



# Major clinical outcomes of the relationship of metabolic syndrome with the success of dental implants: the systematic review

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## Abstract

**Introduction:** Studies show that around 55% of dental implants can be affected by peri-implantitis, a chronic inflammatory process induced by bacteria, which promotes osteoclast-mediated bone resorption and inhibits bone formation, leading to progressive bone loss around the implants. Current evidence points to an increased risk of developing peri-implantitis in both obesity/metabolic syndrome (MS) and diabetes mellitus (DM) conditions compared to the healthy population. **Objective:** It was to develop a systematic review to present the main clinical outcomes of the relationship between metabolic syndrome and the success of dental implants. **Methods:** The PRISMA Platform systematic review rules were followed. The search was carried out from October to December 2023 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 92 articles were found, 26 articles were evaluated in full and 19 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 14 studies with a high risk of bias and 12 studies that did not meet GRADE and AMSTAR-2. Most studies did not show homogeneity in their results, with  $X^2=53.5\%>50\%$ . It was concluded that there is a correlation between the presence of metabolic syndrome and a higher prevalence of some bacterial species in the peri-implant groove, regardless of the peri-implant status. Metabolic

syndrome has been shown to significantly reduce bone formation in the periimplant area in the short term. Metabolic syndrome and diabetes mellitus represent an increased risk of developing peri-implantitis. Peri-implantitis requires treatment to induce new bone formation around an implant. However, this is challenging as peri-implantitis, particularly in obese or diabetic conditions, has a microenvironment that is characterized by increased inflammation.

**Keywords:** Implantology. Peri-implantitis. Metabolic syndrome. Diabetes mellitus. Dental implant success.

## Introduction

In the context of implant dentistry, studies show that around 55% of dental implants can be affected by peri-implantitis, a chronic inflammatory process induced by bacteria, which promotes bone resorption mediated by osteoclasts and inhibits bone formation, leading to progressive bone loss. around the implants. Current evidence points to an increased risk of developing peri-implantitis in both obesity/metabolic syndrome (MS) and diabetes mellitus (DM) conditions compared to the healthy population [1,2].

The predicted increase in peri-implantitis in the world population causes great concern in implant dentistry since hyperglycemic conditions are associated with impaired bone healing, which may occur due to dysfunction of glucose metabolism induced by osteocalcin. The pro-inflammatory systemic condition of MS/DM and the altered immune/microbiome response affect catabolic and anabolic bone healing events that

include increased osteoclastogenesis and impaired osteoblastic activity, which could be explained by the insulin receptor dysfunction that led to the activation of signals related to osteoblastic differentiation [3,4].

Furthermore, chronic hyperglycemia, together with associated micro and macrovascular diseases, causes delayed/impaired wound healing due to the activation of pathways that are particularly important in the initiation of events linked to inflammation, oxidative stress, and cellular apoptosis. This may be through the activation of the AKT/PKB protein, which plays a key role in impulse survival and eNOS signaling [4].

In addition, implant-prosthetic rehabilitations have demonstrated long-term survival rates (over 10 years), however, the massive use of dental implants in recent decades has also led to the development of peri-implant diseases, represented by mucositis and peri-implantitis [1-4]. A meta-analysis study reported a 50% higher risk of detecting peri-implantitis in individuals with diabetes/hyperglycemia compared to patients without diabetes [5].

Among other risk factors, the lack of an appropriate band of keratinized mucosa around dental implants may contribute to the development of peri-implant diseases [6-8], as the peri-implant groove presents a more vulnerable conformation to infection by pathogens [7]. The gingival tissue around the implant neck presents a deeper groove that can transport fluids and bacteria to the implant-abutment junction, creating a deposit for oral pathogens [9,10], with an extension of the inflammatory cell infiltrate more apically than in teeth affected by periodontitis [11].

Although the implant-supported prosthesis is one of the most successful reconstructive strategies in dentistry [8], compromised systemic conditions, such as pro-inflammatory metabolic diseases, have been shown to influence the peri-implant healing process, leading to increased levels of osseointegration failure and initiation and progression of peri-implant disease through severe tissue disruption over time [4].

Also, osseointegration is a complex phenomenon that directly depends on exposure to toxic metabolites and decreased host immune resistance due to the sustained pro-inflammatory state [9,10]. Scientific discoveries have demonstrated that toxic metabolites, such as free fatty acids, can alter tissue function through a direct effect on collagen structure, resulting in compromised bone matrix, as well as the differentiation of mesenchymal stem cells, balance between osteoblastic cells and osteoclastic activity, reducing osteoblast proliferation and function and increasing osteoclast-related activity [4].

Therefore, the present study prepared a systematic review to present the main clinical outcomes of the

relationship between metabolic syndrome and the success of dental implants.

## METHODS

### Study Design

The present study followed the international systematic review model, following the rules of PRISMA (preferred reporting items for systematic reviews and meta-analysis). Available at: <http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1>. Accessed on: 08/14/2023. The methodological quality standards of AMSTAR-2 (Assessing the methodological quality of systematic reviews) were also followed. Available at: <https://amstar.ca/>. Accessed on: 08/14/2023.

### Data Sources and Research Strategy

The literary search process was carried out from October to December 2023 and was developed based on Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various eras to the present. The descriptors (MeSH Terms) were used: *"Implantology. Peri-implantitis. Metabolic syndrome. Diabetes mellitus. Dental implant success"*, and using the Boolean "and" between the MeSH terms and "or" between historical discoveries.

### Study Quality and Risk of Bias

Quality was classified as high, moderate, low, or very low in terms of risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using the Cohen test (d).

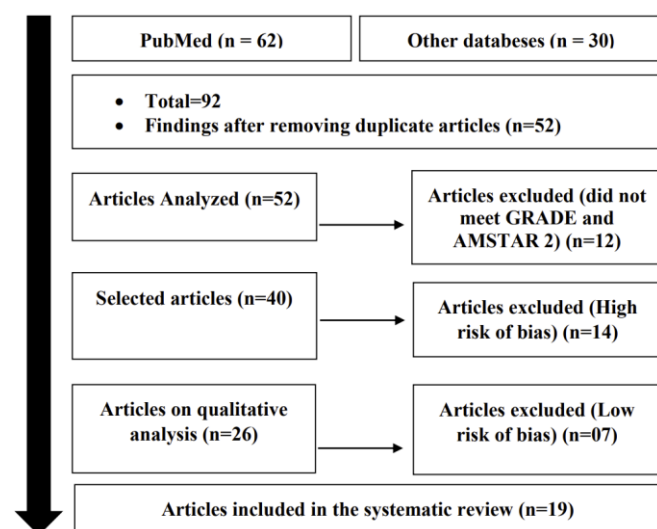
## Results and Discussion

### Summary of Findings

A total of 92 articles were found that were subjected to eligibility analysis, with 19 final studies being selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. The biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with  $X^2=53.5\%>50\%$ . Considering the Cochrane tool for risk

of bias, the overall assessment resulted in 14 studies with a high risk of bias and 12 studies that did not meet GRADE and AMSTAR-2.

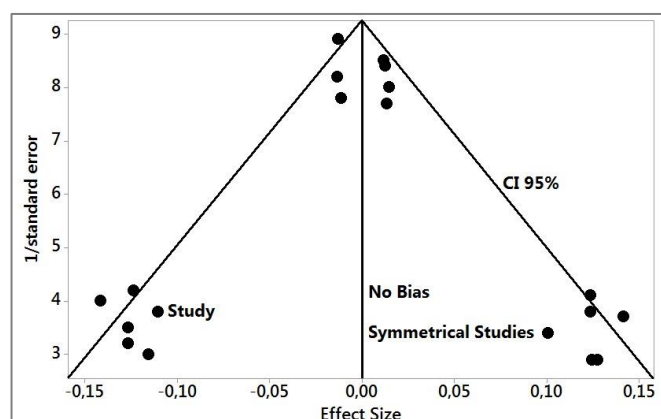
Figure 1. Article selection - exclusion process.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using the Cohen Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both between studies with a small sample size (lower precision) that are shown at the bottom of the graph and in studies with a large sample size that are presented at the top.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies that are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=19 studies).



Source: Own authorship.

## Significance and Clinical Outcomes

Peri-implant diseases, an important group of diseases that cause implant failure, are associated with metabolic abnormalities. Metabolic syndrome (MS) is a common metabolic disorder that comprises abdominal obesity, hyperglycemia, systemic hypertension, and atherogenic dyslipidemia. Previous studies reported that SM and its diverse clinical manifestations may be associated with peri-implant diseases, but the relationship and underlying mechanisms were unclear [12].

A case-control study evaluated the difference in terms of concentrations of oral pathogens in the peri-implant groove of a group of patients affected by metabolic syndrome (Mets) compared to healthy individuals. For each patient, peri-implant sulcular biofilm samples were obtained by inserting two sterile endodontic paper tips into the deepest part of the peri-implant sulcus for 30. A total of 50 patients were included in the study, 25 affected by Mets and 25 healthy. Significantly higher bacterial counts were discovered for *Aggregatibacter actinomycetemcomitans*, *Prevotella intermedia*, and *Staphylococcus aureus* in patients with SM compared to healthy individuals. Considering the peri-implant status and dividing patients by MS diagnosis, no statistically significant differences were found. Therefore, a correlation has been reported between the presence of SM and a higher prevalence of some bacterial species in the peri-implant groove, regardless of the peri-implant status [13].

Still, another study analyzed the clinical results, histological parameters, and bone nanomechanical properties around implants recovered from healthy patients and those with metabolic syndrome (MS). A total of 24 patients with edentulous jaws (12/condition) received four implants between the mental foramina. An additional implant prototype was placed for histological retrieval. The following clinical outcomes were evaluated: insertion torque (TI), implant stability quotient (ISQ) values at baseline and after 60 days of healing, and implant survival. The final study population consisted of 10 women and 11 men (an average of 64 years). A total of 105 implants were placed, and 21 were recovered for histology. Implant survival rates were similar between groups (>99%). Likewise, IT and ISQ analyses did not show a significant association with systemic conditions. Histological micrographs showed similar bone morphology, woven bone, for both conditions. While individuals with MS ( $33 \pm 5.3\%$ ) and healthy individuals ( $39 \pm 6.5\%$ ) did not show a significant difference. Although no significant influence on clinical parameters and bone nanomechanical properties was observed, MS significantly reduced bone

formation in the peri-implant area in the short term [14].

In this scenario, the various definitions for peri-implantitis open up a large discrepancy in the information reported. Also notable is the fact that the most commonly used surrogate markers (pocket probing depth, bleeding, and clinical attachment level) have not been effectively validated with relevant endpoints such as implant failure due to peri-implantitis [15].

Recommendations of combining clinical approaches with conventional radiographic imaging or computed tomography, and with patient-based symptom management, will not only help future clinical research to reevaluate and contribute to the treatment of peri-implantitis.

MS is prevalent at 42% and it is expected to increase [15]. Based on current knowledge, SM and DM represent an increased risk of developing peri-implantitis. Persistent hyperglycemia can cause an exacerbated immunoinflammatory response stimulated by peri-implant pathogens that are responsible for the greater risk and severity of peri-implantitis.

Peri-implantitis requires treatment to induce new bone formation around an implant. However, this is challenging as peri-implantitis, particularly in obese or diabetic conditions, has a microenvironment that is characterized by increased inflammation, which impairs bone regeneration necessary to treat severe bone loss related to peri-implantitis [16].

There is limited translational data on the specific mechanisms and biological components that influence pathogenicity and bone loss around implants under metabolically compromised systemic conditions. Therefore, these investigations are warranted to gain a better understanding of the etiopathogenesis of peri-implant diseases in SM/DM conditions, develop a protocol to halt the progression of peri-implantitis and establish how to effectively regenerate the bone around the dental implant [17-19].

## Conclusion

It was concluded that there is a correlation between the presence of metabolic syndrome and a higher prevalence of some bacterial species in the peri-implant groove, regardless of the peri-implant status. Metabolic syndrome has been shown to significantly reduce bone formation in the peri-implant area in the short term. Metabolic syndrome and diabetes mellitus represent an increased risk of developing peri-implantitis. Peri-implantitis requires treatment to induce new bone formation around an implant. However, this is challenging as peri-implantitis, particularly in obese or diabetic conditions, has a microenvironment that is characterized by increased inflammation.

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## Ethical Approval

Not applicable.

## Informed consent

Not applicable.

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## Data sharing statement

No additional data are available.

## Conflict of interest

The authors declare no conflict of interest.

## Similarity check

It was applied by Ithenticate®.

## Peer Review Process

It was performed.

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