WebLog Journal of Neurosurgery

Research Article
Published: 14 Nov, 2026

A Comparative Cross - Sectional Study of Periodontal Status in Astrocytoma (WHO Grade 2 and 3) *vs.* Oligodendroglioma (WHO Grade 2 and 3) Patients

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WebLog Open Access Publications
Article ID : wjns.2026.k1403
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OPEN ACCESS

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Received Date: *25 Oct 2026*
Accepted Date: *12 Nov 2026*
Published Date: *14 Nov 2026*

Citation:
Chrysanthakopoulos NA, Kotsomiti P. A Comparative Cross - Sectional Study of Periodontal Status in Astrocytoma (WHO Grade 2 and 3) vs. Oligodendroglioma (WHO Grade 2 and 3) Patients. WebLog J Neurosurg. wjns.2026.k1403. https://doi.org/10.5281/zenodo.24280413

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Abstract

Background/Aim: Periodontal Disease (PD) has been associated with several systemic cancers, however, comprehensive data investigating its relationship with gliomas remain scarce. The current research aimed to assess potential variations in periodontal health between individuals suffered from diffuse oligodendroglioma (WHO Grade 2 and 3), and those who suffered from diffuse astrocytoma (WHO Grade 2 and 3).

Materials and Methods: This cross-sectional study involved 52 individuals newly diagnosed with oligodendroglioma (WHO grade 2, and 3), and 87 individuals diagnosed with astrocytoma (WHO grade 2, and 3). Before commencing any oncological treatment, all patients filled out a standardized health questionnaire and received a detailed clinical dental assessment. Periodontal health was assessed by measuring Probing Pocket Depth (PPD), Clinical Attachment Loss (CAL), and Bleeding on Probing (BOP). To isolate independent effects and control for confounding factors, data analysis was performed using both univariate and multivariate logistic regression models.

Results: After controlling for socioeconomic conditions, and smoking habits, the multivariate regression model demonstrated that patients with diffuse astrocytoma exhibited significantly deeper PPD (p= 0.044, 95% CI= 0.606-3.077), and marginally higher CAL values (p= 0.085, 95% CI= 0.760-3.837) in comparison to patients with diffuse oligodendroglioma.

Conclusions: The findings indicated that the specific histological subtype of diffuse glioma were associated with different degrees of periodontal destruction. Specifically, individuals diagnosed with diffuse astrocytoma exhibit significantly worse PPD and borderline higher CAL values than oligodendroglioma patients. These distinct periodontal variations remain evident even after adjusting for smoking habits and socioeconomic confounding factors, suggesting that astrocytoma may influence oral health outcomes.

Keywords: Gliomas; Astrocytoma (WHO Grade 2, and 3); Oligodendroglioma (WHO Grade 2 and 3); Periodontal Disease; Adults

Introduction

Gliomas represent the most prevalent primary solid malignancies originating within the Central Nervous System (CNS) [1]. According to the 2021 World Health Organization (WHO) classification, these neoplasms are stratified into four distinct grades based on integrated histological traits and molecular parameters [2]. Within this revised classification system, Lower-Grade Gliomas (LGGs), corresponding to CNS WHO grades 2 and 3, mainly consist of Astrocytomas (ACs) and oligodendrogliomas (OGs), which typically present clinically in adults during their third and fourth decades of life. Epidemiologic data indicate that these tumors constitute approximately 75% of all diagnosed gliomas and comprise 25% to 30% of primary intracranial malignancies. Glioblastoma, classified as a Grade 4 AC, is the most frequently diagnosed malignant glioma at 58.4%, followed by unclassified malignant gliomas (NOS,7.9%), diffuse AC (7.3%), anaplastic AC (6.8%), pilocytic AC (5.0%), OG (3.5%), and anaplastic OG (1.7%) [2].

The clinical presentation and epidemiological patterns of ACs vary markedly depending on patient age. In pediatric cohorts, low-grade variants, particularly pilocytic AC, are the most frequently encountered subtypes. Conversely, adult populations are disproportionately affected by high-grade, aggressive phenotypes like anaplastic AC and glioblastoma multiforme [3, 4]. Population-based data revealed that the age-adjusted incidence of glioblastoma is substantially higher at 3.23 per 100,000 people, whereas diffuse and anaplastic ACs exhibit much lower rates at 0.46 and 0.42 per 100,000 individuals, respectively. Annually, approximately 15,000 new cases of AC are documented in the United States, representing nearly half of all primary brain malignancies [3, 4]. Furthermore, demographic analyses indicate a slight male predominance in tumor distribution, with a male-to-female ratio spanning between 1.3:1 and 1.5:1 [3, 5].

OGs are categorized as an uncommon type of diffuse neuroepithelial tumors, ranking as the third most frequent primary intracranial malignancy after glioblastoma and diffuse AC, and accounting for roughly 5% of all primary CNS neoplasms [6]. In the United States, the annual incidence of OGs encompasses approximately 1,000 newly diagnosed individuals. From a clinical and histopathological standpoint, OGs are divided into grade 2 and grade 3 (anaplastic) lesions. Although these malignancies predominantly emerge in patients aged 25 to 45 years, the more aggressive grade 3 variants generally present a decade later than lower-grade tumors. OGs remain exceedingly uncommon in both pediatric and geriatric patient groups. A key clinical feature of LGGs is their intrinsic risk of undergoing malignant progression into highly aggressive HGGs. It is widely suspected that anaplastic grade 3 OGs develop from lower-grade precursors via the stepwise acquisition of specific oncogenic genetic modifications [7].

Driven by distinct molecular alterations in line with general oncogenic pathways, the development and progression of OGs rely on genetic biomarkers that provide mandatory diagnostic, prognostic, and predictive insights for modern tumor profiling [8]. Molecularly, establishing a definitive diagnosis of OG strictly requires the detection of an IDH1 or IDH2 mutation [9], which must occur alongside the concurrent, reciprocal chromosomal co-deletion of arms 1p and 19q [2, 10, 11]. Despite substantial progress in molecular biology, the exact cellular cascades and biological triggers modulating oligodendrogliogenesis remain unresolved. Grade 3 OGs display prominent anaplastic features, such as severe nuclear atypia, focal necrosis, hypercellularity, microvascular proliferation, and elevated mitotic activity, culminating in a significantly worse clinical prognosis compared to grade 2 counterparts [8].

While the exact molecular pathways of cranial neoplasms are unclear, therapeutic ionizing radiation to the head and neck is a proven risk factor for glioma onset. Familial history of CNS malignancies significantly increases the risk of developing anaplastic OGs (OR = 2.2), often tied to genetic syndromes like Li-Fraumeni, Turcot, Constitutional Mismatch Repair Deficiency, and Neurofibromatosis type 1 (NF1) [12-16]. Conversely, atopic diseases, like asthma [17], and past varicella-zoster virus infections [18] show an inverse, protective association against these tumors. While exposure to toxic chemicals is heavily analyzed, the link to electromagnetic fields remains ambiguous. Finally, tobacco smoking does not increase CNS cancer risk [19, 20], whereas immunosuppression and older age are linked to higher incidence and worse clinical outcomes [21].

Periodontal Disease (PD), categorized broadly into gingivitis and periodontitis, represents a highly prevalent, destructive, and chronic inflammatory disease affecting approximately 15% of the adult population worldwide. Driven by bacterial pathogens infiltrating the gingival architecture and the supporting elements of the teeth, the development and severity of PD is associated heavily with advanced age, tobacco habits, and inadequate oral hygiene. The introduction of pathogenic oral bacteria [22] alongside concurrent viral factors [23] initiates an intense host immune-inflammatory response. This biological pathway promotes periodontal pocket development, clinical attachment loss, gingival hemorrhage, and alveolar bone resorption, frequently culminating in tooth loss in severe instances. Furthermore, intricate associations involving compromised immune systems, bone density depletion, and distinctive oral microbial characteristics remain areas of ongoing study [24, 25].

Beyond causing localized damage to oral tissues, periodontal pathogens are recognized for placing a heavy systemic burden on several vital organ systems, particularly the respiratory and cardiovascular networks [26]. The cellular mechanism driving this connection involves the overproduction of Reactive Oxygen Species (ROS) and subsequent oxidative damage, which is regulated by acute-phase cytokines and inflammatory mediators like Interleukin (IL)-1, IL-6, and C-Reactive Protein (CRP) that alter the presentation of PD [27]. The systemic spread of these inflammatory biomarkers is thought to occur via a widespread systemic inflammatory state, an immune reaction triggered by periodontal pathogens, or through the direct entry of oral bacteria into the systemic blood supply [28, 29]. Consequently, many epidemiological studies have explored periodontitis as a potential driving factor for systemic illnesses, establishing strong links with cardiovascular and atherosclerotic anomalies, cerebrovascular accidents stroke, Chronic Obstructive Pulmonary Disease (COPD), type 2 diabetes, rheumatoid arthritis, and various forms of cancer [25, 30-37].

An elevated risk of total malignancy [38,39] as well as specific localized cancers [40-42] have been closely linked with inadequate oral hygiene, the advancement of PD, and premature tooth loss. These connections persist even after accounting for standard confounding factors such as age, gender, smoking, and socioeconomic standing.

Although researchers have explored the potential oncogenic role of PD in several anatomical sites, including the oral cavity, esophagus, stomach, pancreas, and lungs [39, 43-46], the compiled data are still a matter of controversy after adjusting for confounders. Additionally, while it is hypothesized that intersecting immuno-inflammatory pathways serve as the underlying link between PD and carcinogenesis, the exact pathophysiological mechanisms connecting periodontitis to heightened cancer susceptibility are still not completely clear.

In contrast, only a small number of studies have examined baseline periodontal conditions or oral clinical findings in groups of patients already diagnosed with malignancies, such as lung, breast, colorectal or gastric carcinomas [47-55]. Most notably, the periodontal status of individuals diagnosed with highly aggressive intracranial tumors, such as primary brain cancers, remains severely underrepresented in current medical research. Furthermore, no studies evaluating the periodontal health of patients diagnosed with two separate malignancies within the exact same organ are available in the literature. To address this paucity of scientific data, this clinical research was initiated to analyze potential differences in periodontal status between patients with histologically verified diffuse OG and those with diffuse AC.

Materials and Methods

Study design and participant cohort

This cross-sectional study was conducted across various clinical environments from June 2023 to August 2026. Calculations for sample size estimation and cohort power assessment were rigorously performed using baseline glioma prevalence data alongside the EPITOOLS software recommendations [56], establishing a 95% Confidence Interval (CI) and a statistical power target of 0.8. Age group stratification was aligned with the epidemiological criteria of the WHO [57] regarding the assessment of CNS malignancy rates [58].

The comprehensive study population encompassed a total of 139 participants. This cohort included individuals aged 33 to 68 years, who were selected from private oncological, medical, and neurological practices. The participants diagnosed with histologically validated gliomas, further differentiated into diffused ACs and OGs. Both cohorts were originated from the same metropolitan area to maximize sample representativeness and mitigate selection bias.

The patients included individuals whose initial suspicion of primary glioma was determined through Magnetic Resonance Imaging (MRI) analysis. Nevertheless, definitive diagnosis was invariably established via the histopathological evaluation of specimens retrieved during surgical resection, utilizing standard cytological, histological, and histochemical protocols [2, 59].

Patient selection and eligibility criteria

To ensure a robust methodology, strict baseline prerequisites were established for the enrollment of individuals into both cohorts. Patients had to be recently diagnosed with, histopathologically validated diffuse glioma, classified as either an AC or an OG in strict accordance with updated WHO diagnostic frameworks [60]. For all participants, clinical characteristics, tumor staging, and diagnostic data were extracted directly from official medical and neuro-oncological databases.

To eliminate potential confounding systemic influences on the biological variables under investigation, participants across both groups were excluded if they had been treated with systemic antibiotics, immunosuppressive therapies, or systemic glucocorticoids within the prior six months. Furthermore, individuals who had undergone any surgical or conservative periodontal interventions during the preceding six months were deemed ineligible. The exclusion protocol also barred individuals presenting with a medical history of advanced cardiovascular pathologies, rheumatoid arthritis, acute respiratory conditions, or any synchronous primary malignancy. These specific clinical conditions were excluded because they possess the potential to alter oral microbial species and periodontal tissue measurements, which could introduce substantial analytical bias [61].

Across both cohorts, specialized neuro-oncological exclusion criteria were applied. Patients presenting with advanced metastatic malignancies secondary to a primary tumor located outside the CNS, as well as individuals with secondary intracranial lesions linked to multi-field carcinogenesis models [62], were excluded from enrollment. In addition, to ensure completely unbiased baseline records, participants were excluded if they had already commenced first-line oncological management, such as surgical resection, adjuvant chemotherapy, targeted molecular regimens, or radiotherapy, prior to the collection of baseline clinical data.

Clinical data acquisition and patient questionnaires

Every eligible patient completed a modified adaptation of the Minnesota Dental School Medical Questionnaire [63]. This validated survey was systematically utilized to acquire comprehensive data concerning the participants' previous medical and dental histories, active systemic diseases, and a broad range of socioeconomic and epidemiological indices.

Evaluation of covariates

Socio-demographic variables were integrated into the statistical models as confounding covariates. The chronological age of the participants across both cohorts was classified into five separate age groups, 33-39, 40-49, 50-59, and over 60 years. Socio-Economic Status (SES) was evaluated using self-reported monthly income and divided into two financial strata, ≤1,000 € and >1,000 €. Tobacco usage profiles were divided into two main clinical groups, lifelong non-smokers (defined as subjects who had smoked fewer than 100 cigarettes in total) and active or former smokers (encompassing individuals with a cumulative lifetime consumption of at least 100 cigarettes, further partitioned into active daily/occasional users and those who had achieved sustained cessation). Finally, obesity profiles were determined via the Body Mass Index (BMI), allowing the stratification of the study sample into normal (<30 kg/m^2) and high (≥30 kg/m^2) adiposity cohorts [64].

Clinical periodontal assessment and index quantitation

Comprehensive clinical oral and periodontal assessments were performed by a calibrated Dental Surgeon. All diagnostic examinations were conducted within a standardized dental operatory utilizing a uniform light source, a dental mouth mirror, and a specialized, pressure-sensitive periodontal probe calibrated to a constant spring-loaded force of 0.2 N (UNC15/Williams type, model DB764R, Aesculap AG & Co. KG, Tuttlingen, Germany) to eliminate inter-examiner measurement variance. To isolate chronic periodontal architectural alterations and prevent acute anatomical confounding, all retained root fragments and third molars were systematically excluded from clinical staging across all quadrants. The baseline periodontal status was recorded through the concurrent evaluation of three standard clinical parameters, the Probing Pocket Depth (PPD), Clinical Attachment Loss (CAL), and Bleeding on Probing (BOP).

To optimize diagnostic sensitivity, clinical measurements were systematically registered across all dental quadrants. For each individual tooth, tissue indices were assessed at six distinct sites encompassing the mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual surfaces. The peak severity values recorded for each parameter were rounded to the nearest 1.0 mm and subsequently operationalized as dichotomous categorical variables for subsequent multivariate statistical modeling.

Periodontal indices were staged based on established PPD classification guidelines. The cohort was stratified into Stage I/II (characterized by a maximum PPD ≤4.0 mm or ≤5.0 mm, respectively, with predominant horizontal bone loss), and Stage III/IV (Stage III: characterized by a maximum PPD ≥6.0 mm with vertical bone loss ≥3.0 mm, Class II/ III furcation involvement, or moderate ridge defects, and Stage IV, meeting Stage III criteria alongside complex rehabilitation requirements driven by masticatory dysfunction, secondary occlusal trauma, tooth mobility ≥degree 2, severe ridge defects, bite collapse, tooth drifting/flaring, or <20 remaining teeth/10 opposing pairs) [65].

Table 1: Univariate analysis of cases and controls regarding each independent variable examined.

Variables	Cases	Controls	*p*-value	Odds Ratio and 95% Confidence Interval
Gender				
Males	27 (53.8)	47 (54.0)	0.984	0.993 (0.498-1.978)
Females	24 (46.2)	40 (46.0)		
Age				
33-39	12 (23.1)	18 (20.7)		
40-49	18 (34.6)	33 (37.9)		
50-59	12 (23.1)	24 (27.6)	**0.000***	_____
60+	10 (19.2)	12 (13.8)		
Socio-economic status				
Low	32 (61.5)	55 (42.5)	0.843	0.931 (0.458-1.891)
High	20 (38.5)	32 (57.5)		
Smoking Status				
Never smokers	21 (40.4)	37 (42.5)	0.804	0.915 (0.455-1.840)
Previous/current smokers	31 (59.6)	50 (57.5)		
Diabetes Mellitus				
No	35 (67.3)	54 (62.1)	0.533	1.258 (0.610-2.594)
Yes	17 (32.7)	33 (37.9)		
Body Mass Index				
<30 kg/m^2	19 (36.5)	36 (41.4)	0.572	0.816 (0.402-1.655)
≥30 kg/m^2	33 (63.5)	51 (58.6)		
Probing pocket depth				
stage I/II	16 (30.8)	37 (42.5)	0.167	0.601 (0.291-1.242)
stage III/IV	36 (69.2)	50 (57.5)		
Clinical Attachment Loss				
stage I/II	21 (40.4)	31 (35.6)	0.575	1.224 (0.604-2.481)
stage III/IV	31 (59.6)	56 (64.4)		
Bleeding on Probing				
Absence	18 (34.6)	28 (32.2)	0.768	1.116 (0.539-2.308)
Presence	34 (65.4)	59 (67.8)		

*p-value: statistically significant

CAL was similarly stratified into Stage I/II (interproximal CAL at the site of maximal destruction measuring 1-2.0 mm or 3-4.0 mm, respectively) and Stage III/IV (Stage III: interdental CAL at the site of greatest loss ≥5.0 mm with a history of ≤4 teeth lost due to periodontitis; Stage IV: interdental CAL ≥5.0 mm with a history of ≥5 teeth lost due to periodontitis) [65].

Assessment of Bleeding on Probing (BOP) was conducted across all six sites per tooth and recorded using a binary classification system, where Score 0 represented absolute clinical health (no bleeding) and Score 1 denoted active hemorrhage. A positive BOP event was documented whenever marginal or sulcular bleeding was visually detected within a 15-second window after the standardized application of the calibrated periodontal probe.

Methodological standardization and intermittent reliability analysis

To confirm the reproducibility of the clinical parameters and rigorously evaluate intra-examiner variability, a random subset of 28 patients (comprising 20% of the comprehensive study population) was isolated for duplicate evaluation. These participants underwent a blinded secondary clinical assessment by the initial evaluating clinician following a strict three-week period. The statistical association between the initial and secondary clinical evaluations revealed an outstanding degree of reproducibility, yielding a calculated Cohen's kappa coefficient of 0.94. To ensure the stability of the intra-examiner records and avoid temporary behavioral modifications that could alter the oral micro-ecology, no oral hygiene counseling or instructions were delivered to the study participants throughout this three-week observational window.

Ethical statement and patient consent

Given the non-interventional structure of this investigation, the research protocol was carried out in strict accordance with institutional guidelines governing exemptions for retrospective database and registry evaluations.

Prior to enrollment in the research protocol, all participants were thoroughly briefed regarding the specific objectives, clinical relevance, and methodological steps of the study, and provided formal written informed consent.

Results

The cohort demonstrated mean ages of 47.3 ± 2.1 for OG patients and 49.7 ± 3.5 for AC patients. Univariate model was used to compare indices between both cohorts for categorical variables. The outcomes showed no statistically significant differences among the PD indices examined between OG and AC patients (Table 1).

The corresponding crude Odds Ratios (ORs) alongside their 95% CIs are summarized in the same table. Following the execution of a multivariate logistic regression model utilizing the Wald stepwise selection method, showed that patients with diffuse AC exhibited significantly deeper periodontal pockets (p= 0.044, 95% CI= 0.606-3.077), and marginally higher CAL values (p= 0.085, 95% CI= 0.760-3.837) in comparison to patients with diffuse OG (Table 2). The adjusted ORs and their respective 95% CIs are documented within the same table.

Discussion

Standard periodontal evaluation typically relies on key clinical indicators, including PPD, CAL, BOP, Gingival Index (GI), Plaque Index (PlI), Bleeding Point Index (BPI), Alveolar Bone Loss (ABL), and measures of missing and retained teeth.

No statistically significant variations were observed between both groups regarding socio-demographic variables, such as age, gender, SES, and smoking habits. Although tobacco consumption is an established risk factor for both the development and exacerbation of PD and various malignancies, it often acts as a confounding variable

Table 2: Presentation of association between AC and OG and variables examined according to Enter (first step1[a]) and Wald (last step 8[a]) method of multivariate logistic regression analysis model.

Variables in the Equation									
		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1[a]	gender	,324	,365	,789	1	,374	1,383	,676	2,828
	age	,113	,194	,045	1	,946	1,013	,692	1,483
	smok.status	,373	,378	,037	1	,847	,930	,443	1,949
	socioec.status	,381	,382	,057	1	,934	,969	,458	2,051
	diab.mellit	,414	,397	1,087	1	,297	1,213	,694	2,298
	bod.mass.ind	,366	,387	,894	1	,344	,693	,325	1,481
	prob.pock.depth	,875	,451	3,758	1	,053	1,417	,672	3,010
	clin.att.loss	,659	,456	2,090	1	,108	1,933	,791	4,725
	bleed.on.prob	,227	,424	,101	1	,988	,993	,433	1,281
	Constant	,618	,545	1,287	1	,000	1,856		
Step 8[a]	prob.pock.depth	,752	,421	3,184	1	,044*	1,571	,606	3,077
	clin.att.loss	,535	,413	1,680	1	,085*	1,708	,760	3,837
	Constant	,660	,327	4,077	1	,000	1,935		

a.Variable(s) entered on step 1: gender, age, smok.status, socioec.status, diab.mellit, bod.mass.ind, prob.pock.depth, clin.att.loss, bleed.on.prob.
**p*-value: statistically significant

in studies exploring the link between PD and oncogenesis, particularly in cancers where smoking plays a direct etiological role [66].

While elevated BMI and obesity are consistently linked to an increased risk of several malignancies, including colorectal [64] and breast cancer [67], this study noted no differrences between OG and AC patients.

Previous studies demonstrated that oral and gingival lesions frequently serve as the initial clinical presentation of several malignancies, such as lung cancer [47], gastric cancer [48] and Multiple Myeloma (MM) [68-70].

The findings indicated a statistically significant difference in PPD between both groups, a trend that remained consistent even after controlling for potential confounders such as smoking status, and SES. To be more specific, individuals diagnosed with diffuse AC exhibit significantly worse PPD, compared to those with diffuse OG. PPD highlights the tissue destruction caused by chronic inflammation and represents a well-recognized marker for evaluating PD severity [71]. Similarly, data from a prospective cross-sectional study revealed that a PPD of 6.0 mm or more was present in 76.0% of individuals with oral or oropharyngeal malignancies, compared to only 10.0% of the control subjects [46]. Comparable trends have been documented in past research involving patients diagnosed with acute leukemia [51]. On the other hand, previous similar researches demonstrated that PPD values did not vary significantly between cases and controls. This lack of statistical significance aligns with outcomes observed in parallel studies on patients with lung [47], gastric [48], colorectal cancer [50], MM [52], and glioblastoma patients [53]. As an additional vital index for determining periodontitis severity, CAL indicates the advanced phases of chronic inflammation and the cumulative outcomes of destructive inflammatory pathways [71]. In this investigation, patients with diffuse AC exhibited marginally higher CAL values in comparison to patients with diffuse OG. Similarly, corresponding research conducted on other anatomical sites demonstrated that individuals with malignancies of the lungs [47], stomach [48], breast [49], as well as those with acute leukemia [51] and glioblastoma [53], presented markedly worse mean scores for this specific index.

Serving as an essential indicator in periodontal evaluation and clinical diagnosis, BOP represents the most reliable indicator of active PD [72], since it captures the host's localized vascular alterations, including hyperemia, capillary expansion, and increased perfusion at the inflammatory focus. While PPD and CAL capture the long-term progression and aggregate structural damage of chronic inflammatory pathways, BOP remains a primary standard for identifying gingival inflammation, with deeper periodontal pockets (≥5.0 mm) demonstrating a substantially higher frequency of bleeding [72].

Following adjustment for potential confounding factors, no statistically significant variation in BOP was detected between both cohorts. These outcomes align with previous data documented in patients with gastric [48], breast [49], colorectal cancer [50], and MM patients [52]. Conversely, distinct variations between case and control subjects have been reported in comparable investigations involving lung cancer [47] and acute leukemia patients [51].

Regarding the pathophysiological mechanisms implicated in the onset or accelerated progression of PD in patients with gliomas, the following suggestions have been proposed. Utilizing genetic data (GWAS), it was demonstrated that a genetic predisposition to glioma causally increases the risk of developing periodontitis. The actual pathophysiological mechanism entails that glioma induces a systemic immune aberration by stimulating CD8 expression on peripheral Natural Killer T-cells (NKT cells), a process that ultimately dysregulates the local immune defense of the gingival tissues [73].

The second mechanism based on Gao *et al.,* study [74]. The researchers clinically examined patients with glioma prior to treatment and found that they exhibited a statistically significant, more severe periodontal destruction (deep pocket depth PD ≥6 mm and clinical attachment loss AL >5 mm) compared to both patients

with benign CNS tumors and the general population.

P. gingivalis LPS significantly increased the mRNA levels of TNF-α, TGF-β, MMP-2, and MMP-9 and had no significant effect on the mRNA levels of IL-1β, IL-6, and IL-10. TNF-α can promote glioma invasion and angiogenesis. TGF-β facilitates glioma growth and immunosuppression and stimulates glioma cell migration and angiogenesis [75].

Furthermore, MMPs are of great importance in facilitating cancer cell migration and invasion by modulating the degradation of the basement membranes and the extracellular matrix. In support of our results, *P. gingivalis* LPS has been shown to upregulate the expression of MMP2 and MMP9 in oral cancer cells [76]. The increased expression of TNF-α, TGF-β, MMP-2, and MMP-9 might explain how the *P. gingivalis* LPS exerts pro-tumor effects. Notably, the Akt signaling pathway has been widely demonstrated to take part in the regulation of inflammatory processes and tumor growth. Previous studies showed that *P. gingivalis* LPS promoted cell growth and cytokine secretion via activating the Akt/NF-κB pathway [76-78].

Moreover, it has been hypothesized that the heightened risk of PD among oncology patients stems primarily from psychological distress, rather than from nutritional inadequacies, modifications in salivary composition and volume, or imbalances in oral microbial and immunological homeostasis brought about by chemotherapy or radiation treatments [79, 80].

Additionally, individuals diagnosed with gliomas might demonstrate a greater vulnerability to periodontal tissue deterioration and exacerbation compared to healthy controls. This potential association may be linked to the unfavorable prognosis characteristically observed in patients presenting with invasive, metastatic histological variants of glioma. This investigation aimed to evaluate various PD indices by comparing patients with diffuse AC and diffuse OG, rather than against epidemiologically matched healthy controls, or establishing a direct causal or risk relationship between PD indices and the onset of OG and AC. As a result, several methodological constraints must be acknowledged. Due to their nature, cross-sectional designs cannot provide the strong causal inferences typical of prospective studies, while selection, recall, and confounding biases can introduce distorted secondary correlations among the studied variables. Furthermore, these designs rely heavily on self-reported questionnaires, which are susceptible to non-response bias or inaccurate data due to participants systematically overestimating or underestimating their objective health status.

Conversely, the primary strengths of this research lie in the thoroughness of the follow-up period and the well-defined cohort, which enabled robust adjustments for confounding factors and a detailed analysis of interactions between confirmed risk variables.

Conclusions

In summary, this study revealed marked disparities between the cohorts, with worse PPD levels and marginally higher CAL values being observed predominantly among patients diagnosed with AC. These distinct profiles remained consistently significant even after controlling for potential confounding factors, including smoking status and SES status.

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