Evaluation of Cognitive Impairment in Type 2 Diabetic Patients with Chronic Periodontitis: A Cross-sectional Study

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Background: Type 2 diabetes mellitus is an important risk factor for dementia; it also shares a bidirectional relationship with periodontitis. It is hypothesized that the increased severity of periodontitis is associated with cognitive decline in patients having uncontrolled diabetes mellitus. An added risk for future development as well as progression of dementia may be prophesied in such a scenario. Therefore, the present study was conducted to find a correlation between the cognitive impairment (CI) and periodontitis in type 2 diabetes mellitus patients. Materials and Methods: A total of 160 older adults aged ≥60 years in Mangalore, Karnataka, India, were included in the present analysis. Known T2DM patients aged ≥ 60 years and diagnosed with periodontitis with a minimum clinical attachment loss (CAL) of $\geq 2 \text{ mm}$ were considered in the present study. Montreal cognitive assessment test assessed the CI. The analysis was carried out using the χ^2 test, an independent *t*-test. Binary logistic regression analysis (enter method) was performed to derive the odds ratios (95% confidence interval). Results: The study included 160 participants, out of which 120 had CI and 40 did not have CI. A statistically significant association was observed between moderate-to-severe periodontitis, HbA1c levels ≥7%, and CI after excluding the confounding factors like age, gender, diet, lifestyle habits, and education. Conclusion: In the present study, cognitive impairment was found to coexist with HbA1c levels ≥7% and moderate-to-severe periodontitis in the elderly diabetics. The clinical implication of these findings adds opportunities to form disease modifiable areas in the elderly diabetic population at a risk for the development of dementia. Additionally, the impact of pre-existing CI on progression of periodontitis and vice versa has been discussed.

Keywords: Cognitive decline, diabetes mellitus, gingivitis, MOCA, periodontitis

INTRODUCTION

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The global burden of dementia, Type 2 diabetes mellitus (T2DM), and periodontitis is rapidly increasing and has become a serious area of concern. Interestingly, T2DM is an important risk factor for dementia^[1-3] and it also shares a bidirectional relationship with periodontitis.^[1] It is reported that the

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treatment of periodontitis has been linked, directly and indirectly, to the improvement of diabetes status

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(HbA1c levels)^[1,4] by various researchers. In the last decade, a link between periodontitis and dementia has been extensively explored.^[2,5-7] Based on the results from a nationwide study, Lee *et al.*^[7] reported a higher risk for the development of dementia exists in older individuals with periodontitis.

Presently, there is no known cure for dementia. The dementia medication only helps in reducing the symptoms like memory loss and confusion and does not affect the underlying pathogenesis of the disease.^[8,9] Hence, in search of better treatment options, the consensus by the British Association for Psychopharmacology emphasized the importance of secondary preventive measures for the management of dementia.^[8] It requires a precise understanding of both the underlying neurodegenerative events which are endogenous to the brain and the influence of exogenous pathological mechanisms which directly and indirectly contribute to neurodegeneration. This may subsequently aid the discovery of a modifiable treatment approach that may prevent or curb the progression of neurodegeneration associated with the different types of dementia.^[2] Chronic systemic inflammation is observed with both T2DM and periodontitis which are modifiable diseases. They have a bidirectional relationship.^[10,11] The possible interrelated mechanisms between T2DM and periodontitis that may contribute to neurodegeneration has been documented in the literature^[12,13]

One of the important parameters in the diagnosis of dementia is cognitive impairment (CI). It is hypothesized that the increased severity of periodontitis is associated with CI in the presence of uncontrolled T2DM. An added risk for the future development as well as progression of dementia may be prophesied in such a scenario. Therefore, the present study was conducted to find a correlation between the cognitive status and periodontitis in T2DM patients. The primary objective was to detect the number of T2DM individuals having CI and periodontitis and the secondary objective being correlating the detected CI with the severity of periodontitis and T2DM status.

MATERIALS AND METHODS

The study was approved by the Institutional Ethics Committee of Manipal College of Dental Sciences, Mangalore, Manipal Academy of Higher Education, Manipal. Data were collected from 200 study participants. The inclusion criteria for the study participants were (i) age 60 years or older; (ii) with the history of T2DM and diagnosed with periodontitis with a minimum clinical attachment loss of $\geq 2 \text{ mm}$; (iii) at least 10 natural teeth. The sample for the present analyses included 160 participants who had completed oral examination, T2DM detail questions, and cognitive evaluation was done for each of the participants.

The individuals visiting outpatient Department of General Medicine, Kasturba Medical College, Mangalore, Karnataka, India, and outpatient Department of Periodontology, Manipal College of Dental Sciences, Mangalore, Karnataka, India, were included in the present cross-sectional study. A written informed consent form was obtained from everyone along with their legally acceptable representatives prior to the enrolment into the study.

Patients with a history of dementia secondary to cerebral trauma, brain tumor, normal pressure hydrocephalus, chronic subdural hematoma, chronic drug intoxication, AIDS, neurosyphilis, cryptococcosis, pellagra, vitamin B12 deficiency, thiamine deficiency, and hypothyroidism; uncontrolled hypertension; inflammatory conditions; and current medication likely to affect cognition were all excluded from the study.^[14,15]

The demographic details for each patient which included age, gender, history of educational status, diet, smoking or alcohol consumption, and medical history were recorded. The status of diabetes was recorded for everyone based on the duration of diabetes, recent medical records for HbA1c levels (not more than 3 months old), and if any diabetic complications were present or absent. If any individual was not able to recall and answer the questions, then their legally acceptable representatives were requested to provide the information. The HbA1c levels were evaluated according to the American Diabetes Association guidelines (ADA) as 4%-6%: normal, <7%: good diabetes control, 7%-8%: moderate diabetes control, and >8%: action suggested to improve diabetes control.^[16]

Intraorally, the number of teeth present were recorded. In the periodontal examination, the probing pocket depth (PPD), clinical attachment level (CAL), and percentage of bleeding sites were recorded. A trained periodontist recorded both PPD and CAL using a periodontal probe with William's markings to the nearest millimeter at all the six sites (mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual) for each tooth. The PPD was determined by measuring the distance from the gingival margin to the base of the pocket and CAL was determined by measuring the distance from the cemento enamel junction (CEJ) to the base of the pocket. The base of the pocket was determined at the level at which maximum resistance was felt while probing the periodontal pocket. In case of a crown, the base of an existing restoration was taken as the fixed reference point. The presence of bleeding was evaluated by carefully probing each tooth with William's periodontal probe and the total percentage of bleeding sites was then recorded for each patient. The case definition of the severity of periodontitis was taken according to Armitage 1999 classification,^[17] i.e., slight: 1–2mm CAL; moderate: 3–4mm CAL; severe: >5mm CAL.

COGNITIVE ASSESSMENT

In the present study, Montreal Cognitive Assessment (MoCA)^[18] was used to screen the individuals for the presence of CI. It is a 30-point test and takes ~10 min. It evaluates multiple cognitive domains by assessing the individuals' visuospatial (5 points), naming (3 points),

memory (5 points), attention (6 points), language (3 points), abstraction (2 points), and orientation (6 points) skills. In the present study, the test was used in the English language. Prior permission was obtained from the developers of the MoCA test to use the test in the present study. Everyone was given the MoCA test after an initial general and intra-oral examination. Step-by-step instructions were given to each individual while they performed the test. In the end. a single trained professional who was unaware of the study interpreted the results. The MoCA scores vary from 0 to 30. The severity of CI is assessed with scores 18-26: mild CI, 10-17: moderate CI and <10: severe CI. In the current study, any score <26 was diagnosed as the presence of CI and that >26 was diagnosed as normal.^[19]

	es of the study population with a	<u>U</u>		<i>P</i> value	
Variables			Cognitive impairment		
		Absent $(n = 40)$	Present $(n = 120)$		
Age		63.15 ± 2.90	69.98 ± 5.22	<0.001ª	
Gender	Female $(n = 75)$	19 (47.5%)	56 (46.7%)	0.9287 ^t	
	Male (<i>n</i> =8 5)	21 (52.5%)	64 (53.3%)		
Education	Nil	0 (0.0%)	0 (0.0%)	< 0.001	
	Primary	0 (0.0%)	1 (0.8%)		
	Class 10	0 (0.0%)	5 (4.2%)		
	Class 12	4 (10.0%)	40 (33.3%)		
	Graduate	23 (57.5%)	67 (55.8%)		
	Professional degrees	13 (32.5%)	7 (5.8%)		
Diet	Vegetarian	10 (25.0%)	31 (25.8%)	0.982 ^b	
	Nonvegetarian	6 (15.0%)	19 (15.8%)		
	Mixed	24 (60.0%)	70 (58.3%)		
Smoking	Yes	2 (5.0%)	0 (0.0%)	0.047 ^b	
	No	32 (80.0%)	102 (85.0%)		
	Former smoker	6 (15.0%)	18 (15.0%)		
Alcohol	Yes	0 (0.0%)	4 (3.3%)	0.4295 ^b	
	No	34 (85.0%)	94 (78.3%)		
	Occasional	6 (15.0%)	22 (18.3%)		
Medical History	Type 2 diabetic	27 (67.5%)	79 (65.8%)	0.847 ^t	
-	Type 2 diabetic + HTN	13 (32.5%)	41 (34.2%)		
Duration of type 2 diabetes (In years)	1-5	8 (20.0%)	7 (5.8%)	0.001 ^t	
	6-10	20 (50.0%)	36 (30.0%)		
	11-15	10 (25.0%)	47 (39.2%)		
	16-20	2 (5.0%)	22 (18.3%)		
	'>20'	0 (0.0%)	8 (6.7%)		
Diabetic Complications	Present	0 (0.0%)	5 (4.2%)	0.189 ^b	
1	Absent	40 (100.0%)	115 (95.8%)		
%BL sites ^c		65.7875±12.3373	75.3808 ± 12.9618	< 0.001ª	
PPD ^d		2.4350±0.5798	3.2375±0.7408	<0.001ª	
CAL ^e		2.9575±0.6857	4.0875±0.7940	< 0.001ª	

^aContinuous Variables (MEAN \pm SD) compared with independent t-test

^bCategorical Variables, Count (Percentage) (N (%)): Compared with chi-square test

°Percentage of Bleeding sites

^dPocket probing depth

^eClinical attachment loss

STATISTICAL ANALYSIS

The association of cognitive impairment with the parameters of gender, education, diet, smoking, alcohol, medical history, duration of diabetes, and complications were compared using χ^2 tests. The continuous variables of age, percentage of bleeding sites, probing depth, and clinical attachment loss were compared using an independent *t*-test. Binary logistic regression analysis (enter method) was performed to derive the odds ratios (95% confidence interval) to predict cognitive impairment. The models were adjusted for the presence of periodontitis, age, gender, duration of diabetes, and HbA1c levels. SPSS 20.0 was used for statistical analysis.

The current study showed that 35% of the individuals with periodontitis (CAL \geq 3) had no CI as opposed to 88% who had CI. Having 160 samples of diabetic participants the effective size of 0.533 using 1 degree of freedom in a χ^2 test at a significance level of 0.005, >90% power was achieved indicating that the present study has an adequate sample to show the association of periodontal status and cognitive impairment.

RESULTS

A total of 160 participants, 75 females and 85 males were included in the study with a mean age of 68.27 ± 5.59 years. The characteristics of the study population with and without CI are illustrated [Table 1]. On the basis of the MoCA test scores, 120 (75%) participants were found to have CI. Forty (25%) participants did not have CI. The mean age of the participants who showed CI was 69.98 ± 5.22 and those did not show CI was 63.15 ± 2.90 . On comparing the participants who showed the presence and absence of CI, no statistically significant difference was found for gender, diet, smoking, and alcohol consumption. However, there was a statistically significant difference for age, education, duration of diabetes, HbA1c levels, percentage of bleeding sites, PD, and CAL.

Periodontal examination revealed that the participants who were screened to have CI had moderate-to-severe periodontitis (CAL \geq 3mm) as suggested by means values of 4.09 \pm 0.79. [Table 1], these results were statistically significant (P < 0.001). The comparison between CAL measurements and MOCA scores revealed a statistically significant association between the severity of periodontitis and the presence of CI [Table 2, P < 0.001]. There was a statistically significant association between tooth loss and the presence of CI (P < 0.001).

Of the 120 participants who were screened for CI, 113 were diabetic for more than 5 years [Table 1]. Fortyseven (39.16%) had HbA1c levels <7% and 73 (60.83%) had HbA1c levels \geq 7%. The comparison between HbA1c levels and MOCA scores revealed a statistically significant association between increased HbA1c levels and the presence of CI [Table 3, *P* < 0.001].

	Table 2: Severity of period	· · · · · · · · · · · · · · · · · · ·		Total	impanment		
		Cognitive	Cognitive impairment		Cognitive impairment		
		Absent	Present				
A: CAL ^b	Slight periodontitis (≤2.9mm)	26 (65.0%)	14 (11.7%)	40 (25.0%)	Chi square value of 46.949 and P value of $< 0.001^{a}$		
	Moderate periodontitis (3-4.9 mm)	14 (35.0%)	89 (74.2%)	103 (64.4%)			
	Severe periodontitis (≥5mm)	0 (0.0%)	17 (14.2%)	17 (10.6%)			
Total		40 (100.0%)	120 (100.0%)	160 (100.0%)			

^aCount (% within Cognitive Impairment): Compared with chi-square test ^bClinical attachment loss

Table 3: Diabetes control (HbA1c) and the presence and absence of cognitive impairment						
		Cognitiv	Cognitive impairment			
		Absent	Present			
Hba1c	4 - 6 %	18 (45.0%)	12 (10%)	30 (18.8%)	Chi square of 40.81 and p-value of	
	>6-7%	19 (47.5%)	35 (29.2%)	54 (33.8%)	<0.001 ^a	
	>7-8 %	3 (7.5%)	51 (42.5%)	54 (33.8%)		
	>8%	0 (0.0%)	22 (18.33%)	22 (13.8%)		
Total		40 (100.0%)	120 (100.0%)	160 (100.0%)		

^aCount (% within Cognitive Impairment): Compared with chi-square test

The CI was present in 67 (97.10%) participants who had CAL \geq 3 and HbA1c \geq 7 out of the total 69 participants who had this combination. These results showed that in participants with HbA1c \geq 7% and moderate-to-severe periodontitis (CAL \geq 3mm), there were 12 times more odds of having CI. Comparison of the odds of CI occurring in cases with HbA1c \geq 7% and periodontitis was 19.156 and 14.061, respectively. The two parameters were seen to be interacting with each other as the adjusted odds reduced to 12.74 and 9.313, respectively, for Hba1C \geq 7% and periodontitis (CAL \geq 3mm). When seen together along with the duration of diabetes the presence of Hba1C \geq 7% had an odds of 10.61 times and periodontitis (CAL \geq 3 mm) had an odds of 9.684 in developing CI [Table 4].

CAL, BOP, and PPD had an unadjusted odds ratio of 7.363, 1.055, and 5.695, respectively, in developing cognitive impairment. The odds ratio was seen to reduce on the inclusion of age, but gender and habits did not significantly alter the odds ratio. The adjusted odds ratio significantly dropped for CAL and PPD from 7.016 to 4.867 and 5.655 to 2.930, respectively, when duration of diabetes and Hba1c levels were included in the model. This indicates that the duration of diabetes and Hba1c levels contribute to the development of CI as compared to age, gender, or habits. Among the periodontal parameters which are clinically assessed the BOP did not show significant alteration in odds ratio, CAL was the best predictor of CI with the odds of 4.867 in favor of developing CI when the value of CAL was >3 [Table 5].

The current study shows that 35% of the individuals with periodontitis (CAL \geq 3) had no CI as opposed to 88% who had CI. Having 160 samples of diabetic participants the effective size of 0.533 using 1 degree of freedom in a χ^2 test at a significance level of 0.005, >90% power was achieved indicating an adequate sample size to show the association of periodontal status and cognitive impairment.

DISCUSSION

The results of the present study revealed that increased severity of both T2DM and periodontitis coexisted

with the presence of CI. Extensive research has been conducted in the past to explore the associations between T2DM and CI as well as between periodontitis and CI. To the best of the author's knowledge, this is the first study to check if any association exists between the status of the severity of both T2DM and periodontitis coexisting together for CI, in elderly individuals.

The definition of the severity of periodontitis in the present study was based on the measurement of CAL ranges as documented by AAP 1999 classification of periodontal diseases.^[17] CAL takes a longer time to develop and is instrumental in assessing the chronic status of the periodontal disease activity. In the present study, the results indicated that the association between increased severity of periodontitis and the presence of CI was statistically significant [Table 2]. These results were in line with the previous studies.^[7,20] Gilmontoya et al.^[20] also found a similar association in the severity of CAL and the presence of CI. They documented that there is a plausibility, attachment loss may precede the development of CI, making CAL a candidate periodontal variable in the predicting risk for the development of CI.

These results do not establish a cause–effect relationship between periodontitis and CI as in the elderly the reverse causality is also possible. In the present study, the individuals screened to have CI had moderate-tosevere periodontitis [Table 2]. Although they were never diagnosed with CI before the study, the pre-existing impacts of CI on their routine oral hygiene practices could have altered their underlying periodontal host tissue response, leading to the development or progression of periodontitis. This possibly explains the relationship between CI and periodontitis as a bidirectional one; however, the severity of which single disease plays a more significant role requires a detailed understanding of pathophysiological interrelated mechanisms.

The HbA1c levels have been established as the risk modifying factor in dementia and have a predictive role in the incidence of mild CI.^[21] The results of the present study found a similar increase in the age-adjusted CI in participants with HbA1c $\geq 7\%$ [Table 5].

Table 4: Binary logistic regression to predict cognitive impairment with uncontrolled diabetes and periodontitis (brackets contains 95% CI of odds ratio)							
Unadjusted Adjusted for Adjusted for diabetes Adjusted for each other and							
	Chaujusteu	periodontitis	Augusten for univeres	duration of diabetes			
Diabetes status (Hba1c	19.156 (5.586, 65.691)	12.764 (3.513, 46.370)		10.641 (2.850, 39.730)			
≥7)							
Periodontitis (CAL ≥3) ^a	14.061 (5.974, 33.097)		9.313 (3.652, 23.751)	9.684 (3.616, 25.935)			
Clinical attachment loss							

^aClinical attachment loss



When the severity of diabetes and periodontitis were evaluated together, it was observed that the presence of Hba1c levels ≥7 with moderate-to-severe periodontitis $(CAL \ge 3 \text{ mm})$ showed greater odds for the presence of CI [Table 4]. However, these results may have been affected due to the presence of several confounding factors. A binary regression model [Table 5] was performed to check the net effect of periodontitis on the presence of CI by eliminating the confounding factors like age, gender, education, habits (smoking and alcohol consumption), along with the duration of T2DM and HbA1C levels. No significant confounding effect was present with gender, education, and habits. The confounding effect of age was present however minimal in comparison to the duration of T2DM and HbA1c levels, which had the most confounding effect. These results indicated a co-existence of increased severity of T2DM, increased severity of periodontitis, and presence of CI.

A large prospective cohort study from the ADVANCE trial^[22] with 11,140 type 2 diabetics (55–88 years) as the study population had found an association between oral disease and dementia. It provided a concrete evidence that an increased risk for both cognitive decline and dementia was associated with tooth loss. The results of the present study found a similar association between tooth loss and presence of CI. Periodontitis is one of the most significant contributing factors for tooth loss in the elderly population. In the current study, the severity of periodontitis was assessed in the elderly diabetics. This helped in estimating the periodontal disease severity in association with the existing T2DM status of the individual. As no alteration in medication was done in the present study, it had an advantage over the ADVANCE trial where a change in medication was done, which could have affected the diabetes control of the study population.

A significant association between increased severity of periodontitis and increased severity of T2DM suggesting a bidirectional relationship between the two have been observed in the present study. These findings were in agreement with past studies which had investigated the association between periodontitis and T2DM^[1,23-26] There are emerging facts for an independent association between periodontitis and incident T2DM in elderly individuals with evidence that moderate to severe periodontitis adversely affects the diabetes control and may also worsen its complications.^[23,25] It may therefore be reasonable to assume that one of these complications may be linked to neurodegeneration underlying progressive CI and dementia. A hypothesis has been reported enumerating the several interrelated mechanisms between T2DM and periodontitis that may be linked to neurodegeneration in CI and dementia.^[12] This is advantageous, as both are associated with dementia and their modification may reduce the cumulative influence on microglial activation and chronic neurodegeneration associated with the development and progression of dementia

In the last decade, a new term "Type 3 diabetes"^[26] (T3DM) was proposed that added an important dimension to the research associated with Alzheimer's disease (AD). AD accounts for >60% of cases with dementia. AD is a form of diabetes that specifically afflicts the brain, to which they coined the term T3DM. They proposed that T3DM may be preventable or treatable with antidiabetic medication. Moreover, though antidiabetic medications are efficacious in the treatment of dementia, it is unclear if this effect is through T2DM control or other alternative mechanisms.^[27]

Treatment of periodontitis and its associated reduction in the systemic inflammatory burden in T2DM individuals may be one of the mechanisms that may help control T2DM status and its consequent effects on the brain. The results from the binary regression analysis [Table 4] in the current study showed that

Tabl	Table 5: binary logistic regression for the prediction of cognitive impairment in terms of clinical measures of periodontitis (brackets contains 95% CI of odds ratio)								
S.	Regression model	CAL ^a Odds ratio	P value	%BL sites ^b Odds ratio	P value	PPD^c Odds ratio	P value		
No.									
1	Unadjusted	7.363 (3.714, 14.598)	< 0.001	1.055 (1.026, 1.086)	< 0.001	5.695 (2.864, 11.322)	< 0.001		
2	Adjusted for Age	7.064 (3.036, 16.440)	< 0.001	1.043 (1.006, 1.081)	0.023	5.485 (2.366, 12.714)	< 0.001		
3	Adjusted for Age & Gender	7.090 (3.029, 16.594)	< 0.001	1.042 (1.004, 1.080)	0.028	5.446 (2.336, 12.697)	< 0.001		
4	Adjusted for Age & Gender and Habits	7.016 (2.819, 17.459)	< 0.001	1.037 (0.997, 1.078)	0.068	5.655 (2.384, 13.418)	< 0.001		
5	Model 4 plus duration of diabetes and HbA1C level	4.867 (1.570, 15.089)	0.006	0.938 (0.882, 0.997)	0.038	2.930 (0.901, 9.524)	< 0.001		

^aClinical attachment loss

^bPercentage of Bleeding sites

^cPocket probing depth

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the presence of HbA1c \geq 7 and moderate-to-severe periodontitis together showed greater odds of having CI in T2DM individuals. Both the medical and dental fraternity have individually arrived at a consensus that the periodontal treatment reduces plasma HbA1c at 3-months and this reduction is equivalent to adding a second drug to a pharmacological regime.^[28,29]

It is noteworthy that a good periodontal maintenance thus may have a potential to prevent or slow the progression of CI or dementia by reducing the systemic inflammatory burden, AGE-RAGE interactions, oxidative stress, and altered cytokine networks. In this way treatment for prevention or progression of a chronic periodontal disease through regular maintenance recall, in individuals with T2DM can be a promising approach to keep a check on their Hba1c levels. Controlled diabetes may, in turn, modulate neurodegenerative mechanisms associated with uncontrolled diabetes.

In the diagnosis of CI, various cognitive assessment tools have been used in the past three decades, out of which mini-mental state examination test (MMSE) has been widely used. In the current study, the MoCA test was used as the cognitive assessment tool to screen for CI. Both MMSE and MoCA tests are independently acceptable cognitive assessment tools for CI. However, several researchers have provided robust evidence that the MoCA test has a higher sensitivity and specificity to detect mild CI in comparison to the MMSE test.^[30] Additionally, in a study, Alagiakrishnan et al. had concluded that superior results were obtained using the MoCA test in comparison to MMSE in assessing mild CI in elderly T2DM participants specifically.^[31] Therefore, the MoCA test was taken as the tool of choice in the current study. Its feasibility to use in any kind of clinical setting without the requirement of any other additional tools provided added advantages to be used in a dental setup.

As oral health professionals, many diabetic individuals are likely to be encountered regularly. If MoCA, MMSE, or any other cognitive assessment screening tools are incorporated into use by the dental professionals, a significantly larger number of individuals can be diagnosed and referred for appropriate treatment. This can be a momentous initiative to reduce a considerable load of dementia expected to rise soon.

Although the current novel exploratory research provides a promising modifying treatment approach for the diabetic population to reduce the future new cases of dementia as well as to prevent the progression of mild CI to AD or other types of dementia, it is still a hypothesis and requires further longitudinal studies to establish its true feasibility. The current research was cross-sectional in design and it had its inherent limitations. Thirty-four percent of the elderly diabetics who had CI were also controlled hypertensives, this may have added another pathological mechanism underlying the existing neurodegeneration. Adults above ≥ 60 years were taken, who may already have a burden of chronic systemic inflammation owing to the emerging concept of "inflammaging",^[12] therefore longitudinal studies taking comparatively younger individuals having diabetes and periodontitis should be conducted in the future as a target group to further strengthen the interrelated mechanism.

CONCLUSION

The findings of the current study revealed the presence of cognitive impairment in the elderly diabetics with HbA1c \geq 7% and moderate to severe periodontitis. The exact interrelated mechanisms between periodontitis and diabetes that participate in neurodegenerative effects need future studies to establish a dose-response relationship. The severity of both periodontitis and diabetes can be controlled and may form an important modifiable factor in the elderly diabetic population at a risk for the development of cognitive impairment or dementia. Conversely, it is very important to diagnose, monitor, and treat periodontitis in patients with preexisting CI to limit its development and progression. Therefore, following a personalized medicine model to deliver overall patient care in the need of the hour. Future studies with a greater sample size and longer follow-ups are required to further validate the results obtained in the current study.

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CONFLICTS OF INTEREST

No potential conflict of interest was reported by the authors.

AUTHORS CONTRIBUTIONS

Ashita Uppoor, Satish Rao, and Keshav Pai have provided contributions in the planning stages of the study, and Shikha Sharma, Sangeeta Nayak, and Srikant N have provided contributions processing of the data. All of them have provided contributions in reviewing the literature and writing the article.

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ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

This study was reviewed and approved by the Institutional ethics and review board, Manipal College of Dental Sciences, Mangalore.

PATIENT DECLARATION OF CONSENT

Not applicable.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

REFERENCES

- Chapple IL, Genco R; Working Group 2 of the Joint EFP/ AAP Workshop. Diabetes and periodontal diseases: Consensus report of the joint EFP/AAP workshop on periodontitis and systemic diseases. J Periodontol 2013;84:S106-12.
- Nascimento PC, Castro MML, Magno MB, Almeida APCPSC, Fagundes NCF, Maia LC, *et al.* Association between periodontitis and cognitive impairment in adults: A systematic review. Front Neurol 2019;10:323.
- 3. Cheng G, Huang C, Deng H, Wang H. Diabetes as a risk factor for dementia and mild cognitive impairment: A meta-analysis of longitudinal studies. Intern Med J 2012;42:484-91.
- Preshaw PM, Alba AL, Herrera D, Jepsen S, Konstantinidis A, Makrilakis K, *et al.* Periodontitis and diabetes: A two-way relationship. Diabetologia 2012;55:21-31.
- Kaye EK, Valencia A, Baba N, Spiro A 3rd, Dietrich T, Garcia RI. Tooth loss and periodontal disease predict poor cognitive function in older men. J Am Geriatr Soc 2010;58:713-8.
- Rai B, Kaur J, Anand SC. Possible relationship between periodontitis and dementia in a North Indian old age population: A pilot study. Gerodontology 2012;29:e200-5.
- Lee YT, Lee HC, Hu CJ, Huang LK, Chao SP, Lin CP, et al. Periodontitis as a modifiable risk factor for dementia: A nationwide population-based cohort study. J Am Geriatr Soc 2017;65:301-5.
- O'Brien JT, Burns A. Clinical practice with anti-dementia drugs: A revised (second) consensus statement from the British Association for Psychopharmacology. J Psychopharmacol 2011;25:997-1019.
- O'Brien JT, Holmes C, Jones M, Jones R, Livingston G, McKeith I, *et al.* Clinical practice with anti-dementia drugs: A revised (third) consensus statement from the British Association for Psychopharmacology. J Psychopharmacol 2017;31:147-68.
- Garcia D, Tarima S, Okunseri C. Periodontitis and glycemic control in diabetes: NHANES 2009 to 2012. J Periodontol 2015;86:499-506.
- 11. Taylor JJ, Preshaw PM, Lalla E. A review of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. J Periodontol 2013;84:S113-34.
- Sharma S, Uppoor AS, Natarajan S. Diabetes and periodontitis Role in cognitive impairment. Dent Hypotheses 2018; 9:20-4.
- Teixeira FB, Saito MT, Matheus FC, Prediger RD, Yamada ES, Maia CSF, *et al.* Periodontitis and Alzheimer's disease: A possible comorbidity between oral chronic inflammatory condition and neuroinflammation. Front Aging Neurosci 2017;9:327.
- 14. Agarwal R. Vitamin B_{12} deficiency & cognitive impairment in elderly population. Indian J Med Res 2011;134:410-2.

- 15. Fenech M. Vitamins associated with brain aging, mild cognitive impairment, and Alzheimer's disease: Biomarkers, epidemiological and experimental evidence, plausible mechanisms, and knowledge gaps. Adv Nutrition 2017:8:958-70. doi: 10.3945/an.117.015610
- American Diabetes Association. 2. Classification and diagnosis of diabetes. Diabetes Care 2017:40(Suppl. 1):S11-S24.
- 17. Armitage GC. Development of a classification system for periodontal diseases and conditions. Ann Periodontol 1999;4:1-6.
- Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, *et al.* The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53:695-9. Erratum in: J Am Geriatr Soc 2019;67:1991.
- Montreal Cognitive Assessment (MoCA) Test: Scoring & Accuracy. Verywell. Retrieved 12 June 2017. Available from: http:// www.mocatest.org/wp-content/uploads/2017/01/MoCANew-Test-8.1-2017-04.pdf [Last accessed on 2020 July 01].
- Gil-Montoya JA, Sanchez-Lara I, Carnero-Pardo C, Fornieles F, Montes J, Vilchez R, *et al.* Is periodontitis a risk factor for cognitive impairment and dementia? A case-control study. J Periodontol 2015;86:244-53.
- 21. Albai O, Frandes M, Timar R, Roman D, Timar B. Risk factors for developing dementia in type 2 diabetes mellitus patients with mild cognitive impairment. Neuropsychiatr Dis Treat 2019;15:167-75. doi: 10.2147/NDT.S189905
- 22. Batty GD, Li Q, Huxley R, Zoungas S, Taylor BA, Neal B, et al.; VANCE Collaborative group. Oral disease in relation to future risk of dementia and cognitive decline: Prospective cohort study based on the action in diabetes and vascular disease: Preterax and Diamicron modified-release controlled evaluation (ADVANCE) trial. Eur Psychiatry 2013;28:49-52.
- 23. Costa KL, Taboza ZA, Angelino GB, Silveira VR, Montenegro R Jr, Haas AN, *et al.* Influence of periodontal disease on changes of glycated hemoglobin levels in patients with type 2 diabetes mellitus: A retrospective cohort study. J Periodontol 2017;88:17-25.
- 24. Taylor JJ, Preshaw PM. A review of the evidence for pathogenic mechanisms that may link periodontitis and diabetes. J Clin Periodontol 2013;40:s14.
- Winning L, Patterson CC, Neville CE, Kee F, Linden GJ. Periodontitis and incident type 2 diabetes: A prospective cohort study. J Clin Periodontol 2017;44:266-74.
- Kandimalla R, Thirumala V, Reddy PH. Is Alzheimer's disease a type 3 diabetes? A critical appraisal. Biochim Biophys Acta Mol Basis Dis 2017;1863:1078-89.
- Ravona-Springer R, Schnaider-Beeri M. The association of diabetes and dementia and possible implications for nondiabetic populations. Expert Rev Neurother 2011;11:1609-17.
- Teeuw WJ, Gerdes VE, Loos BG. Effect of periodontal treatment on glycemic control of diabetic patients: A systematic review and meta-analysis. Diabetes Care 2010;33:421-7.
- Lalla E, Papapanou PN. Diabetes mellitus and periodontitis: A tale of two common interrelated diseases. Nat Rev Endocrinol 2011;7:738-48.
- Freitas S, Simões MR. Montreal cognitive assessment: Validation study for mild cognitive impairment and Alzheimer disease. Alzheimer Disease & Associated Disorders 2013;27:37-43.
- 31. Alagiakrishnan K, Zhao N, Mereu L, Senior P, Senthilselvan A. Montreal cognitive assessment is superior to standardized minimental status exam in detecting mild cognitive impairment in the middle-aged and elderly patients with type 2 diabetes mellitus. Biomed Res Int 2013;2013:1-5.

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