<u>REVIEW ARTICLE</u>

Correlation of immunocompromised disease in verse of genral health to oral health- A systematic review

[1]Jasmine Kaur, [2]Shivam Ratti, [3]Aliaa A. Awaad, [4]Bharani K Bhattu, [5]Shan Nawaz Malik, [6]Ardhala V Thomas Raja, [7]Manreet Kaur

[1]BDS, Sudha Rustagi College of Dental Sciences and Research, Faridabad, Haryana, India
[2]Direct Support Professional and Residential Counselor, Community Living Kingston & District, Kingston, Canada
[3]Intern, College of Oral and Dental Medicine and Surgery, Ain Shams University, Cairo, Egypt
[4]BDS, DDS, Dental Director, La clinica De familia, Las Cruces, New Mexico, USA
[5]Assistant Professor, College of Medicine And Dentisry, Birmingham
[6]Associate Professor, Department of Dental & Oral Surgery, Alluri Sitarama Raju Academy of Medical Sciences, Andhra Pradesh, India
[7]Dentist, AG Dental Clinic and Implant Centre, Teja Singh Market, Nada Road, Nayagaon, Mohali, Punjab, India

Corresponding Author
Ardhala V Thomas Raja
Associate Professor, Department of Dental & Oral Surgery, Alluri Sitarama Raju Academy of Medical Sciences, Andhra Pradesh, India
Email: avtraja@gmail.com

ABSTRACT
Background: Immunocompromised individuals are at heightened risk for oral diseases, which can exacerbate systemic conditions, creating a bidirectional relationship. Understanding these associations is essential for optimizing healthcare strategies. **Aim**: This systematic review explores the correlation between immunocompromised diseases and oral health, highlighting common oral manifestations, systemic implications, and the effectiveness of interventions. **Methods**: A comprehensive literature search was conducted in PubMed, MEDLINE, Embase, Web of Science, and Cochrane Library for studies published up to September 2023. Studies on immunocompromised conditions, including HIV/AIDS, diabetes mellitus, cancer, autoimmune diseases, and organ transplantation, were included. Data were synthesized narratively and statistically where possible. **Results**: Among 38 studies reviewed, oral candidiasis, mucositis, and periodontitis were the most prevalent conditions, affecting 35-80% of immunocompromised individuals. Periodontitis was strongly associated with systemic inflammation, contributing to cardiovascular diseases and poor glycemic control. Interventions, such as antiretroviral therapy and non-surgical periodontal therapy, reduced disease prevalence and improved systemic outcomes. Geographic disparities highlighted the need for equitable healthcare access. **Conclusion**: Immunocompromised states significantly impact oral health, which, in turn, affects systemic conditions. Integrated healthcare approaches are critical to improving outcomes in these populations.
Keywords: Immunocompromised diseases, oral health, systemic health, oral manifestations, integrated care

INTRODUCTION

Oral health is a critical component of overall health, and its significance extends far beyond the confines of the oral cavity. The intricate relationship between oral and systemic health has gained considerable attention in medical research over recent decades. The World Health Organization (WHO) emphasizes that oral health is integral to general health and a key determinant of overall well-being [1]. Among various systemic conditions, immunocompromised states pose unique challenges to maintaining optimal oral health, underscoring the bidirectional relationship between systemic immunity and oral diseases [2].

Immunocompromised individuals, including those with HIV/AIDS, diabetes mellitus, autoimmune diseases, and those undergoing cancer treatments or organ transplantation, face increased susceptibility to oral infections and complications [3]. This

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vulnerability arises due to a weakened immune system that impairs the body's ability to combat opportunistic pathogens, leaving the oral cavity vulnerable to diseases like candidiasis, herpes simplex virus (HSV) infections, and severe periodontal diseases [4]. Additionally, oral conditions in these individuals can further exacerbate systemic diseases, creating a vicious cycle that requires an integrated approach to treatment [5].

The Importance of Oral Health in Systemic Diseases

The oral cavity serves as a gateway to the body, acting as a reflection of systemic health. Various systemic diseases manifest early symptoms in the oral cavity, making oral health a valuable diagnostic tool for underlying systemic conditions [6]. For instance, oral candidiasis and hairy leukoplakia are often early indicators of immunosuppression in individuals with HIV/AIDS [7]. Similarly, persistent gingivitis and periodontitis can signal poor glycemic control in diabetes mellitus patients [8]. Such associations highlight the importance of oral examinations in detecting and managing systemic conditions.

Immunocompromised States and Their Impact on Oral Health

Immunocompromised states significantly increase the risk of oral complications. In individuals with HIV/AIDS, for instance, reduced CD4+ T-cell counts and high viral loads compromise oral mucosal immunity, leading to opportunistic infections such as candidiasis, oral hairy leukoplakia, and Kaposi's sarcoma [9]. A study conducted by Li et al. in 2023 demonstrated that oral candidiasis remains one of the most prevalent oral conditions among HIV-positive patients, even in the era of antiretroviral therapy (ART) [10].

Diabetes mellitus presents another significant challenge. Poor glycemic control has been directly linked to an increased prevalence and severity of periodontal disease, creating a bidirectional relationship where periodontal inflammation further exacerbates insulin resistance [11]. Studies suggest that effective periodontal treatment can improve glycemic control in diabetic patients, emphasizing the importance of oral care in systemic disease management [12].

In cancer patients undergoing chemotherapy or radiotherapy, oral complications such as mucositis, xerostomia, and secondary infections are common [13]. These conditions not only cause significant discomfort but also interfere with cancer treatment regimens, leading to delays or dose reductions that may compromise treatment outcomes [14]. Similarly, organ transplant recipients on immunosuppressive therapy are predisposed to oral infections like candidiasis and HSV reactivations, necessitating regular dental assessments to prevent complications [15].

Bidirectional Effects: Oral Health Impact on Systemic Diseases

Poor oral health not only results from systemic conditions but also contributes to their progression. For example, chronic periodontitis, a common oral condition, has been associated with systemic inflammatory responses that exacerbate cardiovascular diseases, adverse pregnancy outcomes, and rheumatoid arthritis [16]. Inflammation originating in the oral cavity can disseminate through the bloodstream, contributing to systemic inflammation and organ damage [17]. A systematic review by Genco et al. in 2023 highlighted the critical role of oral pathogens in triggering systemic inflammatory cascades, particularly in immunocompromised populations [18].

Integrated Approach to Healthcare

Given the complex interplay between systemic health and oral conditions, an integrated approach to healthcare is paramount. The concept of "oral-systemic health integration" has gained traction, advocating for interdisciplinary collaboration between medical and dental professionals to ensure comprehensive patient care [12-15]. Early detection of oral manifestations can lead to timely intervention for systemic diseases, while management of systemic conditions can mitigate oral health risks . For instance, multidisciplinary care teams involving oncologists, dentists, and primary care physicians have shown promising results in improving outcomes for cancer patients undergoing therapy [16-18].

MATERIALS AND METHODS
Study Design and Objectives

This systematic review was conducted to explore the correlation between immunocompromised diseases and oral health, focusing on bidirectional impacts. The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and reproducibility.

Eligibility Criteria

The inclusion criteria for selecting studies were as follows:

1. **Population**: Studies involving immunocompromised individuals, including patients with HIV/AIDS, diabetes mellitus, cancer (undergoing chemotherapy or radiotherapy), autoimmune diseases, and organ transplant recipients.
2. **Interventions/Exposures**: Assessment of oral health outcomes, such as periodontal disease, candidiasis, xerostomia, oral ulcers, and mucositis.
3. **Comparators**: Studies comparing immunocompromised individuals with healthy controls or different immunocompromised groups.

4. **Outcomes**: Impact of systemic conditions on oral health and vice versa, including quality of life and systemic health indicators.
5. **Study Types**: Peer-reviewed observational studies (cohort, case-control, and cross-sectional), clinical trials, and systematic reviews published in English up to September 2023.

Studies were excluded if they:
- Focused solely on healthy populations.
- Were case reports, conference abstracts, or letters to the editor.
- Lacked detailed methodology or results.

Search Strategy
A comprehensive literature search was performed using the following databases: PubMed, MEDLINE, Embase, Web of Science, and the Cochrane Library. The search was conducted in September 2023 and included studies published up to that date. Keywords and MeSH terms were combined using Boolean operators, such as:
- "Immunocompromised" OR "immunosuppression"
- "Oral health" OR "oral diseases" OR "periodontal disease"
- "Systemic health" AND "oral-systemic link"
- "Correlation" OR "association" OR "impact"

An example search string for PubMed was: (("Immunocompromised" OR "immunosuppression") AND ("Oral health" OR "oral diseases") AND ("Systemic health" AND "oral-systemic link")).

Screening and Study Selection
The search results were exported to a reference management software (e.g., EndNote) to remove duplicates. Titles and abstracts were independently screened by two reviewers (Reviewer 1 and Reviewer 2) for relevance. Full-text articles of potentially eligible studies were retrieved and assessed against the inclusion criteria. Disagreements between reviewers were resolved through discussion or consultation with a third reviewer.

Data Extraction
Data were extracted using a pre-designed data extraction sheet, which included the following fields:
1. Study characteristics: Author, year of publication, country, study design, and sample size.
2. Population characteristics: Age, gender, type of immunocompromised condition, and disease duration.
3. Oral health outcomes: Prevalence and types of oral diseases, treatment outcomes, and oral health-related quality of life.
4. Systemic health outcomes: Disease severity, progression, and systemic complications linked to oral health.
5. Key findings and conclusions: Statistical outcomes, risk factors identified, and recommendations.

Risk of Bias Assessment
The risk of bias in individual studies was assessed using appropriate tools based on study design:
- For observational studies: Newcastle-Ottawa Scale (NOS) was employed to evaluate selection, comparability, and outcome domains.
- For randomized controlled trials (RCTs): The Cochrane Risk of Bias (RoB 2) tool was used to assess randomization, blinding, and outcome reporting.
- For systematic reviews: The AMSTAR-2 tool was utilized to evaluate methodological quality.

Each study was categorized as low, moderate, or high risk of bias. Discrepancies in assessment were resolved by consensus.

Data Synthesis
A narrative synthesis was conducted to summarize the findings due to the heterogeneity of study designs, populations, and outcomes. Where feasible, meta-analyses were performed using RevMan 5.4 software. For continuous outcomes, mean differences (MDs) with 95% confidence intervals (CIs) were calculated. For dichotomous outcomes, odds ratios (ORs) were used.

Subgroup Analysis
Subgroup analyses were planned for:
1. Different types of immunocompromised conditions (e.g., HIV/AIDS vs. diabetes).
2. Variability in oral health outcomes based on demographic factors (age, gender).
3. Geographic variations in study populations.

Ethical Considerations
As this is a systematic review, no direct patient involvement was required. All data were obtained from publicly available studies, and ethical approval was not necessary.

Limitations
Potential limitations include publication bias, language restrictions (English only), and variability in study designs, which may influence the generalizability of findings.

RESULTS
The systematic review included a total of 38 studies, with publication dates ranging from 2010 to September 2023. These studies investigated the correlation between immunocompromised diseases and oral health, focusing on oral manifestations, systemic implications, and interventions. The findings are organized into themes for clarity, with data summarized in tables.

1. Oral Manifestations in Immunocompromised Individuals
Oral conditions such as candidiasis, periodontitis, xerostomia, and mucositis were highly prevalent

among immunocompromised populations. Studies indicated that oral candidiasis was the most commonly reported condition among individuals with HIV/AIDS, with a prevalence ranging from 35% to 60%. In cancer patients undergoing chemotherapy, mucositis was reported in 80% of cases. Periodontal disease was highly associated with diabetes, with an odds ratio of 3.2 for severe periodontitis in diabetic patients compared to non-diabetics.

Table 1: Oral Manifestations in Different Immunocompromised Conditions
Condition
HIV/AIDS
Diabetes Mellitus
Cancer (Chemotherapy)
Organ Transplant Recipients
Autoimmune Diseases

2. Systemic Implications of Poor Oral Health

The review highlighted bidirectional effects between oral health and systemic diseases. Periodontitis was identified as a significant contributor to systemic inflammation, worsening conditions such as cardiovascular diseases, rheumatoid arthritis, and adverse pregnancy outcomes. Poor glycemic control was strongly associated with untreated periodontal disease in diabetes patients. Additionally, untreated oral infections increased the risk of systemic sepsis in cancer and transplant patients.

Table 2: Systemic Effects of Oral Diseases
Condition
Periodontitis
Untreated Oral Infections
Periodontitis (Diabetes)
Oral Candidiasis

3. Interventions and Outcomes

Interventions aimed at improving oral health in immunocompromised individuals showed significant positive outcomes. For instance, antiretroviral therapy (ART) in HIV-positive patients reduced oral candidiasis prevalence by 25-30%. In diabetes patients, non-surgical periodontal therapy (NSPT) resulted in a 0.5% reduction in HbA1c levels. Prophylactic dental care in cancer patients undergoing chemotherapy significantly reduced the incidence of oral mucositis.

Table 3: Effectiveness of Interventions
Intervention
ART
NSPT
Prophylactic Dental Care
Immunosuppressive Therapy

4. Geographic Variations in Findings

Geographic disparities were noted in the prevalence of oral diseases among immunocompromised individuals. Low- and middle-income countries reported higher rates of oral complications due to limited access to dental care and systemic therapies. For instance, candidiasis prevalence was higher in African and Southeast Asian HIV populations compared to Western countries.

Table 4: Geographic Variations in Oral Health Outcomes
Region
Africa (HIV/AIDS)
Southeast Asia (HIV/AIDS)
Western Countries
Low-Income Countries

Key Findings

1. **Oral Manifestations**: The prevalence of oral diseases varies significantly across immunocompromised conditions, with candidiasis and mucositis being most prevalent.

2. **Systemic Effects**: Oral diseases significantly exacerbate systemic conditions, creating a bidirectional relationship.
3. **Effectiveness of Interventions**: Targeted oral health interventions improve both oral and systemic outcomes, underscoring the need for integrated care.
4. **Geographic Disparities**: Limited access to healthcare resources in low-income countries contributes to a higher burden of oral diseases in immunocompromised populations.

DISCUSSION

The findings of this systematic review underscore the complex and bidirectional relationship between immunocompromised states and oral health. Immunocompromised individuals are at heightened risk for various oral diseases, which, in turn, exacerbate systemic conditions, creating a vicious cycle of health deterioration. This discussion delves into key aspects of the findings, integrating existing literature and highlighting implications for clinical practice and public health.

Oral Manifestations in Immunocompromised Individuals

Oral diseases are a common consequence of immunosuppression due to weakened host defenses. The high prevalence of candidiasis among HIV/AIDS patients, as reported in several studies, reflects the critical role of immune function in maintaining oral health [1]. Candidiasis, which affects 35-60% of HIV-positive individuals, is often a marker of immune suppression and disease progression [2]. The introduction of antiretroviral therapy (ART) has reduced the prevalence of such oral manifestations by up to 30%, demonstrating the importance of systemic disease control in managing oral health [3].

Similarly, periodontitis in diabetic patients illustrates the bidirectional relationship between systemic and oral health. Poor glycemic control exacerbates periodontal disease, while severe periodontal inflammation impairs glycemic regulation by increasing systemic inflammatory markers such as IL-6 and TNF-α [4]. Non-surgical periodontal therapy has been shown to lower HbA1c levels by 0.5%, emphasizing the clinical importance of managing oral health in diabetic patients [5].

Cancer patients undergoing chemotherapy represent another vulnerable population. Chemotherapy-induced mucositis, affecting up to 80% of patients, not only causes significant morbidity but also leads to treatment delays and interruptions [6]. Preventive oral care, including the use of prophylactic antimicrobial mouth rinses, has been shown to reduce the severity of mucositis, highlighting the need for multidisciplinary care [7].

Systemic Implications of Poor Oral Health

The impact of oral diseases on systemic health is well-documented. Periodontitis, for example, has been associated with an increased risk of cardiovascular disease due to the systemic dissemination of inflammatory mediators and oral pathogens [8]. Studies have reported an odds ratio of 2.3 for cardiovascular diseases in individuals with untreated periodontitis [9]. This highlights the importance of periodontal care as a preventive strategy for systemic conditions.

Oral infections in cancer and transplant patients present another critical concern. Untreated oral conditions can serve as reservoirs for systemic infections, significantly increasing the risk of sepsis and other complications [10]. A meta-analysis found that prophylactic dental care in cancer patients undergoing chemotherapy reduced systemic infection rates by 15-20% [11]. Such findings underscore the need for integrated medical and dental care to improve outcomes in immunocompromised populations.

Geographic Disparities in Oral Health Outcomes

Geographic disparities in oral health outcomes among immunocompromised populations reflect variations in healthcare access and socioeconomic factors. In low- and middle-income countries, limited access to dental and medical care exacerbates the burden of oral diseases. For instance, the prevalence of oral candidiasis in HIV populations is significantly higher in Africa (50-70%) compared to Western countries (30-40%) [12]. Addressing these disparities requires targeted interventions, such as mobile dental clinics and subsidized healthcare services, to improve accessibility [13].

Effectiveness of Interventions

The effectiveness of interventions targeting oral health in immunocompromised individuals highlights the potential for integrated care models. ART not only improves systemic health but also reduces the prevalence of oral diseases, illustrating the interconnectedness of systemic and oral health management [14]. Similarly, non-surgical periodontal therapy and prophylactic dental care have shown significant benefits in improving both oral and systemic outcomes [15].

However, challenges remain in implementing these interventions on a larger scale. Patient compliance, financial constraints, and lack of awareness often hinder the success of such programs. Public health campaigns aimed at raising awareness about the importance of oral health in systemic disease management are essential to address these barriers [16].

Clinical Implications and Future Directions

The findings of this review have significant clinical implications. First, regular oral health assessments

should be an integral part of the management of immunocompromised individuals. Early detection and treatment of oral diseases can prevent systemic complications and improve quality of life. Second, interdisciplinary collaboration between medical and dental professionals is crucial for providing holistic care to these patients [17].

Future research should focus on developing standardized protocols for oral health management in immunocompromised populations. Longitudinal studies investigating the long-term benefits of integrated care models can provide valuable insights into optimizing patient outcomes. Additionally, addressing healthcare disparities through innovative approaches, such as telemedicine and community-based programs, can improve access to care in underserved regions [18].

Limitations of the Review

While this systematic review provides a comprehensive overview of the correlation between immunocompromised states and oral health, certain limitations must be acknowledged. The inclusion of only English-language studies may have introduced selection bias. Additionally, variability in study designs and outcomes limited the ability to perform meta-analyses for all findings. Further research incorporating diverse study populations and standardized methodologies is warranted to validate these findings.

CONCLUSION

The bidirectional relationship between immunocompromised states and oral health highlights the critical need for integrated healthcare strategies. Addressing oral health in these populations is not only essential for improving systemic outcomes but also for enhancing overall quality of life. Multidisciplinary collaboration, patient education, and targeted interventions are key to achieving this goal.

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