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Relationship between Olfactory Dysfunction and Cognitive Impairment in Elderly Patients with Type 2 Diabetes Mellitus.

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ABSTRACT

Background: Olfactory dysfunctions albeit commonly studied in research study are rarely tested in clinical practice and commonly overlooked in elderly. With ageing, rate of decline in olfactory and cognitive functions increases. Diabetic patients are more prone to develop these olfactory and cognitive dysfunctions. Elderly diabetic patients with olfactory dysfunction were found to have increased incidence of cognitive impairment as compared to patients without olfactory dysfunction. So olfactory function testing can be used as screening tool to detect cognitive impairment at earliest and can halt the progression of cognitive impairment by appropriate measures. **Methods:** A cross-sectional study done on 200 elderly diabetic patients. Olfactory dysfunctions were detected by open essence test and cognitive testing was done with MMSE. Patients with psychosis, apparent dementia, any nasal disease were excluded. **Results:** Out of 200 patients total number of patients with MMSE <23, 24-26 and >26 were 19, 51 and 150 with average Open Essence (OE) score 6.05±, 6.74±0.92 and 8.5±0.54 respectively indicating that patients with lower OE score were found to have lower MMSE score. **Conclusion:** With ageing, olfactory as well as cognitive dysfunction increases. Diabetes accelerates these processes substantially. Olfactory dysfunction precedes the development of cognitive impairment. So elderly patients with diabetes should be screened for olfactory functions so that proper measures could be taken to decrease the incidence or severity of cognitive dysfunction.

Keywords: Olfactory dysfunction, cognitive impairment, type 2 Diabetes Mellitus, elderly patients.

INTRODUCTION

Diabetes mellitus (DM) is increasing worldwide (387 million people with diabetes globally)[1] especially in developing country. India is known as diabetes capital. Diabetes has numerous micro (diabetic nephropathy, neuropathy, retinopathy) as well as macro (peripheral arterial disease, coronary artery disease, cerebrovascular disease) vascular complications. Olfactory dysfunction is known macrovascular complication.[2]

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Olfactory dysfunctions increase with ageing because of decrease in no. of fibres and receptors in olfactory bulb area probably due to ischemic changes.3 Incidence of cognitive dysfunction increases as age advances. Mechanism of cognitive dysfunction can be due to hyperglycemia which causes increased formation of end glycation products and reactive oxygen species with causes inflammation and neuronal and neurovascular demage, insulin resistance also causes altered amyloid metabolism and tau phosphorylation and cerebrovascular disease (complication of DM) causing large vessel disease (stroke) and small vessel disease (lacunae) leading to dementia. This study was done to see the relationship between olfactory dysfunction and cognitive impairment in elderly patients with type 2 diabetes mellitus and we observed elderly diabetic patients with

increased olfactory dysfunction were having greater cognitive impairment. Hence olfactory dysfunction testing can be used to detect cognitive impairment at earliest.

MATERIALS AND METHODS

The present study was prospective cross sectional this study is cross sectional and carried out in Guru Nanak Dev Hospital attached to Govt. Medical College, Amritsar. This study included 200 cases of diabetes mellitus who were sixty or more than sixty years old. The study was conducted after approval from Institutional Thesis and Ethical Committee. The patients recruited in the study after an informed consent.

Inclusion Criteria: Inpatients and outpatients with type 2 diabetes mellitus sixty or more than sixty years old free of clinically-evident cognitive impairment.

The criteria for diagnosis of diabetes mellitus are according to the criteria laid down by the American Diabetes Association, 2015 which include fasting blood glucose >126mg/dl,Postprandial blood glucose >200mg/dl or symptoms of diabetes plus random blood glucose e >200mg/dl.

Exclusion Criteria: The exclusion criteria were (1) patients with severe infections within the preceding 2 weeks, (2) patients scheduled for surgery or who had undergone surgery, (3) patients with severe trauma, (4) patients with psychiatric disorders, (5) patients with hypothyroidism, (6) patients with partial or complete olfactory dysfunction associated with sinusitis, allergic rhinitis, and deviated nasal septum, (7) patients with history of brain tumors, (8) patients on steroid treatment, (9) patients with a Mini-mental State Examination (MMSE) score of less than 18 points. To get 200 elderly patients with type 2 diabetes mellitus that fulfilled the above said criteria, I had to screen 243 patients.

Detailed history was taken regarding presenting complaints, dietary habits, alcohol consumption, smoking or any drug abuse. General physical examination was done in detail and all systems were thoroughly examined. Before the start of study all the patients were investigated for :-

Hemoglobin, Total leukocyte count, Differential leukocyte count, Blood urea, Serum creatinine levels, Fasting blood sugar, Postpranial blood sugar and HbA1C Level.

Procedure: Two hundred patients with type 2 diabetes mellitus both inpatients and outpatients at Guru Nanak Dev Hospital Amritsar were included in the study. Demographic characteristics such as age and sex were recorded. After being informed of the purpose and procedures of the study, olfaction and cognitive tests were performed between 2015 and 2016.

Olfaction test: Smelling sensation was assessed using the Open Essence test (OE test). The OE test was developed as an olfactory identification assessment for Japanese population, and has been used in recent studies. It includes a self-completed olfaction test kit, with which the subject identifies various types of odors using specially prepared paper cards. The OE test consists of 9 odorants, including Indian ink, wood, perfume, menthol, orange, curry, cooking gas, rose, hinoki (Japanese cypress wood). For convenience I slightly modified OE test with respect to smell flavours. I added sandal wood in place of simple wood, peppermint leaves for curry, asfoetida for cooking gas, naphthalene balls for hinoki. For each odorant, the subject was presented with a card showing four odor names and two alternative answers (unknown and not detected) and was asked to select the correct answer. A score of 9 points represents correct identification of all types of odorants, while lower scores indicate olfactory dysfunction.

Mini Mental State Examination (MMSE): Cognitive status was evaluated by the MMSE. The MMSE is widely used for the assessment of cognitive status in both clinical practice and research. The MMSE includes 10 domain items, which measure orientation to time (5 points), orientation to place (5 points), registration (3 points), attention and calculation (5 points), recall (3 points), naming and repetition (3 points), comprehension (3 points), reading ability (1 point), writing ability (1 point), and design copy (1 point). MMSE was assessed and was blinded to the results of the olfaction test. The MMSE scale ranges from 0 to 30, with a higher score indicating better cognitive performance. Patients were divided into three groups: probable dementia group (18≤MMSE score≤ 23), possible cognitive impairment group (24≤MMSE score≤26), and no impairment group (MMSE score ≥27).

Statistical Analysis

Statistical analysis of data was done using SPSS 16 software, chi-square test and results were summarized. “P” value less than 0.05 was consider significant.

RESULTS

Table 1.1 showing distribution of individuals according to age. Number of patients with age 60 years were 42(21%), age 61-70 were 115 (57.5), age 71-80 were 31(15.5%) and more than 80 were 12 (6%). Table1.2 showing relationship between age and cognitive dysfunction. It shows that patients with increased age (mean age 72.15±10.05) shows more decline in cognitive function (MMSE <23) with p-value 0.001 which is statistically significant. Table 1.3 showing relationship between age and olfactory dysfunction. In study I noticed patients who were more aged showed more decline in olfactory function with p-value of 0.001 which was statistically significant. Table 2 showing the relationship between olfactory function and

cognition. Results showing patients with MMSE score ≤23 were having mean OE score of 6.05±1.14, MMSE score 24-26 were having 6.74±0.92 OE score and MMSE score > 26 were having 8.5±0.54 OE score showing patients with lower OE score i.e. olfactory dysfunction were found to have lower MMSE score and vice versa with p-value of 0.001 which is statistically significant.

Table 1.1: Age distribution.

Age group (years)	No.	%age
≤60	42	21.0
61-70	115	57.5
71-80	31	15.5
>80	12	6.0
Total	200	100.0

Table 1.2: Relationship between age and cognitive dysfunction.

Age	MMSE		
	<23 (n=19)	24-26 (n=51)	>26 (n=130)
Mean	72.15±10.05	66.47±6.44	66.70±6.61
p-value	0.001		

Table 1.3: Relationship between age and olfactory dysfunction.

Age	OE					
	4 (n=1)	5 (n=8)	6 (n=26)	7 (n=26)	8 (n=68)	9 (n=61)
Mean	91.00±0.00	70.37±8.79	68.26±7.33	66.26±67.52	67.52±7.33	66.02±5.89
p-value	0.001					

Table 2: OE/MMSE.

OE	MMSE					
	≤23		24-26		>26	
	No.	%	No.	%	No.	%
4	1	5.26	0	0.00	0	0.00
5	6	31.58	2	3.92	0	0.00
6	6	31.58	20	39.22	0	0.00
7	3	15.79	20	39.22	3	2.31
8	3	15.79	6	11.76	59	45.38
9	0	0.00	3	5.88	68	52.31
Total	19	100.00	51	100.00	130	100.00
Mean	6.05±1.14		6.74±0.92		8.5±0.54	

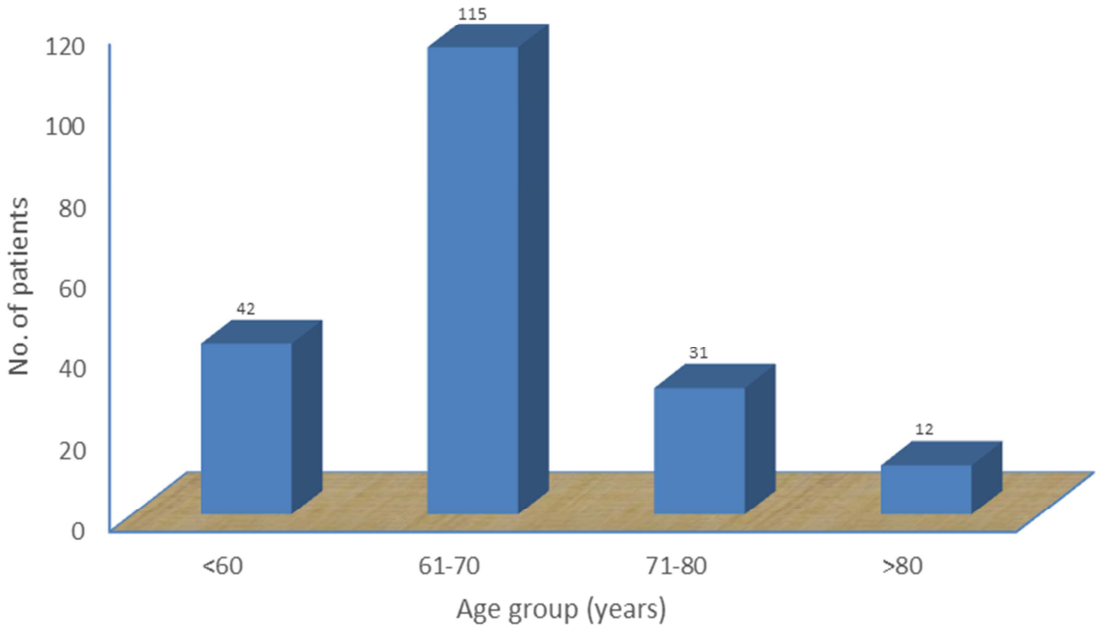

Figure 1: Age distribution.

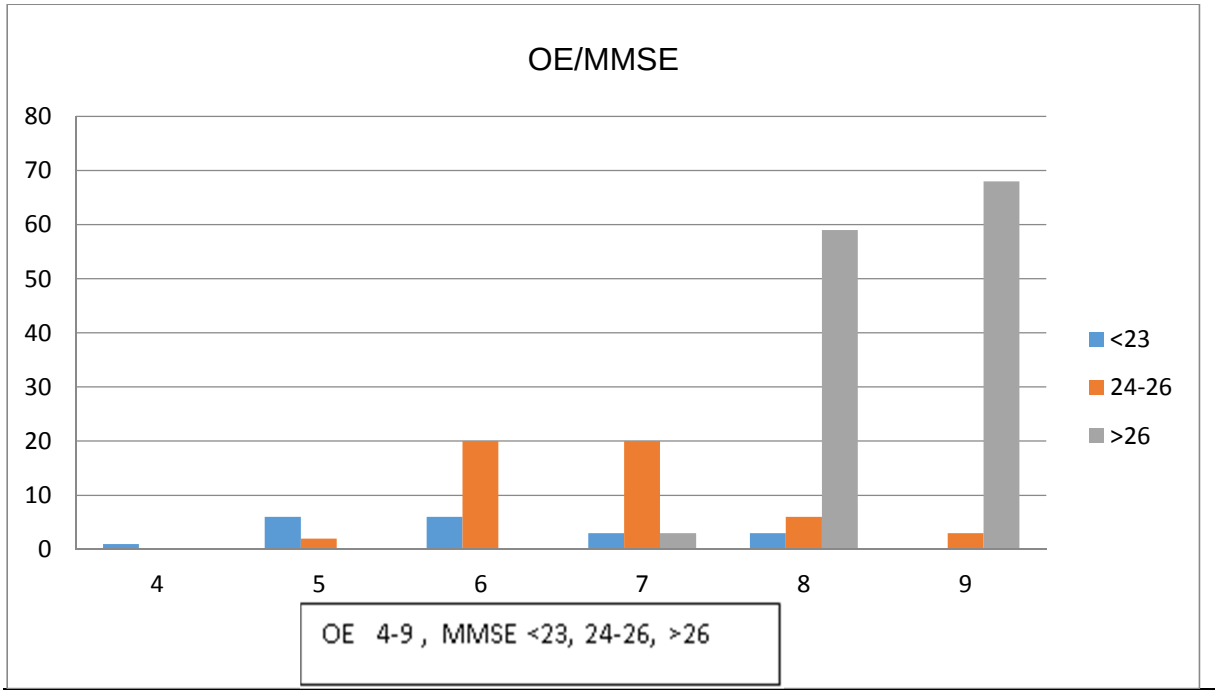

Figure 2: OE/MMSE.

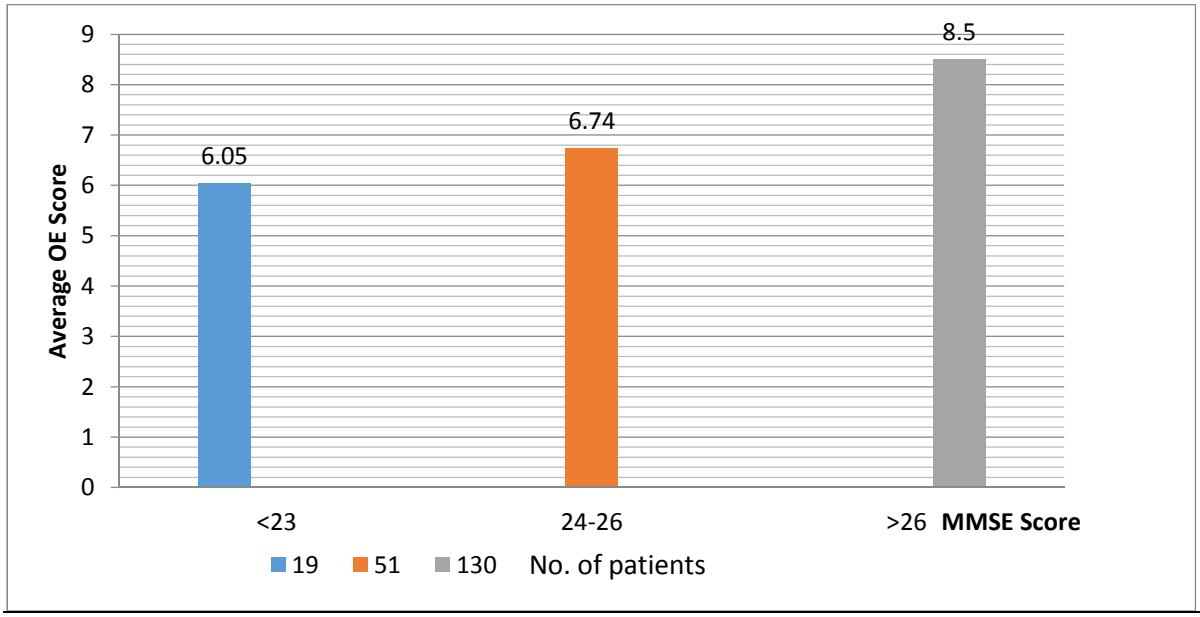

Figure 3: MMSE Score.

DISCUSSION

Olfactory function includes threshold, discrimination and identification of odorant. Threshold for odorant is not associated with cognitive impairment whereas discrimination and identification of odorant are associated significantly.[4] In this study discrimination and identification of odorant (assessed by ability to differentiate between odorant, and ability to identify odorant, respectively) were assessed but not threshold for odorant. Cognitive dysfunction is less addressed complication of DM as compare to cardiovascular complications, retinopathy, nephropahy etc. DM affects different domains of cognition (memory, executive functions, verbal fluency etc.). These patients have significant effect on their daily living if the Mini Mental State Examination score is less than 23.[5]

This study was cross-sectional study and intended to see association between olfactory dysfunction and cognitive impairment in 200 elderly patients with type 2 DM. Patients included in study were without apparent cognitive dysfunction. The mean age of distribution was 61-70 years (57.5%) and 58% patients were female. The results showed a high prevalence of cognitive impairment in elderly patients with type 2 diabetes mellitus who had not

been diagnosed with cognitive impairment. In the study 65% patients were without any cognitive impairment with mean OE score 8.5±0.54, 25.5% fell into possible cognitive impairment group with mean OE score of 6.74±0.92 and 9.5% in probable group with mean OE score of 6.05±1.14 showing patients with impaired olfactory functions were having impaired cognition with p-value of 0.001 which was statistically significant. This finding was consistent with some of previous studies[6-9] but others could not find conclusive results.[10] In this study, significant correlations among low MMSE scores and HbA1c level are found. Results showed greater the HbA1c level lower was the MMSE score among patients with p-value of 0.001 which was statistically significant. This study also correlated HbA1c with olfactory function and found that olfactory function showing patients with decreased open essence score were having higher HbA1c level and vice versa with p-value of 0.001 which was significant. No association could be found between hypertension and olfactory or cognitive dysfunction. When patients with different age group were compared for olfactory and cognitive dysfunction, it was found that with increasing age there was decline in both olfactory and cognitive function with p-value of 0.001 for both, which was statistically significant. Females were found to have better olfaction when compared with males with p-value of 0.001 but there was not significant differences when both sexes were compared for cognitive function (p- value 0.141).

Hence elderly patients with Type 2 DM have more incidence of both olfactory and cognitive dysfunction. As olfactory dysfunction precede the development of cognititve dysfunction and diabetes increases the incidence of cognitive impairment, olfactory dysfunction can be used as screening tool for cognitive dysfunction so that further measures can be taken to control diabetes to halt the progression of cognitive dysfunction in these patients.

CONCLUSION

Diabetes is recognized as a group of heterogeneous disorder with the common element of hyperglycemia and glucose intolerance due to insulin action or both. It is now recognized that it is the low and middle income countries that presently face the greatest burden of diabetes. Epidemiological evidences suggest that without effective prevention and control programmes, diabetes will likely continue to increase globally. This study was aimed to see the relationship between olfactory dysfunction and cognitive impairment in elderly type 2 diabetic patients. The present study was carried out on 200 patients presenting to Guru Nanak Dev Hospital attached to Govt. Medical College Amritsar.

Following conclusions were drawn from study:

■In patients with Type 2 DM as the age advances, there is more decline in olfactory (tested by open essence test) as well as cognitive functions (tested by mini mental state examination).

■Patients who were found to have low open essence score i.e. olfactory dysfunctions were also having low mini mental state examination score i.e. cognitive dysfunctions.

In conclusion, results of this study point to a close relation between olfactory dysfunction and cognitive impairment in elderly patients with type 2 diabetes mellitus. So olfactory function test can be used as screening test for early detection of cognitive dysfunction and better outcome in patients can be expected.

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