J. Health Biol Sci. 2015; 3(1):18-24 doi:10.12622/2317-3076jhbs.v3i1.107p.18.2015

ORIGINAL ARTICLE

Association between periodontitis, gestational diabetes mellitus and diabetes mellitus type 1 and 2 in pregnant women

Associação entre periodontite, diabetes mellitus gestacional e diabetes mellitus tipo 1 e 2 em mulheres grávidas

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Abstract

Introduction: Diabetes is considered a risk factor for periodontitis. However, it is possible that periodontitis induces a systemic inflammatory process which could initiate and propagate an insulin resistance. **Objective:** The aim of this study was to analyze the association between periodontitis, gestational diabetes mellitus (GDM), diabetes mellitus type 1 (DM 1) and diabetes mellitus type 2 (DM 2) in pregnant women. **Methods:** The sample consisted of studying 20 pregnant women with DM 1 or DM 2, 20 women with GDM and 40 pregnant women without any endocrinopathy. Periodontal examination included analysis of bleeding on probing (BOP), probing depth (PD) and clinical attachment level (CAL). Periodontitis was defined as the presence of four or more teeth with at least one site with PD ≥ 4 mm and CAL ≥ 3 mm with BOP associated in the same site. **Results:** Results demonstrated an association between GDM and high maternal age, body mass index (BMI) and hypertension. The prevalence of periodontitis observed was 55%, 40% and 42,5% for women with DM 1 or DM 2 (p=0,360), with GDM (p=0,853) and in the control group, respectively. **Conclusions:** The sample showed high prevalence of periodontitis; however, there was no significant difference between pregnant women with DM 1 or DM 2, women with GDM or pregnant women in the control group.

Keywords: Periodontitis. Diabetes Mellitus. Gestational Diabetes. Pregnant Women.

Resumo

Introdução: O diabetes é considerado um fator de risco para periodontite. No entanto, é possível que a periodontite possa induzir um processo inflamatório sistêmico que poderia iniciar-se e propagar um quadro de resistência à insulina. **Objetivo:** O objetivo deste estudo foi analisar a associação entre a periodontite, o diabetes mellitus gestacional (DMG), o diabetes mellitus tipo 1 (DM1) e o diabetes mellitus tipo 2 (DM 2) em mulheres grávidas. **Métodos**: A amostra foi composta por 20 mulheres grávidas portadoras de DM 1 ou DM 2, 20 mulheres com diabetes gestacional e 40 mulheres grávidas sem qualquer endocrinopatia. O exame periodontal incluiu a análise de sangramento à sondagem (SS), profundidade de sondagem (PS) e nível clínico de inserção (NCI). A periodontite foi definida como a presença de quatro ou mais dentes com pelo menos um sítio com PS ≥ 4 mm e NIC ≥ 3 mm associado a SS no mesmo sítio. **Resultados:** Os resultados demonstraram uma associação entre DMG e idade materna elevada, alto índice de massa corporal (IMC) e hipertensão. A prevalência de periodontite observada foi de 55%, 40% e 42,5% para as gestantes com DM 1 ou DM 2 (p = 0,360), para mulheres com o DMG (p = 0,853) e para as gestantes do grupo controle, respectivamente. **Conclusões:** A amostra apresentou alta prevalência de periodontite; entretanto não houve diferença significativa entre as mulheres grávidas com DM 1 ou DM 2, as mulheres com diabetes gestacional ou mulheres grávidas no grupo de controle.

Palavras-chave: Periodontite. Diabetes Mellitus. Diabetes Gestacional. Gestantes.

INTRODUCTION

Periodontitis comprises a group of disorders characterized by the destruction of periodontal supporting tissue. The production of inflammatory mediators in the pathogenesis of the periodontitis called the attention to the systemic impact of periodontitis and its potential association with other systemic conditions, for example, cardiovascular diseases, diabetes and pregnancy complications[1,2].

Diabetes mellitus (DM) includes a prevalent and heterogeneous group of disorders that affect the metabolism of carbohydrates, lipids and proteins, characterized by a condition of hyperglycemia. Diabetes mellitus type 1 (DM 1) happens in approximately 10% of cases of DM. It results from a destruction of β cells in the pancreas and the consequent absolute insulin deficiency. It is usually diagnosed in children and adolescents. The onset of the disease often occurs abruptly and rarely affects obese individuals. In diabetes mellitus type 2 (DM 2) there is the association of a condition of insulin resistance to a relative deficiency of insulin. It comprises about 90% of all cases of DM. It usually affects people over the forties and many affected individuals are obese. Hyperglycemia has a gradual development, and may remain asymptomatic and undiagnosed for several years[3]. The gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance that has its onset during pregnancy. It has a prevalence of approximately 7%[4]. It usually develops in the second trimester of pregnancy and resolves spontaneously after delivery[5]. Risk factors for developing GDM include obesity, previous GDM, maternal age,

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Conflito de interesse: Não há conflito de interesse por parte de qualquer um dos autores.
Recebido em: 08 Set 2014; Revisado em: 04 Dez 2014; Aceito em: 28 Jan 2015.

and family history of DM[6]. A possible explanation for the etiology and pathogenesis of the GDM includes impaired pancreatic β cell function and decreased tissue sensitivity to insulin[7]. It has also been suggested that inflammatory and infectious processes may contribute to insulin resistance and manifestation of GDM.

DM is considered a risk factor for periodontitis. A change in the immune-inflammatory response of individuals with DM influences the highest prevalence, extent and severity of periodontitis[8]. Additionally, it is possible that periodontitis has a significant impact on the metabolic control of individuals with DM, contributing to the systemic dissemination of inflammatory mediators, microorganisms and bacterial products, inducing a systemic inflammatory process that could initiate and propagate a condition of insulin resistance. A few studies have evaluated the association between periodontitis and diabetes mellitus in pregnant women. The objective of this study was to analyze the association between periodontitis, GMD, DM 1 and DM 2 in pregnant women.

METHODS

Sample

The sample for this case-control study consisted of pregnant women who underwent prenatal care in a public maternity in Belo Horizonte, Brazil. Randomly, 20 pregnant women with DM 1 or DM 2, 20 women with GDM and 40 pregnant women without endocrine disease were selected. Inclusion criteria included pregnancy over 18 years old, singleton pregnancy, gestational age greater than 28 weeks, the presence of at least 12 teeth and no contraindication for periodontal exam. Cases of women undergoing antibiotic therapy or periodontal therapy in the last three months and carriers of acquired immunodeficiency syndrome were excluded. This study was approved by the Ethics Committee of the Federal University of Minas Gerais and by the Ethics Committee in Research of the State of Minas Gerais Hospital Foundation (CAAE 0096.0.287.203-09). The participants were informed about the study and signed an informed consent.

Socio-demographic characteristics

Social and demographic data were collected from each participant using a structured questionnaire. Data origin, age, marital stability, education, parity, smoking, alcohol consumption, history of dental visits, presence of systemic diseases and complications in previous pregnancies were collected. Participants were questioned about the presence, duration and frequency of smoking habit for classification in smokers, nonsmokers and former smokers[9].

Medical data

Through the analysis of medical records, data on gestational age, maternal weight and height and data concerning the metabolic conditions of the pregnant women were collected. Gestational age was established by the physician during prenatal consultation considering the last menstrual period. When it was not possible to determine the date of last menstrual period, gestational age was determined by the examination of obstetric ultrasound.

The body mass index (BMI) was calculated by dividing weight by height squared and the relationship between BMI and gestational age women were classified as underweight, normal weight, overweight and obesity[10].

All the women were subjected to an oral glucose tolerance test (OGTT) in the first prenatal consultation for screening of GDM. When the initial examination showed a negative result for the GDM, this test was performed again in the period between the 24th week and 28th week of gestation. The test was performed with standardized measures of fasting glucose, 1 hour and 2 hours after ingestion of 75g anhydrous glucose. In this curve, the cutoff points were considered 95 mg/dl for the fasting analysis, 180 mg/dl for the sample collected after 1 hour of ingestion of a glucose load and 155 mg/dl for samples collected after 2 hours. A single abnormal value on the OGTT was considered sufficient for the diagnosis of GDM.

Periodontal exam

The periodontal exam was performed after prenatal consultation. Clinical parameters included bleeding on probing (BOP), probing depth (PD) and clinical attachment level (CAL) of all teeth present were recorded. This examination was performed with manual circumferential probing and recording of 4 sites per tooth using a periodontal probe millimeter UNC-15 North Carolina style (UNC-15, Hu-Friedy, Chicago, USA). All participants were examined by a sole practitioner specializing in periodontics (RPEL). The intra-examiner agreement and its unweighted Kappa values were 0.90 to PD and 0.88 for CAL.

The following exclusion criteria were adopted: third molars; impossibility of determining the limit between cementum and enamel; teeth with change in the gingival morphology preventing the execution of the probing; teeth with extensive carious lesion; teeth with iatrogenic restorative procedures; and excessive presence of calculus[11].

The criteria used for the diagnosis of periodontitis was defined as the presence of four or more teeth with at least one site with PD ≥ 4 mm and CAL ≥ 3 associated with BOP at the same site[12].

Statistical Analysis

Descriptive and univariate analysis was performed to compare the characteristics between the groups: control, GDM and DM 1 or DM 2. Both groups were compared regarding age, ethnicity, marital stability, education, smoking, alcohol consumption, first pregnancy, hypertension, BMI, fasting glucose, previous pre-term birth, previous abortion and the presence of periodontitis by Mann-Whitney and chi-square tests when appropriate.

Sample characterization and comparison between the groups in regard to clinical periodontal parameters PD, CAL and BOP was performed by the Mann-Whitney test.

Multinomial regression was performed to examine the association between periodontitis, GDM and DM 1 or DM 2, considering all variables categorized in the sample stratified by blood glucose level. All variables were selected to enter into the models and were manually removed until only significant variables were retained. Interactions were based on their biologic plausibility. Odds Ratios (OR) and respective 95% CIs were calculated and reported.

All data collected were stored in a database, and all analyses were performed by means of statistical software (SPSS v.17.0, IBM, Chicago, USA). Results were considered significant for a probability of less than 5% ($p < 0.05$).

RESULTS

Table 1 presents the characteristics of the sample according to demographic and biological variables of interest. The average age of the sample of DM 1 or DM 2 group was 32.4 years, 32.3 years for the GDM group and 24.75 among pregnant women in the control group. Most pregmant women with DM were between 31 and 35 years, while 57,5% of women in the control group werw between 18 and 25 years old. When the GDM and DM 1 or DM 2 groups were compared to the control group in terms of mean age e and age group in terms of mean age and age group, a satisfically significant difference was observed. The sample consisted of women with low education en the three groupd analyzed. Marital stability was frequently reported in all groups. The first pregnancy was reported by 30% of pregnant women with DM 1 or DM 2, 20% of women with GDM and 37.5% of women in the control group. Smoking and alcohol consumption were infrequent in the sample studied. Hypertension was significantly more common in women with GDM and DM 1 or DM 2. Regarding BMI it was identified a significant difference between the control group and the group of women with GDM. Obesity was diagnosed in 55% of women with GDM. Reports of previous pre-term births were lower in groups, while the report of previous abortions was more frequent among pregnant women in the control group.

Table 2 shows the prevalence of periodontitis among the groups and the characteristics of the sample according to the periodontal condition. Female patients with DM 1 or DM 2 had higher prevalence of periodontitis (55%). However, the prevalence of periodontitis was 40% among women with GDM and 42.5% in the control group. Female patients with DM 1 or DM2 had higher percentage of sites with PD 5 or 6 mm and CAL ≥ 3 mm compared to the control group. There was not any significant difference between groups in the remaining parameters.

A multinomial regression model for blood glucose levels is shown in table 3 and table 4. It was found that only age was significant in the categories of glucose above 106 mg/dl for GDM. Only age was significant in the categories of glucose of 106 to 125 mg/dl for pregnant women with DM 1 or DM 2. Periodontitis was not associated with altered blood glucose levels in any group.

Table 1. Characteristics of the sample according to demographic and biological variables of interest.

Variable	Group				
	Control (n=40)	GDM (n=20)	p*	DM 1 OR 2 (n=20)	p †
Mean age (years)	24.75 ±5.15 (18-36)	32.30 ±5.01 (24-42)	<0.001	32.40 ±7.34 (19-45)	<0.001
Age range (years)					
18 to 25	23 (57.5%)	3 (15.0%)		5 (25.0%)	
26 to 30	12 (30.0%)	4 (20.0%)		2 (10.0%)	
31 to 35	4 (10.1%)	8 (40.0%)		7 (35.0%)	
36 to 40	1 (2.5%)	4 (20.0%)		3 (15.0%)	
≥ 41	0 (0.0%)	1 (5.0%)	<0.001	3 (15.0%)	<0.001
Marital Stability					
With partner	33 (82.5%)	18 (90.0%)		16 (80.0%)	
Without partner	5 (12.5%)	1 (5.0%)		3 (15.0%)	
Other	2 (5.0)	1 (5.0%)	0.658	1 (5.0%)	0,964
Education level (years)					
Illiterate	1 (2.5%)	0 (0.0%)		1 (5.0%)	
≤ 8	20 (50.0%)	11 (55.0%)		10 (50.0%)	
9 to 12	17 (42.5%)	8 (40.0%)		9 (45.0%)	
≥13	2 (5.0%)	1 (5.0%)	0.900	0 (0.0%)	0.736

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Variable	Group				
	Control (n=40)	GDM (n=20)	p*	DM 1 OR 2 (n=20)	p †
Smoking					
Nonsmoker	31 (77,5%)	15 (75.0%)		16 (80.0%)	
Smoker	3 (7,5%)	1 (5.0%)		3 (15.0%)	
Former Smoker	6 (15,0%)	4 (20.0%)	0.845	1 (5.0%)	0.386
Alcohol consumption	1 (2,5%)	1 (5.0%)	0.611	1 (5.0%)	0.611
Primiparity	15 (37,5%)	4 (20.0%)	0.170	6 (30.0%)	0.566
Chronic hypertesion	2 (5,0%)	7 (35.0%)	0.002	5 (25.0%)	0.023
BMI					
Underweight	5 (12,5%)	1 (5.0%)		2 (10.0%)	
Normal weight	18 (45,0%)	3 (15.0%)		5 (25.0%)	
Overweight	9 (22,5%)	5 (25.0%)		6 (30.0%)	
Obese	8 (20,0%)	11 (55.0%)	0.025	7 (35.0%)	0.397
Fasting Glucose (mg/dl)	NA	117.25±20.15 (97 – 183)		105.55±25.96 (65 – 183)	NA
Range of glucose					
≤ 95 mg/dl	NA	0 (0.0%)		5 (25.0%)	
96 a 105 mg/dl	NA	6 (30.0%)		7 (35.0%)	
106 a 125 mg/dl	NA	9 (45.0%)		5 (25.0%)	
≥ 126 mg/dl	NA	5 (25.0%)	NA	3 (15.0%)	NA
Previous pre-term delivery	0 (0,0%)	0 (0.0%)	NA	1 (5.0%)	0.154
Previous abortion	10 (25,0%)	2 (10.0%)	0.171	1 (5.0%)	0.059

* comparison between control and GDM groups; †comparison between DM 1 or DM 2 and control groups; NA = not applicable

Table 2. Prevalence of periodontitis and the periodontal condition of the sample.

Variable	Group				
	Control (n=40)	GDM n=20	p*	DM 1 or 2 (n=20)	p †
Periodontitis	17 (42.5%)	8 (40.0%)	0.853	11 (55.0%)	0.360
Teeth present (n)	26.17±2.07 (19 – 28)	25.10±2.69 (18 – 28)	0.118	25.55±2.06 (20 – 28)	0.173
Sites with BOP (%)	21.55	29.85	0.104	25.45	0.307
Sites with CAL ≥ 3 mm (%)					
and PD 4 mm	4.80	4.45	0.841	5.30	0.589
and PD 5 to 6 mm	2.82	2.55	0.575	4.05	0.016
and PD ≥ 7 mm	0.10	0.15	0.479	0.45	0.185

*comparison between control and GDM groups; †comparison between DM 1 or DM 2 and control groups; BOP = bleeding on probing; PD = probing depth; CAL = clinical attachment level.

Table 3. Multinomial regression model for blood glucose levels in the GDM group.

Variable	GDM group		
	Coefficient	OR (95% CI)	p
Blood glucose 96 to 105 mg/dl			
Constant	-8.090	NA	0.013
Age	0.189	1.208 (0.976 to 1.496)	0.083
Hypertension	3.412	30.340 (2.898 to 317.635)	0.004
Blood glucose 106 to 125 mg/dl			
Constant	-10.071	NA	0.001
Age	0.293	1.341 (1.111 to 1.617)	0.002
Hypertension	1.354	3.872 (0.322 to 46.562)	0.286
Blood glucose ≥ 126 mg/dl			
Constant	-12.253	NA	0.002
Age	0.342	1.408 (1.109 to 1.788)	0.005
Hypertension	1.180	3.256 (0.162 to 65.294)	0.440

NA = not applicable.
Main effects model; reference category = controls.

Table 4. Multinomial regression model for blood glucose levels in the DM 1 or 2 groups.

Variable	DM 1 or 2 group		
	Coefficient	OR (95% CI)	p
Blood glucose 96 to 105 mg/dl			
Constant	-7.883	NA	0.002
Age	0.218	1.243 (1.055 to 1.466)	0.009
Blood glucose 106 to 125 mg/dl			
Constant	-11.899	NA	0.002
Age	0.329	1.389 (1.102 to 1.750)	0.005
Blood glucose ≥ 126 mg/dl			
Constant	-7.373	NA	0.026
Age	0.174	1.190 (0.961 to 1.475)	0.111

NA = not applicable.
Main effects model; reference category = controls.

DISCUSSION

Diabetes mellitus comprises a group of metabolic disorders characterized by high blood glucose levels. Changes in the immune and inflammatory system caused by a condition of hyperglycemia are responsible for increasing the susceptibility of individuals with DM up to complications such as cardiovascular diseases, visual disorders, neuropathy and nephropathy. Periodontitis has also been considered a complication associated with DM[8]. Results of our study showed a high prevalence of periodontitis in pregnant women with DM 1 or DM 2 as compared to pregnant women without endocrine abnormality, although this difference was not considered statistically significant. The small sample size of our study is a limitation that may reflect this result.

High blood glucose levels lead to the formation of the advanced glycation end products (AGEs). These AGEs seem to be primarily responsible for the observed changes in individuals with DM. Individuals with DM have reduced their neutrophil function. However, monocytes and macrophages are more reactive and produces pro-inflammatory cytokines in an exaggerated manner. Additionally, these individuals may experience changes in homeostasis, maturation and collagen synthesis[13,14]. These changes may explain the relationship between DM and periodontitis.

The complications associated with DM, including periodontal changes, are directly related to the glycemic control. Additionally, the time of exposure to a hyperglycemic condition exerts a significant impact on the expression of complications[15]. Many studies have associated DM 2 with greater prevalence, extent and severity of periodontitis[16-20]. DM 2 has been demonstrated as a risk factor for periodontitis; however, the evidence is insufficient to establish a relationship between DM 1 and periodontitis[8]. The low age of individuals with DM 1 involved in research may be responsible for the lack of association between DM 1 and periodontitis, since periodontitis in different settings affects more individuals over 35-45 years of age[11].

Regarding the GDM, it is not expected that the glycemic change may influence the development of periodontitis, since the hyperglycemia that begins during pregnancy occurs in a short period and it is insufficient to lead to loss of periodontal supporting tissues. This is an important difference when compared to other types of DM, as DM 2 or DM 1. Time is critical for the interaction of AGEs and, consequently, for the involvement in the pathogenesis of complications associated with DM[7]. However, periodontitis as an infectious process might contribute to the manifestation of the insulin resistance observed in women with GDM.

Alongside with the GDM presence, well-established risk factors such as high maternal age, high BMI and a history of GDM, other factors may also be involved in the pathogenesis. Thus, the possibility that a systemic infectious process contributes to a framework for insulin resistance and consequently a manifestation of GDM has been discussed[21]. The possible association between GDM and periodontitis is guided by the fact that periodontitis is a significant source of inflammatory mediators; bacterial products and antigens may be significant factors in the development of the GDM process. Additionally, periodontal therapy can contribute to reducing the levels of key inflammatory molecules such as IL-6 and C - reactive protein, directly related to significant systemic changes.[22] Despite the high prevalence of reported periodontitis, the results of our study did not show any significant differences between women with GDM and pregnant women in the control group in relation to periodontitis.

A limited number of studies have evaluated the association between GDM and periodontitis[23-29]. Additionally, the results of these studies differ, without convergence to a robust conception of this relation. Similar to our work, three studies reported a lack of association between GDM and periodontitis[23,25,29]. Moreover, four studies demonstrated positive results that support the hypothesis about the association between periodontitis and GDM[24,26-28]. Besides the number of trials that is extremely reduced, significant methodological differences are observed between them. Remarkable differences especially in the diagnostic criteria for both GDM and periodontitis.

The definition of periodontitis is a timely issue and remains difficult to establish a consensus case definition of periodontitis without underestimating or overestimating the disease. That really reflects an inflammatory and infectious process that may have systemic effects. A criterion might reveal a strong impact in the prevalent rates of the disease[30].

Results of our study demonstrated an association between GDM and high maternal age, high BMI and chronic hypertension corroborating the results of previous studies[26,27,29,31-33].

The GDM is a unique opportunity for early intervention to prevent the development of DM 2, because women with GDM are at increased risk of developing DM after pregnancy. This fact reflects the importance of deepening studies of GDM. Moreover, the GDM can still have serious consequences such as maternal and infant, for example, macrosomia and maternal hypertensive disorder[4]. Indeed, the limited number of studies of the association between GDM and periodontitis and their conflicting results converge to the need for additional studies on this association.

Regarding the association of GDM and periodontitis, the possibility of future development of DM 2 in women with GDM should be emphasized. The fact that the DM 2 is a risk factor for periodontitis suggests the importance of preventive measures for periodontitis in the group of women with GDM.

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Como citar este artigo/How to cite this article:

Lima RPE, Costa FO, Cota LOM, Cyrino RM. Association between periodontitis, gestational diabetes mellitus and diabetes mellitus type 1 and 2 in pregnant women. J Health Biol Sci. 2015 Jan-Mar; 3(1):18-24