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Evaluation of Glycosylated Hemoglobin Level in Patients with Chronic Periodontitis

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ABSTRACT: Diabetes and periodontal disease have an established two way relation. Glycosylated hemoglobin (HbA1c) is a time tested method for estimating glycemic control in diabetic patients. Some studies have also shown an increase in HbA1c level in patients with who are not diabetic but have chronic periodontitis.

AIM: To evaluate glycosylated hemoglobin level in systemically healthy individuals with chronic periodontitis.

40 patients fulfilling the inclusive and exclusive criteria were selected from the OPD of a dental college and divided into

The patients were divided into 4 groups

Group A: Diabetics patients with chronic periodontitis (according to AAP International Workshop for Classification of Periodontal Disease, 1999.)

Group B: Non –diabetic patients with chronic periodontitis (according to AAP International Workshop for Classification of Periodontal Disease, 1999.)

Group C: Diabetics patients without chronic periodontitis

Group D: Heathy Individuals

A detailed case history was recorded. Clinical parameters such as Plaque index (Silness And Loe 1964), Gingival index (Loe and Silness1963), Russell Periodontal Index 1956 and Pocket Probing Depth (PPD) were recorded. Blood samples of the patient were taken and sent to the pathology lab for HbA1c test. ADA's diagnostic criteria used for the diagnosis of type 2 diabetes based on HbA1c values. The values were estimated by turbid metric inhibition immunoassay (TINIA).

Result:PI,GI,PPD and Russell Periodontal Index were higher in group A and group B. here was statistically significant difference between Group B and Group C ($p<0.001$) as well as Group B and Group D ($p<0.001$) There was statistically significant difference between Group C and Group D with ($p<0.001$).

CONCLUSION:From this current study, it was observed that glycated hemoglobin levels for non-diabetic patients with chronic periodontitis were close to pre-diabetic levels. More studies need to be conducted to assess if Hba1c can be identified as a risk indicator for not only diabetes but for chronic periodontitis

Keywords: glycated hemoglobin, periodontitis, two-way relationship, diabetes mellitus

I. INTRODUCTION

Many bodily disturbance are first observed in the oral cavity. Systemic diseases like diabetes mellitus, chronic obstructive pulmonary disease, acute bacterial pneumonia, obesity etc, alter host tissues and physiology, which may impair the host's barrier function and immune defense against periodontal pathogens, thereby creating the opportunity for destructive periodontal diseases to progress. Diabetes mellitus is a metabolic disorder due to dysfunctional insulin regulation [1]. It can be classified as type I (insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes")and typeII non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes", [2]. Type 1 is due to insufficient production of insulin in the Langerhans in the pancreas whereas type II due defective uptake of insulin by the body.

In 1996, during the world workshop in periodontics, the concept of periodontal medicine was proposed by Offenbacher as a rapidly emerging branch of periodontology focusing on the wealth of new data establishing a strong

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relationship between periodontal health or disease and systemic health or disease. Various cross – sectional and longitudinal study in the 1990s investigating PIMA Indian population established the importance of diabetes as a major risk factor for periodontitis.[3,7]In the early 1990s, periodontitis was recognized to be the 'sixth complication of diabetes by the American diabetic association [4] establishing its two way relationship. [6]

In 1950, Ray and Orban observed that the degeneration of tissues and the presence of calcified bodies in and around small blood vessels of the gingiva are cause of the basic structural changes in the diabetic periodontium.[15] Decreased level of cyclic Adenosine Monophosphate [16] , impairment of PolyMorphonuclear Neutrophil chemotaxis[17] ,decreased antibody productionand presence of lipid deposits causing vascular insufficiency in small blood vessels , as well as, prostaglandin E2 hyper secretory response to lipopolysaccharides in monocytes ;[18] and impaired production of bone matrix component by osteoblasts, decreased collagen synthesis by gingiva and periodontal ligament fibroblasts, and increased collagenase activity[19] were observed to be diabetes associated factors which increase the severity of periodontitis.

On the other hand, Periodontitis could have a negative effect on glycemic control as well.Chronic gram-negative periodontal infections may result in increased insulin resistance and poor glycemic control[20].In periodontitis, the core immuno-inflammatory dysregulation shows an impairment of glycemic control due the increase in cytokine level.

Glycated hemoglobin (glycohemoglobin, HbA1c, hemoglobin A1C, A1C, or less commonly HbA1c, HgbA1c, Hb1c, etc.) is a form of hemoglobin (Hb) that is chemically linked to sugar. When glucose binds to hemoglobin it formsglycosylated hemoglobin and this tested to monitor the long-term control of diabetes mellitus. Glycated hemoglobin causes an increase of highly reactive free radicals inside blood cells. Radicals alter blood cell membrane properties. This leads to blood cell aggregation and increased blood viscosity, which results in impaired blood flow [8]. It has been that the risk as well as the severity of periodontitis in diabetic patients increases with the elevated hba1c level.[9, 19,] Of late some studies have shown that glycated hemoglobin level increasein chronic inflammatory condition like chronic periodontitis even in individual not suffering from diabetics. Hence the current study aimed at studythe association between periodontitis and glycated hemoglobin

II. MATERIALS AND METHOD:

40 patients above the age of 25 years fulfilling the inclusive and exclusive criteria were selected from the OPD of a dental college in Maharashtra.

Inclusion criteria:

1) Patients with mild to moderate chronic periodontitisas proposed by American Academy of Periodontology (AAP) 1999
2) Patients with no history of use of antibiotics and anti-inflammatory therapy in the past 6 months.
3) Patients with no history of use of oral antiseptics or mouthwashes in the past 6 months.
4) Patients willing to participate in the study.

Exclusion criteria

1) Patients with any habit like history of tobacco use insmoked or smokeless form
2) Patients who have undergone any periodontal therapy inthe past 6 months.
3) Patients with any history of drugs, alcohol or substance abuse

The patients were informed about the study and their writtenconsent was taken.

The patients were divided into 4 groups

Group A: type IIDiabetics patients with chronic periodontitis

Group B: Non –diabetic patients with chronic periodontitis

Group C: type IIDiabetics patients without chronic periodontitis

Group D: Heathy Individuals

A detailed case history was recorded. Clinical parameters such as Plaque index (Sinless And Loe 1964), Gingival index (Loe and Silness1963), Russell Periodontal Index 1956 and Pocket Probing Depth (PPD) were recorded. Blood samples of the subject were taken and sent to the pathology lab for HbA1cestimation. The values were estimated by turbid metric inhibition immunoassay (TINIA).

	Normal glucose tolerance	Prediabetes	Type 2 diabetes
HbA1c	≤5.7% (39 mmol/mol)	5.7%-6.4% (39-46 mmol/mol)	≥6.5% (48 mmol/mol)

ADA = American Diabetes Association.

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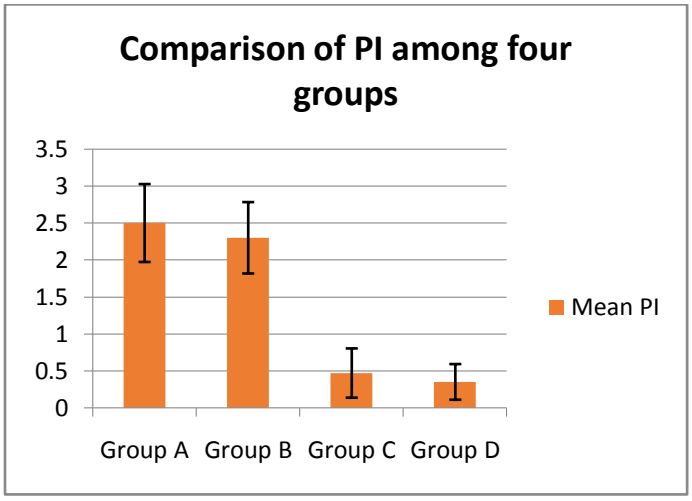
Statistical Data Analysis:
All the data were entered into Microsoft Excel 2010. Descriptive statistics for all five parameters were expressed as mean ± standard deviation (SD) for each group. Four groups (Group A Group B Group C and Group D) were compared for five parameters by Analysis of variance (ANOVA) followed by Tukey's Post hoc Test for pairwise comparison.
Simple/Multiple bar chart were used for graphical representation.
All the above test 'p' value was considered statistically significant when it was <0.05. The software used was SPSS (Statistical Package for Social Sciences) version 19.

III. RESULTS:

Comparison of PI among four groups by Analysis of variance followed by intergroup comparison by Tukey's post hoc test.

ANOVA p <0.001*

	Group A (2.500±.5270)	**Group B** (2.300±.4830)	**Group C** (.470 ± .3335)	**Group D** (.350 ± .2415)
Group A **(2.500±.5270)**	-	-	-	-
Group B **(2.300±.4830)**	**.701**	-	-	-
Group C **(.470 ± .3335)**	**<0.001***	**<0.001***	-	-
Group D **(.350 ± .2415)**	**<0.001***	**<0.001***	**0.915**	-



- There was statistically significant difference among four groups for Plaque Index.
- Intergroup comparison showed that there was statistically significant difference between Group A and Group C (p<0.001) as well as Group A and Group D (p<0.001) However; The difference between group A and Group B with p=0.701 were statistically insignificant
- Intergroup comparison showed that there was statistically significant difference between Group B and Group C (p<0.001) as well as Group B and Group D (p<0.001). However, the difference between Group C and Group D with p=0.901were statistically insignificant

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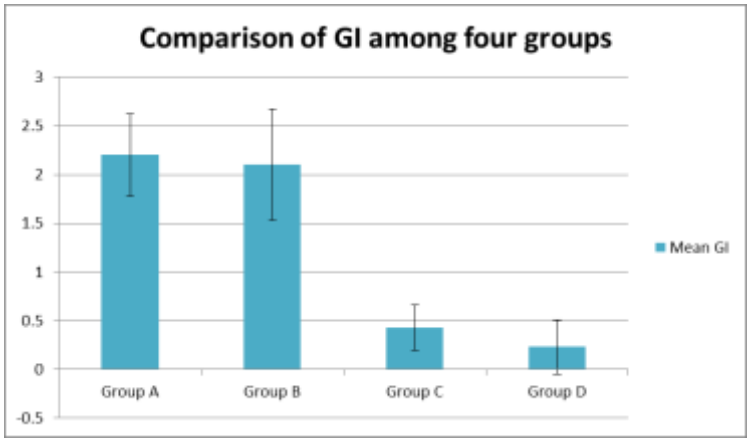
Comparison of GI among four groups by Analysis of variance followed by intergroup comparison by Tukey's post hoc test

ANOVA p <0.001*

	Group A (2.200 ±..4216)	**Group B** (2.100±..5676)	**Group C** (.430 ± .2312)	**Group D** (.230 ± .2791)
Group A (2.200 ±..4216)	-	-	-	-
Group B (2.100±..5676)	**0.942**	-	-	-
Group C (.430 ± .2312)	**<0.001***	**<0.001***	-	-
Group D (.230 ± .2791)	**<0.001***	**<0.001***	**0.676**	-



- There was statistically significant difference among four groups for **Gingival Index.**
- Intergroup comparison showed that there was statistically significant difference between Group A and Group C (p<0.001) as well as Group A and Group D (p<0.001) However; The difference between group A and Group B with p=0.942 were statistically insignificant
- Intergroup comparison showed that there was statistically significant difference between Group B and Group C (p<0.001) as well as Group B and Group D (p<0.001) However; the difference between Group C and Group D with p=0.676942 were statistically insignificant

Comparison of PPD among four groups by Analysis of variance followed by intergroup comparison by Tukey's post hoc test

ANOVA p <0.001*

	Group A (6.500 ± .8498)	**Group B** (6.500 ± .5270)	**Group C** (2.400 ± .5164)	**Group D** (2.500 ± .5270)
Group A (6.500 ± .8498)	-	-	-	-

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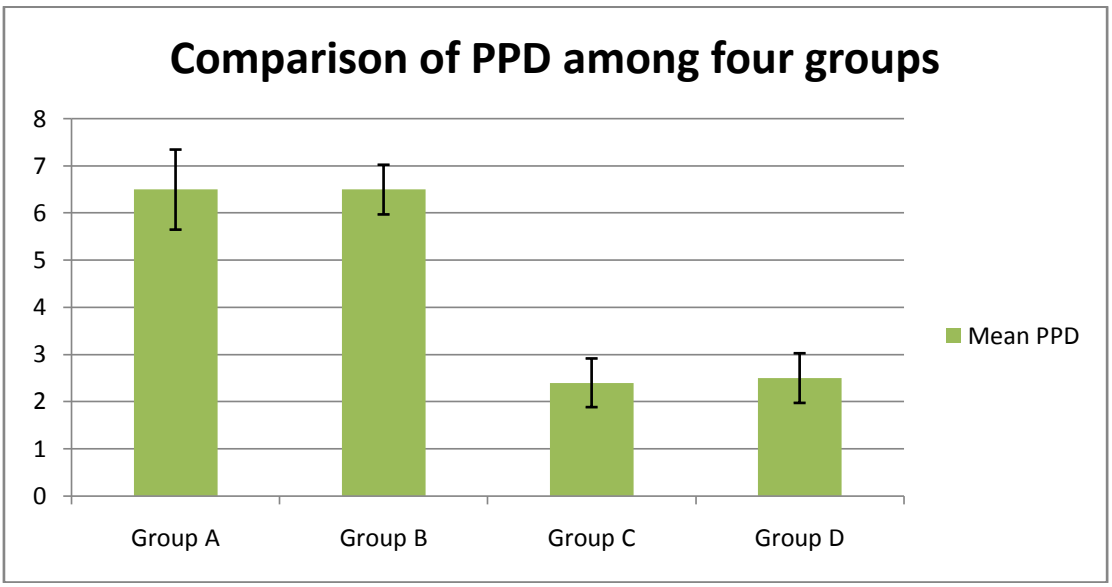
Group B (6.500 ± .5270)	1.000	-	-	-
Group C (2.400 ± .5164)	**<0.001***	**<0.001***	-	-
Group D (2.500 ± .5270)	**<0.001***	**<0.001***	**0.984**	-



- There was statistically significant difference among four groups for **PPD.**
- Intergroup comparison showed that there was statistically significant difference between Group A and Group C (p<0.001) as well as Group A and Group D (p<0.001) However; The difference between group A and Group B with p=1.000 942 were statistically insignificant
- Intergroup comparison showed that there was statistically significant difference between Group B and Group C (p<0.001) as well as Group B and Group D (p<0.001) However; The difference between Group C and Group D with p=0.984 942 were statistically insignificant

Comparison of RPI among four groups by Analysis of variance followed by intergroup comparison by Tukey's post hoc test

ANOVA p <0.001*				
	Group A (5.430 ± .4498)	**Group B** (5.170 ± .3561)	**Group C** (.440 ± .2319)	**Group D** (.150 ± .0707)
Group A (5.430 ± .4498)	-	-	-	-
Group B (5.170 ± .3561)	.260	-	-	-
Group C (.440 ± .2319)	**<0.001***	**<0.001***	-	-
Group D (.150 ± .0707)	**<0.001***	**<0.001***	**0.178**	-

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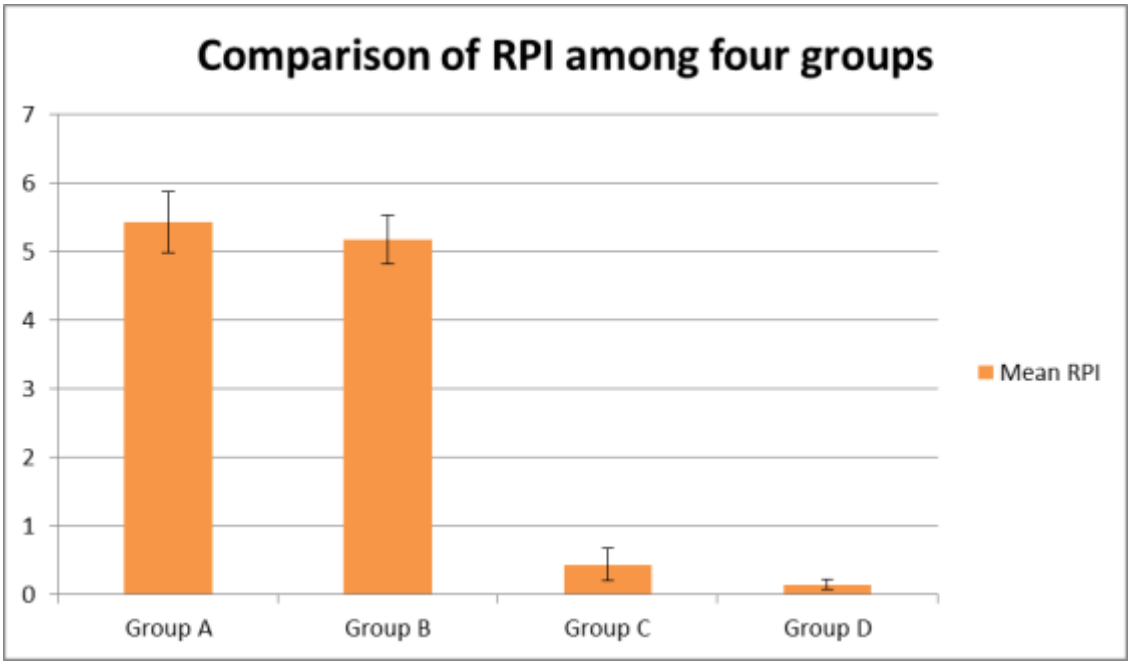
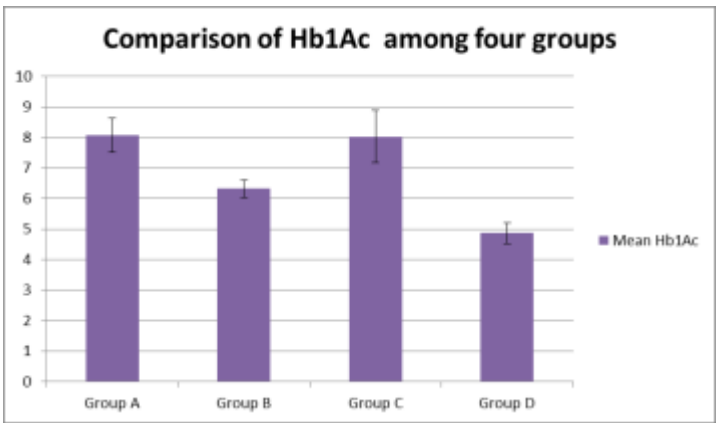


- There was statistically significant difference among four groups for **Russell's periodontal index.**
- Intergroup comparison showed that there was statistically significant difference between Group A and Group C (p<0.001) as well as Group A and Group D (p<0.001) However; The difference between group A and Group B with p=0.260942 were statistically insignificant
- Intergroup comparison showed that there was statistically significant difference between Group B and Group C (p<0.001) as well as Group B and Group D (p<0.001) However; The difference between Group C and Group D with p=0.178942 were statistically insignificant.

Comparison of Hb1Ac among four groups by Analysis of variance followed by intergroup comparison by Tukey's post hoc test.

ANOVA p <0.001*				
	Group A (8.070 ±.5458)	**Group B** (6.320 ± .2781)	**Group C** (8.030 ± .3335)	**Group D** (4.870 ± .3401)
Group A (8.070 ±.5458)	-	-	-	-
Group B (6.320 ± .2781)	**<0.001***	-	-	-
Group C (8.030 ± .3335)	**0.998**	**<0.001***	-	-
Group D (4.870 ± .3401)	**<0.001***	**<0.001***	**<0.001***	-



- There was statistically significant difference among four groups for **Hb1Ac**
- Intergroup comparison showed that there was statistically significant difference between Group A and Group B ($p<0.001$) as well as Group A and Group D ($p<0.001$) However; There was statistically insignificant difference between Group A and Group C with $p=0.998$
- Intergroup comparison showed that there was statistically significant difference between Group B and Group C ($p<0.001$) as well as Group B and Group D ($p<0.001$) There was statistically significant difference between Group C and Group D with ($p<0.001$).

IV. DISCUSSION:

In recent years, a lot of research has focused on association between oral health and systemic diseases. Diabetes and periodontal diseaseare complex chronic diseases, linked by an established bidirectional relationship. Risk for periodontitis is increased two to three times in people with diabetes compared to individuals without[21].Periodontitis is characterized by chronic inflammation, and inflammation can promote insulin resistance and dysregulate glycaemia.

Glucose can bind irreversibly to hemoglobin through a non-enzymatic reaction to form glycosylated hemoglobin (HbA). Hemoglobin A1C, or HbA1c, is the major subfraction of HbA. HbA1c is considered as a beneficial indicator of long-term homeostasis, reflecting an average blood glucose concentration for the past 2-3 months.[11]

Wolff et al [12] in the year 2002 found that periodontitis is associated with a slight elevation in glycated hemoglobin. Nibali ET al[13] found slightly, but statistically significant, higher non-fasting glucose levels in periodontitis cases compared to healthy controls. Bethesda[14]

Hence the current study aimed at studythe association between periodontitis and glycated hemoglobin.

In the present study, we observed the levels of glycated hemoglobin are elevated level in patients in the group suffering from with diabetes than that of patients without diabetics and among the diabetic patients,those suffering chronic periodontitis had higher level glycated hemoglobin. An interested observation which patients with chronic periodontitis have hba1c level were in the range of pre diabeticlevel as proposed by American Diabetes Association (5.7%-6.4%). This can be attributedto the persistent systemic challenge with periodontopathic bacteria and their products result in an up-regulation of the immunoinflammatory response, with elevation in serum levels of proinflammatory mediators such as IL-1β, TNF-α, and IL-6. This is similar to well-recognized systemic infections but on a more persistent, chronic basis. Increased serum levels of several cytokines, including TNF-α and IL-6, are associated with increased insulin resistance. This mechanism would explain the worsening of glycemic control associated with severe periodontitis.

V. CONCLUSION.

It can be concluded current study, it was observed that glycated hemoglobin levels for non-diabetic patients with chronic periodontitis fell in the range of pre-diabetic levels. This association between periodontitis and glycemic level needs to be further investigated.

More randomized clinical trial, withlarger sample size,need to be carried out to assess if Hba1c can be established as a risk indicator for chronic periodontitis as well.

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