

## A Study to Evaluate the Association between Dental Procedures and the Acquisition of Infective Endocarditis

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### Abstract

**Aim:** The aim of the present study was to evaluate the association between dental procedures and the acquisition of infective endocarditis.

**Material & Methods:** A retrospective study was conducted in the Department of Dentistry, RDJMMCH, TURKI, Muzaffarpur, Bihar, India for 24 month to compare the odds of exposure to dental procedures within 3 months preceding hospitalization with that during matched control periods when no infective endocarditis developed. 200 patients were included in the study.

**Results:** The mean age was 56.0 (18.6) years; 40% of patients were 65 years and older. Men accounted for 65% of all patients. In terms of co-morbidities, hypertension was the most common followed by diabetes and ischemic heart disease. Out of 200 patients, 43 patients were exposed to infective endocarditis.

**Conclusion:** In conclusion, using a case-crossover design, this population-based study found that dental procedures are not significantly associated with the risk of IE.

**Keywords:** Infective Endocarditis, Dental Procedures.

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### Introduction

Infective endocarditis (IE) is a rare but life-threatening disease. It is an infection of the endocardial surface of the heart, which may involve  $\geq 1$  heart valves can result from bloodstream infection caused by a spectrum of bacterial and fungal organisms entering the circulation. If patients with IE do not receive appropriate treatment, they may develop serious complications or die. The annual incidence of IE is  $\approx 3$  to 9 cases per 100000 persons in industrialized countries, with the mean age varying between 36 and 69 years, and the incidence is higher in men than in women. [1,2] Mitral valve prolapse, congenital heart disease, rheumatic heart disease, previous IE, and previous cardiac valve surgery are risk factors for IE. [3]

IE is an uncommon but potentially devastating disease, with an estimated annual incidence ranging from 2 to 7.9 per 100,000 individuals per year. [4,5] and a short-term mortality of 10% to 30%. [6] Through the breakdown of mucocutaneous barriers and induction of bacteraemia, dental therapy and other invasive procedures have been linked to seeding of heart valves and the development of IE. [7,8,9] The possibility that some cases of IE might be linked to invasive dental procedures (IDPs) was first suggested by Lewis and Grant in 1923 [10] and

supported in 1935 by Okell and Elliott, [11] who demonstrated that 61% of individuals develop a transient bacteraemia with oral viridians group streptococci (OVGS) following a dental extraction and that OVGS could be isolated from the heart valve vegetations of 40–45% of individuals with IE. However, the evidence supporting the effectiveness of antibiotic prophylaxis was poor, deriving solely from animal studies, case series, and assessments of bacteraemia risk. [3,12,13] Notably, the AHA guidelines in 1997 did acknowledge that most IE cases are not attributable to resulting from certain invasive procedures, but rather random bacteraemia from routine daily activities such as tooth brushing or chewing, and thus suggesting that prophylaxis may only prevent a small number of cases of IE. [14]

Invasive dental treatments (IDTs) have been considered a potential risk factor of IE; however, the association between IDTs and IE remains controversial. Dental treatments were considered IDTs when the treatments might cause bleeding and introduce oral bacteria into the bloodstream, such as dental cleaning, scaling and root planning, extraction, odontotomy, and periodontal surgery. IDTs can yield temporary bacteraemia that may attach to abnormal heart valves or damaged heart

tissue, giving rise to IE. Few epidemiological studies have been carried out in this area. [12, 15,16] In these studies, however, IE risk associated with different types of dental procedures was estimated based on small sample sizes.

The aim of the present study was to evaluate the association between dental procedures and the acquisition of infective endocarditis.

### Materials & Methods

A retrospective study was conducted in the Department of Dentistry, RDJMMCH, Turki, Muzaffarpur, Bihar, India for 24 months to compare the odds of exposure to dental procedures within 3 months preceding hospitalization with that during matched control periods when no infective endocarditis developed. 200 patients were included in the study.

This self-matching design thus avoids the control selection bias and the confounding by measured and unmeasured risk factors that are time invariant within subjects but differ between subjects.

The date of hospital admission served as the index date. Patients were excluded if they were less than 18 years old at the time of hospitalization. To ensure a 2-year claims history, we excluded patients who did not enrol in NHI 2 years before their index date.

### Case and Control Periods

For each patient, we defined a period of 12 weeks preceding the index date as the case period A. This prehospitalization "at risk" period of 12 weeks had been a time interval frequently used in the literature [18,19] although the incubation period between bacteraemia and the onset of symptoms of IE was estimated to be 7 to 14 days. [10,18] The rationale for using this time frame was to take into account the prolonged duration of symptoms. In a previous study, the mean duration of symptoms in patients with IE was 49.6 days, and only 24.7% of patients were hospitalized within 10 days of symptom onset. [23] We defined a second 12-week period starting from days 85 before the index date as the case period B, which was used for the purpose of sensitivity analysis, based on a prior assumption that the IE risk would less likely manifest in relation to dental procedures occurring more than 13 weeks before the index date. Three 12-week control periods

were matched to each case period. For both case periods A and B, the control period ended 12 weeks before the start of its corresponding case period to prevent carryover effects.

### Exposure to Dental Procedures

The dental procedures of interest are 5 common dental services provided in both inpatient and outpatient settings, including tooth extraction, surgery, dental scaling, periodontal treatment, and endodontic treatment.

### Data Analysis

To describe the characteristics of patients with IE, we presented the distribution of age, sex, and comorbidities. A patient was identified as having a comorbidity if, within 2 years before the index date, he or she had a ICD-9-CM diagnosis code of that comorbidity on at least 2 outpatient claims or any inpatient claim. We also analysed antibiotics related to dental procedures, defined as a prescription of antibiotics on the same date on which claims were made for dental procedures during the case periods and their corresponding control periods.

For each of the 5 categories of dental services, we described exposure frequency during the case periods and the matched control periods. The exposures are dichotomous variables. Patients were exposed to a dental service if they had any inpatient or outpatient claim for that dental service during each specific time period.

We used the conditional logistic regression to compare the likelihood of exposure to dental procedures during case period A versus its matched control periods. The model yielded matched odds ratios (ORs) and 95% confidence intervals (CIs), which can be estimated by the ratio of the number of discordant pairs with exposed case period to the number of discordant pairs with non-exposed case periods. To adjust for potential time-varying confounders, we included antibiotics related to dental procedures in the multivariable models. We performed the adjusted and unadjusted models for each category of dental services. All these analyses were repeated using case period B and its matched control periods. Analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

### Results

**Table 1: Patient characteristics**

Age groups in years	N%
18-25	12 (6)
26-35	24 (12)
36-45	22 (11)
46-55	30 (15)
56-65	32 (16)
66-75	44 (22)
>75	36 (18)

Mean (standard deviation)	56.0 (18.6)
Male	130 (65)
Female	70 (35)
<b>Comorbidities</b>	
Hypertension	90 (45)
Diabetes	50 (25)
Ischemic stroke	28 (14)
Hemorrhagic stroke	4 (2)
Congestive heart failure	40 (20)
Liver disease	34 (17)
Chronic renal failure or dialysis therapy	28 (14)
Valvular heart disease	36 (18)
Ischemic heart disease	48 (24)

The mean age was 56.0 (18.6) years; 40% of patients were 65 years and older. Men accounted for 65% of all patients. In terms of co-morbidities, hypertension was the most common followed by diabetes and ischemic heart disease.

**Table 2: Concordant and Discordant Pairs of Exposures to Dental Procedures in Patients with Infective Endocarditis**

Dental procedures	N
<b>Tooth extraction N=55</b>	
Non-exposed	40
Exposed	15
<b>Dental scaling N=40</b>	
Non-exposed	32
Exposed	8
<b>Surgery N=25</b>	
Non-exposed	18
Exposed	7
<b>Periodontal treatment N=20</b>	
Non-exposed	17
Exposed	3
<b>Endodontic treatment N=60</b>	
Non-exposed	50
Exposed	10

Out of 200 patients, 43 patients were exposed to infective endocarditis.

### Discussion

Infective endocarditis (IE), is a rare but serious condition which currently still carries a mortality of up to 25%. [17] A yearly incidence of 3–10 per 1000,000 people has been reported. [18] Clinical features of IE are non-specific and include high fever (which may be absent in the elderly or immunocompromised), loss of weight, lethargy, shortness of breath, new or changing heart murmurs and possibly skin manifestations. Major complications include sepsis, stroke and heart failure from valvular dysfunction. Treatment is with prolonged intravenous antibiotics with a significant proportion requiring valvular surgery. Long term complications include the increased risk of re-infection, mechanical complications requiring repeated procedures and possibly life-long

anticoagulation with its own attendant complications if prosthetic heart valve replacement is needed. [18,19]

The mean age was 56.0 (18.6) years; 40% of patients were 65 years and older. Men accounted for 65% of all patients. In terms of co-morbidities, hypertension was the most common followed by diabetes and ischemic heart disease. Out of 200 patients, 43 patients were exposed to infective endocarditis. In a study by van der Meer et al, 23% of 275 patients with IE had undergone a procedure with an indication for prophylaxis within 180 days of onset, and in only 11.3% of the patients the procedures had been within 30 days of onset. [20] Guntheroth extracted from published reports that the prevalence of dental extractions within 2 months preceding onset of IE was surprisingly low, only 3.6% for 1322 cases. [21] Studies suggest that the incubation period of IE is usually 7 to 14 days for viridians group streptococci or enterococci, with 78% of cases

occurring within 7 days of bacteraemia and 85% within 14 days. [22]

As reported by Roberts, the cumulative risk of bacteraemia over 1 year from routine daily activities is 5.6 million times greater than that from a single tooth extraction. [23] Given the far higher cumulative risk of bacteraemia resulting from routine daily activities, it would be difficult to determine whether the bacteraemia that provoked IE originated from these routine activities or from a dental procedure during the same period. In other words, the association of dental procedures and acquisition of IE might be coincidental, even performed within a short incubation period.

Antibiotic prophylaxis has been recommended for the prevention of IE in patients with a high risk of IE. However, the effectiveness of antibiotic prophylaxis has remained a controversial issue for decades. In a previous study, Duval et al [24] used population data in France to show that the risks of developing IE were 1 in 46 000 and 1 in 150 000 for dental procedures without and with antibiotic prophylaxis, respectively. According to their results, the number needed to treat is therefore  $\approx 66\ 346$  patients [25]; that is, 66 346 patients would have had to be given antibiotic prophylaxis to prevent a case of IE. A 2013 Cochrane Database systematic review of antibiotic prophylaxis of IE in dentistry [26], concluded that there is no evidence to determine whether antibiotic prophylaxis before dental procedures is effective or ineffective. A recent publication by Cahill TJ et. al., 2017 [27] is the most extensive systematic review and meta-analysis of all studies available from 1960 to 2016 on antibiotic prophylaxis for infective endocarditis.

### Conclusion

In conclusion, using a case-crossover design, this population-based study found that dental procedures are not significantly associated with the risk of IE. This result may argue against the conventional assumption on which the rationale of prophylaxis for IE is based. We believe that the result with its implication is of great relevance to the practice of both physicians and dentists. Further confirmatory studies with larger scale or direct causal effects studies of IE are needed and the AHA guidelines for prevention of IE should to be reinvestigated accordingly.

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