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Association between human herpes virus and aggressive periodontitis: A systematic review

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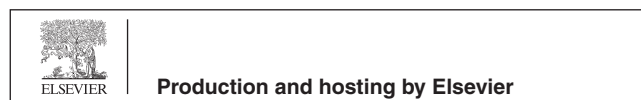
KEYWORDS

Herpes simplex virus;
Cytomegalovirus;
Epstein–Barr virus;
Aggressive periodontitis;
Systematic review

Abstract *Objectives:* to elucidate the association between HHVs [Human Herpes Viruses–human cytomegalovirus (HCMV), Epstein–Barr virus (EBV) and herpes simplex virus (HSV)] and risk of aggressive periodontitis (AgP) and advanced periodontitis (AP). *Materials and methods:* the addressed focused question was: “Is there an association between HHVs and AgP and do HHVs implicate in the pathogenesis of AgP and AP?” Electronic search of the MEDLINE/PubMed, EMBASE, Scopus, ISI Web of knowledge, and Google-Scholar databases was combined with hand searching of articles published from 1970 up to and including March 2016 using relevant MeSH terms. Review papers, in-vitro and experimental studies, case reports, commentaries, interviews, updates and duplicate publications were excluded. *Results:* twelve studies were included. Three studies reported elevated percentage of HSV1 carriage in AgP patients whereas two studies reported comparable percentage levels of HSV1 among AgP patients and periodontally healthy patients. Seven studies reported significantly higher percentage levels of HCMV in AgP patients as compared to healthy controls whereas four studies showed comparable levels of HCMV among AgP and healthy controls. Six studies reported higher EBV carriage in AgP patients than healthy controls whereas five studies showed comparable EBV percentage levels among AgP and periodontally healthy patients. *Conclusion:* overall, human herpes virus (HSV, CMV and EBV) levels are increased and are found to be associated with AgP and AP as compared to healthy individuals. However a possible involvement of HHVs in the pathogenesis of AgP warrants further investigation.

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1. Introduction

1.1. Rationale

Aggressive periodontitis (AgP) is a rapidly progressive periodontal disease in adults associated with limited amount of dental plaque, in otherwise systemically healthy individuals.¹ The etiopathogenesis of AgP involves multifactorial risk factors such as immunologic, genetic, and environmental factors. The current understanding of the pathogenesis of AgP suggests that it is associated with anaerobic gram-negative pathogenic bacteria such as *Aggregatibacter actinomycetemcomitans* (Aa), *Prevotella intermedia* and *Porphyromonas gingivalis* (Pg).^{2,3} However, several studies have reported that deep periodontal pockets are also associated with human herpesviruses (HHVs) and may be the source of periodontal tissue destruction.^{4–7}

Human herpesviruses are a group of enveloped DNA viruses which belong to the family herpesviridae. The most common types of HHVs affecting humans are herpes simplex virus (HSV) type 1 and 2; cytomegalovirus (CMV); and Epstein–Barr virus (EBV).⁸ Aggressive periodontitis patients are associated with a state of elevated localized inflammatory burden due to increased gingival crevicular fluid cytokine levels.⁹ Herpesvirus infection is thought to stimulate local cytokine production through macrophages and other inflammatory cells which may lead to the impairment of local periodontal immune defense.¹⁰

Herpesviruses target host cells by attachment onto the cell surface through glycoproteins present in the viral envelope.¹¹ A number of studies suggest that HHVs are associated with clinical periodontal parameters in AgP.^{12–14} These viruses with bacteria, may be implicated in causing periodontal destruction.

In this context, it may be hypothesized that the subgingival carriage of herpesvirus in patients affected by AgP should be elevated as compared to periodontally healthy individuals and may be implicated in causing the disease. Moreover, what drives these viruses for causing AgP is still unclear. In the past decade, a number of microbiological studies have been conducted to elucidate the role of HHVs in the pathogenesis of AgP and advanced periodontal lesions.^{7,15} The present study is designed to clarify the periodontopathogenic role of HHVs in AgP and advanced periodontitis (AP).

1.2. Objective

Therefore, the aim of the present study was to elucidate the association between HHVs [Human Herpes Viruses–human cytomegalovirus (HCMV), Epstein–Barr virus (EBV) and herpes simplex virus (HSV)] and risk of AgP and AP.

2. Materials and methods

2.1. Focused question

This review was registered at the National Institute for Health Research PROSPERO, International Prospective Register of Systematic Reviews, registration number CRD42015013792. Based on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines,¹⁶ a specific question was constructed. The addressed focused question was “Is there an association between HHVs and AgP and do HHVs implicate in the pathogenesis of AgP and AP?”

PECO Question (Patient, Exposure, Comparative, Outcome)

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