ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 11, Issue, 01, pp.162-167, January, 2019

DOI: https://doi.org/10.24941/ijcr.33553.01.2019

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

PERIODONTITIS AND GESTATIONAL DIABETES MELLITUS: A CASE CONTROL STUDY

[1*]Saindhya Tora Sonowal, [2]Swarga Jyoti Das, [3]Gokul Chandra Das and [4]Pawan Kumar

[1]Registrar, Dept., Of Dentistry, Tezpur Medical College and Hospital, Tezpur, Assam
[2]Prof and HOD Deptt., Of Periodontics, Regional Dental College, Bhangagarh, Guwahati, Assam
[3]Prof & HOD Deptt., Of Obstetrics and Gynaecology, Guwahati Medical College and Hospital, Bhangagarh, Guwahati, Assam
[4]PhD Scholar, Tezpur Central University, Assam

ARTICLE INFO

Article History:
Received 09th October, 2018
Received in revised form
26th November, 2018
Accepted 24th December, 2018
Published online 30th January, 2019

Key Words:

Gestational Diabetes Mellitus,
Oral Glucose tolerance test,
Periodontitis.

ABSTRACT

Context: Gestational diabetes mellitus (GDM) is a special form of diabetes mellitus (DM) that begins or is first detected during pregnancy. Periodontal disease has been found as a risk factor for different systemic conditions, among which DM has been widely studied. Though some studies show the association between periodontal disease and GDM, others fail to observe such correlations. **Aims:** The present study was planned to determine the association of maternal periodontal disease and GDM. **Methods:** The study comprised of 40 pregnant women, of which 20 were cases and 20 were controls. All subjects underwent a laboratory screening test for GDM between 24 to 30 weeks of gestation based on the recommendation of the Obstetricians and Gynaecologists. The subjects were divided into two groups: Group A (control) and Group B (case) based on the blood glucose level of oral glucose tolerance test (OGTT), as per the criteria of ADA (2004). For the periodontal status, a full mouth periodontal examination was performed assessing the gingival index (GI), probing pocket depth (PPD), relative attachment level (RAL) and plaque index (PI) using a UNC -15 probe by a single examiner who was blinded on the diabetic status of the pregnant women. To compare the means, student's t-test was performed. **Results:** GI score in women with GDM was 2.60 ± 0.66 (range 1.05 - 3.00) whereas those without GDM 1.94 ± 0.77 (range 1.07 - 3.00), ($p<0.01$). The mean PPD of control group was 2.50 ± 0.70 (range 1.38 - 3.71) mm and of case group was 3.91 ± 0.96 (range 2.42 - 5.05) mm; ($p<0.001$). The mean RAL of control group was 8.23 ± 1.83 (range 3.57 - 11.14) mm and of case group was 9.82 ± 0.76 (range 8.71 - 11.25) mm; ($p<0.01$). The mean PI of control group was 1.42 ± 0.48 (range 0.69 - 1.97) and in case group was 2.09 ± 0.90 (range 0.04 - 2.63); ($p<0.001$). **Conclusions:** GI, PI, PPD and RAL were more in subjects with GDM than those without GDM. Hence, GDM is associated with periodontal disease.

Citation: ***Saindhya tora Sonowal, Swarga Jyoti Das, Gokul Chandra Das and Pawan Kumar*. 2019.** "Periodontitis and gestational diabetes mellitus: a case control study", *International Journal of Current Research*, 11, (01), 162-167.

INTRODUCTION

Over the past two decades, possible role for periodontal disease as a risk factor for systemic conditions have been investigated by a number of studies (O'Reilly, 2000). Recent advances in the field of molecular biology including the microbiology, immunology and genetics have lead researchers to resume the study of the relationship between oral and systemic conditions with a more scientifically oriented approach. Thus, the theory of "focal infection" is to some extent revisited, which came to an end in the early 1950s. This theory proposed that certain bacteria and its products within the periodontal pocket could enter the bloodstream and thus could be harmful to the whole body (Thoden et al., 1984).

Corresponding author: **Dr. Saindhya Tora Sonowal,**
Registrar, Dept., Of Dentistry, Tezpur Medical College and Hospital, Tezpur, Assam.

The systemic involvement includes the cardiovascular (Humphrey et al., 2018), and respiratory systems (Scannapieco et al., 2003) outcome of pregnancy (Pitiphat, 2008) and diabetes (Mealey, 2009). Recently, some emerging evidence has indicated an association of periodontitis with kidney disease, rheumatoid arthritis and pancreatic cancer also (Henderson, 2009). Among the various disorders mentioned above, diabetes mellitus is widely studied so far. Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia due to the defective secretion or activity of insulin or both. It is classified as Type 1, 2, gestational and others due to different genetic defects in pancreatic β-cell function and insulin action (American Diabetes Association, 2001). Gestational diabetes mellitus (GDM) is a special form of DM that begins or is first detected during pregnancy (American Diabetes Association, 2004).

It affects ~ 7% of all pregnancies. Detection of GDM is very important considering its association with maternal and fetal complications like an increased risk of macrosomia, preeclampsia and perinatal death (Tracy, 2005). These complications can be reduced with medical nutrition therapy, close monitoring of glucose levels and insulin therapy. Besides, the history of GDM increases the risk for subsequent development of type 2 diabetes. GDM is diagnosed by detecting the blood glucose levels every hour up to 3hrs after administration of either 75 or 100 gm of glucose orally (oral glucose tolerance test; OGTT). The diagnostic criteria given by American Diabetic Association (ADA) and World Health Organization (WHO) are given in Table 1.

In pregnancy, resistance to insulin with a compensatory increase in β-cell response occurs which results in hyperinsulinemia. The insulin sensitivity is reduced by as much as 80%. This phenomenon usually begins in the second trimester and progresses throughout the remaining period of pregnancy. The causes of insulin resistance during pregnancy include the placental secretion of hormones, *e.g.* progesterone, cortisol, placental lactogen, prolactin and growth hormone variant. The insulin resistance is likely to ensure that the fetus has an adequate supply of glucose by changing the maternal energy metabolism from carbohydrates to lipids (Cianni, 2003). The women with GDM have a greater severity of insulin resistance compared to the insulin resistance seen in normal pregnancies. Moreover, they also have impairment in insulin secretion, particularly in the first phase of secretion. This decrease in first phase insulin release may be a marker for deterioration of β-cell function (Xiang et al., 1999). There is also a subset of women with GDM who have evidence of islet cell autoimmunity (1.6-38%). The women with GDM may be at risk for developing an autoimmune form of diabetes later in life and also for defect in the β-cell, such as a mutation in glucokinase (Maurico et al., 1996). GDM is coupled with both fetal and maternal complications. Fetal complications include macrosomia, neonatal hypoglycemia, perinatal mortality, congenital malformation, hyperbilirubinemia, polycythemia, hypocalcemia and respiratory distress syndrome (Sheffield et al., 2002). Perinatal mortality (including stillbirths and neonatal deaths) was reported to be more in women with GDM (Wood, 2000).

The incidence of a major malformation in an infant whose mother is GDM is 4.8%, in contrast to 1-3% with no history of diabetes (Jeanne, 2002). In addition, long-term complications of GDM to the offspring include an increased risk of glucose intolerance, diabetes and obesity (American Diabetes Association, 2004). Maternal complications associated with GDM include hypertension, preeclampsia and an increased risk of cesarean delivery (Schmidt, 2011). Therefore, diagnosis of GDM plays an important role to take up an intervention that improves insulin sensitivity, which may further help in prevention of these fetal as well as the maternal complications (Seely, 2003). In addition, women with a history of GDM have an increased risk of developing diabetes after pregnancy compared to the general population, with a conversion rate of up to 3% per year (Cianni, 2003). Periodontal disease is caused by bacteria present in dental plaque, especially the gram-negative rods, *e.g. Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis* and *Tanerella forsythus* (Haffajee, 1994). These pathogens, particularly *P. gingivalis* have the ability to invade the deep vascular endothelium within the periodontium (Chun, 2005).

They can also initiate and perpetuate the inflammatory responses either directly by the release of noxious substances, such as ammonia (NH3) and hydrogen sulfide (H2S) or by activating the immune-inflammatory response through the production of a variety of inflammatory mediators and destructive enzymes, such as cytokines (*e.g.* IL-1β and TNF-α), prostanoids (PGE2) and matrix metalloproteinases (MMPs). Again, these microorganisms can gain entrance to the blood and circulate throughout the body leading to transient bacterimia (Amar, 2003). Thus, viable bacteria, bacterial products and proinflammatory cytokines from the inflammed periodontal tissues may enter the circulation and trigger a maternal systemic inflammatory response. This may induce insulin resistance and further destruction of the pancreatic β-cell (Moller, 2000). Pregnancy itself is a stressful state with increased inflammatory activity (Williams, 2003), and thus, leads to increased insulin resistance (Xiong, 2009). Since infection leads to insulin resistance, maternal chronic periodontal disease could induce a sustained systemic inflammatory response that may result in a state of insulin resistance. Such an infection-induced insulin resistance in response to periodontal infection could exacerbate the preexisting pregnancy-induced insulin resistance and may cause impaired glucose tolerance and the manifestation of GDM (Figure 1).

Aims and Objective

The present study was planned to determine the relationship of periodontal health and GDM considering the clinical parameters: gingival index (GI), probing pocket depth (PPD), relative attachment level (RAL) and plaque index (PI).

MATERIALS AND METHODS

The study was conducted partly in the Department of Periodontology and Oral Implantology, Regional Dental College and Hospital, Guwahati and partly in the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati. The concerned gynaecologist was well informed regarding the study design. No change in the medication or diet was made for the patients. A total number of 40 pregnant women participated in this study. The subjects included in the study were explained the entire procedure in details and their consent was taken.

Method of Data Collection: Thorough medical history and the laboratory investigation of the subjects were obtained in details. All the pregnant women underwent a laboratory test for GDM between 24-30 weeks of gestation. The subjects were divided into two groups: Group A (control) and Group B (case) based on the blood sugar level of OGTT with the administration of 100 gm of glucose orally, as per the criteria of ADA. Besides, all the subjects included in the study were free from any other types of diabetes. A full mouth periodontal examination was performed in all the subjects included in the study on day 0. To judge the periodontal status, the parameters recorded were: GI, PPD, RAL and PI. The parameters were recorded manually at four sites per tooth (Mesial, distal, mid facial/buccal and mid palatal/lingual) using UNC-15 probe**.** In addition to the above mentioned examination, oral hygiene habits were also discussed with all the subjects. The data collected were analysed statistically. Student's t –test was performed in the study. All the analysis was performed using SPSS16.

RESULTS AND OBSERVATIONS

The mean age was 24.00 ± 0.64, (range of 21-32 years). The mean GI in the subjects of group A was found to be 1.94 ± 0.77 (range of 1.07 - 3.00). Again, the mean GI in the subjects of group B was found to be 2.60 ± 0.66 (range of 1.05 - 3.00), as shown in Table 2 and represented graphically in Figure 2. The mean PPD in the subjects of group A was found to be 2.50 ± 0.70 (range 1.38 - 3.71) mm, while the same in the subjects of group B was found to be 3.91 ± 0.96 (range 2.42 - 5.05) mm as shown in Table 2 and graphically represented in Figure 3.

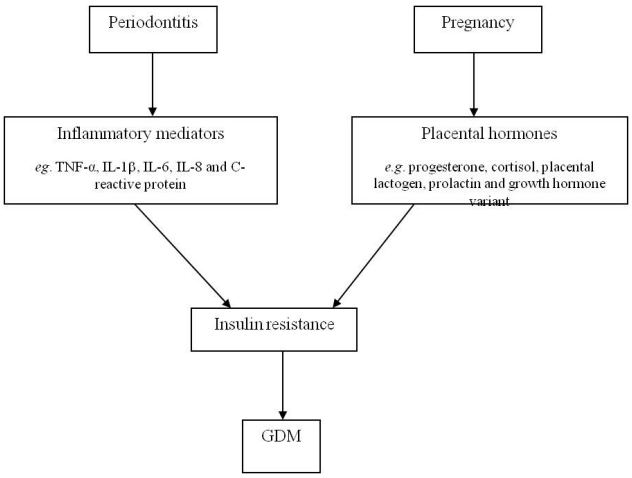

Figure 1. Interrelationship between periodontitis and GDM

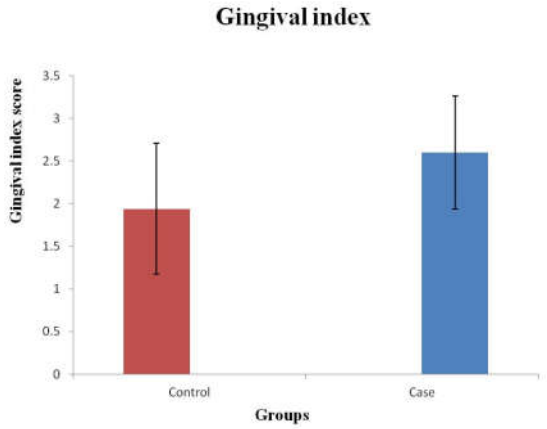

Figure 2. Mean gingival index in control and case groups

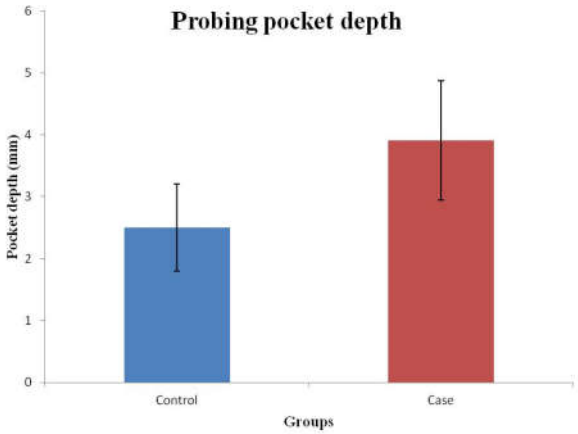

Figure 3. Mean PPD (in mm) in control and case

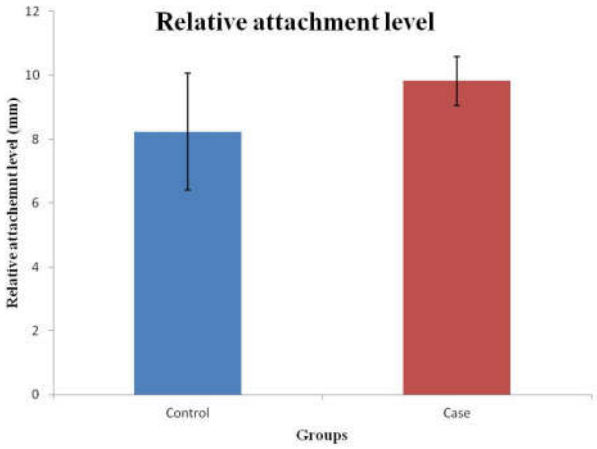

Figure 4. Mean RAL (in mm) in control and case

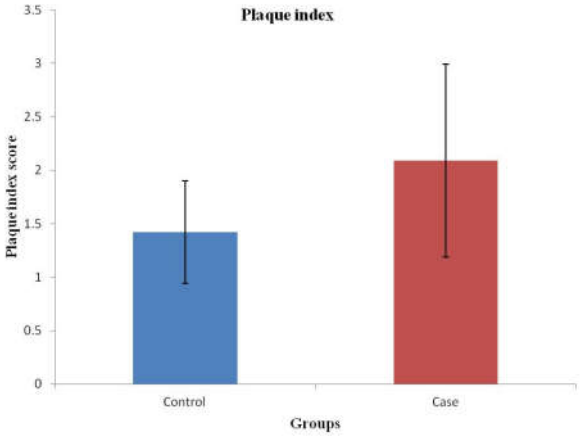

Figure 5. Mean plaque index in control and case

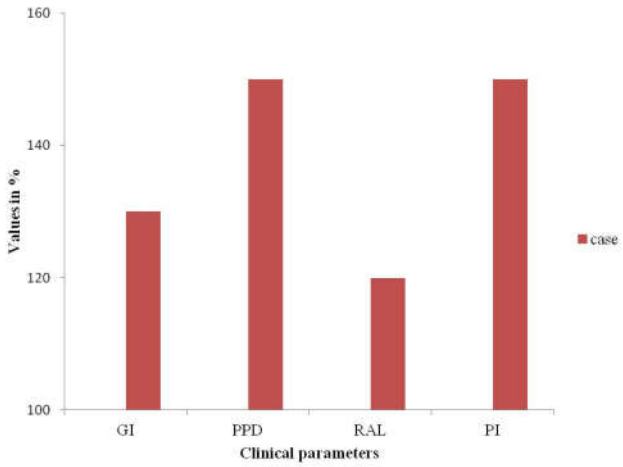

Figure 6. Clinical parameters in % as found in cases compared to controls

Table 1. ADA and WHO criteria for the diagnosis of GDM

	Threshold Levels Blood Glucose (mg/dL)		
	ADA		WHO
	OGTT (100 gm)	OGTT (75 gm)	OGTT (75gm)
Fasting	95	95	126
1hour PP	180	180	-
2 hour PP	155	155	140
3hour PP	140	-	-

Table 2. Clinical parameters in control and case

Clinical parameters	Groups		t-value	*p* value
	Control (n=20)	Case (n=20)		
Gingival Index	1.94 ± 0.77 (1.07 - 3.00)	2.60 ± 0.66 (1.05 - 3.00)	-2.90	0.00623
Probing Pocket Depth	2.50 ± 0.70 (1.38 - 3.71)	3.91 ± 0.96 (2.42 - 5.05)	-5.33	0.00000
Relative attachment level	8.23 ± 1.83 (3.57 - 11.14)	9.82 ± 0.76 (8.71 - 11.25)	-3.57	0.00098
Plaque Index	1.42 ± 0.48 (0.69 - 1.97)	2.09 ± 0.90 (0.04 - 2.63)	-2.91	0.00603

As shown in Table 2, the mean RAL in the subjects of group A was found to be 8.23 ± 1.83 (range of 3.57 - 11.14) mm and the mean RAL in the subjects of group B was found to be 9.82 ± 0.76 (range of 8.71 - 11.25) mm. The finding is represented graphically in Figure 4. The mean PI in the subjects of group A was found to be 1.42 ± 0.48 (range of 0.69 - 1.97) and that in the subjects of group B was found to be 2.09 ± 0.90 (range of 0.04 - 2.63) as shown in Table 2 and represented graphically in Figure 5. As shown graphically in Figure 6, it is seen that all the parameters showed higher values in the case group in comparison to the controls. It is clear that GI was found to be 130% more in the cases than in the controls, represented as 100. Similarly, the PPD, RAL and PI were recorded as 150%, 120% and 150% more in the cases than the controls.

DISCUSSION

Periodontal disease has been shown to be associated with an increased risk of GDM and a 'dose–response' relationship *i.e.* an increased risk of GDM with increased severity of periodontal disease has been observed (Khader, et al., 2006). Gingival health is assessed by the gingival index. Here it is seen that the gingiva is more inflamed in the subjects of case group than in the controls, so there is a possibility of influence of gingival inflammation on blood glucose level. It has been shown in other studies that gingival inflammation is more in diabetics than in nondiabetics (Khader et al., 2008). Thus, the present study supports the observation of the previous investigators. PPD and RAL are important clinical parameters and it is seen that PPD is more in the subjects of case group than in the controls. It has been shown by Hugoson *et al*., (1989), Khader *et al*., (2006), Kasaj *et al*., (2006) that pocket depth is more in diabetics than in nondiabetics. Also the present study reveals more loss of attachment in the case group than in the control. Thus, the present study also supports their observation and indicates that periodontal health is more detoriated in the diabetics than in nondiabetics. Increased in PPD and RAL in the case group than in the control suggests a possibility of influence of periodontal disease on blood glucose level. The same was observed by Guthmiller *et al.,*(2001), Khader *et al*., (2006), Seppala *et al*., (2005). The mean PI of control (A) group was found to be 1.42 ± 0.48 (range of 0.69 - 1.97), in contrast of 2.09 ± 0.90 (range of 0.04 - 2.63) observed in the case (B) group; ($p<0.001$). It has been shown in other studies that PI is more in diabetics than in nondiabetics (Khader *et al*., 2006, Kasaj *et al*., 2008, Li *et al*., 2007). Thus, the present study supports the observation of these investigators. Again, reduction in blood glucose level has been reported after periodontal therapy by few studies (Tsiavou et al., 2004). So, the periodontal infection may be a potent etiological factor for GDM, which may occur due to increased resistance to insulin (Kinane, 2003 and Kim, 2002). Periodontal disease has been shown to be associated with GDM in cross-sectional and case-control studies (Xiong, 2006 and Tsiavou, 2004).

Though it still remains to be determined whether periodontal disease is a causal risk factor for GDM or is a result of GDM, it is well established that periodontal disease is more prevalent in type 1 and 2 diabetics compared to the healthy controls. The observation of association between the periodontal disease and GDM might be explained by the fact that GDM causes periodontitis, similar to type 1 and 2 diabetes. However, compared to them, GDM only represents an early stage of glucose dysregulation and a temporary impaired glucose tolerance that occur in later pregnancy. The elevated glucose levels in the majority of women diagnosed with GDM will usually return to normal after parturition. Therefore, the hyperglycemia of GDM may be too mild and of too short duration to have a significant effect on gingival tissues and to cause destruction of the supporting structures manifesting as periodontitis. An alternative explanation is that periodontal disease may be a cause, instead of the result, of GDM. Periodontal infection, a local and chronic sub-clinical inflammation, triggers a maternal systemic inflammatory response. Since pregnancy itself is a stressful state with increased inflammatory activity and marked insulin resistance such an infection-induced insulin resistance in response to maternal periodontal infection may thus worsen the preexisting pregnancy-induced insulin resistance that may cause impaired glucose tolerance and the manifestation of GDM.

There may also be a common genetic cause for both of the periodontal disease and GDM, which may results in the observed association between these two disorders. Though a clear correlation between the gene polymorphisms and GDM is lacking, few studies have 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 preexisting genetic polymorphisms may result in imbalances between the inflammatory cytokine systems, predisposing to both periodontal disease and GDM simultaneously. To ensure the validity as well as to limit the potential biases in the study, several measures were taken like: periodontal examinations were performed by only one examiner to eliminate inter-examiner variability, more objective approaches were used to assess periodontal disease by comparing the mean levels of periodontal indices, namely GI, PPD, RAL, PI and the subjects of both groups were selected from the same source which limits the potential selection bias that may occur in a single hospital-based case-control study. It is reported that 35–60% of women with GDM develops type 2 DM within 10 years (Kim, 2002). Diabetes, especially type 2, has become one of the most common chronic diseases. GDM thus provides a window of opportunity for early interventions to prevent later development of type 2 diabetes in young women. It has also been reported that women with a previous history of GDM after parturition have a sustained higher prevalence of periodontitis compared to those without diabetes , which is also supported by the present study. Since women with GDM are at higher risk of developing type 2 diabetes and periodontal disease has been implicated as a risk factor for type 2 diabetes, periodontal disease may contribute to future development of diabetes in women with a previous history of GDM. Periodontal disease is preventable and curable. If periodontal disease is confirmed as a risk factor for GDM, this will open one of the doors to prevent this dreaded condition of the modern age. However, it needs further studies to prove that periodontal disease is a positive contributory factor of GDM through some intervention studies.

In that case, improving oral health and treating periodontal disease before or during pregnancy may not only reduce the maternal and infant morbidity associated with GDM during pregnancy, but also prevent type 2 DM later in life.

Conclusion

The influence of DM on periodontal health and that of periodontal health on the glycemic control is widely discussed in the dental literature. Association of periodontal disease and GDM is frequently considered. However, contradictory conclusions have been put forwarded by various investigators, thus it remains uncertain. Considering this, the present study was carried out to evaluate the correlation of these two conditions, namely periodontal health and GDM. In the light of the present study carried out, the following conclusions are drawn: GI score, PPD, RAL and PI score are more in women with GDM (130%, 150%, 120% and 150%, respectively) than those of without GDM and are significant statistically. Both periodontal disease and pregnancy have been reported to be associated with significant metabolic derangement in the host. Thus, health education plays an important role in prevention as well as reduction of both of the conditions. Observation of the present study that increased in prevalence of periodontal diseases among the women with GDM also indicates the requirement of strong steps towards the primary prevention, including the health education system.

It should start as early as possible to have a practical impact to attain positive outcome. Screening could detect females with uncontrolled metabolic state, which may demand aggressive primary preventive strategies and further, induction of preventive strategies may relieved the future society from an important unwanted social burden. Similarly, there is a demand that periodontists should 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. However, further study involving larger sample size and of longer duration is required to confirm the findings of the present study. And an intervention study to evaluate the effects of periodontal therapy on GDM is also required. Thus, a long term, follow up study is on demand for better understanding of these commonly associated conditions, namely periodontitis and GDM.

REFERENCES

Amar S and Han X. 2003. The impact of periodontal infection on systemic diseases. *Med Sci Monit*., 9:RA291–299.

American Diabetes Association. Gestational diabetes mellitus (Position Statement). Diabetes Care. 2004: 27 (Suppl. 1):S88–S90.

American Diabetes Association. Gestational diabetes mellitus. *Diabetes Care*. 2004: 27 (Suppl. 1):S88–S90.

American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. 2001: *Diabetes Care*. 24(supp 1): S5-S20.

Buchanan TA and Xiang AH. 2005. Gestational Diabetes Mellitus. *J Clin Invest*., 115:485–491.

Chun YH, Chun KR, Olguin D and Wang HL. 2005. Biological foundation for periodontitis as a potential risk factor for atherosclerosis. *J Periodontal Res.* 40:87–95.

Cianni GD, Miccoli R, Volpe L, Lencioni C and Del Prato S. 2003. Intermediate metabolism in normal pregnancy and in gestational diabetes. *Diabetes Metab Res Rev*. 19:259–270.

Cianni GD, Miccoli R, Volpe L, Lencioni C and Del Prato S. 2003. Intermediate metabolism in normal pregnancy and in gestational diabetes. *Diabetes Metab Res Rev*., 19:259–270.

Guthmiller JM, Hassebroek-Johnson JR, Weenig DR, Johnson GK, Kirchner HL, Kohout FJ, Hunter SK. 2001. *J Periodontol*., 72:1485.

Haffajee AD and Socransky SS. 1994. Microbial etiological agents of destructive periodontal diseases. *Periodontol 2000*. 5:78–111.

Henderson B. Periodontal medicine and systems biology. Chichester, UK 2009. Ames, Iowa: Wiley-Blackwell.

Humphrey LL, Fu R, Buckley DI, Freeman M and Helfand M. 2008. Periodontal disease and coronary heart disease incidence: a systematic review and meta-analysis. J. Gen. Intern. Med., 23: 2079-2086.

Jeanne S. Sheffield, Erin L. Butler-Koster, Brian M. Casey, Donald D. McIntire and Kenneth J. Leveno. 2002. Maternal Diabetes Mellitus and Infant Malformations. *Obstetrics & Gynecology*.,100:5:925-930.

Kasaj A, Zafiropoulos GG, Tekyatan H, Pistorius A and Willershausen. 2006. Periodontal Disease Status of Pregnant Women with Diabetes Mellitus. *Coll. Antropol*., 32(1):115-118.

Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A. and Batayha WQ. 2006. Periodontal Status of Diabetics Compared with Nondiabetics: A Meta-Analysis. 20(1):59-68

Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A and Batayha WQ. 2006. Periodontal Status of Diabetics Compared with Nondiabetics: A Meta-Analysis. 20(1):59-68

Kim C, Newton KM and Knopp RH. 2002. Gestational Diabetes and the Incidence of Type 2 Diabetes: A Systematic Review. *Diabetes Care*. 25:1862–1868.

Kinane DF and Hart TC. 2003. Genes and Gene Polymorphisms Associated with Periodontal Disease. *Crit Rev Oral Biol Med*., 14:430–449.

Lamster IB, Lalla E, Borgnakke WS and Taylor GW. 2008. The Relationship between Oral Health and Diabetes Mellitus. *J Am Dent Assoc*. 139 (Suppl):19S–24S.

Li Z, Sha YQ, Zhang BX, Zhu L and Kang J. Prevalence and 2007. Related Factors of Periodontitis in Community-Dwelling Chinese with Diabetes. *Zhonghua Kuo Qiang yi Xue Za Zhi*., 42(2):100-1

Maurico D, Balsells M, Morales J, Corcoy R, Puig-Domingo M and de Leiva A. 1996. Islet cell autoimmunity in women with gestational diabetes and risk of progression to insulin-dependent diabetes mellitus. *Diabetes Metab Rev*., 12:275–285.

Mealey BL. and Oates TW. 2006. Diabetes mellitus and periodontal diseases. *J Periodontology*. 77: 1289-1303.

Moller DE. 2000. Potential role of TNF-alpha in the pathogenesis of insulin resistance and type 2 diabetes. *Trends Endocrinol Metab*., 11:212–217.

O'Reilly PG and Claffey NM. 2000. A history of oral sepsis as a cause of disease. Periodontol, 2000: 23:13-18.

Pitiphat W, Joshipura KJ, Gillman MW, Williams PL, Douglass CW and Rich-Edwards JW. 2008. Maternal periodontitis and adverse pregnancy outcomes. *Community Dent.Oral Epidemiol.* 2008: 36: 3-11.

Scannapieco FA, Bush RB and Paju S. 2003. Associations between periodontal disease and risk for nosocomial bacterial pneumonia and chronic obstructive pulmonary disease. A systematic review. *Ann.Periodontol.* 8: 54-69.

Schmidt MI, Duncan BD, Reichelt AJ, Branchtein L, Matos MC, Forti A, Spichler ER, Pousada J, Teixeira MM and

Yamashita T. Gestational diabetes mellitus diagnosed with a 2-h 75-g oral glucose tolerance test and adverse pregnancy outcomes. *Diabetes Care*. 2001:24:1151–1155.

Seely EW and Solomon CG. Insulin resistance and its potential role in pregnancy-induced hypertension. *J Clin Endocrinol Metab*. 2003:88:2393–2398.

Seppala B, Seppala M and Ainamo J. 2005. A Longitudinal Study on Insulin-Dependent Diabetes Mellitus and Periodontal Disease. *Journal of Clinical Periodontology*. 20(3):161-165.

Sheffield JS, Butler-Koster EL, Casey BM, McIntire DD and Leveno KJ. 2002. Maternal diabetes mellitus and infant malformations. *Obstet Gynecol*. 100:925–930.

Teeuw WJ, GErdes VEA and Loos BG. 2010. Effect of Periodontal Treatment on Glycemic Control of Diabetic Patients. *Diabetes Care*. 33:421–427.

Thoden V. and Abraham-Inpijn L. 1984. Plaque and systemic disease: a reappraisal of the focal infection concept. *J.Clin.Periodontol*. 11: 209-220.

Tracy L Setji, Ann J. Brown and Mark N. Feinglos. 2005. Gestational Diabetes Mellitus. Clinical diabetes. 23:1:17-24.

Tsiavou A, Hatziagelaki E, Chaidaroglou A, *et al*.. TNF-alpha, TGF-beta1, IL-10, IL-6, Gene Polymorphisms In Latent Autoimmune Diabetes Of Adults (LADA) and Type 2 Diabetes Mellitus. *J Clin Immunol*. 24:591–599.

Williams D. Pregnancy: a stress test for life. *Curr Opin Obstet Gynecol*. 2003:15:465–471.

Wood SL, Sauve RS, Ross S, Brant R and Love E. Prediabetes and perinatal mortality. *Diabetes Care*. 2000:23:1752–1754.

Xiang AH, Peters RK, Trigo E, Kjos SL, Lee WP and Buchanan TA. 1999. Multiple metabolic defects during late pregnancy in women at high risk for type 2 diabetes. *Diabetes*. 48:848–854.

Xiong X, Buekens P, Fraser W, Beck J, Offenbacher S. 2006. Periodontal Disease and Adverse Pregnancy Outcomes: A Systematic Review. *BJOG.* 113:135–143.

Xiong X, Buekens P, Vastardis S and Pridjian G. Periodontal Disease and Gestational Diabetes Mellitus. 2006. *Am J Obstet Gynecol*., 195:1086–1089.

Xiong X, Elkind-Hirsch KE, Vastardis S, Delarosa RL, Pridjian G and Buekens. 2009. Periodontal Disease Is Associated With Gestational Diabetes Mellitus: A Case-Control Study. *J Periodontol.* 80(11) :1742-1749.

****