

**UNIVERSITI TEKNOLOGI MARA**

**INFLAMMATORY BIOMARKERS IN  
THE GINGIVAL CREVICULAR FLUID  
OF PERIODONTITIS PATIENTS  
WITH AND WITHOUT  
TYPE 2 DIABETES MELLITUS  
AND THEIR CONCENTRATION  
CHANGES AFTER NON-SURGICAL  
PERIODONTAL THERAPY:  
A SYSTEMATIC REVIEW &  
META-ANALYSIS**

**NAJWA BINTI BAHARUDIN**

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## ABSTRACT

**Introduction:** There's emerging evidence that periodontitis and diabetes mellitus share the same pathophysiological process through inflammation. There are numerous inflammatory biomarkers found in gingival crevicular fluid (GCF) identified in patients with periodontitis modified by type 2 diabetes mellitus (T2DM) but their significance has yet to be determined.

**Objective:** This systematic review and meta-analysis aims to identify and evaluate all relevant studies that investigated on the various inflammatory biomarkers, other than cytokines, detected in GCF of patients with periodontitis and T2DM (P+DM) compared to periodontitis and healthy (P+H) subjects (clinical question 1 – CQ1) as well as their concentration changes after nonsurgical periodontal therapy (NSPT) (clinical question 2 – CQ2). **Material &**

**Method:** Two separate systematic reviews with predetermined PICOS were done to fulfil the objectives and answer the two clinical questions. Electronic search using set search strategies were done via five databases: Scopus, Medline Complete, PubMed, Web of Science and Ovid. All relevant studies published between January 2000 and December 2021 were identified and stepwise processes were taken to select the studies that will be included in the two SRMA. Risk-of-bias assessment were also done to ascertain the quality of each of the studies selected and meta-analysis were done for level and changes in concentration of inflammatory biomarkers with at least 2 comparable studies answering CQ 1 & 2 separately. **Results:** From the literature search, 28 studies included for CQ 1 & 2. From the 28, 24 studies included for CQ 1 and 13 studies (9 studies included in both CQ) were included for CQ 2. All of the studies were evaluated using 2 types of risk-of-bias tool (RoB 2.0 and Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS)) done based on study design. Three randomised studies evaluated using RoB 2.0 and 25 non-randomised studies assessed using RoBANS. All 3 randomised studies evaluated with RoB 2.0 have high risk of bias. RoBANS domain shows that the highest percentage of high risk-of-bias is the blinding of outcome assessment and the domain with the highest percentage of low risk-of-bias is the incomplete outcome data. Meta-analysis for CQ1 revealed significant increase of visfatin and hs-CRP and non-significant increase of resistin & PGE2 in P+DM group compared to P+H group. For CQ2, only resistin significantly reduced while, visfatin and MMP-9 non-significantly reduced after NSPT for P+DM subjects. **Conclusion:** With careful consideration, it can be suggested that visfatin and hs-CRP in the CGF have great promise to be used as the inflammatory biomarker for P+DM

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# CHAPTER ONE

## INTRODUCTION

### 1.1 Research background

Periodontitis is a multifactorial chronic non-reversible inflammatory disease affecting the supporting structures of dentition due to interaction between host's defense mechanism and periodontal pathogenic bacteria. Previous studies have shown that periodontitis may have profound effects on systemic health (Iacopino & Cutler, 2000). The inflammatory associated pathogenesis of periodontal disease has been related as the source of these effects with studies have suggested periodontal inflammation to influence systemic disorders that share the common inflammatory pathways. Some of these systemic disorders include arthritis, atherosclerosis, as well as type 2 diabetes mellitus (de Molon et al., 2019). At the same time, substantial evidence of systemic conditions affecting periodontal condition also have build-up throughout the years so much so that it has been recognized in the 2017 classification of periodontal disease and conditions. In one of the supporting literatures published, a comprehensive list has been introduced outlining the systemic diseases and conditions that have an influence on the periodontium directly or periodontal disease process indirectly (Albandar et al., 2018). Some of the common systemic diseases and conditions listed are obesity, diabetes mellitus, tobacco smoking with nicotine dependence as well as emotional stress and depression. It is interesting to note that diabetes mellitus has been associated in both ways of interaction between systemic condition and periodontitis supporting the strong notion of bidirectional relationship between the two disease conditions (Preshaw et al., 2012).