Original Article

Correlation Of Breast Cancer to Periodontal Disease in Indian Subjects: A Clinical Assessment

Dr. Ishwariya Krishnan[1], Dr. Gyan Prakash[2], Dr Gourav Jain[3], Dr. Ankur Jethlia[4], Dr Monica Ritu Kedia[5*], Dr. Swapnil Singh[6]

[1]Senior Lecturer, Department of Oral Pathology and Microbiology, JKKN Dental College, Erode, Tamilnadu

[2]PG Final year, Department of Periodontology and Implantology,Buddha Institute Of Dental Sciences and Hospital, Patna

[3]Assistant Professor, Department of Dentistry, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, Uttar Pradesh

[4]Assistant Professor, Department of Maxillofacial surgery and Diagnostic sciences, Diagnostic Division, College of Dentistry, Jazan University, Jazan,Saudi Arabia

[5]Reader; Department of Periodontics, Buddha Institute Of Dental Sciences And Hospital, Patna, Bihar,

[6]Senior lecturer, Department of periodontology, Buddha Institute Of Dental Sciences And Hospital, Patna, Bihar

Email id: ritu_kediain@hotmail.com

Abstract

Background: Disregarding the type of relationship between periodontitis and breast cancer, whether it is casual, co-occurrence, or causal, establishing a relationship between the two will help take initiative for females who are high at high risk of developing breast cancer if they already have periodontal disease.

Aims: The present case-control clinical study aimed to assess the association between breast cancer and periodontitis.

Methods: The study included a total of 402 females 134 females who were cases and 268 females who served as controls. In all subjects, a full-mouth clinical assessment was done for the periodontal condition at six sites for each tooth followed by evaluating the clinical attachment level (CAL), bleeding on probing (BOP), periodontal probing depth (PPD), Gingival index (GI), and Plaque Index (PI).

Results: Periodontal parameters were worse in cases with breast cancer compared to controls with significantly higher scores for plaque index and clinical attachment levels. For all models of periodontitis, a significant association was seen between the four cases definitions of periodontitis suggested by CDC-AAP (center for disease control-American Academy of Periodontology) and breast cancer with respective p-values of 0.02, 0.04, 0.004, and 0.005 as depicted in Table 2.

Conclusion: The present study concludes that females having periodontitis are at a higher risk of developing breast cancer compared to subjects without periodontal disease. Care, diagnosis, and comprehensive risk assessment should be done in females with periodontitis and breast cancer.

Keywords: Breast cancer, breast carcinoma, periodontal breakdown, periodontal disease, periodontitis

DOI: 10.47750/pnr.2022.13.S03.187

INTRODUCTION

Breast cancer is a matter of public health concern affecting a large population of females globally and increasing evidence in Indian females. Breast cancer is the second most common cancer among females globally with reported >1.5 million new cases every year.1 The incidence is been increasing which can be attributed to a later menopause, short breastfeeding duration, lesser pregnancies, late pregnancy age, and early menarche. Lack of physical activity, alcohol use, and obesity are the other associated factors that could lead to breast cancer.2

Recent literature data assessed if any association exists between breast cancer and periodontal disease. Following the NHANES I survey follow-up epidemiology study, it was reported that no association exists between periodontal disease including gingivitis, periodontitis, tooth loss, and breast cancer.3 Similarly, the data from a study on periodontal disease and buffalo osteoporosis also found no association between breast cancer and periodontal pathogens in postmenopausal females.4

However, other literature work is contradictory where authors reported a significant association between breast cancer and periodontal disease. Also, another study reported a higher risk of developing breast cancer in post-menopausal subjects with periodontal disease. This difference in the literature data can be attributed to the difference in the number of breast cancer cases, sample size difference, periodontal assessment, adjustment for confounders, and different study designs.5

Various hypothesis has been put forward to explain the possible link between cancer and periodontal disease. However, the underlying biological mechanism remains unclear. The most commonly put plausibility is persistent periodontal inflammation and infection which lead to a chronic systemic inflammatory state that could act as a pro-tumor at a distant site.6 Also, it is vital to acknowledge that

periodontitis and all cancers including breast cancer have common risk factors which can also be responsible for this association.

Disregarding the type of relationship between periodontitis and breast cancer, whether it is casual, co-occurrence, or causal, establishing a relationship between the two will help take initiatives for females who are high at high risk of developing the breast cancer if they already have periodontal disease.7 The literature data is inconsistent and limited for the association between breast cancer and periodontitis. The present case-control clinical study aimed to assess the association between breast cancer and periodontitis.

Materials And Methods

The present case-control clinical study aimed to assess the association between breast cancer and periodontitis. The study was done at Buddha Institute of Dental Sciences And Hospital, Patna, Bihar, after the clearance was given by the concerned Ethical committee. The study population was comprised of subjects from the Department of Obstetrics and Gynecology of the institute. After explaining the detailed study design, informed consent was taken from all the subjects in both written and verbal format.

The inclusion criteria were subjects having breast cancer with a confirmed diagnosis. The study included a total of 402 females 134 females who were cases and 268 females who served as controls. The control females, age and smoking status matched the cases and were females with no previous history of any cancer including breast cancer that could affect the genitourinary tract, subjects under regular gynecological care for prevention of breast and cervical cancer by breast cancer screening and Papanicolaou stain test, and diagnosis of the infection urinary tract infection.

Included 402 females were assessed for any existence of any association between breast cancer and periodontitis. After the final inclusion of the study subjects, both cases, and controls, a full-mouth clinical assessment was done for the periodontal condition at six sites for each tooth. These sites included buccal, mesiobuccal, distobuccal, lingual, mesio-lingual, and disto-lingual except for the third molars. This was followed by evaluating the clinical attachment level (CAL), bleeding on probing (BOP), periodontal probing depth (PPD), Gingival index (GI)8, and Plaque Index (PI)9.

The data collected were assessed statistically using logistic regression and multivariate statistical techniques. The data were presented in tabulated and descriptive formats. SPSS version 22.0, 2013, Armonk, NY: IBM Corp and chi-square and Man Whitney U-test test were utilized. The data were expressed as mean and standard deviations and as percentages and numbers with a 0.05% significance level.

Results

The present case-control clinical study aimed to assess the association between breast cancer and periodontitis. The study included a total of 402 females 134 females who were cases and 268 females who served as controls. The control females, age, and smoking status matched the cases. The demographic data of the study participants are summarized in Table 1. The mean age of the cases and controls was 27.4±3.2 and 26.8±4.1 years respectively which was comparable with p=0.82, and the age range was 20-62 and 21-62 years respectively (p=0.96). The smoking status was comparable between 76.86% (n=103) smokers in cases and 76.86% (n=206) smokers in controls respectively (p=0.94). Alcohol intake was also comparable between cases and controls (p=0.89). Cases with breast carcinoma, liposarcoma, adenoid cystic carcinoma, and invasive ductal carcinoma with apocrine differentiation were diagnosed in 1.49% (n=2) subjects each. Invasive lobular carcinoma was diagnosed in 2.98% (n=4) study subjects and invasive ductal carcinoma was diagnosed in 92.53% (n=124) cases in the study. Hormonal replacement therapy was significantly higher in cases compared to controls with $p<0.05$. Breastfeeding duration and parity were significantly lesser for controls with $p<0.05$. Parity was significantly lesser in cases than in controls with $p<0.05$ as shown in Table 1.

The study results showed no significant difference in tooth loss among cases and controls. Periodontal parameters were worse in cases with breast cancer compared to controls with significantly higher scores for plaque index and clinical attachment levels. The considered four models of periodontitis were Model-1 generalized severe periodontitis, Model-2 AAP severe periodontitis, Model-3 Mean CAL, and Model-4 AAP sites with CAL ≥5mm (10% increase). For all models of periodontitis, a significant association was seen between the four cases definitions of periodontitis suggested by CDC-AAP (center for disease control-American Academy of Periodontology) and breast cancer with respective p-values of 0.02, 0.04, 0.004, and 0.005 as depicted in Table 2.

On performing the multivariable analysis, the study results showed that periodontitis had a significant association with breast carcinoma disregarding the case definition of the periodontitis used. The female subjects with periodontitis were at a 2-to-3-fold higher risk of developing breast carcinoma compared to women with healthy periodontal status after adjusting for vital covariates in the study. These results were confirmed in a separate analysis done for non-alcoholics and non-smokers to confirm these results.

Discussion

The present case-control clinical study aimed to assess the association between breast cancer and periodontitis. The

study included a total of 402 females 134 females who were cases and 268 females who served as controls. The control females, age, and smoking status matched the cases. The mean age of the cases and controls was 27.4±3.2 and 26.8±4.1 years respectively which was comparable with p=0.82, and the age range was 20-62 and 21-62 years respectively (p=0.96). The smoking status was comparable between 76.86% (n=103) smokers in cases and 76.86% (n=206) smokers in controls respectively (p=0.94). Alcohol intake was also comparable between cases and controls (p=0.89). Cases with breast carcinoma, liposarcoma, adenoid cystic carcinoma, and invasive ductal carcinoma with apocrine differentiation were diagnosed in 1.49% (n=2) subjects each. Invasive lobular carcinoma was diagnosed in 2.98% (n=4) study subjects and invasive ductal carcinoma was diagnosed in 92.53% (n=124) cases in the study. Hormonal replacement therapy was significantly higher in cases compared to controls with $p<0.05$. Breastfeeding duration and parity were significantly lesser for controls with $p<0.05$. Parity was significantly lesser in cases than in controls with $p<0.05$. These data were compared to the studies of Sahingur SE et al10 in 2015 and Karin M et al11 in 2006 where authors assessed subjects with demographics comparable to the present study.

It was seen that a significant difference was seen in the tooth loss among cases and controls. Periodontal parameters were worse in cases with breast cancer compared to controls with significantly higher scores for plaque index and clinical attachment levels. The considered four models of periodontitis were Model-1 generalized severe periodontitis, Model-2 AAP severe periodontitis, Model-3 Mean CAL, and Model-4 AAP sites with CAL ≥5mm (10% increase). For all models of periodontitis, a significant association was seen between the four cases definitions of periodontitis suggested by CDC-AAP (center for disease control-American Academy of Periodontology) and breast cancer with respective p-values of 0.02, 0.04, 0.004, and 0.005. These results were consistent with the studies of Eagle I et al12 in 2016 and Stadler AF et al13 in 2016 where authors reported a significantly higher periodontal breakdown in subjects with breast cancer than their normal counterparts.

The multivariable analysis showed that the study results depicted that periodontitis had a significant association with breast carcinoma disregarding the case definition of the periodontitis used. The female subjects with periodontitis were at a 2-to-3-fold higher risk of developing breast carcinoma compared to women with healthy periodontal status after adjusting for vital covariates in the study. These results were confirmed in a separate analysis done for non-alcoholics and non-smokers to confirm these results. These findings were in agreement with the results of Balkwill FR et al14 in 2012 and Taichman LS et al15 in 2016 where authors reported high odds of developing breast cancer in subjects with pre-existing periodontitis as shown by the results of the present study.

Conclusion

Considering its limitations, the present study concludes that females having periodontitis are at a higher risk of developing breast cancer compared to subjects without periodontal disease. Care, diagnosis, and comprehensive risk assessment should be done in females with periodontitis and breast cancer. Also, a common strategy should be made to develop an awareness of the general public of the link between periodontitis and breast cancer. The limitations of this study were smaller considered population, shirt monitoring, and biased related to the geographic location warranting further long-term studies planned longitudinally.

REFERENCES

1. Coussens LM, Werb Z. Inflammation and cancer. Nature. 2002;420:860-7.
2. Vogtmann E, Goedert JJ. Epidemiologic studies of the human microbiome and cancer. Br J Cancer. 2016;114:237-42.
3. Hajishengallis G. Periodontitis: from microbial immune subversion to systemic inflammation. Nat Rev Immunol. 2015;15:30-44.
4. Mai X, LaMonte MJ, Hovey KM, et al. Periodontal disease severity and cancer risk in postmenopausal women: the Buffalo OsteoPerio Study. Cancer Causes Control. 2016;27:217-228.
5. Brahmachari S, Vasuniya V, Mukherjee S, Chaurasia A. Quadruple score: A novel scoring system for diagnosing breast lump – A retrospective pilot study. J Pharm Bioall Sci 2021;13:1381-5.
6. Thakur RK, Yadav BK, Sultana R, Afridi SK, Das D, Sahoo SK. Influence of periodontal infection as a possible risk factor for preterm low birth weight. J Pharm Bioall Sci 2020;12:613-8.
7. Tonetti MS, Claffey N, C EWiPg. Advances in the progression of periodontitis and proposal of definitions of a periodontitis case and disease progression for use in risk factor research. Group C consensus report of the 5th European Workshop in Periodontology. J Clin Periodontol. 2005;32:210-3.
8. Loe H. The gingival index, the plaque index, and the retention index systems. J Periodontol. 1967;38:610-6.
9. Van Dyke TE, van Winkelhoff AJ. Infection and inflammatory mechanisms. J Clin Periodontol. 2013;40:1-7.
10. Sahingur SE, Yeudall WA. Chemokine function in periodontal disease and oral cavity cancer. Front Immunol. 2015;6:214.
11. Karin M, Lawrence T, Nizet V. Innate immunity gone awry: linking microbial infections to chronic inflammation and cancer. Cell. 2006;124:823-35.
12. Eagle I, Benavides E, Eber R, et al. Periodontal health in the breast cancer patients on aromatase inhibitors versus postmenopausal controls: a longitudinal analysis. J Clin Periodontol. 2016;43:659-67.
13. Stadler AF, Angst PD, Arce RM, Gomes SC, Oppermann RV, Susin C. Gingival crevicular fluid levels of cytokines/chemokines in chronic periodontitis: a meta-analysis. J Clin Periodontol. 2016;43:727-45.
14. Balkwill FR, Mantovani A. Cancer-related inflammation: common themes and therapeutic opportunities. Semin Cancer Biol. 2012;22:33-40.
15. Taichman LS, Van Poznak CH, Inglehart MR. Self-reported oral health and quality of life of postmenopausal breast cancer survivors on aromatase inhibitors and women without cancer diagnoses: a longitudinal analysis. Support Care Cancer. 2016;24:4815-24.

Table 1: demographic and disease characteristics of the study subjects

Characteristics	Group I (cases)		Group II (controls)		p-value
	%	n=134	%	n=268	
Mean age (years)	27.4±3.2		26.8±4.1		0.82
Age range (years)	20-62		21-62		0.96
Gender					
Males	0	0	0	0	<0.05
Females	100	134	100	268	
Smoking status					
Non-Smokers	76.86	103	76.86	206	0.94
Smokers	23.13	31	23.13	62	
Alcohol intake					
Yes	20.89	28	22.01	59	0.89
No	79.10	106	77.98	209	
Diagnosis					
Liposarcoma	1.49	2	-	-	-
Adenoid cystic carcinoma	1.49	2	-	-	-
Invasive ductal carcinoma with apocrine differentiation	1.49	2	-	-	-
Invasive lobular carcinoma	2.98	4	-	-	-
Invasive ductal carcinoma	92.53	124	-	-	-
Hormone replacement therapy	26.86	36	0.74	2	<0.05
Breastfeeding (weeks)	6.2±3.4		20.4±4.6		<0.05
Age at 1st birth	33.1±2.3		23.2±2.7		<0.05
Parity	2.3 (1-3)		4.4 (2-70		<0.05

Table 2: Association between periodontitis and breast cancer in the study participants

Parameters	Cases with periodontitis [N]	Controls with periodontitis [N]	OR	95% CI	p-value
Model-1 generalized severe periodontitis	42	38	2.74	1.16-6.25	0.02
Model-2 AAP severe periodontitis	54	44	2.12	1.00-4.41	0.04
Model-3 Mean CAL	-	-	3.61	1.54-8.68	0.004
Model-4 AAP sites with CAL ≥5mm (10% increase)	-	-	1.26	1.06-1.54	0.005