Journal of Dental Health and Oral Research

Open Access

Research Article

Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis

Minusha Grace S[1], Sheela Kumar Gujjari[2*], Manjunath S Shetty[3], Sumana MN[4]

[1]Periodontist, Department of Periodontology, JSS Dental College and Hospital, India

[2]Professor, Department of Periodontology, JSS Dental College and Hospital, India

[3]Professor and Head of Department of Nephrology, Department of Periodontology, JSS Dental College and Hospital, India

[4]Professor, Department of Microbiology, JSS Dental College and Hospital, India

[*]**Corresponding Author:** Sheela Kumar Gujjari, Professor, Department of Periodontology, JSS Dental College and Hospital, India; Email: sheelagujjari@gmail.com

Received Date: 16-07-2022; **Accepted Date:** 13-08-2022; **Published Date:** 20-08-2022

Abstract

Background: Diabetes and Periodontitis share a bidirectional relationship. Hyperglycaemia and duration of diabetes can cause the micro-organisms to thrive in the periodontium leading to the activation of the innate i mmune system and cause low grade inflammation leading to systemic diseases such as Chronic Kidney Disease (CKD). The co mmonly used markers of CKD are Serum Creatinine and Albumin. Antibodies like IgG have been found to be elevated with decreased Kidney Function which is also elevated in inflammatory conditions like Diabetes and Periodontitis. As there are no studies done to detect the progression of diabetes and periodontitis to early chronic kidney disease stages by using IgG antibody titre against *P. gingivalis* as a biomarker. The present study evaluated the same.

Methods: Patients were divided into the following group two Groups of 40 each; Group 1 Periodontitis without diabetes) and Group 2 (Periodontitis with Diabetes). Periodontal parameters were recorded. Serum Creatinine, urine albumin and estimated Glomerular Filtration Rate (eGFR) were calculated in both the groups. Serum IgG antibody titre against *P. gingivalis* was detected using ELISA.

Grace SM | Volume 3; Issue 2 (2022) | JDHOR-3(2)-061 | Research Article

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

Results: IgG antibody titre against *P. gingivalis* was detected in both groups with no statistical significance (p-value 0.166). eGFR were significantly (p-value-0.007) lower in diabetics with Periodontitis compared with non-diabetics with periodontitis. A significant (p-value-0.002) association was found when IgG antibody against *P. gingivalis* compared with eGFR in both the groups. Serum Creatinine and urine albumin were significantly higher [p-value- 0.001 and p-value- 0.040] in diabetics with Periodontitis compared to non-Diabetics with Periodontitis.

Conclusion: IgG antibody titre against *P. gingivalis* was similar in both the groups with no significant difference but it was associated with decreased eGFR which revealed that IgG antibody titre against *P. gingivalis* may be used to detect the progression of diabetes to Early chronic kidney Disease Stages. Hence more studies are required to establish it as a potential marker in diabetic patients with periodontitis.

Abbreviations

IgG: Immunoglobulin-G; CKD: Chronic Kidney Disease; CAL: Clinical Attachment Level; PPD-Pocket Probing Depth

Keywords

IgG Antibody; *P. Gingivalis*; Early Chronic Kidney Disease; Diabetes, Periodontitis

Introduction

Chronic Kidney Disease (CKD) is a universal health burden with a high economic cost to healthcare systems [1]. It is a silent killer as it doesn't cause any symptoms until most of the kidney is damaged. The worldwide approximated prevalence of CKD was found to be 13.4%. The major risk factors of CKD include diabetes, CKD and Cardiovascular disease in addition to other risk factors like Periodontitis. A mediation Analysis have revealed that periodontitis and diabetes have a convincing direct and indirect effect through each other on escalating the incidence of Chronic Kidney Disease (CKD) [2]. It was observed that periodontal pathogens and inflammatory cytokines from the contaminated Periodontium travel through the bloodstream and affect the endothelial functions of nephrons [2]. Subgingival biofilms remain a major source of gram-negative bacteria and also the periodontium act as a reservoir of many inflammatory mediators. Previous studies have revealed gram-negative bacteria like *Porphyromonas gingivalis*, Aggregatibacter actinomycetemcomitans, and Tannerella forsythia as the main causative agents in periodontal disease and also have been found to be associated with systemic disease [3].

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

These microorganisms activate the host i mmunologic system which produces specific Immunoglobulins (Ig). Serum antibody titre to specific pathogens Aggregatibacter actinomycetemcomitans, Fusobacterium nucleatum including *P. gingivalis* is elevated in patients with Periodontitis and it has been found to be improved after periodontal therapy. *P. gingivalis* demonstrate diverse virulence factors which boost up its survival and spread causing sustained systemic inflammation.

Microorganisms play an important role in the association of Diabetes and Periodontitis as well. *P. gingivalis* is one among the microorganisms which thrive in the periodontal pocket of diabetics due to the release of Lipopolysaccharides which trigger inflammatory cytokines causing infection and it is also associated with insulin resistance [4]. Interestingly, it was also found that an association exists between IgG antibody titre against periodontal pathogens like *P. gingivalis* and chronic kidney disease [5]. There is no literature regarding this.

CKD is classified into 5 stages based upon its severity defined by the eGFR (estimated Glomerular Filtration Rate levels). Out of the 5 stages, Stages 1, 2, 3 are considered to be the early stages. Most of the patients remain asymptomatic in these stages. According to the data given by the National Institutes of Health and National Institute of Diabetes and Digestive Kidney Diseases, diabetes is more common in patients with stage 1 to 3 CKD (20%) than in patients without CKD (5%) [6].

Though studies have shown an association exists between systemic antibody titre against *P. gingivalis* and chronic kidney disease there are hardly any studies of the same in diabetic patients with periodontitis correlating it with Early Chronic Kidney Disease. If an association can be established, then IgG antibody titre against *P. gingivalis* could be used as a biomarker to early detect, screen, educate and prevent the progression of Periodontitis and Diabetes to early chronic kidney disease.

Patients and Methods

The research protocol was approved by the Institutional Review Board at JSS Dental College [IEC NO:45\2019], Mysore prior to commencement of the study and was registered in Clinical Trial Registry [CTRI/2020/10/028747]. An informed written consent was obtained from all the subjects and the study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000. Patients were recruited from September 2020 to October 2021.

80 individuals who met the inclusion criteria and were divided in to two groups consisting of of 40 each. Group 1-Periodontitis without diabetes and Group 2-Periodontitis with diabetes.

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

They were selected from the outpatient, Department of Periodontology, JSS Dental College and Hospital, Constituent College of JSS AHER, Mysore. The inclusion criteria consisted of diabetic patients of more than 6 years of duration and diabetic patients of more than 6.5% glycated hemoglobin level and with eGFR 30-59 ml\min or more (CKD stage 1, 2 and 3) in both groups. Periodontitis Patients with diabetes and non-diabetes of pocket depth of 4 mm or more than 4 mm and within the age group of 35-68 years of both male and female were included in the study. Patients with eGFR 15-29 ml/min or less than that (CKD stage 4 and Stage 5) in diabetic with Periodontitis and non-diabetic patients with Periodontitis and people who had undergone hemodialysis, peritoneal dialysis or kidney transplantation were not included.

Patients with systemic Diseases that could acutely affect the GFR (rapid progressive glomerulo-nephritis, active glomerular diseases) and renal stones were excluded from the study. Patients undergoing or undergone periodontal therapy in the past 3 months. Pregnant and gestational diabetes, Hypertension and Smokers were also excluded.

Periodontal Clinical Examination

The periodontal condition was assessed by the Modified CPI Index [7]. The Percentage of bleeding sites was calculated. In CPI index bleeding on probing is scored as 0 = Absence of the condition, 1 = Presence of the condition, 9 = Tooth excluded, X = Not present. The percentage of sites with probing pocket depth 4-5 mm and more than 6 mm was calculated. In CPI index probing pocket depth was scored as: 0 = Absence of condition, 1 = Pocket 4-5 mm, 2 = Pocket 6 mm or more, 9 = Tooth excluded, X = Tooth not present.

Clinical Attachment loss was measured as the distance from the cementenamel junction to the base of the pocket and the mean periodontal Attachment Loss (AL) per subject was calculated. In CPI index for clinical attachment level was scored as:
0 = 0-3 mm
1 = 4-5 mm Cemento-Enamel Junction (CEJ) within black band
2 = 6-8 mm CEJ between upper limit of black band and 8.5 mm ring
3 = 9-11 mm CEJ between 8.5 mm and 11.5 mm ring
4 = 12 mm or more CEJ beyond 11.5 mm ring
X = Excluded sextant
9 = Not recorded

Measurement of Kidney Function

Serum Creatinine and Urine albumin test was done for both diabetic and non-diabetic group.

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

Serum creatinine levels were measured. eGFR was calculated according to CKD-EPI equation from the serum creatinine levels obtained [8].

eGFR =141 x min (SCr/κ, 1) α x max (SCr /κ, 1)-1.209 x0.993Age x1.018 [if female] x1.159 [if Black]. Urine albumin was measured using Dipstick method.

Microbiological Investigation

Serum was collected and stored in -20 degree9 to assess titres of serum Immunoglobulin G (IgG) antibody against *P. gingivalis*. It was measured by enzyme-linked immunosorbent assay (ELISA). The assay was done using commercially available Human IgG antibody Elisa Kit for *P. gingivalis* from Chondrex Inc. (https://www.chondrex.com/). The procedure was followed by the instruction provided in the assay kit by the company. BIO-RAD Automated Elisa Reader was used and results were obtained by Magellan Data Analysis Software.

Statistical Analysis

Collected data was analysed using SPSS for Windows (Statistical Presentation System Software, SPSS Inc.) version 17.0. In our study Chi square test was used to find out the association between two variables (i.e., periodontal parameter between both the groups, eGFR between both the groups, IgG antibody titre against *P. gingivalis* between both the groups). Pearson correlation test was used to find the correlation between the variables (i.e. IgG antibody titre against *P. gingivalis* and periodontal parameters, IgG antibody titre against *P. gingivalis* and duration of diabetes).

Results

A total of 80 patients were recruited in the study and divided in to two groups of 40 each, periodontitis without diabetes and periodontitis with diabetes.

The majority of the male patient in the control group was 44% (19\40) and female patient in the group was 56.8% (21\40). The majority of the male patient in the control group was 55.8% (21\40) and female patient in the group was 43.2% (16\40).

Table 1,2 shows the comparison of Age, Periodontal paramaters, Hb, Serum Creatinine between the groups. It was observed (Table 1) that the mean age of the patients was found to be statistically higher (p-value- 0.001) in the group with Periodontitis and Diabetes. The mean Bleeding on Probing (BOP) was statistically higher (p-value- in the group with Periodontitis

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

and Diabetes. The mean Hb levels were equally less (Control group-10.3, Test group-10.5) in both the groups with no statistical significance between the groups. The mean Serum Creatinine levels were significantly higher (p-value-0.001) in patients with periodontitis and diabetes. With regard to periodontal condition assessed, BOP was significantly higher in Periodontitis patients with diabetes. Pocket Probing Depth (PPD) was equally more in both the groups with significant difference. When comparing Clinical Attachment Loss (CAL) between the groups, it was found that CAL was significantly higher (p-value-0.010) in Periodontitis patients with diabetes (Table 2).

Albumin detected was significantly higher (p-value-0.010) in diabetics with periodontitis (Table 3). eGFR calculated from serum creatinine levels were significantly lower in diabetics with Periodontitis compared with non-diabetics with periodontitis (Table 3). IgG antibody titre againgst *P. gingivalis* was equally detected in both the groups with no statistical significance (Table 3). When eGFR was compared with IgG antibody titre against *P. gingivalis* there was a significant (p-value-0.002) increase in the titre levels when the eGFR levels were low (Table 4) (Fig. 1).

Variable	Groups	N	Mean	Std. Deviation	Std. Error Mean	P-value
Age	Control	40	46.25	7.132	1.128	0.001*
	Test	40	52.28	8.042	1.271	
BOP %	Control	40	38.68	18.306	2.894	0.027*
	Test	40	47.89	18.184	2.875	
PPD 4-5 mm %	Control	40	27.45	14.837	2.346	0.832
	Test	40	28.15	14.441	2.283	
PPD >6 mm %	Control	40	19.60	13.030	2.060	0.729
	Test	40	18.63	12.074	1.909	
Hb %	Control	40	10.30	1.791	.28327	0.583
	Test	40	10.53	1.938	.30644	
SCr mg\dl	Control	40	.41	.301	.04774	0.001*
	Test	40	.89	.417	.06602	

BOP: Bleeding on Probing; PPD: Pocket Probing Depth; Hb: Hemoglobin; SCr: Serum creatinine; N: Number of patients; SD: Descriptive statistics

Table 1: Descriptive statistics.

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

Variable			Groups		P-value
			Control Group	Diabetic Group	
CAL	0	N	15	4	0.010*
		%	78.9%	21.1%	
	4-5 mm	N	8	18	
		%	30.8%	69.2%	
	6-8 mm	N	8	10	
		%	44.4%	55.6%	
	9-11 mm	N	7	3	
		%	70.0%	30.0%	
	>12 mm	N	2	5	
		%	28.6%	71.4%	
CAL: Clinical Attachment Loss; N: Number of patients; Chi-square test					

Table 2: Comparison of clinical attachment loss in diabetic and non-diabetic groups.

Variable			Groups		P-value
			Control Group	Diabetic Group	
Albumin	-	N	40	36	0.040*
		%	52.6	42.2	
	+	N	0	4	
		%	0.0%	100.0%	
eGFR	G1	N	33	21	0.007*
		%	61.1%	38.9%	
	G2	N	7	10	
		%	41.2%	58.8%	
	G3a	N	0	8	
		%	0.0%	100.0%	
	G3b	N	0	1	
		%	0.0%	100.0%	

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

IgG Antibody Titre against P gingivalis units\ml	**Not Detected**	**N**	22	15	0.166
	Detected	**%**	**59.5%**	**40.5%**	
	Not Detected	**N**	18	25	
	Detected	**%**	41.9%	58.1%	
eGFR: Estimated Glomerular Filtration Rate; G1, G2, G3a,G3b: Stages of GFR; IgG: I mmnunoglobulin G; N:Number of patients; Chi-square test					

Table 3: Comparison of albumin eGFR and IgG antibody titre against *P. gingivalis* in both the groups.

Variable			**IgG Antibody Titre against P gingivalis units\ml**		**P-value**
			Not Detected	**Detected**	
eGFR	**G1**	N	33	21	0.002*
		%	89.2%	48.8%	
	G2	N	3	14	
		%	8.1%	32.6%	
	G3a	N	1	7	
		%	2.7%	16.3%	
	G3b	N	0	1	
		%	0.0%	2.3%	

Table 4: Comparison of eGFR and IgG antibody titre against *P. gingivalis*.

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

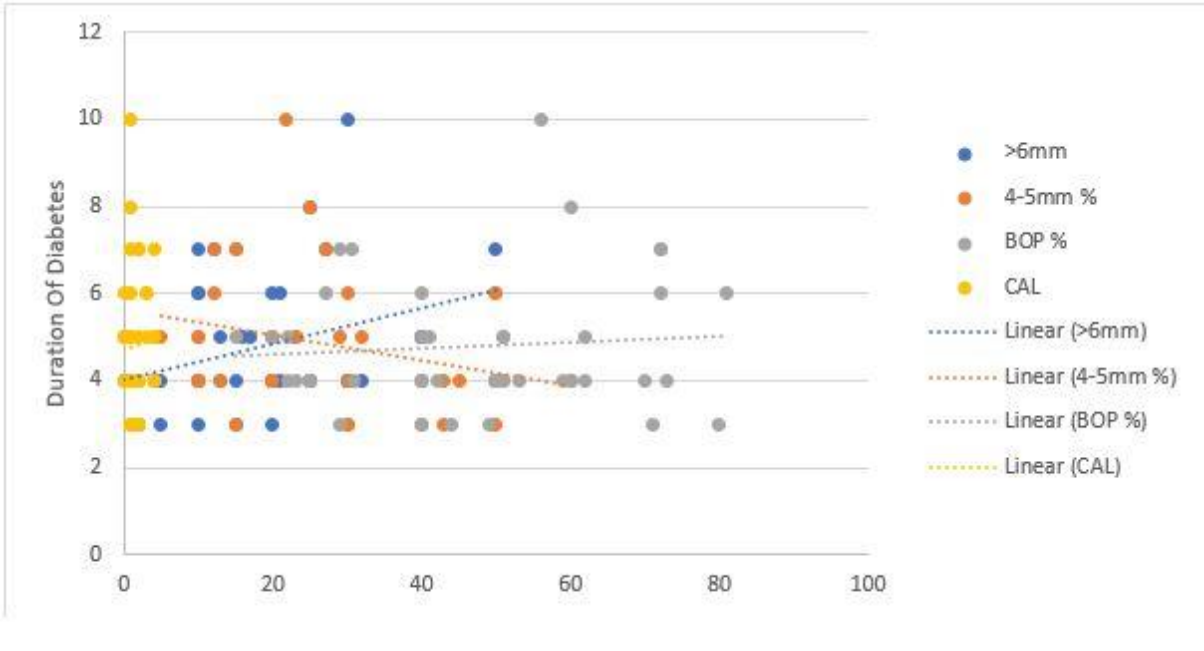

Figure 1: Periodontal parameters and duration of diabetes.

Discussion

Even though studies have found association of IgG antibody titre against *P. gingivalis* with periodontitis and CKD. There are no studies done in diabetic patients with periodontitis. This study was based on the fact that periodontitis has been found to have a systemic link mainly through inflammation. Both diabetes and Periodontitis have been associated with chronic kidney disease and early chronic kidney disease is asymptomatic and can be undiagnosed. So, this study was done to to study the association between IgG antibody titre against *P. gingivalis* and Early Chronic Kidney disease stages in diabetics with Periodontitis and non-diabetics with Periodontitis.

The present study investigated IgG antibody titre against *P. gingivalis* in both groups. It was found that IgG antibody titre against P.gingivalis was detected in both the groups with no significant difference. This could be due to periodontal severity being equally similar in both the groups.

The present study showed the mean BOP% significantly higher in Diabetics with Periodontitis that could be due to Poor Glycaemic control causing vascular changes and collagen destruction. These results were in agreement with the results of the study done by Kaisa M, et al., were they found increased bleeding on probing in diabetic patients with periodontitis [10]. BOP %, when compared with IgG antibody titre against *P. gingivalis*, found a significantly higher association

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

in diabetics compared to non-diabetics with Periodontitis. This could be due to the Immunoinflammatory responses caused by P. *gingivalis* which led to gingival inflammation.

In our study, the mean Probing depth was found to be similar in both groups with no significant difference. This could be due to periodontal destruction being similar in both groups. The results were found to be similar to a meta-analysis done by Khader, et al., where they found no difference in terms of probing depth between diabetics and non-diabetics with periodontitis [11]. But CAL was significantly higher in the diabetic group with periodontitis. This could be due to high glycaemic levels and impaired bone matrix leading to insufficient osteoblast production in Diabetic patients which led to increased attachment loss when compared to the non-diabetic group. The results were in agreement with the study done by Botero, et al., where they found increased Clinical attachment loss in periodontal individuals with diabetes [12]. PD and CAL did not show a significant difference when compared with serum IgG titre against *P. gingivalis* which contradicts the study done by Takahasi, et al., where they found Serum IgG antibody levels against *P. gingivalis* were significantly elevated in diabetics with periodontitis [13]. The results of the present study could be due to periodontal destruction being similar in both groups which led to a similar immunoinflammatory response.

Diabetes increases with age which could be due to various reasons like long-time consumption of sugar, genetics, and lifestyle modification. Also, it is known that the complications of diabetes increase with age [14]. In the present study as the age advanced the individuals had diabetes which is in accordance with the study done by Kyungdo Han, et al., [15]. Also in the present study, Age when correlated with periodontal parameters revealed a significant correlation with Clinical Attachment loss. The correlation of CAL with age could be due to various factors like increased proinflammatory cytokines and immunosenescence associated with age [16].

In the present study, we assessed HbA1c and the duration of diabetes in diabetic patients. The results have shown the mean duration of diabetes was 4.8 years with the maximum duration being 10 years. When correlated with the periodontal parameters, a correlation was found between the duration of diabetes with pockets more than 6 mm. These findings were similar to the study done by Kim, et al., where they also found a correlation between the duration of diabetes and periodontal parameters [17].

In the current study, the mean HbA1c levels were found to be 8.3% with a maximum of up to 12% [18]. When the duration of diabetes was compared with the glycated Hb levels (HbA1c), there was no significant association found even though there are studies such as the one done by Verma, et al., where HbA1c levels showed a significant increase with the duration of diabetes [19]. These contradictory results could be due to the difference in sample size and the

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

techniques used or due to the misinformation by the patient regarding their diabetes status and its duration.

Chronic Kidney Disease is diagnosed through various markers such as Serum Creatinine (SCr), Cystatin C, Serum, Urine Albumin, etc. [20]. In our study we have used Serum Creatinine and Urine albumin. Though albumin in the urine is associated with chronic kidney disease it is seen also in non-kidney diseases [21]. We have also estimated GFR from serum Creatinine which was calculated through the CKD-EPI equation. "Chronic Kidney disease is defined as the presence of Kidney damage or eGFR less than 60 ml\min\1.73 m^2 which persist for 3 months or more than that irrespective of its cause" [22]. In the current study eGFR was categorized into G1, G2, G3a, G3b based upon its severity following the in which G1 implies 90 ml\min\1.72 m^2, G2 implies 60-89 ml\min\1.73 m^2, G3a implies 45-59 ml\min\1.73 m^2, G3b implies 30-44ml\min\1.73 m^2. These eGFR rates are in accordance with early chronic kidney disease stages CKD1, CKD2, CKD3, CKD3a, CKD3b.

In the present study, 4 individuals in the Diabetic group with Periodontitis were found to have albumin in urine whereas none of the patients in the control group had albumin in the urine. This could be due to the severity of diabetes and inflammation. The current study was in agreement with the previous study done by Han, et al., where the results showed a positive association with urine albumin in diabetics with Periodontitis. This might be explained by the fact that in diabetics' inflammation is more [15].

Serum creatinine levels are considered normal up to 1.2 mg\dl in the Indian population [23]. The mean SCr in the control group was found to be 0.4 with the maximum of up to 1.1 and the mean SCr in the diabetics were found to be 0.8 with the maximum levels up to 1.8 and a statistically significant difference between the diabetics with periodontitis and non-diabetics with periodontitis was observed. The results were in agreement with the study done by Bamanikar, et al., where they found significantly higher SCr levels in diabetics with periodontitis [24].

In the control group 33 out of 40 patients belongs to G1,10 out of 40 patients belong to G2,8 out of 40 patients belong to G3a and 1 out of 40 patients belongs to G3b which again implies a significant number of individuals in the diabetic group had lower estimated Glomerular Filtration Rate. A study done by Nata, et al., has shown an increased prevalence of decreased eGFR among diabetics which is in agreement with the present study [25]. In the current study, eGFR was calculated at one point of time for the initial inclusion of patients but it has to be monitored for 3 months to confirm the stage of CKD. Also, eGFR can be reduced even in the absence of CKD with factors such as age. So, it should be noted that Serum Creatinine levels are influenced by various other factors which include muscle mass, diet, and also medications such as Cephalosporins and aminoglycoside antibiotics [26].

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

Furthermore, hemoglobin was also assessed as an additional parameter to know the overall health condition of the patient. The mean hemoglobin levels were significantly less in both groups. This could be due to inflammation which reduced the number of erythrocytes in blood and the reduction in erythrocytes could have contributed to low eGFR due to less production of erythropoietin which is essential for kidney function.

When comparing IgG antibody titre against *P. gingivalis* and eGFR it was found that antibody titre against *P. gingivalis* was significantly higher in patients with decreased eGFR in diabetic patients with periodontitis. This could be due to direct cellular damage to the nephron unit or its vasculature caused by the systemic circulation of the pathogens. A study done by Kshirsagar, et al., found high levels of Serum IgG titre against periodontal pathogens including Porphyromonas gingivalis, Treponema denticola, and Aggregatibacter actinomycetemcomitans [27]. Another study done by Iwasaki, et al., investigated the association between serum antibody to the periodontal pathogen Porphyromonas gingivalis (*P. gingivalis*) and CKD in 215 individuals and the results showed that participants with elevated serum antibody to *P. gingivalis* were 2.6 times more likely to have CKD which is in agreement with our study [28].

A Mediation Analysis was done by Lertpimonchai, et al., which showed a direct effect of periodontitis on the incidence of ckd as well as the indirect effect of periodontitis through diabetes on the incidence of CKD [2]. In the present study also periodontitis through diabetes would have shown the signs of progression towards early chronic kidney disease stages since serum creatinine, eGFR, and albumin was significantly associated with the diabetic group compared to the non-diabetic group with Periodontitis. Moreover, in our study, it is observed IgG antibody titre against *P. gingivalis* was associated with reduced eGFR in diabetic compared to the non-diabetic group. So, it could be used as a biomarker to see the early progression of chronic kidney disease in diabetics with periodontitis.

A potential limitation in our study was lack of systemically healthy group without chronic periodontitis. Also, participants were from outpatient of the department of Periodontology who were diabetics so there might be a chance of selection bias which led to over or underestimation of the true association among the two groups. Another limitation was IgG antibody titre against other periodontal pathogens other than *P. gingivalis* was not measured in our study.

Further studies with larger samples and serum titre to other periodontal pathogens would be useful to find out the progression of diabetes with Periodontitis to early chronic kidney disease and also would be necessary to substantiate the present study results. Future studies should evaluate the role of periodontal therapy as it is believed to reduce the chronic inflammatory burden caused by periodontitis in diabetics thereby reducing the risk of progression towards early chronic kidney disease. Studies should come up with monitoring of eGFR for 3 months

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216

to know the actual progression of early chronic kidney disease. So, more research is required to establish it as a marker.

Conclusion

Though studies have shown an elevation of IgG titres in periodontitis as well as in diabetes. In this study IgG antibody titre against *P. gingivalis* was found similar in both diabetic and non-diabetic group with periodontitis and had a statistical significance with eGFR in diabetics with Periodontitis which showed that it can be used as a biomarker to detect the early progression of CKD in diabetics as well as non-diabetics with periodontitis. Further studies are required to prove this association in diabetics with periodontitis.

Acknowledgement

This study was supported by a grant (5293) from JSS Academy of Higher Education and Research (JSSAHER).

Conflict of Interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the manuscript.

References

1. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global prevalence of chronic kidney disease - A systematic review and meta-analysis. PLoS ONE. 2016;11(7).
2. Lertpimonchai A, Rattanasiri S, Tamsailom S, Champaiboon C, Ingsathit A, Kitiyakara C, et al. Periodontitis as the risk factor of chronic kidney disease: Mediation analysis. J Clin Periodont. 2019;46(6):631-9.
3. Zambon JJ. Section IIB periodontal diseases: microbial factors question set. Annals Periodontol. Buffalo; 1996;1:879-925.
4. Almeida-Santos A, Martins-Mendes D, Gayà-Vidal M, Beja-Pereira A, Quintas A, de Gaia N, et al. Characterization of the oral microbiome of medically controlled type-2 1 diabetes patients 2. 2020:1-28.
5. Iwasaki M, Taylor GW, Manz MC, Kaneko N, Imai S, Yoshihara A, et al. Serum antibody to Porphyromonas gingivalis in chronic kidney disease. J Dental Res. 2012;91(9):828-33.
6. Qaseem A, Hopkins RH, Sweet DE, Starkey M, Shekelle P. Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease: a clinical practice guideline from the american college of physicians. 2013. Last accessed on: August 12, 2022 www.annals.org
7. Beltrán-Aguilar ED, Eke PI, Thornton-Evans G, Petersen PE. Recording and surveillance systems for periodontal diseases. Periodontol 2000. 2012;60(1):40.
8. Levey AS, Stevens LA, Schmid CH, Zhang Y, Castro III AF, Feldman HI, et al. Authors current mailing address: 8. paul eggers kidney and urology branch, NIDDK, National Institutes of Health, 6707 Democracy Blvd. Ann Intern Med. 2009;150(9).

9. Fernando C, Flores Y, De Las Á, Pineda MH, Cevallos Bonilla VM, Sáenz-Flor K. Sample management: stability of plasma and serum on different storage conditions. EJIFCC. 2020;31(1):46-55.
10. Karjalainen, Kaisa M, Maril. The onset of diabetes and poor metabolic control increases gingival bleeding in children and adolescents with insulin-dependent diabetes mellitus. J Clin Periodontol. 1996;96(2):1060-7.
11. Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A, Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a meta-analysis. J Diabetes and its Complications. 2006;20(1):59-68.
12. Botero JE, Yepes FL, Roldán N, Castrillón CA, Hincapie JP, Ochoa SP, et al. Tooth and periodontal clinical attachment loss are associated with hyperglycemia in patients with diabetes. J Periodontol. 2012;83(10):1245-50.
13. Takahashi K, Nishimura F, Kurihara M. Subgingival microflora and antibody responses against periodontal bacteria of young Japanese patients with type 1 diabetes mellitus. J Int Acad Periodontol. 2001;3(4):104-11.
14. Chentli F, Azzoug S, Mahgoun S. Diabetes mellitus in elderly. Ind J Endocrinol and Metabolism. 2015;19(6):744-52.
15. Han K, Park JB. Clinical implications of age and sex in the prevalence of periodontitis in Korean adults with diabetes. Experimental and Therapeutic Medicine. 2018;15(4):3865-73.
16. Ebersole JL, Dawson DA, Emecen Huja P, Pandruvada S, Basu A, Nguyen L, et al. Age and Periodontal Health-Immunological View. Curr Oral Health Rep. 2018;5(4):229-41.
17. Kim EK, Lee SG, Choi YH, Won KC, Moon JS, Merchant AT, et al. Association between diabetes-related factors and clinical periodontal parameters in type-2 diabetes mellitus. BMC Oral Health. 2013;13(1).
18. Rajan P, Nera M, Pavalura AK, Medandrao N, Kumar C. Comparison of glycosylated hemoglobin (HbA1C) levels in patients with chronic periodontitis and healthy controls. Dental Res J. 2013;10;389.
19. Verma M, Paneri S, Badi P, Raman PG. Effect of increasing duration of diabetes mellitus type 2 on glycated hemoglobin and insulin sensitivity. Ind J Clin Biochem. 2006:21.
20. Lopez-Giacoman S. Biomarkers in chronic kidney disease, from kidney function to kidney damage. World J Nephrol. 2015;4(1):57.
21. Prasad RM, Tikaria R. Microalbuminuria. Treasure Island: StatPearls Publishing. 2022.
22. SatyaNarayana R Vaidya, Narothoma R Arddula. Chronic renal failure. Treasure Island (FL): Stat Pearl. 2020.
23. Ray AS, Kare PK, Makwane HS, Saxena T, Garg C. Estimation of serum creatinine, serum urea, glomerular filtration rate and proteinuria among apparently healthy adults to assess the renal impairment and its association with body mass index: An observational hospital-based study. Studies. 2020;6:7.
24. Bamanikar S, Bamanikar A, Arora A. Study of serum urea and creatinine in diabetic and non-diabetic patients in in a tertiary teaching hospital. J Med Res. 2016;2(1):12-5.
25. Nata N, Rangsin R, Supasyndh O, Satirapoj B. Impaired glomerular filtration rate in type 2 diabetes mellitus subjects: a nationwide cross-sectional study in Thailand. J Diabetes Res. 2020;2020:1-9.
26. National kidney foundation. Measurement of kidney function 4.
27. Kshirsagar AV, Offenbacher S, Moss KL, Barros SP, Beck JD. Antibodies to periodontal organisms are associated with decreased kidney function. The Dental Atherosclerosis Risk in Co mmunities Study. 2007;25:125-32.
28. Iwasaki M, Taylor GW, Manz MC, Kaneko N, Imai S, Yoshihara A, et al. Serum antibody to Porphyromonas gingivalis in chronic kidney disease. J Dental Res. 2012;91(9):828-33.

Citation: Gujjari SK, et al. Association of Serum IgG Antibody to *P. gingivalis* and Early Chronic Kidney Disease in Diabetics and Non-Diabetics with Periodontitis. J Dental Health Oral Res. 2022;3(2):1-14.

DOI: https://doi.org/10.46889/JDHOR.2022.3216