

Evaluation of clinical and biochemical parameters in Periodontal Disease in Relation with Gestational Diabetes Mellitus

Dr. Zewar A. Al-Qassab*¹, Dr. Bakhtiar M. Ahmed*², Dr. Khadija M. Ali*³

1. Department of Periodontology, College of Dentistry, Hawler Medical University, Erbil, Iraq.
2. Department of Basic Sciences, College of Dentistry, Hawler Medical University, Erbil, Iraq.
3. Department of Periodontology, College of Dentistry, Hawler Medical University, Erbil, Iraq.

E-mail: drbakhtiarmn@yahoo.com

Abstract

Periodontal disease is a chronic bacterial inflammation can induce a sustained systemically inflammatory response that may result in a state of insulin resistance. This study was carried out to assess the association between the periodontal disease and gestational diabetes mellitus (GDM). 80 pregnant women were participated in this study, 40 of them were diagnosed with GDM. Full mouth periodontal examination with some serum biochemical, and inflammatory parameters were performed for all participants. The results of the study showed a significant increase in serum triglyceride (TG), C-reactive protein, and alkaline phosphatase (ALP) in periodontitis groups, while high density lipoprotein (HDL) showed a significant decrease in periodontitis groups as compared with nonperiodontitis groups in both pregnant women with and without GD. Serum total cholesterol (TC) and low density lipoprotein (LDL) showed non-significant differences among the groups. The results of this study support the hypothesis of the association of periodontal disease with GDM.

Keywords: Periodontitis, Gestational diabetes mellitus, Lipid profile, alkaline phosphatase.

1. Introduction

Diabetes Mellitus is a group of metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (ADA, 2013). It is classified according to its etiology into; type 1, type 2, gestational diabetes and other specific types (Negarato *et al*, 2013).

Gestational diabetes mellitus is a condition of carbohydrate intolerance of varying severity that begins or recognized during pregnancy (NIH, 2013). Inadequate pancreatic β -cell response to increased insulin requirements during fetal development within physiological, pregnancy-associated insulin resistance, is implicated in the pathophysiology of this common pregnancy complication (Lovrenčić *et al*, 2013). Clinical manifestations of GDM have been attributed mainly to the condition of hyperglycemia, hyperlipidemia, and hyperinsulinemia (Metzger *et al*, 2007). One of the symptoms of GDM is the change in biochemical markers including serum glucose, serum HbA1c, leukocyte count (Xiaohong and Xiufang, 2007), alkaline phosphatase (Wojcicka-Bentyn *et al*, 2004), serum ferritin (Amiri *et al*, 2013), C-reactive protein, TNF- α , and IL-6 (Salmi *et al*, 2012, Edalat *et al*, 2013).

Periodontal disease is a slowly progressive disease (Newman *et al*, 2012), which induces local and host immune response and is able to produce transient bacteremia (Garcia *et al*, 2000, Amar and Han, 2003). The link between pregnancy and periodontal inflammation has been known for many years, as a result of alteration in the composition of subgingival plaque that occurs during pregnancy (Newman *et al*, 2012). Viable bacteria and bacterial products (e.g., lipopolysaccharide) from subgingival plaque and pro-inflammatory cytokines (TNF- α , IL-6, C-reactive protein) from inflamed periodontal tissue can enter circulation and trigger maternal systemic inflammatory response (Garcia *et al*, 2000, Amar and Han, 2003).

It is known that pancreatic beta cell destruction can result from pro-inflammatory imbalance created by sustained elevations of cytokines (Moller, 2000), therefore maternal chronic periodontal disease could induce sustained systemic inflammatory response that may result in a state of insulin resistance (Xiong *et al*, 2009).

Aim of the study:

This study was carried out to examine whether periodontal disease is associated with an increased risk of GDM and to evaluate the intensity of the condition, and inflammatory status in GDM women with periodontitis, through assessing some serum biochemical parameters and inflammatory markers.

2. Subjects and method

2.1 Subjects:

Eighty pregnant women with age range of 22-32 years were included in this study who attained diabetes center in maternity Hospital and pregnancy unit at health centers in Erbil city. These women were about 26-32 weeks of gestation; according to the last menstrual cycle or based on ultrasound examination. These pregnant women were divided into four groups:

The first group included 20 pregnant women without GDM and periodontal disease.

The second group included 20 pregnant women without GDM, but they had periodontal disease. The third group included 20 pregnant women with GDM but without periodontal disease. Finally the fourth group included 20 pregnant women with both GDM and periodontal disease. Ethical approval for this study was obtained from localized ethical committee.

Depending on the health document during pregnancy; the GDM pregnant women were diagnosed using oral glucose tolerance test (OGTT) basing on Carpenter and Constant criteria (Amiri *et al*, 2013). All the participants agreed to sign a consent form. Patients case history was recorded which included general information of the patient, medical history and drug history.

Exclusion criteria included obese pregnant women (Body mass index more than 25 Kg/m²), pregnant women with systemic disease, history of drug treatment for hyperlipidemia, history of periodontal treatment in past 6 months.

2.2 Methods:

Body mass index was calculated using the following formula (Park, 2005):

$BMI = \text{Weight (Kg)} / (\text{Height (m)})^2$ (Negarato *et al*, 2013).

A full-mouth periodontal examination was performed for each pregnant woman by one periodontist. The measurements were taken at six sites per tooth (mesio-buccal, mesio lingual, distobuccal, disto-lingual, mid-buccal and mid-lingual), using manual UNC-15 periodontal probe and mouth mirror under ordinary light. The periodontal status was diagnosed according to the clinical parameters only avoiding using x-ray, since pregnant women cannot be exposed to radiographic examination. The clinical measures of periodontal conditions included; plaque index (PI), probing pocket depth (PPD) which represent the distance between the base of the pocket and the gingival margin, and clinical attachment level (CAL) which represent the distance between the base of the pocket and cement-enamel junction (Newman *et al*, 2012). Severity of PPD and CAL were estimated (total PPD/CAL divided by affected surface) (Bortold *et al*, 2003).

After periodontal examination, (5ml) Fasting blood sample was drawn from each subject, then the sample was centrifuged and the serum was separated, and transferred into a plain tube containing no anticoagulant and stored in an ice-box for transferring to chemical laboratory for the estimation of the following serum biochemical: glucose levels, HbA1c, total cholesterol (TC), triglycerides (TG), HDL, LDL, Alkaline phosphatase (ALP), and C-reactive protein (CRP). All biochemical parameters were determined by colorimetric methods using specific kits.

2.3 Statistical analysis:

Data were analyzed using the statistical package for social sciences (SPSS, Version 19). One way descriptive analysis was done to calculate mean \pm SD. Analysis of variance (ANOVA) was used to compare among means of the studied groups. A post Hoc test (LSD) was used to find out significant differences between each two groups (out of the four study groups). A "P" value of ≤ 0.05 was considered statistically significant.

3. Results:

This study included 80 pregnant women that divided into four groups. The age, BMI, and gestational weeks were matched for these groups (table 1). The results showed that there were non-significant differences in the age ranges among the groups. In general the ages for all the groups were nearly in the range of (25.5 – 26) years.

Regarding to the BMI values for the groups, the results indicated that non-significant differences in BMI values were found among the groups. In general the BMI values for all the groups were nearly 24 – 25 kg/m². Concerning gestational weeks; a non-significant difference also was found among the groups ($P > 0.05$).

The periodontal clinical parameters PPD, CAL are shown in figure (1); in which the PPD (G2 and G4: 4.89 \pm 0.43, 5.45 \pm 0.50 respectively) and CAL (G2 and G4: 4.93 \pm 0.60, 5.58 \pm 0.43 respectively) were significantly higher in periodontitis groups when compared with nonperiodontitis groups (PPD in G1 and G3: 3.05 \pm 0.53, 3.20 \pm 0.33, and CAL in G1 and G3 1.44 \pm 0.35, 1.53 \pm 0.42 respectively) for both pregnant women with and without GDM.

Figure (2) indicates the serum fasting glucose (SFG) levels for the groups. The results showed a significantly high SFG levels in both GDM groups (group 3 & 4) (154.30 \pm 38.38 and 165 \pm 11.68 mg/dl, respectively). The blood sugar of these two groups were uncontrolled, this is according to their high serum HbA1c % values (7.21 \pm 0.8 and 7.90 \pm 0.6 percentage respectively) as shown in figure (3).

The serum lipid profile for the groups, are shown in figure (4). The results showed that; serum TG was significantly higher in periodontitis groups (G2 and G4: 189.35 \pm 7.75, 219.50 \pm 16.39 respectively) when compared with nonperiodontitis groups (G1 and G3: 180.55 \pm 7.63, 208.4 \pm 7.65 mg/dl, respectively), while serum Cholesterol and serum LDL did not affected by periodontal disease in both pregnant women with and without GDM. On the other hand serum HDL was significantly lower in periodontitis groups (G2 and G4: 49.70 \pm 7.17, 44.90 \pm 7.14 respectively) when compared with nonperiodontitis groups (G1 and G3: 54.05 \pm 8.64, 48.80 \pm 7.95 respectively).

Regarding to Serum ALP activity, the results showed higher values of serum ALP activities in periodontitis groups (G2 and G4: 249 ± 44.01 , 282 ± 41.42 respectively) when compared with non-periodontitis groups (G1 and G3: 207 ± 42.45 , 280 ± 60.83 respectively) (Figure 5).

In case of C-reactive protein, its levels increased significantly in both groups with periodontal disease (G2 and G4: 6.50 ± 1.88 , 13.40 ± 3 respectively) when compared with nonperiodontitis groups (G1 and G3: 4.30 ± 0.98 , 9.1 ± 2.40 respectively), as shown in (Figure 6).

4. Discussion

Increasing evidence supported that there are distinct degree of subclinical inflammation in women with GDM, and inflammatory effect plays an important role in the process for insulin resistance to GDM (Xiaohong and Xiufang, 2007). Periodontal disease is a chronic inflammation which can induce changes in the functions of immune cells that cause metabolic derangement of lipids and glucose metabolism through mechanisms involving pro-inflammatory cytokines (Fawzia, 2009). (TNF- α , IL-1 β , IL- α , and C-reactive protein (Garcia, 2000) and there is a negative relation between TNF- α and insulin sensitivity index is found in gestational diabetics (Wang *et al.*, 2004). Furthermore, it has been shown that both TNF- α and IL-1 inhibit the production of lipoprotein lipase, thus causing lipid metabolism disturbance (Wu *et al.*, 2000).

David *et al.* in cross-sectional study found that endotoxin / lipopolysaccharide of *P. gingivalis* from patient with severe periodontal disease positively correlated with serum TG and negatively correlated with serum HDL and no correlation was found between endotoxin / lipopolysaccharide and total cholesterol and LDL (David *et al.*, 2008).

The results of the present study showed a statistically significant elevation in serum TG and a significant reduction in HDL level in both groups with periodontal disease (group 2 and group 4). Morita *et al.* observed that mean TG level was significantly higher in patients with periodontal disease than in patients without periodontal disease (Morita *et al.*, 2004). Bullon *et al.* also showed that serum TG levels were higher in patients with periodontitis than in patients without periodontitis²⁴, while In contrast, Sandi *et al.* showed that no significant increase found in serum TG and HDL in patients with chronic periodontitis when compared with nonperiodontitis, they observed a significant increase in serum cholesterol and LDL in patients with chronic periodontitis (Sandi *et al.*, 2014).

In our study we found no significant differences in the levels of serum TC and LDL in periodontitis and non-periodontitis pregnant women with and without GDM. Beside that Swati *et al.* found that the serum levels of TG, TC, and LDL were significantly higher for periodontitis group as compare with nonperiodontitis group. They showed that HDL cholesterol levels were significantly lower in periodontitis group than in nonperiodontitis group (Swati *et al.*, 2013). It was reported that normal pregnancy can induce major alteration in lipid metabolism (Gillmer, 1996).

According to the significant elevation in serum TG in both groups with periodontitis in the present study, the periodontal disease could play a role in GDM status. Studies done by Wiznter *et al.*, 2009 and Niromanish *et al.*, 2012, indicated that elevation of serum levels of TG are associated with GDM. This may be because there is a positive correlation between hypertriglyceridemia and hyperinsulinemia (Akbari *et al.*, 2013).

Alkaline phosphatase (ALP) can be considered as periodontal disease marker (Malhotra *et al.*, 2010). The level of ALP activity directly correlated with intensity of inflammatory process of periodontal tissue (Aiinname *et al.*, 1990). We observed that, the activity of ALP was significantly higher in non-GDM women with periodontal disease when compared with those free from periodontitis (group 1 and group 2). Possible explanation for this difference is that; ALP is released by secondary granules of neutrophils and its concentration increases significantly with plaque accumulation and increasing inflammation (Randhir and Geeta, 2011). Ishikawa and Cimasoni showed positive correlation of ALP in periodontitis patient with increased pocket depth (Ishikawa and Cimasoni, 1970). GDM can also cause extremely elevation in ALP activity (Wojcicka-Bentyn *et al.*, 2004). Thus, our result showed that both GDM and periodontitis together can elevate serum ALP.

Elevation in CPR levels in women with GDM can suggest a role of inflammation in the etiology of GDM (Dasanayake *et al.*, 2008). In the present study pregnant women with periodontitis showed higher CPR levels when compared with those with nonperiodontitis. It was also found that CRP levels in GDM women were higher comparing with non GDM women. These results are consistent with outcomes of investigations, which reported an elevation of CRP levels in pregnant women with periodontal disease compared with those without periodontal disease (Waranuch *et al.*, 2006, Anupria *et al.*, 2009, Oksan *et al.*, 2013).

Studying CRP levels during pregnancy is of great important value. There is evidence for CRP elevation during the first trimester of pregnancy (Wolf *et al.*, 2003, Oksan *et al.*, 2013). Qui *et al.* in their study which included women were recruited before 16 weeks of gestation and were followed until delivery. They showed that elevated CRP was associated with an increased risk of GDM status, and the association is independent of maternal pre-pregnancy adiposity (Qui *et al.*, 2004). While other studies failed to demonstrate the association between maternal elevated CRP and GDM (Ravi *et al.*, 2003, Mahdieh *et al.*, 2011). The possible explanation for the mechanism of this association is that, viable bacteria, bacterial product from subgingival plaque and pro-

inflammatory cytokines (TNF- α ,IL-1 β ,IL-6 ,IL-8 and C-reactive protein) enter the circulation and trigger maternal inflammatory response (Garcia et al, 2000, Amar and Han, 2003), and it is known that pancreatic β -cell destruction can result from the pro-inflammatory-imbalance created by sustained elevation of cytokines (Moller, 2000).

5. Conclusion

The results of this study support the hypothesis of association between periodontal disease and GDM through alteration of some serum biochemical parameters. If periodontal disease is confirmed as a risk factor for GDM in further studies, dentists are in a unique position to contribute to the improvement of this health care problem and improving oral health treatment of periodontal disease before and during pregnancy to reduce the risk of GDM.

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Table (1): Some characteristics of the studied groups (age, BMI, and gestational weeks)

Variables	Groups	N	Mean	SD	p (ANOVA)	Significance by LSD
AGE	G1	20	26.15	4.31	.986	NA
	G2	20	26.25	3.64		
	G3	20	25.80	4.05		
	G4	20	26.10	3.61		
BMI	G1	20	24.73	.34	.106	NA
	G2	20	24.57	.36		
	G3	20	24.79	.41		
	G4	20	24.83	.27		
WEEKS	G1	20	29.13	1.33	.450	NA
	G2	20	28.87	1.32		
	G3	20	28.65	1.98		
	G4	20	28.36	1.50		

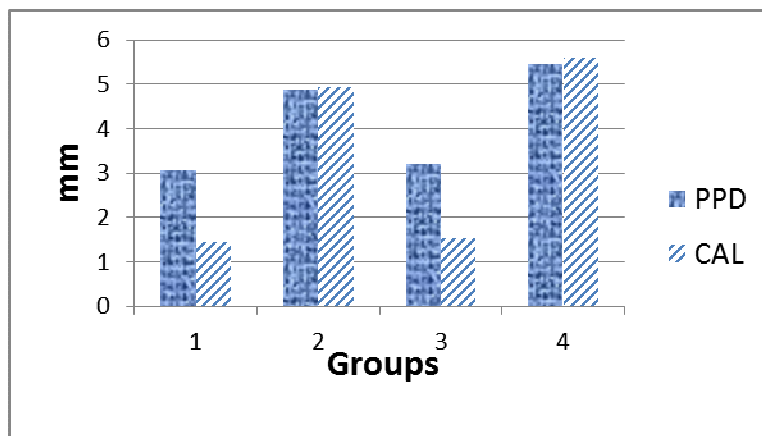


Figure (1): The clinical measures of periodontal conditions including; The probing pocket depth (PPD) and the clinical attachment level (CAL).

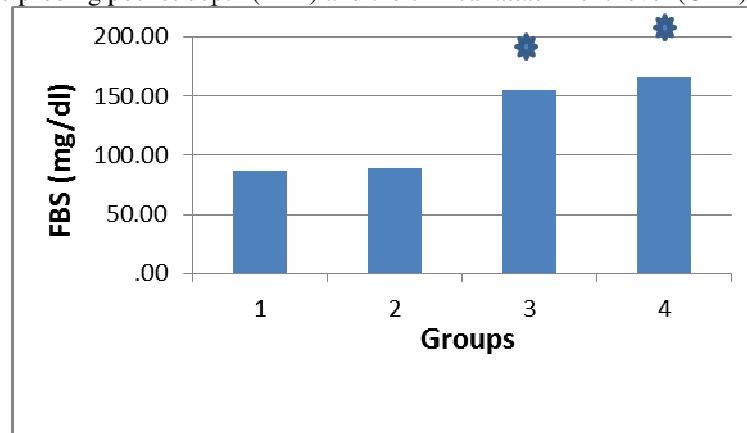


Figure (2): The serum fasting glucose levels for the groups.

✱ = significance.

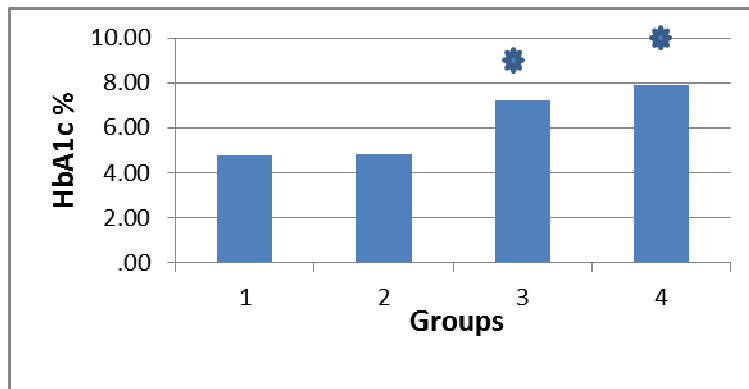


Figure (3): The percentage of glycosylated hemoglobin (HbA1c %).
* = significance.

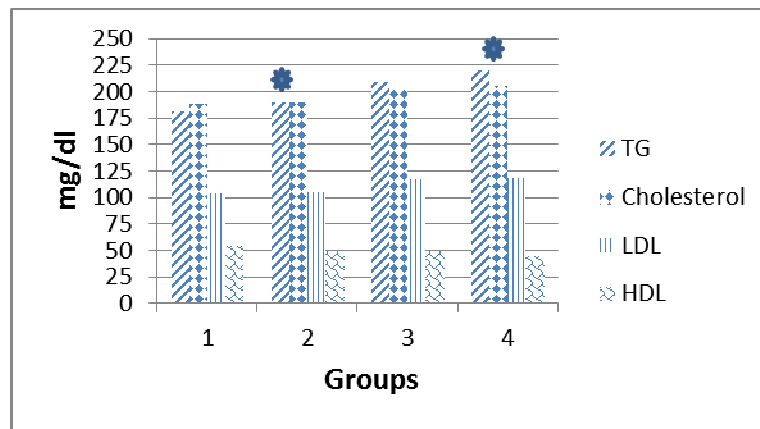


Figure (4): Serum Lipid profile for the groups.
* = significance.

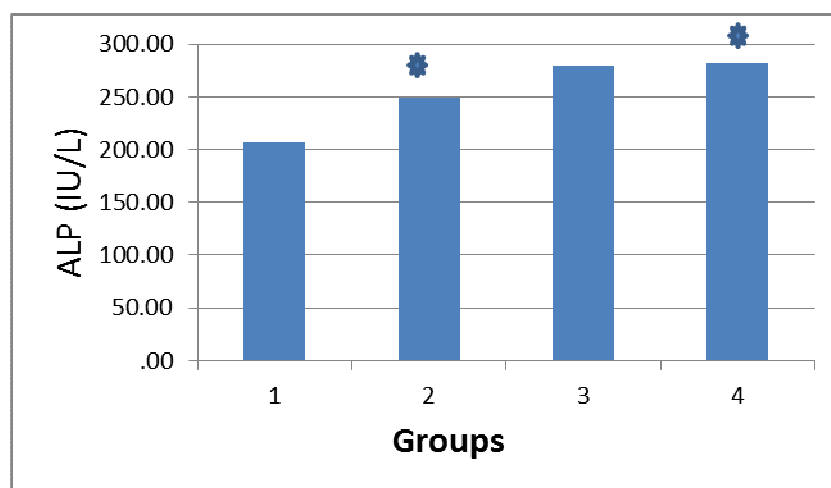


Figure (5): Serum alkaline phosphatase activities for the groups.
* = significance.

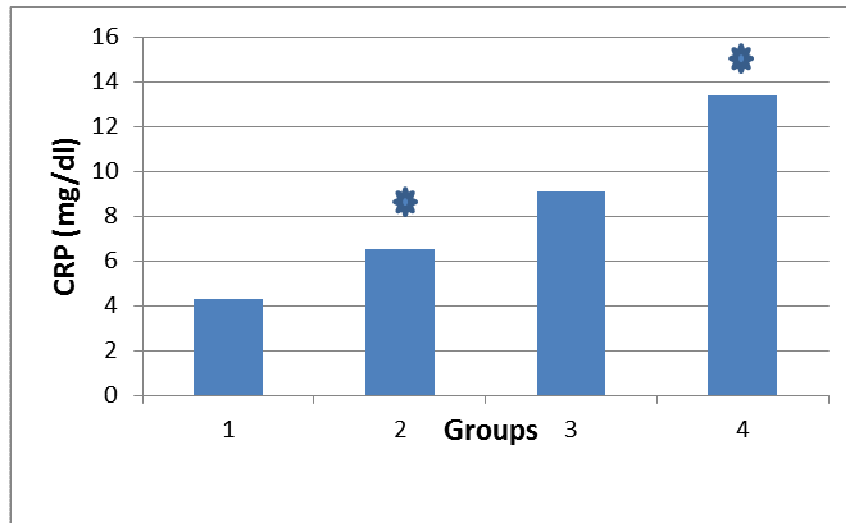


Figure (6): Serum C-reactive protein levels for the groups.
* = significance.

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