

Evaluation of Salivary and Serum Levels of Alkaline Phosphatase and Acid Phosphatase in Chronic Periodontitis Patients before and after Scaling and Root Planing with or without Systemically Administered Doxycycline: A Comparative Study

Surbhi Sinny¹, R. Padma², Vivek Kumar², Rana Praween Kumar², Ayon Gupta², Dhananjay Kumar²

¹Private Practitioner and Consultant, Dhanbad, Jharkhand, India.

²Department of Periodontology, Awadh Dental College and Hospital, Jamshedpur, Jharkhand, India.

Abstract

Background: In oral diagnostics, there is a great challenge to determine biomarkers for screening and evaluating the disease activity. Biomarkers can also serve as a useful tool to measure the efficacy of the therapy. Hence, the aim of the present study is to determine the serum and salivary levels of alkaline phosphatase (ALP) and acid phosphatase (ACP) in patients diagnosed with chronic periodontitis before and after phase I therapy with or without adjunct to systemically administered doxycycline. **Materials and Methods:** 60 participants in the age range of 40 and 56 years reporting to the Outpatient Department of Periodontics who qualified for the inclusion criteria were included in this study. Clinical parameters recorded were plaque index (PI), gingival index (GI), sulcus bleeding index (SBI), probing pocket depth, and clinical attachment level. Saliva and serum samples were collected for the estimation of ALP and ACP. **Results:** The serum ALP levels reduced significantly when baseline values of Group A (109.20 ± 22.48) were compared to 3-month post-therapy of Group B (283.50 ± 34.68) and also 3-month post-therapy of Group C (186.75 ± 38.05). Salivary ALP levels also showed a significant difference when baseline values of Group A (132.25 ± 26.48) were compared to 3-month post-therapy of Group B (306.50 ± 47.60) and Group C (158.75 ± 30.25). A significant difference was also found with respect to serum and salivary ACP levels at 3-month post-therapy. **Conclusion:** Salivary diagnosis extends an easy, safe, economical, and non-invasive approach to disease detection and possesses a high perspective to reconstitute the next generation of diagnostics.

Keywords: Acid phosphatase, Alkaline phosphatase, Chronic periodontitis.

INTRODUCTION

Periodontal disease is an inflammatory lesion moderated by complex host-parasite interaction which leads to loss of connective tissue attachment and alveolar bone loss.^[1] If untreated, the disease progresses causing tooth mobility and subsequent tooth loss.^[2]

Conventional methods used to diagnose periodontal diseases are measurement of probing depth, attachment level, and assessment of bone loss using radiographs to diagnose the pathology only after the disease process has occurred. One can predict the disease risk by assessing the serum and salivary levels of certain compounds. Enzymes, immunoglobulins, hormones of host origin, and bacterial products are some of

the salivary constituents that are used for the estimation of the disease risk which have been termed as biomarkers.^[3]

Of the various enzymes that can be estimated for early diagnosis of periodontal disease, alkaline phosphatase (ALP), and acid phosphatase (ACP) are important as they play a

Address for correspondence: Dr. Vivek Kumar,
Department of Periodontology, Awadh Dental College and Hospital,
Jamshedpur, Jharkhand, India.
Email: drvivek1909@gmail.com

Received: May. 19, 2024; **Accepted:** Jun. 02, 2024; **Published:** Jun. 25, 2024

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online

Website:
www.jrad.co.in

DOI:
<https://doi.org/10.53064/jrad.2024.15.6.572>

How to cite this article: Sinny S, Padma R, Kumar V, Kumar RP, Gupta A, Kumar D. Evaluation of Salivary and Serum Levels of Alkaline Phosphatase and Acid Phosphatase in Chronic Periodontitis Patients before and after Scaling and Root Planing with or without Systemically Administered Doxycycline: A Comparative Study. J Res Adv Dent 2024;15(6):1-5.

crucial role.^[4] ALP, a membrane-bound glycoprotein produced by cells such as polymorphonuclear leukocytes, fibroblasts, macrophages, and osteoblasts is a hydrolyzing enzyme that removes the phosphate groups from various molecules and is a marker of bone metabolism.^[5]

ACP which is produced by desquamated epithelial cells, macrophages, and bacteria such as *Capnocytophaga*, *Veillonella*, and *Actinobacillus* is mainly correlated with the osteoclastic activity of bone metabolism.^[6,7]

A literature search has shown that various studies have assessed the salivary and serum levels of ALP^[8] and ACP^[9] and correlated the same with the clinical parameters.^[10] In adjunct to scaling and root planing (SRP), local and systemic antimicrobials are used to maintain long-term stability in patients with poor oral hygiene maintenance.^[11]

Tetracyclines are being used extensively in the treatment of periodontal disease as they are effective against rapidly multiplying bacteria.^[12] Doxycycline has an indistinct ability to reduce the degeneration of the collagen matrix by inhibiting the action of matrix metalloproteinases.^[13]

The current study was done to determine the serum and salivary levels of ALP and ACP in patients diagnosed with chronic periodontitis before and after phase I therapy with or without adjunct to systemically administered doxycycline.

MATERIALS AND METHODS

A total number of 60 participants in the age range of 40 and 56 years were chosen from the Outpatient Department of Periodontics and Implantology. The sample size was estimated using G* power 3.9.2 software and keeping the alpha error as 5% and the power of the study as 90%. Ethical clearance was obtained from the ethical committee of the institution.

The participants were divided into 3 groups (Groups A, B, and C). Group A which formed the control group comprised 20 periodontally healthy subjects. Groups B and C (test groups) comprised 20 subjects each of who were diagnosed with chronic generalized periodontitis.

Inclusion criteria for the control group were study participants with sulcus depth of ≤ 3 mm with no attachment loss and bleeding on probing present in $<20\%$ sites. The test group participants had to have a having a probing depth ≥ 5 mm and clinical attachment loss ≥ 5 mm in a minimum of two teeth of each quadrant and BOP in more than 30% of sites.

Written informed consent was obtained from all the individuals who participated in the study.

Clinical parameters were recorded at baseline in Group A and at baseline and 3-month post-therapy in Group B and Group C. The parameters assessed included plaque index (PI),^[14] gingival index (GI),^[15] sulcus bleeding index (SBI),^[16] probing depth (PD), and clinical attachment level (CAL). This was followed by saliva and blood sample collection. Saliva

samples were collected in the morning from 10 A.M. to 11 A.M. to standardize the collection according to the circadian rhythm.^[17] 5 mL of unstimulated saliva was collected in a sterile container and the same was transported to the laboratory immediately.

10 mL of blood sample was collected from the median cubital vein of each participant and transported to the laboratory immediately. The transported saliva and blood samples were centrifuged at 3000 rpm. for 5 min. Both salivary and serum ALP and ACP were analyzed by spectrophotometry using a semi-auto analyzer.

After the sample collection, all the participants received a detailed periodontal examination. In all the test group participants, SRP was performed using an ultrasonic scaler and hand instruments and chlorhexidine mouthrinse was prescribed twice daily for 1 month.

Patients in Group C were instructed to follow a systemic antibiotics regimen of 100 mg doxycycline twice a day on the 1st day, then once a day for 14 days.^[18] Clinical parameters and serum and salivary samples were recorded 3-month post-therapy.

Statistical analysis

The data were arranged in Microsoft Excel and analyzed with SPSS v.24 software. The variables have been expressed with mean and standard deviation. To assess the clinical parameters at baseline and 3-month post-operative, a paired t-test was applied. ALP and ACP levels in saliva and serum between the test groups at baseline and post-operative and with the control were assessed using one-way ANOVA.

RESULTS

On comparing the clinical parameters such as PI, GI, SBI, probing depth, and CAL of Group A with Group B and C, there was a significant difference showing a $P = 0.001$ at 3-month post-therapy (Table 1).

There is a significant improvement in PI, GI, SBI, probing depth, and gain in CAL when the baseline values of Group A were compared to 3-month post-therapy of Group B and C. When 3-month post-therapy values of Group B and C were compared, it showed a $P = 0.003$ which was found to be statistically significant (Table 2).

The serum ALP levels reduced significantly when baseline values of Group A (109.20 ± 22.48) were compared to 3-month post-therapy of Group B (283.50 ± 34.68) and also 3-month post-therapy of Group C (186.75 ± 38.05). Salivary ALP levels also showed that a significant difference when baseline values of Group A (132.25 ± 26.48) were compared to 3-months post-therapy of Group B (306.50 ± 47.60) and Group C (158.75 ± 30.25). Both Groups B and C also showed a significant difference in salivary and serum ALP levels when baseline values were compared to 3-month post-therapy. However, there was no significant difference when serum

and salivary levels of Group B were compared to Group C at 3-month post-therapy showing a $P = 0.109$ and 0.065 for serum and saliva, respectively (Table 3).

The serum ACP levels reduced significantly when baseline values of Group A (2.19 ± 0.34) were compared to 3-month post-therapy of Group B (3.04 ± 0.42) and also 3-month post-therapy of Group C (2.87 ± 0.35). Similarly, there is a significant difference when salivary ACP levels of Group A at baseline (2.54 ± 0.38) were compared to 3-month post-therapy of Group B (5.07 ± 0.29) and Group C (5.64 ± 0.28). Both serum and salivary ACP levels showed a significant difference when baseline values were compared to 3-month post-therapy in Group B and C. However, there was no significant difference when serum and salivary levels of Group B were compared

to Group C at 3-month post-therapy showing a $P = 0.139$ and 0.127 for serum and saliva, respectively (Table 4).

DISCUSSION

A periodontal diagnostic tool in general provides relevant information for differential diagnosis, localization of disease, and severity of infection. The diagnosis of an active phase of periodontal disease and recognition of patients at risk for active disease are challenges for clinicians.^[19]

Saliva could serve as a conducive vehicle to simultaneously evaluate multiple factors that predict the level of activity known to occur in the progression of periodontitis. Studies reveal an assuring outlook for saliva as a key diagnostic

Table 1: Comparing the clinical parameters such as PI, GI, SBI, PD, and CAL of Group A with Groups B and C

Groups	GI	PI	SBI	PD	CAL
Control (Group A)	0.23±0.19	0.47±0.24	1.15±0.36	2.55±0.51	0.00±0.00
Test group B					
Before phase I therapy	2.63±0.27	2.68±0.23	3.70±0.80	5.85±0.81	6.30±1.12
After phase I therapy	1.48±0.20	1.56±0.26	2.75±0.71	4.60±0.75	5.30±1.12
F-value	616.156	369.609	68.727	107.047	245.259
P-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Significance	HS	HS	HS	HS	HS
Test group C					
Before phase I therapy	2.67±0.22	2.76±0.17	4.00±0.79	5.75±0.78	6.40±0.94
After phase I therapy	0.48±0.16	0.70±0.36	1.85±0.97	3.39±0.94	4.15±1.03
F-value	959.126	393.432	97.931	87.523	326.711
P-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Significance	HS	HS	HS	HS	HS

PI: Plaque index, GI: Gingival index, SBI: Sulcus bleeding index, PD: Probing depth, CAL: Clinical attachment level

Table 2: Significant improvement in PI, GI, the SBI, PD, and gain in CAL when the baseline values of Group A were compared to 3-month post-therapy of Groups B and C

Group	GI	PI	SBI	PD	CAL	Significance
Group B (3 months post therapy)	1.48±0.20	1.56±0.26	2.75±0.71	4.60±0.75	5.30±1.12	0.003
Group C (3 months post therapy)	0.48±0.16	0.70±0.36	1.85±0.97	3.39±0.94	4.15±1.03	

PI: Plaque index, GI: Gingival index, SBI: Sulcus bleeding index, PD: Probing depth, CAL: Clinical attachment level

Table 3: The comparison of serum and salivary alkaline phosphatase levels of Group A compared to 3-month post-therapy of Group B and Group C

Groups	Serum alkaline phosphatase level			Salivary alkaline phosphatase level		
	Mean	SD	P-value	Mean	SD	P-value
Group A	109.20	22.48	<0.001 (H.S)	132.25	26.48	<0.001 (H.S)
Group B (after 3 months)	283.50	34.68		306.50	47.60	
Group A	109.20	22.48	<0.001 (H.S)	132.25	26.48	<0.001 (H.S)
Group C (after 3 months)	186.75	38.05		158.75	30.25	
Group B (baseline)	340.00	39.20	<0.001 (H.S)	420.00	39.06	<0.001 (H.S)
Group B (after 3 months)	283.50	34.68		306.50	47.60	
Group C (baseline)	314.00	23.03	<0.001 (H.S)	404.50	47.18	<0.001 (H.S)
Group C (after 3 months)	186.75	38.05		158.75	30.25	
Group B (after 3 months)	283.50	34.68	0.109 (N.S)	306.50	47.60	0.065 (N.S)
Group C (after 3 months)	186.75	38.05		158.75	30.25	

Table 4: The comparison of serum and salivary acid phosphatase levels of Group A compared to 3-month post-therapy of Group B and Group C

Groups	Serum acid phosphatase level			Salivary acid phosphatase level		
	Mean	SD	P-value	Mean	SD	P-value
Group A	2.19	0.34	<0.001 (H.S)	2.54	0.38	<0.001 (H.S)
Group B (After 3 months)	3.04	0.42		5.07	0.29	
Group A	2.19	0.35	<0.001 (H.S)	2.54	0.38	<0.001 (H.S)
Group C (After 3 months)	2.87	0.35		2.64	0.28	
Group B (Baseline)	3.39	0.45	<0.001 (H.S)	5.99	0.31	<0.001 (H.S)
Group B (After 3 months)	3.04	0.42		5.09	0.29	
Group C (Baseline)	3.54	0.44	<0.001 (H.S)	6.06	0.24	<0.001 (H.S)
Group C (After 3 months)	2.87	0.35		2.64	0.28	
Group B (After 3 months)	3.04	0.42	0.139 (N.S)	5.07	0.29	0.127 (N.S)
Group C (After 3 months)	2.87	0.35		2.64	0.28	

medium for determining systemic diseases of the health status of an individual.^[20,21] Highly enriched content of disease biomarkers that can be deciphered and analyzed, ease of collection, and surplus availability make saliva a key diagnostic medium.^[22] Salivary ALP takes part in the normal turnover of the periodontal ligament, alveolar bone, and root cementum formation.

ALP creates a pH favorable for hydroxyapatite crystal formation in the bone matrix. Their increased activity might be an aftermath of a destructive process in alveolar bone in the advanced stages of the development of periodontal disease.^[23] The potential value of ALP as a biomarker of periodontal disease was identified by Ishikawa and Cimasoni.^[24]

They showed a significant correlation between ALP concentration in gingival crevicular fluid and pocket depth. Our study showed a significant increase in the serum and salivary ALP levels in chronic generalized periodontitis patients. Following phase I therapy, there was a significant reduction in the serum and salivary levels which is in accordance with the study by Dabra and Singh.^[25]

ACP is among the enzymes associated with bone metabolism. It is present in neutrophils and is considered a lysosomal marker. Our study showed us a statistically significant increase in the activity of ACP in patients with chronic periodontitis when compared to healthy subjects. Similar results were reported by Todorovic *et al.*^[26]

Contrary to our study Zombon *et al.*^[27] reported no change in the levels of ACP activity when pretreatment levels were compared to its posttreatment.

The results of our study reveal a promising outlook for saliva as a key diagnostic medium as it provides sensitivity and specificity for discriminating periodontitis from health and also identifying those individuals who might be at risk for continued chronic inflammation.^[28,29] Some bacteria are inclined to get away from the host defenses after non-surgical periodontal therapy due to restricted means of entry to the root surfaces in addition to the tissue-invading capacity of the pathogens.^[30,31] A

variety of antibiotics have been tried to battle these phenomena. Systemic doxycycline has been tried as an adjunct to SRP.^[32,33]

Similar results were found by Akincibay *et al.* and Baltacioglu *et al.* They evaluated the effect of systemic doxycycline in patients with aggressive periodontitis after SRP and found that the use of doxycycline is superior to SRP alone.^[34,35]

Contrary to our study Grellmann *et al.* showed that the use of doxycycline did not significantly improve probing depths.^[36] The results of our study have shown significant improvement in the clinical parameters when doxycycline was used as an adjunct to SRP. This was in accordance with the results shown by Eickholz^[37] and Hagh.^[38]

CONCLUSION

Saliva, like blood, contains a myriad of protein and nucleic acid molecules that reflect physiological status. Unlike other body fluids, salivary diagnosis extends an easy, safe, economical, and non-invasive approach to disease detection and possesses a high perspective to reconstitute the next generation of diagnostics.

Although the future of periodontal disease diagnosis using salivary diagnostics looks promising, hurdles to these approaches may unfold in the clinical setting. Endorsement of novel periodontal diagnostics will need to be benchmarked with existing “gold standard” of diseases such as alveolar bone levels and CAL in large patient populations.

Systemic antibiotics as a complementary therapy in addition to scaling and root planing in patients with severely affected sites by periodontitis improve the clinical results further thereby decreasing the need for surgical periodontal therapy.

REFERENCES

1. Fiyaz M, Ramesh A, Ramalingam K, Thomas B, Shetty S, Prakash P. Association of salivary calcium, phosphate, pH and flow rate on oral health: A study on 90 subjects. *J Indian Soc Periodontol* 2013;17:454-60.
2. Offenbacher S. Periodontal diseases: Pathogenesis. *Ann Periodontol* 1996;1:821-78.
3. Hulka BS. Overview of biological markers. In: Hulka BS, Griffith JD,

- Wilcosky TC, editors. Biological markers in epidemiology. New York: Oxford University Press; 1990. p. 3-15.
4. Koppolu P, Sirisha S, Mishra A, Deshpande K, Lingam AS, Alotaibi DH, *et al.* Alkaline phosphatase and acid phosphatase levels in saliva and serum of patients with healthy periodontium, gingivitis, and periodontitis before and after scaling with root planing: A clinico-biochemical study. *Saudi J Biol Sci* 2021;28:380-5.
 5. Chapple IL, Garner I, Saxby MS, Moscrop H, Matthews JB. Prediction and diagnosis of attachment loss by enhanced chemiluminescent assay of crevicular fluid alkaline phosphatase levels. *J Clin Periodontol* 1999;26:190-8.
 6. Desai S, Shinde H, Mudda JA, Patil V. Levels of alkaline phosphatase (ALP) in saliva of patients with chronic periodontitis; a clinical and biochemical study. *Internet J Dent Sci* 2008;8:1.
 7. Sanikop S, Patil S, Agrawal P. Gingival crevicular fluid alkaline phosphatase as a potential diagnostic marker of periodontal disease. *J Indian Soc Periodontol* 2012;16:513-8.
 8. Kunjappu JJ, Mathew VB, Hegde S, Kashyap R, Hosadurga R. Assessment of the alkaline phosphatase level in gingival crevicular fluid, as a biomarker to evaluate the effect of scaling and root planing on chronic periodontitis: An *in vivo* study. *J Oral Maxillofac Pathol* 2012;16:54-7.
 9. Hue AC, Burrill DY, Fosdick LS. Correlation of blood constituents with periodontal disease acid and alkaline phosphatase. *J Periodontol* 1961;32:35-7.
 10. Lang NP. Indications and rationale for non-surgical periodontal therapy. *Int Dent J* 1983;33:127-36.
 11. Cattabriga M, Pedrazzoli V, Cattabriga A, Pannuti E, Trapani M, Verrocchi GC. Tetracycline fiber used alone or with scaling and root planing in periodontal maintenance patients: Clinical results. *Quintessence Int* 1996;27:395-400.
 12. Christersson LA, Norderyd OM, Puchalsky CS. Topical application of tetracycline-HCl in human periodontitis. *J Clin Periodontol* 1993;20:88-95.
 13. Tripathi KD. *Essentials of Pharmacology for Dentistry*. New Delhi: Jaypee Brothers; 2011. p. 378.
 14. Loe H. The Gingival Index, the plaque index and the retention index systems. *J Periodontol* 1967;38:1610-6.
 15. Turesky S, Gilmore ND, Glickman I. Reduced plaque formation by the chloromethyl analogue of vitamin C. *J Periodontol* 1970;41:41-3.
 16. Mühlemann HR, Son S. Gingival sulcus bleeding--a leading symptom in initial gingivitis. *Helv Odontol Acta* 1971;15:107-13.
 17. Navazesh M. Methods for collecting saliva. *Ann N Y Acad Sci* 1993;694:72-7.
 18. Akalin FA, Baltacıoğlu E, Sengün D, Hekimoğlu S, Taşkin M, Etikan I, *et al.* A comparative evaluation of the clinical effects of systemic and local doxycycline in the treatment of chronic periodontitis. *J Oral Sci* 2004;46:25-35.
 19. Reddy MS, Geurs NC, Jeffcoat RL, Proskin H, Jeffcoat MK. Periodontal disease progression. *J Periodontol* 2000;71:1583-90.
 20. Amritage GC. Periodontal diseases: Diagnosis. *Ann Periodontol* 1996;1:37-215.
 21. Burt B, Research, Science and Therapy Committee of the American Academy of Periodontology. Position paper: Epidemiology of periodontal disease. *J Periodontol* 2005;76:1406-19.
 22. Wong DT. Salivary diagnostic for oral cancer. *J Colip Den Assoc* 2006;34:303-8.
 23. Sophia K, Suresh S, Sudhakar U, Jayakumar P, Mathew D. Salivary alkaline phosphatase level in post menopausal women. *J Clin Diagn Res* 2017;11:122-4.
 24. Ishikawa I, Cimasoni G. Alkaline phosphatase in human gingival fluid and its relation to periodontitis. *Arch Oral Biol* 1970;15:1401-4.
 25. Dabra S, Singh P. Evaluating the levels of salivary alkaline and acid phosphatase activities as biochemical markers for periodontal disease: A case series. *Dent Res J (Isfahan)* 2012;9:41-5.
 26. Todorovic T, Dozic I, Vicente-Barrero M, Ljuskovic B, Pejovic J, Marjanovic M, *et al.* Salivary enzymes and periodontal disease. *Med Oral Patol Oral Cir Bucal* 2006;11:E115-9.
 27. Zombon JJ, Nakopmura M, Slots J. Effect of periodontal therapy on salivary enzyme activity. *J Periodontal Res* 1985;26:652-9.
 28. Morrison EC, Ramfjord SP, Hill RW. Short-term effects of initial, nonsurgical periodontal treatment (hygienic phase). *J Clin Periodontol* 1980;7:199-211.
 29. Ehmke B, Moter A, Beikler T, Milian E, Flemmig TF. Adjunctive antimicrobial therapy of periodontitis: Long-term effects on disease progression and oral colonization. *J Periodontol* 2005;76:749-59.
 30. Tsalikis L, Sakellari D, Dagalis P, Boura P, Konstantinidis A. Effects of doxycycline on clinical, microbiological and immunological parameters in well-controlled diabetes type-2 patients with periodontal disease: A randomized, controlled clinical trial. *J Clin Periodontol* 2014;41:972-80.
 31. Socransky SS, Haffajee AD. Periodontal microbial ecology. *Periodontol* 2000 2005;38:135-87.
 32. Herrera D, Alonso B, León R, Roldán S, Sanz M. Antimicrobial therapy in periodontitis: The use of systemic antimicrobials against the subgingival biofilm. *J Periodontol* 2008;35:45-66.
 33. Ramfjord SP, Caffesse RG, Morrison EC, Hill RW, Kerry GJ, Appleberry EA, *et al.* 4 modalities of periodontal treatment compared over 5 years. *J Clin Periodontol* 1987;14:445-52.
 34. Akincibay H, Orsal SO, Sengün D, Tözüm TF. Systemic administration of doxycycline versus metronidazole plus amoxicillin in the treatment of localized aggressive periodontitis: A clinical and microbiologic study. *Quintessence Int* 2008;39:e33-9.
 35. Baltacıoğlu E, Aslan M, Saraç Ö, Saybak A, Yuva P. Analysis of clinical results of systemic antimicrobials combined with nonsurgical periodontal treatment for generalized aggressive periodontitis: A pilot study. *J Can Dent Assoc* 2011;77:b97.
 36. Grellmann AP, Sfreddo CS, Maier J, Lenzi TL, Zanatta FB. Systemic antimicrobials adjunct to periodontal therapy in diabetic subjects: A meta-analysis. *J Clin Periodontol* 2016;43:250-60.
 37. Eickholz P. Systemic doxycycline and nonsurgical periodontal treatment in diabetic patients. *Evid Based Dent* 2007;8:14.
 38. Hagh GL. Clinical effect of scaling and root planning with or without doxycycline in type 2 diabetic patients with chronic periodontitis. *Jundishapur Med J* 2010;9:149-56.