

Periodontitis during pregnancy: a case control study

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Abstract

Periodontal diseases are a common group of conditions that cause inflammation and destruction to the supporting structures of the teeth. When it's found during pregnancy may lead to adverse pregnancy outcomes.

Objective: To evaluate the relation ship between periodontal diseases and adverse pregnancy outcomes.

Patients and methods: 300 pregnant women were assessed for periodontal status by the criteria commonly used in epidemiological studies, probing depth (PD), Plaque index (PI), Gingival index (GI), Radiological Assessment and clinical attachment level (CAL). Women were then classified according to periodontal status in to two patient groups (150 pregnant women with periodontitis) and control group (150 pregnant women without periodontitis). For all participants C-reactive protein (CRP) assay was performed, follow up of all participants until delivery was done to evaluate obstetric complications associated with each group.

Results: In general periodontal disease (PD) is significantly associated with adverse pregnancy outcomes P. value <0.001. Also PD is significantly associated with preterm labor and low birth weight P. value 0.04 & 0.004 respectively. Also there is a highly significant difference between both case and control group in relation to the presence of positive C. reactive protein. 74.7% VS 8.7% for patient and control group respectively ($P < 0.001$).

Key words: periodontal disease, adverse pregnancy outcomes, C. reactive protein.

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Introduction

Increased levels of the hormones progesterone and estrogen can have an effect on the small blood vessels of the gingiva, making it more permeable. "Barak, et al (2003)"

This increases the mother's susceptibility to oral infections, allowing pathogenic bacteria to proliferate and contribute to inflammation in the gingiva. This hyperinflammatory state increases the sensitivity of the gingiva to the pathogenic bacteria found in dental biofilm. Females often see these changes during other periods of their life when hormones are fluctuating, such as puberty, menstruation, pregnancy, and again at menopause (American Academy of Periodontology; 2011)

Recently it is suggested that the presence of maternal periodontitis has been associated with adverse pregnancy outcomes, such as preterm birth (Offenbacher, et al (2001), preeclampsia, (Boggess, et al; 2003), gestational diabetes (Xiong, et al;2006), delivery of a small-for-gestational-age infant Boggess, et al; 2006) and fetal loss (Moore, et al; (2004). The strength of these associations ranges from a 2-fold to 7-fold increase in risk. The increased risks suggest that periodontitis may be an independent risk factor for adverse pregnancy outcomes.

Periodontal diseases are a group of conditions that cause inflammation and destruction to the supporting structures of the teeth. These chronic oral infections are characterized by the presence of a biofilm matrix that adheres to the periodontal structures and serves as a reservoir for bacteria. Dental plaque biofilm is a complex structure of bacteria that is marked by the excretion of a protective and adhesive matrix "Thomas, et al (2006)".

CRP is an acute-phase reactant synthesized by the liver in response to the inflammatory cytokines, interleukin (IL)-6, IL-1, and tumor necrosis factor-alpha. Circulating CRP levels are a marker of systemic inflammation and are associated with periodontal disease. CRP could amplify the inflammatory response through complement activation, tissue damage, and induction of inflammatory cytokines and may mediate the relationship between periodontitis and adverse pregnancy outcomes. "Craig RG et al. 2003".

Aim of the study

To evaluate the relation ship between periodontal diseases and adverse pregnancy outcomes. In Bany-Mazar, El-Minia, Egypt.

Patient and method

Study design

This is a case control study that evaluates the relationship between PD and some adverse pregnancy outcome.

Study Population

300 pregnant women attending the prenatal outpatient clinic at Bany Mazar general hospital (El-Minia-Egypt) and voluntarily agreed to participate in the study after signing an informed consent form during the period 2012-2013.

Inclusion criteria

Maternal age 20 to 35 years old., Gestational age \leq 32 weeks at recruitment., Singleton pregnancy and absence of chronic pregestational conditions that may affect pregnancy outcomes as pre gestational diabetes and chronic hypertension.

Exclusion criteria

Maternal age below 20 or above 35 years., Women with multiple pregnancy due to greater risk of preterm and/or low birth weigh., Uterine or cervical anomalies and any previous history of preterm, any chronic pre gestational conditions that may affect pregnancy outcomes as pre gestational diabetes and chronic hypertension.

Each participant was subjected to all of the following

A) Assessment of periodontal status: a single periodontal examination on the day of a scheduled prenatal visit was carried out once during pregnancy before 32 weeks of gestation by the same periodontist and an assistant who provided technical support and who filled the data collection forms. Periodontal status was assessed by the criteria commonly used in epidemiological studies, And Clinical periodontal parameters and Radiological Assessment in evaluation of periodontal disease. state as follow :

1-Clinical periodontal parameters**A)Plaque index (PI) (Løe and Silness, 1963)**

Measured to assess plaque accumulation around gingival margin. The degree of plaque accumulation was assessed as follows:

0= No plaque around the gingival margin.

1= A thin film of plaque around the gingival margin .the plaque may be recognized only by running a probe across the tooth surface.

2= Moderate accumulation of soft deposits on the gingival margin and/or adjacent tooth surface, which can be seen by naked eye.

3= Abundance plaque accumulation within the gingival pocket and/or on the gingival margin and adjacent tooth surface and hard deposits on the tooth surface are seen.

B) Gingival index (GI) (Løe and Silness, 1963)

Used to measure gingival inflammation .the degree of gingival inflammation was assessed as follow:

0= Normal gingiva. & 1= Mild inflammation, slight change in color, slight edema and no bleeding on probing. & 2= Moderate inflammation, redness, edema and bleeding on probing. & 3= Severe inflammation, marked redness, edema and tendency to spontaneous bleeding.

C) Pocket depth (PD)

The measurements were recorded by using graduated periodontal probe. PD was measured as the distances(to nearest mm)from the free gingival margin to the base of the periodontal pocket at six sites, each include midbuccal, mesiobuccal, distobuccal ,midlingual, mesiolingual, and distolingual for each teeth and the degree was assessed as follows:

· 3-5= mild periodontitis & · 5-7= moderate periodontitis & · >7= severe periodontitis

2-Radiological Assessment

X ray was done to assess bone loss.

Study populations were then classified according to their periodontal status in to two groups:

Group I (patient group): consists of 150 patients with periodontities.

Group II (control group): consists of 150 patients without periodontities.

A) Pregnant women were then referred directly to the prenatal outpatient clinic to receive additional information and sign the informed consent form immediately afterwards.

All patients will be subjected to

- 1] Detailed history taking.
- 2] General, abdominal and local examination to exclude {general medical disorders as hypertension, diabetes and rheumatic heart, or any local or abdominal problems.
- 3] Routine investigation "Complete blood picture, urine analysis – random blood sugar.
- 4] C. reactive protein assay as a marker of inflammatory process. C- reactive protein is an acute phase reactant; its levels are considered as a marker of systemic inflammation and are associated with periodontal disease. Each participant provided a blood sample at the initial study visit or shortly thereafter. Plasma samples were stored in EDTA, refrigerated for several hours, and then transported on ice to the laboratory, where they were centrifuged, aliquotted, and frozen in liquid nitrogen until the time of analysis. Plasma samples were thawed and assayed using clinically validated immunoturbidimetric assays on an analyzer with reagents and calibrators. One laboratory technician who was blinded to the participants' periodontal condition and pregnancy outcome performed all assays.
- 5] Abdominal ultrasound: to confirm gestational age, estimate fetal weight, diagnose IUGR, and for evaluation of other parameters as amniotic fluid and placenta.

Diagnosis of gestational diabetes depended on: presence of glucose in urine or increased random blood glucose level more than 180 mg/dl., And confirmed by oral glucose tolerance test (OGTT) "Xu Xiong 2009".

Diagnosis of preeclampsia depended on: Maternal systolic blood pressure \geq 140mm.Hg or diastolic pressure \geq 90mm Hg with proteinuria (0.3 g/24 h). Or lower limb edema.

Diagnosis of preterm labor (PTL) is defined as: labor occurring after 28 weeks and before 37 weeks of gestation "Khader 2009"

Low birth weight (LBW) is defined as: birth weight below 2500 gm "Khader 2009".

Prelabor rupture of membranes (PROM) is defined as: Rupture of membranes occurring before the onset of labor, diagnosed clinically by sudden gush of watery vaginal discharge, and decreased amount of amniotic fluid confirmed by ultrasound scan "Gomez-Lopez. 2012"

Statistical Analysis

When each case was finished, with information on delivery and perinatal outcomes available, the form was checked for completeness and correctness. Then the information was entered to feed a computer database specifically prepared for this study.

Differences between periodontitis cases and controls were compared using two sample t tests or Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables.

P value >0.05 = non-significant

P value <0.05 = significant

P value <0.001 = highly significant

Results

In general, all pregnant women presented similar socio-demographic Characteristics and habits in both groups. Likewise, the groups did not present significant differences regarding the number of prenatal visits, time of odontologists visiting, frequency of tooth brushing, systemic antibiotic use in pregnancy or mode of delivery.

Table 1 shows comparison between cases & control as regards to socio-demographic characteristics data. We found that the higher educational level of the patient, the lower the affection by periodontal disease. because of better personal and oral hygiene (P. value 0.03), There a significant difference between both groups in relation to age between (25:30) years old. We found that this age was less affected by periodontal disease (P. value 0.04).

Table 1: Comparison between cases & control as regards to socio-demographic data

clinical characteristics	Cases (N=150)	Control (N=150)	P. value
Gestational age			
• <30 weeks	88(58.7%)	96(64%)	0.4
• >30 weeks	62(41.3%)	54(36%)	0.4
Maternal age			
• <25 years	79(52.7%)	63(42%)	0.08
• 25-30 years	64(42.7%)	83(55.3%)	0.04
• >30years	7(4.7%)	4(2.7%)	0.5
Parity			
• Primigravida	51(34%)	46(30.7%)	0.62
• Multigravida	99(66%)	104(69.3%)	0.62
Educational level			
• Not educated	112(74.7%)	94(62.7%)	0.03
• Highly educated	38(25.3%)	56(37.3%)	0.03

- P value > 0.05 = non-significant
- P value < 0.05 = significant
- P value < 0.001 = highly significant

Table 2: Comparison between cases & control as regards to Clinical finding. It was found that mixed vaginal infection was significantly higher in patient group compared to control group. (P. value 0.003)

Table 2: Comparison between cases & control as regards to Clinical finding

Clinical finding	Cases (N=150)	Control (N=150)	P. value
Lower limb edema			
• No	135(90%)	137(91.3%)	0.8
• Minimal	2(1.3%)	3(2%)	0.9
• Moderate	11(7.3%)	8(5.3%)	0.6
• Severe	2(1.3%)	2(1.3%)	0.6
Vaginal infection			
• Clinical free	90(60%)	107(71.3%)	0.05
• Vaginal candidiasis	10(6.7%)	7(4.7%)	0.6
• Bacterial vaginosis	8(5.3%)	16(10.7%)	0.1
• Mixed vaginal infection	42(28%)	20(13.3%)	0.003

Table 3: Comparison between cases & control as regards to laboratory investigations we found that the presence of anemia (hemoglobin<11 mg/dl) was significantly higher in case group compared to control group.(P. value 0.004), as regards to presence positive C reactive protein was significantly higher in patient group compared to control group. (P. value < 0.001). also the presence of normal clear urine was significantly higher in control group compared to case group.(P. value 0.01).

Table (3): Comparison between cases & control as regards to Lab investigation

Laboratory investigation	Cases (N=150)	Control (N=150)	P. value
Presence of anemia			
• Haemoglobin<11 mg/dl	91(60.7%)	65(43.3%)	0.004
Urine			
• Clear	96(64%)	117(78%)	0.01
• Urate	13(8.6%)	9(6%)	0.5
• glucose	5(3.3%)	3(2%)	0.7
• Albumin	14(9.3%)	9(6%)	0.4
• Pus cells	22(14.7%)	12(8%)	0.1
Random blood sugar			
• >180 mg/dl	5(3.3%)	3(2%)	0.7
• ≤180 mg/dl	145(96.6%)	147(98%)	0.7
CRP			
• +ve	112(74.7%)	13(8.7%)	<0.001

Table (4): Comparison between cases & control as regards to normal pregnancy outcome and adverse pregnancy outcomes (PE. Preclampsia, LBW low birth weight, PROM pre mature rupture of membrane, PTL preterm labor and DM diabetes mellitus) we found that preterm labor was significantly higher in case group compare to control group(P. value < 0.04) , also as regards to low birth weight was significantly higher in case group compare to control group (P. value < 0.004). in general normal pregnancy outcome was significantly higher in control group compare to case group (P. value < 0.001).

Table 4: Comparison between cases & control as regards to pregnancy outcome

Pregnancy outcome	Cases (N=150)	Control (N=150)	P. value
Normal	73(48.7%)	110(73.3%)	<0.001
PE	14(9.3%)	9(6%)	0.4
PTL	19(12.7%)	8(5.3%)	0.04
PROM	29(19.3%)	20(13.3%)	0.2
DM	5(3.3%)	3(2%)	0.7
LBW	10(6.7%)	0(0%)	0.004

- P value >0.05 = non-significant
- P value <0.05 = significant
- P value <0.001 = highly significant

Table 5: shows the strength of the relation between periodontal disease and (pregnancy outcomes, educational level, C. reactive protein and vaginal infection) There was a strong positive relation between all of the above except educational level was inversely related to periodontal disease.

Table 5: The relation between types of periodontitis and pregnancy outcome and other significant relations

Types of periodontitis (Mild & Moderate & sever)		
	R	P. value
Educational level	-0.2	<0.001
Vaginal Infection	0.2	<0.001
CRP	0.7	<0.001
Pregnancy outcome Normal and (adverse pregnancy outcomes)	0.52	<0.001

- (+) R. factor : Relation factor
 0.00 to 0.24 = WEAK or no association
 0.25 to 0.49 = FAIR association
 0.50 to 0.74 = MODERATE association
 0.75+ = STRONG association
 (-) R. factor : Relation factor
 Means inverse relation

Table 6: Show the strength of the relation between (The severity of periodontal disease and it's types (Gingivitis, Mild Periodontitis, Moderate Periodontitis, Sever Periodontitis and Sever Periodontitis with bone loss) in relation to adverse pregnancy outcomes "Preclampsia, preterm labor, premature rupture of membrane, diabetes mellitus with pregnancy and low birth weight" we found a significant relation between Pre. Eclampsia, preterm labor in relation to types of periodontitis P. value was 0.01 & 0.03 respectively. and highly significant relation in case of presence of premature rupture of membrane in relation to the severity of periodontitis P. value = 0.001, there is no significant relation between diabetes mellitus and low birth weight and the severity of periodontitis.

Table "6" : Types of periodontitis in relation to adverse pregnancy outcome

Types of periodontitis N (%)	No Periodontitis 150 (50%)	Gingivitis 48 (16%)	Mild Periodontitis 29 (9.7%)	Moderate Periodontitis 10 (3.3%)	Sever Periodontitis 48 (16%)	Sever Periodontitis With bone loss 15 (5%)	P. value
Pregnancy outcome	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
PE	9(6%)	0(0%)	1(3.4%)	5(50%)	7(14.6%)	1(6.7%)	0.01
PTL	8(5.3%)	0(0%)	0(0%)	0(0%)	14(29.2%)	5(33.3%)	0.03
PROM	20(13.3%)	0(0%)	0(0%)	0(0%)	23(47.9%)	6(40%)	0.001
DM	3(2%)	0(0%)	0(0%)	2(20%)	2(4.2%)	1(6.7%)	0.7
LBW	0(0%)	0(0%)	3(10.3%)	3(30%)	2(4.2%)	2(13.3%)	0.9

Discussion

Periodontal disease refers to an inflammatory condition of the soft tissues surrounding the teeth (i.e., gingivitis) and the destruction of the supporting structures of the teeth, including the periodontal ligament, bone, cementum and soft tissues (i.e. periodontitis) "Manau, et al 2008".

There is increasing evidence suggesting that periodontal disease is associated with an increased risk of systemic diseases such as cardiovascular diseases, respiratory diseases, diabetes mellitus and osteoporosis "Pihlstrom, et al 2005".

The relation between periodontal diseases and pregnancy complications is a matter of controversy and has been investigated during the last decade to evaluate the actual association with different obstetric complications. Periodontal disease (PD) has been suggested to be associated with preterm, low birth weight (PTB/LBW), and small for gestational age neonates (SGA) with higher risk of perinatal and neonatal mortalities, development of health problems during childhood (neurological, respiratory, gastrointestinal and cardiovascular), and risk of diseases during adulthood "Marianna, et al 2010".

This study was conducted to evaluate the relation of periodontal disease with the adverse pregnancy outcomes and to highlights the possible pathogenesis for this adverse pregnancy outcomes.

In this study We found that the patients with periodontitis were associated highly significantly with adverse pregnancy outcomes ($p < 0.001$) and the presence of periodontal disease among pregnant women nearly double the risk of developing pregnancy complication suggesting a strong positive association between PD and adverse pregnancy outcomes.

Also, in this study we found that the higher educational level of the patient, the lower the affection by periodontal disease because of better personal and oral hygiene (P. value 0.03) in accordance to "Darby. "2003)" "Sarlati, et al (2004)".

In the current study we found that the incidence of GDM was higher in patient group compared to control group (3.3% vs. 2%) but this increase did not reach statistical significance. In accordance with "Dasanayake et al 2008" how found an increased incidence of GDM in women with clinical periodontal disease compared to women without periodontal disease but this increase did not reach statistical significance. However "Xiong, et al 2006", "Xu Xiong, et al 2009", and "Ahmed, et al 2012". Found that that maternal periodontitis is significantly associated with increased risk of developing GDM.

In this study the incidence of preeclampsia was higher in patient group compared to control group (9.3% vs. 6%) but this increase did not reach statistical significance. This result is comparable with "Rustveld LO, Kelsey SF, et al 2008", "Cathy Nabet, et al 2010" and also, "Ahmed, et al 2012" who found that maternal periodontitis nearly double the risk of developing PE.

In the present study the incidence of preterm labor and low birth weight were significantly higher in patient group compared to control group (12.7% vs. 5.3% and 6.7% vs. 0.0% for PTL and LBW respectively). In accordance with "Ahmed, et al 2012" and also our result is comparable to Ismail et al, 2008" and "Dolapo et al, 2010", who found that periodontitis increase the risk of preterm low birth weight almost 4 times. However on contrary to our results "Marianna et al, 2010", found no association between periodontitis and PTL and "Cathy et al, 2010", found a significant association between generalized periodontitis and induced preterm birth for preeclampsia but not for spontaneous PTL.

In this study the incidence of prelabor rupture of membranes was higher in patient group compared to control group (19.3% vs. 13.3%) this result is comparable with "Marianna et al, 2010" and "Ahmed, et al 2012".

In this study, we found that the (+) level of CRP was higher among patient group compared to control group and the difference was statistically highly significant (74.7% vs. 8.7%). ($P < 0.001$)

This result is comparable to "Waranuch et al, 2006" who found 65% higher CRP levels among pregnant women with periodontitis compared to periodontally healthy women. And in accordance with "Ahmed, et al 2012"

In the present study we measured CRP in a single blood sample, which is reasonable as there is little seasonal or diurnal variation in CRP levels "Meier, et al 2001". In addition, most participants in the study had CRP levels below 10 mg/l, the standard threshold associated with acute-phase effects, reducing the possibility that CRP levels were raised as a result of acute infections or trauma "Ridker. 2003".

The association between PD and the adverse outcomes of pregnancy that were found in this study are consistent with those in other studies, for example. "Meier, 2001", "Ridker, 2003", "Xiong, 2006", "Waranuch, 2006", "Bogges, 2006",

“Ismail, 2008”, “Khader, 2009”, “Shetty, 2010”, “Jagan, 2012” and “Ahmed, et al 2012”.

However they differ from outcomes of a study carried out by many investigators “Dasanayake, 2008”, “Marianna, et al 2010”, and “Cathy, 2010”, which either used a partial periodontal evaluation that does not include important periodontal clinical parameters, such as CAL, or used different criteria for diagnosis. We observed a difference between the conclusions of the studies due to distinct definitions of periodontitis “Manau, et al 2008”.

One of the goals of this study was to found an explanation to the pathogenesis by which periodontal disease affects pregnancy outcome. This study suggests the presence of local and systemic inflammatory reaction associated with periodontitis, as evidenced by elevated levels of CRP. Maternal infections, acts as a reservoir of gram-negative anaerobic microorganisms results in a state of transient bacteremia. Viable bacteria and bacterial products (e.g., lipopolysaccharide) from the sub gingival plaque and proinflammatory cytokines (tumor necrosis factor α , IL-1 β , IL-6, IL-8, prostaglandin E2 and C-reactive protein) from the inflamed periodontal tissues can enter the circulation and trigger a maternal systemic inflammatory response amplified by CRP leads to complement activation, tissue damage, and induction of inflammatory cytokines that mediate the relationship between periodontitis and some adverse pregnancy outcomes as preeclampsia, PTL, LBW and PROM “Rustveld, et al. 2008”, and “Waranuch, 2006”.

The pathogenesis for GDM may be explained by the same mechanism mentioned before. The pro-inflammatory cytokines from the inflamed periodontal tissues trigger a maternal systemic inflammatory response. Pregnancy itself is a stressful state with increased inflammatory activity and increased insulin resistance “Xu Xiong et al. 2009”.

It is known that pancreatic β -cell destruction can result from the pro-inflammatory imbalance created by sustained elevation of cytokines. It is well accepted that infection results in a state of insulin resistance. Therefore, 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 could exacerbate the preexisting pregnancy-induced insulin resistance and may cause impaired glucose tolerance and the manifestation of GDM “Xu Xiong, et al. 2009”.

The pathogenesis for preeclampsia may be explained by the same mechanism mentioned before. As any endothelial damage in the placental vascular bed may be initiated by a number of mechanisms. This damage results in oxidative and inflammatory vascular damage, which may ultimately result in the development of preeclampsia. “Dekker, et al (1999)”.

Conclusion

In conclusion, findings of our study showed a significant relationship between periodontal disease and adverse pregnancy outcomes in Bani Mazar – El Minia – Egypt. The majority of studies all over the world showed such positive association between periodontitis in pregnancy and adverse pregnancy outcomes. From this study we emphasize that periodontal examination and early treatment in antenatal care units and good counseling of pregnant women about the benefit of oral hygiene is a way for healthy pregnancy and healthy outcome.

Recommendations

- Periodontal examination should be a routine in antenatal care unit as in developed country early treatment as possible can give better results in pregnancy outcomes.
- Counseling of the women about regular antenatal care and its benefits.
- Education of mothers that oral hygiene gives them healthy pregnancy and healthy baby.
- Any decrease of adverse pregnancy outcomes means decrease of the morbidity and mortality which means decrease in the cost of health care programs, as periodontal disease is a treatable condition. And so we can prevent it. And decrease this risk.
- More researches is needed to show the exact relation between periodontal disease and adverse pregnancy outcomes, and the proper treatment and the optimum timing of this treatment which can decrease the adverse pregnancy outcomes.

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