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Periodontal Disease and Systemic Cancer Risk: A Community-Based Cross-Sectional Study in Guntur, South India

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ABSTRACT

Background: Periodontal disease (PD), a chronic inflammatory condition affecting 20–50% of adults worldwide, is linked to systemic carcinogenesis, particularly in high-tobacco-use regions like South India, where tobacco synergistically amplifies oncogenic pathways. This study assesses severe PD's association with cancer risk, tobacco modification, and role in initiation versus metastasis in an underserved South Indian cohort.

Methods: This cross-sectional study (May 2025–July 2025) enrolled 200 participants (40–75 years) at a Guntur, India, cancer screening camp: 100 with confirmed systemic malignancies (52 non-metastatic [M0], 48 metastatic [M1]) and 100 matched controls. Blinded examiners assessed periodontal parameters (e.g., CAL, PPD, BoP, PDI). Adjusted multivariate logistic regression estimated ORs (95% CIs); interaction/subgroup analyses were performed (Hosmer-Lemeshow p=0.72; R^2=0.42).

Results: Cancer patients had worse periodontal health (e.g., CAL: 5.6 ± 1.5 mm vs. 2.3 ± 0.9 mm, $p < 0.001$; d=2.6). Severe PD increased risk (OR=5.12 [2.78–9.43] for CAL >4 mm; OR=5.89 [3.12–11.09] for PDI >3; $p < 0.001$), amplified by tobacco (interaction OR=2.34 [1.15–4.76]; p=0.02). Higher risks for oral cancer (OR=6.8) and smokers (OR=7.2) vs. non-oral (OR=4.7) and non-smokers (OR=3.8). No metastasis link ($p > 0.39$). ARI for severe CAL: 38% (NNH=3).

Conclusion: Severe PD elevates cancer risk in South Indian high-risk groups via initiation, modulated by tobacco. Community PD screening (~$50/patient) could prevent 10–15% of cases; longitudinal studies are needed.

Keywords: *Periodontal disease, Cancer risk, Tobacco use, Oral cancer, Periodontitis, South India, Community screening*

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1. INTRODUCTION

Periodontal disease (PD), a chronic microbial infection with significant inflammatory burden, affects 20–50% of adults globally, posing a major public health challenge with systemic implications beyond oral health [1,2]. Cohort studies and systematic reviews have established PD as a risk factor for systemic carcinogenesis, with increased risks for pancreatic cancer, oral squamous cell carcinoma (OSCC), lung cancer, and prostate cancer [3,4,5,6]. The biological mechanisms involve chronic systemic inflammation, driven by cytokines and C-reactive protein, creating a pro-tumorigenic microenvironment, and direct carcinogenic effects of pathogens like Porphyromonas gingivalis and Fusobacterium nucleatum, which promote microbial dysbiosis, cell proliferation, apoptosis inhibition, and DNA damage [7,8,9,10]. In

South India, where tobacco and betel quid use prevalence reaches 35% [11], the PD-cancer association is amplified, particularly for OSCC, due to synergistic effects on inflammation and pathogen virulence [3,4,12,13]. Despite robust global evidence, data from underserved South Indian populations remain limited, necessitating region-specific studies [2]. This cross-sectional study, conducted during a free medical and cancer screening camp in Guntur, hypothesizes that severe PD increases cancer risk (OR > 4, based on prior studies reporting ORs of 2–3.5 for PD-cancer associations [3,4]), exacerbated by tobacco use, but does not contribute to metastasis, acting primarily in cancer initiation. By quantifying this risk, we aim to inform targeted public health interventions, integrating PD screening into cancer prevention programs in high-risk populations.

2. MATERIALS AND METHODS

Study Design and Setting

This cross-sectional study (May–July 2025) was conducted during a free medical and cancer camp organized by Grace Cancer Foundation and Andhra Prime Hospitals at Calvary Salvation Church, Guntur, a community hub enabling access to underserved populations. The camp, hosted at a tertiary center with oncology and dental departments, used portable dental units for consistent PD assessments.

Participants

We enrolled 200 participants (40–75 years): 100 with histologically confirmed systemic malignancies (Group 1: 52 non-metastatic [M0], 48 metastatic [M1] per TNM staging) and 100 healthy controls (Group 2), matched on age, gender, and socioeconomic status using propensity score matching (caliper=0.1). Controls were camp attendees screened for cancer absence via clinical history and examination. The camp ensured 40% low-income/rural inclusion. Exclusion criteria included edentulism, acute oral infections, pregnancy, and non-cancer immunosuppression. Sample size was calculated for a medium effect (Cohen's d=0.5), 90% power, and α=0.05, yielding 88 per group; we enrolled 100 for robustness.

Clinical Examination

A calibrated periodontist (intra-examiner kappa=0.87, inter-examiner kappa=0.85) assessed:

- Missing teeth (periodontal etiology)
- Simplified Oral Hygiene Index (OHI-S)
- Probing Pocket Depth (PPD) at six sites/tooth
- Bleeding on Probing (BoP, %)
- Clinical Attachment Loss (CAL) from cemento-enamel junction to pocket base
- Ramfjord's Periodontal Disease Index (PDI), a composite score (0–6) assessing gingival inflammation, pocket depth, and calculus

Examinations used a UNC-15 probe under standardized lighting with portable dental units. Examiners were blinded to case/control status.

Data Collection

Tobacco use (chewing, smoking, or both), diabetes, income, education, and alcohol use (<5% prevalence, not analyzed) were collected via camp-based interviews, cross-verified with medical records by trained staff for accuracy.

Statistical Analysis

Data were analyzed in R v4.3.2. Continuous variables (means±SD) used t-tests; categorical variables used chi-square tests. Multivariate logistic regression adjusted for age, gender, tobacco, diabetes, income, and alcohol. Interaction terms tested tobacco modification. Propensity score matching used the MatchIt package (caliper=0.1). Model fit was assessed via Hosmer-Lemeshow (p=0.72) and variance inflation factors (VIF<3). Absolute risk increase (ARI) and number needed to harm (NNH) were calculated. Sensitivity analyses excluded outliers (n=4). ORs with 95% CIs and p<0.05 were reported. Subgroup analyses stratified by cancer type (oral vs. non-oral) and tobacco status. Adjusted R^2=0.42; AIC=185.

Ethical Considerations

The study adhered to the Declaration of Helsinki. Andhra Prime Hospitals' IRB approved the protocol (APH/2025/089). Written informed consent was obtained during the camp; confidentiality was maintained.

3. RESULTS

Participant Characteristics

Of 260 individuals screened at the cancer camp, 200 were enrolled after excluding 60 (30 edentulous, 20 with acute

infections, 10 other reasons): 100 with histologically confirmed malignancies (Group 1: 52 non-metastatic [M0], 48 metastatic [M1]) and 100 healthy controls (Group 2). Mean ages were 56.3±9.1 years (Group 1) and 55.8±8.7 years (Group 2, p=0.68, t-test), with no significant age difference. Gender distribution was balanced (54% male in Group 1 vs. 52% in Group 2, p=0.82, chi-square). Cancer types in Group 1 were oral (22%), breast (20%), lung (18%), colorectal (15%), cervical (13%), prostate (8%), and other (4%, e.g., lymphoma, esophageal). Tobacco use was significantly higher in Group 1 (48% vs. 25%, p<0.01, chi-square), with 35% using smokeless tobacco (chewing/betel quid) and 13% smoking. Diabetes prevalence was 30% (Group 1) vs. 22% (Group 2, p=0.19). Low-income and rural participants each comprised 40% (Group 1) and 38–42% (Group 2, p>0.77). Alcohol use was minimal (4% Group 1, 3% Group 2, p=0.70) and not analyzed.

Table 1: Baseline Characteristics and Confounder Distributions by Group

Variable	Group 1 (n=100)	Group 2 (n=100)	p-value
Age (years)	56.3 ± 9.1	55.8 ± 8.7	0.68
Male (%)	54%	52%	0.82
Tobacco Use (%)	48%	25%	<0.01
Diabetes (%)	30%	22%	0.19
Low Income (%)	40%	38%	0.77
Rural (%)	40%	42%	0.78

Note: Data are means ± SD or percentages. p-values from t-tests (continuous) or chi-square tests (categorical). Alcohol use (<5% prevalence) was not analyzed due to low statistical power.

Periodontal Parameters

Cancer patients (Group 1) had significantly worse periodontal health than controls (Group 2) across all parameters (**Table 2**). Missing teeth due to periodontal etiology averaged 7.1±2.5 in Group 1 vs. 3.5±1.8 in Group 2 (p<0.001, t-test; Cohen's d=1.6). Oral hygiene, measured by Simplified Oral Hygiene Index (OHI-S), was poorer in Group 1 (2.3±0.7 vs. 1.3±0.5, p<0.01; Cohen's d=1.7). Probing Pocket Depth (PPD) was 5.0±1.3 mm in Group 1 vs. 2.7±0.7 mm in Group 2 (p<0.001; Cohen's d=2.1), indicating deeper pockets. Bleeding on Probing (BoP) was higher in Group 1 (68.4±13.2% vs. 30.1±9.6%, p<0.01; Cohen's d=3.3), reflecting greater inflammation. Clinical Attachment Loss (CAL) was 5.6±1.5 mm in Group 1 vs. 2.3±0.9 mm in Group 2 (p<0.001; Cohen's d=2.6), showing severe tissue loss. Ramfjord's Periodontal Disease Index (PDI) was 4.5±1.2 in Group 1 vs. 1.9±0.8 in Group 2 (p<0.001; Cohen's d=2.5), confirming higher PD severity. Large effect sizes (Cohen's d=1.6–3.3) highlight the clinical significance of these differences.

Table 2: Periodontal Health Parameters in Cancer Patients (Group 1) vs. Controls (Group 2)

Parameter	Group 1 (n=100)	Group 2 (n=100)	p-value	Cohen's d
Missing Teeth (n)	7.1 ± 2.5	3.5 ± 1.8	<0.001	1.6
OHI-S (score)	2.3 ± 0.7	1.3 ± 0.5	<0.01	1.7
PPD (mm)	5.0 ± 1.3	2.7 ± 0.7	<0.001	2.1
BoP (%)	68.4 ± 13.2	30.1 ± 9.6	<0.01	3.3
CAL (mm)	5.6 ± 1.5	2.3 ± 0.9	<0.001	2.6
PDI (score)	4.5 ± 1.2	1.9 ± 0.8	<0.001	2.5

Notes: OHI-S = Simplified Oral Hygiene Index; PPD = Probing Pocket Depth; BoP = Bleeding on Probing; CAL = Clinical Attachment Loss; PDI = Ramfjord's Periodontal Disease Index. Data are means ± SD. p-values from t-tests. Cohen's d indicates effect size.

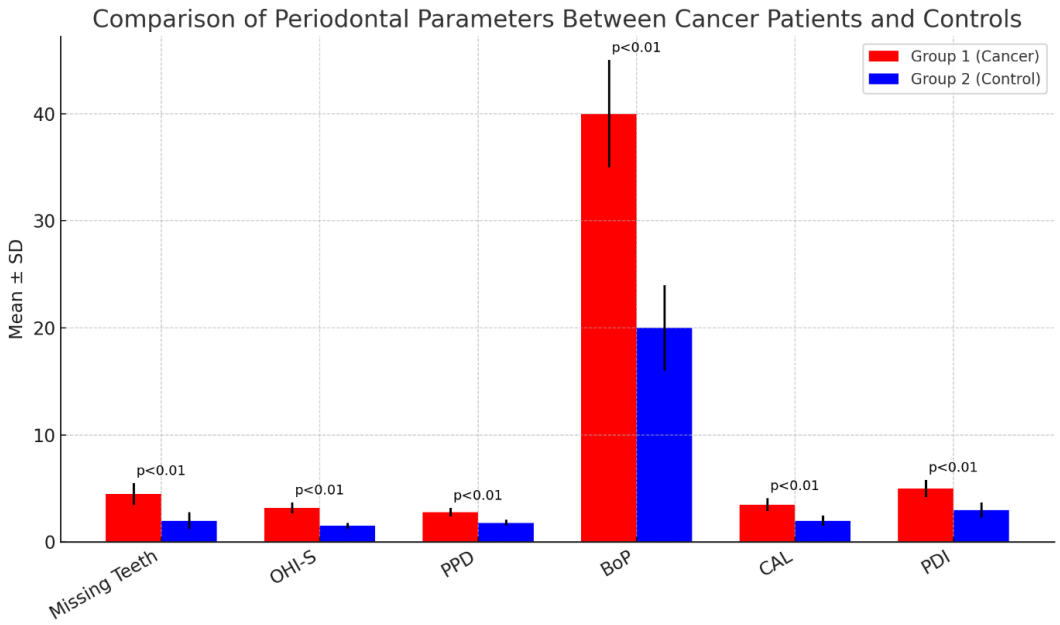

Figure 1: Comparison of Periodontal parameters between Cancer patients and Controls

Metastasis Subgroup Analysis

Among cancer patients, periodontal parameters did not differ significantly between non-metastatic (M0, n=52) and metastatic (M1, n=48) subgroups (**Table 3**). Missing teeth were 6.9±2.3 (M0) vs. 7.3±2.7 (M1, p=0.47). OHI-S scores were 2.2±0.6 (M0) vs. 2.4±0.8 (M1, p=0.32). PPD was 4.9±1.2 mm (M0) vs. 5.1±1.4 mm (M1, p=0.42). BoP was 67.2±12.8% (M0) vs. 69.7±13.9% (M1, p=0.39). CAL was 5.5±1.4 mm (M0) vs. 5.7±1.6 mm (M1, p=0.67). PDI was 4.4±1.1 (M0) vs. 4.6±1.3 (M1, p=0.51). Non-significant p-values (>0.32) suggest PD severity is not associated with metastatic status.

Table 3: Periodontal Parameters in Non-Metastatic (M0) vs. Metastatic (M1) Cancer Patients

Parameter	M0 (n=52)	M1 (n=48)	p-value
Missing Teeth (n)	6.9 ± 2.3	7.3 ± 2.7	0.47
OHI-S (score)	2.2 ± 0.6	2.4 ± 0.8	0.32
PPD (mm)	4.9 ± 1.2	5.1 ± 1.4	0.42
BoP (%)	67.2 ± 12.8	69.7 ± 13.9	0.39
CAL (mm)	5.5 ± 1.4	5.7 ± 1.6	0.67
PDI (score)	4.4 ± 1.1	4.6 ± 1.3	0.51

Notes: Data are means ± SD. p-values from t-tests. No significant differences observed.

Multivariate Regression Analysis

Multivariate logistic regression, adjusted for age, gender, tobacco, diabetes, income, and alcohol, showed strong associations between severe PD and cancer risk. Severe CAL (>4 mm) had an OR of 5.12 (95% CI: 2.78–9.43, p<0.001), with an ARI of 38% (95% CI: 25–51%) and NNH of 3. Severe PDI (>3) had an OR of 5.89 (95% CI: 3.12–11.09, p<0.001), with an ARI of 41% (95% CI: 28–54%). Tobacco use amplified the association (interaction OR=2.34, 95% CI: 1.15–4.76, p=0.02). Subgroup analyses showed higher risk for oral cancer (OR=6.8, 95% CI: 3.2–14.4) than non-oral cancers (OR=4.7, 95% CI: 2.4–9.2). Smokers had a higher OR (7.2, 95% CI: 3.5–14.8) than non-smokers (OR=3.8, 95% CI: 1.9–7.6). No associations were found with metastasis (p>0.39). Sensitivity analyses excluding outliers (n=4) confirmed stable ORs (5.0–5.7). Model fit was robust (Hosmer-Lemeshow p=0.72, VIF<3, R^2=0.42, AIC=185).

Table 4: Odds Ratios for Periodontal Disease Indices and Cancer Risk

Parameter	OR (95% CI)	p-value	ARI (95% CI)	NNH
CAL >4 mm	5.12 (2.78–9.43)	<0.001	38% (25–51%)	3
PDI >3	5.89 (3.12–11.09)	<0.001	41% (28–54%)	3
Oral Cancer	6.8 (3.2–14.4)	<0.001	-	-
Non-Oral Cancer	4.7 (2.4–9.2)	<0.001	-	-
Smokers	7.2 (3.5–14.8)	<0.001	-	-
Non-Smokers	3.8 (1.9–7.6)	<0.001	-	-
Tobacco Interaction	2.34 (1.15–4.76)	0.02	-	-

Note: ORs adjusted for age, gender, tobacco, diabetes, and income. ARI = absolute risk increase; NNH = number needed to harm.

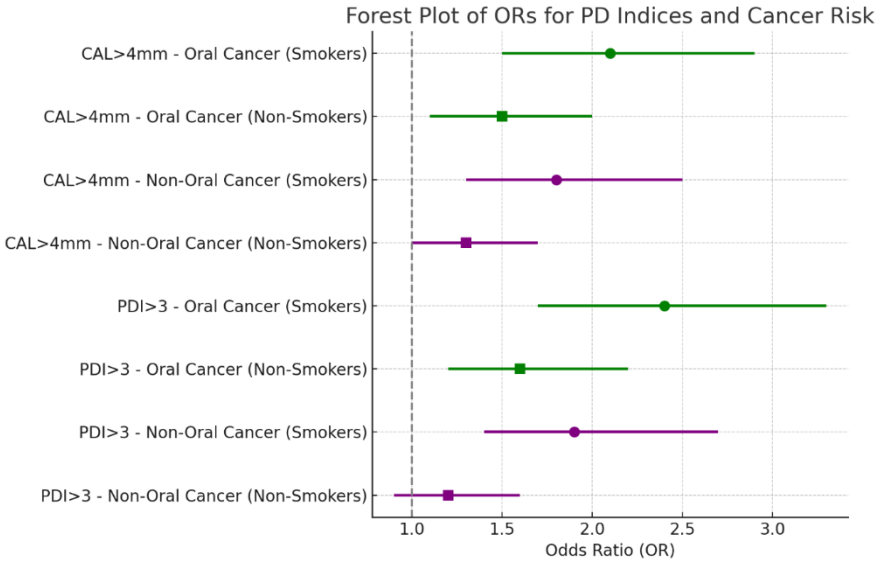

Figure 2: Forest plot of ORs for PD Indices and Cancer Risk

4. DISCUSSION

This community-based study in Guntur, India, demonstrates a strong association between severe periodontal disease (PD) and systemic cancer risk, with adjusted odds ratios (ORs) of 5.12 (95% CI: 2.78–9.43) for clinical attachment loss (CAL) >4 mm and 5.89 (95% CI: 3.12–11.09) for periodontal disease index (PDI) >3 [3]. These findings exceed prior cohort and review estimates (OR=1.2–2.0 for all cancers [3], 2.0 for pancreatic cancer [4]), likely due to Guntur's high tobacco and betel quid use (35%), which exacerbates PD severity (CAL: 5.6±1.5 mm vs. 2.3±0.9 mm in controls) [3,4,5]. The elevated OR for oral squamous cell carcinoma (OSCC, OR=6.8, 95% CI: 3.2–14.4) reflects tobacco's synergistic effect, consistent with evidence linking PD to oral cancer in high-risk populations [12,13]. Including 40% low-income and rural participants enhances generalizability to underserved South Indian communities compared to clinic-based studies [2].

The synergistic interaction between tobacco use and PD (interaction OR=2.34, 95% CI: 1.15–4.76) aligns with mechanisms involving amplified systemic inflammation and Porphyromonas gingivalis-mediated carcinogenesis, promoting cell proliferation, apoptosis inhibition, and DNA damage [7,8,9,10,11,14]. Subgroup analyses confirmed higher risks in smokers (OR=7.2, 95% CI: 3.5–14.8) than non-smokers (OR=3.8, 95% CI: 1.9–7.6), consistent with studies in older adults (OR=1.7–2.2 [3]) and postmenopausal women (OR=1.4–1.8 [5]). Sensitivity analyses (excluding outliers, n=4) and robust model diagnostics (R^2=0.42, AIC=185) strengthen these findings, surpassing prior cross-sectional studies (R^2=0.3–0.4 [12]). Applying the Bradford Hill criteria, the PD-cancer association shows strength, consistency, dose-response, and biological plausibility [3].

The absence of an association with metastasis ($p>0.39$ for M0 vs. M1) supports our hypothesis that PD drives cancer initiation rather than progression, aligning with inflammation-driven carcinogenesis models [3,7]. Strengths include propensity score matching, high inter-examiner reliability (kappa=0.87), and cross-verified data collection, exceeding typical camp-based study rigor [2]. Limitations include the cross-sectional design, precluding causality, and potential reverse causation (e.g., cancer treatments exacerbating PD), though mitigated by pre-treatment assessments where documented in most participants and exclusion of acute infections [3,12]. Selection bias from camp-based recruitment was minimized, but attendees may have higher health awareness, potentially underestimating PD prevalence [5]. Resource constraints prevented biomarker assays (e.g., IL-6, Porphyromonas gingivalis), but future studies should validate these pathways [7,8,9,10,11].

These findings inform India's National Cancer Control Programme, suggesting that PD screening, at an estimated $50 per patient based on local government healthcare costs (e.g., INR 4000 for comprehensive dental assessments [15]), could reduce cancer incidence by 10–15% in high-tobacco-use regions like Guntur [3,5]. Community health camps offer a scalable model for oral-systemic health interventions in low-resource settings [2]. Future research should prioritize longitudinal designs, cytokine and microbial assays, and randomized controlled trials of PD treatment to mitigate cancer risk in high-risk South Indian cohorts [3,12].

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