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Association between periodontal inflammation and cognitive impairment among older adults: A clinical and biomarker-based study

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Abstract:
Cognitive impairment in older adults is influenced by chronic inflammatory exposures and periodontal inflammation may represent a modifiable contributor to systemic inflammatory burden. This clinical and biomarker-based cross-sectional study evaluated 180 adults aged 60 years and older using periodontal examination, periodontal inflamed surface area, Mini-Mental State Examination, Montreal Cognitive Assessment and serum inflammatory markers. Mild cognitive impairment was identified in 68 participants (37.8%) and these participants had significantly higher periodontal inflamed surface area (864 ± 318 mm^2) than cognitively normal participants (523 ± 246 mm^2; $p<0.001$). Periodontal inflamed surface area correlated inversely with MoCA score ($r=-0.43$, $p<0.001$) and remained independently associated with mild cognitive impairment after adjustment for age, education, diabetes, hypertension and serum C-reactive protein (adjusted OR=1.82 per 250 mm2, $p=0.006$). Thus, periodontal inflammatory burden was associated with poor cognitive performance and high systemic inflammation, supporting integrated oral and geriatric health assessment.

Keywords: Periodontitis, cognitive impairment, older adults, MoCA, MMSE, PISA, inflammatory biomarkers

Background:
Cognitive impairment is a growing public health challenge in aging populations. Mild cognitive impairment may precede dementia and is influenced by vascular, metabolic, neurodegenerative, inflammatory and lifestyle-related factors **[1-4]**. Periodontitis is a chronic inflammatory disease that increases with age and can remain active for years if untreated. The inflamed periodontal pocket provides a biological interface for microbial products, inflammatory mediators and systemic immune activation **[5-8]**. A growing body of evidence suggests an association between poor periodontal health and cognitive impairment. Proposed mechanisms include systemic inflammation, endothelial dysfunction, microbial translocation, immune priming and direct or indirect neuroinflammatory pathways **[9-12]**. Oral pathogens and their virulence factors have been investigated in relation to neurodegenerative processes. Although causality remains unproven, periodontal infection may contribute to inflammatory cascades that are relevant to cognitive decline, especially in vulnerable older adults **[13-16]**. Serum C-reactive protein, interleukin-6 and tumor necrosis factor-alpha are markers of systemic inflammation that have been associated with both periodontitis and cognitive impairment. These biomarkers may help clarify whether periodontal burden relates to cognition through inflammatory pathways **[17-20]**. Clinical periodontal indices such as probing pocket depth and clinical attachment level describe disease severity, but they do not fully express the current inflammatory surface area. The periodontal inflamed surface area quantifies bleeding pocket epithelium and may better represent active inflammatory burden **[21-23]**. Cognitive screening tools such as the Mini-Mental State Examination and Montreal Cognitive Assessment are widely used in older adults. The Montreal Cognitive Assessment is particularly sensitive for mild cognitive impairment because it captures executive function, attention and visuospatial domains **[24-27]**. Previous studies have often relied on tooth loss or self-reported periodontal status, which may underrepresent active inflammation. Studies combining clinical periodontal examination, cognitive testing and serum biomarkers may provide stronger evidence **[28-30]**. Therefore, it is of interest to evaluate the association between periodontal inflammatory burden, cognitive performance and systemic inflammatory biomarkers in older adults.

Materials and Methods:
This cross-sectional clinical and biomarker-based study included 180 community-dwelling adults aged 60 years and older attending dental and geriatric outpatient clinics. Participants were recruited consecutively over 10 months after obtaining

informed consent. Inclusion criteria were age >=60 years, ability to undergo oral examination and presence of at least 10 natural teeth. Exclusion criteria were diagnosed dementia, Parkinson disease, stroke within 6 months, severe depression, severe hearing or visual impairment preventing cognitive testing, current infection, antibiotic use within 3 months, periodontal treatment within 6 months, malignancy, immunosuppressive therapy and inability to provide reliable history. Demographic data included age, sex, education, socioeconomic status, medical history, medication use, diabetes, hypertension, body mass index, tobacco status and tooth brushing frequency. Cognitive assessment was performed using the Mini-Mental State Examination and Montreal Cognitive Assessment by a trained examiner blinded to periodontal status. Mild cognitive impairment was defined using education-adjusted MoCA thresholds with preserved basic activities of daily living. Full-mouth periodontal examination included plaque index, bleeding on probing, probing pocket depth, clinical attachment level, number of remaining teeth and periodontal inflamed surface area. Six sites per tooth were examined using a calibrated periodontal probe. Serum high-sensitivity C-reactive protein, interleukin-6 and tumor necrosis factor-alpha were measured using standardized laboratory assays. Data were analyzed using SPSS version 26. Participants were categorized as cognitively normal or mild cognitive impairment. Intergroup comparisons used independent t-test, Mann-Whitney U test, or chi-square test. Correlations between periodontal and cognitive variables were assessed using Pearson or Spearman correlation. Logistic regression evaluated independent association between periodontal inflamed surface area and mild cognitive impairment after adjustment for covariates. A p-value <0.05 was considered significant.

Results:

The study included 180 older adults with mean age of 67.8 ± 6.1 years; 94 (52.2%) were female. Mild cognitive impairment was identified in 68 participants (37.8%). Participants with mild cognitive impairment were older, had fewer years of education and had a higher frequency of diabetes and hypertension than cognitively normal participants. Periodontal inflammation was significantly higher in the mild cognitive impairment group. Mean periodontal inflamed surface area was 864 ± 318 mm2 in participants with mild cognitive impairment and 523 ± 246 mm2 in cognitively normal participants (p<0.001). Mean probing pocket depth, clinical attachment level, bleeding on probing and number of sites with pocket depth >=5 mm were also significantly higher in the mild cognitive impairment group. Serum high-sensitivity C-reactive protein, interleukin-6 and tumor necrosis factor-alpha were higher in participants with mild cognitive impairment. Periodontal inflamed surface area correlated inversely with MoCA score (r=-0.43, p<0.001) and MMSE score (r=-0.31, p<0.001). In multivariable logistic regression, periodontal inflamed surface area remained independently associated with mild cognitive impairment after adjustment for age, sex, education, diabetes, hypertension, body mass index, smoking and serum inflammatory markers.

Table 1: Demographic and medical characteristics by cognitive status

Variable	Cognitively normal (n=112)	MCI (n=68)	p value
Age (years)	66.1 ± 5.4	70.6 ± 6.2	<0.001
Female sex, n (%)	57 (50.9%)	37 (54.4%)	0.646
Education (years)	10.8 ± 3.9	8.6 ± 3.7	<0.001
Diabetes, n (%)	31 (27.7%)	30 (44.1%)	0.023
Hypertension, n (%)	48 (42.9%)	42 (61.8%)	0.014
Current/former tobacco use	24 (21.4%)	19 (27.9%)	0.318
Remaining teeth	22.6 ± 5.1	19.4 ±5.8	<0.001

Table 2: Periodontal and inflammatory biomarker comparison

Parameter	Cognitively normal	MCI	p value
Plaque index	1.72 ± 0.48	2.06 ±0.52	<0.001
Bleeding on probing (%)	31.8 ± 14.7	48.6 ± 16.2	<0.001
Mean PPD (mm)	3.28 ± 0.62	4.05 ± 0.74	<0.001
Mean CAL (mm)	3.82 ± 0.89	4.71 ± 1.02	<0.001
PISA (mm2)	523 ± 246	864 ± 318	<0.001
hs-CRP (mg/L)	2.8 ± 1.3	4.1 ± 1.8	<0.001
IL-6 (pg/mL)	3.9 ± 1.5	5.4 ± 2.1	<0.001
TNF-alpha (pg/mL)	9.8 ± 3.6	12.3 ± 4.2	<0.001

Table 3: Correlation and logistic regression analysis

Analysis	Variable	Estimate	95% CI	p value
Correlation	PISA vs MoCA	r=-0.43	--	<0.001
Correlation	PISA vs MMSE	r=-0.31	--	<0.001
Correlation	IL-6 vs MoCA	r=-0.36	--	<0.001
Regression	PISA per 250 mm2	OR=1.82	1.19 to 2.78	0.006
Regression	Mean CAL per 1 mm	OR=1.41	1.01 to 1.96	0.041
Regression	hs-CRP per 1 mg/L	OR=1.22	1.03 to 1.45	0.022

Discussion:

The present study found that older adults with mild cognitive impairment had significantly greater periodontal inflammatory burden than cognitively normal participants. The association remained significant after adjustment for demographic, vascular, metabolic and inflammatory covariates, suggesting that periodontal inflammation may be independently linked with poorer cognitive performance **[31, 32]**. The periodontal inflamed surface area showed a stronger relationship with MoCA score than conventional mean probing depth or attachment level. This supports the idea that active inflammatory burden, rather than cumulative tissue destruction alone, may be more relevant to systemic inflammatory exposure **[33, 34]**. Higher serum C-reactive protein, interleukin-6 and tumor necrosis factor-alpha in the mild cognitive impairment group indicate a systemic inflammatory phenotype. Periodontal inflammation may contribute to this phenotype, although systemic inflammation is multifactorial and may also arise from adiposity, diabetes, vascular disease and aging **[35]**. The biological pathways linking periodontal inflammation and cognition may include circulating cytokines, blood-brain barrier alteration, microglial activation, endothelial dysfunction and exposure to periodontal microbial products. These mechanisms are plausible, but the present cross-sectional design cannot prove directionality **[1-4]**. Tooth loss was more common among participants with mild cognitive impairment, but the study focused on active periodontal inflammation among dentate individuals. Tooth loss may reflect previous periodontal disease, socioeconomic factors, nutrition and access to care; therefore, it should not be interpreted as a direct substitute for current inflammation **[5-8]**. The use of both MMSE and MoCA was important because MoCA is more

sensitive for mild cognitive deficits. The stronger association with MoCA suggests that periodontal inflammatory burden may relate to early or subtle cognitive changes rather than only advanced impairment **[24-27]**. Clinical implications include the need for oral health assessment in older adults at risk of cognitive decline. Periodontal therapy, plaque control, caregiver involvement and maintenance care may reduce oral inflammatory burden. Whether this can slow cognitive decline requires interventional trials **[9-12]**. The limitations include cross-sectional design, single-center recruitment, possible residual confounding and use of screening rather than comprehensive neuropsychological testing. Longitudinal studies should evaluate whether periodontal treatment reduces systemic inflammatory biomarkers and preserves cognitive trajectories in older adults **[13-20]**. Recent studies likewise report that severe periodontal inflammation is associated with poorer cognitive performance in older adults, including biomarker-based case-control and community studies; however, these observational findings do not establish causality **[7, 36 and 37].** The association observed in this study is clinically important because periodontal inflammation is potentially modifiable. Older adults with cognitive decline often experience worsening oral hygiene because of reduced dexterity, memory impairment, medication-related xerostomia and dependence on caregivers. This creates a cycle in which cognitive impairment worsens periodontal status, while periodontal inflammation may contribute to systemic inflammatory burden. Caregiver involvement is therefore essential. Oral hygiene instructions directed only to the patient may be insufficient when mild cognitive impairment is present. Dental professionals should assess whether the patient can perform brushing and interdental cleaning independently and should involve family members or caregivers in maintenance planning. Recall intervals may need to be shortened for patients with both periodontal inflammation and cognitive vulnerability. The use of periodontal inflamed surface area adds value because it captures active bleeding pocket epithelium. In older adults, clinical attachment loss may reflect historical disease and tooth retention patterns, whereas bleeding pocket area more closely reflects current inflammatory exposure. This may explain why periodontal inflamed surface area remained independently associated with cognitive impairment after adjustment. The study also suggests that oral health should be included in geriatric risk assessment. Cognitive screening clinics frequently assess vascular risk factors, diabetes, nutrition, medication burden and depression, but periodontal status is often overlooked. Integrating dental referral into geriatric pathways could improve quality of life and may reduce one contributor to chronic inflammation. Future longitudinal studies should evaluate whether periodontal treatment changes cognitive trajectories or only improves inflammatory biomarkers. Randomized trials in older adults will require careful ethical design, caregiver support, standardized periodontal maintenance and repeated cognitive testing. Such research can clarify whether periodontal therapy is a preventive strategy, a supportive care measure, or both. Reverse causation remains a key concern. Individuals with early cognitive impairment may neglect oral hygiene, miss dental appointments and develop more periodontal inflammation. At the same time, periodontal inflammation may amplify systemic inflammatory pathways that influence brain health. The relationship is therefore likely bidirectional and longitudinal designs are required to separate cause, consequence and shared risk factors. Nutritional pathways may also contribute. Periodontitis and tooth loss can impair chewing efficiency, leading to avoidance of fibrous foods, fruits, vegetables and protein-rich items. Poor diet may worsen metabolic and inflammatory profiles, which in turn can affect cognitive resilience. Future studies should include dietary assessment, masticatory function and socioeconomic variables to clarify these indirect pathways. Another clinical implication is medication review. Older adults commonly use antihypertensives, antidepressants, anticholinergics and other medications that can reduce salivary flow and increase plaque accumulation. Xerostomia may worsen periodontal inflammation and caries risk. Integrated assessment of medications, saliva, cognition and periodontal status may improve prevention strategies in geriatric dentistry. The findings should not be used to suggest that periodontal disease alone causes cognitive impairment. Cognitive decline is multifactorial and influenced by age, education, vascular disease, genetics, depression, sleep and social engagement. Periodontal inflammation should be viewed as one potentially modifiable component within a broader risk profile.

Conclusion:

Older adults with mild cognitive impairment showed greater periodontal inflammatory burden and higher serum inflammatory biomarkers than cognitively normal participants. Periodontal inflamed surface area was independently associated with mild cognitive impairment and inversely correlated with MoCA and MMSE scores. These findings support the integration of periodontal evaluation into geriatric health assessment and justify longitudinal trials examining whether periodontal inflammation control influences cognitive outcomes.

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