

## **Interleukin-6-572C/G polymorphism is associated with the risk of chronic periodontitis.**

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### **Abstract**

Previous studies investigated the association between the IL-6-572C/G polymorphism and chronic periodontitis risk. However, the results were inconclusive. Therefore, we performed this study to assess the association between IL-6-572C/G polymorphism and chronic periodontitis risk. We included 231 patients with chronic periodontitis and 259 healthy controls. IL-6 sequence amplification was done using polymerase chain reaction (PCR). Subjects with CG genotype showed an increased risk of chronic periodontitis (OR=1.52, 95% CI 1.06-2.21). In addition, individuals with GG genotype had a higher risk of chronic periodontitis (OR=4.53, 95% CI 1.43-14.21). Carriage of the G-allele was significantly associated with chronic periodontitis risk (OR=1.62, 95% CI 1.19-2.22). In conclusion, this study found a significant association between IL-6 -572C/G polymorphism and chronic periodontitis risk.

**Keywords:** Chronic periodontitis, Interleukin 6, Polymorphism.

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### **Introduction**

Chronic periodontitis is a multi-factorial infectious disease that occurs as a result of the host immune inflammatory response to pathogenic microorganisms, leading to the destruction of periodontal tissues, bone resorption and ultimately tooth loss [1]. It is more likely that the cumulative effects of the disease occur over a lifetime. In addition to bacterial infection, individuals' susceptibility to periodontitis is likely to be of major importance in determining the manifestation and progression of the disease [2].

Chronic periodontitis induces local and systemic elevation of proinflammatory cytokines, and these molecules contribute to soft and hard periodontal tissue destruction and loss of dental elements [3]. Thus, inflammatory responses play an important role in the development of chronic periodontitis. Interleukin 6 (IL-6) is an interleukin that acts as both a pro-inflammatory and anti-inflammatory cytokine [4]. It is a predominant cytokine associated with bone destruction in advanced periodontal disease [5]. The level of IL-6 in the sera of periodontitis patients was seen to be higher than those of healthy controls [6]. Previous studies investigated the association between the IL-6 -572C/G polymorphism and chronic periodontitis risk [7,8]. However, the results were inconclusive. Therefore, we performed this study to assess the association between IL-6 -572C/G polymorphism and chronic periodontitis risk.

### **Methods**

#### **Study subjects**

A total of 490 subjects, including 231 patients with periodontitis and 259 controls, were suitable to participate in this study. Written informed consent was obtained from the patients who agreed to participate in the study. This study was approved by People's Hospital of Henan Province.

#### **Genotyping of IL-6-572C/G polymorphism**

The quality and the quantity of DNA were confirmed by agarose gel electrophoresis and spectrophotometry, respectively. IL-6 sequence amplification was done using polymerase chain reaction (PCR) with 3 thermal protocols of 94°C for 30 s, 56°C for 30 s and 72°C for 30 s. This cycle was repeated 30 times.

#### **Statistical analysis**

Results on continuous measurements are presented as mean  $\pm$  SD and categorical measurements are presented in number (%). Student's t test was used to find the significance of study parameters on a continuous scale between the two groups. Odds ratios (OR) and their corresponding 95% confidence intervals (CI) were used to assess the association of IL-6-572C/G polymorphism and chronic periodontitis risk. All statistical analyses were performed by SPSS software (20.0; SPSS, Inc., Chicago, IL, USA).

## Results

This was a case-control study with 58 females and 173 males in the study group (n=231) and 79 females and 180 males in the control group (n=259). There was no significant difference between the age and gender distribution between the study and control groups. Among periodontitis patients, 37.3% were smokers, while this was 21.2% among controls (P<0.05). All the periodontal parameters were significantly higher in the study group (Table 1).

**Table 1.** Baseline characteristics of the patients and controls.

Characteristics	Chronic periodontitis (n=231)	Healthy controls (n=259)	p
Age (years)	45.0 ± 5.2	46.6 ± 4.1	>0.05
Gender			
Male	173	180	>0.05
Female	58	79	
Smoking habit (%)	37.7%	21.2%	<0.05
Pocket depth (PD)	2.1 ± 0.6	1.8 ± 0.2	<0.05
Plaque index (PI)	2.2 ± 0.2	1.6 ± 0.3	<0.05
Gingival index (GI)	2.5 ± 0.3	1.8 ± 0.1	<0.05

**Table 2.** Genotype distributions and allele frequencies of this study.

Genetic model	Case (n)	Control (n)	OR	95% CI	p
Genotype model					
CC	120	167			
CG	98	88	1.52	1.06-2.21	<0.05
GG	13	4	4.53	1.43-14.21	<0.05
Allele model					
C	338	422			
G	124	96	1.62	1.19-2.22	<0.05

The genotype distributions and allele frequencies were showed in Table 2. Subjects with CG genotype showed an increased risk of chronic periodontitis (OR=1.52, 95%CI 1.06-2.21). In addition, individuals with GG genotype had a higher risk of chronic periodontitis (OR=4.53, 95%CI 1.43-14.21). Carriage of the G-allele was significantly associated with chronic periodontitis risk (OR=1.62, 95%CI 1.19-2.22).

## Discussion

We included 231 patients with chronic periodontitis and 259 healthy controls. We found that subjects with CG genotype showed an increased risk of chronic periodontitis. In addition, individuals with GG genotype had a higher risk of chronic periodontitis. Carriage of the G-allele was significantly associated with chronic periodontitis risk.

IL-6 is a pro-inflammatory cytokine that has different pleiotropic activities including induction of acute phase proteins and stimulation of T and B cells, synoviocytes and osteoclasts. These inflammatory reactions result in cartilage and bone damage as well as other systemic manifestations [9]. Amr et al. found that No association was found between IL-6-572G/C gene polymorphism and rheumatoid arthritis [10]. Ma et al. suggested that the -572 C>G polymorphism was proved to be significantly associated with hypertension [11]. Shi et al. indicated that CC genotypes of the IL-6 gene polymorphisms at position -572 may confer a high risk of cervical cancer [12]. Yin et al. suggested a significant association between the IL-6 gene -572 G allele and increased risk of type 2 diabetes mellitus [13]. Qi et al. showed that IL-6-572 C/G polymorphism could decrease the risk of Alzheimer's disease [14].

In conclusion, this study found a significant association between IL-6-572C/G polymorphism and chronic periodontitis risk. Carriage of the G-allele was significantly associated with chronic periodontitis risk. Large well-designed cohort studies are needed to confirm our results.

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