

4-30-2021

Periodontal Parameters and Anti-Cardiolipin Antibodies Following Periodontal Therapy in Chronic Periodontitis

Wan Majdiah Wan Mohamad

School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia,
wmajdiah@usm.my

Noor Rashidah Saad

Unit of Periodontics, Klinik Pergigian, Jalan Putra, 36000 Teluk Intan, Perak, Malaysia,
rashi_5758@yahoo.com

Siti Lailatul Akmar Zainuddin

School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia,
lailatul@usm.my

Haslina Taib

School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia,
haslinakk@usm.my

Follow this and additional works at: <https://scholarhub.ui.ac.id/jdi>



Part of the [Dental Hygiene Commons](#), [Dental Materials Commons](#), [Endodontics and Endodontology Commons](#), [Health Economics Commons](#), [Oral and Maxillofacial Surgery Commons](#), [Oral Biology and Oral Pathology Commons](#), [Orthodontics and Orthodontology Commons](#), [Pediatric Dentistry and Pedodontics Commons](#), and the [Periodontics and Periodontology Commons](#)

Recommended Citation

Wan Mohamad, W., Saad, N., Zainuddin, S., & Taib, H. Periodontal Parameters and Anti-Cardiolipin Antibodies Following Periodontal Therapy in Chronic Periodontitis. *J Dent Indones.* 2021;28(1): 15-21

This Article is brought to you for free and open access by the Faculty of Dentistry at UI Scholars Hub. It has been accepted for inclusion in *Journal of Dentistry Indonesia* by an authorized editor of UI Scholars Hub.

Periodontal Parameters and Anti-Cardiolipin Antibodies Following Periodontal Therapy in Chronic Periodontitis

Cover Page Footnote

ACKNOWLEDGEMENTS We would like to express our utmost gratitude to all patients and staff who direct or indirectly involved in this study. This study was funded by USM Short Term Grant (304/PPSG/61311040).

ORIGINAL ARTICLE

Periodontal Parameters and Anti-Cardiolipin Antibodies Following Periodontal Therapy in Chronic Periodontitis

Wan Majdiah Wan Mohamad^{1*}, Noor Rashidah Saad², Siti Lailatul Akmar Zainuddin¹, Haslina Taib¹

¹School of Dental Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

²Unit of Periodontics, Klinik Pergigian, Jalan Putra, 36000 Teluk Intan, Perak, Malaysia

*Correspondence e-mail to: wmajdiah@usm.my

ABSTRACT

Anti-cardiolipin (anti-CL) antibodies are autoantibodies which are directed against cell membrane phospholipids. A significant number of periodontitis patients showed positive for anti-CL antibody. **Objective:** This study aimed to determine the periodontal parameters and anti-CL antibodies levels before and after non-surgical periodontal therapy in chronic periodontitis. **Methods:** This cross-sectional study had been carried out at Periodontal Clinic, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia. Thirty five chronic periodontitis (CP) and 39 non-periodontitis (NP) patients underwent clinical periodontal examination at baseline. Plaque index (PI), gingival index (GI), periodontal pocket depth (PPD), and clinical attachment loss (CAL) were measured. Scaling and polishing was performed and blood samples were taken for IgG and IgM anti-CL antibodies analysis. Re-evaluation was performed four weeks after initial therapy. CP patients were re-examined, all periodontal parameters were recorded and blood samples were taken for reassessment of IgG and IgM anti-CL antibodies. **Results:** Significant difference means of PI ($p=0.001$), GI ($p=0.000$), PPD ($p=0.000$) and, CAL ($p=0.000$) were found between CP and NP groups. All periodontal parameters were significantly reduced ($p\leq 0.05$) after four weeks of therapy. The mean levels of IgG and IgM anti-CL antibodies at baseline were significantly higher in CP than NP group (IgG=4.46 vs 3.22, $p=0.002$; IgM=3.28 vs 2.57, $p=0.019$). No significant difference of the median levels of IgG ($p=0.82$) and IgM anti-CL antibodies ($p=0.35$) following therapy. **Conclusion:** All periodontal parameters were significantly reduced following periodontal therapy. Higher level of Anti-CL antibodies in CP indicates stimulation of autoantibodies production by periodontal infection. Nonetheless no significant changes of this anti-CL antibodies levels despite significant reduction of the clinical parameters after periodontal therapy.

Key words: periodontal parameters, anti-CL antibodies, chronic periodontitis, non-surgical periodontal therapy

How to cite this article: Wan Mohamad WM, Saad NR, Zainuddin SLA, Taib H. Periodontal parameters and anti-cardiolipin antibodies following periodontal therapy in chronic periodontitis. J Dent Indones. 2021;28(1):15-21

INTRODUCTION

Anti-cardiolipin (anti-CL) antibodies are autoantibodies which are directed against cell membrane phospholipids. These antibodies are classified as immunoglobulin M (IgM), immunoglobulin G (IgG), and immunoglobulin A (IgA) or as $\beta 2$ -glycoprotein dependent or independent forms¹ which have been found in about 15% to 20% of aggressive and chronic periodontitis patients at higher concentration than those found in 95% of healthy adult population.² These antibodies were typically found in patients with autoimmune disease such as systemic lupus erythematosus (SLE) and antiphospholipid

syndrome (APLS), characterized by thrombosis and recurrent pregnancy loss.² A significant number of periodontitis patients showed positive for anti-CL antibody, most probably due to bacterial antigens homologous to the target antigen of anti-CL antibody on the serum protein $\beta 2$ glycoprotein-1 ($\beta 2$ GPI), thus can induce production of anti-CL by molecular mimicry mechanism.³

Chronic periodontitis (CP) is an inflammatory disease due to bacterial infections affecting tissues surrounding the teeth, periodontal pocket formation, loss of clinical attachment, and alveolar bone resorption. In

advanced CP, it may lead to tooth mobility, and/or tooth migration, and tooth loss.⁴ The role of periodontal pathogens, notably *Porphyromonas gingivalis* (*P. gingivalis*), in the onset or exacerbation of systemic diseases has been proposed. *P. gingivalis* expresses several virulence factors that promote its survival, spreading, and sustaining systemic inflammation.⁵ Schenkein et al. reported increase in IgG anti-CL antibody titres has been found in 18.9% of periodontitis patients compared to periodontally healthy subjects (7.5%).⁶ They hypothesized that these antibodies trigger the endothelial cells to produce monocyte chemoattractant protein-1 (MCP-1) which may elucidate the link between periodontitis and systemic conditions.

Previous studies^{2,7} have proven that *P. gingivalis*, *Haemophilus influenza* or *Neisseria gonorrhoea*, and cytomegalovirus, stimulate the production of anti-CL antibodies. These pathogens were found to have similar peptide sequences to the TLRVYK peptide of β 2GPI. Three peptides sequence in the arg-gingipain protease of *P. gingivalis* was found to be similar to the TLRVYK peptide of β 2GPI which may induce cross-reactive autoantibodies in periodontitis patients.^{2,8} Interestingly, a number of studies^{2,3,6} had reported that infection by periodontal pathogens may stimulate the production of anti-CL antibodies in periodontitis.

In periodontitis, oral hygiene instruction and motivation is the key message for the patients to control chronic infection. Non-surgical periodontal therapy is considered the gold standard for the initial treatment of periodontitis which involves plaque removal, plaque control, supragingival and subgingival scaling root planing, as well as adjunctive use of chemical agents. Other various methods which are used in non-surgical periodontal therapy include hand instrumentation, ultrasonic and sonic scalers, and ablative laser therapy.⁹

Scaling and polishing removes plaque and calculus from tooth and root surfaces. Regular removal of these deposits may reduce gingivitis and prevent progression to periodontitis.¹⁰ Scaling and root planing remain the essential parts for successful periodontal therapy to reduce the number of pathogenic bacteria species.¹¹ However, if the periodontal pockets persist at 5mm or more, root planing is required to remove embedded calculus, necrotic cementum, and to smoothen the root surfaces.¹² These procedures result in decrease in inflammation of the periodontium due to a lesser bacterial load, subsequently leads to beneficial clinical changes.⁹ In addition, Gunupati et al.¹³ had done a study among chronic periodontitis patients with acute myocardial infarction. They found that there was a significant alteration in the concentrations of IgM ($p=0.008$) and IgG ($p<0.001$) anti-CL antibodies along with periodontal parameters following non-surgical periodontal therapy. However, currently the findings are still controversial. Thus, this study has been carried out to determine whether there is an improvement

in periodontal parameters as well as the decrease in anti-IgG and IgM anti-CL antibodies levels following non-surgical periodontal therapy.

METHODS

A prospective study had been conducted at Periodontal Clinic, Hospital Universiti Sains Malaysia, Kelantan, Malaysia. A total of 35 chronic periodontitis (CP) patients and 39 non-periodontitis (NP) subjects with the age over 18 years old without any medical problem had participated in this study. The criteria for CP were those with clinical attachment loss (CAL) of >2 mm and periodontal pocket depth (PPD) of >3 mm.^{4,14} The NP group were those with healthy periodontium with CAL of ≤ 2 mm, and PPD of ≤ 3 mm.

The exclusion criteria for the study includes pregnant and lactating mothers, smokers, patients who had chronic medical conditions, patients with history of trauma or tooth extraction two weeks prior to the study, patients who received antibiotics and chronic medications within the past three months, and patients who underwent periodontal treatment for the past six months.

Written informed consent was obtained from all subjects. The study protocol was approved by Human Research Ethics Committee Universiti Sains Malaysia [USM/KK/PPP/JEPeM (232.3(1))].

Clinical examination

Clinical periodontal examination was performed twice on CP patients, during the baseline and four weeks after scaling and polishing. All the periodontal parameters were recorded. The clinical periodontal examination was carried out by a calibrated examiner with patient sitting on dental chair in supine position. Plaque index (PI), Gingival index (GI), PPD, and CAL were then measured by using Michigan 'O' William's periodontal probe which are Plaque index, Gingival index and Periodontal pocket depth and clinical attachment loss.^{15,16}

Plaque Index¹⁵

PI was used to assess the presence of plaque on tooth surfaces. and The PI scores as follows: 0) No plaque in gingival area, 1) Thin plaque layer at gingival margin and adjacent area of the tooth, only detectable by scrapping with a probe, 2) Moderate layer of plaque within the gingival pocket, or on the tooth surface and along the gingival margin, plaque is visible with the naked eye, 3) Abundant plaque within the gingival pocket or on tooth surface and the gingival margin.

Gingival Index¹⁶

GI was used to determine the gingival status. The GI scores can be interpreted as follows: 0) Normal gingival, absence of gingival inflammation, 1) Mild

Table 1. General characteristics of the subjects (n=74)

Characteristics	Non Periodontitis (n=39)		Chronic Periodontitis (n=35)	
	Mean (SD)	Frequency (%)	Mean (SD)	Frequency (%)
Age (Years)	34.97 (10.88)		43.23 (11.40)	
Gender				
Male		16 (41.0%)		16 (45.7%)
Female		23 (59.0%)		19 (54.3%)
Ethnics				
Malay		37 (94.9%)		31 (88.6%)
Chinese		2 (5.1%)		4 (11.4%)

*SD: standard deviation

Table 2. The baseline data of periodontal parameters of the subjects (n=74)

Variables	NP (n=39)	CP (n=35)	Mean difference (95% CI)	t-statistic (df)	p value*
	Mean (SD)	Mean (SD)			
PI	0.51 (0.34)	0.89 (0.55)	-0.38 (-0.59, -0.16)	-3.5 (55)	0.001
GI	0.47 (0.25)	0.99 (0.48)	-0.52 (-0.70, -0.34)	-5.7 (50)	<0.001
PPD (mm)	1.71 (0.33)	2.66 (0.63)	-0.95 (-1.18, -0.71)	-7.0 (50)	<0.001
CAL (mm)	0.14 (0.29)	1.16 (1.33)	-1.02 (-1.49, -0.55)	-4.4 (37)	<0.001

*Independent t-test

NP=NonPeriodontitis; CP=Chronic Periodontitis; SD=standard deviation; PI=Plaque index; GI=Gingival index; PPD=Periodontal pocket depth; CAL= Clinical attachment loss

inflammation – slight change in colour, slight oedema, no bleeding on pressure. 2) Moderate inflammation – moderate glazing, redness, oedema and hyperthropy, bleeding on pressure. 3) Severe inflammation – marked redness, oedema and hyperthropy, tendency to spontaneous bleeding.

All the periodontal parameters were recorded at four sites (distal-facial, facial, mesial-facial and lingual/palatal) of six index teeth (maxillary right first molar, maxillary right lateral incisor, maxillary left first premolar, mandibular left first molar, mandibular left lateral incisor and mandibular right first premolar). The score for each index tooth was calculated and averaged for each subjects.

Periodontal pocket depth and clinical attachment loss

PPD and CAL were measured were determined at six sites per tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual-palatal, mid-lingual-palatal, and disto-lingual-palatal) for all teeth. The total of PPD and CAL measurements from all teeth then were averaged to get a mean score for each subject respectively.

Blood samples collection

A standard venepuncture procedure was performed twice, which is during the baseline and four weeks after scaling and polishing. Three millilitres of venous blood was withdrawn during each visit. The blood samples

were then transferred into plain bottles and immediately transported to the Immunology Laboratory for anti-CL antibodies analysis.

Anti-CL antibodies analysis

The blood samples were allowed to clot for one hour at room temperature. Centrifugation was done for 5 minutes at 4,500 rpm using Hettich Zentrifugen Universal 32 R Centrifuge at 4°C. The sera then were separated, placed in microcentrifuge tubes and stored in the refrigerator at -80°C until assayed. The IgG and IgM anti-CL antibodies levels then were analysed using commercially available enzyme linked immunosorbent assay (ELISA) kits according to the manufacture's protocol. The normal values of IgG and IgM anti-CL antibodies were reported as < 10GPL Unit/mL and <7MPL Unit/mL respectively.

Re-evaluation

Full mouth scaling and polishing were performed on CP patients. However, out of 35 CP patients, only 23 patients were able to turn up after four weeks for re-evaluation of periodontal parameters as well as IgG and IgM anti-CL antibodies levels. This is due to problem in answering follow up call; some of them claimed to have forgotten their appointment, and some had problem in transportation particularly those who stayed in the rural area. NP subjects were advised for six monthly routine dental check-up.

Table 3. The periodontal parameters at baseline and after 4 weeks of scaling and polishing in chronic periodontitis patients (n=23)

Variables	Baseline	After 4 weeks	Z statistic*	p-value*
	Median (IQR)	Median (IQR)		
PI	0.75 (0.92)	0.42 (0.26)	-2.85	0.005
GI	0.83 (0.75)	0.63 (0.67)	-2.89	0.004
PPD (mm)	2.36 (0.83)	2.23 (0.71)	-2.86	0.004
CAL (mm)	0.44 (0.69)	0.44 (0.70)	-3.55	<0.001

*Wilcoxon Signed Rank Test

IQR=Interquartile Range; PI=Plaque index; GI=Gingival index; PPD=Periodontal pocket depth; CAL= Clinical attachment loss

Table 4. Comparison of baseline data of the means of IgG and IgM anti-cardiolipin antibodies levels between non-periodontitis and chronic periodontitis groups (n=74)

Anti-CL antibodies	Anti-CL antibody levels Mean (SD)		Mean difference (95% CI)	t-statistic (df)	p-value*
	NP (n= 39)	CP (n=35)			
IgG (GPL Unit/mL)	3.22 (1.35)	4.46 (1.89)	-1.24 (-1.99, -4.89)	-3.29 (72)	0.002
IgM (MPL Unit/ mL)	2.57 (0.91)	3.28 (1.57)	-0.71 (-1.29, -0.12)	-2.40 (72)	0.019

*Independent t- test

NP=Non-Periodontitis; CP=Chronic Periodontitis; SD=Standard Deviation; CI=Confidence Interval; df=degree of freedom

Table 5. The median levels of IgG and IgM anti-cardiolipin antibodies levels at baseline and 4 weeks after scaling and polishing in chronic periodontitis patients (n=23)

Variables	Before treatment	After treatment	Z statistic	p-value*
	Median (IQR)	Median (IQR)		
IgG (GPL Unit/mL)	4.41 (2.49)	4.69 (3.39)	-0.228	0.82
IgM (MPL Unit/mL)	2.97 (1.69)	3.36 (1.77)	-0.943	0.35

*Wilcoxon Signed Rank Test; IQR: Interquartile Range

Statistical Analysis

All data were analysed using the Statistical Package for the Social Sciences (SPSS) version 20.0. Descriptive statistics of demographic variables were expressed as frequency and percentage. Independent t-test was used to compare the baseline data of the means of periodontal parameters and anti-CL antibodies (IgG and IgM) levels for NP and CP groups, while Wilcoxon Signed Rank Test was used to determine the median (IQR) of periodontal parameters and anti-CL antibodies (IgG and IgM) at baseline and 4 weeks after scaling and polishing in CP patients. The p-value of <0.05 was considered as statistically significant.

RESULTS

Seventy four subjects were recruited at baseline of the study; 35 CP and 39 were NP with the mean age

of 43.23±11.40 and 34.97±0.88 years respectively. Majority of the subjects were female (59.0%) and Malay (94.9%) (Table 1). Table 2 shows the baseline data of periodontal parameters of NP and CP patients. Significant differences of the means of PI (p=0.001), GI (p<0.001), PPD (p<0.001) and CAL (p<0.001) were found between both groups. In CP patients, the PI, GI, PPD, and CAL were significantly reduced (p<0.05) at 4 weeks after scaling and polishing (Table 3).

Table 4 shows the baseline levels of IgG and IgM anti-CL antibodies in NP and CP patients. The mean levels of IgG and IgM anti-CL antibodies at baseline were significantly higher in chronic periodontitis than non-periodontitis group (IgG=4.46 vs 3.22, p=0.002; IgM=3.28 vs 2.57, p=0.019). Re-evaluation of IgG and IgM anti-CL antibodies for the 23 CP patients after 4 weeks of scaling and polishing showed slightly increase

in antibodies levels but no significant changes (IgG: $p=0.82$ and IgM: $p=0.35$) compared to the baseline (Table 5).

DISCUSSION

In this study, the mean age of chronic periodontitis patients was 43.23 years, which was older than non-periodontitis subjects (34.97 years). This reflects periodontitis is common in older age. Khan et al.¹⁷ and Kiany and Hedayati¹⁸ reported the mean age of CP patients in their study were 43.9 and 40.55 years respectively, which were almost similar with our study. Most patients were female and from Malay ethnic group.

Significant difference means of PI ($p=0.001$), GI ($p<0.001$), PPD ($p<0.001$) and, CAL ($p<0.001$) were found between NP and CP groups. In fact, the means of PI ($p=0.005$), GI ($p=0.004$), PPD ($p=0.004$) and CAL ($p=0.000$) in CP patients were found to be reduced significantly after full mouth scaling and polishing. As mentioned previously, non-surgical periodontal therapy reduces inflammation and subsequently improve the periodontal parameters.⁹ These findings are consistence with previous studies^{18, 19} which reported a significant reduction in PI, GI, PPD, and CAL following non-surgical periodontal therapy. In addition, a number of studies also reported the similar significant reduction of PI, GI, PPD and CAL following non-surgical periodontal therapy involving scaling and root planing.^{3,13,18}

Our study shows IgG and IgM anti-CL antibodies in CP patients were significantly higher compared to NP subjects, although the levels were within the normal range based on the kit manufacturer. The results are consistent with the finding from previous studies^{2,8} that reported a significant number of periodontitis patients have demonstrated elevated serum concentration of anti-CL antibodies. The increase in anti-CL antibodies in our patients most probably due to production of autoantibodies triggered by periodontal pathogens. As mentioned previously, anti-CL antibodies are commonly found in patients with SLE and APLS² and can increase in some infectious diseases.⁷ These pro-thrombotic auto-antibodies are also associated with adverse pregnancy outcomes such as fetal involution, prematurity, low birth weight with cardiovascular sequelae such as atherosclerosis, stroke and myocardial infarction. All of these conditions are remarkable similar to systemic condition associated with periodontitis.² Since infectious diseases may induce production of anti-CL antibodies, it is hypothesized that CP patients may have increased anti-CL antibodies levels.

The median levels of IgG and IgM anti-CL antibodies were increased at four weeks following full mouth scaling in chronic periodontitis patients. The increase

in IgG and IgM anti-CL antibodies might be due to the possibility of 'immunization' effect where the instrumentation induced bacteremia results in increase antibody production. However, this may be temporary. Since the duration of measurement of antibodies during final visit is only four weeks after scaling and polishing, thus these antibodies levels may need longer time to be decreased following non-surgical periodontal therapy. According to Syrjanen et al.²⁰ transient bacteremia can be directly related to dental disease and its treatment. Bacteremia frequently occurs after treatment procedures such as extractions, scaling, scaling and root planing, periodontal probing, periodontal surgery, suture removal, orthodontic treatment, restorative dentistry, non-surgical root canal treatment. Apart from professional treatment, chewing, subgingival irrigation, oral hygiene procedures such as tooth brushing and flossing have been reported to give rise to bacteremia. However, the results showed considerable variability due to the techniques used, timing of blood sample collection, and periodontal status and identification methods for the isolation of microorganisms.²¹ On the contrary, Chaston et al.²² reported there was a significant reduction of IgM anti-CL antibody following non-surgical periodontal therapy but not for IgG anti-CL antibodies.

Our study shows no significant changes of the median IgG and IgM anti-CL antibodies levels at baseline and four weeks after scaling and polishing in CP patients (IgG: $p=0.82$ and IgM: $p=0.35$). This may indicate longer time interval is needed for the reduction of anti-CL levels following periodontal therapy. However, several studies reported contradictory findings. Kiany and Hedayati¹⁸ found that there was a significant difference of mean levels of IgM ($p=0.003$) and IgG ($p=0.001$) anti-CL antibodies before and after six weeks of non-surgical periodontal therapy. In 2011, Gunupati et al.¹³ reported there was a significant changes in IgG anti-CL antibodies ($P<0.001$) and IgM anti-CL antibodies ($p=0.008$) in CP patients with acute myocardial infarction following one month of non-surgical periodontal therapy.

In this study, the levels of anti-CL antibodies in CP patients were increased compared to NP group. The most possible cause of increase in anti-CL antibodies in CP patients is due to periodontal infections. Although the levels of anti-CL antibody in periodontitis patients are mostly lower than those currently recommended in the classification criteria for diagnosis of APS², these antibodies have nevertheless been shown to enhance cytokine release from human vascular endothelial cells⁶. Therefore, this will further promote the inflammatory process in chronic periodontitis. Periodontal infections triggered the production of anti-CL antibodies by molecular mimicry mechanism. Molecular mimicry occurs when a self-antigen (protein $\beta 2$ GP1) is similar to antigens from a microorganisms (antigens with peptide sequences of periodontal pathogens) or

other source in the environment.²³ Furthermore, anti-CL antibodies can be induced by immunization of animals with certain periodontal pathogens, including *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, and *Treponema denticola*. This is an example of molecular mimicry mechanism. Since all these pathogens have antigens with peptide sequences with significant homology to that of a critical antibody binding site in the serum protein β 2GPI, the target antigen of anti-CL antibody,⁶ thus this will lead to increase production of pathogenic anti-CL antibodies in chronic periodontitis.

CONCLUSION

This study has some limitations. A number of patients did not turn up during second visit. This may affect the results. Therefore some rules need to be enforced during patients' recruitment to avoid this problem. The levels of anti-CL antibodies in CP patients were increased compared to NP group, although within normal range. The normal range is actually depends on the manufacture's kit which are differs between population, depending upon the prevalence of anti-CL antibodies in the population.

Significant different means were found in PI, GI, PPD, and CAL when comparing non-periodontitis and chronic periodontitis group. PI, GI, PPD, and CAL also had improved after scaling and polishing in chronic periodontitis patients. Since periodontitis patients with no evidence of systemic disease demonstrate higher levels of IgG and IgM anti-CL antibodies than periodontally healthy subjects, it can be postulated that these pathogenic autoantibodies production is induced by various periodontal pathogens. However, no significant changes noted in the antibodies levels following non-surgical periodontal therapy. This might be due to insufficient time needed for the decrease in anti-CL antibodies levels following therapy. Therefore, we recommend longer time interval is needed for re-evaluation of the anti-CL antibodies following non-surgical periodontal therapy. Additionally testing specific antibodies towards these periodontal pathogens may be more beneficial compared to anti-CL antibodies in future studies to obtain more conclusive findings.

ACKNOWLEDGEMENTS

We would like to express our utmost gratitude to all patients and staff who direct or indirectly involved in this study. This study was funded by USM Short Term Grant (304/PPSG/61311040).

CONFLICT OF INTEREST

All authors declare no conflict of interest.

REFERENCES

1. Shen X, Liu D, Lin Y, Zhu YZ, Lin LR, Tong ML, et al. The characteristics of beta glycoprotein I-dependent anticardiolipin antibody and blood coagulation status in subjects with classical biological false-positive syphilis reaction. *Int Immunopharmacol*. 2018; 62:132-8.
2. Schenkein HA, Thomas RR. Anticardiolipin (aCL) in sera from periodontitis subjects activate Toll-like receptor 4 (TLR4). *PLOS ONE*. 2018; 13(9):e0203494.
3. Chaston R, Sabatini R, Koertge TE, Brooks CN, Schenkein HA. Serum Anticardiolipin concentrations in patients with chronic periodontitis following scaling and root planing. *Journal of Periodontology*. 2014; 85(5):683-7.
4. Flemmig TF. Periodontitis. *Annals of Periodontology*. 1999; 4(1):32-8.
5. Mullhal H, Huck O, Amar S. *Porphyromonas Gingivalis*, a Long-Range Pathogen: Systemic Impact and Therapeutic Implications. *Microorganisms*. 2020; 8(6):869.
6. Schenkein HA, Sabatini R, Koertge TE, Brooks CN, Purkall DB. Anti-cardiolipin from periodontitis patients induces MCP-1 production by human umbilical vein. *J Clin Periodontol*. 2013; 40(3):212-7.
7. Martirosyan A, Aminov R, Manukyan G. Environmental Triggers of Autoreactive Response: Induction of Antiphospholipid Antibody Formation. *Front. Immunol*. 2019; 01609.
8. Tew J, El Shikh M, El Sayed R, Schenkein H. Dendritic cells, antibodies reactive with oxLDL, and inflammation. *Journal of Dental Research*. 2012; 91(1):8-16.
9. Tanwar J, Hungund SA, Dodani K. Nonsurgical periodontal therapy: A Review. *Journal of Oral Research and Review*. 2016; 8(1):39-44.
10. Lamont T, Worthington HV, Clarkson JE, Beirne PV, Cochrane Oral Health Group. Routine scale and polish for periodontal health in adults. *Cochrane Database Syst Rev*. 2018; 12:CD 004625.
11. Newman M, Takei H, Klokkevold P, Carranza F. *Carranza's Clinical Periodontology*. 11th ed. Missouri: Saunder, Elsevier. 2011.
12. Eley BM, Soory M, Manson JD. *Periodontics Book*. 6th ed. British Library. Publisher: Edinburgh; New York. Churchill Livingstone. Elsevier. 2010.
13. Gunupati S, Chava VK, Krishna BP. Effect of phase I periodontal therapy on anticardiolipin

- antibodies in patients with acute myocardial infarction associated with chronic periodontitis. *Journal of periodontology*, 2011; 82(12):1657-64.
14. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Annals of Periodontology*. 1999; 4(1):1-6.
 15. Silness J, L e H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontologica*. 1964; 22(1):121-35.
 16. L e H, Silness, J. Periodontal disease in pregnancy I. Prevalence and severity. *Acta Odontol Scand*. 1963;21:533-51.
 17. Khan S, Saub R, Vaithilingam RD, Safii SH, Vethakkan SR, Baharuddin NA. Prevalence of CP in an obese population: a preliminary study. *BMC Oral Health*. 2015; 15: Article number:114.
 18. Kiany F, Hedayati A. Evaluation of serum anti - cardiolipin antibodies after non - surgical periodontal treatment in chronic periodontitis patients. *Odontology*. 2015; 103(2):203-9.
 19. Khan S, Khalid T, Bettiol S, Crocombe LA. Non-surgical periodontal therapy effectively improves patient-reported outcomes: A systematic review. *International Journal of Dental Hygiene*. 2021; 19(1):18-28.
 20. Syrjanen J, Valtonen VV, Iivanainen M, Kaste M, Huttunen JK. Preceding infection as an important risk factor for ischaemic brain infarction in young and middle aged patients. *Br Med J (Clin Res Ed)*. 1988;296:1156–60.
 21. Waghmare AS, Vhanmane PB, Savitha B, Chawla RL, Bagde HS. Bacteremia following scaling and root planing: A clinico-microbiological study. *J Indian Soc Periodontol*. 2013; 17(6):725-30.
 22. Chaston RW. Serum anti-phosphorylcholine and anti-cardiolipin concentrations following periodontal scaling and root planing. Virginia Commonwealth University, Virginia. 2006.
 23. Su arez LJ, Garzon H, Arboleda S, Rodriguez A. Oral Dysbiosis and Autoimmunity: From Local Periodontal Responses to an Imbalanced Systemic Immunity. A Review. *Front Immunol*. 2020; 11. 591255.

(Received September 25, 2020; Accepted April 1, 2021)