

**Original Research**

## Clinical and Metabolic changes after the Non- surgical Periodontal Therapy in patients with Type-2 Diabetes Mellitus with Chronic periodontitis with or without the Systemic administration of Azithromycin - A Randomized Controlled Clinical Trial

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**Abstract**

**Background & Objectives:** *There is growing evidence that periodontitis may affect general health. Periodontal disease is now recognized as the sixth complication of diabetes. It has been suggested that an alteration in glucose metabolism occurs as a result of antibacterial periodontal therapy. The present study is aimed to evaluate the clinical and metabolic changes in type-2 diabetic patients with chronic periodontitis after non-surgical periodontal therapy with or without the systemic administration of azithromycin.*

**Method:** *In our study 24 patients with type-2 diabetes having chronic periodontitis were included. Group I included 12 patients who underwent scaling and root planing (SRP) only and group II 12 patients who underwent SRP with concomitant systemic administration of azithromycin 500mg once daily for 3 days. At baseline, plaque index (PI), gingival index (GI), probing depths (PD) were recorded and glycated haemoglobin (HbA1c) levels were evaluated. Patients were followed for 30-90 days.*

**Results:** *The mean decrease in glycosylated hemoglobin (HbA1c) was  $0.18 \pm 0.5$  after nonsurgical periodontal treatment in group I on comparing the baseline ( $8.98 \pm 0.99$ ) and final values ( $8.8 \pm 1.10$ ), and in group II was  $1.18 \pm 0.47$  on comparing the baseline ( $9.01 \pm 1.18$ ) and final values ( $3.36 \pm 1.87$ ) proved statistically significant ( $P \leq 0.05$ ).*

**Conclusion:** *A decrease in HbA1c was observed in group II (SRP+Azithromycin 500mg once daily 3 days) thus indicating improved blood glucose control in Type 2 diabetics with periodontal disease compared to group I (SRP only).*

**Keywords:** *Non-surgical therapy; Haemoglobin A1c; Diabetes Mellitus; Chronic Periodontitis; Periodontal Disease; Antibiotics; Azithromycin; Diabetes Mellitus.*

**Introduction**

Periodontitis is a multifactorial disease that is associated with loss of the supporting tissues (i.e., periodontal ligament and alveolar bone) around the tooth. A major objective of periodontal therapy is to

remove soft and hard, supra and sub gingival deposits from the root surface to stop disease progression. Mechanical scaling and root debridement have shown to be an effective treatment approach for periodontal disease.<sup>1</sup>

Diabetes mellitus and periodontal disease are two highly prevalent chronic disorders. The inter relationship between periodontal disease and diabetes mellitus provides an example of a cyclical association whereby a systemic disease predisposes the individual to oral infections, and, once the oral infection is established, it exacerbates the systemic disease.<sup>2</sup> Intervention trials<sup>3</sup> have assessed the potential effects of periodontal therapy on glycemic control in subjects with diabetes and found a marked improvement in glycemic control in type 2 diabetic patients following periodontal therapy.

Measurement of hemoglobin A1C is of major clinical value as per the recent ADA guidelines and accurately reflects the mean blood glucose concentration over the preceding 1–3 months. Strauss *et al.*<sup>4</sup> in a pilot study examined whether a novel diabetes screening approach using gingival crevicular blood (GCB) could be used to test for hemoglobin A1c (HbA1c) during periodontal visits. Over the years, numerous trials<sup>5</sup> have sufficiently documented the benefits of adjuvant administration of antibiotics in combination to SRP. Azithromycin possesses good oral absorption and is characterised by extremely good resilience toward gastric acids. It is an interesting drug which has a similar spectrum of activity to erythromycin. It possesses high effectiveness toward gram-negative bacteria and *Aggregatibacter actinomycetemcomitans* in particular.<sup>6</sup> It is concentrated in fibroblasts and phagocytes and is transported to areas of inflammation as a result of chemotactic effects exerted on the phagocytes thus targeting the drug at those sites.

Tissue concentrations greatly exceed the concomitant serum levels by 10–100 folds. In addition tissue release is slow leading to prolonged excretion with azithromycin still detectable in the tonsils for over a week after a single 500 mg dose although it is more commonly given as a once a day 500mg dose for 3–5 days. Thus the present study is aimed to evaluate the clinical and metabolic changes in type-2 diabetic patients with chronic periodontitis after non-surgical periodontal therapy

with or without the systemic administration of azithromycin.

### Materials and Method

The present triple blinded randomized controlled trial was carried out at a single center. The subjects were enrolled for the study from April 2016 to March 2017. All subjects were given information about the study, and oral and written informed consent was obtained from all participants prior to study. The patients for this study were selected from outpatient section. Ethical committee of the institution approved the study. Twenty four patients diagnosed with type 2 diabetes mellitus and chronic periodontal disease were included in the study those who visited the outpatient department of periodontics.

### Inclusion criteria

- Patients with type 2 DM  $\geq$  5 years
- No major diabetic complications
- No history of systemic antibiotic administration within the last 3 months
- No periodontal treatment 6 months prior to the study
- At least one site  $>$ 5mm and two sites with attachment loss  $>$ 6mm
- Signed informed consent

### Exclusion Criteria

- Pregnant or lactating females
- Deleterious habits like smoking/alcohol/tobacco consumption
- Use of antibiotics within 6 months prior to the study
- Active periodontal treatment within last 6 months
- Other Systemic disease
- Insulin utilization.

### Screening and Examinations

A total of 55 patients were screened out of which 24 patients with the age group of 24-55 years (15 males & 9 females) were enrolled in the clinical trial. The following clinical parameters including Plaque index (PI)<sup>7</sup>, Gingival index (GI)<sup>8</sup>, Probing Depths (PD), were recorded at Baseline, for 30-90 days. All

measurements were performed by one experienced periodontal examiner, allowing an intra-experimental comparison of the values. Percentage agreement with another examiner within 1mm was > 96%. The reading was recorded to the nearest millimeter.

EDTA Blood samples were collected under aseptic precautions at baseline 30-90 days after the periodontal therapy to monitor the glycated haemoglobin which was tested by ion exchange chromatography method.

### Randomization

After baseline examination, a simple randomization approach<sup>9</sup> using computer-generated random numbers was employed to assign patients into two groups (the sequence was concealed until interventions were assigned) to one of the following treatment modalities:

**Group I:** Scaling and root planing (SRP) only.

**Group II:** SRP & systemic administration of Azithromycin 500mg (Tab. Azivent 500mg) once daily for 3 days.

### Periodontal & adjunctive treatments

A specific treatment protocol was designed to manage the periodontal disease associated with type 2 diabetes mellitus. The subjects were divided into two groups. Group I underwent a scaling and root planing and Group II underwent scaling and root planing along with the systemic administration of azithromycin 500mg once daily for 3 days. All

patients received routine oral hygiene instructions & one-stage full-mouth conventional scaling and root planing (SRP) employing both hand instruments (Hu-Friedy, USA) & a piezoelectric ultrasonic hand piece (EMS) under local anaesthesia of 2% lidocaine with 1:80000 adrenaline (Lignox 2% A; Indoco Remedies Ltd, L-32,Goa). Group II patients were prescribed with azithromycin 500mg (Tab. Azivent 500mg) once a day for 3 days. Patients were asked to maintain same diet and medications for the diabetes.

### Statistical Analysis

The data were analyzed using the SPSS -software 19.00 program (SPSS Inc., Chicago, IL, USA). One-way ANCOVA (analysis of covariance) was done to determine significant differences between the two groups. Differences were considered as statistically significant at  $p < 0.005^*$ .

### Results

Significant reduction in plaque index (PI) was seen in group II (74.44 %<sup>\*</sup>) compared to group I (63.59 %<sup>\*</sup>) (Table 1). Significant reduction in gingival index (GI) was seen in group II (68.83 %<sup>\*</sup>) compared to group I (60.98 %<sup>\*</sup>) (Table 2). Mean reduction in probing depth (PD) in group II was  $2.45 \pm 0.82$  and in group I  $2.09 \pm 0.54$  was found to be statistically significant ( $P < 0.05$ ) in group II (Table 3). There was greater % of HbA1c reduction in group II at the end of 0 days compared to group I (Table 4).

**Table 1:** Mean, standard deviation (SD) and percentage reduction at baseline and after 30-60 days for plaque index (PI) for each group

Variance	Groups	Before		After		Gain (difference)	
		Mean	SD	Mean	SD	Mean	SD
PI-INDEX	I	2.07	0.48	0.75	0.17	1.1318	0.4708
	II	2.02	0.44	0.51	0.24	1.509	0.3448
	% of reduction in I					63.59% <sup>*</sup>	
	% of reduction in II					74.44% <sup>*</sup>	
	F -value	0.0529 <sup>+</sup>		7.5953 <sup>#</sup>			
	P- value	0.8218		0.01256 <sup>*</sup>			

<sup>\*</sup>P < 0.05, <sup>+</sup>indicates one way ANOVA, <sup>#</sup>indicates analysis of covariations by baseline values on covariate (ANCOVA)

**Table 2:** Mean, standard deviation (SD) and percentage reduction at baseline and after 30-60 days for gingival index(GI) for each group

Variance	Groups	Before		After		Gain (difference)	
		Mean	SD	Mean	SD	Mean	SD
GI-INDEX	I	2.21	0.40	0.88	0.21	1.3273	0.3844
	II	2.10	0.43	0.65	0.24	1.4455	0.3205
	% of reduction in I					60.98%*	
	% of reduction in II					68.83%*	
	F -value	0.3510 <sup>+</sup>		5.7948 <sup>#</sup>			
	P- value	0.5660		0.2026*			

\*P <0.05, <sup>+</sup>indicates one way ANOVA, <sup>#</sup>indicates analysis of covariations by baseline values on covariate (ANCOVA)

**Table 3:** Mean, standard deviation(SD) and percentage reduction at baseline and after 30-60 days for probing depth (PD) for each group

Variance	Groups	Before		After		Gain (difference)	
		Mean	SD	Mean	SD	Mean	SD
PD-DEPTH	I	6.27	1.10	4.18	1.902	2.09	0.54
	II	5.82	1.17	3.36	0.50	2.45	0.82
	% of reduction in I					33.33%*	
	% of reduction in II					42%*	
	F -value	0.8803 <sup>+</sup>		5.7812 <sup>#</sup>			
	P- value	0.3593		0.0265*			

\*P <0.05, <sup>+</sup>indicates one way ANOVA, <sup>#</sup>indicates analysis of covariations by baseline values on covariate (ANCOVA).

**Table 4:** Mean, standard deviation (SD) and percentage reduction at baseline and after 30-60 days for glycated hemoglobin (HbA1c) for each group

Variance	Groups	Before		After		Gain (difference)	
		Mean	SD	Mean	SD	Mean	SD
HbA1c	I	8.98	0.99	8.8	1.10	0.18	0.5
	II	9.01	1.18	3.36	1.87	1.18	0.47
	% of reduction in I					2%	
	% of reduction in II					13%*	
	F -value	0.0034 <sup>+</sup>		25.9295 <sup>#</sup>			
	P- value	0.9539		0.0006*			

\*P <0.05, <sup>+</sup>indicates one way ANOVA, <sup>#</sup>indicates analysis of covariations by baseline values on covariate (ANCOVA).

## Discussion

In view of the growing number of people with unrecognized diabetes and the increased risk for diabetes among periodontal patients, diabetes screening at the time of the dental visit is a promising public health opportunity. The present study there was significant improvement in PI, GI, PD and HbA1c in both the groups but there was significant improvement in group II when compared to group I. In a randomized double-blind placebo-controlled parallel-designed studies by Emingil et al.<sup>10</sup> Gomi et al.<sup>11</sup>, Oteo et al.<sup>12</sup>, Smith et al.<sup>13</sup>, SRP + Azithromycin (Test group) (500 mg, 3 days) SRP + Placebo (Control) (3 days), all clinical parameters

(PD, CAL, PI, BOP) improved over 30-60days period similar to our study group II showed significant improvement in all the parameters compared to group I at the end 30-90 days.

A recent systemic review and meta-analysis by Antonio Renatus<sup>5</sup> concluded use of AZM as an adjuvant to SRP for generalized chronic periodontitis improves clinical and microbiological findings compared to SRP therapy alone. In our study also there was improvement in clinical parameters (PI, GI, and PD) in group II over 30-90days period and there was greater % of HbA1c reduction when compared to group I but there was no statistical difference between both the groups.

In are view Taylor<sup>14</sup> examined the body of evidence and concluded that there may be an effect of periodontal treatment on glycaemic control in Type 2 DM. In another review, Grossi & Genco<sup>15</sup> identified eight studies and reported that the three studies combining antimicrobial therapy with mechanical periodontal debridement all showed an improvement in metabolic control.

Limitations of the study include the manner in which SRP is performed. The variations refer to the number of treatment sessions (1-6 sessions) and also the intervals between the individual appointments (1-4 weeks). On the other hand there exist clear limitations regarding different study designs and composition of the investigated population between the studies. Moreover it has to be mentioned that there is no generally accepted definition of periodontal disease and examination.

### Conclusion

A decrease in HbA1c was observed in group II (SRP+Azithromycin 500mg once daily for 3 days) thus indicating improved blood glucose control in Type 2 diabetics with periodontal disease compared to group I (SRP only). Use of Azithromycin as an adjuvant to SRP for generalized chronic periodontitis improves clinical and improved blood glucose control in Type 2 diabetics compared to SRP therapy alone. Further studies regarding the adjunctive use of AZM in patients with aggressive periodontitis are needed.

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