



GESTATIONAL DIABETES MELLITUS AND CHRONIC PERIODONTITIS-EXPLORING THE LINK BY IMMUNOLOGICAL BIOMARKERS-A REVIEW

Ashwini S* and Shivani

Department of Periodontology, Faculty of Dental Science, Ramaiah university of Applied Science
Bengaluru, India

ARTICLE INFO

Article History:

Received 4th September, 2018

Received in revised form 25th
October, 2018

Accepted 23rd November, 2018

Published online 28th December, 2018

Key words:

GDM, Pregnancy, Periodontitis, Diabetes
mellitus, Inflammatory cytokines

ABSTRACT

Periodontal disease is one of the most common chronic disorders of infectious origin known in humans. It has found to be associated with systemic diseases such as cardiovascular diseases, diabetes mellitus and adverse pregnancy outcomes. Diabetes mellitus (DM) has been proposed to be biologically linked with chronic periodontitis. Moreover, periodontitis has been considered the sixth complication of DM. Therefore, the relationship between periodontitis and DM is widely accepted. Maternal chronic periodontal disease could induce a sustained systemic inflammatory response that may result in a state of insulin resistance in response to periodontal infection exacerbating the pre-existing pregnancy induced insulin resistance and cause impaired glucose tolerance and the manifestation of Gestational Diabetes Mellitus. It has been hypothesized that periodontitis, as an infectious process could contribute to the insulin resistance observed in woman with gestational diabetes mellitus and thus affect the overall health of patient. Based on the inclusion and exclusion criteria defined, titles isolated from the electronic databases were analysed. The abstracts of selected titles were screened by one reviewer. The full texts of 30 publications selected by the reviewer were further studied, which led to the exclusion of 19 articles. Finally, 11 publications were included in the review. In the present review, it was noticed that immunological cytokines play a significant role in causation as well as resolution of inflammation in periodontitis as well as Gestational Diabetes Mellitus. It was also observed that periodontitis is one of the risk factors enhancing glycaemic levels in pregnant women thus leading to GDM.

Copyright©2018 **Ashwini S and Shivani**. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Chronic periodontitis, also known as adult periodontitis, is an infectious inflammatory disease caused by the bacteria of the dental plaque, resulting in the progressive destruction of the tissues that support the teeth. Periodontal disease is characterized by periods of exacerbation interspersed with periods of remission and presents a local microbial burden that initiates local inflammation and local tissue destruction. It has also been suggested that the hormonal changes during pregnancy, particularly the marked increases in oestrogen and progesterone, may be in part responsible for the increased risk of developing periodontitis. Other possible factors that may be involved in the aetiology include changes in blood flow to the gingiva.

Although limited by numerous confounding factors, the relationship between periodontal disease and health status has gained widespread interest in the medical and dental literature. Observational studies performed over the past 10 years have

connected periodontal disease with cardiovascular disease, diabetes mellitus, respiratory infections, and Alzheimer's disease, among others. Similarly, periodontal infection has also shown a bidirectional association with many systemic disease.

It has been seen that chronic periodontitis is associated with the incidence of coronary heart disease (CHD) among younger men, independent of established cardiovascular risk factors (HH Mawardi et al- 2015). Cumulative evidence supports a causal association between periodontal infection and atherosclerotic cardiovascular disease or its sequelae. Also results of various studies have concluded that there exists link between hypertension and periodontitis as hypertension increases the risk of various adverse cardiovascular events such as atherosclerosis, stroke, and coronary heart disease. Studies also showed that periodontitis was associated with respiratory disease. Following a previous systematic review of the association between respiratory diseases and oral health (Xin-Fang Leong *et al* 2014), it was concluded that there is a fair evidence of an association of pneumonia with oral health. A significant association is also noted between rheumatoid arthritis and periodontal disease (J Koziel - 2014).

***Corresponding author: Ashwini S**

Department of Periodontology, Faculty of Dental Science,
Ramaiah university of Applied Science Bengaluru, India

Review Studies

S.No	Author	Year	Research Focus	Methods and Methodology	Findings	Conclusion
1.	Janet M. Guthmiller, Jeanne R. Hassebroek-Johnson, Duane R. Weenig, Georgia K. Johnson, H. Lester Kirchner, Frank J. Kohout, and Stephen K. Hunter	2001	To examine the association of type 1 diabetes mellitus (DM) on the periodontal status of pregnant women.	<p>STUDY DESIGN- Observational study</p> <p>STUDY POPULATION- Pregnant women between 20 to 39 weeks gestation. 33 patients-13 subjects with type 1 DM and 20 non-diabetics</p> <p>STUDY SETTING- University of Iowa Hospitals and Clinics Obstetrical Clinics</p> <p>METHODS AND METHODOLOGY- The mean age of the diabetics and non-diabetics was 28.5±7.1 and 27.0±7.3</p> <p>The following parameters were assessed at Ramfjord's index teeth: (PI), (GI),(PD), (GM) location, and (CAL).</p>	<p>Diabetic subjects had significantly (P <0.001) higher PI (1.48 ± 0.69) and GI (1.77 ± 0.44) scores than non-diabetics (PI = 0.63 ± 0.38; GI = 0.93 ± 0.48).</p> <p>Mean PD for diabetics (2.95 ± 0.69 mm) was significantly different (P <0.024) from that of non-diabetics (2.44 ± 0.32 mm). Significant differences were seen for GI (P <0.001), PD (P = 0.005), GM location (P <0.001), and CAL (P <0.001) when assessing the effect of diabetes and controlling for plaque.</p> <p>While when assessment of the effect of plaque and after controlling variables for diabetes, the only significant difference was GI (P = 0.001).</p>	The results of this study demonstrate that periodontal inflammation and destruction are increased in pregnant diabetics as compared to non-diabetic pregnant patients
2.	Karen F. Novak, George W. Taylor, Dolphus R. Dawson, James E. Ferguson II, John Novak.	2006	Women with a history of gestational diabetes mellitus (GDM) during pregnancy would exhibit more severe periodontal disease than controls without a history of diabetes during pregnancy	<p>STUDY DESIGN- Cross-Sectional Study, Observational.</p> <p>STUDY POPULATION- 4244 females. (20-59yrs)</p> <p>STUDY SETTING- United States Of America</p> <p>METHODS AND METHODOLOGY- One hundred and thirteen had a history of GDM (GDM+), while 4,131 had no history of diabetes before or during their pregnancies (GDM-). Women were further classified by the presence or absence of diabetes mellitus (DM+ or OM-) at the time of their NHANES III examination. The oral health data-based on random half mouth evaluation of two sites per tooth. Statistical analyses included assessing bivariate associations and 3-way stratified associations of important covariates with periodontitis.</p> <p>STUDY DESIGN- Observational, cross-sectional study.</p> <p>STUDY POPULATION- 256 pregnant and 4234 non-pregnant women.</p> <p>Women were classified into those with gestational diabetes mellitus (GDM) in current pregnancy, with GDM in previous pregnancy, and with type 1 or 2 diabetes. (age 15-44 years)</p> <p>STUDY SETTING- Unites States Of America.</p> <p>METHODS AND METHODOLOGY- The study population was divided into patients who developed GDM in current pregnancy, patients with GDM in previous pregnancy, and with type 1 or 2 diabetes. Diagnosis and assessment of periodontal disease was based on clinical criteria (CAL and PD).</p> <p>Univariate analysis was performed to compare the difference in prevalence between different groups.</p>	<p>The PD prevalence among women who were GDM+DM- was 9.0% and 4.8% for those who were GDM-DM-. PD prevalence for women who were GDM+DM+ subjects was 30.5% and 11.6% respectively.</p> <p>Alogistic regression model, controlling for age, calculus, smoking, and income estimated women who were GDM+DM+ were more likely to have periodontal disease than women who were GDM-DM- (0r-8.7% CI-2.9,29.8) and women who were GDM-DM+.</p> <p>The GDM+DM- group also tended to be more likely to have PD more than the GDM-DM- and GDM-DM+ groups. However, the odds ratios were not statistically significant</p>	These results support the hypothesis that women with gestational diabetes mellitus (GDM) during pregnancy may be at greater risk for developing more severe periodontal disease than pregnant women without GDM.
3.	Xu Xiong, Pierre Buekens, Sotirios Vastardis, Gabriella Pridjian.	2006	To examine the relationship between periodontal disease and different types of diabetes in pregnant and non-pregnant women.	<p>STUDY DESIGN- Observational, cross-sectional study.</p> <p>STUDY POPULATION- 256 pregnant and 4234 non-pregnant women.</p> <p>Women were classified into those with gestational diabetes mellitus (GDM) in current pregnancy, with GDM in previous pregnancy, and with type 1 or 2 diabetes. (age 15-44 years)</p> <p>STUDY SETTING- Unites States Of America.</p> <p>METHODS AND METHODOLOGY- The study population was divided into patients who developed GDM in current pregnancy, patients with GDM in previous pregnancy, and with type 1 or 2 diabetes. Diagnosis and assessment of periodontal disease was based on clinical criteria (CAL and PD).</p> <p>Univariate analysis was performed to compare the difference in prevalence between different groups.</p>	<p>In pregnant women, the prevalence of periodontitis was 44.8% in women with GDM and 13.2% in non-diabetic women, with adjusted odds ratio (aOR) of 9.11 (95% confidence interval [CI] 1.11-74.9).</p> <p>In non-pregnant women, the prevalence of periodontitis was 40.3% in women with type 1 or 2 diabetes, 25.0% in women with previous history of GDM, and 13.9% in non-diabetic women, with a OR of 2.76 (1.03-7.35) for women with type 1 or 2 diabetes.</p>	An association between periodontal disease and GDM was found.
4.	Steven Offenbacher, Dongming Lin, Robert Strauss, Rosemary McKaig, Joanna Irving, Silvana P. Barros, Kevin Moss, David A. Barrow, A. Hefli, and James D. Beck	2006	The present study examined the effects of periodontal therapy during pregnancy.	<p>STUDY DESIGN- A Randomized, delayed-treatment, controlled pilot trial</p> <p>STUDY POPULATION- 74 Patients were included.</p> <p>STUDY SETTING- Wake County, North Carolina Human Services prenatal Clinic.</p> <p>METHODS AND METHODOLOGY- Intervention group received SRP and polishing and they were given a sonic power toothbrush. Control group received SRP-6 weeks post-partum. Clinical parameters were recorded. GCF, subgingival and serum samples were collected. Eight oral pathogens and levels of GCF, IL-1beta, PGE2 and IL-6 were assessed. Serum levels of IL-6, ICAM, GP-130 and CRP were analyzed</p>	<p>Periodontal intervention resulted in a significantly decreased incidence odds ratio (OR) for preterm delivery (OR = 0.26; 95% confidence interval = 0.08 to 0.85), adjusting for baseline periodontal status which was unbalanced after randomization.</p> <p>Pregnancy without periodontal treatment was associated with significant increases in probing depths, plaque scores, GCF IL-1b, and GCF IL-6 levels.</p> <p>Intervention resulted in significant improvements in clinical status (attachment level, probing depth, plaque, gingivitis, and bleeding on probing scores) and significant decreases in levels of Prevotellanigrescens and Prevotella intermedia, serum IL-6sr, and GCF IL-1b.</p>	<p>Study showed further evidence supporting the potential benefits of periodontal treatment on pregnancy outcomes.</p> <p>Treatment was safe, improved periodontal health, and prevented periodontal disease progression. Pregnancy without periodontal treatment was associated with increase in clinical parameters and GCF IL-1 beta and IL-6 levels. A significant decrease in Prevotellanigrescens and Prevotella intermedia, serum IL-6sr, and GCF IL-1b was observed in intervention group</p>

5.	Adrian Kasaj, Gregor Georg Zafropoulos, HakiTekyatan, Alex Pistorius and Brita Willershausen	2008	To evaluate the association between type I diabetes mellitus (DM) and periodontal disease in pregnant women.	<p>STUDY DESIGN-CASE-CONTROL STUDY</p> <p>STUDY POPULATION-52 pregnant women aged 27.9±6.9 years with type I DM. 42 non-pregnant type I female diabetics (mean age: 27.9±6.1 years) and 121 healthy non-pregnant women (mean age: 29.1±5.7 years) without diabetes formed the control group.</p> <p>STUDY SETTING- General Hospital (Munich-Schwabing),Germany.</p> <p>METHODS AND METHODOLOGY-All subjects were given a clinical periodontal examination (PPD), (CAL),assessment of plaque and gingivitis scores (SBI).The periodontal measurements were recorded at 6 sites on each of the 6 Ramfjord teeth (16, 21, 24, 36, 41, 44) using a pressure sensitive probe. Blood parameters included levels of hemoglobin, glycosylated hemoglobin, total cholesterol, triglyceride and leukocytes.</p> <p>SPSS software used to perform stastical analysis along with paired t-test.</p>	The pregnant diabetic subjects showed despite a good metabolic control significantly higher values for the SBI compared to the controls. Pregnant diabetic subjects displayed a significant correlation between the dose of insulin per day and PPD (p≤0.05) as well as the CAL (p≤0.05).	The results of the study indicate that pregnant diabetics demonstrate a higher degree of periodontal inflammation and destruction compared to non-pregnant diabetics and healthy non-pregnant patients despite a good metabolic control compared to non pregnant diabetics with poor metabolic control.
6.	Xu Xiong , Karen E. Elkind-Hirsch, SotiriosVastardis, Robert L. Delarosa, Gabriella Pridjian, and Pierre Buekens	2009	To examine whether maternal periodontal disease is associated with GDM.	<p>Study Design- Case-control study</p> <p>Study Population- 53 pregnant women with GDM and 106 pregnant women without GDM</p> <p>Study Setting-Woman’s Hospital, Baton Rouge, USA.</p> <p>Methods And Methodology- Single blinded examiner.</p> <p>-The severity of periodontal disease was measured in quartiles of PD and CAL.</p> <p>-Univariable analysis and multivariable logistic regression were used.</p>	The percentage of periodontitis was 77.4% in women with GDM and 57.5% in pregnant non-GDM women with an odds ratio (OR) and 95% confidence interval (CI) of 2.5 (1.2–5.3).	This study supports the hypothesis of an association between periodontal disease and GDM.
7.	Fawzia A. Habib	2009	To evaluate periodontal status among females with gestational diabetes in Ohud Hospital, Al Madinah Al-Munwarrah and to assess its effect on insulin sensitivity and lipid metabolism.	<p>Study Design- CROSS-Sectional Descriptive Study</p> <p>Study Population- 250-100 pregnant with gestational diabetes (GDM), and 100 were pregnant without GDM and 50 were normal non pregnant females.</p> <p>Study Setting- Ohud Hospital, Al Madinah Al-Munwarrah.</p> <p>Methods and Methodology- Case history followed by physical examination and assessment of periodontal status. Laboratory tests include fasting blood sugar, insulin levels, Homeostasis Model Assessment Insulin Resistance (HOMA-IR) test and serum lipids. Serum levels of inflammatory markers (CRP, ESR, IL-1 , and TNF-) was also measured. The periodontal health status was assessed using the Community Periodontal Index of Treatment Needs.</p>	Females with GDM showed higher systolic and diastolic blood pressure, fasting insulin, HOMA-IR, serum lipids and serum inflammatory markers levels than the other groups. Serum fasting insulin levels, HOMA-IR, triglyceride levels, and serum inflammatory markers were higher in females with severe periodontal diseases.	The prevalence of periodontal disease is high among pregnant females especially those with GDM. Periodontal disease had important deleterious effects on carbohydrates and lipids metabolism. Strategies are needed to improve dental health care and to reduce periodontal diseases among pregnant females.

9.	Priyam Mishra, Bagavad Gita and Chandrasekaran SC	2014	To assess the periodontal status in patients with and without GDM To examine any association between maternal periodontal disease and GDM	<p>Study design-case- control study</p> <p>Study population-90 patients, out of which 30 were cases & 60 were controls .</p> <p>Study Setting-SreeBalaji Dental College & Hospital & Primary Health Centre, Adyar, Chennai between October 2009 and August 2011.</p> <p>Methods And Methodology- To assess the periodontal status, a full-mouth periodontal examination, assessing the probing depth, clinical attachment level, bleeding on probing and gingival recession was performed on all study participants, using the WHO periodontal probe by a single trained examiner.</p> <p>Tests for proportions and associations were performed by using chi-square statistics.</p>	<p>The results showed that only age of the mother OR 1.387 (95% CI 1.129, 1.704), body mass index OR 1.190 (95% CI 1.029, 1.377), and family history of DM OR3.98 (95% CI 1.09, 14.49) were significant predictors of GDM.</p> <p>None of the periodontitis condition was found to be significant predictor of GDM.</p>	The study did not show any positive correlation between GDM & periodontal disease.
10.	Zahra Kashi, ZohrehEhsani, AvidehMaboodi, Adele Bahar, Nadia Rezai	2015	To investigate the relation between periodontitis and related inflammatory mediators and gestational diabetes mellitus	<p>Study Design- Case Control Study.</p> <p>Study Population- 100 singleton pregnant women with gestational diabetes and 100 singleton pregnant women with normal glucose level (gestational age >20 weeks).</p> <p>Study Setting- Mazandaran University of Medical Sciences, Sari, Iran</p> <p>Methods And Methodology- The patients underwent dental examinations and those with periodontitis and gingivitis were identified. Blood samples were taken and ESR and hsCRP were measured in all patients. Data was analyzed in SPSS applying independent t-test and Chi- square.</p>	<p>The prevalence of periodontitis in patients and controls were 36% and 28%, respectively (P= 0.22). All periodontitis were moderate and no severe periodontitis was observed. Gingivitis was seen in both pregnant women with diabetes (74%) and control patients (83%) (P= 0.12).</p> <p>Among the subjects 18% of patients and 22% of the control group had severe gingivitis while others had moderate to mild gingivitis (P= 0.45). Dental plaques were seen in 73% of pregnant women with diabetes and 91% of the control group (P= 0.01).</p> <p>No significant relationship was seen in inflammatory mediators between the individuals with/without periodontitis and gingivitis.</p>	In this study, no relationship was found between gestational diabetes, gingivitis, severity of gingivitis, periodontitis, and inflammatory markers. According to the lower levels of dental plaque in pregnant women with gestational diabetes other reasons rather than poor oral hygiene are believed to be involved.
11.	ÖzgünÖzçaka, Banu Ceyhan-Öztürk, Pınar Gümüş, AliyeAkcalı, Nalbantsoy, NurcanBuduneli	2016	To compare clinical periodontal findings, GCF and serum levels of tumor necrosis factor-alpha (TNF- α), interleukin-10 (IL-10), and IL-33 between women with and without GDM.	<p>Study Design-Case Control</p> <p>Study Population-161 patients.</p> <p>Study Setting- Endocrinology and Metabolism outpatient clinic, State Hospital of Aydın, Turkey</p> <p>Methods And Methodology-Case: 96 females(22-24 yrs) with GDM Controls: 65 non-diabetic pregnant females age(19-38 yrs)</p> <p>Full-mouth plaque index, bleeding on probing and probing depth were recorded.</p> <p>Serum and GCF samples were collected.</p> <p>Age, smoking status, pre-pregnancy body mass index, and pregnancy outcomes were recorded.</p> <p>Serum and GCF IL-10, IL-33, TNF-α level were determined.</p>	<p>The GDM group was significantly older than the control group with an age difference of 3.27 years (mean ages were 32.05 and 28.78 years, respectively)(p < 0.0001).</p> <p>Plaque Index (50.0 and 30.0 p = 0.005), bleeding on probing (50.0 and 30.0 p = 0.003) values were significantly higher in the GDM group.</p> <p>Serum TNF-a concentrations were significantly higher in the non GDM group than the GDM group (p = 0.001). GCF IL-10 concentrations and total amounts were significantly higher in the GDM group than the controls (p = 0.004 and p < 0.0001, respectively)</p>	Plaque Index, bleeding on probing values was significantly higher in the GDM group. Serum TNF- α concentration was significantly higher in the non GDM group than the GDM group. IL-10 concentrations and total amounts were significantly higher in the GDM group than the controls.

Recent studies have also shown that periodontal disease is often found to be related to adverse pregnancy outcomes seen during pregnancy and can also lead to enhanced insulin level in pregnant patients thus further enhancing the periodontal destructive process (Patricia Weidlich et al, 2018).

Approximately 40% of pregnant women have some form of periodontal disease. The most common maternal oral diseases that potentially could impact pregnancy outcome include dental caries, gingivitis, and periodontitis. It was seen that there is a significant association between preterm birth and/or low birth weight and periodontitis, irrespective of parity, race, and maternal age. It has also been stated that periodontitis appears to be an independent risk factor for poor pregnancy outcome and preliminary evidence suggests that periodontal intervention may reduce this adverse pregnancy outcome. While it has been established that people with diabetes are more prone to developing periodontal disease, new research is suggesting that periodontal disease may, in turn, be a risk factor for diabetes. The association between periodontal disease and type 1 or 2 diabetes has been well established. However, few studies have examined the relationship between periodontal disease and GDM.

Gestational diabetes mellitus (GDM) is a condition defined as any degree of glucose intolerance that starts or is first recognized during pregnancy, and it is characterized by recent hyperglycaemia as a consequence of an association between insulin resistance and inadequate insulin secretion (Buchanan et al, 2007). A few studies have suggested that pregnancy is a modifying factor of periodontal disease (Laine, 2002; Mascarenhas et al, 2003).

Periodontal disease induces local and host immune responses and is able to cause transient bacteraemia. Studies by Dasanayake et al., 2008 concluded that the presence of *T. forsythia* in vaginal flora is a potential risk factor for gestational diabetes mellitus, but this should be confirmed in future studies. Although there is lack of clear correlation between the gene polymorphisms and GDM, a few studies suggested that cytokines such as TNF- α , IL-6, and IL-1 polymorphisms may be associated with the risk of insulin resistance or type 2 diabetes as well as periodontal disease. Therefore, there is a possibility that pre-existing genetic polymorphisms result in imbalances between the pro vs. anti-inflammatory cytokine systems predisposing to both periodontal disease and GDM simultaneously. So, the purpose of this review was to identify the best available evidence to establish the relationship between GDM and periodontitis.

Study Selection

Publications were deemed eligible for inclusion in this review, if following parameters were present:

- Clinical trials
- Immunological Biomarkers associating GDM and periodontitis.
- Clinical Parameters assessing efficacy of NSPT in periodontitis and diabetes.
- Criteria followed for exclusion of publications were:
- Review article
- Immunological Studies-in vivo or in vitro

- Not in the English language

Outcome Measures

The primary outcome measure was to check whether there is a relationship between chronic periodontitis and gestational diabetes mellitus and to assess efficacy of non-surgical periodontal therapy in pregnant females and diabetic patients.

Information Sources and Literature Search

A search was done in PubMed and Google scholar by using the following keywords Pregnancy, Diabetes, Periodontitis, GDM, Immunological Biomarkers, Gingival Crevicular Fluid, and Periodontal Clinical Parameters. The search was restricted to papers published in humans and clinical trials.

In addition hand search of most relevant scientific journals in periodontology such as journal of clinical periodontology and journal of periodontology was also done. Researches with relevant information and published in English language were considered for inclusion in the review.

Based on the inclusion and exclusion criteria defined, titles isolated from the electronic databases were analysed. The abstracts of selected titles were screened by one reviewer. The full texts of 30 publications selected by the reviewer were further studied, which led to the exclusion of 19 articles. Finally, 11 publications were included in the review.

DISCUSSION

Periodontal disease induces local and host immune responses and is able to cause transient bacteraemia. Viable bacteria, bacterial products (e.g., lipopolysaccharide) from the subgingival plaque and pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6, IL-8, and C-reactive protein) from the inflamed periodontal tissues can enter the circulation and trigger a maternal systemic inflammatory response. Pregnancy itself is a stressful state with increased inflammatory activity, increased gingival inflammation and increased insulin resistance. It is known that pancreatic β -cell destruction can result from the pro-inflammatory imbalance created by sustained elevation of cytokines (e.g., IL-1 β and TNF- α). Therefore, maternal chronic periodontal disease could induce a sustained systemic inflammatory response that may result in a state of insulin resistance.

Studies have shown relationship between GDM and periodontitis based on periodontal clinical parameters i.e., Bleeding on Probing, Clinical Attachment Level, Probing pocket depth and immunological biomarkers which include TNF- α , IL-1 β , IL-6, IL-8, IL-10, IL-33 and C-reactive protein. It was also found that there was an effect of non-surgical in reduction of periodontal clinical parameters in patients with GDM and periodontitis.

In a study by Janet M. Guthmiller et al, in 2001, it was seen that periodontal inflammation and destruction are increased in pregnant diabetics as compared to non-diabetic pregnant patients. According to study done by Kasaj et al., in 2008 it was concluded that pregnant diabetics demonstrate a higher degree of periodontal inflammation and destruction compared to non-pregnant diabetics and healthy non-pregnant patients despite a good metabolic control compared to non-pregnant diabetics with poor metabolic control.

In a study done by Xu Xiong et al., in 2006 it was found that there exists an association between periodontal disease and GDM. Another study by Novak et al., in 2006 it was observed that women with gestational diabetes mellitus (GDM) during pregnancy may be at greater risk for developing more severe periodontal disease than pregnant women without GDM.

Several studies study done by Xu Xiong et al., in 2009, Anyarat Chokwiriyachit et al in 2013, Lima et al in 2013, Priyam Mishra et al in 2014, Kalra et al in 2016 with an aim was to examine whether maternal periodontal disease is associated with GDM it was found that there exists an association between periodontal disease and GDM.

According to study by Habib et al., in 2009, to evaluate periodontal status among females with gestational diabetes and to assess its effect on insulin sensitivity and lipid metabolism, it was concluded that the prevalence of periodontal disease is high among pregnant females especially those with GDM. It was also found that periodontal disease had important deleterious effects on carbohydrates and lipids metabolism. Strategies are needed to improve dental health care and to reduce periodontal diseases among pregnant females.

A study by Ruiz et al in 2011, it was found that the presence of periodontal disease was significantly higher in Brazilian diabetic pregnancies (GDM and T1DM) when compared to non-diabetic pregnant women. The degree of periodontal disease was similar between the GDM and T1DM groups. Authors further stated that age, pre-gestational BMI, and HbA1c were factors related to CAL development in these two types of diabetes mellitus.

A study by Bullon et al in., 2013 with an aim to establish the relationship between metabolic syndrome in pregnant women affected by gestational glucose metabolism disorder, authors concluded that Pre-pregnancy weight, Pre-pregnancy BMI, systolic and diastolic blood pressure, VLDL cholesterol and glucose parameters were higher in GDM patients.

In a systematic review and meta-analysis of observational studies done by Samuel A. Abariga et al in 2016 with an aim to summarize available data regarding the association between periodontitis and GDM. A total of 10 observation studies and 5724 patients were included, the authors concluded that periodontitis is associated with a statistically significant increased risk for GDM compared to women without periodontitis.

Most of the studies established an association between GDM and periodontitis based on clinical parameters and immunological biomarkers as the study done by Nitin H. Dani et al in 2016 where it was found that Gestational Diabetes resulted in increased values of Gingival Index, plaque index and also gingival recession along with an increased value of probing pocket depth and clinical attachment level.

Another study by Özçaka et al in 2016 where a comparison was made between clinical periodontal findings, GCF and serum levels of tumor necrosis factor-alpha (TNF- α), interleukin-10 (IL-10), and IL-33 between women with and without GDM it was seen that plaque Index, bleeding on

probing values was significantly higher in the GDM group. Serum TNF- α concentration was significantly higher in the non GDM group than the GDM group. IL-10 concentrations and total amounts were significantly higher in the GDM group than the controls.

However there were a few studies which showed that there exists no significant association between GDM and periodontitis as shown by Kashi et al in 2015 where, no relationship was found between gestational diabetes, gingivitis, severity of gingivitis, periodontitis, and inflammatory markers. According to the study it was found that lower levels of dental plaque in pregnant women with gestational diabetes other reasons rather than poor oral hygiene are believed to be involved.

A systematic review and meta-analysis done by Rafael Paschoal Esteves Lima et al in 2016 where four cross-sectional studies and two case-control studies were included, it was concluded that the scientific evidence cannot affirm a positive association between periodontitis and GDM and thus More studies like this should be performed to confirm the association between the two.

Most of the studies concluded that there exists a relationship between GDM and periodontitis. It was also seen that when non-surgical periodontal therapy was performed in pregnant patients having diabetes, a significant reduction was seen in clinical parameters and also on adverse pregnancy outcomes in such patients.

Offenbacher et al in 2006 did a study to examine the effects of periodontal therapy during pregnancy and it was concluded that there are potential benefits of periodontal treatment on pregnancy outcomes. It was found that non-surgical periodontal treatment was safe, improved periodontal health, and prevented periodontal disease progression. Pregnancy without periodontal treatment was associated with increase in clinical parameters and GCF IL-1 beta and IL-6 levels. A significant decrease in *Prevotella intermedia*, serum IL-6sr, and GCF IL-1b was observed in intervention group.

Research gaps identified

Studies done till date showed that there exists a relationship between Gestational Diabetes and periodontitis however-

- Limited studies are done taking into consideration the immunological status of patients along with assessment of clinical parameters to establish the association between GDM and Periodontitis.
- There has been a considerable variation seen in definition of periodontitis and GDM from study to study and standardized criteria has not been used for defining neither Gestational Diabetes nor periodontitis.
- Till this date, studied literature review showed that few interventional studies have been carried out to evaluate effect of Non-Surgical periodontal therapy in GDM patients with periodontitis.

Recommendations for future research

In the present reviewed articles, it was found that GDM is associated with periodontitis. Most of articles have given this association based on clinical parameters or combined with microbiological parameters. So, further research should concentrate on establishing the association between GDM and periodontitis based on immunological biomarkers. Till date few studies have been done to analyse effect of NSPT in patients with GDM and Periodontitis so, further future studies should be also done to evaluate effect of NSPT in patients with GDM and Periodontitis.

CONCLUSION

In the present review, it was noticed that immunological cytokines play a significant role in causation as well as resolution of inflammation in periodontitis as well as Gestational Diabetes Mellitus. It was also observed that periodontitis is one of the risk factors enhancing glycaemic levels in pregnant women thus leading to GDM. Similarly, it was also found that GDM could also lead to periodontitis by enhancing inflammatory cytokine level. Therefore, based on the results of the reviewed articles, it can be correctly stated that there is a significant association between periodontitis and Gestational Diabetes Mellitus.

References

Abariga, S.A. and Whitcomb, B.W., 2016. Periodontitis and gestational diabetes mellitus: a systematic review and meta-analysis of observational studies. *BMC pregnancy and childbirth*, 16(1), p.344.

Bullon, P., Jaramillo, R., Santos-Garcia, R., Rios-Santos, V., Ramirez, M., Fernandez-Palacin, A. and Fernandez-Riejos, P., 2014. Relation of periodontitis and metabolic syndrome with gestational glucose metabolism disorder. *Journal of periodontology*, 85(2), pp.e1-e8.

Chokwiriyaichit, A., Dasanayake, A.P., Suwannarong, W., Hormdee, D., Sumanonta, G., Prasertchareonsuk, W., Wara-Aswapati, N., Combellick, J. and Pitiphat, W., 2013. Periodontitis and gestational diabetes mellitus in non-smoking females. *Journal of periodontology*, 84(7), pp.857-862.

Dani, N.H., Beldar, A.M., Khedkar, S.U. and Andhale, S.K., 2016. Effect of gestational diabetes on plaque micro flora and periodontal health. *Journal Of Applied Dental and Medical Sciences*, 2, p.2.

Engelbreton, S. and Kocher, T., 2013. Evidence that periodontal treatment improves diabetes outcomes: a systematic review and meta-analysis. *Journal of clinical periodontology*, 40(s14).

Esteves Lima, R.P., Cyrino, R.M., de Carvalho Dutra, B., Oliveira da Silveira, J., Martins, C.C., Miranda Cota, L.O. and Costa, F.O., 2016. Association between periodontitis and gestational diabetes mellitus: systematic review and meta-analysis. *Journal of periodontology*, 87(1), pp.48-57.

Guthmiller, J.M., Hassebroek-Johnson, J.R., Weenig, D.R., Johnson, G.K., Kirchner, H.L., Kohout, F.J. and Hunter, S.K., 2001. Periodontal disease in pregnancy complicated by type 1 diabetes mellitus. *Journal of periodontology*, 72(11), pp.1485-1490.

Habib, F.A., 2009. Evaluation of periodontal status among saudi females with gestational diabetes and its relation to glucose and lipid homeostasis in ohud hospital, Al madina Al-munwarrah. *International journal of health sciences*, 3(2), p.143.

Kasaj, A., Georg Zafiroopoulos, G., Tekyatan, H., Pistorius, A. and Willershausen, B., 2008. Periodontal disease status of pregnant women with diabetes mellitus. *Collegium antropologicum*, 32(1), pp.115-118.

Kashi, Z., Ehsani, Z., Maboodi, A., Bahar, A. and Rezai, N., 2015. Relationship between Periodontitis and Inflammatory Factors with Gestational Diabetes. *Journal of Mazandaran University of Medical Sciences*, 25(131), pp.24-31.

Kalra, M., Tangade, P., Punia, H., Gupta, V., Sharma, H. and Jain, A., 2016. Assessment of two-way relationship between periodontal disease and gestational diabetes mellitus: A case-control study. *Indian Journal of Dental Research*, 27(4), p.392.

Lima, R.P.E., Costa, F.O., Cota, L.O.M. and Cyrino, R.M., 2015. Association between periodontitis, gestational diabetes mellitus and diabetes mellitus type 1 and 2 in pregnant women. *Journal of Health & Biological Sciences*, 3(1), pp.18-24.

Mishra, P., Gita, B. and Chandrasekaran, S., 2014. Assessment of periodontal status in association with gestational diabetes mellitus: a case-control study. *J DiabMetab*, 5(467), p.2.

Novak, K.F., Taylor, G.W., Dawson, D.R., II, J.E.F. and Novak, M.J., 2006. Periodontitis and gestational diabetes mellitus: exploring the link in NHANES III. *Journal of public health dentistry*, 66(3), pp.163-168.

Offenbacher, S., Lin, D., Strauss, R., McKaig, R., Irving, J., Barros, S.P., Moss, K., Barrow, D.A., Hefti, A. and Beck, J.D., 2006. Effects of periodontal therapy during pregnancy on periodontal status, biologic parameters, and pregnancy outcomes: a pilot study. *Journal of periodontology*, 77(12), pp.2011-2024.

Ruiz, D.R., Romito, G.A. and Dib, S.A., 2011. Periodontal disease in gestational and type 1 diabetes mellitus pregnant women. *Oral diseases*, 17(5), pp.515-521.

Tamashiro, N.S., Duarte, P.M., Miranda, T.S., Maciel, S.S., Figueiredo, L.C., Faveri, M. and Feres, M., 2016. Amoxicillin plus Metronidazole Therapy for Patients with Periodontitis and Type 2 Diabetes: A 2-year Randomized Controlled Trial. *Journal of dental research*, 95(7), pp.829-836.

How to cite this article:

Ashwini S and Shivani (2018) 'Gestational diabetes Mellitus And Chronic Periodontitis-Exploring The link by Immunological Biomarkers-A Review', *International Journal of Current Advanced Research*, 07(12), pp. 16413-16419. DOI: <http://dx.doi.org/10.24327/ijcar.2018.16413.3034>