Assessment of serum Interleukin-1β and its correlation with periodontal health status during pregnancy

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ABSTRACT

Background: Pregnancy is a stressful state of increased inflammatory activity, and pregnancy – associated hormone changes can influence periodontal tissues, these inflammatory activity lead to production of inflammatory mediators. Interleukin 1 beta (IL-1β) is a potent pro-inflammatory cytokines that is consistently associated with periodontal diseases. This study was designed to determine the periodontal health status and detect the serum level of IL-1β in the healthy pregnant women at first, second and third trimester and compare it with healthy non pregnant women, and determine its correlation with different clinical periodontal parameters.

Materials and Methods: Subjects included in the study were sixty six (66) healthy pregnant women with an age range of 20-35 years old. They were divided into three subgroups according to gestational age, as twenty two (22) women in each trimester. Also the sample included fifteen (15) married, non pregnant women and didn't take contraceptive pills, as control group with same age rang of 20- 35 years. Clinical periodontal parameters were measured in this study (plaque index, gingival index, bleeding on probing, probing pocket depth and clinical attachment level). Blood samples were collected from all women under study (pregnant & non pregnant women) to asses concentrations of IL-1β by mean of enzyme – linked immune sorbent assay (ELISA).

Results: Highly significant statistical differences were observed among the study groups regarding the gingival index (GI)with p-value(0.007) and the percentages of bleeding on probing (BOP) p- value(0.00), a significant difference regarding the probing pocket depth (PPD) with p-value (0.046) ,and non significant statistical differences regarding the plaque index (PLI), p-value(0.6) and clinical attachment level (CAL) with p-value (0.371). Interleukin 1-beta (IL-1β) serum level showed a highly statistical significant difference among the study groups with p-value (0.00).A pregnant women showed higher level than non pregnant with a higher value in the second trimester.

Conclusions: The present result revealed that the serum level of IL-1β was higher in pregnant women than non pregnant women with a highly significant difference. The IL-1β serum concentration reaches the maximum value in the second trimester of pregnancy. Nevertheless there were weak correlations between clinical periodontal parameters and serum level of IL-1β.

Key words: Interleukin 1β, Pregnancy, Periodontal health status. (J Bagh Coll Dentistry 2014; 26(2): 111-115).

الخلاصة

الخلفية. الحمل هو حالة مرهقة من زيادة النشاط الالتهابي , كما ان التغيرات الهرمونية المصاحبة للحمل تؤثر في انسجة ماحول الاسنان . يؤدي هذا النشاط الالتهابي الى انتاج وسطاء التهابات مثل السايتوكينات .المدور الخلوي 1 بيتا هو من السايتوكينات الموالية للالتهابات القوية الذي يرتبط باستمرار مع امراض انسجة ماحول الاسنان .تم تصميم هذه الدراسة لتحديد الحالة الصحية لانسجة ماحول الاسنان وكشف المستوى المصلي للسايتوكين 1 بيتا في النساء الحوامل في فترات مختلفة من الحمل ومقارنتها مع النساء غير الحوامل , وتحديد علاقته مع معلمات ماحول الاسنان السريرية المختلفة .

المواد وطرائق العمل. شمل البحث ستة وستين(66) من النساء الحوامل تراوحت اعمارهن بين (20-35) سنة تم تقسيمهن الى ثلاث مجموعات فرعية وفقا لعمر او مرحلة الحمل الى 22 امراءة حامل في كل فصل من فصول الحمل الثلاثة . وشملت العينة خمسة عشر(15) من النساء المتزوجات غير الحوامل ولم ياخذن حبوب منع الحمل , كمجموعة مقارنة بنفس متوسط الاعمار من (20-35) سنة . كانت معلمات ماحول الاسنان المستخدمة في هذه الدراسة هي مؤشر الصفيحة الجرثومية و مؤشر التهابات اللثة والنزف عند التسمير وعمق جيوب اللثة وفقدان الانسجة الرابطة. تم جمع عينات الدم من جميع النساء قيد الدراسة (الحوامل وغير الحوامل) لتقييم التركيزات المصلية للسايتوكين 1بيتا باستخدام تقنية مقايسة الانزيم المرتبط الممتز المناعية

النتائج .لوحظ وجود فروق ذات دلالة احصائية عالية بين مجموعات الدراسة يشأن مؤشر التهاب اللثة ومؤشر النزف عند التسمير ,هناك فرق كبير فيما يتعلق بعمق جيوب اللثة . لاتوجد فروق فيما يتعلق بمؤشر الصفيحة الجرثومية وفقدان الانسجة الرابطة. اظهر المستوى المصلي للمدور الخلوي 1بيتا فروقات ذات دلالة احصائية عالية بين مجموعات الدراسة مع . واظهرت.اعلى قيمة للمدور الخلوي1بيتا في الفصل الثاني من الحمل .p=0.00.

الاستنتاج كشفت النتيجة الحالية أن المستوى المصلي من المدور الخلوي 1بيتا كان أعلى في النساء الحوامل من النساء غير الحوامل مع فروق ذات دلالة إحصائية عالية.التركيز المصلي للمدور الخلوي 1بيتا يصل القيمة القصوى في الثلث الثاني من الحمل . ومع ذلك كان هناك وجود علاقة ضعيفة بين المعلمات السريرية ومستوى المصل من المدور الخلوي 1بيتا.

INTRODUCTION

Periodontal disease is a common chronic inflammatory condition of infectious origin that results in breakdown of the periodontium .When the inflammation is confined to the soft tissue, it is called gingivitis. Gingivitis is often caused by inadequate oral hygiene, and it is reversible with appropriate oral home care. Untreated gingivitis may develop into periodontitis, which results in loss of connective tissue attachment and bone around teeth [(1)].

In some individuals, gingivitis may exist as an independent clinical condition without progressing to periodontitis. How gingivitis progresses to periodontitis is still unclear. On the other hand, periodontitis appears to be more specific inflammatory response to specific periodontal pathogens residing in the subgingival biofilm. Nonetheless, it must be noted that, although bacteria are necessary for disease initiation, they are not sufficient to cause disease progression unless there is an associated inflammatory response within a susceptible host [(2)]. The bacterial insult at the biofilm-gingival interface results in the direct destruction of host tissues through bacterial virulence factors such as collagenases and leukotoxins, and indirectly through the activation of host inflammatory cells such as neutrophils and macrophages ,which in response to the pathogenic biofilm release effector molecules such as prostaglandin E2 [(3)] and proinflammatory cytokines such as interleukin-

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1beta (IL-1β) [4], tumor necrosis factor-alpha (TNF-α) [5]. These signaling molecules modulate the inflammatory process through the autocrine and paracrine activation of inflammatory cells, through mechanisms of chemotaxis [6]. Interleukin-1 is one of the major pro-inflammatory cytokine involved in the pathogenesis of periodontitis [7]. Its effects range from regulation of inflammatory mediators to catabolic effects on osteoclasts and activation of matrix metalloproteinases [8].

Pregnancy is a physiological process that affects profoundly even healthy women and there are many physiological ,anatomic and biochemical changes that mimic disease processes .[9]In most studies changes in oral health of pregnant women have been noticed in the condition of the dental hard tissue (dental caries) and soft tissue (periodontium) ,where many results showed an increase in the severity of dental caries and periodontal diseases especially gingivitis.[10,11] During pregnancy, progesterone levels increase 10-fold and estrogen level 30-fold compared to those observed on menstrual cycle due to their continuous production. Physiological changes in metabolism include oral microbial species, immune response and cell metabolism. The increase in progesterone results in greater vascular permeability, gingival edema, crevicular fluid levels and prostaglandin production, which may lead to gingival inflammation [12]. The depth of periodontal pockets may increase as pregnancy progresses [13,14]; however, the level of activity of the disease does not necessarily result in loss of periodontal clinical attachment level [14]. There is, nonetheless, a consensus that pregnant women suffer a decline in periodontal health status. In spite of some studies showing no association between periodontitis and adverse perinatal outcomes [15] a growing number of studies indicate that the consequences of periodontitis activity during pregnancy may affect delivery outcomes, contributing towards prematurity, neonates with low birth weight, small for gestational age and fetal growth restriction [3,16,17].

Within the last two decades, a large number of cross-sectional, case-control, and cohort observational studies were carried out to investigate periodontal disease as a risk factor for adverse pregnancy outcomes [18]. Which involved miscarriage, preeclampsia, preterm birth (PTB), low birth weight (LBW), and/or preterm low birth weight (PLBW) [19]. Results of these studies presented conflicting findings. Most studies reported positive association [20-22]. While the researches reporting no significant association took up a small portion [23,24]. The classical theory of 'focal infection' speculated that oral foci of infection might be a contributing factor in triggering systemic inflammatory response. Investigators hypothesized that hematogenous translocation of periodontal bacteria and their products or pro-inflammatory mediators from sites of periodontal infection into the fetal membranes, placenta, and amniotic cavity would induce pathological processes that could result in adverse outcomes [25].

MATERIALS AND METHODS

Subjects included in the study were drawn from patients attending the health care center of AL-Ameen city and AL-Alweea teaching hospital. The study groups included sixty six pregnant women with an age range of 20-35 years old. They were divided into three subgroups according to gestational age, as twenty two women in each trimester, also the sample included fifteen married, non pregnant women and didn't take contraceptive pills, as control group with an age range of 20-35 years old.

Exclusion criteria: **1-** smokers, **2-** systemic antibiotic therapy or anti inflammatory therapy within the last three months, **3-** previous periodontal treatment within the last three months.

Clinical periodontal parameters were measured for all women by using periodontal probe by same examiner. The four surfaces of all teeth except 3rd molar were examined, the collected data included: PLI, GI, BOP, PPD and CAL. Two ml of venous blood were drawn from pregnant women and non pregnant (control group). Blood sample was collected in a serum separator tube (SST) and allow samples to clot for 30 minutes before centrifugation for 15 minutes at 1000 rpm. Collect serum and stored samples at –20°C. till used .The analysis was done by Enzyme Linked Immuno Sorbent Assay (ELISA) for quantitative determination of interleukin1β (IL-1β) in serum. The laboratory analysis was done in the Teaching Laboratories of Baghdad Medical City.

RESULTS

Non significant statistical differences were observed among the study groups regarding the plaque index (PLI), p-value (0.6) (Table 1).Highly significant statistical differences were observed among the study groups regarding the gingival index (GI) with p-value (0.007) (Table2), and the percentages of bleeding on probing (BOP) p-value (0.00) (Table 3), a significant difference regarding the probing pocket depth (PPD) with p-value (0.046) (Table4). Non significant

statistical differences were observed in clinical attachment level (CAL) with p-value (0.371) (Table5). Interleukin 1-beta (IL-1β) serum level showed a highly statistical significant difference among the study groups with p-value (0.00) (Table6), also showed the higher value of IL-1β in the second trimester. The correlation between means of serum IL-1β and means of PLI for each study group (Table7). In the 1st trimester, there was a significant positive strong correlation between the means of PLI & IL-1β. While there were non significant positive correlation between the mean of plaque &IL-1β in the 2nd, 3rd trimester and control group. Also show positive non significant correlations between IL-1β serum level and means of GI in the 1st and 2nd trimesters while there were negative non significant correlation in the 3rd trimester and control group (Table7). IL-1β serum concentration show positive but non significant correlations with the percentages of bleeding on probing (BOP) (Table 8) and probing pocket depth (PPD) (Table9) in all study groups . Positive non significant correlations also observed between IL-1β &CAL in the 1st trimester & control group while there is significant positive correlation in the 3rd trimester and there is no correlation in the 2nd trimester (Table 9).

Table1: The mean values of PLI of each study group with comparison of sig. among the groups

Groups	Mean Pl.I	+ S.D.	p.value	Sig.
1st	1.45	0.46	0.60	N.S.
2nd	1.25	0.58		
3rd	1.43	0.36		
Control	1.06	0.48		
ANOVA = 2.578				

Table 2: The mean values of GI of each study group with comparison of sig. among the groups

Groups	Mean GI.	+ S.D.	p.value	Sig.
1st	1.115	0.22	0.007	HS
2nd	1.231	0.36		
3rd	1.346	0.37		
Control	1.050	0.10		
ANOVA = 4.297				

Table 3: The Chi values of BOP with comparison of sig. among the groups

Groups	Chi	DF	P.value	Sig.
1st	60.682	3	0.00	HS
2nd				
3rd				
Control				

Table 4: The mean values of PPD of each study group with comparison of sig. among the groups

Groups	Mean PPD.	+ S.D.	p.value	Sig.
1st	2.22	2.09	0.046	S
2nd	2.54	1.96		
3rd	2.72	1.90		
Control	0.93	1.94		
ANOVA = 2.783				

Table 5: The mean values of CAL of each study group with comparison of sig. among the groups

Groups	Mean CAL.	+ S.D.	p.value	Sig.
1st	1.045	1.58	0.371	NS
2nd	1.22	1.52		
3rd	1.36	1.46		
Control	0.53	0.96		
ANOVA =0.371				

Table 6: The mean values of IL-1β of each study group with comparison of sig. among the groups

Groups	Mean IL-1β	+ S.D.	p.value	Sig.
1st	17.227	0.585	0.00	HS
2nd	19.282	1.22		
3rd	18.841	1.23		
Control	17.477	0.51		
ANOVA =21.754				

Table 7: The correlations between mean of PLI, GI for each study group with the means of IL-1β

Parameters	Serum IL-1β		
	Groups	r	p. value
PL	1st	0.659	0.01
	2nd	0.196	0.382
	3rd	0.247	0.268
	Control	0.358	0.19
GI	1st	0.13	0.564
	2nd	0.191	0.395
	3rd	-0.271	0.223
	Control	-0.235	0.399

Table 8: The correlations between mean of BOP for each study group with the means of IL-1β

Parameter	Serum IL-1β		
	Groups	r	p. value
BOP	1st	0.115	0.609
	2nd	0.255	0.252
	3rd	0.154	0.49
	Control	0.396	0.144

Table 9: The correlations between mean of PPD, CAL for each study group with the means of IL-1β

Parameters	Serum IL-1β		
	Groups	r	p. value
PPD	1st	0.388	0.74
	2nd	0.146	0.517
	3rd	0.051	0.823
	Control	0.223	0.423
CAL	1st	0.203	0.366
	2nd	0.023	0.92
	3rd	0.505	0.016
	Control	0.152	0.588

DISCUSSION

The present study showed that mean of plaque index was higher among pregnant groups especially in the first trimester followed by third trimester. This finding is in agreement with other study [26]. This finding may be due to increased in the oral hygiene negligence during pregnancy especially in the fist trimester due to nausea and gag reflex. While during third trimester pregnant women may become restless, exhausted and anxious also it has been thought that pregnant women tend to avoid dental care because they believe poor oral health to be a routine consequence of pregnancy and because of fear that dental care would harm the fetus [27].The increased in the severity of gingivitis during pregnancy may be exaggerated due to arise in circulation level of progesterone affecting the gingival microvasculature [28]. Elevated progesterone levels in pregnancy enhance capillary permeability and dilatation, resulting in increased gingival exudate [29].

In the present study there was gradual increase in the numbers and percentages of bleeding sites during pregnancy, this could be related to the increased level of estrogen and progesterone during pregnancy has a special effect on the periodontium, which would enhance the reaction to local stimulation and lead to the occurrence or increase of inflammation in gingival [30]. This study reported that the probing depth scores increased gradually in the first, second and in the third trimester when reach maximum level, this result in accordance with other studies [31-33]. This could be related to the extended period of the inflammation. Also could be attributed to the quick effect of increasing progesterone & estradiol level which lead to the formation of prostaglandins & also the presence of high counts of Prevotella Intermedia [33].

There was no statistical difference between pregnant and non pregnant women (control group) in the CAL, this agreed with other study [34]. In this study, they reported there was no support to the assumption that the wider distribution and increased severity of gingival inflammation in the course of pregnancy will cause lasting injuries to the periodontium.

In this investigation we can notice the serum level of IL-1β increased from first to the third trimester .This finding was in accordance with [35,36] who demonstrated that the serum level of IL-1β, IL-6 and IL-8 increased during the gestation period, and reached the maximum value in the second trimester of pregnancy. This may be related to increased gingival inflammation during second trimester which will affect the level of inflammatory mediators produced by fibroblast and macrophage [37]. Nevertheless there were weak correlations between clinical periodontal parameters and serum level of IL-1β, this may be due to small samples size in this study.

As conclusion; pregnant women have higher PLI, GI, BOP, deeper periodontal pockets and more clinical attachment loss in comparison with non pregnant women. Deep pockets and clinical attachment loss were low among pregnant women. The serum level of IL-1β was higher in pregnant women than non pregnant women with a highly significant difference. The IL-1β serum concentration reaches the maximum value in the second trimester of pregnancy. Nevertheless there were weak correlations between clinical periodontal parameters and serum level of IL-1β.

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