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

Fawzia A Habib[1]; Mohamed Y Abdul Aziz[2]; Abdul-Kader R Allam[3]; Amal M Shaheen[4]; Khalid AA Al Nahdi[5], Hassan Hemida[6]

Obstetric & Gynecology[1] ; Internal Medicine[2] and Cardiology[3] – College of Medicine , Taibah University . Obstetrics & Gynecology [4]; Dental Care Center[5] and Laboratory[6] – Ohud Hospital, Al Madina Al Munawarrah.

Abstract:

Objectives: Due to the lack of pregnant based oral health studies in our country, we conducted this study 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.

Methods: This cross-sectional descriptive study was conducted from January 2008 till June 2008. The sample includes 250 Saudi females, 100 were pregnant with gestational diabetes (GDM), and 100 were pregnant without GDM and 50 were normal non pregnant females. The study cases were matched age and body mass index. All the participants were subjected to history taking, physical examination and assessment of their 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-1β, and TNF-α) also measured. The periodontal health status was assessed using the Community Periodontal Index of Treatment Needs (CPITN).

Results: Severe periodontal diseases were elicited in 37% of the pregnant females with GDM, 29% of the pregnant females without GDM and 14% of non pregnant normal control group. 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. Females with recurrent GDM were found to have higher Body Mass Index (BMI), severe periodontal diseases, as well as higher HOMA-IR, than those presented for first time with GDM.

Females with GDM; also shows significant positive correlation between CPITN scoring and patient age, HOMA-IR and inflammatory markers.

Conclusions: 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.

Correspondence:
Dr. Fawzia A. Habib
College of Medicine,
Department of Obstetrics, Taibah University,
Post Box: 30001, Madinah, Saudi Arabia

Introduction

Diabetes mellitus (DM) is a common chronic disease, and its prevalence in Saudi Arabia, particularly type 2 DM, is increasing. Periodontal diseases are common conditions among Saudi population. The association between diabetes and periodontal diseases is well documented. Patients with DM have increased incidence and severity of periodontal diseases. Poor glycemic control has been consistently associated with periodontal disease severity [(1)].

Inflammation affecting the supporting structures of the teeth (periodontitis) is usually caused by anaerobic gram-negative microorganisms. This infection causes destruction of the supporting alveolar bone and can lead to tooth loss. Diabetic patients are at greater risk of developing periodontitis and may not respond well to periodontal therapy as non-diabetic patients, and may require more aggressive treatment to manage periodontitis [(2)].

Insulin resistance and progressive pancreatic β-cell dysfunction have been identified as the two fundamental features in the pathogenesis of type 2 DM. As a widely validated clinical and epidemiological tool for estimating insulin resistance and β-cell function, the homeostasis model assessment (HOMA) is derived from a mathematical assessment of the balance between hepatic glucose output and insulin secretion from fasting levels of glucose and insulin [(3 -4)].

The major contributing factor for insulin resistance is currently considered to be the pro-inflammatory cytokine tumor necrosis factor-alpha (TNF-alpha). Periodontal surgery may cause transient bacteremia which affects the serum TNF-alpha level, and this in turn suppresses insulin action [5].

Studies have demonstrated that TNF-alpha suppresses insulin action via its specific receptor; hence, it exacerbates insulin resistance. TNF-alpha produced due to periodontal inflammation may be an additional important factor influencing insulin sensitivity. This interaction mechanism is a possible relationship between type 2 DM and periodontal disease [(6 -7)].

There is a current interest in the associations of circulating inflammatory markers (CRP, white cell count, and ESR) in prediction of insulin resistance, impaired glucose tolerance and cardiovascular events in the general population [(8)].

The pro-inflammatory cytokines (interleukin (IL)-1 beta, IL-6, and TNF-alpha) produce the characteristic deregulation of lipid metabolism associated with type 2 DM. They have effects on pancreatic beta cells. In addition, evidence supports the role of cytokine elevation in the pathophysiology and metabolic abnormalities associated with DM [(9)].

Recent evidence suggests that periodontitis itself may lead to elevated Low Density Lipoproteins /Triglycerides (LDL/TRG). Periodontitis-induced bacteremia/endotoxemia,also produce alterations in lipid metabolism[(10)].

In terms of the potential relationship between periodontitis and systemic disease, it is possible that periodontitis-induced changes in immune cell function, causes metabolic deregulation of lipid metabolism through mechanisms involving pro-inflammatory cytokines. Sustained elevations of serum lipids and/or pro-inflammatory cytokines may have a serious negative impact on systemic health [(6)].

The Community Periodontal Index of Treatment Needs (CPITN), developed jointly by Federation Dentaire International (FDI) and the World Health Organization (WHO), was the most widely used tool for the assessment of periodontal health [11]. CPITN acts as a surrogate marker of periodontal disease [(12)].

The present study is carried out to assess the periodontal status among pregnant females with gestational diabetes in Ohud Hospital,Al Madinah Al-Munwarrah, and to assess its effect on insulin sensitivity and lipid metabolism.

Methods

This cross-sectional descriptive study was performed at Ohud Hospital, Al Madinah Al-Munwarrah. All consecutive pregnant females (100) with gestational diabetes who attended the outpatient gestational diabetes clinic during a 6-month period from January to June in 2008 were included in this study. Simultaneously, another 100 non-diabetic pregnant females were randomly selected from the Obstetric antenatal clinics and another 50 healthy non pregnant or lactating females in childbearing age as a control group of similar age group were also randomly selected from the same hospital. Informed consent for the interview and examinations were obtained from each participant.

Exclusion criteria includes pre pregnancy diabetes, chronic illnesses such as chronic renal diseases, chronic hepatic diseases, cardiac & respiratory diseases, endocrine disease, collagen or vascular diseases, and current use of corticosteroids.

The diagnosis of GDM was made using a two-step approach. Patients were initially screened by measuring the plasma glucose concentration 1 h after a 50-g oral glucose challenge test at 28 weeks of gestation. A diagnostic oral glucose Tolerance test was performed on the subset of females whose plasma glucose concentrations exceeded the glucose threshold value (140 mg/dl). The diagnostic criteria for GDM were the Carpenter/Coustan conversion as recommended by the American Diabetes Association [(13)].

All participants were interviewed for demographic data including: age, obstetrical, gynecological medical, family, social and drug history. This was followed by complete physical assessment including: anthropometric measurements of height (measured to nearest 0.5 cm) and weight (measured to nearest 0.1 kg) that obtained using a medical scale and calculated body mass index (BMI), blood pressure measurements, and complete medical and obstetrical examination.

Dental Examination

CPITN as an indicator of periodontal status was used for this assessment. It includes the presence of gingival bleeding, supra- or sub gingival calculus, and periodontal pockets, subdivided into shallow (4 to 5 mm) and deep (6 mm or more). Periodontal probing was carried out with a plane mouth mirror (number 5) and an ordinary dental probe. Each tooth was examined from the buccal and lingual/palatal surfaces at three points (mesial, medial and distal); the greatest probe depth was registered in mm. The mean value of the pocket depth was obtained by calculating the arithmetic mean of the greatest values obtained in the explored teeth. Periodontal status was scored as follows: 0, periodontal health; 1, gingival bleeding; 2, calculus detected during probing; 3, pocket 4- to 5-mm depth; and 4, pocket 6-mm or more depth [(14)]. Dental examinations were performed by two specific dentists; who were not aware of the clinical and diabetic status of the patients.

Blood Samples

Blood samples were collected after a 12 hour fast; 10 mls of venous blood were withdrawn and aliquot into tubes under aseptic conditions as follows: sodium fluoride plasma for determination of glucose, lipid profile determination (total cholesterol, HDL-C, LDL-C and triglycerides) and serum insulin level. The EDTA samples were stored on ice (-80) till the time of centrifugation for determination of Serum IL-1 & TNF-alpha levels.

The plasma glucose level was measured by an automated enzymatic method. The HbA1c was measured by HPLC.

Serum levels of total cholesterol, triglyceride, and HDL cholesterol were measured by enzymatic methods using an auto analyzer. LDL-cholesterol is calculated using the Friedewald formula [15] as follows:

LDL-C = total cholesterol – [HDL-C – (TG/2.2)]

where all quantities are expressed in mmol/L

Insulin resistance is measured using calculated HOMO test (HOMA-IR) as follow:

HOMA-IR = (fasting insulin (µU/ml) x fasting glucose in mmol/L) / 22.5 [16]

Serum insulin was measured using an immunoradiometric assay kit .The intra- and inter assay coefficients of variation of the assay were 2.0% and 2.1%, respectively.

A high sensitivity enzyme linked immunosorbent assay (ELISA) is used to evaluate CRP, IL-1 and TNF-alpha levels. Erythrocyte sedimentation rate (ESR) was done to all cases.

Statistical Analysis

Statistical evaluation of all data was done on IBM-PC microprocessor computer using SPSS software for windows (Statistical Package for Social Sciences version 11.5, USA) for data management and analysis and the excel for figures. Quantitative data were presented as mean ± SD. Quantitative variables with normal distribution were analyzed with a two-tailed, paired Student's *t* test. ANOVA (F) test with Bonferroni multiple comparisons were used for comparison between more than 2 groups. Qualitative variables such as comparison between proportion & percentage by Chi square with Yates correction as necessary, and Fisher's test. Pearson correlation coefficient was used to correlate between variables. The coefficients of correlation and Odds ratio of 95% Confidence interval were used to studied association between CPITN score, HOMA-IR and the levels of glucose, insulin, lipids, and Inflammatory markers.

Results

The age and BMI are matched in pregnant females with GDM, pregnant females without GDM and healthy females (32.2±6.1, 31.3±4.7 & 31.1±4.8 years and 30.7±5.1, 29.8±6.5 & 29.2±7.8 respectively). The severity of CPITN Score is significantly higher in females with GDM than other groups (37% versus 29% and 14% respectively) (Table-1). Females with GDM showed significant higher systolic, diastolic blood pressure, serum triglycerides levels and HOMA-IR and lower HDL levels than other two groups, Table (1).

Table (2) showed higher BMI, systolic; mean blood pressure, HOMA-IR, serum triglyceride levels, serum IL-1 and TNF-α in gestational diabetic female with severe periodontal diseases (CPITN 3-4) than those with mild or no periodontal diseases.

Females with recurrent GDM show significant higher BMI, CPITN score , higher systolic blood pressure, as well as higher HOMA-IR and serum TNF-α than those presented with GDM for first time (32.9±4.4, 41.8%, 122±8, 14.9±6.1 and 0.024±0.027 versus 29.1±4.1, 31.2%, 116±9, 10.6±6.4 and 0.011±0.022 respectively as shown in table (3).

Table (4) shows a significant positive correlation between CPITN scoring and patient age, BMI, HOMA-IR (figure-1) in females with GDM. (r=0.67, p=0.001: r=0.52, p=0.05: r=0.66, p=0.001 respectively).

Concerning insulin resistance index (HOMA-IR); it is positively correlated with age, BMI, serum triglyceride and TNF-α, (figure-2) (r=0.62, p=0.001: r=0.35, p=0.05: r=0.62, p=0.001 and r=0.47, p=0.01 respectively).

Table (1). Demographic data with comparison between pregnant diabetic females (Group-1), pregnant non diabetic females (Group-2) and a control group (Group-3).

	Group-1 (GDM)	Group-2 (Pregnant)	Group-3 (Control)	P value
Number (%)	100	100	50	
Age: years	32.2±6.1	31.3±4.7	31.1±4.8	0.49
BMI	30.7±5.1	29.8±6.5	29.2±7.8	0.52
CPITN score				
0	29/29%abc	44/44%	33/66%	0.001**
1-2	34/34%abc	27/27%	10/20%	0.001**
3-4	37/37%abc	29/29%	7/14%	0.001**
Blood pressure				
SBP	120±9ab	109±11	109±10	<0.05*
DBP	77±7ab	67±8	68±8	0.001**
MBP	91 ± 7ab	81±8	81±.8	0.001**
Glycemic State				
FBG	6.77±1.25ab	4.61±0.44	4.6±0.45	0.001**
FI	42.6±24.6ab	18.2±5.8	15.2±7.9	0.001**
HOMA-IR	12.8±7.9ab	3.7±1.3	3.1±1.6	0.001**
HA1C (gm %)	6.6±0.94ab	5.2±0.3	5.2±0.33	0.001**
TC (mmol/L)	5.31±1.17	5.13±1.24	4.93±1.04	0.56
HDL (mmol/L)	1.24±0.25ab	1.42±0.24	1.41±0.12	0.001**
LDL (mmol/L)	3.26±1.13	2.93±1.13	2.55±0.97	0.23
TG (mmol/L)	1.79±0.69ab	1.44±0.34	1.40±0.27	0.001**
CRP (mg/dl)	0.24±0.45	0.22±0.52	0.15±0.40	0.34
ESR (mm/1h)	50.8±22.6ab	33.5±17.4	32.1±12.1	0.001**
IL-1(pg/ml)	3.12±5.36ab	1.43±3.87	1.19±3.31	0.001**
TNF-a (ng/ml)	0.023±0.021ab	0.004±0.011	0.001±0.003	0.001**

*Comparison between the different groups by using ANOVA test for numerical data and Chi square test for percentages. * P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01).*

GDM: Gestational DM. BMI: Body mass index. CPITN: Community periodontal index of treatment needs. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. MBP: Mean blood pressure. FBG: Fasting blood glucose. FI: Fasting insulin. HOMA-IR: Homeostasis model assessment-Insulin resistance. HAIC: hemoglobin A1c. TC: Total cholesterol. HDL: High density lipoprotein. LDL: Low density lipoprotein. TG: Triglycerides. CRP: C- reactive protein. ESR: Erythrocyte sedimentation rate. IL-1: Interleukin-1. TNF-α: Tumor Necrosis Factor-alpha.

Table (2). Characteristics of gestational diabetic females according to CPITN scores.

	Group-1 (CPITN 3-4)	Group-2 CPITN 1-2	Group-3 CPITN 0	P value
Number (%)	37	34	29	
Age: years	32.5±6.6	34.7±6.2	33.4±7.2	0.61
BMI	32.9±4.4abc	29.1±4.1	26.8±1.7	<0.05*
Blood pressure				
SBP	121±9ab	118±9	113±11	<0.05*
DBP	79±6	78±7	75±10	0.39
MBP	94±6ab	89±7	87±10	<0.05*
Glycemic State				
FBG	6.8±1.2	6.5±1.2	6.9±1.3	0.17
FI	54.7±23.2ab	23.6±10.4	20.5±8.6	0.001**
HOMA-IR	16.4±7.7ab	6.8±3.4	6.6±3.8	0.001**
HA1C (gm %)	6.7±1.1	6.3±0.9	6.71±0.93	0.23
TC (mmol/L)	5.33±1.31	5.21±0.96	4.96±1.04	0.23
HDL (mmol/L)	1.21±0.26ac	1.27±0.21	1.47±0.25	0.001**
LDL (mmol/L)	3.31±1.12	3.27±0.76	3.11±0.87	0.31
TG (mmol/L)	1.84±0.72ac	1.78±0.61	1.33±0.66	0.001**
CRP (mg/dl)	0.30±0.47	0.14±0.41	0.11±0.28	0.13
ESR (mm/1h)	54.1±23.4ab	43.4±16.7	42.7±24.6	0.001**
IL-1(pg/ml)	4.81±6.17abc	2.21±0.001	0.53±1.34	0.001**
TNF-a (ng/ml)	0.024±0.028abc	0.007±0.001	0.002±0.009	0.001**

*Comparison between the different groups by using ANOVA test for numerical data. * P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01).*

NS: non-significant. BMI: Body mass index. CPITN: Community periodontal index of treatment needs. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. MBP: Mean blood pressure. FBG: Fasting blood glucose. FI: Fasting insulin. HOMA-IR: Homeostasis model assessment-Insulin resistance. HAIC: hemoglobin A1c. TC: Total cholesterol. HDL: High density lipoprotein. LDL: Low density lipoprotein. TG: Triglycerides. CRP: C- reactive protein. ESR: Erythrocyte sedimentation rate IL-1: Interleukin-1. TNF-α: Tumor Necrosis Factor-alpha.

Table (3). Comparison between females presented with recurrent gestational diabetes and those for the first time.

	Recurrent GDM group	First GDM Group	P Value
Number (%)	55 (55%)	45 (45%)	
Age: years	32.5±6.6	34.7±6.2	0.08
BMI	32.9±4.4*	29.1±4.1	<0.05
CPITN score			
0	15/27.3%	15/33.3%	0.63
1-2	17/30.9%	16/35.5%	0.72
3-4	23/41.8%*	14/31.2%	<0.05
Blood pressure			
SBP	122±8*	116±9	<0.05
DBP	77±6	76±7	0.60
MBP	92±6	90±7	0.27
Glycemic State			
FBG	6.8±1.2	6.5±1.2	0.14
FI	48.5±25.7*	37.1±23.1	<0.05
HOMA-IR	14.9±6.1*	10.6±6.4	<0.05
HA1C (gm %)	6.95±0.96*	6.2±0.8	<0.05
TC (mmol/L)	5.34±1.19	5.40±1.24	0.81
HDL (mmol/L)	1.23±0.27	1.23±0.22	0.71
LDL (mmol/L)	3.31±1.19	3.31±1.13	0.95
TG (mmol/L)	1.77±0.75	1.83±0.59	0.68
CRP (mg/dl)	0.32±0.50	0.16±0.40	0.09
ESR (mm/1h)	56±21*	42±24	<0.05
IL-1(pg/ml)	3.93±5.93	2.44±4.66	0.19
TNF-a (ng/ml)	0.024±0.027*	0.011±0.022	<0.05

*Comparison between the different groups by using t test for numerical data and Chi square test for percentages. * P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01).*

GDM: Gestational DM. NS: non-significant. BMI: Body mass index. CPITN: Community periodontal index of treatment needs. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. MBP: Mean blood pressure. FBG: Fasting blood glucose. FI: Fasting insulin. HOMA-IR: Homeostasis model assessment-Insulin resistance. HAIC: hemoglobin A1c. TC: Total cholesterol. HDL: High density lipoprotein. LDL: Low density lipoprotein. TG: Triglycerides. CRP: C- reactive protein. ESR: Erythrocyte sedimentation rate. IL-1: Interleukin-1. TNF-α: Tumor Necrosis Factor-alpha.

Table (4). Correlations between periodontal Status scoring system (CPITN) and different characteristics of females with gestational diabetes.

Parameters	CPITN		Parameters	CPITN	
HA1C	r	0.37	**Age**	R	0.67
	p	<0.05*		P	0.001**
TC	r	0.14	**BMI**	R	0.52
	p	0.31		P	<0.05*
TG	r	0.56	**SBP**	R	0.23
	p	0.001**		P	0.12
LDL	r	0.08	**DBP**	R	0.17
	p	0.89		P	0.19
ESR	r	0.34	**HOMA-IR**	R	0.66
	p	<0.05*		P	0.001**
IL-1	r	0.49	**TNF-α**	R	0.59
	p	<0.05*		P	0.001**

Table (5). Correlations between Insulin Sensitivity index (HOMA-IR) and different characteristics of females with gestational diabetes.

Parameters	HOMA-IR		Parameters	HOMA-IR	
HA1C	R	0.16	**Age**	R	0.62
	P	0.37		P	0.001**
TC	R	0.04	**BMI**	R	0.35
	P	0.91		P	<0.05*
TG	R	0.61	**SBP**	R	0.05
	P	0.001**		P	0.87
LDL	R	0.02	**DBP**	R	0.04
	P	0.95		P	0.91
HDL	R	-0.22	**CPITN Score**	R	0.66
	P	0.16		P	0.001**
ESR	R	0.13	**CRP**	R	0.19
	P	0.43		P	0.32
IL-1	R	0.41	**TNF-α**	R	0.47
	p	<0.05*		P	<0.01**

** P: mildly statistically significant (P<0.05). ** P: highly statistically significant (P<0.01).*

NS: non-significant. BMI: Body mass index. CPITN: Community periodontal index of treatment needs. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. HOMA-IR: Homeostasis model assessment-Insulin resistance. HAIC: hemoglobin A1C. TC: Total cholesterol. HDL: High density lipoprotein. LDL: Low density lipoprotein. TG: Triglycerides. CRP: C- reactive protein. ESR: Erythrocyte sedimentation rate. IL-1: Interleukin-1. TNF-α: Tumor Necrosis Factor-alpha.

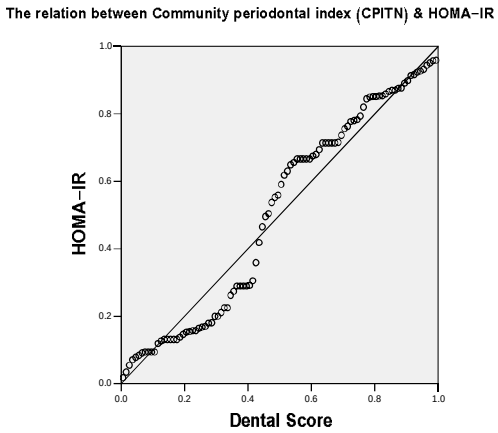

Fig. (1). The relation between periodontal Status index (CPITN) & HOMA-IR.

CPITN: Community periodontal index of treatment needs. HOMA-IR: Homeostasis model assessment-Insulin resistance. TNF-α: Tumor Necrosis Factor-alpha

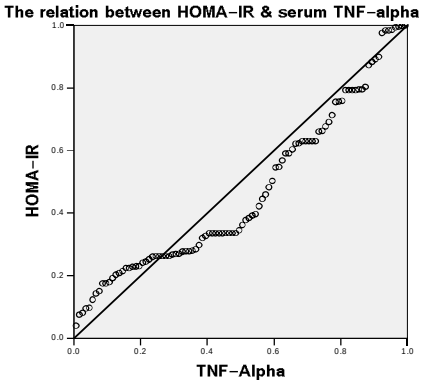

Fig. (2). The relation between HOMA-IR & serum TNF-α .

Discussion

In terms of the potential relationship between periodontitis and systemic diseases such as diabetes and insulin resistance, it is possible that periodontitis-induced changes in the function of the immune cell cause metabolic derangement of lipid and glucose metabolism through mechanisms involving pro-inflammatory cytokines.

One of the reasons for carrying out this study is to establish a relation between periodontal disease and the metabolic abnormalities associated with gestational diabetes and so screening could detect females with uncontrolled metabolic state, deserving initiating aggressive primary preventive strategies.

Periodontal diseases (CPITN Score of 3-4) was elicited in 37% of pregnant females with gestational diabetes, 29% of pregnant females without gestational diabetes and 14% of non pregnant control group. Also it was noticed that in patients with gestational diabetes; 37% of them with CPITN 3-4 (severe periodontal diseases), 34% with CPITN 1-2 (mild periodontal diseases) and 29% with CPITN 0 (no periodontal diseases). This observation, may dictate that the periodontal diseases should be screened in every pregnant females and managed aggressively in order to achieve proper primary prevention.

Females with gestational diabetes showed significant higher fasting insulin and HOMA-IR than other two groups. This is consistent with previous studies which show that females with gestational diabetes have decreased insulin sensitivity in comparison with weight-matched control groups. Ryan *et al* [16] were the first to report a 40% decrease in insulin sensitivity in females with gestational diabetes in comparison with a pregnant control group in late pregnancy using a euglycemic clamp.

Decreased maternal pre pregnant insulin sensitivity (insulin resistance) coupled with an inadequate insulin response is the pathophysiological mechanisms underlying the development of gestational diabetes. Insulin-regulated carbohydrate, lipid and protein metabolism are all affected to a variable extent. The prevalence of gestational diabetes increased in developed countries from 2.9% to 8.8% [(17)] The underlying pathophysiology of gestational diabetes is a function of decreased maternal insulin sensitivity or increased insulin resistance. Insulin resistance results in the inability of insulin to suppress lipolysis. [(18)]

Decreased insulin response to a glucose challenge was demonstrated by Xiang *et al* [19] in females with gestational diabetes in late gestation. Garvey *et al* [20] were the first to demonstrate that there were no significant differences in the concentration of the glucose transporter (GLUT 4) responsible for insulin action in skeletal muscle of pregnant compared with non-pregnant females despite reduced insulin-stimulated glucose transport.

In our study, overall mean serum lipids were higher in females with gestational diabetes with significant high serum triglycerides and low HDL levels.

The presence of periodontal pockets can harbor pathogenic microorganisms and evoke a host response causing a systemic effect. The presence of periodontal pockets as measured by CPITN was positively associated with total cholesterol and LDL-cholesterol [21].

Knopp *et al* [22] reported that females with gestational diabetes show an increase in triglyceride and decrease in high-density lipoprotein concentration, while; Koukkou *et al* [23] reported an increase in total triglyceride but lower low-density lipoprotein cholesterol .

Concerning inflammatory markers; the mean serum levels of IL-1 and TNF-α were significantly higher in females with gestational diabetes than pregnant without gestational diabetes and normal control group. This is consistent with the study reported by Deepa *et al* [24] which shows that inflammatory markers (CRP, IL-6, and VCAM-1) increase with increasing degrees of glucose intolerance.

Fasting plasma TNF-alpha levels in pregnant females with gestational diabetes is significantly higher than in normal pregnant females. A negative relationship between TNF-alpha and insulin sensitivity index is found in gestational diabetics, suggesting that an increased TNF-alpha may contribute to insulin resistance in pregnant females with gestational diabetes [25].

Our results also demonstrate that C-reactive protein (CRP), fibrinogen and leukocyte count are increased in the insulin resistance state and this could predict type 2 DM. The increase of inflammatory markers may be one of the first detectable disorders in healthy females at high risk of type 2 DM and insulin resistance state, like those with a gestational DM history [26].

In a population at risk for type 2 DM our results provide evidence that sub-clinical inflammation underlies the metabolic syndrome, through association to one of its primary anomalies-insulin resistance, whereas no association was found to impaired insulin secretion [27].

Leipold *et al* [28] suggest that in females with gestational diabetes the CRP concentration is primarily related to the degree of adiposity until the second trimester and thereafter impaired glucose metabolism appears to be the predominant predictor of changes in CRP. The same assumption applies and to a greater extent to the data of Ferraz *et al* [29] which suggests that the presence of metabolic syndrome in females with previous gestational DM is associated with high levels of CRP.

Systemic inflammation is associated with the development of type 2 DM. In females who develop GDM, there is evidence of increased inflammation during the first trimester [30]. Moreover, a higher level of CRP, a marker of chronic low-grade inflammation, is present in a subset of females with gestational DM, independently of metabolic syndrome [8].

The findings in this study demonstrate that low-grade systemic inflammation is associated to GDM, in particular for pregnant females without conventional risk factors for gestational hyperglycemia, whose insulin resistance seems unexplainable [7].

There were significant higher BMI, systolic and mean blood pressure, serum fasting insulin levels, HOMA-IR, serum triglyceride levels, serum IL-1 and TNF-α in females with severe periodontal diseases (CPITN 3-4) in comparison to those with mild or no periodontal diseases.

Serum CRP level was related with gestational and weight gain during pregnancy and this is expected and consistent with previous study [31]. The relation of obesity-related insulin resistance and type 2 DM is also confirmed [32].

Females with recurrent gestational diabetes in their pregnancies proved to have higher BMI, systolic blood pressure, severity of periodontal diseases as well as higher serum fasting insulin & HOMA-IR, high ESR and serum TNF-α ,in comparison to those presented for the first time with gestational diabetes.

This is consistent with that reported by Tamas and Keremji [33] which show that insulin resistance is a prominent feature in females with previous gestational DM. O'Sullivan [34] had found that females with previous gestational DM were at greater risk for hypertension and hyperlipidemia. In 1996; Meyers-Seifer and Vohr [35] demonstrated that mean total cholesterol, triglycerides, LDL and systolic blood pressure were significantly higher among females with recurrent gestational DM. The same assumption applies and to a greater extent to gestational DM which may be considered a possible marker or risk factor for IRS in later life.

Our study shows significant positive correlation between CPITN scoring and patient age, BMI, HbA1c, serum triglycerides, HOMA-IR, TNF-α and IL-1.

The level of glycaemic control as measured by HbA1c emerged as the most consistent risk factor associated with the extent and severity of periodontal disease [(36)]. Also, the severity of periodontal disease is associated with advancing patient age and diabetes [37]. Previous study showed that periodontal treatment is associated with improved glycaemic control in type 2 DM and could be undertaken along with the standard measures for the diabetic patient care [(38)].

The severe periodontal disease is associated with changes in serum acute-phase response [39]. The serum triglyceride level might be a potential indicator for the presence of periodontal disease [(40)] and the periodontal therapy significantly decreased Lipid peroxide and oxidative stress index in type 2 diabetic patients with periodontal disease [(41)].

Concerning insulin resistance index (HOMA-IR); it is positively correlated with age, BMI, CPITN Score of periodontal diseases, serum triglyceride, IL-1 and TNF-α..

The results in our study demonstrate that TNF-α may play an important role in insulin resistance, and that is in accordance with similar studies showing that TNF-alpha produced due to periodontal inflammation synergistically affects insulin resistance in type 2 diabetic patients. Periodontal diseases treatment is effective in improving metabolic control in diabetics, possibly through reduced serum TNF-alpha and improved insulin resistance [42].

Conclusion

Periodontal diseases and gestational diabetes are considered as common association. Periodontal diseases are associated with significant metabolic derangement in gestational DM. Findings also indicate increased prevalence of periodontal diseases among pregnant females necessitating strong steps in primary prevention including health education that should start as early as possible to have a practical impact on the final outcome. Screening could detect females with uncontrolled metabolic state, deserving initiating aggressive primary preventive strategies.

The emergence of periodontal medicine demands that dentists assume a larger responsibility for the overall health of their patients, and acquire knowledge of relevant systemic conditions as diabetes, to interact more meaningfully with medical colleagues to achieve the ultimate goal of providing better patient care.

Acknowledgements

Financial funding for this study was provided by the Dean ship of Scientific Research at Taibah University. We would like to thank the unit management staff of Ohud Hospital for their time and work. We would also like to extend our gratitude to Dr. M Helaly for producing the statistics.

References

1. Engebretson SP, Hey-Hadavi J, Ehrhardt FJ, *et al*. Gingival fluid levels of interleukin-1beta and glycemic control inpatients with chronic periodontitis and type 2 diabetes. J Periodontol. Sep 2004; 75(9):1203-8.
2. Pucher J & Stewart J (2004): Periodontal disease and diabetes mellitus. Curr Diab Rep. 2004; 4(1):46-50.
3. Matthews DR, Hosker JP, Rudenski AS, *et al*. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. July1985, 28(7):412–419.
4. Yiqing S, JoAnn E., Lesley T., *et al*. Insulin Sensitivity and Insulin Secretion Determined by Homeostasis Model Assessment (HOMA) and Risk of DM in a Multiethnic Cohort of Women: Diabetes Care. July 2007; 30(7): 1747–1752.
5. Nishimura F, Kono T, Fujimoto C, *et al*. Negative effects of chronic inflammatory periodontal disease on diabetes mellitus. J Int Acad Periodontal. 2000 Apr; 2(2):49-55
6. Iacopino AM & Cutler CW: Pathophysiological relationships between periodontitis and systemic disease: recent concepts involving serum lipids. J Periodontal. Aug 2000; 71(8):1375-84
7. Bo S, Signorile A, Menato G, *et al*. C-reactive protein and tumor necrosis factor-alpha in gestational hyperglycemia. J Endocrinol Invest. Oct 2005; 28(9):779-86.
8. Di Cianni G, Lencioni C, Volpe L, *et al*. C-reactive protein and metabolic syndrome in women with previous gestational diabetes. Diabetes Metab Res Rev. Feb 2007; 23(2):135-40.
9. Grossi SG: Treatment of periodontal disease and control of diabetes: an assessment of the evidence and need for future research. Ann Periodontal. Dec 2001; 6(1):138-45

10. Iacopino AM. Periodontitis and diabetes interrelationships: role of inflammation. Ann Periodontal. Dec 2001; 6(1):125-37.
11. Ainamo J, Barmes D, Beagrie G *et al*. Development of the World Health Organization (WHO) Community Periodontal Index of Treatment Needs (CPITN). Int Dent J. Sep 1982; 32(3):281-91.
12. Cutress TW, Ainamo J, Sardo-Infirri J *et al*. The community periodontal index of treatment needs (CPITN) procedure for population groups and individuals. Int dental J, Dec 1987, 37(4):222–33.
13. American Diabetes Association: Gestational diabetes mellitus. Diabetes Care. 2000; 23 (Supp1 1):S77–S79.
14. Available at: http://www.whocollab.od.mah.se/expl/methods.html. Accessed December 19, 2005.
15. Friedewald W T, Levy R I and Fredrickson D S. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, with out the use of the preparative ultracentrifuge. Clin. Chem. Jun 1972, 18(6):499-502.
16. Ryan EA, O'Sullivan MJ, Skyler JS *et al*. Insulin action during pregnancy. Studies with the euglycemic clamp technique. Diabetes. Apr 1985, 34(4): 380–389.
17. Betscher, NA, Wein P, Sheedy MT & Steffer B. Identification and treatment of women with hyperglycemia diagnosed during pregnancy can significantly reduce perinatal mortality rates. Aust. N. Z. J. Obstet. Gynaecol. 1996, 36: 239–247.
18. *Patrick M, John P, Sylvie H et al.* Gestational DM and Insulin Resistance: Role in Short- and Long-Term Implications for Mother and Fetus. J. Nutr. 2003, 133:1674S-1683S.
19. Xiang AH, Peters RH, Trigo E *et al*. Multiple metabolic defects during late pregnancy in women at high risk for type diabetes. Diabetes. Apr 1999, 48(4): 848–854.
20. Garvey WT, Maianu L, Hancock JA, *et al*. Gene expression of GLUT4 in skeletal muscle from insulin-resistant patients with obesity, IGT, GDM, and NIDDM. Diabetes Apr 1992, 41(4): 465–475.
21. Joseph Katz. Association between Periodontal Pockets and Elevated Cholesterol and Low Density Lipoprotein Cholesterol Levels. Journal of Periodontology. May 2002, 73(5): 494-500.
22. Knopp RH, Chapman M, Bergelin RO, *et al*. Relationship of lipoprotein lipids to mild fasting hyperglycemia and diabetes in pregnancy. Diabetes Care 1980, 3: 416–420.
23. Koukkou E, Watts GF, Lowy C *et al*. Serum lipid, lipoprotein and apolipoprotein changes in gestational diabetes mellitus: a cross-sectional and prospective study. J. Clin. Pathol. Aug 1996, 49(8): 634–637.
24. Deepa R, Velmurugan K, Arvind K, *et al*. Serum levels of interleukin 6, C-reactive protein, vascular cell adhesion molecule 1, and monocyte chemotactic protein 1 in relation to insulin resistance and glucose intolerance--the Chennai Urban Rural Epidemiology Study (CURES). Metabolism. Sep 2006; 55(9):1232-8.
25. Wang SL, Liu PQ, Ding Y, *et al*. Maternal serum tumor necrosis factor alpha concentration and correlation with insulin resistance in gestational diabetes. Zhonghua Fu Chan Ke Za Zhi. Nov 2004; 39(11):737-40.
26. Di Benedetto A, Russo GT, Corrado F *et al*. Inflammatory markers in women with a recent history of gestational diabetes mellitus. J Endocrinol Invest. Jan 2005; 28(1):34-8.
27. Temelkova-Kurktschiev T, Siegert G, Bergmann S *et al*. Subclinical inflammation is strongly related to insulin resistance but not to impaired insulin secretion in a high risk population for diabetes. Metabolism. Jun 2002; 51(6):743-9.
28. Leipold H, Worda C, Gruber CJ, *et al*. Gestational diabetes mellitus is associated with increased C-reactive protein concentrations in the third but not second trimester. Eur J Clin Invest. Dec 2005; 35(12):752-7.
29. Ferraz TB, Motta RS, Ferraz CL, *et al*. C-reactive protein and features of metabolic syndrome in Brazilian women with previous gestational diabetes. Diabetes Res Clin Pract. Oct 2007; 78(1):23-9. Epub 2007 Apr 20.
30. Wolf M, Sandler L, Hsu K, *et al*. First-trimester C-reactive protein and subsequent gestational diabetes. Diabetes Care. Mar 2003;26(3):819-24.
31. Rota S, Yildirim B, Kaleli B, *et al*. C-reactive protein levels in non-obese pregnant women with gestational diabetes. Tohoku J Exp Med. Aug 2005; 206(4):341-5.

32. Al-Harithy RN & Al-Ghamdi S. Serum resistin, adiposity and insulin resistance in Saudi women with type 2 diabetes. Ann Saudi Med. Jul-Aug 2005;25(4):283-7.
33. Tamas G & Keremji Z. Gestational diabetes: current aspects on pathogenesis and treatment. Exp Clin Endocrinol Diabetes. 2001, 109 (Suppl 2):S400–S411.
34. O'Sullivan JB. Subsequent morbidity among GDM women. In: Sutherland HW, Stowers JM, eds. Carbohydrate metabolism in pregnancy and the newborn. New York: Churchill Livingstone. 1984, 174–180.
35. Meyers-Seifer CH & Vohr B. Lipid levels in former gestational diabetic mothers. Diabetes Care. Dec 1996, 19(12):1351–1356.
36. Lim LP, Tay FB, Sum CF *et al*. Relationship between markers of metabolic control and inflammation on severity of periodontal disease in patients with diabetes mellitus. J Clin Periodontol. Feb 2007; 34(2):118-23.
37. Al-Shammari KF, Al-Khabbaz AK, Al-Ansari JM, *et al*. Risk indicators for tooth loss due to periodontal disease. J Periodontol. Nov 2005; 76(11):1910-8.
38. Kiran M, Arpak N, Unsal E *et al*. The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. J Clin Periodontol. Mar 2005; 32(3):266-72.
39. Craig RG, Yip JK, So MK *et al*. Relationship of destructive periodontal disease to the acute-phase response. J Periodontol. Jul 2003; 74(7):1007-16.
40. Morita M, Horiuchi M, Kinoshita Y, *et al*. Relationship between blood triglyceride levels and periodontal status. Community Dent Health. Mar 2004; 21(1):32-6.
41. Sonoki K, Nakashima S, Takata Y *et al*. Decreased lipid peroxidation following periodontal therapy in type 2 diabetic patients. J Periodontal. 2006; 77(11):1907-13.
42. Iwamoto Y, Nishimura F, Nakagawa M *et al*. The effect of antimicrobial periodontal treatment on circulating tumor necrosis factor-alpha and glycated hemoglobin level in patients with type 2 diabetes. J Periodontol. Jun 2001; 72(6):774-8.