DAYTIME SLEEPINESS AND COGNITIVE FUNCTIONS IN TYPE 2 DIABETES MELLITUS PATIENTS IN INDIAN POPULATION: A CROSS-SECTIONAL STUDY

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ABSTRACT
Aim and Background: Daytime sleepiness is difficulty to stay awake and due to insufficient sleep. The wide range of complications of type 2 diabetes mellitus is responsible for the poor quality of sleep in the working population. There are psychomotor deficits have been found in these patients. Study aims to evaluate the effect of daytime sleepiness on cognitive functions in patients of type 2 diabetes mellitus in Indian population. **Material and Methods:** We have conducted a cross-sectional study in Pune to study the daytime sleepiness on cognitive functions in type 2 diabetes mellitus with the help of the pretested Epworth sleepiness scale for daytime sleepiness and Trail making test for cognitive functions. Sample size calculated to be 74. Patients divided in to 3 groups based on The ESS. ANOVA applied for statistical analysis and data analyzed with the help of SPSS v2020. **Results:** There is a significant difference seen between the means of the groups of ESS and TMT B with the P value of <0.05. **Conclusion:** This states that the groups of type 2 diabetes mellitus patients of higher Epworth Sleepiness Scale take more time to complete the trail making test B which indicates impairment in the executive function.
Keywords: Daytime sleepiness, ESS, Cognitive functions, Type 2 diabetes mellitus.

INTRODUCTION
Daytime sleepiness is commonly the result of concealed ailments or insufficient sleep [1]. Daytime sleepiness is characterized by difficulty in staying alert and awake during major waking times of day, with sleep occurring unintentionally during the wake period [2]. Epidemiological studies have demonstrated an association between sleep disturbance and adverse health outcomes like impaired glucose tolerance, obesity, hypertension, and other cardiovascular disorders (CVD) [3]. Sleep deprivation studies suggest that habitual short sleep results in a reduction in insulin sensitivity, and a risk factor for the later development of diabetes [4]. Diabetic patients are more sleepy during the daytime [5]. The wide range of complications of type 2 diabetes mellitus is responsible for the poor quality of sleep in the

working population [6]. Deficits have been seen in areas of psychomotor alertness, episodic memory, semantic memory, and working memory.

Considering the importance of self-management requirements in diabetes treatment and the high complexity of diabetes treatment plans, diabetic patients with cognitive dysfunction may experience significant difficulty managing their diseases [7]. There are very few studies conducted to examine in the Indian subcontinent on daytime sleepiness in patients of type 2 Diabetes Mellitus and its association with cognitive function, which may impact functional and social outcomes of society. The study is focused on evaluating the effect of daytime sleepiness on cognitive functions in patients of type 2 diabetes mellitus.

MATERIAL AND METHODS

We have conducted cross sectional study in the Department of Physiology, at the tertiary care centre of western Maharashtra, India. The study carried out in between the years 2019 – 2021 and approval of the institutional ethical committee was taken on 18 Oct 2019. The participants of the study were adult patients and diagnosed cases type 2 DM (Type 2 DM already diagnosed as per International Diabetic Federation criteria 2019) [8]. Sample size calculated to be 74. Patients were divided in to 3 groups based on The ESS. ANOVA applied for statistical analysis. Data analysis was done with the help of SPSS v2020.

The focus was to study the daytime sleepiness on the cognitive functions in diabetes mellitus patients with help of the Epworth sleepiness scale and Trail making test for Cognitive functions particularly the executive functions [9]. The selected age group for the study was between 40 to 60 yrs old and who were diagnosed case of diabetes mellitus type 2 as per the IDF -2019 updates [8]. Only the stable patients were selected. Patients with complications of diabetes mellitus type 2 like acute kidney failure, severe infections, acute cases of metabolic syndrome were not a part of the study. Patients with cardiovascular, cerebrovascular and neurovascular complications were excluded from the study. Patients with Psychiatric illnesses like Schizophrenia, dementia, delirium were out of the study. Chronic Alcoholics patients, as well as night shift workers, were not a part of this study. The participants who were already suffering from sleep disorders like obstructive sleep apnea, restless leg syndrome were not part of the study.

Epworth Sleepiness Scale (ESS), self-administered questionnaire that is shown to provide a measurement of the subject's general level of daytime sleepiness. This scale is developed by Murray W. Johns Sleep Disorders Unit, Epworth Hospital, Melbourne, Victoria, Australia in the year 1991.Every situation mentioned is scored from 0 to 3 based on individuals' tendency to fall asleep and their total score is calculated as an ESS score. Interpretation of ESS is done as per score done for daytime sleepiness. More the ESS of the patient higher is daytime sleepiness. 0-7: Unlikely that you are abnormally sleepy. 8-9: You have an average amount of daytime sleepiness. 10-15: You are excessively sleepy depending on the situation. You may want to take an advice for medical attention. 16-24: You are excessively sleepy, and you should consider seeking medical attention [10]

Further, they were asked to complete the Trail Making Test. This test is developed by Halstead-Reitan as a Neuropsychological Battery test and consists of parts A and part B. The Trail Making Test is principally regarded as a test of visual conceptual and visio-motor tracking [11]. Trail making tests Part A and Part B are used from the from study Gaudino EA *et al.* [12]. Each part of the test consists of 25 spots encircled each one of them on an 8.5" X 11" sheet of paper, which the participants have to connect by pen mark. Part A contains numbered spots only, connected in sequence, starting from 1 through 25. Part B consists of numbers and letters

mingled in between the numbers, connected in alternating fashion: 1 to A, A to 2, 2 to B, and so on. Tests are studied for total time taken is noted in seconds by the patients on each part to complete (9)

Study Protocol: Data is was collected from a total of 74 volunteered patients with Diabetes Mellitus type 2 patients (46 males and 28 females), visiting the tertiary care hospital. The procedure of the study was explained to the participants and willingly informed written consent was obtained. Relevant history was obtained and recorded. This includes demographic details of the patients like the name, age, sex and physical parameters noted were height, weight, and BMI. Patients were also asked about the history of the duration of the diabetes mellitus from the diagnosis to date, any history of smoking in any form, and comorbidities including hypertension were asked. Particularly, those who were suffering from psychological disorders, sleep disorders, obstructive sleep apnoea, alcohol intake, night shift workers are not included in the study. Patients were briefed about the questionnaire of ESS and instructed to give appropriate scores for all 8 questions according to each question in the set, and its total score was recorded. The patient who required help have been dictated the exact connotation to complete their score. Total ESS was calculated by adding the score of all 8 questions.
Then, the same patients were given a paper of the Trail making test part A and part B to perform. The time taken to perform both tests was noted separately in seconds on the same paper and recorded for data analysis. Due care has been taken that if the patients were suffering from myopia, they should use their spectacles while performing the test. They were not allowed to lift the pen once they have started the exercise, not to repeat the same number.

Statistical Analysis

The sample size has been calculated on the basis of mean ± SD of the Epworth sleepiness scale from the available previous study and calculated to be 74. Data were expressed in terms of mean ± SD. One sample Kolmogorov Smirnov test is used to check the normality of distribution. The comparison between the groups is analyzed by one-way analysis of variance (ANOVA). A type of multiple comparison test Bonferroni (ANOVA-post hoc Test) test is also used to check the difference between quantitative data between the groups after checking the homogeneity. IBM SPSS software version 20.0 has been utilized to analyze the data.

RESULTS

The present study was performed to measure ESS and Trail making test part A and Part B in type 2 DM patients. A total no of 74 patients of diabetes type 2, who fulfilled the inclusion and exclusion criteria, were voluntarily recruited in the study.
The patients have been diagnosed cases of diabetes mellitus type 2 as per IDF criteria year 2019 and updates. Their reports of blood glucose levels have been noted, which may include random blood glucose levels or fasting and postprandial glucose or HbA1c or 2-hour postprandial report is noted.
The results were compiled and analyzed after the end of data collection of the study. Out of the total 74 patients, 46 men and 28 are women. All the patients were in between the age group of 40 to 60 years, the mean age was 51.3 ± 6.9 years. The Mean duration of the diabetes was 6.1±6.2 years, Mean ESS was 5.4 ± 2.4 and the TMT A and TMT B were 59.6±19.9 and 100.7±39.7 in seconds respectively. Groups 1,2 and 3 of the ESS are the patients having ESS scores between 0-7, 8-9, more than 10. ANOVA has been applied to see the difference between the means of groups of ESS and TMT A and TMT B Table (1 and 2).

Table 1: Descriptive statistics between the groups of ESS and TMT A and B

	Group	N	mean	SD	p value.
ESS_TMT A	0-7	61	58.6	19.1	0.16
	8-9	6	74.4	28.5	
	≥10	7	56.5	15.9	
	Total	74	59.6	19.9	
ESS_TMT B	0-7	61	95.2	33.6	0.005*
	8-9	6	148.9	57.0	
	≥10	7	108.0	50.2	
	Total	74	100.0	39.7	

Table 2: One way ANOVA between the groups of ESS and TMT A and TMT B

		Sum of Squares	df	Mean Square	F	Sig.
ESS_TMT A	Between Groups	1445.133	2	722.567	1.863	.163
ESS_TMT B	Between Groups	16191.681	2	8095.841	5.787	.005*
TMT A, and B: Trail making test A and B, df: degrees of freedom, F: F-test, p value <0.05 is statistically significant shown by *						
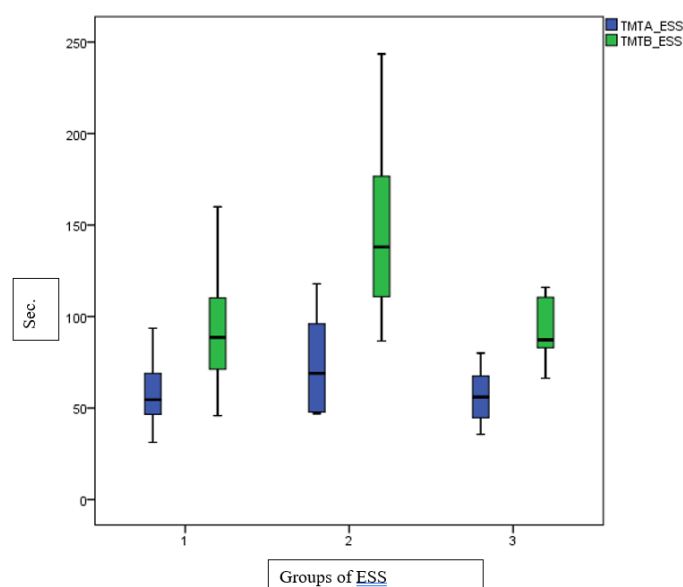
Figure 1: Whisker Box Plot of the groups of ESS and TMT A and TMT B.

It is found that there is a significant difference is seen between the means of the groups of ESS and TMT B with a p-value of 0.005 (Table 2). ANOVA post hoc test (Bonferroni test) applied and found that there is a significant difference found in group 1 (ESS 0-7) and 2 (ESS 8-9) and the p-value is 0.001. There is no statistically significant difference in groups ESS and TMT A and the p-value is 0.16 (Table 1 and 2). Whisker boxplot shows the group 2 of having ESS 8-9 taking more time to complete the TMT (Fig.1).

DISCUSSION

The present study was designed to evaluate the effect of daytime sleepiness on cognitive functions in type 2 diabetes mellitus (type 2 DM). Out of the total 74 patients, 46 men and 28 were women. All the patients were in between the age group of 40 to 60 years. The mean age was 51.3 ± 6.9 years. The average BMI of the patients was 26.9 ± 5.5. The Mean Duration of the diabetes was 6.1 ± 6.2 years, Mean ESS was 5.4 ± 2.4 and the TMT A and TMT B were 59.6 ± 19.9 and 100.7 ± 39.7 in seconds respectively.

There was a significant difference is seen between the means of the groups of ESS and TMT B where the p-value is 0.005 (Table 2). This is found in group 2 who were having ESS of 8-9 and the p-value is 0.005. This states that the groups of the diabetic patients of ESS between 8-9 take more time to complete the trail making test B which is an indicator for declined cognitive functions in the form of Executive functions [13]This finding is in support of the previous numerous studies. A review of the literature by Audrey Gabelle *et al.* at the University of Montepellier, in France, was done to identify self-reported sleep-wake disturbances over a 1-year follow-up in patients of age group more than 70 yrs. They have used clinical interviews and numerous validated questionnaires, like Epworth Sleepiness Scale for measuring excessive daytime sleepiness (EDS). They concluded that the risk of cognitive decline is higher in subjects with EDS (MMSE decline (OR = 2.46; 95% CI, p-value = 0.007) [14].

The presence of a cognitive decline in the given age groups of excessive daytime sleepiness may be symptomatic for an early change in circadian rhythm due to neurological damage [15]. The cycle is influenced by factors such as physical activity and, especially, environmental light. If this normal physiological cycle becomes desynchronized with the sleep period or with the daily schedule, the EDS may be experienced [16]. This neurological damage may involve grey matter, and white matter, which comprises the cortex and thalamus, and basal ganglia, which covers demyelination of the axons, and damage of the connections between grey matter areas. The damage to certain areas is responsible for convinced deficits. Insult to the parietal lobe can cause the inability to dress or visuospatial function. When there is damage to the frontal lobe systems, it can cause deficits in planning, and abstract understanding and damage to the temporal lobes cause deficits in language and memory [17]

Strengths of the study:

Our study is targeted towards the specific population of diabetes between the age group of 40 to 60 years and conducted in a particular in the Indian subcontinent. India is highly prevalent with cases of diabetes mellitus this study stands very relevant to society.

Limitations of the Study:

One limitation of the study is that the patients educational level can be considered while performing the test. While performing TMT different groups will have different values of TMT (18). The study can be targeted towards populations of type 2 DM follow-up for particular duration, their control of hyperglycemia and control of potential confounders.

Prospective studies and case-control studies have been recommended in future to demonstrate a causal relationship between Hyperglycemia and daytime sleepiness and cognitive functions.

CONCLUSION

The result of the study shows that the patients with more Epworth sleepiness scale (ESS) among type 2 diabetes mellitus (type 2 DM) patients show significant cognitive deterioration in the form of delayed executive functions.

It is important to understand the role of daytime sleepiness in the impairment of cognitive functions in diabetes mellitus type 2 patients. For this reason, all the patients with type 2

diabetes mellitus coming to OPD should be evaluated for sleep and on the domain of cognitive parameters along with the treatment of type 2 diabetes mellitus.

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