INPLASY

Unravelling the Impact of TNFA -308 (rs1800629) on Periodontitis Susceptibility: A Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 January 2026 and was last updated on 7 January 2026.

INTRODUCTION

Review question / Objective To systematically evaluate and quantitatively synthesize available evidence on the association between TNFA rs1800629 (–308 G/A) gene polymorphism and the risk and susceptibility of periodontitis, including chronic and aggressive forms, across different ethnic populations
PICOS Framework

P (Population):
Individuals diagnosed with periodontitis (chronic periodontitis and aggressive periodontitis) and periodontally healthy controls from different ethnic backgrounds.

I (Intervention / Exposure):
Presence of the TNFA rs1800629 (–308 G/A) polymorphism, particularly carriers of the A allele.

C (Comparison):
Individuals without the polymorphism (GG genotype or non-carriers of the A allele).

O (Outcome):
Increased susceptibility to or risk of periodontitis, measured using odds ratios (ORs) and 95% confidence intervals (CIs).

S (Study Design):
Case–control and nested case–control genetic association studies included in a meta-analysis.

Rationale Periodontitis is a multifactorial inflammatory disease characterized by the destruction of tooth-supporting tissues, where disease onset and progression are influenced not only by microbial factors but also by host genetic susceptibility. Among host-related factors, pro-inflammatory cytokines play a critical role in modulating the immune response to periodontal pathogens. Tumor necrosis factor-alpha (TNF-α) is a key cytokine involved in inflammation, immune regulation, and bone resorption, and elevated levels of TNF-α have been consistently observed in periodontal tissues and gingival crevicular fluid of affected individuals. The TNFA rs1800629 (–308 G/

A) polymorphism, located in the promoter region of the TNFA gene, has been shown to influence transcriptional activity and TNF-α production. The A allele is associated with increased cytokine expression, which may intensify inflammatory responses and accelerate periodontal tissue breakdown. Numerous case–control studies have investigated the association between this polymorphism and periodontitis; however, their findings remain inconsistent, likely due to limited sample sizes, ethnic variability, differences in disease classification (chronic vs. aggressive periodontitis), and methodological heterogeneity. Given these inconsistencies, a comprehensive meta-analysis is warranted to enhance statistical power, resolve conflicting evidence, and provide a more precise estimate of the relationship between TNFA rs1800629 polymorphism and periodontitis susceptibility. Furthermore, subgroup analyses based on ethnicity and type of periodontitis are essential to clarify population-specific genetic effects and to better understand the role of TNF-α–related genetic variation in periodontal disease pathogenesis. This evidence may contribute to improved risk assessment, personalized preventive strategies, and a deeper understanding of gene–inflammation interactions in periodontitis.

Condition being studied Periodontitis (chronic and aggressive forms) — a chronic inflammatory disease affecting the supporting tissues of the teeth.

METHODS

Search strategy A comprehensive literature search was conducted to identify studies evaluating the association between TNFA rs1800629 (–308 G/A) gene polymorphism and periodontitis. Electronic databases including PubMed, Google Scholar, and ScienceDirect were systematically searched. The search strategy used combinations of Medical Subject Headings (MeSH) terms and free-text keywords such as: “Tumor Necrosis Factor Alpha” OR “TNFA”, “rs1800629” OR “–308 G/A”, combined with “periodontitis”, “chronic periodontitis”, “aggressive periodontitis”, and “genetic polymorphism”.

Reference lists of relevant articles and reviews were also manually screened to identify additional eligible studies. Only English-language case–control or nested case–control studies with sufficient genotype data to calculate odds ratios (ORs) and 95% confidence intervals (CIs) were included. Duplicate publications and studies lacking adequate genetic data were excluded.

Participant or population Individuals diagnosed with chronic or aggressive periodontitis and periodontally healthy control subjects from different ethnic populations.

Intervention Presence of the TNFA rs1800629 (–308 G/A) gene polymorphism, particularly carriage of the A allele.

Comparator Individuals without the TNFA rs1800629 (–308 G/A) polymorphism, specifically those carrying the GG genotype (non-carriers of the A allele).

Study designs to be included Case–control and nested case–control genetic association studies.

Eligibility criteria Case–control or nested case–control studies evaluating the association between TNFA rs1800629 (–308 G/A) polymorphism and periodontitis; studies involving patients with chronic or aggressive periodontitis and healthy controls; studies providing sufficient genotype data to calculate odds ratios (ORs) and 95% confidence intervals (CIs); and studies in which genotype distributions in control groups conform to Hardy–Weinberg equilibrium.
Exclusion criteria:
Studies published in languages other than English; duplicate publications; reviews, meta-analyses, case reports, or editorials; and studies lacking adequate or extractable genotype frequency data.

Information sources Electronic databases including PubMed, Google Scholar, and ScienceDirect were searched for relevant studies. In addition, reference lists of retrieved articles and related reviews were manually screened to identify additional eligible publications.

Main outcome(s) Association between TNFA rs1800629 (–308 G/A) polymorphism and risk of periodontitis, measured using pooled odds ratios (ORs) with 95% confidence intervals (CIs) under allelic, dominant, and recessive genetic models.

Data management Data were independently extracted from eligible studies into a standardized data extraction form, including first author, publication year, country, ethnicity, study design, type of periodontitis, genotyping method, and genotype frequencies in cases and controls. Extracted data were checked for accuracy and completeness before analysis. The compiled dataset was then entered into the MetaGenyo web tool.

Quality assessment / Risk of bias analysis The methodological quality of included studies was assessed by evaluating study design, selection of cases and controls, genotyping methods, and conformity of genotype distributions in control groups with Hardy–Weinberg equilibrium. Potential sources of bias, including selection bias and publication bias, were examined. Publication bias was further assessed using Begg's funnel plots and Egger's regression test, while sensitivity analyses were performed to evaluate the robustness of the pooled results.

Strategy of data synthesis Data were quantitatively synthesized using meta-analysis. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to evaluate the association between the TNFA rs1800629 (–308 G/A) polymorphism and periodontitis under allelic, dominant, and recessive genetic models. Between-study heterogeneity was assessed using Cochrane's Q test and the I^2 statistic. Subgroup analyses were conducted based on ethnicity and type of periodontitis (chronic or aggressive). Sensitivity analyses (leave-one-out method) were performed to test the stability of the results.

Subgroup analysis Subgroup analyses were performed to explore potential sources of heterogeneity by stratifying studies according to ethnicity (Asian, Caucasian, and mixed populations) and type of periodontitis (chronic periodontitis and aggressive periodontitis). Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated within each subgroup to assess population- and disease-specific associations between the TNFA rs1800629 (–308 G/A) polymorphism and periodontitis risk.

Sensitivity analysis Sensitivity analysis was conducted using a leave-one-out approach, in which each study was sequentially excluded to assess its influence on the overall pooled effect estimates. The consistency of the results after removal of individual studies indicated the robustness and stability of the association between the TNFA rs1800629 (–308 G/A) polymorphism and periodontitis risk.

Language restriction Only studies published in the English language were included in this review and meta-analysis.

Country(ies) involved India.

Keywords Periodontitis; TNFA; TNF-α; rs1800629; –308 G/A polymorphism; genetic polymorphism; chronic periodontitis; aggressive periodontitis; meta-analysis.

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