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Correlation between Diabetes Mellitus and Oral Potentially Malignant Disorders - A Literature Review

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Abstract

With the global diabetic population projected to reach 642 million by 2040, understanding the oral health complications associated with diabetes is crucial. Diabetes mellitus (DM) significantly impacts oral health, leading to various pathologies including fungal infections, periodontitis, changes in salivary flow, oral cancer, and oral potentially malignant disorders (OPMDs). This study aims to investigate the correlation between DM and OPMDs through a comprehensive literature review. A systematic search was conducted, retrieving studies published in English until December 31, 2023, from databases including PubMed, Scopus, and Google Scholar. Eligible studies included observational studies, randomized controlled trials, and meta-analyses focusing on diabetic individuals diagnosed with OPMDs. Results from the reviewed studies indicate a significant association between DM and various OPMDs, particularly oral leukoplakia, erythroplakia, and oral lichen planus. While some studies report a moderate to strong association between DM and specific OPMDs, others found no significant correlation. The discussion highlights the need for further research to elucidate underlying mechanisms and develop preventive strategies. Proactive diabetes management is emphasized as crucial for improving oral health outcomes and reducing the burden of OPMDs among diabetic populations. Interdisciplinary collaboration between medical and dental professionals is recommended for comprehensive care and early detection of OPMDs in diabetic patients.

Keywords: Diabetes Mellitus, Oral Potentially Malignant Disorders, Oral Leukoplakia, Oral Submucous Fibrosis, Oral Lichen Planus, Erythroplakia, Oral Health, Correlation, Literature Review

Introduction

With the global diabetic population projected to reach 642 million by 2040, understanding the oral health complications associated with diabetes becomes increasingly crucial [1]

Diabetes mellitus (DM) is a heterogeneous group of clinical and genetic metabolic disorders recognised by abnormally high levels of glucose in the blood. Type 1 diabetes (DM I) and type 2 diabetes (DM II) are the two general categories into which it is divided. In diabetes mellitus I, the death of β-cells results in a complete loss of insulin production. The most prevalent kind of diabetes mellitus (DM) is called non-insulin dependent (DM II), and it is caused by a gradual deficiency in insulin secretion or resistance of the body to the effects of insulin [2].

Oral cavity is among all the organs and systems affected in the course of DM. Most common and significant pathologies include fungal infections, periodontitis (PD), changes in salivary flow, oral cancer, and oral potentially malignant disorders (OPMDs)[1].

Diabetes is a chronic illness that has been shown to greatly influence oral health[3]. The risk of developing oral diseases in diabetic individuals reaches as high as 67.8%. Diabetes patients have poor oral hygiene, hyposalivation, and xerostomia, which may increase their susceptibility to infections and the development of oral mucosal diseases[4]. Patients with diabetes mellitus (DM) are more likely to develop fungal infections,particularly those caused by the genus Candida. The rates of Candidal species colonizing oral mucosa are much greater in DM1 (85%) and DM2 (68%) patients than in non-diabetics (27%)[1].

Oral potentially malignant disorders (OPMDs) are defined as a group of oral mucosal lesions with an increased risk of malignant transformation. These disorders include a number of diseases with varying clinical appearances, histology, etiologies and comprise various entities, such as leukoplakia, erythroplakia, erythroleukoplakia, oral lichen planus(OLP), oral submucous fibrosis (OSF) and oral dysplasia [5,6] Of these, oral lichen planus(OLP) and leukoplakia are associated with considerable malignant transformation rates[1].Numerous researches have discovered an association between diabetes and the emergence of potentially malignant oral disorders [7,8]. For instance, a meta-analysis shows that oral leukoplakia occurs with a prevalence of 2.49% in the diabetic population (2490 per 100,000 patients with DM), making the risk of developing oral leukoplakia in a diabetics 4.34 times higher compared to the general population. Similarly, patients with DM present a prevalence of OLP of 2.72% (2720 per 100,000) with a chance of developing OLP 1.87 times higher than in the non-diabetics. [1]

This correlation gains significant importance when considering that up to 80% of oral cancers are reported to arise from pre-existing OPMDs[9], highlighting the critical need for focused research on this topic. While studies have explored links between diabetes mellitus (DM) and specific oral potentially malignant disorders (OPMDs) like leukoplakia or lichen planus, a clear picture of the overall statistical connection across various OPMDs in diabetic patients is missing. This lack of comprehensive data makes it difficult to accurately assess the combined risk for developing OPMDs in diabetic populations. Additionally, large-scale studies examining the prevalence of different OPMDs within diabetic groups are uncommon. Understanding this association through robust statistical analysis, including factors like demographics and other health conditions, is crucial. By addressing this critical gap in knowledge, this study aims to provide valuable

insights for both medical professionals and researchers. This will ultimately lead to the development of more targeted preventative strategies and improved oral health outcomes for diabetic patients.

Methods

Search Protocol and Study Selection

Comprehensive electronic research was performed till 31st December, 2023 for studies published within the last 37Ora years using the following databases: PubMed, Scopus; to retrieve articles in the english language. To expedite the literature search, Google Scholar was utilised alongside academic databases.

Search Strategy

Appropriate keywords and Medical Subject Heading(MeSH) terms were selected and combined with Boolean operators like and.the search strategy was as follows:(diabetes mellitus and opmds)(diabetes mellitus and leukoplakia)(diabetes mellitus and erythroplakia)(diabetes mellitus and oral lichen planus)(diabetes mellitus and oral submucous fibrosis). In the selection phase, articles that did not meet the inclusion criteria were excluded.

Eligibility Criteria

Inclusion criteria

1. Observational studies (cohort, case-control), retrospective studies with strong methodology.
2. Randomized controlled trials (RCTs) if relevant to specific aspects of the association.
3. Studies involving human participants diagnosed with diabetes mellitus (Type 1 or Type 2).
4. Studies investigating the prevalence or incidence of specific OPMDs (e.g.,leukoplakia, lichen Planus, Oral Submucous Fibrosis, Erthroplakia) in diabetic populations.
5. Studies including relevant clinical and demographic data (e.g., age, sex, duration of diabetes) for statistical analysis.

Exclusion criteria

1. Reviews, opinion pieces, case reports, studies with weak methodology.
2. Studies on animal models or non-diabetic populations.
3. Studies solely focusing on OPMD diagnosis or treatment without considering diabetes status.
4. Studies in language other than English.
5. Studies published before 1st January, 1987.
6. Studies with limited or unavailable data for analysis.
7. Studies not fully available in the database.

Study Characterstics

A comprehensive summary outlining the descriptive characteristics of all the incorporated studies is presented in [Table/Fig-1]. Data assessment encompassed studies investigating diabetes mellitus and four major Oral Potentially Malignant Disorders (OPMDs): Oral Lichen Planus (OLP), Oral Submucous Fibrosis (OSF), Leukoplakia, and Erythroplakia. Correlation analyses were conducted and evaluated across multiple studies:

Oral Leukoplakia was evaluated in three studies [11,12,13], Erythroplakia in one study[12], OSF in one study[12], OLP in one study[14], and Oral Premalignant Lesions in one study[10].

Results

The results of the reviewed studies elucidate a notable correlation between diabetes mellitus (DM) and various Oral Potentially Malignant Disorders (OPMDs). Meisel et al. (2010)[11] identified a significant association between diabetes and Oral Leukoplakia, reporting an odds ratio (OR) of 1.51 (CI=1.08-2.12). This association was found to be

augmented by smoking and positively correlated with A1C concentrations. Dikshit et al. (2005)[12] further corroborated these findings, noting a twofold increase in the risk of Oral Leukoplakia among diabetic women (OR=2.0, CI=1.4-2.9), with no significant excess risk observed in men. Vikas et al. (2023)[13] found that poor glycemic control was linked to an increased risk of Oral Leukoplakia. Conversely, Dikshit et al. (2005)[12] observed no significant association between diabetes and Submucous Fibrosis, while the risk of Erythroplakia was more than threefold higher among diabetic women (OR=3.2, CI=1.3-7.9), with no significant excess risk in men. Additionally, a meta-analysis by Mallah et al. (2021)[14] revealed a moderate association between diabetes mellitus and Oral Lichen Planus (pooled OR=1.87, CI=1.57-2.22). These findings collectively underscore the need for further investigation into the mechanisms underlying the observed associations and the development of potential preventive strategies.

Sn.	Author/Year	Sample Size	Age of study population	Gender M/F (cases)	Type of OPMD study	Type of OPMD diagnosed	Statistical methods/ measures reported for correlation between OPMDs and Diabetes Mellitus	Conclusion
1.	Sandeep Kumar et al.,(2015)[10]	1241	20-65 years	656/585	Cross-sectional study	Oral premalignant lesions	OR=2.21, P-value=0.014	Diabetic individuals were more likely to suffer from OPMDs compared to non-diabetics
2.	Peter Meisel et al.,(2010)[11]	4310	20-80 years	Not mentioned	Cross-sectional study	Oral Leukoplakia	OR=1.51, CI=1.08-2.12	Diabetes is associated with the risk of Oral Leukoplakia, which is exaggerated by smoking. The risk is positively correlated with A1C concentrations.
3.	Rajesh P. Dikshit et al.,(2005)[12]	927	Not specified	516/411	Cross-sectional study	Oral Leukoplakia	OR=2.0, CI=1.4-2.9	The OR for developing leukoplakia was 2-foldamong women with a history of diabetes. No statistically significant excess risk, however, could be observed for men.
4.	Rajesh P. Dikshit et al.,(2005)[12]	170	Not specified	31/139	Cross-sectional study	Submucous fibrosis	insignificant	No increased risk for submucous fibrosis among men and women observed for individuals with positive history of diabetes.
5.	Rajesh P. Dikshit et al.,(2005)[12]	100	Not specified	51/49	Cross-sectional study	Erythroplakia	OR=3.2, CI=1.3-7.9	The OR for developing Erythroplakia was more than 3-fold among women with a history of diabetes. No statistically significant excess risk, however, could be observed for men.
6.	Vikas et al.,(2023)[13]	207	>18 years	134/73	Case control study	Oral Leukoplakia		Patients having poor glycaemic control had increased risk of developing Oral Leukoplakia
7.	Narmeen Mallah et al.,(2021)[14]	32 unique studies	-	-	Systematic review and meta-analysis	Oral lichen planus	Pooled OR=1.87, CI=1.57-2.22	The meta-analysis shows that there is a moderate association between Diabetes mellitus and Oral Lichen Planus.

Discussion

The primary aim of this literature review was to investigate the correlation between diabetes mellitus (DM) and Oral Potentially Malignant Disorders (OPMDs), synthesizing existing research to offer insights into this association. The results of the reviewed studies underscore a significant correlation between DM and various OPMDs, highlighting potential implications for clinical practice and future research directions.

Summarizing the key findings, Meisel et al. (2010)[11] identified a noteworthy association between diabetes and Oral Leukoplakia, reporting an odds ratio (OR) of 1.51 (CI=1.08-2.12). This association was found to be heightened by smoking and positively correlated with A1C concentrations. Similarly, Dikshit et al. (2005)[12] observed a twofold increase in the risk of Oral Leukoplakia among diabetic women (OR=2.0, CI=1.4-2.9), with no significant excess risk observed in men. Moreover, Vikas et al. (2023)[13] emphasized the impact of poor glycemic control on the risk of Oral Leukoplakia, emphasizing the critical role of diabetes management in oral health.

However, Dikshit et al. (2005)[12] did not find a significant association between diabetes and Submucous Fibrosis. Nonetheless, they noted a more than threefold increase in the risk of Erythroplakia among diabetic women (OR=3.2, CI=1.3-7.9), with no significant excess risk observed in men. Additionally, a meta-analysis by Mallah et al. (2021)[14] revealed a moderate association between diabetes mellitus and Oral Lichen Planus (pooled OR=1.87, CI=1.57-2.22), further supporting the correlation between DM and OPMDs.

Acknowledging the scarcity of precise, high-quality research papers on this topic, it is evident that while the studies included in our review significantly contribute to understanding the association between DM and OPMDs, further research is warranted. Future investigations should not only explore the correlation between OPMDs and different systemic diseases individually but also delve into the underlying etiology and pathological mechanisms driving these associations.

Moreover, there is a pressing need for research focusing on the correlation between the progression of systemic diseases, such as DM, and the development of OPMDs. A comprehensive understanding of these interactions could inform more effective treatment strategies and prognostic measures, ultimately contributing to the prevention or reduction of cancerous lesions in the population.

In conclusion, this paper endeavors to provide a comprehensive review of the existing literature on the correlation between diabetes mellitus and OPMDs, prioritizing studies that are characterized by high quality, precision, and relevance to the topic. While the findings discussed contribute significantly to the understanding of this relationship, further research is essential to fully elucidate the intricate mechanisms underlying these associations and their clinical implications.

Conclusion

Based on our comprehensive review, a significant correlation emerges between diabetes mellitus (DM) and Oral Potentially Malignant Disorders (OPMDs). Notably, associations are evident with Oral Leukoplakia, Erythroplakia, and Oral Lichen Planus, underscoring the importance of understanding underlying mechanisms. These findings emphasize the necessity for targeted interventions to manage diabetes and mitigate OPMDs risk. Proactive diabetes management emerges as pivotal in enhancing oral health outcomes and alleviating the burden of OPMDs among diabetic populations. Furthermore, interdisciplinary collaboration between dental and medical professionals is essential to provide comprehensive care for diabetic individuals at risk of developing these oral disorders. Continuous monitoring and early detection of OPMDs in diabetic patients can facilitate timely intervention and improve long-term oral health outcomes, ultimately enhancing the quality of life for individuals affected by both diabetes and OPMDs.

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