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ORIGINAL ARTICLE

Is Oral Bacterial Flora with Dental Disease a Risk Factor for Recurrence of Peptic Ulcer Disease? A Retrospective Study on 644 Patients

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ABSTRACT

Background: From last few years, peptic ulcer disease (PUD) had a significant role in morbidity and mortality. *Helicobacter pylori* infections of the stomach are common worldwide. In the presence of dental diseases, oral bacterial flora usually contains relevant bacteria.

Aims and objectives: The aim of this study was to verify the effect of oral bacterial flora associated with dental disease on the recurrence of PUD.

Materials and methods: A retrospective cohort study was conducted on 644 patients who were admitted and diagnosed with PUD in the rural medical institute in Udaipur city, Rajasthan, India. Patients' oral bacterial flora with dental disease assisted by gastroscopic test findings were recorded before and after the exposure period. Patients were divided into two groups as exposed group (patient with one of the dental diseases in oral cavity) and nonexposed group (patient without one of the dental diseases in oral cavity). There was a follow-up of 6 months in order to evaluate recurrence of PUD. The recurrence of PUD was considered as the outcome of the study, and effect of oral bacterial flora with dental disease on the recurrence of PUD was investigated according to a logistic regression model.

Results: Out of the total, 644 patients fulfilled the inclusion criteria and all patients have history of PUD. The 6-month follow-up results were the oral bacterial flora with dental disease, a 1.54 times the odds of the PUD recurrence with existing systemic factors [p = 0.128; 95% confidence interval (CI) for odds ratio (OR) ranged from 0.88 to 2.68], whereas it was 1.95 times the odd of PUD recurrence without existing systemic factors (p = 0.010; 95% CI for OR ranged from 1.17 to 3.23) for exposed and nonexposed group, in which statistically significant difference was seen.

Conclusion: Within the limitations of the study, it can be concluded that there is an evident association between the oral bacteria flora with dental disease and PUD recurrence, but further prospective studies with large sample size will be useful in confirming the findings.

Keywords: Cohort study, Dental disease, *Helicobacter pylori*, Oral bacterial flora, Peptic ulcer disease, *Streptococcus*.

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BACKGROUND

Following the last decades of the 20th century, PUD has demonstrated a noticeable contribution toward morbidity and mortality.[1] Peptic ulcer disease has a common occurrence in the stomach and proximal duodenum with predisposing factors, such as *H. pylori* infection, and nonsteroidal anti-inflammatory drugs like aspirin, acetaminophen, ibuprofen, and many more are commonly used in control of dental pain because of their analgesic and anti-inflammatory actions.[2] *Helicobacter pylori* mainly damages gastric epithelium which leads to gastric inflammation.[3,4] The main risk factor for PUD is tobacco smoking, use of minor tranquilizers, and intake of alcohol.[4-6] Recently, specific bacterial species in the oral cavity have been found in several systemic diseases like aspirational pneumonia, cardiovascular diseases, osteomyelitis in children, and bacterial endocarditis.[7-9] There are more than 700 species of bacteria that have been detected in different sites of the oral cavity. Some authors[10] have suggested that *H. pylori* that is primarily responsible for PUD may belong to the normal oral flora of the human oral cavity, maintaining a commensal relation with the host, but present in very low numbers such that reliable identification is difficult. Others[11] have suggested that *H. pylori* is not consistently present in dental plaque and, when present, may be the result of occasional gastroesophageal reflux.

The purpose of this study was to test the hypothesis that oral bacterial flora with dental disease, which was considered in the study as a bacterial presence (especially *Streptococcus* genera), plays an important role in the recurrence of PUD.

MATERIALS AND METHODS

Study Design

The present study was designed as a retrospective cohort study, mainly highlighting the effect of oral bacterial flora with dental disease on the recurrence of PUD. This report was conducted according to STROBE (Strengthening the Reporting of Observational studies in Epidemiology) Statement.[12]

Ethical Clearance, Official Permission, and Informed Consent

Study protocol was obtained from the Ethical Committee of Pacific Dental College & Hospital, Udaipur, Rajasthan, India. Official permission was obtained from the Pacific Institute of Medical Sciences, Umarda, Udaipur. Informed consent was taken from the included patients in the study who were willing to participate.

Participants

The study was started with the sorting of the data from the patients undergoing treatment in our rural medical institute (Pacific Institute of Medical Sciences), Udaipur city, Rajasthan, India. All the patients suffering from PUD who were admitted and continuing the treatment between December 2015 and December 2016 were first considered the eligible population. A 6-month follow-up was considered for all patients and follow-up visit were scheduled between December 2015 and December 2016. The data were collected and analyzed between January 2016 and February 2017 in different visits.

In regular practice, the patient with PUD is usually evaluated for different findings before the treatment and no treatment or surgery was rendered if systemic findings were not under control. The most common systemic risk factors like smoking habits, use of minor tranquilizers, and alcohol habits that existed in patients were included in the study. Hence, the oral bacterial flora with dental disease was the only hypothetical risk factor exposed during the follow-up period, which could affect the outcome of the results.

Within the population of eligible patients, only those who had medical history of PUD, gastroscopic test findings, and other reports available were selected. The excluded patients were those who were not undergoing treatment or noncompliant with the follow-up program.

Variable and Data Sources

The data about oral bacterial flora with dental disease, tobacco smoking, use of minor tranquilizers, and use of alcohol were collected from the patient's record. The first factor considered as exposure in the study was the oral bacterial flora with dental disease and the last three considered as effect analyzers, which were associated systemic risk factors for which, so far, an evident association with PUD has been demonstrated.

The oral bacterial flora without any dental disease or bacterial infection present was considered to be normal. The gastroscopic test findings with oral bacteria presence were considered to be recurrence of PUD. A 6-month follow-up was considered for all included patients in the study. The outcome taken into consideration was the recurrence of PUD. All findings and outcome events were finally registered in a patient's file and in a special register. The patient's file and the special register were then matched in order to cross-check the recurrence events.

Statistical Methods

The univariate effect of oral bacterial flora with dental disease on the recurrence of PUD was investigated via a logistic regression model, and the OR and related 95% CI based on robust standard error were calculated. Wald's chi-square test was applied for evaluation of factor significance and the analysis was performed at the patient level only. Then data were statistically significant only if $p < 0.05$. Independent variable oral bacterial flora with dental disease as exposure was categorized either "0" exposed group or "1" nonexposed group in the analysis. Tobacco smoking, use of minor tranquilizers, and use of alcohol were initially analyzed and were found that they did not significantly affect or modify the PUD events. And for the complete analysis, every model was repeated with and without these systemic risk factors. Logistic regression model was performed with Statistical Package for the Social Sciences software (version 20.0 SPSS Inc. Chicago, Illinois, USA).

RESULTS

Out of 673 patients, 645 were eligible for the study, 28 were excluded because their original scanned reports were not available and one patient died during further treatment due to the severity of the disease. Hence, total 644 patients were included in the study. All patients were observed for 6-month follow-up for evaluation of recurrence events and all 644 patient's data were analyzed. Of these 644, 43.79% were men and 56.21% women. When these populations first visited the institute, their average age was 56.9 [standard deviation (SD) 11.6 and range

between 20 and 82]. Out of 644 patients, 388 (60.25%) were exposed to bacterial flora with dental diseases, 162 (25.16%) were tobacco smokers, 22 (3.42%) were users of minor tranquilizers, and 132 (20.50%) were alcohol consumers (Table 1).

Within the patients of exposed group, PUD was observed in 42 out of 388 and 25 out of 256 were seen in the nonexposed group, which means a cumulative 6-month follow-up recurrent rate was 10.82 and 9.77% respectively, at the patient level along with effect modifiers. Hence, no statistically significant ($p > 0.10$) recurrence of PUD was seen in exposed and nonexposed groups (Table 2).

Logistic regression model with systemic risk factors (tobacco smoking, use of minor tranquilizers, and use of alcohol) did not highlight any statistical significance on recurrence of PUD ($p > 0.1$) (Table 2).

The oral bacterial flora with dental disease effect rate was not statistically significant in exposed and nonexposed groups: a 1.54 greater odds of PUD recurrence ($p > 0.1$; 95% CI for OR ranged from 0.88 to 2.68, Table 2). In smokers, users of minor tranquilizers, and alcoholics, no statistical significance was found, so they did not alter the risk of recurrence PUD (OR = 1.54, $p = 0.128$; OR = 0.96, $p = 0.907$; and OR = 1.33, $p = 0.781$ respectively; Table 3).

After repeating the analysis without systemic risk factors, the recurrence effect of PUD was similar; in fact, the relationship between oral bacterial flora with dental disease in exposed and nonexposed groups on recurrence of PUD was statistically significant ($p < 0.1$, Table 4).

The oral bacterial flora with dental disease effect rate was statistically significant in exposed and nonexposed groups with a 1.95 greater odds of PUD recurrence ($p = 0.010$, 95% CI for OR ranged from 1.17 to 3.23; Table 4). Thus, the effect of oral bacterial flora with dental disease even without the modifiers remained the same in both groups on recurrence of PUD.

DISCUSSION

To our knowledge, this is the first study in literature that evaluates the effect of the oral bacterial flora with dental disease on the recurrence of PUD as a retrospective cohort study. The analysis highlighted a significant tendency for oral bacterial flora with dental disease patients to have PUD recurrence (Table 2, model with effect modifiers and Table 4, model without effect modifiers). In studies, the oral bacterial flora with dental disease can be directly or indirectly related to infecting gastric flora which ultimately increases the peptic ulcer incidence in the stomach which was in conjunction with the results of our study that demonstrated a similar relationship between oral bacterial flora with dental diseases and PUD.[13,14]

Table 1: Comparison of demographic and clinical features of the two cohorts

Oral bacteria flora with dental diseases	*Exposed group*	*Nonexposed group*	*Total*
Number of patients	388	256	644
Age (SD)	53.6 (12.9)	59.1 (10.1)	56.9 (11.6)
Male:female ratio	174:214	108:148	282:362
Smokers	84	78	162
Users of minor tranquilizers	12	10	22
Alcoholics	76	56	132
Total effect modifiers	172	144	316
Total without effect modifiers	216	112	328

Note: Effect modifiers—smokers, users of minor tranquilizers, and alcoholic

Table 2: Effect of oral bacterial flora with dental diseases on recurrence of PUD (logistic regression model with effect modifiers)

	Seen/absent in exposed group	*Seen/absent in nonexposed group*	*OR*	*95% CI*	*p-value*
PUD recurrence	42/130 = 0.3	25/119 = 0.21	1.54	0.88–2.68	0.128

p-value: level of significance

Table 3: Effect of systemic factors on recurrence of PUD (logistic regression model with effect modifiers)

	OR	*95% CI*	*p-value*
Oral bacterial flora with dental diseases	1.54	0.88–2.68	0.128
Smokers	0.96	0.52–1.79	0.907
Users of minor tranquilizers	1.33	0.18–10.12	0.781
Alcoholics	0.99	0.49–1.99	0.974

p-value: level of significance

Table 4: Effect of oral bacterial flora with dental disease on recurrence of PUD (logistic regression model without effect modifiers)

	Seen/absent in exposed group	*Seen/absent in nonexposed group*	*OR*	*95% CI*	*p-value*
PUD recurrence	85/131	27/85	1.95	1.17–3.23	0.010*

*Statistically significant difference; p-value: level of significance

Because of the retrospective design of the study, the cohort study approach for this might appear questionable since observational studies like cohort and case–control studies are used to verify the hypothesis and the cohort studies select individuals based on exposure conditions, and in most of the cases, they are prospective. Nevertheless, any cohort studies can be retrospective, when exposure measurements are taken into consideration before the onset of disease. In the present study, all the exposures to the systemic disease-related data, whether it is oral bacterial flora with dental disease or effect modifiers (systemic risk factors), were acquired and filed before the further treatment or surgery.

In our analysis, all the systemic risk factors that had been demonstrated to be related to the recurrence of PUD were considered as effect modifiers. No patients in critical state were included because such patients are not considered suitable for further treatment or surgery before appropriate control on disease has been obtained; some other uncommon factors, such as diabetes, hypertension, and human immunodeficiency virus infection were not considered, and no patients affected by them were present in both cohorts in the study.

As the limitation of the study, the evaluation of oral bacterial flora with dental diseases only considers the presence of bacteria (especially *Streptococcus* genera) in gastric flora in results of gastroscopic tests. The different bacteria with actual factor associated with oral bacterial flora with dental diseases were not considered due to the lack of data on it. It is also important that the presence of bacteria (especially *Streptococcus* genera) in gastric flora in gastroscopic test is a good indicator of PUD in the stomach. In fact, this study shows same relationship between exposure and diseases as speculated in past studies.[15-17]

In summary, in this retrospective cohort study, we found a significant association between oral bacterial flora with dental diseases and recurrence of PUD. Despite the limitations of the study, it can be suggested that evaluation of oral bacterial flora with dental diseases could be advisable before relevant PUD treatment procedures are performed.

CONCLUSION

Within the limitations of the study, it can be concluded that there is an evident association between the oral bacteria flora with dental disease and the PUD recurrence, but further prospective studies with large sample size will be useful in confirming the findings.

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