

ORIGINAL ARTICLE

CHRONIC PERIODONTITIS, PREECLAMPSIA AND SERUM INTERLEUKIN-8: IS THERE A LINK?

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Background: Association of periodontitis with preeclampsia through mediators has currently been in consideration. Present study aimed to compare serum IL-8 levels in normotensive and preeclamptic gravid women with and without chronic periodontitis in antepartum and postpartum phases. **Methods:** It was a longitudinal cohort study of pregnant women of Narowal aged 18–34 years. Out of seventy subjects, 30 had normal periodontium (6 preeclamptics+24 normotensives), while 40 had periodontitis (6 preeclamptics+34 normotensives). Blood samples were first taken in antepartum and again in postpartum phase of the same women. Periodontium assessment by CPITN probing and preeclampsia verification was done through medical record and blood pressure. IL-8 estimation was done using ELISA. Data were analysed on Microsoft Excel. **Results:** Periodontally healthy normotensives exhibited 4% raised IL-8 in ante partum while preeclamptics showed increased IL-8 by 0.04% postpartumly. Periodontitis with normotensives showed 46% increased IL-8 in postpartum whereas periodontitis with preeclampsia showed 10% high IL-8 in antepartum. In antepartum, normotensives periodontitis revealed 1% increased IL-8 while normotensives with healthy periodontium revealed 14% increased IL-8. In postpartum normotensives, with periodontitis exhibited 62% more IL-8 while normotensives with healthy periodontium revealed 10% more IL-8. In antepartum, normotensives with healthy periodontium exhibited 2.3% raised IL-8 while preeclamptics with periodontitis showed 11% raised IL-8. In postpartum normotensives with periodontitis showed 49% more IL-8 while periodontally healthy preeclamptics showed 0.5% more IL-8. **Conclusion:** Raised serum IL-8 levels were observed in normotensives affected with chronic periodontitis and those who were with healthy periodontium in antepartum and postpartum phases. Highest serum IL-8 was observed in normotensives with chronic periodontitis in their postpartum phase.

Keywords: Interleukin 8, Chronic Periodontitis, Preeclampsia, Normotensives, Healthy Periodontium

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INTRODUCTION

Chronic periodontitis is a severe infectious periodontal pathology caused mainly by gram negative bacteria, i.e., Porphyromonas gingivalis, Treponema denticola, Aggregatibacter actinomycetemcomitans and Tannerella forsythia that ultimately lead to decay of bony and soft tissue supporting structures of the tooth.¹ Worldwide prevalence of chronic periodontitis is about 50% in adults and 60% in aged population², while prevalence of preeclampsia is 22.8% in Pakistan³. The virulent sub-gingival microbiota in the dental plaque initiate host immune response that primarily causes migration of immune-mediated leukocytes to the site of inflammation through a series of complement cascade.⁴

Many studies revealed the role of periodontitis in adverse pregnancy conditions such as preeclampsia through activation of pro-inflammatory cytokines which are induced by infective bacteria to distant organs of the body via circulation. Moreover, many bio-researchers have proposed a two directional relation between periodontitis and preeclampsia. The two pathologies may influence each other and there

may be a connection between these two multifactorial disorders.⁵

In present era, periodontal pathologies have been linked to numerous systemic illnesses like arthritis, coronary heart diseases, diabetes, lung disorders and poor gestational outcomes such as preeclampsia and low birth weight.⁶ The gravid body already encounters a gentle shift of immunity under the hormonal effects of pregnancy.⁷ Preeclampsia is a prime community health concern because it is considered the commonest cause of maternal as well as foetal mortality. It is one of the adverse pregnancy outcome characterized by hypertension and proteinuria that is established about 20th week of gestation.⁸ Preeclampsia is a multifactorial pathology, in which genetic history is the leading cause. Others include shift of immune-inflammatory tolerance.⁹

Many cytokines act as regulators to promote or inhibit the inflammation which is induced by infective pathogens. Studies suggested the elevated level of certain cytokines in preeclamptic women such as TNF- α , IL-6, IL-1 β and IL-8.¹⁰ IL-8 is a chemokine that causes chemotaxis and migration of polymorphs to the focal site of injury. Its raised levels in gingival

crevicular fluids (GCF) in periodontitis suggested it as a biomarker for chronic periodontitis. IL-8 along with other cytokines like IL-1 β , IL-6 and IL-10 has been associated with chronic periodontitis by the literature.⁶ However various epidemiological data proposed a contradiction in regard to this association.¹ Oral health care may prevent poor pregnancy results and even reduce the rate of maternal and neonatal morbidity and mortality.⁴ Present study aimed to compare serum IL-8 levels in normotensive and preeclamptic gravid women with and without chronic periodontitis in antepartum and postpartum phases.

MATERIAL AND METHODS

It was a prospective longitudinal cohort study conducted on pregnant population of Narowal District of Punjab, Pakistan, using convenience sampling technique. The sampling duration was from June 2016 to February 2018 with age of participants between 18 and 34 years.

Sample size was calculated through Cochran’s Formula and estimated portion of population (p) was calculated through surveying prior to sampling of the local population, to estimate the prevalence of chronic periodontitis in gravid women. No previous research was available in this regard. We found 57% prevalence of chronic periodontitis in gravid rural population. Thus in total 70 pregnant women were taken in this study, out of which 30 were with healthy periodontium that were again categorized as 6 preeclamptics and 24 normotensives. The remaining 40 females were infected with chronic periodontitis, with further subdivision with 6 preeclamptics and 34 normotensives. Consent was documented by each participant after informed purpose of study and examination procedures. The study was completed in two phases. In first phase sera collection was taken from participants in their second trimester and in second phase sera were again gathered from the same population of first phase, when they were in their postpartum period.

Dentist evaluated the periodontium through CPITN (Community Periodontal Index for Treatment Need) probing technique and marked the severity of periodontal loss in mm. To rule out preeclampsia the routine blood pressure profile was checked by her physician. Sera in eppendrofs were refrigerated at -80 °C till analysis.

Sandwich ELISA plates each with 96 wells were used to detect the serum concentrations of IL-8 in pg/ml, separately for antepartum and postpartum sera. Statistical analysis was performed through Microsoft Excel and Minitab version 18. Student’s *t*-test was used as a statistical test to see the significant difference between two categories and alpha was considered as ≤ 0.05 .

RESULTS

In normotensive subjects with healthy periodontium 4% raised serum IL-8 (pg/ml) was measured in antepartum period than postpartum period ($p=0.26$), while in preeclamptics with healthy periodontium only 0.04% rise was noticed in postpartum period ($p=0.98$). In normotensives affected with chronic periodontitis 46% increased serum IL-8 (pg/ml) level were observed in postpartum period compared to antepartum period ($p=0.26$), whereas in preeclamptics with chronic periodontitis 10% rise was observed in antepartum state than postpartum ($p=0.28$). All comparisons were statistically non-significant ($p>0.05$) (Table-1).

In second trimester normotensives with periodontitis exhibited 0.7% high serum IL-8 (pg/ml) levels in comparison to preeclamptics periodontitis patients ($p=0.95$) and in the same phase of pregnancy periodontally healthy normotensives showed 14% more serum IL-8 (pg/ml) levels than that of periodontally healthy preeclamptics ($p=0.015$).

In postpartum period normotensive with periodontitis showed 62% raised serum IL-8 (pg/ml) levels as compared to preeclamptics with periodontitis ($p=0.56$) and in the same phase normotensives with healthy periodontium exhibited 9.5% high serum IL-8 levels as compared to preeclamptics with healthy periodontium ($p=0.09$) (Table-2).

In antepartum period normotensives with healthy periodontium exhibited 2.3% raised serum IL-8 (pg/ml) levels as compared to preeclamptics affected with chronic periodontitis ($p=0.71$) and in the same period preeclamptic subjects affected with chronic periodontitis revealed 10.7% increased IL-8 (pg/ml) levels in comparison to preeclamptics with normal periodontium ($p=0.22$).

In postpartum phase normotensives affected with periodontitis showed 48.5% raised serum IL-8 (pg/ml) levels compared to normotensives with healthy periodontium ($p=0.32$) and in the same phase preeclamptics with periodontitis showed 0.5% more serum IL-8 levels than that of preeclamptics with healthy periodontium ($p=0.91$). However all comparisons were statistically non-significant ($p>0.05$), (Table-3).

Table-1: Gestational comparison of IL-8 levels between subjects with and without preeclampsia, in relation to periodontitis (pg/ml)

Comparative categories		Pregnancy state				p
		Ante partum (2 nd trimester)		Postpartum		
Periodontal status	History of Preeclampsia	n	Mean \pm SEM	n	Mean \pm SEM	
Healthy	No	24	26.32 \pm 0.61	24	25.31 \pm 0.62	0.26
	Yes	6	23.09 \pm 0.41	6	23.1 \pm 0.54	0.98
Chronic Periodontitis	No	34	25.74 \pm 1.25	28	37.6 \pm 11.4	0.26
	Yes	6	25.56 \pm 1.86	6	23.22 \pm 0.89	0.28

Table-2: IL-8 in subjects with and without preeclampsia, in relation to periodontitis and gestation (pg/ml)

Comparative categories	History of preeclampsia				p
	Without		With		
	n	Mean±SEM	n	Mean±SEM	
Antepartum (2nd trimester)					
Chronic Periodontitis	34	25.74±1.25	6	25.56±1.86	0.95
Healthy	24	26.32±0.61	6	23.09±0.41	0.015*
Postpartum (Puerperium)					
Chronic Periodontitis	28	37.6±11.4	6	23.22±0.89	0.56
Healthy	24	25.31±0.62	6	23.1±0.54	0.09

*Significant

Table-3: IL-8 in subjects with and without periodontitis in two gestational phases in connection to preeclampsia (pg/ml)

Comparative categories	Preeclampsia	Periodontal status				p
		Healthy Periodontium		Chronic Periodontitis		
		n	Mean±SEM	n	Mean±SEM	
Ante partum	No	24	26.32±0.61	34	25.74±1.25	0.71
	Affected	6	23.09±0.41	6	25.56±1.86	0.22
Postpartum	No	24	25.31±0.62	28	37.6±11.4	0.32
	Affected	6	23.1±0.54	6	23.22±0.89	0.91

DISCUSSION

Chronic periodontitis is clinically characterized by loss of periodontal structures that deteriorate alveolar anatomy and ultimately loosening of tooth occurs in the socket.¹¹ In this regard the host mediated immune responses against subgingival pathogens have been placed as vital importance in the pathogenesis of periodontitis.¹²

Periodontitis directly and indirectly contributes to preeclampsia, directly through dissemination of virulent periodontal pathogens from periodontal pockets (>2 mm sulcus depth) to fetoplacental membrane. The indirect route is facilitated via enhanced systemic inflammatory cytokines and interleukins.^{6,13}

Bio-researchers also claimed that IL-1β, IL-6, IL-8, IL-12p70, IL-13, and IL-15 are elevated with the advancement of even normal pregnancy.⁹ Immune modulation is essential component throughout pregnancy and according to epidemiological studies this altered immunity may be a central cause of preeclampsia.¹⁴ There are multiple dynamics of preeclampsia like imbalance of Th1/Th2 mediated functions and raised serum levels of pro-inflammatory mediators.¹⁵

Interleukin 8 is a chemo attractant protein that mainly trigger neutrophils at inflammatory front and its raised level has been observed in patients of periodontitis and preeclampsia.^{9,10} Porphyromonas gingivalis is a key contributor of chronic periodontitis and is said to potentiate chemotactic paralysis of neutrophils that is why it inhibits IL-8 expression and inversely

related with Polymorphonuclear Leukocytes recruitment.¹⁰ Uwitonze AM *et al* concluded that P. gingivalis and F. nucleatum exhibited increased circulating levels of IL-6 and IL-8.⁶

Finoti LS, *et al* declared higher concentrations of IL-8 in plasma of patients affected with chronic periodontitis.¹³ Our results are in line with Finoti LS *et al*. A contradiction is seen in literature about the association of IL-8 with both pathologies; many studies have exhibited the decrease in serum IL-8 levels in preeclamptic mothers¹⁶, similar to our findings, and also a decrease serum levels of IL-8 in periodontitis patients^{17,18} compared to controls. IL-8 is secreted by various cellular populations such as monocytes, epithelial cells and endothelial cells, as well as gingival fibroblasts, in reaction to IL-1β¹⁹ and TNF-α induced inflammatory processes¹⁸.

Studies also revealed the raised levels of IL-8 in GCF in chronic periodontitis, which has made IL-8 as a possible indicator of periodontal disease.¹ IL-8 has also been detected from human perivascular cells around blood vessels of endometrium/decidua.^{7,20} A study supported the notion that IL-8 is modulated by up- or down-regulation of progesterone in gestation. Due to this connection IL-8 has been observed to suppress by increase in progesterone levels.²¹

CONCLUSION

Raised serum IL-8 levels were observed in normotensives affected with chronic periodontitis and those who were with healthy periodontium in antepartum and postpartum phases. Highest serum IL-8 was observed in normotensives with chronic periodontitis in their postpartum phase.

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