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Original Research Article

Cognitive function in hypothyroid patients: a tertiary care-based cross-sectional study

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ABSTRACT

Background: Estimation of cognitive impairment among hypothyroid individuals plays an important role in intervening in the disease progress at the earliest. The present study was conducted to measure the cognitive impairment in a hypothyroid state.
Methods: A cross-sectional study was conducted among 260 sample of hypothyroid patients at Agartala Government Medical College Hospital from January to June 2024 using a case record form where pregnant state, acute illnesses, and co-morbidities were excluded. The General Practitioner Assessment of Cognition scale was used to measure the cognitive impairment. Both descriptive and inferential statistics were used using SPSS vs 21.0.
Results: Out of 260 cases of hypothyroidism, 32.7% have cognitive impairment. Only 16.9% of the subjects with sub-clinical states showed cognitive impairment but 58% of them with visible clinical manifestations showed cognitive impairment (p-value .001). The cognitive function was more impaired among males (51.8%) than females (28.0%) which is found to be statistically significant (p-value .004).
Conclusions: The study concluded that every third person had cognitive impairment among hypothyroid patients. Clinical hypothyroidism, advance age, and males were associated with cognitive impairment. Newly diagnosed cases were found to show increased impairment.

Keywords: Cognitive function, Cognitive impairment, Hypothyroidism, Thyroid

INTRODUCTION

Hypothyroidism may occur due to primary gland failure or insufficient thyroid gland stimulation by the hypothalamus or pituitary gland. It is characterized by the reduction or low production of T3 (triiodothyronine) and T4 (thyroxine) hormones.[1] Overt hypothyroidism is defined as an increased serum TSH level with a low free T4 (fT4) level, while mild or "subclinical" hypothyroidism is defined as an elevated TSH with a normal fT4.[2] The reason for the higher thyroid-stimulating hormone in India compared with Western countries is possibly linked to chronic iodine deficiency.[2] The highest prevalence of hypothyroidism (13·1%) is noted in people aged above 45 years, with people of middle-aged years being less affected (7·5%).[3] Cognitive impairment is one of the common complications that occur among patients with hypothyroidism.[4] Cognitive impairment is a condition in which a person has difficulty recalling, learning new things, concentrating, and making

decisions that affect his/her everyday life.[5] There are different causes for cognitive impairment such as genetic factors, exposure to toxic substances, head injury, chronic illnesses, malnutrition, and other lifestyle factors like smoking, chat chewing, and alcoholism. From those wide ranges of causes, hypothyroidism is one of the diseases of the thyroid gland that can cause cognitive impairment.[6]

There are pieces of evidence across the world that claim cognitive impairment is a common problem among these patients. A few studies demonstrated that cognitive impairment affected about 17%-32% of hypothyroid patients.[7-9] Therefore, recognition at the earliest stage of the pathophysiological process of cognitive impairment is very important so that early interventions can be applied to improve cognition or at least prevent further progression. [10, 11]

The prevalence of hypothyroidism in the state of Tripura is 16.6% according to the only study conducted in the year 2016[12] and no local data is available regarding the prevalence of cognitive impairment in hypothyroid patients. The present study was conducted to estimate the proportion of cognitive impairment among the hypothyroid patients attending Agartala Government Medical College and GBP Hospital and to determine the associated factors (such as age, gender, and duration of hypothyroidism) for cognitive impairment among the hypothyroid patients.

METHODS

A hospital-based cross-sectional study was conducted at Agartala Government Medical College GBP Hospital from January to June 2024 after obtaining institutional ethical approval. Sample size was determined by using the single population proportion formula; $n=z^2pq/e^2$. Based on a previous study, the prevalence (p) of cognitive impairment in hypothyroid is 31.06%.[9] Keeping a 95% confidence interval ($Z\alpha/2=1.96$) and a 6% margin of error and adding a 10% non-response rate, the sample size calculated was 260. Patients with established hypothyroidism of different categories based on fT3, fT4, and TSH levels were selected for the study. Patients having hypothyroidism associated with any acute illnesses or chronic diseases or other co-morbidities (like diabetes, hypertension, malignancies, CVA, etc) and pregnancy were excluded from the study. A predesigned and pretested case study form was used for data collection.

Hypothyroidism was categorized as per the cut-off value established for patients tested in the central laboratory of Agartala Government Medical College Hospital which also follows that of standard clinical references set at International System of Units (SI Units):[13] Assessment of Cognition among the recruited hypothyroid patients attending Agartala Government Medical College Hospital was done using the guidelines of GPCOG (General Practitioner Assessment of Cognition) Score.[14] Each correct answer was valid for one point leading to a maximum score of 9 (fewer points indicate more impairment). The informant interview asks six historical questions from an informant/next of kin who knows the patient well. He or she was asked to compare the patient's current function with his/her performance a few years ago. Areas that are covered in the informant interview include memory, word-finding difficulties, trouble managing finances, difficulties managing medication independently, and needing assistance with transportation.

The informant interview was to be conducted if further information about the patient's function is required (i.e. cognitive test scores 5 to 8). It consists of six questions which can be answered with “yes” (=impairment), “no” (=no impairment), “don’t know” or “N/A”. Each question was worth one point. As a “yes” answer indicates impairment it is scored 0, while all other answers score 1 point each; (hence higher scores indicate less impairment).

Data analysis was done by SPSS software version 21. Descriptive statistical tools such as frequencies, proportions, and the mean with standard deviation were used. The Chi-square test and Student’s t-test were also used to see the association or relation among variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 260 cases of hypothyroidism were included in the study with a median age of 39 years ranging from 15 years to 79 years. In the study, the female was 79.2%, the majority of the middle-class family (57.0%), only 18.8% were employed and only 15.8% of the participants were involved in vigorous type of physical activity (Table 1).

Table 1: Sociodemographic profile of the study participants (n=260)

Sociodemographic profile	Frequency	%
Sex		
Male	54	20.8
Female	206	79.2
Social class		
Lower class	50	19.2
Lower middle class	21	8.1
Middle class	148	57.0
Upper middle class	41	15.7
Occupation		
Employed	49	18.8
Self-employed	99	38.1
Homemaker	112	43.1
Physical activity		
Sedentary	133	51.1
Moderate	86	33.1
Heavy/vigorous	41	15.8

Table 2: Thyroid profile and hypothyroid state (n=260).

Thyroid profile	Frequency/Median	%/Range
Thyroid profile		
T3	12.0 pmol/l	4.0-20.9
T4	3.68 pmol/	1.2-8.40
TSH level	9.86 mIU/l	1.30-120.0
Hypothyroid state		
Sub-clinical	160	61.5
Clinical	100	38.5

mIU/l=milli international units/liter, pmol/l=picomole per litre

Table 3: Association between hypothyroidism patterns and cognitive function (n=260)

Hypothyroidism patterns	Cognitive function		P value
	Impaired N (%)	Intact N (%)	
Sub-clinical state	27 (16.9)	133 (83.1)	0.001
Clinical hypothyroidism	58 (58.0)	42 (42.0)	

Table 4: Association between age, gender, and duration of illness and cognitive impairment among the study subjects (n=260).

Demographic profile and duration of illness	Cognitive function		P value
	Impaired N (%)	Intact N (%)	
Gender			
Male	28 (51.8)	26 (48.2)	0.004
Female	57 (28.0)	203 (72.0)	
Age in years (mean, SD)	44.83±4.12	37.71±51	0.01
Duration of illness			
Newly diagnosed	39 (46.9)	44 (53.1)	0.001
Diagnosed in the past 1 year	19 (35.8)	36 (64.2)	
Above 1 year to 5 years	16 (26.7)	44 (73.3)	
Above 5 years	11 (17.7)	51 (82.3)	

Table 5: Factors associated with cognitive impairment among adult hypothyroid patients.

Factors/variables	Cognitive impairment		Crude odds ratio	P value
	Yes (n=85) N (%) /mean±SD	No (n=175) N (%) /mean±SD		
Age (in years)	44.83±4.12	37.71±51	1.039 (1.016-1.063)	0.001
Gender				
Male	28 (51.8)	26 (48.2)	12.065 (0.82-5.19)	0.123
Female	57 (28.0)	203 (72.0)		
Duration of illness (years)	1.2 years	4.5 years	2.15 (1.16-7.21)	0.04

The thyroid function test of the study participants shows the median value of T3 12.0 pmol/l, T4 3.68 pmol/l, and thyroid stimulating hormone (TSH) 9.86 mIU/l. More than half of the participants were in a sub-clinical state of hypothyroidism (53.6%) and 46.4% of the participants were in a clinical state of hypothyroidism (Table 2). The present study shows that 32.7% of the hypothyroidism subjects have cognitive impairment and 67.3% (175 out of 260) were of intact cognitive function (Figure 1).

The association of cognitive function with the hypothyroid state where the cognitive function was more intact when the disease state was in the sub-clinical stage (83.1%) but when there were visible clinical manifestations or deranged thyroid function test, 58% showed cognitive impairment among them. There was a significant association found between altered thyroid hormone or clinical state of hypothyroidism and cognitive impairment among the study subjects with a p value of 0.001 (Table 3).

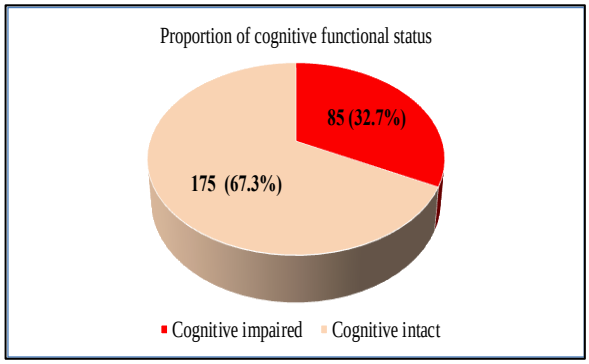

Figure 1: Proportion of cognitively impaired among hypothyroidism (n=260).

The study also found that gender, age, and duration of illness were associated with impaired cognitive function. The cognitive function was more impaired among males (51.8%) than females (28.0%) which is found to be statistically significant (p value 0.004). Similarly, higher-aged people and new cases are more associated with higher impaired cognitive status (p value 0.01 and 0.001 respectively). Binary logistic regression analysis shows age in years (COR is 1.039 (1.016-1.063) with a p value 0.001) and duration of hypothyroid state in years (COR is 2.15 (1.16-7.210) with a p value 0.04) had higher odds among cognitively impaired than those who had not developed impairment.

DISCUSSION

Numerous studies have addressed the association of cognitive impairment with hypothyroidism. [9,10,15,16] The present study was done to estimate the proportion of cognitive impairment among the hypothyroid patients attending Agartala Government Medical College and GBP Hospital and also to determine the associated factors

(such as age, gender, and duration of hypothyroidism) for cognitive impairment among the hypothyroid patients.

In the present study, 32.7% were found to have a cognitive impairment, which is inconsistent with the study done in India (32.2%), Ethiopia (27.3%), and Los Angles (28.2).[8-10] On the other hand, the result of the present study is higher than that of the study conducted in Minnesota (17%).[7] The discrepancy may be elucidated by differences in sociodemographic characteristics of the participants mainly the educational level. Higher educational levels among Minnesota participants might be associated with health literacy which increases the degree to which individuals can obtain, process, and understand basic health information and services needed to make appropriate health decisions.[17] In addition to the above, the discrepancy may be due to the use of different assessment techniques. In the current study, the GPCOG **(**general practitioner assessment of cognition**)** scale was used while in the study conducted in Minnesota battery of psychometric tests was involved.[7]

In the current study, a significant association was found between altered thyroid hormone or clinical state of hypothyroidism and cognitive impairment among the study subjects. Numerous studies [18-21] have reported that overt hypothyroidism can affect a range of cognitive domains. Studies report decrements in general intelligence, attention/concentration, memory, perceptual function, language, psychomotor function, and executive function. Memory is the most consistently affected domain, with specific deficits in verbal memory. Imaging studies provide objective evidence that brain structure and function are altered in hypothyroid patients, with decreased hippocampal volume, cerebral blood flow, and function globally and in regions that mediate attention, visuospatial processing, working memory, and motor speed.[22,23-26]

In the current study, cognitive impairment among hypothyroid patients was significantly associated with increased age, which is supported by a study conducted in Los Angeles and Ethiopia.[10,27] This increased prevalence of cognitive impairment with an increase in age could be due to aging-induced changes in T4 transport into the brain areas that are important for cognitive function, altered brain conversion of T4 into T3, decreased brain thyroid receptor number or affinity. Decreased T4 and T3 levels might be associated with a decreased metabolic activity that consequently decreases the brain glucose-consuming process needed for neurotransmission, memory, and other higher brain functions involved in cognitive function.[28] Additionally, it may be due to age-related changes in the structure and function of synapses and changes in neuronal networks involved in higher brain functions including cognition.[29]

Unlike other studies where long duration of illness was associated with cognitive impairment among hyperthyroid patients, in the present study it was seen that new cases are more associated with higher impaired cognitive status. [10,28] This may be because of the initiation of treatment of hypothyroidism which might have slowed the cognitive impairment or stopped it from any further deterioration.[30] A study conducted by Bono G et al showed that after L-thyroxine treatment, an increase in serum fT4 was detected in parallel with thyroid stimulating hormone (TSH) reduction.[31] A positive correlation was found between TSH reduction and improved mood scores. Verbal fluency and depression scores showed a slight improvement.

It was not possible to establish causal relationships because of the cross-sectional nature of the study. More prospective observational studies are needed in the future with a control group. Undiagnosed neurodegenerative diseases might have affected the performance of the study subjects on the GPCOG score.

CONCLUSION

The study concluded that the proportion of cognitive impairment among hypothyroid patients was high. Clinical hypothyroidism, increased age, and females were associated with cognitive impairment. Newly diagnosed cases were found to show increased impairment. Hence, early screening of hypothyroidism in general and cognitive function, in particular, should be emphasized to increase the quality of life and to decrease the economic burden on individuals and the country level. Moreover, early screening can decrease the progression of mild cognitive impairment to dementia by giving appropriate replacement therapy. Early diagnosis of hypothyroidism and periodic screening of cognitive functions among hypothyroid patients should be emphasized to prevent further complications.

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