex topics, are all examples of cognitive disorders. [5] Secondary

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disorders in particular. Bradycardia, face puffiness, peripheral edoema, delayed tendon reflex, Carpel Tunnel Syndrome, and serous

depression has been linked to hypothyroidism in the past. Almost all people with hypothyroidism experience some degree of depression at some point during their illness. (5) Untreated hypothyroidism can culminate in psychosis, which is referred to as "myxoedema madness." Clinical hypothyroidism is connected with significant cognitive and affective changes, and it is regarded to be one of the contributing factors to so-called "reversible dementia." [5] Even though a lot of research have been reported from the Western world, there is a scarcity of literature on psychiatric problems, psychiatric symptoms, and cognitive impairment in individuals with hypothyroidism in the Indian subcontinent, according to the authors.

**Objectives of the Study**

1. To evaluate the frequency of psychiatric disorders in patients with hypothyroidism.
2. To evaluate the frequency and nature of psychiatric symptoms in patients with hypothyroidism.
3. To evaluate the frequency of cognitive impairment in patients with hypothyroidism.

**Source of Data:**

This clinical investigation was conducted in the departments of Psychiatry, Endocrinology and Medicine of Ayaan Institute of Medical Sciences, HYderabad. This study commenced from November 2019 and was completed by August 2021.

**Methods of Collection of data**

Population for the investigation consisted of patients suffering from hypothyroidism attending endocrinology outpatient department and inpatients in the department of endocrinology. 100 consecutive patients with diagnosis of hypothyroidism satisfying inclusion and exclusion criteria formed the sample of the study. Patients diagnosed with essential hypertension attending medical outpatient department were the population for control group. 100 consecutive patients with hypertension meeting inclusion and exclusion criteria constituted the control group. Following were the inclusion and exclusion criteria

**Inclusion Criteria for Sample**

1. Patients diagnosed to have hypothyroidism in endocrinology outpatient department
2. Age 18-60 years
3. Both males & females
4. Patients consenting for study

**Exclusion Criteria for Sample**

1. Patients with hypertension.
2. Patients with other significant medical co morbidities like diabetes mellitus, chronic renal failure and other chronic debilitating medical conditions.
3. Patients with known primary psychiatric disorders.

**Inclusion Criteria for Control**

1. Patients diagnosed with essential hypertension
2. Age 18-60 years
3. Both males and females
4. Patients consenting for study

**Exclusion Criteria for Control**

1. Patients with thyroid disease.
2. Patients with other significant medical co-morbidities like diabetes mellitus and other endocrine disorders ,chronic renal failure and other chronic debilitating medical conditions
3. Patients with known primary psychiatric disorders

**Type of Study**

This was an observational, descriptive, cross-sectional, case control, comparative clinical study

**Tools for Assessment**

The following tools were used for assessment of psychiatric disorders, psychiatric symptoms and cognitive impairment

1. Mini International Neuropsychiatric Interview Plus (MINI Plus).<sup>(44)</sup>
2. Comprehensive Psychopathological Rating Scale(CPRS).<sup>(45)</sup>
3. Standardized Mini Mental Scale Examination (SMMSE).<sup>(46)</sup>
4. Brief Cognitive Rating Scale (BCRS).<sup>(47)</sup>

**Results**

**Table 1: Data regarding age distribution**

Age	Group		Total
	Sample	Controls	
18-30	22	2	24
31-40	21	8	29
41-50	19	20	39
51-60	18	50	68
Total	80	80	160

Patients in the age group of 18 – 30 years constituted the major part of sample (27.5%), followed by age group of 31-40 years (26.25 %) and in control group, patients aged 51- 60(62.5 %), followed by patients

in the age group of 41-50 years (25 %). There is statistically highly significant difference between age of hypothyroidism patients and control group(P<0.01).

**Table 2: Data regarding gender distribution**

Gender	Group		Total
	sample	Control	
Male	12	45	57
Female	68	35	103
Total	80	80	160

There was statistically highly significant difference between gender of patients with hypothyroidism and control groups (P=0.000 (<0.01)).In

sample majority of patients are females (85 %) and in controls 56.25 % are males and 43.75 % females.

**Table 3: Data regarding symptoms suggestive of hypothyroidism**

Symptoms	No of patients	Frequency
Weight gain + lethargy + fatigue + intolerance to cold + constipation + bodyaches + hair loss	20	25 %
Lethargy + fatigue + bodyaches	16	20 %
Lethargy + bodyaches + voice alteration	6	0.75%
Lethargy + fatigue	12	15 %
Weight gain	11	13.75 %

Lethargy	5	0.62%
Fatigue	8	1%
Hair loss	2	0.25 %

25 % of the patients have multiple symptoms. It includes Weight gain, lethargy, and fatigue, intolerance to cold, constipation, body aches and hair loss. 20 % of the patients have Lethargy, fatigue and body aches.

**Table 4:** Data regarding clinical examination findings

Clinical examination	Sample	Frequency
Pedal oedema + menstrual irregularities	3	3%
Pedal oedema + carpal tunnel syndrome	4	3%
Hair loss + menstrual irregularities	18	19%
Hair loss	2	2%
Bradycardia	2	2%
Coarse/dry skin	6	5%
Pedal oedema	11	12%
Delayed ankle jerk	2	2%
Carpal tunnel syndrome	4	4%
Menstrual irregularities	16	26%
Nil	12	22%

26% of patients presented with only menstrual irregularities.19% with hair loss and menstrual irregularities. There are no statistical significant difference in psychiatric disorders, psychiatric symptoms and cognitive impairment with the clinical examination

**Table 5:** Data regarding duration of symptoms suggestive of hypertension

Duration	Controls	Frequency
<1 year	18	22.5%
1-4 year	20	25.0 %
>4 years	42	52.5%

Majority of Control (52.5%) had symptoms for more than four years. 25 % ofpatients had symptoms suggestive of hypertension between 1-4 years.

**Table 6:** Data regarding frequency of psychiatric disorders

Mini Plus	Patients	frequency	Controls	Frequency
Dysthymia	22	27.5%	3	3.75%
Alcohol dependence syndrome	0	0%	8	10.0%
Panic disorder	4	5%	1	1.25%
Mixed anxiety depressive disorder	4	5%	0	0%
Major depressive episode	4	5%	0	0%
Adjustment disorder	1	1.25%	0	0%
Generalized anxiety disorder	2	2.5%	0	0%
Nil	37	46.25%	56	70%

**Table 7:** Relation between serum T4 abnormality and frequency of psychiatricdisorders

Serum T4 abnormality	Dysthymia	Panic disorder	Mixed anxiety depressive disorder	Major depressive episode	Adjustment disorder	Generalize danxiety disorder
Present	5	3	0	2	0	0
	18.5%	37.5%	0%	50.0%	0%	0%
Absent	22	5	5	2	1	2
	81.5%	62.5 %	100%	50.0%	100%	100%
Total	27	8	6	4	1	2
	100%	100%	100%	100%	100%	100%

There is no significant difference in hypothyroidism patients in the frequency of psychiatric disorders in relation to serum T4 abnormalities (p=0.076>0.05).However this analysis reveals that there is significant increased frequency of psychiatric disorders in patients without serum T4 abnormality

**Table 8:** Relation between serum T3 abnormality and frequency of psychiatricdisorders

Serum T4 abnormality	Dysthymia	Panic disorder	Mixed anxiety depressive disorder	Major depressive eepisode	Adjustment disorder	Generalized anxiety disorder
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Present	5	3	1	1	1	0
	15.6%	50%	16.7%	20.0%	100%	0%
Absent	27	3	5	4	0	2
	84.4%	50%	83.3%	80.0%	0%	100%
Total	32	6	6	5	1	2
	100%	100%	100%	100%	100%	100%

There is no significant difference in hypothyroidism patients in the frequency of psychiatric disorders in relation to serum T3 abnormalities (p=295>0.05). However this analysis reveals that there

is increased frequency of psychiatric disorders in patients without serum T3 abnormality.

**Table 9:** Correlation of TSH levels with psychiatric disorders

TSH Levels	Dysthymia	Panic Disorder	Mixed Anxiety Depressive Disorder	Major Depressive Episode	Adjustment Disorder	Generalized Anxiety Disorder	Nil
0.27-4.2	2 20%	0	0	0	0	0	8 80%
4.21-10	11 22.6%	1 1.9%	2 3.8%	1 1.9%	0	0	38 69.8%
10.1-20	14 70%	1 5%	2 10%	0	0	1 5%	2 10%
20.1-50	4 44.4%	2 22.2%	1 11.1%	1 11.1%	0	1 11.1%	0
>50	2 20%	2 20%	1 10.0%	3 30.0%	2 20%	0	0

This analysis reveals increasing levels of TSH have more psychiatric disorder .present study shows that almost all individuals with TSH

level more than 20 are diagnosed with psychiatric disorders. There is highly statistically significant difference with p<0.0001.

**Table 10:** Data regarding psychiatric symptoms

CPRS	Diagnosis	N	Mean	Std. deviation	Median	Mannwhitney test	p value
Reported	Hypothyroidism	80	9.40	4.56	9	8.69	.000 HS
	Hypertension	80	2.62	3.02	2		
Observed	Hypothyroidism	80	1.01	1.33	1	6.22	.000 HS
	Hypertension	80	.14	.37	0		
Total CPRS Scores	Hypothyroidism	80	10.22	6.32	1	9.08	.000 HS
	Hypertension	80	2.61	3.38	1		

There is statistically highly significant difference between patients and control in domains of Reported, Observed and Total score (p<0.01).

The patients have a higher mean value compared to control group in all the domains indicating more psychopathology in the patient

**Table 11:** Data regarding cognitive function tests

BCRS	Diagnosis	N	Mean	Std. Deviation	Median	Mannwhitney test	P Value
Concentration	Hypothyroidism	80	1.64	0.59	1	1.56	.057
	Hypertension	80	1.42	0.57	1		
Recent Memory	Hypothyroidism	80	1.23	0.40	1	0.72	.586
	Hypertension	80	1.21	0.28	1		
Past Memory	Hypothyroidism	80	1.01	0.12	1	1.01	.303
	Hypertension	80	1.00	.00	1		
Orientation	Hypothyroidism	80	1.00	0.00	1	.000	1.00
	Hypertension	80	1.00	0.03	1		
Functioning of care	Hypothyroidism	80	1.38	0.62	1	1.65	.071
	Hypertension	80	1.19	0.76	1		
Total	Hypothyroidism	80	1.34	0.40	1	2.03	.042 Sig
	Hypertension	80	1.03	0.24	1		

There is a statistically significant difference in the total score of BCRS between the patients and the control group (p<0.05). The patients have a higher mean value (1.34) compared to Control group (1.03), indicating cognitive impairment in the patients.

There is no statistical significance in other domains. The patients have a higher mean value compared to control group in the domains of concentration, recent memory, past memory and functioning of care indicating cognitive impairment in the patients.

**Table 12:** Data regarding cognitive function tests

SMMSE	Diagnosis	N	Mean	Std. Deviation	Median	Mannwhitney test	P Value
Orientation	Hypothyroidism	80	9.83	0.46	15	2.64	.0081 HS

	Hypertension	80	9.55	0.80	12		
Registration	Hypothyroidism	80	2.93	0.24	4	1.53	.064
	Hypertension	80	2.83	0.43	3		
Attention and concentration	Hypothyroidism	80	4.42	0.74	7	1.13	.303
	Hypertension	80	4.23	0.66	7		
Recall	Hypothyroidism	80	2.50	0.38	5	.66	.511
	Hypertension	80	2.29	0.64	3		
Language	Hypothyroidism	80	7.99	0.12	7	3.32	.001 HS
	Hypertension	80	7.86	0.28	6		
Construction	Hypothyroidism	80	0.90	0.30	4	4.17	.000 HS
	Hypertension	80	0.73	1.05	1		
Total	Hypothyroidism	80	25.87	1.64	30	1.22	0.132
	Hypertension	80	21.41	2.50	20		

There is highly significant difference in domains of Orientation, language and construction ( $p < 0.01$ ) between the patients and the control group. However no statistically significant differences in the domains of registration ( $p = .067$ ), recall ( $p = .511$ ) and attention and concentration ( $p = 0.303$ ). The mean score attained by the patients is 25.87 and control group is 21.41, a score below 24 on the SMMSE indicate cognitive impairment.

#### Discussion

The present investigation is carried out on 180 patients with hypothyroidism who attended the outpatient and inpatient departments of Endocrinology and 80 patients with hypertension who attended outpatient and inpatient Departments of Medicine of Ayaan Institute of Medical Sciences, Hyderabad. By and large patients coming to this hospital belong to the middle and lower socioeconomic class. This hospital has six general medical units with bed strength of 200-250 and one endocrinology super speciality unit with bed strength of 30-40. The average number of patients attending the endocrinology outpatient department is around 60 – 80 and medical outpatient is around 250-300. The present study is conducted from July 2019 and the data collection is completed by 30st June 2021.

#### Sociodemographic and Clinical Variables

The sample and control groups do not significantly differ in term of religion, education, income and socioeconomic status. However there is statistical significant difference in terms of age, gender, marital status and domicile distribution. The sample has more patients in the age group of 18-30 years followed by 31 – 40 years and control has more patients in the age group of 51-60 years. This finding can be explained on the basis that hypertension is more prevalent in older age group, whereas hypothyroidism is more common in younger individuals. In the sample majority of patients are females (68 %). This finding substantiates that hypothyroidism is more common in females.

#### Frequency of Psychiatric Disorders

The present investigation reveals that patients with hypothyroidism have higher frequency of psychiatric disorders compared to control. There is statistically high significant difference between patients with hypothyroidism and those in control in terms of presence of psychiatric disorders. ( $p = 0.000 < 0.01$ ). The psychiatric disorders are diagnosed in 42 hypothyroidism patients and 11 hypertension patients. Among the 42 hypothyroidism patients, 22 patients have dysthymia, four have panic disorder, four have mixed anxiety depressive disorder, four have major depressive episode, two have generalized anxiety disorder and one patient is diagnosed to have adjustment disorder. The diagnosis is made using Mini International Neuropsychiatric Interview Plus (MINI Plus). In the present investigation 40% and 6.25% of hypothyroidism patients have dysthymia and major depressive episode respectively. The findings of the present investigation are consistent with those of earlier studies. [1,2]. Carta G M et al find the prevalence of the depressive disorder to be 50% in patients with hypothyroidism. [1] A study done by Demartini B et al find that 17.9% of patients with hypothyroidism have depressive episode. [3] The present investigator finds that 2% of hypothyroidism patients have generalised anxiety disorder and 7.5 %

patients each have mixed anxiety depressive disorder and panic disorder. Earlier studies also report presence of anxiety disorders in patients with hypothyroidism. [4,5,6,7,8,9]

#### Psychiatric Disorders and Clinical Variables

Present investigation finds that psychiatric disorders are more common in patients with multiple symptoms compared to those with single symptom. Multiple symptoms include weight gain, lethargy, fatigue, intolerance to cold, constipation, bodyaches, hair loss and menstrual irregularities. There is increased frequency of depressive disorders as well as anxiety disorders in these patients, but there is no statistical significant difference.

#### Frequency and Nature of Psychiatric Symptoms

The results of the present investigation revealed that patients with hypothyroidism have higher frequency of psychiatric symptoms compared to control. This study used Comprehensive Psychopathological Rating Scale (CPRS) to evaluate the frequency and nature of psychiatric symptoms. There is statistical highly significant difference on the reported score, observed score and total score between sample and control on CPRS.

Majority of the patients in the sample reports sadness, inability to feel, inner tension, lassitude, fatigability, failing memory, concentration difficulties, reduced sexual interest and aches and pains. [8]

The current study reveals that psychiatric symptoms are more common in individuals with multiple symptoms compared to single symptom in domains of reported and total CPRS Score. But there is no significant difference in hypothyroidism patients in all domains of CPRS Score in relation to symptoms of hypothyroidism. This indicates that there is no particular symptom contributes completely to psychiatric symptoms in hypothyroidism patients. Present investigator fails to find earlier studies which relate symptoms of hypothyroidism to psychiatric symptoms.

Present investigator attempts to find relationship between Serum FT4, T4 and T3 abnormality and psychiatric symptoms. Present investigation reveals that psychiatric symptoms are more common in individuals with serum FT4 abnormality. However there is no significant difference noted in all domains of CPRS Score. Psychiatric symptoms are more common in individuals with serum T4 abnormality. But there is no significant difference in hypothyroidism patients in all domains of CPRS Score. There is no significant difference in hypothyroidism patients in all domains of CPRS Score in relation to Serum T3 abnormality as well. Present investigator fails to find earlier studies which evaluated relationship between serum FT4, T4 and T3 levels and psychiatric symptoms. [9]

#### Cognitive Impairment

Present investigation finds that cognitive impairment assessed with BCRS and SMMSE are present in a significant proportion of patients with hypothyroidism. It finds that attention and concentration, recent memory, recall, registration, language, construction, past memory and functioning of care are impaired in these patients. Presence of cognitive impairment have been documented in multiple domains including the inability to concentrate, poor attention, bradyphrenia

calculation difficulties and difficulty understanding complex questions. [10]

In the current study the total mean score obtained by patients with hypothyroidism on SMMSE is 25.87 and control scores 21.41. The result of the present study indicates that there is highly significant difference in domains of orientation, language and construction on SMMSE ( $p < 0.01$ ) between the sample and the control group. However no statistically significant differences is found in the domains of registration ( $p = .067$ ), recall ( $p = .511$ ) and attention and concentration ( $p = 0.303$ ). Multiple comparison analysis reveals that there is significant difference in the domain of orientation, recall, construction and total score.

Present investigation finds statistically significant difference in the total score of BCRS between the sample and the control groups ( $p < 0.05$ ). The patients have a higher mean value (1.34) compared to control group (1.03) indicating cognitive impairment in the sample. There is no statistically significant difference in other domains of BCRS.

Current investigation reveals that there is significant cognitive impairment with increasing levels of TSH. There is statistically high significant difference with increasing TSH levels in patients with hypothyroidism in respect to domains of concentration and total score on BCRS ( $p < 0.01$ ). There is statistically significant difference between TSH levels in patients with hypothyroidism in respect to domains of recent memory and orientation on BCRS. There is statistical highly significant difference in the domains of attention and concentration and total score on SMMSE ( $p < 0.01$ ). Present investigator fails to find earlier studies which correlates TSH levels with cognitive impairment.

#### Conclusion

According to the findings of the current study, people with hypothyroidism are more likely to have substantial psychiatric illnesses, psychiatric symptoms, and cognitive impairment. The levels of serum FT4 and serum TSH are associated with psychiatric illnesses. TSH levels in the blood are associated with both psychiatric symptoms and cognitive impairment.

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