

ASSOCIATION OF sICAM-1 IN PREGNANCY RELATED PRE-ECLAMPSIA AND CHRONIC PERIODONTITIS

Ayesha Sadiqa¹, Abdul Majeed Cheema²

^{1,2}Institute of Molecular Biology and Biotechnology, The University of Lahore, Lahore, Pakistan

Address for Correspondence:

Ayesha Sadiqa

Department of Physiology Shalamar Medical and Dental College, Lahore, Pakistan.

Emails: ayeshaias@yahoo.com

Date Received: February 17, 2019

Date Revised: March 24, 2019

Date Accepted: May 27, 2019

Contribution

AMC conceived the idea and designed the study. AS did data collection and manuscript writing. AMC did final review. All authors contributed equally to the submitted manuscript.

All authors declare no conflict of interest.

This article may be cited as: Sadiqa A, Cheema AM. Association of sICAM-1 in pregnancy related pre-eclampsia and chronic periodontitis. Pak Heart J 2019; 52 (03):266-70

ABSTRACT

Objective: To investigate any association between periodontitis and preeclampsia in connection to sICAM-1 (ng/ml) levels in pregnant subjects in pregnancy and post-pregnancy phases.

Methodology: A cross-sectional study on pregnant subjects aged between 18-34 years, was conducted from June 2016 to February 2018 in Narowal District by using convenience sampling technique was performed. All subjects were first visited in their 2nd trimester for their blood sample and then in postpartum. From 73 subjects, 45% were with healthy periodontium (from which 6 were preeclamptic and 27 with no preeclamptic history) and 55% were with periodontitis (from which 6 were preeclamptic and 34 with no preeclamptic history). CPITN probing technique was used to examine periodontium and history of preeclampsia was confirmed by the concerned doctor and monthly check-up reports of the subject. Through centrifugation sera were taken and sandwich ELISA technique was used to estimate sICAM-1 in ng/ml. Microsoft Excel and Minitab were used as software system to analyze data.

Results: A total of 73 subjects were included. In subjects with healthy periodontium and without preeclampsia, 28.44% higher sICAM-1 levels were found in postpartum than antepartum and 25% raised sICAM-1 (ng/ml) was observed in postpartum in subjects without preeclampsia but affected with periodontitis. While a rise of 26% in sICAM-1 was assessed again in postpartum phase, where subjects were with both disorders. In subjects without preeclampsia, elevated sICAM-1 levels were found in those that were with healthy periodontium in both antepartum and postpartum, while in preeclamptics excessively raised sICAM-1 was noticed in subjects with periodontitis in both phases.

Conclusion: Pregnancy normally reduces sICAM-1 levels. Chronic periodontitis alone was not related to increased sICAM-1 levels, but in patients with preeclampsia, it showed many times raised levels of sICAM-1.

Key Words: Chronic Periodontitis, sICAM-1, Preeclampsia, Pregnancy.

INTRODUCTION

Pregnancy is a state of high oxidative stress, because of raised metabolic activity in mitochondria of placenta and immense release of superoxide.¹ Preeclampsia usually appeared as a complicated obstetric disorder after 20th gestational week in a formerly normotensive female and as a hypertensive malady of pregnancy it has been accountable for 15% neonatal deaths in the world.² Chronic periodontitis is an oral multifactorial infectious disorder of tooth supporting structures.³ Prevalence range of pregnancy related periodontitis has been documented as 5-20% globally.⁴ There has been still an unsettled debate regarding the association of periodontitis and preeclampsia. Abundant immunological studies suggested the causative association of chronic periodontitis with a variety of systemic pathologies such as coronary heart disease⁵, cerebrovascular diseases⁵, pulmonary disorders and adverse pregnancy outcomes like preterm labour and preeclampsia.⁶

Many researchers found that maternal infections caused by periodontal pathogens, raised circulating mediators IL-1 β , IL-6, IL-8, IL-17, and TNF- α , all have been known too for preeclampsia.^{4,5} Bacteria along with their toxins leaked deep into periodontal tissues and interact with fibroblasts and dendrite cells, which then released pro-inflammatory cytokines and finally caused complement activation.⁷ All these events also influenced vascular endothelial cells, expressed as adhesion molecules (ICAM and VCAM) that brought immune cells.⁸ Cellular adhesion molecule (CAM), is a protein that adheres to the surfaces of gingiva, sulcular epithelium and even to the junctional epithelium. Its main purpose is to provide a connection between cell and the extracellular matrix. CAM is found to be present in raised concentration in periodontitis. sICAM-1 stands for soluble Intercellular adhesion molecule-1, that is broadly located on WBCs, endothelial and epithelial cells.² Literature endorsed the elevated serum ICAM-1 levels in periodontitis as sICAM-1 has been positively linked with plaque accumulation on the surfaces of teeth, which further trigger endothelial cells as well as leukocytes at the focal sites.⁷ A study has found an increased level of sICAM-1 in the plasma of pregnant women with preeclampsia, though it was a non-significant increase.⁹ Our purpose is to detect the association of sICAM-1 with preeclampsia and chronic periodontitis and also to observe the effect of preeclampsia on healthy and as well as chronic periodontitis subjects through estimation of sICAM-1 serum levels in pregnancy.

METHODOLOGY

A cross-sectional study was conducted on only pregnant population of Narowal District of Punjab, Pakistan. Convenience sampling technique was employed and the total duration of study was from June 2016 to February 2018.

The age of all participants was between 18–34 years. Subjects were sampled for sera collection and periodontal evaluation in their second trimester and then again visited for sera collection in their postpartum phase after six week of child birth.

Every time 4 cc blood was taken in sterile syringe after taking consent from each participant, and then preserve in a glass vial for centrifugation. The drawn serum was stored at -80°C. The examination of oral cavity was assured by a dentist with the help

of CPITN (Community Periodontal Index for Treatment Need) probing technique, through which the degree of clinical attachment loss was measured in mm by placing the tip of the probe in the area of gingival sulcus and severity of periodontitis was determined and recorded in a sample Performa in which other specific information related to medical and drug history of the subject was already mentioned.

To verify a subject for preeclampsia, her routine record of Blood pressure was taken by her doctor/gynecologist, after her due permission.

96 welled preformed ELISA kits for serum sICAM-1 detection were used separately for antepartum and postpartum sera samples. All the readings were taken through interpolation on the calibrated curve.

Microsoft Excel and Minitab version 18 were used to analyze the data. Unpaired Student's t-test was used as a statistical test to assess the level of significance. Alpha was set as 0.05. Comparative Line graph was plotted to show the difference in sICAM-1 (ng/ml) concentration in each related category.

RESULTS

From 73 total patients, 33 were with healthy periodontium, that were again classified into 6 as preeclamptic and 27 were with no history of preeclampsia. The remaining 40 gravid women were with chronic periodontitis that were again subdivided into 6 preeclampted and 34 were with no effects of preeclampsia. In subjects without history of preeclampsia, a 28.44% increased sICAM-1 levels were observed in postpartum phase as compared to antepartum phase, moreover all subjects were with healthy periodontium ($p=0.02$) and a rise of 25% in sICAM-1 levels were found again in postpartum phase compared to antepartum phase, in non-preeclampted subjects effected with chronic Periodontitis ($p=0.03$). Both differences proved statistically significant. In gravid preeclampted subjects effected with healthy periodontium, a 26% high sICAM-1 concentrations were assessed in postpartum than antepartum phase ($p=0.36$), whereas only 8% rise in sICAM-1 was observed in preeclampted sufferers of periodontitis in antepartum phase ($p=0.89$). Although the differences proved statistically insignificant. (Table-1)

The subjects in second trimester and effected with chronic periodontitis, showed a 75.4% more sICAM-1 level in preeclamptics than non-preeclamptics and also with statistical significance ($p=0.04$). Whereas subjects in second trimester with healthy periodontium showed 13.4% raised sICAM-1 in non-preeclampted ones, though with insignificant difference ($p=0.42$). The subjects with chronic periodontitis in postpartum phase, expressed 30% raised sICAM-1 levels in preeclamptics compared to those who were with without preeclampsia ($p=0.42$). While the subjects with healthy periodontium in postpartum period, exhibited a 16% high sICAM-1 concentrations in non-preeclamptic over those who were preeclamptics ($p=0.46$). Though the differences were statistically insignificant (Table-2).

In antepartum phase, with non-preeclamptic only 4% increased sICAM-1 was noticed in only those who were with healthy periodontium than sufferers of periodontitis. While in the same

phase preeclamped showed a greater rise of 82% in sICAM-1 levels in those effected with also periodontitis. Similarly in postpartum phase, non-preeclamptics with healthy periodontium showed 7% high sICAM-1 levels than those ones who were effected with periodontitis. Whereas in the same phase,

preeclamptics exhibited a much increased sICAM-1 i.e. up to 40%, in those effected with periodontitis than those that were with healthy periodontium. However all differences were not statistically significant ($p < 0.05$) (Table-3).

Table 1: Gestational Comparison of sICAM-1 (ng/ml) levels between subjects with and without Preeclampsia, in relation to Periodontitis

GESTATIONAL PHASE						
STUDIED GROUPS		Antepartum		Postpartum		p-value
Periodontium	Preeclampsia	n	Mean±SEM	n	Mean±SEM	
Healthy	No	27	5.66±0.35	24	7.27±0.59	0.02*
	Effected	6	4.99±0.76	6	6.29±1.13	0.36
Chronic Periodontitis	No	34	5.44±0.45	28	6.78±0.36	0.03*
	Effected	6	9.54±4.22	6	8.83±2.71	0.89

* statistical significant as $p < 0.05$.

Table 2: Difference between sICAM-1 (ng/ml) in subjects with and without Preeclampsia, in relation to Periodontitis and Gestation

HISTORY OF PREECLAMPSIA						
STUDIED GROUPS		No		Postpartum		p-value
Gestational Phase	Periodontal Status	n	Mean±SEM	n	Mean±SEM	
Antepartum (2 nd trimester)	Ch. Periodontitis	34	5.44±0.45	6	9.54±4.22	0.04*
	Healthy	27	5.66±0.35	6	4.99±0.76	0.42
Postpartum (Puerperium)	Ch. Periodontitis	28	6.78±0.36	6	8.83±2.71	0.16
	Healthy	24	7.27±0.59	6	6.29±1.13	0.46

* statistical significant as $p < 0.05$.

Table 3: Comparison of sICAM-1 (ng/ml) between subjects with and with periodontitis in two gestational phases, in connection to Preeclampsia

PERIODONTAL STATUS						
STUDIED GROUPS		Healthy Periodontium		Chronic Periodontitis		p-value
Periodontium	Preeclampsia	n	Mean±SEM	n	Mean±SEM	
Healthy	No	27	5.66±0.35	24	5.44±0.45	0.71
	Effected	6	4.99±0.76	6	9.54±4.22	0.31
Chronic Periodontitis	No	34	7.27±0.59	28	6.78±0.36	0.46
	Effected	6	6.29±1.13	6	8.83±2.71	0.41

* statistical significant as $p < 0.05$.

DISCUSSION

Chemically Intercellular adhesion molecule-1 (ICAM-1) is a known trans-membrane glycoprotein protein derived from endothelial cells and leukocytes.¹⁰ ICAM-1 has been observed to direct WBCs adhesion and extra-vasation in reaction to inflammatory trigger caused by antigenic substance, which can be a pathogen (bacterium) as well. This response has been placed a vital effect on the health of normal periodontium.¹¹ A

study in UK observed raised sICAM-1 levels in the patients of periodontitis compared to healthy controls. sICAM-1 altered leukocytes function in relation to periodontitis via by blocking the receptor site. So it hindered the leukocytes adhesion mechanism.¹² Similar to our findings, another study from Kuwait by Austgulen et al. also concluded that elevated serum concentrations of sICAM-1 have been significantly noticed in preeclamptic gestations compared to healthy pregnancies.¹³

A Canadian study exhibited the causative relation of periodontitis with poor gestational outcomes like preeclampsia.¹⁴ The association between chronic periodontitis and preeclampsia has now been more focused and studied by the researchers of life sciences in all over the World.¹⁵ A group of bio-researchers from Poland found no association between these two disorders, though the same study has found an insignificant raised level of sICAM-1 in the plasma of preclamptic women¹⁶, these results are similar to our observations as we also noticed raised sICAM-1 levels in preeclamptic women in both phases i.e. antepartum and postpartum. Moreover previous studies from China & USA proved no association of sICAM-1 with normal pregnancy^{17,18} our results are also in the same lines.

A comparative research conducted between preeclamptic and normotensive women explored that chronic periodontitis has no relation with preeclampsia.¹³ However a study on the same association from Iran documented that most of the times a preeclamptic women pronouncedly showed higher clinical attachment loss and gingival recession than healthy gravid women.¹⁵ Canacki et al along with another study verified that females effected with preeclampsia, showed more severity in periodontal decay.¹⁹ Furthermore a study on Chinese population proposed that ICAM-1 owned a vital role in early deterioration of periodontium in patients with chronic periodontitis, where ICAM-1 is itself induced by pro-inflammatory mediators such as IL-1 β , TNF- α , IFN- γ .⁸

It has also been suggested by the literature that pregnancies effected with periodontitis, exhibited clinical features of preeclampsia because of imbalanced enhanced maternal immune-inflammatory reactions.¹³ Infact there are many confounding elements that effect the results of preeclampsia related periodontal outcomes in terms of several mediators. Some of those confounders are difference in socioeconomic status, method of measuring clinical attachment loss, ethnicity, dietary and hygienic habits, history of preeclampsia, sample size and most importantly the type of gravidity (primiparous or multiparous).¹⁴

CONCLUSION

Elevated sICAM-1 in ng/ml was reported in postpartum period compared to antepartum, in healthy subjects without periodontitis and preeclampsia. Moreover sICAM-1 (ng/ml) was positively associated with preeclampsia in those subjects that were with periodontitis in antepartum as well as postpartum phases.

REFERENCES

1. Tettamanti L, Lauritano D, Nardone M, Gargari M, Silvestre-Rangil J, Gavoglio P, et al. Pregnancy and periodontal disease: does exist a two-way relationship? *Oral Implantol (Rome)* 2017;10(2):112-8.
2. Wu P, van den Berg C, Alfirevic Z, O'Brien S, Röthlisberger M, Baker PN, et al. Early pregnancy biomarkers in preeclampsia: a systematic review and meta-analysis. *Int J MolSci* 2015;16(9):23035-56.
3. Sadiqa A, Cheema AM, Malik S. Chronic periodontitis a possible threat towards CVD. *Biomedica* 2016;32(1):29-32.
4. Desai K, Desai P, Duseja S, Kumar S, Mahendra J, Duseja S. Significance of maternal periodontal health in preeclampsia. *J IntSocPrev Community Dent* 2015;5(2):103-7.
5. Sadiqa A, Cheema AM, Malik S. Mild chronic periodontitis: a possible threat towards CVD in males with raised C-RP. *Pak J Physiol* 2015;11(3):18-21.
6. da Silva HEC, Stefani CM, de Santos Melo N, de Almeida de Lima A, Rösing CK, Porporatti AL, et al. Effect of intra-pregnancy nonsurgical periodontal therapy on inflammatory biomarkers and adverse pregnancy outcomes: a systematic review with meta-analysis. *Syst Rev* 2017;6(1):197.
7. Leishman SJ, Seymour GJ, Ford PJ. Local and systemic inflammatory responses to experimentally induced gingivitis. *Dis Markers* 2013;35(5):543-9.
8. Wang L, Li XH, Ning WC. Evaluation of ICAM-1 and VCAM-1 Gene Polymorphisms in Patients with Periodontal Disease. *Med SciMonit* 2016;22:2386-91.
9. Conde-Agudelo A, Papageorgiou AT, Kennedy SH, Villar J. Novel biomarkers for the prediction of the spontaneous preterm birth phenotype: a systematic review and meta-analysis. *BJOG* 2011;118(9):1042-54.
10. Erdemir EO, Hendek MK, Keceli HG, Apan TZ. Crevicular fluid levels of interleukin-8, interleukin-17 and soluble intercellular adhesion molecule-1 after regenerative periodontal therapy. *Eur J Dent* 2015;9(1):60-5.
11. Witkowska AM, Borawska MH. Soluble intercellular adhesion molecule-1 (sICAM-1): an overview. *Eur Cytokine Netw* 2004;15(2):91-8.
12. Fraser HS, Palmer RM, Wilson RF, Coward PY, Scott DA. Elevated systemic concentrations of soluble ICAM-1 (sICAM) are not reflected in the gingival crevicular fluid of smokers with periodontitis. *J Dent Res* 2001;80(7):1643-7.
13. Raghupathy R. Cytokines as key players in the pathophysiology of preeclampsia. *Med Princ Pract* 2013;22Suppl 1:8-19.
14. Taghzouti N, Xiong X, Gornitsky M, Chandad F, Voyer R, Gagnon G, et al. Periodontal disease is not associated with preeclampsia in Canadian pregnant women. *J Periodontol* 2012;83(7):871-7.
15. Sayar F, Hoseini MS, Abbaspour S. Effect of periodontal disease on preeclampsia. *Iran J Public Health* 2011;40(3):122-7.
16. Djurovic S, Schjetlein R, Wisløff F, Haugen G, Berg K. Increased levels of intercellular adhesion molecules and vascular cell adhesion molecules in pre-eclampsia. *Br J ObstetGynaecol* 1997;104(4):466-70.
17. Zhao J, Zheng DY, Yang JM, Wang M, Zhang XT, Sun L, et al. Maternal serum uric acid concentration is associated with the expression of Tumor Necrosis Factor- α and Intercellular Adhesion Molecule-1 in patients with preeclampsia. *J Hum Hypertens* 2016;30(7):456-62.
18. Chaiworapongsa T, Romero R, Yoshimatsu J, Espinoza J, Kim YM, Park K, et al. Soluble adhesion molecule profile in

normal pregnancy and pre-eclampsia. J Matern Fetal Neonatal Med 2002;12(1):19-27.

19. Contreras A, Herrera JA, Soto JE, Arce RM, Jaramillo A, Botero JE. Periodontitis is associated with preeclampsia in pregnant women. J Periodontol 2006;77(2):182-8.