

## Original article

# A cross sectional study on evaluation of cognitive function in subclinical hypothyroidism

<sup>1</sup>Dr.K.Soundariya, <sup>2</sup>Mr.Selvam.V.S, <sup>3</sup>Miss.Nivethitha.N

<sup>1</sup>Professor, Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry – 605107

<sup>2</sup>Clinical Psychologist, Department of Psychiatry, Sri Manakula Vinayagar Medical College and Hospital, Puducherry – 605107

<sup>3</sup>Final MBBS Student, Sri Manakula Vinayagar Medical College and Hospital, Puducherry – 605107

Corresponding author: .K.Soundariya ; Email ID: drsoundariya@gmail.com



## Abstract

**Background:** While the cardiovascular and neurologic sequelae of a full blown hypothyroidism is well established, there is lack of evidence on the influence of subclinical hypothyroidism on the cognitive functioning of the individuals. Screening of the individuals for subclinical hypothyroidism at an earlier age and identification of subtle cognitive dysfunction in early stages, may help to decide on the initiation of management.

**Aim:** The present study aimed to study and compare the cognitive function between the normal individuals and subclinical hypothyroidism

**Methodology:** The cognitive function was assessed in 52 Subclinical hypothyroidism patients and 50 normal individuals with Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment Test (MoCA). Baseline characteristics and the cognitive parameters were compared between subclinical hypothyroid patients and the normal individuals.  $p < 0.05$  was considered statistically significant.

**Results:** There was no statistically significant difference in the MMSE and MoCA scores between the subclinical hypothyroid patients and normal individuals. However MMSE scores were significantly different between the illiterate normal and individuals with subclinical Hypothyroidism. A positive correlation was observed between the TSH values and the MMSE scores.

**Conclusion:** Cognition is not affected in subclinical hypothyroidism in literate individuals. However decrement in the cognitive function with advancing age may not be excluded.

**Key words:** Cognition, MMSE, Subclinical Hypothyroidism

## Introduction

Hypothyroidism is the most common of thyroid disorders in India, affecting one in ten adults.<sup>[1]</sup> Hypothyroidism is characterized by a broad clinical spectrum ranging from an overt state of myxedema, end-organ effects and multisystem failure to an asymptomatic or subclinical condition. Subclinical Hypothyroidism is defined as elevated TSH levels in the presence of normal circulating Free T<sub>3</sub> and T<sub>4</sub> concentrations.<sup>[2]</sup> Subclinical Hypothyroidism is known to affect 3-15% of the general population.<sup>[3]</sup> Thyroid hormones exhibit profound effects on central nervous

system. Elevated Thyroid Stimulating Hormone (TSH) levels have been associated with enhanced risk of cognitive deficits.<sup>[4]</sup> While the cardiovascular and neurologic sequelae of a full blown hypothyroidism is well established, there is lack of evidence on the influence of subclinical hypothyroidism on the cognitive functioning of the individual. Patients with subclinical hypothyroidism have a higher rate of progression to clinically overt hypothyroidism, even in the absence of thyroid peroxidase antibodies.<sup>[5]</sup> Literature on cognitive function in subclinical hypothyroidism remain sparse and inconclusive.<sup>[6,7]</sup>

The management of subclinical hypothyroidism always remain a matter of debate,<sup>[8]</sup> some recommend intervention, others suggest a mere observation. Most of the time, the decision on the management of subclinical hypothyroidism is based on biochemical parameters. As the incidence of subclinical hypothyroidism is known to increase with age,<sup>[9]</sup> screening of the individuals for subclinical hypothyroidism at an earlier age and identification of subtle cognitive dysfunction in early stages, may help to decide on the initiation of management, because there are evidences that recommend administration of thyroxine to reverse the mild cognitive dysfunction to normal.<sup>[10]</sup> Montreal cognitive Assessment test (MoCA) and Mini Mental State Examination (MMSE) are widely used to assess the mild cognitive impairment.<sup>[9,10]</sup> Hence the present study aimed to evaluate the cognitive function of the individuals with subclinical hypothyroidism.

#### **Materials and Methods**

**Study setting:** The present study was conducted at the research laboratory, Department of Physiology of our Institution.

**Study Design:** Cross sectional study.

**Study Participants and Sample size:** The sample size was estimated to be 102, using software open epi version 3.01 taking into consideration mean (S.D) of MMSE of normal and subclinical hypothyroid individuals as 28.2(1.3) and 27.5 (1.2) respectively, based on a previous study,<sup>[11]</sup> with 80% power and 95% confidence interval.

**Study Duration:** May -June 2018

**Inclusion criteria:** Both genders, 20 – 50 years, newly diagnosed subclinical hypothyroid individuals with TSH levels between 5.5 – 10 mIU /L, both literate and illiterate individuals were included in the study

**Exclusion criteria:** Age > 50 years, TSH levels < 5.5 mIU/L or > 10mIU/L, H/O smoking, alcoholism, known hypertensives, known diabetics, subjects with any form of mental illness like depression, mental retardation, individuals on sedatives, anti-psychotic drugs, clinically evident cognitive dysfunction, on treatment with thyroid hormones were excluded from the study

#### **Methodology:**

Prior approval was obtained from the Research committee and the Institutional Ethics committee before the commencement of the study. The study participants (normal controls and individuals with subclinical Hypothyroidism) were selected from the biochemistry laboratory register, based on the Thyroid Profile. Only subjects satisfying the inclusion and exclusion criteria were included for the study. Informed consent was obtained from all the study participants. After obtaining medical history, a thorough physical examination was performed on all the study participants. All demographic details were recorded through a structured questionnaire.

The study participants were divided into two groups as follows:

Group I – Normal

Group II – Subclinical Hypothyroidism

Individuals with subclinical Hypothyroidism will be divided into three subgroups based on their TSH levels as follows:

Group IIa - TSH between 5.5 – 6.9 mIU/L

Group IIb – TSH between 7 – 8.49 mIU/L

Group IIc – TSH between 8.5 – 10 mIU/L

### **Study Tools:**

The principal investigator was trained by a Clinical Psychologist from the department of Psychiatry regarding the administration of questionnaire to the study participants. The study subjects were explained in detail regarding the need, nature and usefulness of the study tools. The details of the study tools were clearly explained to the study participants in their own language and then administered.

Two tools were used to assess the cognitive functioning of the study participants. The mini-mental state examination (MMSE) a questionnaire comprising of 11 questions tests the individual's orientation, calculation, attention, recall, language and motor skills, making to a total score of 30. A score of 25 and above is considered as normal.

Montreal Cognitive assessment (MoCA) (tamil version) is a rapid screening tool to assess mild cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuospatial constructional skills, conceptual thinking, calculations and orientation. The total possible score is 30 points; a score of 26 or above is considered normal. This tool was used for literate individuals with minimum 6 years of primary education.

### **Statistical Analysis:**

Description of categorical variables were done by using percentage and continuous variables using mean and standard deviation. Mean scores of the cognitive tests were compared between the normal and subclinical hypothyroid individuals using student t test. Scores within the three subgroups of subclinical hypothyroid individuals was by one way ANOVA. Pearson correlation test was used to correlate the TSH levels with cognitive scores.  $p < 0.05$  was considered statistically significant. SPSS version 20 was used for statistical analysis.

### **Results**

Table 1 shows the basic parameters of the study participants. Of the 102 study participants, 8.8% were males, 91.2% were females. 52 study participants were diagnosed as subclinical hypothyroidism and remaining 50 study participants were normal individuals with normal thyroid profile. The mean age of the study participants were  $37.09 \pm 9.97$ . The TSH values were significantly different between the two groups.

Table 2 shows the comparison of MMSE and MoCA scale scores between Literate normal individuals and individuals with subclinical hypothyroidism. TSH values were significantly different between both the groups. The total scores and the scores of individual domains of MoCA and MMSE were not statistically different between the two groups. However the scores in language domain of MMSE was significantly lower in individuals with subclinical hypothyroidism.

**Table 1: Basic Parameters of the study participants**

Parameters	Normal	Subclinical Hypothyroidism
n	50	52
Age	36.28 ± 10.20	37.88 ± 9.79
Free T <sub>3</sub>	2.70 ± 0.47	2.73 ± 0.44
Free T <sub>4</sub>	1.10 ± 0.36	1.02 ± 0.15
TSH	2.31 ± 1.28	7.25 ± 1.35*

n - Number of the study participants, \* p < 0.001, TSH – Thyroid stimulating Hormone

**Table 2: Comparison of cognition scores between literate normal and individuals with subclinical Hypothyroidism**

Parameters		Normal	Subclinical Hypothyroidism
n		25	27
Age		33.20 ± 10.07	34.55 ± 10.69
Free T <sub>3</sub>		2.63 ± 0.40	2.66 ± 0.49
Free T <sub>4</sub>		1.08 ± 0.24	1.01 ± 0.14
TSH		2.39 ± 1.23	6.98 ± 1.04*
MoCA Scale Scores	Visuospatial	4.16 ± 0.55	4.11 ± 0.42
	Naming	3.00 ± 0	2.96 ± 0.19
	Attention	5.68 ± 0.62	5.29 ± 0.82
	Language	3.00 ± 0	3.00 ± 0
	Abstraction	1.80 ± 0.40	1.85 ± 0.30
	Delayed Recall	3.48 ± 1.22	3.40 ± 1.04
	Total	27.12 ± 1.78	26.55 ± 1.64
MMSE Scale Scores	Orientation	10.00 ± 0	10.00 ± 0
	Registration	3.00 ± 0	3.00 ± 0
	Attention	4.72 ± 0.54	4.66 ± 0.62
	Recall	2.64 ± 0.70	2.77 ± 0.42
	Language	8.76 ± 0.43	8.07 ± 1.03*
	Total	29.12 ± 1.16	28.48 ± 1.50

n – Number of study participants, TSH – Thyroid stimulating hormone, MoCA – Montreal Cognitive Assessment, MMSE – Mini Mental State Examination, \* p < 0.05

Table 3 shows the comparison of MMSE scores between illiterate normal individuals and individuals with subclinical hypothyroidism. TSH values were significantly different between both the groups. The total scores MMSE were lower in subclinical hypothyroidism compared to the normal individuals. The scores in calculation domain of MMSE was significantly lower in individuals with subclinical hypothyroidism. However the scores in the other domains were not statistically significant.

**Table 3: Comparison of cognition scores between illiterate normal and individuals with subclinical Hypothyroidism**

Parameters		Normal	Subclinical Hypothyroidism
n		25	25
Age		39.36 ± 9.54	41.4 ± 7.33
Free T <sub>3</sub>		2.78 ± 0.53	2.81 ± 0.38
Free T <sub>4</sub>		1.12 ± 0.45	1.03 ± 0.15
TSH		2.23 ± 7.54	1.36 ± 1.58*
MMSE Scale Scores	Orientation	8.76 ± 0.87	8.24 ± 0.96
	Attention	6.40 ± 0.81	6.16 ± 1.02
	Calculation	4.92 ± 0.40	4.28 ± 0.93*
	Recall	2.52 ± 0.58	2.20 ± 0.57
	Language	5.00 ± 0	4.96 ± 0.20
	Total	27.6 ± 1.89	25.8 ± 1.90*

n – Number of study participants, TSH – Thyroid stimulating hormone, MMSE – Mini Mental State Examination, \* p < 0.05

Table 4 shows the comparison of the cognitive scores within the subgroups of subclinical hypothyroidism. There was no statistically significant difference in the cognitive scores between the three subgroups of subclinical hypothyroidism.

Table 5 shows the correlation between the TSH values and the cognition scores. There was a significant negative correlation between the TSH values and the MMSE total score (p < 0.05).

**Table 4: Comparison of cognition scores between the subgroups of subclinical hypothyroidism**

Parameters	Subclinical Hypothyroidism		
	II <sub>a</sub>	II <sub>b</sub>	II <sub>c</sub>
MoCA scores	26.00 ± 1.41	26.81 ± 1.77	26.42 ± 1.65
MMSE scores	28.00 ± 1.41	27.90 ± 1.81	29.00 ± 1.10

MoCA – Montreal Cognitive Assessment, MMSE – Mini Mental State Examination

**Table 5: Correlation between TSH values and the cognitive scores**

Parameters	MMSE score		MoCA Score	
	r	p	r	p
TSH	-0.312	0.024*	-0.165	0.243

MoCA – Montreal Cognitive Assessment, MMSE – Mini Mental State Examination,

\* statistically significant

### Discussion

Several studies have addressed the association of cognitive impairment with hypothyroidism.<sup>[12,13]</sup> Literature on cognitive function in subclinical hypothyroidism remain sparse and inconclusive. In the present study there was no significant difference in the cognitive scores between the normal individuals and individuals with subclinical hypothyroidism. Similar results were observed by other studies using global cognitive measurement scales.<sup>[14,15]</sup>

However a significant difference was observed in the global cognitive scores between illiterate normal individuals and illiterate sub clinically hypothyroid individuals. Bajaj et al reported a higher prevalence of cognitive impairment in subclinical hypothyroidism using MMSE and clock drawing test.<sup>[9]</sup> Similar results were observed by Baldini et al<sup>[16]</sup> and Cook et al.<sup>[17]</sup> But in the present study a significant correlation was observed between TSH values and MMSE scores. These results go in consistency with that of Bajaj et al<sup>[9]</sup> and Hogervorst et al.<sup>[18]</sup>

These controversies could be explained by the fact that in the present study the sample size was small and the age group was between 20 – 50 years, whereas the studies that showed cognitive impairment in subclinical hypothyroidism were carried out in elderly individuals. However as TSH levels has shown a significant correlation with MMSE scores, care need to be taken for the individuals with subclinical hypothyroidism, as they advance in age, they are easily prone for developing overt hypothyroidism and are still at higher risk of developing cognitive impairment.

### Conclusion

While the neurological manifestations of overt hypothyroidism are well addressed, literature on cognitive function in subclinical hypothyroidism remain sparse and inconclusive. In the present study MMSE and MoCA scores did not show a significant difference in cognitive scores between normal individuals and individuals with subclinical hypothyroidism. Hence future studies with large sample size and sensitive cognitive measurements with different scales may be recommended for early identification of cognitive impairment in subclinical hypothyroidism.

### Acknowledgment:

We would like to thank the Department of Biochemistry, Sri Manakula Vinayagar Medical College and Hospital for extending their support in the selection of study subjects.

### References:

1. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian Journal of Endocrinology and Metabolism*. 2013;17(4):647-652.
2. Wiersinga WM. Guidance in Subclinical Hyperthyroidism and Subclinical Hypothyroidism: Are we making progress?. *Eur Thyroid J* 2015;4:143-148.
3. Deshmukh V, Behl A, Iyer V, Joshi H, Dholye JP, Varthakavi PK. Prevalence, clinical and biochemical profile of subclinical hypothyroidism in normal population in Mumbai. *Indian Journal of Endocrinology and Metabolism*. 2013;17(3):454-459.
4. Akintola AA, Jansen SW, van Bodegom D, van der Grond J, Westendorp RG, de Craen AJ et al. Subclinical hypothyroidism and cognitive function in people over 60 years: a systematic review and meta-analysis. *Frontiers in Aging Neuroscience*. 2015;7:150.
5. Sankareswari A, Affiya Shreen L, Vigil TD, Naveen S, Chandrasekhar M. Evaluation of peripheral nerve conduction and visual evoked potential in newly diagnosed hypothyroid females. *Int J Med Res Health Sci*. 2016;5:43-6.
6. Cook SE, Nebes RD, Halligan EM, Burmeister LA, Saxton JA, Ganguli M et al. Memory impairment in elderly individuals with a mildly elevated serum TSH: the role of processing resources, depression and cerebrovascular disease. *Aging, Neuropsychology and Cognition*. 2002;9(3):175-183.
7. Osterweil D, Syndulko K, Cohen SN, Pettler-Jennings PD, Hershman JM, Cummings JL, et al. Cognitive function in non-demented older adults with hypothyroidism. *Journal of the American Geriatrics Society*. 1992;40(4):325-335
8. Raza SA, Mahmood N. Subclinical hypothyroidism: Controversies to consensus. *Indian J Endocr Metab* 2013;17, Suppl S3:636-42.
9. Bajaj S, Sachan S, Misra V, Varma A, Saxena P. Cognitive function in subclinical hypothyroidism in elderly. *Indian J Endocr Metab* 2014;18:811-4.
10. Jensovsky J, Ruzicka E, Spackova N, Hejdukova B. Changes of event related potential and cognitive processes in patients with subclinical hypothyroidism after thyroxine treatment. *Endocrine Regulations*. 2002;36(3):115-122
11. Davis JD, Tremont G. Neuropsychiatric aspects of hypothyroidism and treatment reversibility. *Minerva Endocrinol*. 2007;32:49-65.
12. Constant EL, Adam S, Seron X, Bruyer R, Seghers A, Daumerieet C, et al. Anxiety and depression, attention, and executive functions in hypothyroidism. *J Int Neuropsychol Soc*. 2005;11:535-544.
13. Resta F, Triggiani V, Barile G, Benigno M, Suppressa P, Giagulli VA, et al. Subclinical hypothyroidism and cognitive dysfunction in the elderly. *Endocr Metab Immune Disord Drug Targets*. 2012; 12:260- 267

14. Miao YU, Ying Y, Song CHI, Fang W. The characteristics of cognitive impairment in patients with primary hypothyroidism. Chinese Journal of Behavioral Medical and Brain Science.2013;4:332-334.
15. Osterweil D, Syndulko K, Cohen SN, Pettler-Jennings PD, Hershman JM, Cummings JL, et al. Cognitive function in non-demented older adults with hypothyroidism. J Am Geriatr Soc. 1992;40:325–35.
16. Luboshitzky R, Oberman AS, Kaufman N, Reichman N, Flatau E. Prevalence of cognitive dysfunction and hypothyroidism in an elderly community population. Isr J Med Sci. 1996;32:60–5.
17. Baldini IM, Vita A, Mauri MC, Amodei V, Carrisi M, Bravin S, et al. Psychopathological and cognitive features in subclinical hypothyroidism. Prog Neuropsychopharmacol Biol Psychiatry. 1997;21:925–35.
18. Cook SE, Nebes RD, Halligan EM. Memory impairment in elderly individuals with a mildly elevated serum TSH: The role of processing resources, depression and cerebrovascular disease. Aging Neuropsychol Cogn. 2002;9:175–83.
19. Hogervorst E, Huppert F, Matthews FE, Brayne C. Thyroid function and cognitive decline in the MRC funded cognitive function and ageing study. Psychoneuroendocrinology. 2008;33:1013–22.

Date of Submission: 30 June 2020

Date of Peer Review: 12 July 2020

Date of Acceptance: 2 Aug 2020

Date of Publishing: 15 September 2020

Author Declaration: Source of support: Nil, Conflict of interest: Nil

Ethics Committee Approval obtained for this study? YES

Was informed consent obtained from the subjects involved in the study? YES

For any images presented appropriate consent has been obtained from the subjects: YES

Plagiarism Checked: YES

Author work published under a Creative Commons Attribution 4.0 International License



Creative Commons Attribution

CC BY

DOI: 10.36848/IJBAMR/2020/18215.55592