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Original Article

Serum IL-1 B Levels in Preeclamptics and Non-Preeclamptics Affected With or Without Periodontitis

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ABSTRACT

Literature supported the association of bio-inflammatory cytokines in multifactorial pathologies such as preeclampsia and periodontitis. **Objectives:** To compare serum IL-1β in non-preeclamptic and preeclamptic pregnancies affected with/without periodontitis. **Methods:** Longitudinal cohort study was conducted on 73 pregnant women of Narowal (Pakistan) aged between 18-34 years, after seeking their consent. Wherein 33 subjects were periodontally healthy (6 preeclamptics, 27 non-preeclamptics) while 40 subjects were with periodontitis (6 preeclamptics, 34 non-preeclamptics). Serum samples were collected in antepartum and postpartum periods of the same subjects. Periodontium was examined by CPITN index, preeclampsia via blood pressure records. IL-1β was estimated through ELISA. **Results:** Raised IL-1β(pg/L) were observed in postpartum than antepartum i.e. 76% in non-preeclamptics with periodontitis(p=0.099), 89% in periodontally healthy non-preeclamptics(p=0.082), 313% in preeclamptics with periodontitis(p=0.242), and 34% in preeclamptics with healthy periodontium(p=0.351). Likewise, elevated IL-1β levels were found in non-preeclamptics than preeclamptics in antepartum and postpartum i.e. 327% in antepartum of periodontitis-affected non-preeclamptics(p=0.251), 0.43% in antepartum of periodontally healthy normotensives(p=0.983), 82% in postpartum of periodontitis affected non-preeclamptics(p=0.382), and 41% in postpartum of periodontally healthy non-preeclamptics(p=0.611). Similarly, high IL-1β levels were estimated in antepartum: 23% in non-preeclamptics with periodontitis than periodontally healthy non-preeclamptics(p=0.553) and 248% in periodontally healthy preeclamptics than periodontitis-affected preeclamptics(p=0.011). Also, increased IL-1β levels were noticed in postpartum: 15% in normotensives with periodontitis than periodontally healthy non-preeclamptics(p=0.694) and 12% in periodontally healthy preeclamptics than periodontitis-affected preeclamptics(p=0.853). **Conclusion:** Pregnancy suppressed IL-1β in preeclamptic and non-preeclamptics, while periodontitis without preeclampsia raised IL-1β in pregnancy and post-pregnancy phases.

INTRODUCTION

Periodontitis and preeclampsia are multifactorial pathologies that are supposed to be linked together through systemic inflammatory mediators or cytokines. Even though researchers are persistently trying to find the nature of the association between periodontitis and preeclampsia, the true association is yet to be ascertained [1]. Periodontal pathologies are bacterial-plaque-induced infectious diseases of the bony and soft tissues supportive structures around the teeth [2]. Those infectious periodontal tissues locally raise the concentration of certain cytokines like interleukin-1 β (IL-1 β), prostaglandin E-2(PGE-2), interleukin-6(IL-6), and tumor necrosis factor-α (TNF-α) [3, 4]. Those cytokines through systemic circulation exacerbate inflammatory reactions [1]. Microbiota involved in periodontitis is linked to the systemic pathologies through the release of direct or indirect immune-mediated destructive mediators [5]. Similarly, periodontitis has also been related to preeclampsia by many researchers [6, 7]. A study in 2017 revealed a high level of IL-8 in the gingival crevicular fluid (GCF) among the

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patients affected with periodontitis while the same type of patients exhibited an increased concentration of IL-6 in another study conducted in 2018 [8, 9]. Preeclampsia as a gestational syndrome is considered an alarming ailment, mainly characterized by the onset of hypertension with proteinuria after the 20th week of pregnancy. According to a study, preeclampsia is responsible for about 6-10% of total neonatal and maternal mortalities in the world [10]. Though many studies could not reveal the exact pathophysiology of preeclampsia [2, 11]. However, a few studies found out the cause of preeclampsia by proposing different pathogenesis like atypical trophoblastic development, placental malfunctioning, and immune-inflammatory pathology [10, 12]. Moreover, other studies also mentioned various genetic, environmental, socioeconomic, ethnic, and immune-inflammatory factors that influence the onset and severity of preeclampsia [2, 13]. A study in the same lines claimed the rise of numerous circulatory cytokines in preeclamptic subjects. IL-1 β, IL-2, IL-6, and INF-γ showed a positive association with preeclampsia. IL-1 β a pro-inflammatory mediator is released by several cellular varieties including monocytes, macrophages, keratinocytes, fibroblasts, synoviocytes, and epithelial cells [14]. Another study from North India supported the argument that IL-1 β stimulates the production of other cytokines like TNF-α, INF-γ, IL-2, and IL-12 [1,15]. In 2014 a group of researchers found the enhanced placental expression of IL-1 β in preeclamptic women [13]. The present study aims to compare serum IL-1 β concentrations in both preeclamptic and non-preeclamptic pregnant women either affected with periodontitis or otherwise.

METHODS

A prospective longitudinal cohort study was carried out in rural, under-developed city of Narowal, Pakistan by using convenience sampling approach. The study spanned just over one and half years, from June 2016 to February 2018. Pregnant women aged 18–34 years within 14-24 weeks of pregnancy belonging to rural areas of Narowal District affected with or without periodontitis were included in the study. While pregnant women aged under 18 or above 34 years, with less than 14 or more than 24 weeks of pregnancy, or affected with some other periodontal pathology like gingivitis were excluded from the study. Cochran's Formula was used to calculate the sample size. To get an estimated population portion (p) a thorough survey of the local population was carried out prior to the sampling. According to the best of our knowledge, no previous study was available to readily give an estimation of the prevalence of pregnant women affected with periodontitis in Pakistan. However, the survey conducted on the study population determined a 57% prevalence. There were a total of 73 pregnant women who participated in the study in two consecutive phases (antepartum and postpartum), So serum samples were first taken in their antepartum phase and serum samples were again collected from the same subjects in their postpartum phase. Out of 73 subjects, 40 were with periodontitis (further subdivided as 34-nonpreeclamptics, and 6-preeclamptics) and 33 were with healthy periodontal status (further subdivided as 27-nonpreeclamptics, and 6-preeclamptics). The study was also approved by the Ethical Review Board of the Institute. Written consent was sought from the subjects after duly informing about the study purpose and routine examination procedure. The periodontal status of each participant was thoroughly evaluated by using CPITN (Community Periodontal Index for Treatment Need) index in the presence of an adequate light source. The assessment of clinical attachment loss at gingival sulcus in millimeters was categorized according to the criterion given by 'American Dental Association/American Academy of Periodontology 1999'. Pocket depth of more than 3mm for ten indexed teeth including: 11, 16, 17, 26, 27, 31, 36, 37, 46, and 47 as per 'Federation Dentaire Internationale' (FDI) numbering system, with all four sides of each tooth i.e. mesial, distal, buccal / labial and lingual / palatal, was labelled as periodontitis. Moreover, as an incentive the oro-dental diagnosis of each participant was shared with her and the related treatment options were also recommended subsequently. Participants were professionally advised about the ways to take care of their periodontium on daily basis. Serum samples were collected from the participants in two successive gestational phases. Firstly, in the antepartum phase i.e. between 14-24 week of gestation. Secondly, from the same participants in their postpartum period (within 6 weeks after child birth). To confirm preeclampsia, the blood pressure record of the subjects was acquired from their physician/gynecologist after seeking their permission. Pregnant women having normal blood pressure profile before pregnancy but characterized by high blood pressure and clinical features of edema, severe headache, dizziness, vision changes, nausea, and vomiting during pregnancy were labelled as preeclamptics. Labelled serum samples were kept in Eppendrofs and then refrigerated at -80°C. Ninety six-welled ELISA plates specified for serum IL-1 β levels (pg/L) were used separately for the estimation of IL-1 β levels of antepartum and postpartum serum samples and the values were observed through interpolation method. The data was analyzed by using Microsoft Excel and Minitab®18. Student T-Test was employed as a statistical test to determine the significant difference between the two groups. All the statistical tests were performed with 95% confidence interval.

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RESULTS

Non-preeclamptic subjects with healthy periodontium showed 89% increased IL-1 β (pg/L) serum levels in the postpartum period compared to the antepartum period (p=0.082). Whereas, preeclamptic subject with healthy periodontium exhibited 34% high IL-1 β (pg/L) serum levels in the postpartum period than in the antepartum period (p=0.351) (Table 1). Non-preeclamptic subjects with periodontitis displayed 76% increased IL-1 β (pg/L) serum levels in postpartum period compared to the antepartum period, (p=0.099). While preeclamptic subject affected with periodontitis revealed 313% higher IL-1 β (pg/L) serum levels in the postpartum period than in the antepartum period (p=0.242) (Table 1).

Studied Groups		Gestational Phase				p-value
		Antepartum		Postpartum		
Periodontium	Preeclampsia	n	Mean±SEM	n	Mean±SEM	
Healthy i.e. ≤3mm sulcus depth with no gingival inflammation	Without	27	37.41±5.03	24	70.7±19.5	0.082
	With	6	37.57±9.45	6	50.16±8.56	0.351
Periodontitis i.e. >3mm sulcus depth with inflamed gingiva, at least grade I mobility)	Without	34	46.1±12.5	28	81.3±18.4	0.099
	With	6	10.8±0.71	6	44.64±27.67	0.242

Table 1. Gestational Comparison of serum IL-1 β Levels (pg/L) among studied groups

Non-preeclamptic subjects affected with periodontitis in their second trimester presented 327% raised serum IL-1 β levels (pg/L) compared to preeclamptic subjects (p=0.251). On the other hand, Non-preeclamptic subjects with healthy periodontium in their second trimester showed only 0.43% high serum IL-1 β levels (pg/L) than that of preeclamptic subject (p=0.983) (Table 2). In postpartum phase subjects with periodontitis revealed 82% more serum IL-1 β levels (pg/L) in non-preeclamptics than preeclamptics (p=0.382), while in the same phase the subjects with healthy periodontium showed 41% raised serum IL-1 β levels (pg/L) in non-preeclamptics than preeclamptics (p=0.611) (Table 2). In the antepartum period, non-preeclamptics affected with periodontitis exhibited 23% more serum IL-1 β levels (pg/L) compared to non-preeclamptics with healthy periodontium (p=0.553). Whereas, in the same phase, preeclamptics with healthy periodontium revealed 248% increased serum IL-1 β levels (pg/L) than those affected with periodontitis (p=0.011). Besides the difference proved statistically very significant (Table 2). In the postpartum phase, non-preeclamptic subjects having periodontitis showed 15% high serum IL-1 β levels (pg/L) than those without periodontitis (p=0.694) while the preeclamptics in the same phase showed 12% more serum IL-1 β levels (pg/L) in those who possessing healthy periodontal status compared to periodontitis affected patients (p=0.853). Although the differences were proved statistically insignificant (p>0.05) (Table 2).

Comparative Groups		Periodontal Status				p-value
		Healthy Periodontium		Periodontitis		
Periodontium	Preeclampsia	n	Mean±SEM	n	Mean±SEM	
Antepartum	Without	27	37.41±5.03	34	46.1±12.5	0.553
	With	6	37.57±9.45	6	10.8±0.71	0.011*
p-value		0.983		0.251		
Postpartum	Without	24	70.7±19.5	28	81.3±18.4	0.694
	With	6	50.16±8.56	6	44.64±27.67	0.853
p-value		0.611		0.382		
* Statistically significant as p≤0.05.						

Table 2. Serum IL-1 β Levels (pg/L) in comparative groups with respect to periodontitis and preeclampsia

DISCUSSION

In periodontal pathology, there are alternate episodes of periodontal decay and retardation, mainly because of gram-negative bacteria [16, 17]. Periodontitis is an infectious disorder that constantly devastates the periodontium of the tooth, though in a sluggish manner by supra and sub-gingival bacterial pathogens [3]. Periodontitis is a severe periodontal ailment affecting 5-20% of pregnant women across the World [1]. Many studies suggest that pregnant women with periodontitis are more prone to preeclampsia due to the possible translocation of periodontal pathogenic bacteria to the fetoplacental membranes that ultimately lead to immense inflammation and oxidative stress [18, 19]. Intense inflammation stimulated by oral infection may contribute to uteroplacental atherosclerosis, as observed in preeclamptic patients [2]. Other studies conclude that the presence of pathogens at placental cells activates Natural killer cells in the uterus to release pro-inflammatory cytokines such as TNF-α and IL1-β that more deleteriously affect placental membranes [19, 20]. Although the clear etiopathogenesis of preeclampsia is yet to be defined, still there is consensus by many researchers on the role of placental modifications in the ultimate pathology of preeclampsia. Increased serum levels of many cytokines such as TNF-α (Tumor necrosis factor-α), GM-CSF (Granulocyte-macrophage colony-stimulating factor), IL-10, and TGF-β1 (Transforming growth factor-beta 1) are examined in the focal placental tissues in preeclamptics. Similarly, raised serum levels of many angiogenic mediators like PlGF (Placental growth factor), VEGF (Vascular endothelial growth factor), and Flt-1(Fms Related Tyrosine Kinase 1) are also observed in the focal placental tissues in preeclamptics [18]. Similar to the findings of the current study, another study also revealed that the pregnancy hormones -progesterone and estradiol - promote prostaglandin E-2 levels and reduce the release of cytokine IL-1β [21]. The current study has been conducted with relatively small sample size. Also, the daily nutritional intake of the studied population and their BMIs have not been recorded. In the future, a study with large sample size,

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varied ethnicity, and wide range of age may better explore the relation of periodontitis with adverse gestational consequences.

CONCLUSIONS

Periodontitis in non-preeclamptics increases serum IL-1 β levels in antepartum as well as in the postpartum phases. Likewise, periodontitis in preeclamptics decreases serum IL-1 β levels in both phases. Moreover, periodontitis markedly elevates IL-1 β levels in the postpartum phase, both in preeclamptics and non-preeclamptics. Besides in preeclamptics and non-preeclamptics, pregnancy suppresses IL-1 β levels in subjects with and without periodontitis.

Conflicts of Interest

The authors declare no conflict of interest

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