GINGIVA CHANGES IN DIABETES MELLITUS PATIENTS: LITERATURE REVIEW
(PERUBAHAN GINGIVA PADA PASIEN DIABETES MELITUS: *LITERATURE REVIEW*)

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ABSTRAK

Latar belakang: Diabetes melitus merupakan penyakit metabolik kronis yang sering kali menyebabkan komplikasi oral, termasuk perubahan dan kerusakan gingiva akibat peningkatan inflamasi. Insidensi penyakit periodontal meningkat dua hingga tiga kali lebih besar dibandingkan dengan individu tanpa diabetes, yang memperburuk kerusakan jaringan gingiva dan memperlambat penyembuhan. Hiperglikemia memicu pembentukan *advanced glycation end-products* (AGEs), yang meningkatkan produksi sitokin proinflamasi. Penulisan artikel bertujuan untuk mengidentifikasi perubahan pada gingiva yang terkait dengan diabetes melitus. **Metode:** Penelitian ini menggunakan metode *literature rewiew* terhadap artikel yang dipublikasikan secara daring melalui database seperti *Google Scholar* dan *Pubmed*. Artikel yang dianalisis merupakan publikasi dari tahun 2019 hingga 2024, dengan total 21 artikel yang memenuhi kriteria inklusi serta relevan dengan tujuan penelitian. **Hasil:** Hasil kajian menunjukkan perubahan pada gingiva pasien diabetes melitus disebabkan oleh interaksi antara hiperglikemia, peningkatan stres oksidatif, serta gangguan pada sistem imun, yang memperburuk peradangan dan kerusakan jaringan gingiva. Faktor-faktor seperti peningkatan radikal bebas, gangguan penyembuhan jaringan akibat disfungsi vaskular, serta penurunan produksi kolagen turut memperparah kerusakan jaringan. **Kesimpulan:** Perubahan fisiologis tubuh yang terjadi meningkatkan risiko terjadinya penyakit periodontal pada pasien diabetes melitus. Gingivitis dan periodontitis merupakan dua bentuk umum dari penyakit periodontal yang disebabkan oleh biofilm patogen di sekitar gigi.

Kata kunci: Status gingiva; Penyakit periodontal; Diabetes melitus.

ABSTRACT

Background: *Diabetes mellitus is a chronic metabolic disease that leads to oral complications generally, including changes and damage to the gingiva due to increased inflammation. The incidence of periodontal disease is two to three times higher compared to individuals without diabetes, which exacerbates gingival tissue damage and slows down healing. Hyperglycemia triggers the formation of advanced glycation end-products (AGEs), which increase the production of pro-inflammatory cytokines. This article aims to identify changes in the gingiva associated with diabetes mellitus.* ***Method:*** *The method used is a literature review of articles published online through databases such as Google Scholar and PubMed. The analyzed articles are publications from 2019 to 2024, with a total of 21 articles meeting the inclusion criteria and relevant to the research objectives.* ***Result:*** *The study results indicate that the interaction between hyperglycemia causes changes in the gingiva of diabetic patients, increased oxidative stress, and dysfunction in the immune system, which worsens inflammation and gingival tissue damage. Factors such as increased free radicals, impaired tissue healing due to vascular dysfunction, and decreased collagen production also contribute to the exacerbation of tissue damage.* ***Conclusion:*** *Physiological changes in the body can increase the risk of periodontal disease in patients with diabetes mellitus. Gingivitis and periodontitis are two common forms of periodontal disease caused by pathogenic biofilms around the teeth.*

Keywords: Gingival status; Periodontal disease; Diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a chronic endocrine and metabolic disorders characterized by increased blood glucose levels, insulin resistance, and relative insulin deficiency which causes disturbances in carbohydrate, protein, and lipid metabolism. These disorders affects more than 415 million people of all ages woldwide and is expected to affect 592 million people by 2035 (SriChinthu et al., 2021; H. Sun et al., 2023; Xu et al., 2023; Zhao et al., 2023). This disease has long-term complications such as retinopathy, nephropathy, neuropathy, cardiovascular disorders, as well as various oral manifestations such as changes in saliva flow, xerostomia, burning mouth syndrome, candidiasis, cheilosis, caries, gingivitis, and periodontitis (Reddy & Gopalkrishna, 2022).

Gingival changes in DM sufferers are caused by interactions between hyperglycemia, increased oxidative stress, and immune system dysfunction that worsen inflammation (Tabatabaei et al., 2021). Excessive inflammation response and vascular disruption in periodontal tissue also contribute to gingival changes. Hyperglicemia triggers the formation of *advanced glycation end-products* (AGEs), which increase the production of proinflammation cytokines such as IL-1β, IL-6, and *tumor necrosis factor-alpha* (TNF-α), causes inflammation and demage to gingival tissue. Diabetes also disrupts neutrophil function, making it easier for periodontopathogenic bacterial infections and slowing tissue healing due to vascular dysfuction and decreased collagen production. Accumulation of AGEs and increased production of free radicals exacerbate tissue demage which increases the risk of gingivitis and periodontitis in diabetes sufferers (Rapone et al., 2021; H. Sun et al., 2023).

DM sufferers often has various disorders or abnormalities in the epithelial tissue in the oral cavity (Graves et al., 2020). These complications include periodontal disease such as gingivitis and periodontitis. Uncontrolled diabetes also increases the risk of oral health problems such as fungal infections, increased risk of caries, gingivitis, and bone loss associated with periodontal diseases (Rapone et al., 2021).

Gingivitis and periodontitis are two common features of periodontal disease caused by pathogenic biofilms around the teeth (Alqedra & Aljeesh, 2020). Pathogenis bacterial infections in periodontal pockets can spread through the bloodstream and infect other parts of the body. Moreover, there are other oral complication including halitosis, xerostomia, taste disorders, burning mouth syndrome, aphthous stomatitis, and risk of pre-cancer infections in the oral cavity (Agustina et al., 2022; Rohani, 2019).

The intensity of diabetes complications is generally proportional to the degree and duration of hyperglicemia. Uncontrolled blood sugar levels can also affect white blood cells, including neutrophils, monocytes and macrophages which play an important role in the body's defense against infection, making DM sufferers more susceptible to infection because the ability of body to fight bacteria decreases. An increase in the number of bacteria in the oral cavity in diabetes patients can cause changes and abnormalities of gingiva.

Reviewing various disorders and complications of DM in the oral cavity, especially changes in the gingiva which can ultimately reduce the patient's quality of life. Several studies have been conducted to explore gingival changes in DM patients, but there are still

limitations in previous studies. Based on the results of field observations and literature review, this article aims to identify changes in the gingiva that are associated with DM.

METHOD

The research method used *literature review* by taking references as a basis for forming a clear theoretical framework related to the problem or question being studied. This method involves reviewing and outlining theories, as well as reviewing other relevant research sources. Through the literature review method, researchers examine several articles whose content and discussion are in accordance with the topic and research objectives, so that they can provide a strong foundation for understanding the problem being studied. The analysis method was carried out by selecting articles that met the inclusion criteria.

Search for articles via the internet and research journal databases including Google Scholar and Pubmed with the Indonesian and English keywords "status gingiva" OR "gingival status" "penyakit periodontal" OR "periodontal disease", dan "diabetes melitus" OR "diabetes mellitus" accompanied by boolean operators (AND, NOT, and OR). The information obtained from references then selected to obtain data that matces the predetermined criteria. In the inclusion criteria, studies were considered eligible for systematic review with the target group of patients suffering from DM. Selected articles come from publications within a 5 year period (2019-2024) and must be open access articles. Exclusion criteria included filtering out data that was irrelevant or did not provide the requires information, as well as articles that only presented abstracts or used literature review methods. The authors specified the population, sampling, methods, and documents that did not discuss gingival changes in DM patients were excluded. Research is reviewed in English and Indonesian, with a maximum publication year limit of 5 years.

Researchers obtained 274.600 articles based on keywords in Google Scholar and 72.880 Pubmed, then sorted them into 37.591 articles. Articles were sorted again according to the criteria, namely 123 articles. There are 21 articles that are relevant to the research objectives. The strategy for searching data uses the Preferred Repoting Items for Systematic Review and Meta-Analysis (PRISMA) flowchart diagram (Figure 1).

RESULT AND DISCUSSION

The result of a literature review of artcles published in the 2019-2024 period using Indonesian and English, in total found 21 articles that met the inclusion criteria, namely focusing on discussing gingival changes in DM sufferers.

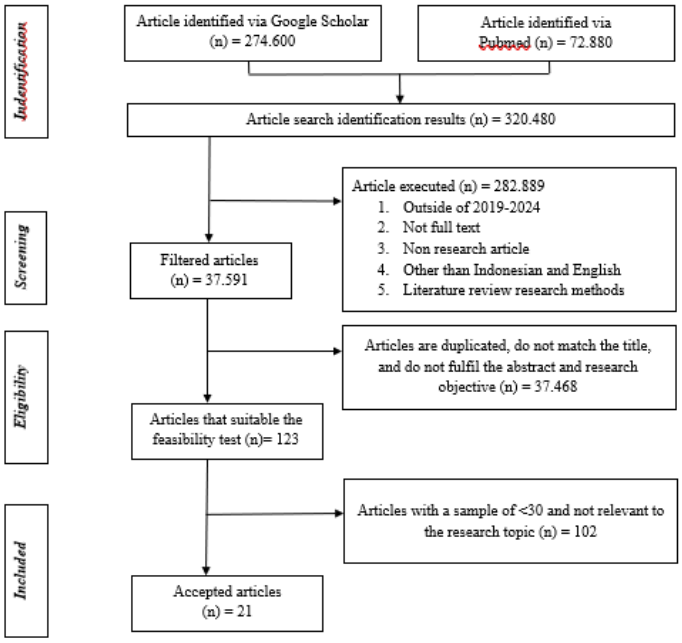

Figure 1. Article search flow based on PRISMA flowchart.

Research articles that meet the inclusion criteria will be collected and summarized, including information such as article title, author, year of publication, research objectives, methodology, samples used, results or findings, as well as similar and different aspects. A summary of the articles reviewed by researchers is presented briefly in Table 1 below.

Table 1. Matrix of reviewed articles.

Article Title, Author, Publication year	Objective	Research design	Result
Exfoliative Cytology of Buccal and Gingival Mucosa in Diabetes Mellitus Type 2, (Andini et al., 2024)	Analyzing the relationship between high blood glucode levels in Type II DM and condition of buccal and gingival cytology cells, using Giemsa stain and Periodic Acid Schiff (PAS)	Analytical observational study with a cross sectional approach, involving 16 respondents with diabetes mellitus (DM) who underwent glucose level checks using Point of Care Testing (POCT)	Observation of buccal cells showed that 10 people had normal cells (62,5%) and 6 people had mild demage (37,5%). In gingival cells, 8 people had normal cells (50%) 6 people had mild cell demage (37,5%), and 2 people had moderate cell demage (12,5%). Examination of epithelial cells using PAS staining showed normal condition in 10 people (62,5%), slight demage in 3 people (18,8%), and moderate demage in 3 people (18,8%). There was No. significant relationship between blood glucose levels and abnormalities of the buccal mucosa and gingiva (p=0.105 foe buccal, p=0.151 for gingiva). There was a significant correlation in epithelial

			cells stained with PAS (p=0.048)
Evaluation of gingival and periodontal status in obese and non-obese type II diabetic patients – a cross sectional study (SriChinthu et al., 2021)	Evaluating gingival and periodontal status in obese and non-obese type II diabetes patients.	Analytical observational research with a cross sectional approach, the study population consisted of 75 subjects divided into three different groups.	The average gingival index scores in group 1, group 2, and group 3 were 1,58, 1,54, and 1,25, respectively. Periodontal status showed increased periodontal pockets in the obese diabetic group (15,4%), followed by the non-obese diabetic (4,66%), and the obese non-diabetic group (2%). Clinical attachment loss (CAL) was severe in the obese diabetic group (60,7%), followed by non-obese diabetic (45,9%) and non-obese diabetic (15,3%)
Periodontal Status Differences between Chronic Periodontitis Patient with and Without Type 2 Diabetes Mellitus, (Nadhia Anindita Harsas, Robert Lessang, Yuniarti Soeroso, 2019)	To assess the comparison of periodontal status of type II DM and non-diabetic patients with chronic periodontitis. Periodontal status: periodontal pocket depth, gingival recession, and clinical attachment loss (CAL)	Analytical observational study with a cross sectional approach, involving 97 subjects with type II DM and 97 subjects without type II DM, at the Periodontics Clinic, Dental Hospital, Faculty of Dentistry, University of Indonesia during 2007-2016.	Periodontal status in T2DM subjects had a higher value compared to subjects without T2DM. The periodontal status that has the highest value is clinical attachment loss (CAL), while gingival recession has the lowest value. There were significant differences in pocket depth (p=0.003), gingival recession (p=0.000), and clinical attachment loss (CAL) (p=0.000) in subjects with type II DM compared to subjects without type II DM (pvalue < 0.05)
Prevalence of Periodontal Disease in Type 2 Diabetes Mellitus Patients: A Cross-sectional Study, (Monika Singh, Vivek Kumar Bains, Rajesh Jhingran, Ruchi Srivastava & Shubhash Chandra Maurya, 2020)	To assess the prevalence of periodontal disease in type II DM patients in North India.	Analytical observational study with a cross sectional approach, involving 427 respondents from type II DM patients at the outpatient clinic of the Department of Periodontology, Saraswati Dental College, Lucknow, and Dr. Ram Manohar Lohia Combined Hospital, Gomti Nagar, Lucknow.	More than 95% of type II DM patients experience periodontal demage. 27,1% of respondents had good oral hygiene, 68,8% fair, and 3,9% poor. The prevalence of severe periodontitis in respondents with good, fair, and poor oral hygiene status was 0,8%, 17%, and 29,4%, respectively. The prevalence of severe periodontitis in respondents with good, adequate, and poor oral hygiene status with poor glycemic control (glycated hemoglobin >8%) was 2,5%, 28,1%, and 30,7%, respectively.
Assessment of periodontal health among patients with diabetes mellitus: a retrospective study, (Masitah et al., 2021)	Assessing periodontal health among patients with DM.	A cross-sectional retrospective study was conducted at Saveetha Dental College and Hospital, using medical records of 200 patients diagnosed with DM, aged over 30 years with more than 6 remaining teeth.	Total of 200 diabetes patients, 116 patients experienced gingivitis and 84 patients experienced periodontitis. The prevalence of both gingivitis and periodontitis was higher among patients in the age group 45-54 years and in men than in women. The association between age and periontal status was found to be statistically significant with p value= 0.04.
Oral health status and knowledge among 10-15years old type 1 diabetes	Assessing oral health status and knowledge among children and young	Analytical observational study with a case control approach in 175	Periodontal status showed that subjects with healty periodontal tissue were less in the diabetes group compared to the control

mellitus children and adolescents in Bengaluru, (Geetha et al., 2019)	adolescents using the Community Periodontal Index and the carious teeth/ missing teeth/ filled teeth index (DMFT/dmft).	children aged 10-15 years with T1DM and 175 non-diabetic controls at Bangalore Diabetes Hospital.	group. There were more patients with bleeding and calculus in the diabetes group than in the control group. The difference between the diabetes group and the control group was statiscally significant (p=0.001). the mean number of DMFT/dmft was less in diabetics (0,07±0.006)/ (0.26±0.05) compared with the control group (0.1±0.01)/(0.84±0.2), respectively. Overall, oral health knowledge was higher in diabetes patients (8.3±1.7) compared with controls (7.5±1.8).
Gingival crevicular fluid biomarkers in type 1 diabetes mellitus: A case–control study, (Sereti et al., 2021)	Comparing Gingival crevicular fluid (GCF) levels of interleukin 8 (IL-8), matrix metalloproteinase 8 (MMP-8), and advanced glycated-end products (AGEs) in a group of type I diabetes (T1D) subjects and healthy controls.	Analytical observational study with a case control approach on 50 subjects with TIDM in the Diabetology Unit of the Geneva University Hospital, and 50 control subjects. Samples were tested for IL-8 and MMP-8 using a bead array multianalytic detection system and for AGEs using ELISA.	TIDM subjects showed more gingival plaque and inflammation as well as more sites with bleeding on probing compared with controls. GCF levels of IL-8, MMP-8, and AGEs were not significantly different between the two groups. Further analysis of GCF markers in younger (<40 years) and older (≥40 years) cohorts showed no significant differences between younger diabetics and controls or between older diabetics and controls. When groups were divided according to glycemic status (HbA1c 6.1-8, and >8%), no significant differences could be identified for any biochemical markers.
Comparative evaluation of periodontal status among diabetic and non-diabetic population in davangere city: A cross-sectional study, (Yavagal & L, 2020)	Assess and compare the prevalence and severity of periodontal disease among diabetic and non-diabetic populations aged 25-64 years in Davangere City.	A cross-sectional comparative study was conducted among subjects aged 25-64 years, consisting of 210 diabetic subjects and 300 non-diabetic subjects in Davangere City. Community Periodontal Index (CPI) and loss of attachment (LOA) are used to assess periodontal status.	There was highly signigficant relationship between diabetes status and periodontal status (p<0.001). the severity of periodontal disease was higher among diabetics than non-diabetics (p<0.001)
Comparison of Caries and Gingival Status in Patients with Type 2 Diabetes and Healthy Children, (Wang et al., 2024)	Comparing caries and gingival status in patients with TIIDM and healthy children to improve understanding and attention of patients with TIIDM towards oral health.	A retrospective study with a case-control method using clinical data from 60 TIIDM patients and 60 healthy patients aged under 10 years with TIIDM at the Department of Endocrinology, Children's Hospital, Capital Institute of Pediatrics.	The prevalence of dental plaque (DP) (91,67%) and moderate to severe PD (45%) in the diabetic group was significantly higher compared to the healthy group (73,33% and 23,33%) [1,25, 95% CI (0,96, 1,63), P<0.001]. The prevalence of caries and CA was also significantly higher in the diabetic group (75% vs. 21,67%, 2,88 vs. 1,06), and the incidence of gingivitis was higher (63,33% vs. 16,67%) [1,93, 95% CI (1,38, 2,70),

			P<0.001]. Meanwhile, the diabetic group showed significantly higher PI (2,31±0,13), GCBI (2,45±0,28), AL (5,62± 0,47 mm), and TL (0,85±0,17 mm), with obvious differences compared with the healthy group (0,92±0,21, 0,86±0,23, 1,65±0,46 mm, 0,36±0,08 mm) [3,46, 95% CI (2,33, 5,15), p<0.001]
Periodontal health in a cohort of subjects with type 1 diabetes mellitus, (Roy et al., 2019)	Evaluate periodontal health and oral health behaviors using gingival index (GI), plaque index, pocket depth (PD), bleeding on probing (BOP), and clinical attachment level (CAL), and record self-reported attitudes and behaviors related to dental care.	Cohort study in a group of TIDM subjects, 50 people with TIDM (30 men and 20 women; mean age: 35,2 years) were recruited from the Diabetology Unit of the Geneva University Hospital.	There were no significant differences between two groups in mean PD, CAL, and mean number of sites with PD >4mm that bleed on probing. Subjects with diabetes had significantly more plaque and gingival inflammation and more sites with BOP compared to control subjects. Further analysis of younger (<40 years) and older (>40 years) subjects revealed significant differences in GI between younger healthy subjects and controls.
Osteocalcin levels in gingival crevicular fluid periodontitis patients with and without type 2 Diabetes Mellitus, (Wildan et al., 2023)	To assess octeocalcin (OC) levels in gingival crevicular fluid in periodontitis patients with uncontrolled type II DM and non-DM patients.	Analytical observational study with a case control approach, using gingival crevicular fluid taken from 20 periodontitis patients with type II DM (TIIDMP) and 20 non-DM periodontitis patients and analysis of OC levels using the Osteocalcin ELISA Kit at the UGM Prof. Soedomo Dental and Oral Hospital and the KORPAGAMA Family Doctor Clinic.	OC levels in the TIIDMP group were lower with an average of 0,369±0,140, while the non-DM periodontitis group had levels of 0,664±0,141.
Severity of Periodontal Status in Type I and Type II Diabetes Mellitus, (Batool et al., 2022)	Comparing the severity of periodontal status in patients with type I and type II DM	A cross-sectional descriptive study of 178 patients with type I and type II DM from the diabetes clinic of Liaquat University Hospital (Hyderabad) was assessed to record oral findings, periodontal disease and severity with the help of Community Periodontal Index of Treatment Need (CPITN) index.	Of the 89 patients with type I DM, 60 patients scored 1 according to the CPITN assessment (bleeding on probing, indicating periodontal disease). In comparison, of the 89 patients with type II DM, 51 patients scored 3 according to the CPITN assessment (meaning pathological pocket depth (4-5) indicating a higher severity of periodontal disease). The relationship between the CPITN score was significant with both types of DM (p value = 0.001)
Assessment of Oral Hygiene, Gingival,	To assess oral hygiene, gingival	A case-control study of 80 children (40	There were no significant differences between diabetic and

and Periodontal Health, and Teeth Eruption among Type 1 Diabetic Saudi Children, (Mandura et al., 2022)	and periodontal health and eruption of permanent teeth in children with type I DM and healthy children.	children with type I DM and 40 healthy children) aged 6-12 years, was clinically examined using the simplified oral hygiene index, Loe and Silness gingival index, clinical attachment loss (CAL), and Logan and Kronfeld tooth eruption stage.	healthy children regarding oral hygiene and gingival health. Most children had poor oral hygiene (52,5% in the case group and 60% in the control group), with fairly good gingival health (70% in the case group and 55% in the control group). Children with DM had significantly more periodontitis (p=0.05) compared to healthy children. Teeth in advanced eruption stages were significantly higher in DM children compared to control subjects (p=0.048 in stage V and p=0.003 in stage VI).
Association between metabolic control and oral health in children with type 1 diabetes mellitus, (Ferizi et al., 2022)	Analyzing the impact of metabollic control on saliva, dental caries, dental plaque, gingival inflammation, and caries-causing bacteria in saliva.	Epidemiological case-control study in children with type I DM (34 children with good metabolic control (HbA1c < 7,5%) and 46 children with poor metabolic control (HbA 1c >7,5%). Oral status was evaluated using the Decay, Missing, and Filled Teeth indeks for permanent teeth (DMFT), plaque indeks and gingival indeks.	The diabetic group with poor metabolic control had significantly higher DMFT index, plaque index, and gingival index, as well asa more colonies and higher risk of Streptococcus mutans and Lactobacillus compared to children with good metabolic control (p<0.001). The level of diabetic metabolic control did not affect salivary flow rate (p>0.05). The majority of both groups, both with good and poor metaboliccontrol, brushed their teeth once a day and visited the dentist only when necessary (61,3%).
Comparison of the inflammatory states of serum and gingival crevicular fluid in periodontitis patients with or without type 2 diabetes mellitus, (Xu et al., 2023)	To compare the inflammatory state in gingival crevicular fluid (GCF) in periodontitis patients with or without TIIDM and healthy subjects.	Case control study on 100 samples divided into 20 subjects with healthy periodontal conditions (Group H), 40 subjects with periodontitis (Group CP), and 40 subject with periodontitis and type II DM (group DC). Fasting blood glucose (FBG) and HbA1c testing were performed. GCF volume and serum levels of interleukin (IL) 17, visfatin, and the ratio of RANKL (receptor activator of nuclear factor-kappa B ligand)/ osteoprotegerin (OPG) were measured.	GCF volume, total IL-17, visfatin, and RANKL/OPG ratio in GCF and their concentrations in serum were higher (p <0.05) in the CP and DC groups compared with the H group. These values were also higher (p<0.05) in the DC group compared with the CP group, except for visfatin in GCF and IL-17 in serum. At sample sites with pocket depth (PD)≥3mm, GCF volume, IL-17, visfatin, and RANKL/OPG ratio in the DC and CP groups were higher (p<0.05) compared with the H group, and also higher in DC group compared with the CP Group, both with PD≥3mm. The inflammatory state in GCF was positively correlated with systemic inflammation and both were positively correlated with FBG.
Evaluation of Periodontal Status Amongst the Diabetic Patients Visiting Private	Determining periodontal status and treatment needs using the Community	Cross sectional study of 102 diabetic patients in the out patients clinic of a private dental clinic in Ahmedabad,	The age group of 56-65 years showed the worst periodontal status among all groups and required the highest periodontal treatment. This group of diabetic patients is more

Dental Clinic in Ahmedabad Using CPITN, (Patel et al., 2022)	Periodontal Indeks of Treatment Needs (CPITN) indeks in adult diabetic patients.	screened by a single examiner based on WHO criteria, using a mouth mirror and CPITN probe.	susceptible to the development of destructive forms of periodontal disease. Periodontitis is a periodontal disease that is found to occur more frequently than gingivitis in patients with TIIDM.
The association between Type 1 diabetes mellitus and periodontal diseases, (K. T. Sun et al., 2019)	Analyzing a nationwide population-based study in Taiwan, with a follow-up period of 14 years, to investigate the risk of periodontal diseases (PDs) in TIDM patients.	Cohort study indentifying newly diagnosed patients with TIDM from 1998 to 2011. Participants consisted of 4248 patients in the TIDM cohort and 16992 individuals in the non TIDM cohort.	TIDM patients showed an increased risk of PDs compared to non TIDM individuals (aHR 1,45). TIDM patients who visited the emergency room more than twice per year had a higher aHR of 13,0 for developing PDs, and the aHR for PDs in TIDM patients who were hospitalized more than twice per year was 13,2.
Periodontal Status of Type 2 Diabetic Patients Attending UNRWA Health Centers in Gaza Governorates, (Alqedra & Aljeesh, 2020)	Evaluating periodontal status in TIIDM patients visiting UNRWA health centers in the GAZA Strip.	Cross-sectional analytical study of 406 TIIDM patients selected through systematic random sampling from 5 UNRWA health centers. Basic method tools from the World Health Organization (WHO) were used to cllect data and assess oral health.	16.4% of participants did not experience gingival bleeding, with an average number of teeth without gingival bleeding of (9,79), experiencing gingival bleeding of (9,91), and not present for bleeding test of (9,14). 2,4% of participants did not have periodontal pockets, with an average number of teeth without periodontal pockets of (7,15), having 4-5 mm pockets of (7,84), having 6 mm or more pockets of (4,96), and not present for pocket measurement of (9,13). Gingival bleeding was statiscally significantlyassociated with gender and frequency of toothbrushing, but there was no statiscally significant association between gingival bleeding and periodontal pockets, social demographics, HbA1c levels and duration of diabetes.
Effect of diabetes mellitus on periodontal health status, salivary flow rate and salivary pH in patients with chronic periodontitis, (Ibraheem et al., 2020)	To determine and compare the severity of periodontal health and salivary parameters in diabetic and non-diabetic patients with chronic periodontitis.	Case control study on 70 patients divided into three groups: Group 1 consisted of 25 patients with type II DM and chronic periodontitis, Group 2 consisted of 25 patients with chronic periodontitis without a history of systemic disease, and Group 3 consisted of 20 subjects with healthy periodontium and healthy systemic conditions, with periodontal parameters (plaque index, gingival index, pocket depth, and clinical attachment level) recorded for each patient.	All clinical periodontal parameters were highest in group 1 compared with groups 2 and 3. Comparison between pairs of groups revealed significant differences between groups 1 and 2 for plaque index, gingival indeks, pocket depth, and clinical attachment level, and highly significant differences for plaque indeks and gingival indeks between groups 2 and 3, and between groups 1 and 3. Salivary flow rate and pH were lower in group 1 compared with groups 2 and 3. Intergroup comparison for salivary parameters also showed significant differences between groups 1 and 2, with No. significant differences between groups 2 and 3.

Oral health-related quality of life in type 2 diabetic patients of Yogyakarta General Hospital, (Agustina et al., 2022)	Evaluating oral health-related quality of life (OHRQoL) of outpatients with type II DM, using the Geriatric Oral Health Assessment Indeks (GOHAI) and Xerostomia Inventory (XII])	Analytical observational study with a cross-sectional approach, involving 50 male outpatients and 32 female outpatients with type II DM (Aged 40-81 years) at RSU Yogyakarta.	A total of 49 (59,76%) subjects had low GOHAI scores and 33 (40,24%) high; 78 (95,12%) with and 4 (4,88%) without periodontal tissue abnormalities; 79 (96,34%) with poor OH and 3 (3,66%) WITH good OH; 17 (20,73%) with coated tongue ≤50%; >50% and 65 (79,27%) with coated tongue ≤50%; 34 (41,46%) with the number of teeth <20 and 48 (58,54%) with the number of teeth ≥20; and 39 (47,56%) with xerostomia and 43 (52,44%) with normal status. The nuber of teeth was significantly correlated with the proportion of GOHAI status in patients with type II DM (p=0.032). type II DM patients with ≥20 teeth had a significantly higher proportion of high GOHAI status compared to <20 teeth the majority of outpatients with type II DM had poor OHRQoL as a reflection of oral conditions which were partly influenced by patients with <20 teeth.

Inflammation and Damage to Periodontal Tissue

One of the main effects of DM is increased inflammation in various body tissue. This condition occurs due to increased levels of TNF-α (Rohani, 2019). DM causes increased expression of inflammatory cytokines in periodontal tissues, such as increased IL-1β and prostaglanddin E2 found in gingival crevicular fluid (GCF) in patients with type I and type II DM (Chung et al., 2024). Various studies have reported increased expression of TNF-α, IL-1β, IL-17, IL-23, and IL-6 in the gingiva of patients with DM. increased expression of these inflammatory cytokines causes increased blood vessel permeability and recruitment of inflammatory cells, as well as increased bone resorption (Graves et al., 2020).

Increased inflammation also induces greater production and activation of matrix metalloproteinases, connective tissue demage, and increased apoptosis of matrix-producing cells such as fibroblast and osteoblasts, thereby slowing the healing process. the production of anti-inflammatory factors such as IL-4, IL-10, and transforming growth factor-β (TGF-β), contribute to increased periodontal inflammation in diabetics. Several anti-inflammatory cytokines produced by T cells and M2 macrophages are reduced in diabetic complications along with decreased anti-inflammatory activity of peroxisome proliferator-activated receptor-α, thereby increasing periodontal inflammation and gingival changes in diabetics (SriChinthu et al., 2021).

Other conditions resulting from the influence of chronic high glucose levels, trigger cytokine expression and responses to cytokine stimulation, including the production of reactive oxygen species (ROS). High glucose levels in all tissues of people with DM causes an increase, which then contributes to cell and DNA demage and increased inflammation (Graves et al., 2020). The interaction of AGEs with their receptors AGEs (RAGE) can stimulate the production of ROS, triggering the expression of inflammatory cytokines (Alqedra and Aljeesh, 2020).

Periodontal examination showed higher pocket depth and clinical attachment loss (CAL) levels in the DM group compared to the non-DM periodontitis group, indicating that periodontitis patients with DM experience more severe periodontal tissue demage (Patel et al., 2022).

Hyperglycemia in DM increases AGEs, which accelerate pro-inflammatory effects, thus affecting various body systems, including periodontal tissues. Several studies evaluating gingival status using gingival indeks, showed that gingival health was worse in obese and non-obese diabetic patients compared to non-diabetic obese patients (SriChinthu et al., 2021).

Distribution of gingival status based on blood sugar control showed that the most severe cases were found in subjects with poor blood sugar control, namely 10 people (52,6%). This condition occurs because poor blood sugar control greatly affects the health of gingival tissue in diabetics. Uncontrolled diabetes causes demage to white blood cells, making teeth more susceptible to infection and increasing the risk of gingival problems to changes in gingival status (Zahrawi Astrie Ahkam, Hasrini, Amirah Maritsa, Arfiah Jauharuddin, 2023).

Damage to Periodontal Ligament Cells, Osteoblasts, and Osteocytes

DM causes a decrease in the number of periodontal ligament cells, osteoblasts, and osteocytes, and increases apoptosis which ultimately has an impact on gingival changes and regeneration of periodontal and bone tissue (Rohani, 2019). In periodontal ligament cells, DM reduces the number of fibroblasts that are important for the maintenance of periodontal structures. Patients with type I DM have a 6-7 times higher risk of fracture with reduced bone mineral density, while patients with type II DM have a 1,5 times higher risk of fracture

with decreased bone strength without reduced bone mineral density (Wildan et al., 2023).

DM significantly reduces bone formation, associated with decreased expression of transcription factors such as Runt-related transcription factor 2 (RUNX2), the human homologue of the distal-less gene in drosophilia, and C-fos. Diabetes reduces the number of bone-lining cells, osteoblasts and periodontal ligament fibroblast, and increases apoptosis of these cells. AGE products may contribute to the decrease in osteoblast precursors seen in diabetes. Diabetes also increases apoptosis of mesenchymal stem cells and periodontal ligament cells, and reduces differentiation of mesenchymal stem cells into osteoblasts (Agustina et al., 2022; Rohani, 2019).

Accumulation of AGEs in bone tissue also triggers osteoblast apoptosis and impairs bone regeneration. RAGE inhibitors have been shown to reduce TNF production and periodontal bone loss. Increased binding between RAGE and AGE activates nuclear transcription factor-κB (NF-κB), leading to increased expression of NF-κB receptor activator ligand (RANKL), which mediates osteoclastogenesis. Accumulation of AGEs can also stimulate IL-6 which will reduce osteoblast proliferation and activity and increase osteoclast activity. Another study explained that IL-6 reduces osteoblast formation and fuction, thereby reducing the number of osteoblasts in DM patients (Perraudin, 2019).

High pro-inflammatory mediators in patients with DM increase lipid peroxidation and dyslipidemia resulting in osteoclastogenesis. High levels of TNF-α increase the RANK/ osteoprotegrin (OPG) rasio causing increased bone resorption. Chronic inflammation stimulates the expression of pro-apoptotic genes such as bcl-2-like protein (BAX) and decreases the expression of genes that stimulate osteoblast formation such as Fos antigen and RUNX2, resulting in more severe bone damage (Rapone et al., 2021; Zahrawi Astrie Ahkam, Hasrini, Amirah Maritsa, Arfiah Jauharuddin, 2023).

Periodontal Disease

Poor glycemic control is associated with the onset and progression of gingivitis, periodontitis, and alveolar bone loss. Periodontal disease has been reported to have a higher incidence and prevalence in patients with type I and type II diabetes. The prevalence of severe periodontitis in diabetic patients compared to non-diabetics was found to be 59,6%: 39% (Rohani, 2019).

The most striking changes is uncontrolled diabetes are a decrease in the body's defense mechanisms and an increased susceptibility to infection, leading to destructive periodontal disease. Glucose content in gingival fluid and blood is higher in individuals with diabetes compared to those without diabetes, even though plaque scores and the GI are similar (Tabatabaei et al., 2021). Increased glucose in the gingival fluid and blood in diabetic patients can alter the microflora environment, triggering qualitative changes in bacteria that contribute to the severity of periodontal disease seen in patients with uncontrolled diabetes. In patients with uncontrolled diabetes, polymorphonuclear granulocytes (PMNs) and monocytes/ macrophages are impaired, thus reducing the primary defense of PMNs against periodontal pathogens and increasing bacterial proliferation (Chung et al., 2024; Costa et al., 2023).

Mechanisms explaining increased susceptibility to periodontal disease include alterations in host defense responses (such as neutrophil dysfunction), subgingival microbial flora, collagen structure and metabolism, vascularization, and gingival crevicular fluid, as well as heredity. Several risk factors have been reported to make patients with DM more susceptible to the development of periodontal disease, including poor oral hygiene, poor metabolic control, longer duration of DM and smoking (Zahrawi Astrie Ahkam, Hasrini,

Amirah Maritsa, Arfiah Jauharuddin, 2023).

Several studies have shown that periodontal disease has a negative impact on diabetes and treatment of periodontal disease has a positive effect on blood sugar control. Elimination of pathogens through treatment reduces inflammation which ultimately reduces insulin resistance, thus lowering glucose levels. Therefore, there is a bidirectional relationship between periodontal disease and diabetes. In the adult population, periodontal disease is the leading cause of tooth mobility and ultimately tooth loss (Costa et al., 2023; Nadhia Anindita Harsas, Robert Lessang, Yuniarti Soeroso, 2019).

a. Gingivitis

Gingivitis is the early stage of periodontal disease, characterized by inflammation limited to the gingiva, gingiva bleeding and swollen gums, and can be treated with good oral hygiene (Batool et al., 2022). This disease can progress to periodontitis if left untreated, characterized by inflammation, loss of connective tissue, and irreversible destruction of periodontal tissue. Several previous studies have identified diabetes as a risk factor for the prevalence of gingivitis (Nadhia Anindita Harsas, Robert Lessang, Yuniarti Soeroso, 2019).

b. Periodontitis

Periodontitis is a chronic inflammatory disease characterized by demage to tooh-supporting structures such as the periodontal ligament and alveolar bone. The prevalence of severe periodontitis is 10% to 15% in the general population (Stødle et al., 2021) periodontitis is known as a complication of DM, increasing the gingival response to bacterial plaque due to high glucose levels in GCF, neutrophil dysfunction, and changes in collagen metabolism (Kudiyirickal & Pappachan, 2024). Inflammation of the periodontal tissues triggered by the long-term presence of subgingival biofilm (dental plaque). This inflammatory response is characterized by secretion of inflammatory mediators and the destruction of periodontal tissues. the most studied mediators include IL-1β, IL-6, PGE2, TNF-α, RANKL, and MMPs; especially MMP-8, MMP-9, and MMP-13, as well as T-cell regulatoru cytokines (e.g. IL-12, IL-18) and chemokines. The complexity of the cytokine network in periodontal pathogenesis is becoming increasingly clear and it is recognized that there is significant heterogeneity in the inflammatory response between individuals. This heterogeneity occurs not only between individuals, but also within individuals over time, and is influenced by genetic, epigenetic, and enviromental factors. The sum of the inflammatory responses in the periodontal tissues determines the pattern and rate of disease progression (Rohani, 2019; Xu et al., 2023).

CONCLUSION

Based on literature review of 21 articles, researchers concluded that changes in gingival status in patients with DM are caused by the interaction between hyperglycemia, increased oxidative stress, and immune system dysfunction that worsens inflammation and gingival tissue damage. Increased free radical production, tissue healing due to vascularization dysfuction, and decreased collagen production exacerbate tissue damage, thereby increasing the risk of periodontal disease in diabetics. Therefore, it is hoped that the public will be more concerned about implementing a healthy lifestyle, including increasing the frequency of physical activity, regulating diet by paying

attention to the amount and frequency of food (2-3 times a day), and the type and time of meals. In addition, it is important to reduce smoking habits and check blood sugar levels regu;ary, especially for individuals over 45 years of age and those with a family history of diabetes, to prevent oral complications due to DM. Medical personnel are also expected to continue to improve health services and be more active in providing education to ht public regarding risk factors and complications of DM.

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