

## ‘A Prospective Observational Study to Analyze the Cognitive Functions in Patients with Type II Diabetes Mellitus at Tertiary Care Teaching Hospital’

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### ABSTRACT

**Background and objectives:** - Diabetes is considered as self-contained risk factor for cognitive impairment and dementia. In this study we assess the cognitive function in patients with type 2 diabetes mellitus by using MMSE and also found correlation of age duration of diabetes and HbA1c with cognitive function among the diabetics.

**Materials and Methods:**-100 type 2 DM subjects of both sexes between 40-60 years age group and a total of 100 apparently healthy individuals taken as control group who were age, sex, BMI and education matched. Both the group are undergone through MMSE scores and the correlation between age, duration of diabetes and HbA1c was done.

**Result:-** In this study 100 type 2 diabetic patient where taken as study group and 100 age, sex, BMI, and education matched healthy individuals where taken as cognitive group, the cognitive status of type 2 DM subjects and healthy controls without diabetes who was evaluated through MMSE about 89% had mild cognitive impairment and 11% had moderate cognitive impairment in the study group and 78% had normal cognitive and 22% had mild cognitive control group after making correction for age and educational qualification there was a significant decrease in MMSE score among the diabetic ( $p < 0.001$ )

**Conclusion:-**Cognitive decline was observed in all the three age groups, but the comparison of significant MMSE scores between the groups was not significant. In this study it was observed that individuals with higher HbA1c levels performed poorly in cognitive examination suggesting that glycemic control has an influence on cognitive function.

**Keywords**Type 2 diabetes, cognitive impairment, MMSE, blood glucose, HbA1c, duration of diabetes.

### I. INTRODUCTION

Diabetes Mellitus is a chronic disease characterized by dysfunction of secretion and usage of insulin, leading to hyperglycemia<sup>1</sup>. Diabetes is considered as non-communicable illness, with around 173 million individuals all over the world. As population is expanding, getting more seasoned, more self-evident and stationary, the number of people with diabetes moreover increments<sup>2</sup>. Type I diabetes mellitus is characterized by autoimmune destruction of beta cells in pancreas leading to absolute insulin deficiency. Type 2 diabetes mellitus predominantly shows resistance to insulin<sup>3</sup>.

Irrespective of the mechanism underlying this cognitive impairment, patients with DM 2 moreover show a wide variety of comorbidities and related disease requiring extensive care. In fact, cognitive dysfunction might contribute to a declining within the clinical condition of such patients, who may disregard medications or become more confined in their social lives. In this manner evaluating the cognitive conditions of DM 2 patient should form routine medical practice and not relying upon highly specialized (and often difficult to obtain) neurophysiological tests<sup>1</sup>.

If early dementia is properly recognized and treated, progression can be prevented by regulating blood glucose and planning cognitive exercises<sup>10</sup>. Both type 1 and type 2 diabetes mellitus have shown to cause deficiencies in various dominants of cognitive function<sup>5</sup>. Type 2 diabetes is related with accelerated cognitive decline and increased risk of dementia particularly in older individuals. Previous studies have shown decrements in memory function, executive function and information processing speed. These decrements in cognitive capacities are related with modest brain atrophy and vascular lesions on brain magnetic resonance imaging. Diabetes related

factors, such as insulin resistance, persistent hyperglycemia, hypertension and lipid disorders likely are significant determinants<sup>6</sup>.

As diabetes could be a heterogeneous illness that is easily composed by hypertension, dyslipidemia and so on, it is considered to be a clinical condition that is adjusted by numerous components. In any cases, for cognitive dysfunction, the fundamental conditions are blood glucose disorders, such as insulin resistance and insulin insufficiency, have been shown to lead to cognitive dysfunction<sup>7</sup>. Length of the diabetes have moreover been related with cognitive decrements such as immediate verbal recall, delayed verbal recall and abstract reasoning. Pre-diabetes, poor control and longer duration of disease where related with more prominent late-life cognitive decline<sup>9</sup>.

Cognitive impairment is defined as difficulty in remembering, learning things, concentrating or making choices that influence everyday life. It is a major community concern since it results in functional disability and it increases healthcare cost. It might antagonistically influence the administration plan or cause serious harm especially in patients with diabetes. Since patients concepts with respect to the need for regular follow-up, self-care, adherents to diet, exercise and medications develop mainly on an in-fact memory<sup>10</sup>.

Diabetes is the 5<sup>th</sup> cause of hospitalization and a fundamental cause of death among the ten major causes of mortality in our nation. As specified by many studies about more than 50% of these patients will pass away from cardiovascular disease. Other than diabetes these patients generally have other comorbidities such as hypertension, weight and dyslipidemia. Nowadays there is solid proof that bear an intensive control of glycaemia, blood pressure, cholesterol and weight to intercept cardiovascular and diabetes persistent obstacles pointing to diminish morbidity and mortality of the illness. Due to departed incidents patients ought to alter their way of life and take numerous diverse pills to attain a great control of all parameters. These components make it troublesome for patients who are not able to perform themselves or have poor educational and cognitive levels, which may head to false elucidation of medicine and as a result, an adequate adhesion to treatment<sup>11</sup>.

MMSE was developed by Folstein et al. It is broadly utilized to identify cognitive disability around the world. It does not require any medical equipment for testing and can be executed by any

healthcare worker with a short training<sup>12</sup>. Mini-Mental State Examination (MMSE) was utilized to evaluate the level of cognitive impairment. The standard MMSE form was managed to each patients. The scale of MMSE ranges from 0-30 points, where lower score demonstrates way better cognitive execution. The MMSE form incorporates 19 questions conceived to assess the patients mental status being isolated into the following 5 categories: 10 questions about orientation (year, season, date, day, month, state, city, close street, floor and location) 2 items with respect to memory (repeat the words car, window and vase and after delayed recall) 1 item about calculation 5 language items and one constructional items (copy overlapping pentagons). MMSE scores < 27 revealed a normal cognitive, score between 21 and 26 indicated MCI scores between 11 and 20 reported moderate cognitive impairment and scores < 10 were classified as serious cognitive impairment<sup>14</sup>. Cognitive impairment might be another factor associated with poor diabetes control and also with bad adherence of patients to educational approach such as diet orientations<sup>2</sup>.

## II. METHODOLOGY

The study was conducted in the outpatient department of Chigateri District Hospital, Davangere, Karnataka (A tertiary care teaching hospital). A cross sectional observational study will be conducted in the outpatient medicine department in Chigateri District Hospital, Davangere. The data required for the study will be collected from demographic details of patient. Outpatient in general medicine department with or without comorbidities meeting the inclusion criteria will be enrolled in the study. The demographic details age, gender, bodyweight, height, social history, duration of diabetes mellitus and laboratory data will be collected using a suitably designed data collection form. The cognitive impairment will be assessed by using Mini Mental State Examination and result would be analysed by statistical method with IBM SPSS version 25 for Windows. The ethical approval for the study was obtained from the institutional ethics committee of SCS College of Pharmacy.

## III. RESULT

### TABLE 1:- AGE DISTRIBUTION:

Group I: In 41-45 age group 33 patients (33%), in 46-50 age group 36 patients (36%) and in 51-55 age group 31 patients (31%) were present.

Group 2: In 41-45 age group 36 healthy subjects (36%), in 46-50 age group 31 healthy subjects (31%) and in 51-55 age group 33 healthy subjects (33%) were present.

Age wise distribution is same in both study and control group. The mean age in group 1 & group 2 was 48.19 years and 47.96 years respectively.

Age	Group-I	Group-II
Range	41 - 55	41 - 55
Mean	48.19	47.96
SD	4.11	4.41
P value	0.703, Not Significant	

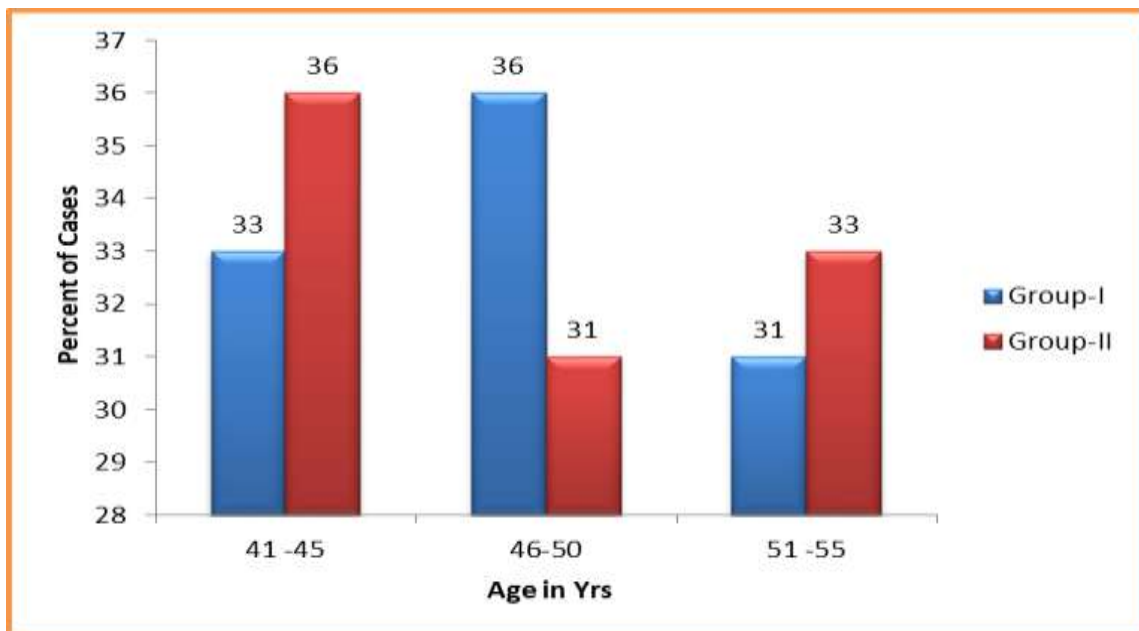


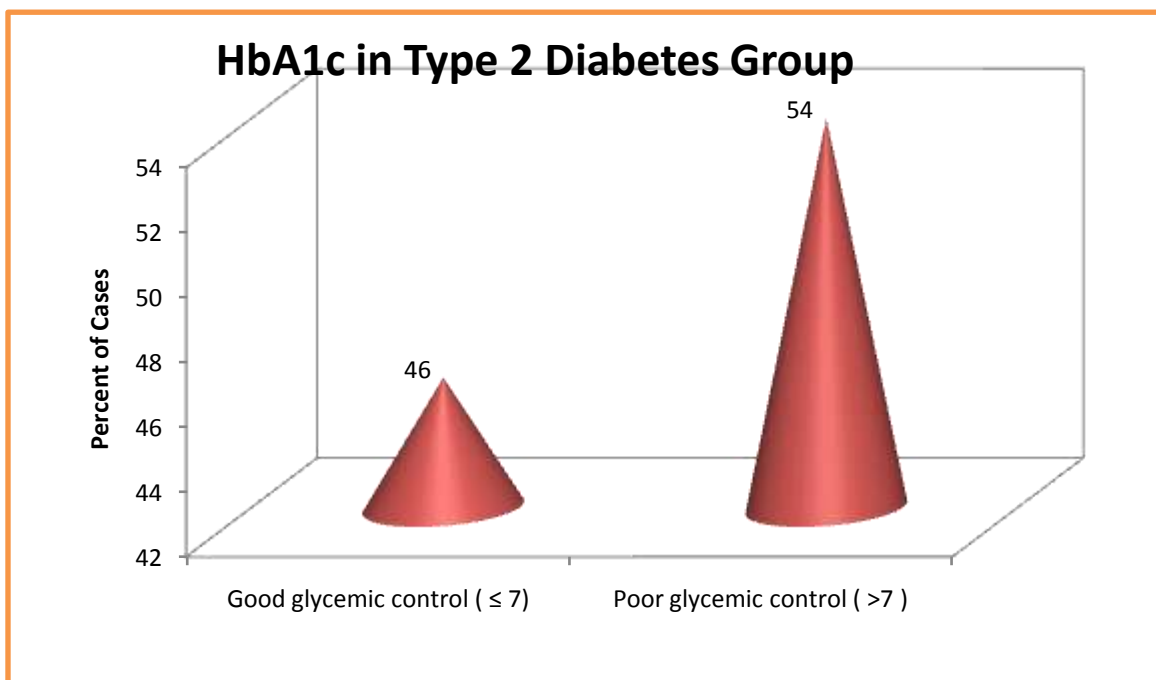
Figure 1: Age distribution in Group I & Group II.

**TABLE 2: GENDER DISTRIBUTION:**

In Group 1 number of male patients were 29(29%) and number of female patients were 71(71%).

In Group 2 number of male patients were 29 (29%) and number of female patients were 71(71%). Gender wise distribution is same in both the study and the control group.

Gender	Group-I		Group-II	
	n	%	N	%
Male	29	29	29	29
Female	71	71	71	71
Total	100	100	100	100
P value	1.00, Not Significant			



**Figure 2:** Gender Distribution in Group I & Group II.

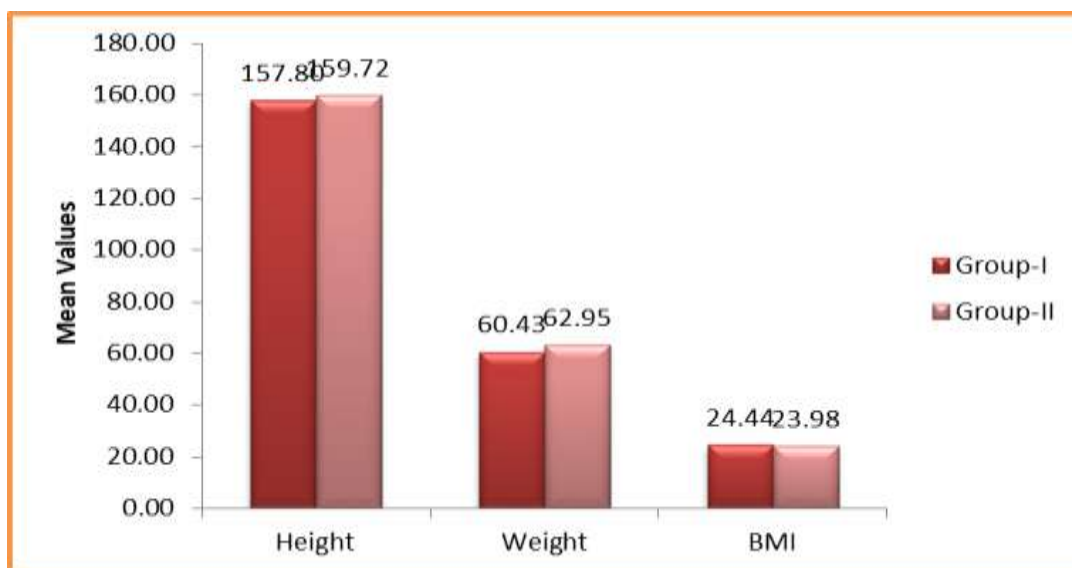
**TABLE 3: COMPARISON OF HEIGHT, WEIGHT & BMI BETWEEN GROUP 1 & GROUP 2.**

In Group I mean height was 157.80, mean weight was 60.43 and mean BMI was 24.44.

In Group II mean height was 159.72, mean weight was 62.95 and mean BMI was 23.98.

There is no statistical difference in height, weight and BMI between group I & group II.

Parameters	Group-I		Group-II		Unpaired t Test P Value
	Mean	Std. Deviation	Mean	Std. Deviation	
Height	157.80	7.95	159.72	8.04	0.076, Not Sig
Weight	60.43	10.12	62.95	9.22	0.067, Not Sig
BMI	24.44	3.43	23.98	2.61	0.287, Not Sig



**Figure 3:** Comparison of height, weight and BMI between Group I & Group II.

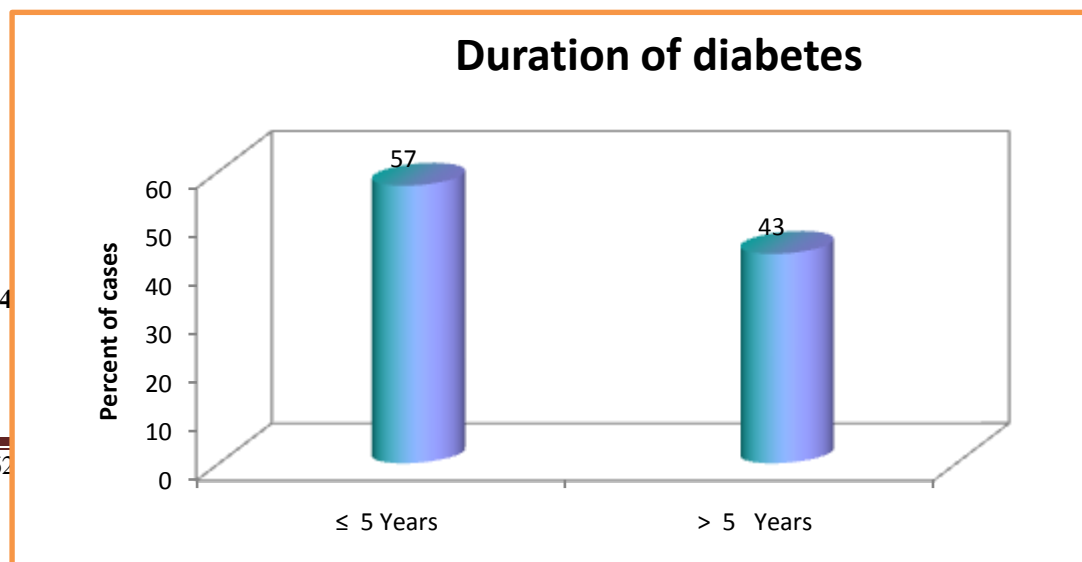
**TABLE 4: DISTRIBUTION OF TYPE 2 DIABETIC SUBJECTS ACCORDING TO HbA1c LEVELS.**

In accordance with HbA1c level 46(46%) patients were under good glyceemic control and 54(54%).patients were under poor glyceemic control.

There is equal distribution of cases in type 2 DM subjects having good glyceemic control and poor glyceemic control.

HbA1c	Type 2 Diabetes Group	
	N	%
Good glyceemic control ( $\leq 7$ )	46	46
Poor glyceemic control ( $> 7$ )	54	54
Total	100	100
<b>HbA1c</b>		
Mean	23.01	
SD	1.74	

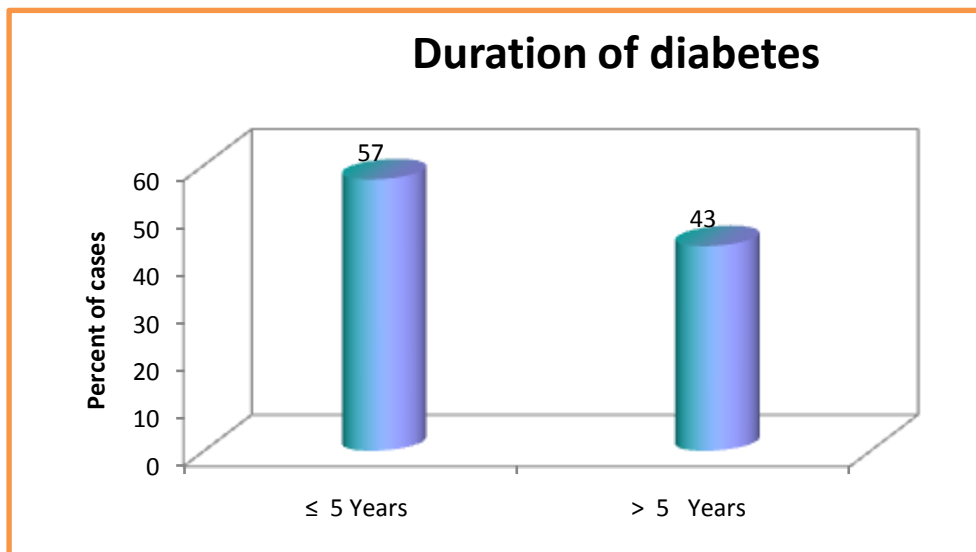
Figure 4



**TABLE 5: DISTRIBUTION OF TYPE 2 DIABETIC PATIENTS ACCORDING TO DIABETIC DURATION.**

According to the duration of diabetes  $\leq 5$  Years were 57(57%), and  $>5$  Years were 43(43%). There is equal distribution of type 2 diabetic subjects with diabetic duration below 5 years and more than 5 years.

Group-I		
Duration of diabetes	Type 2 Diabetes Group	
	N	%
$\leq 5$ Years	57	57
$> 5$ Years	43	43
<b>Total</b>	100	100



**Figure 5:** Distribution of type 2 Diabetic patients according to diabetic duration.

**TABLE 6: DISTRIBUTION OF SUBJECTS ACCORDING TO MMSE GRADES.**

In Group I normal cognition was 0, 89 patients had mild cognition, 11 patients had moderate cognition and severe cognition was 0.

In Group II 100 patients had normal cognition. About 89% of them have mild cognitive impairment and 11% of them have moderate cognitive impairment in group I.

MMSE – SEVERITY	Group-I		Group-II	
	n	%	N	%
Normal Cognition (> 27)	0	0	100	100
Mild cognitive impairment (21 – 26)	89	89	0	0
Moderate cognitive impairment (11- 20)	11	11	0	0
Severe cognitive impairment (< 10 )	-	-	-	-
Total	100	100	100	100
Chi Square test P value	0.001, Significant			

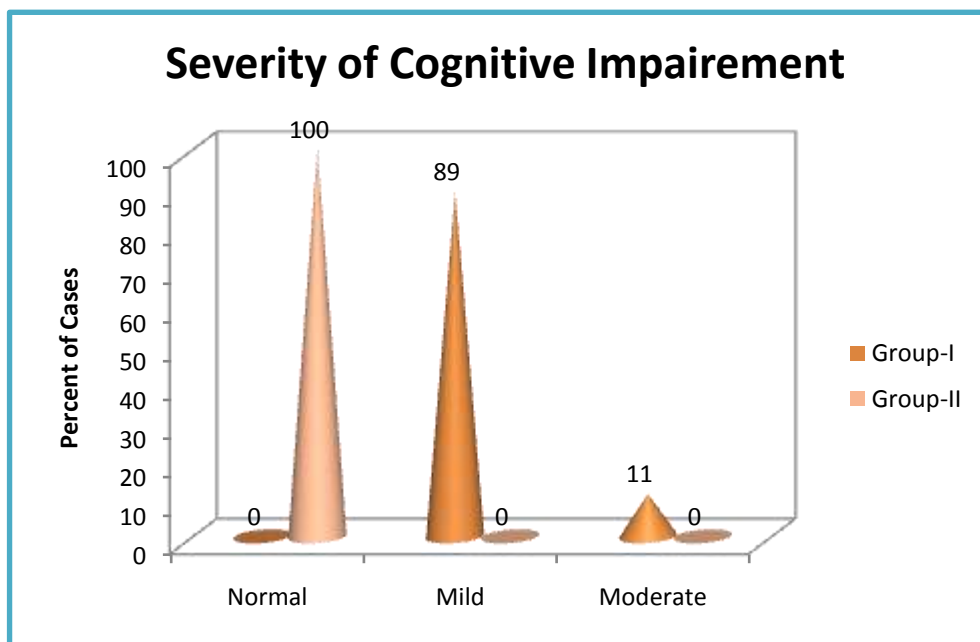


Figure 6: Distribution of subjects according to MMSE grades.

**TABLE 07: COMPARISON OF VARIOUS COGNITIVE DOMAINS OF MMSE**

The mean MMSE score was  $23.01 \pm 1.74$  in study subjects whereas in control subjects it was  $29.01 \pm 1.05$ .

Comparison of the mean scores of various cognitive domains in group I & group II was significant.

CMMSE	Group-I		Group-II		Unpaired t Test Value	P
	Mean	Std. Deviation	Mean	Std. Deviation		



Orientation (10)	7.79	0.82	9.68	0.60	<0.001 Significant
Registration (3)	2.39	0.49	2.88	0.33	<0.001 Significant
Attention & Calculation (5)	3.61	0.53	4.92	0.27	<0.001 Significant
Recall (3)	2.23	0.47	2.86	0.35	<0.001 Significant
Language & visual construction (9)	7.01	0.72	8.70	0.61	<0.001 Significant
Total points (30)	23.01	1.74	29.01	1.05	<0.001 Significant

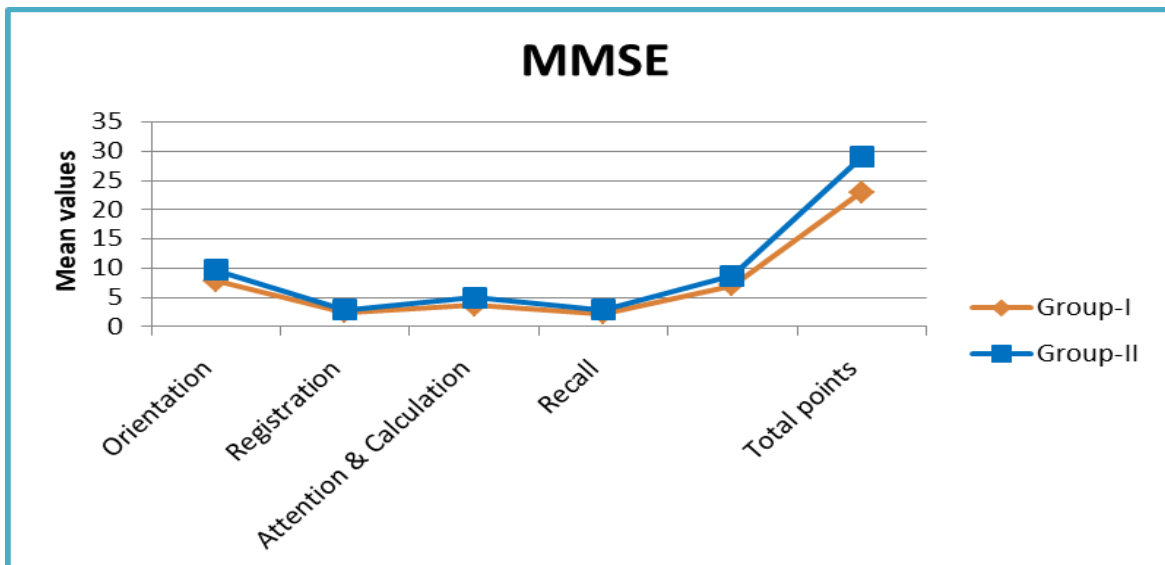


Figure 07: Comparison of various cognitive domains of MMSE.

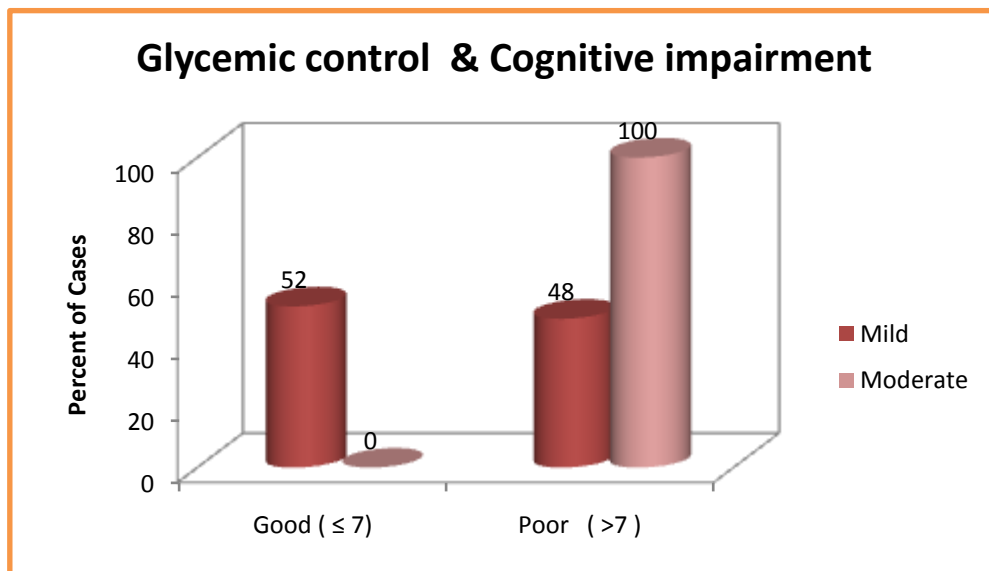
**TABLE 08: COMPARISON OF GLYCEMIC CONTROL AND COGNITIVE IMPAIRMENT.**

In patients with good glycemic control 46(52%) had mild cognitive impairment and had moderate cognitive impairment.

In patients with poor glycemic control 43(48%) had mild cognitive impairment and 11 had moderate cognitive impairment.

Glycemic control	Cognitive impairment			
	Mild		Moderate	
	N	%	N	%

Good ( $\leq 7$ )	46	52	0	0
Poor ( $>7$ )	43	48	11	100
Total	89	100	11	100
Fisher's Exact test P Value	<0.001, Significant			



**Figure 08:** Comparison of glycemic control and cognitive impairment

**TABLE 09: COMPARISON OF DURATION OF ILLNESS AND COGNITIVE IMPAIRMENT.**

Patients with duration  $< 5$  years have 52(58%) had mild cognitive impairment and 5(45%) had moderate cognitive impairment.

Patients with duration  $> 5$  years have 37(42%) had mild cognitive impairment and 6(55%) had moderate cognitive impairment.

Duration of Illness	Cognitive impairment			
	Mild		Moderate	
	N	%	N	%

≤ 5 Years	52	58	5	45
> 5 Years	37	42	6	55
Total	89	100	11	100
Chi Square test P Value	0.412, Not Significant			

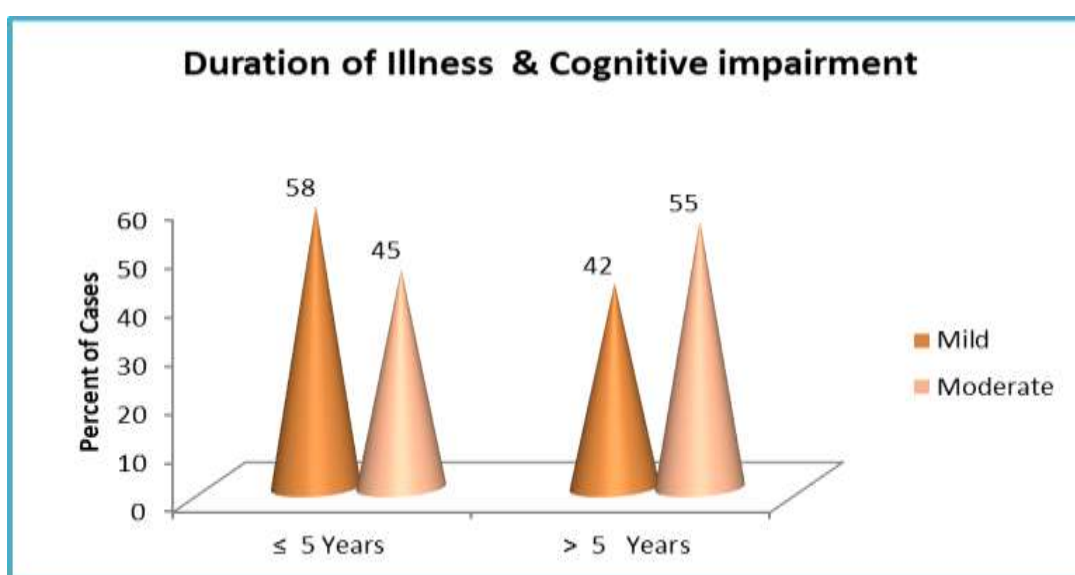


Figure 9: Comparison of duration of illness and cognitive impairment.

#### IV. DISCUSSION

In this study 100 type 2 diabetic patient were taken as study group and 100 age, sex, BMI, and education matched healthy individuals were taken as cognitive group, the cognitive status of type 2 DM subjects and healthy controls without diabetes who was evaluated through MMSE about 89% had mild cognitive impairment and 11% had moderate cognitive impairment in the study group and 78% had normal cognitive and 22% had mild cognitive control group after making correction for age and educational qualification there was a significant decrease in MMSE score among the diabetic ( $p < 0.001$ ). The mean MMSE score was  $23.01 \pm 1.5$  in study subjects, where as in control subject it was  $29.01 \pm 1.05$ . These findings in the current study show the presence of cognitive dysfunction in type 2 subjects. This is similar to various studies which also specified impairment in cognitive function in type 2 diabetes.

Age wise distribution is same in both the study group and control group. The mean age in group I & group II was 48.19 and 47.96 years respectively.

The gender wise distribution is same in both the study and control group.

There is no statistical difference in height, weight and BMI between group I & group II.

There is equal distribution of cases in type 2 DM subjects having good glycemic control and poor glycemic control.

There is equal distribution of type 2 diabetic subjects with diabetic duration below 5 years and more than 5 years.

About 89% of them had mild cognitive impairment and 11% of them had moderate cognitive impairment in group I.

By comparing glycemic control and cognitive impairment, out of 46 good glycemic control patients 46 of them had mild cognitive impairment

and out of 54 poor glycemic control patients 43 had mild cognitive impairment and 11 had moderate cognitive impairment. This shows that glycemic control plays an important role in cognitive impairment.

#### MEAN MMSE SCORE & AGE

In this current study, the men MMSE score of 41-45 years age group was  $23.21 \pm 1.69$  where as in 46-50 years age group was  $22.75 \pm 1.65$  and for those between 51-55 years was  $23.10 \pm 1.92$  cognitive decline is observed in all the 3 age categories but the contrast of the significant MMSE score between the category was not remarkable, this indicate that type 2 diabetes might be a necessary contributing component for cognitive decline in contrast with ageing.

Aimen Malik et al, suggested that advanced age could be a threat for the advancement of cognitive disability in type 2 diabetes. As diabetes mellitus and old age are both unconventional possibilities for developing Alzheimer's disease, vascular dementia and other disorders associating to the pinnacle of cognitive decline a sequences of both can contribute to a superior prevalence of cognitive impairment over older diabetics.

Sandip.k.Dash reported in his study that the frequency of type 2 DM develops with age and the degree of dementia also increases in old age consequently the co-occurrence of diabetes and dementia accelerates with ageing.

#### MEAN MMSE SCORE & HbA1c LEVEL:

The mean MMSE score of type 2 DM subjects with glycosylated Hemoglobin levels were examined and it established that participants with greater HbA1c levels represented unsatisfactorily in cognitive test indicating that glycemic control has an impact on cognitive function. Correlation coefficient between MMSE score and HbA1c was invalid in this study from which it is concluded that rise in HbA1c level is related with depletion in MMSE scores.

Rania Naguib et al, disclosed that the degree of HbA1c was considerably higher in individual with serious cognitive impairment and the chance of cognitive impairment and severe cognitive impairment rises as the grade of HbA1c increases.

OguzTekin et al, established in their study that the length of the disease, high serum HbA1c levels are significant additional risk factors of DM.

#### MEAN MMSE SCORE & TYPE 2 DM DURATION:

In the present study it was also observed that knock off in mean MMSE score in type 2 DM having a timespan above 5 years was prominent when compared to those with timespan less than 5 years. It exhibits that prolonged timespan has a consequence over cognitive function.

Mohammed Abdul hannanzariet al, it coveys that diabetes with  $\leq 5$  years of disease duration and those with  $>5$  years of disease duration revealed remarkable differentiation.

EmreCakiret al, introduced a prominent association among duration of diabetes and cognitive dysfunctions.

#### V. CONCLUSION

A study was conducted on 100 type 2 DM subjects of both sexes between 40-60 years age group and a total of 100 apparently healthy individuals taken as control group who were age, sex, BMI and education matched. The current study implies that cognitive dysfunction was significantly related to type 2 DM and there was a strong relation of cognitive decline with diabetic duration and glycemic control.

Cognitive decline was observed in all the three age groups between 41-45 years, 46-50 years and 51-55 years but the comparison of significant MMSE scores between the groups was not significant. In this study it was observed that individuals with higher HbA1c levels performed poorly in cognitive examination suggesting that glycemic control has an influence on cognitive function. It was also seen that longer duration of type 2 DM has an effect over cognitive function. So perminantly high blood glucose levels and long duration of diabetes can accelerate cognitive impairment. The early implementation of mini mental, which is a simple method of execution, can be done to detect early stages of dementia.

It was carried out with the purpose that it will provide information on cognitive impairment and associated factors among type 2 diabetes mellitus patients to concerned bodies in designing diagnosis and management strategies particularly focusing on counseling in preventing risk factors.

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#### AUTHOR'S CONTRIBUTION

All the authors have contributed equally.

#### CONFLICT OF INTEREST

All the authors declare no conflict of interest.

#### ETHICS DECLARATION

The protocol was verified by the Institutional Ethic Committee of SCS College of Pharmacy.

Informed consent was obtained from all the residence in the hospital.

#### CONSENT FOR PUBLICATION

All authors have given their consent for publication

#### COMPETING INTERESTS

The authors declare that they have no competing interests.

#### AUTHORS FUNDING

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