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INTERLEUKIN 6 (IL-6), TUMOR NECROSIS FACTOR ALPHA (TNF-α), NUCLEAR FACTOR KAPPA BETA (NFκβ), OSTEOPROTEGERIN (OPG), RECEPTOR ACTIVATOR NUCLEAR FACTOR KAPPA (RANK) AND SOLUBLE RECEPTOR ACTIVATOR NUCLEAR FACTOR KAPPA LIGAND (sRANKL) AS A POTENTIAL DIAGNOSTIC BIOMARKER FOR PERI-IMPLANT-DISEASES

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ABSTRACT

Peri-implant diseases, including peri-implant mucositis and peri-implantitis, pose a growing challenge to the long-term success of dental implants. Early diagnosis and effective management of these conditions are essential to preserve their functions and prevent failure. This study evaluated the potential of IL-6, TNF-α, NFκβ, OPG, RANK and sRANKL in peri-implant crevicular fluid (PICF) as potential diagnostic tools for peri-implant diseases. These biomarkers were selected due to their important roles in inflammatory processes and bone metabolism, which are central to the pathogenesis of peri-implant diseases. A prospective study was conducted involving 21 patients with 32 dental implants. Based on the clinical examinations and radiographical evaluation, the dental implants were categorised into peri-implant health (PH), peri-implant mucositis (PM), and peri-implantitis (PI) groups. Clinical parameters recorded in this study were probing pocket depth (PPD), full-mouth bleeding score (FMBS), full-mouth plaque score (FMPS), modified plaque index (mPI), and modified bleeding index (mBI). PICF samples were collected using standardised PerioPaper™ strips. Both clinical parameter measurement and PICF sample collection were done at baseline and after 3 months of non-surgical periodontal therapy (NSPT). NSPT was conducted only to reduce peri-implant inflammatory levels and to see any changes in the biomarker concentration. The PICF samples were then analysed and quantified using the ELISA test. Statistical analyses were performed to compare the concentrations of biomarker levels between groups and to discern intergroup differences before and after NSPT to allow the assessment of the changes in biomarker concentration after NSPT. The results revealed that IL-6, TNF-α, NFκβ, RANK, and sRANKL were detectable in all three groups of peri-implant conditions. Statistical significance was also seen in the concentrations of RANK and IL-6 ($p > 0.05$) when intergroup comparisons were made comparing PI to PM and PH. Significant reductions in concentrations of IL-6, TNF-α, NFκβ, RANK, and sRANKL were also observed after three months of NSPT ($p < 0.05$). Heterogeneity of results was observed where statistical significance was only seen in the PH group involving TNF-α and sRANKL ($p < 0.05$). In contrast, statistical significance was noted in PM and PI in IL-6, NF-κB, and RANK ($p < 0.05$). However, despite numerical reduction across all groups post-treatment, OPG did not show any significant statistical changes ($p > 0.05$). Significant improvement of PPD, mPI, and mBI was seen involving PH ($p < 0.05$), and both PH and PM showed significant improvement of FMBS and FMPS ($p < 0.05$). This study underscores the potential of PICF biomarkers as valuable tools for early detection and monitoring of peri-implant diseases. The findings also suggest that NSPT effectively reduce inflammation and improves clinical outcomes in peri-implant mucositis; however, peri-implantitis cases require surgical approaches in addition to NSPT. Incorporating biomarkers in addition to the standard practice of diagnosis may facilitate earlier detection of peri-implant disease progression and enable more targeted, individualised therapeutic strategies.

TABLE OF CONTENTS

CHAPTER 1
INTRODUCTION

1.1 Research Background

Placing implant-supported prostheses has transformed restorative dentistry, offering patients improved functionality, aesthetics, and overall quality of life. Dental implants, which integrate directly with the alveolar bone through osseointegration, are now widely recognised as the gold standard for tooth replacement in partially and fully edentulous patients (Schnitman & Han, 2015; Wang et al., 2015). Unlike removable prostheses, which can cause irritation and discomfort, implants restore natural oral function, enhancing chewing efficiency, speech clarity, and aesthetic outcomes (Severino et al., 2016; Güncü et al., 2013; Stellingsma et al., 2004).

The global market capital of dental implants was estimated to be over US $4.6 billion in 2022. These numbers are expected to increase tremendously, reaching 2030 at an annual rate of 10%. The rising demand for dental implants and their placement are associated with increased demand for managing their treatments, including supportive care to avoid biological or mechanical complications (Grand View Research, 2024; Alani et al., 2014).

The dental biofilm induces inflammation in the peri-implant tissues. These inflammatory reactions lead to two distinct types of peri-implant diseases: peri-implant mucositis and peri-implantitis. Inflammation of the peri-implant mucosa without any progressive marginal bone loss is termed peri-implant mucositis (Heitz-Mayfield & Salvi, 2018). Peri-implantitis, on the other hand, is defined as the peri-implant biofilm-associated pathological condition involving peri-implant mucosa, characterised by peri-implant mucosal inflammation and the presence of progressive bone loss (Berglundh et al., 2018; Schwarz et al.,2018). Peri-implant mucositis is a reversible condition. It occurs due to the disruption in the balance between host and microbial flora. However, peri-implantitis is similar to periodontitis and is no longer reversible (Heitz-Mayfield & Salvi, 2018; Schwarz et al.,2018; Herrera et al., 2023).

Epidemiologically, peri-implant diseases are a significant public health concern due to their high prevalence and potential to compromise implant longevity. Eleven studies from a systematic review reported that peri-implant mucositis affects