

Glucose as a risk factor for periodontitis in kidney transplantation patients

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Research Article

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Abstract

Background: Various factors including diabetes and oxidative stress are associated with periodontal inflammation. In patients with end stage renal disease (ESRD), accumulation of uremic toxin leads to various systemic abnormalities, including cardiovascular disease, metabolic abnormalities, and infection. Even after kidney transplantation (KT), various factors are known to be associated with inflammation. Our study, therefore aimed to study risk factors associated with of periodontitis in KT patients.

Methods: Patients, who visited Dongsan Hospital, Daegu, Korea, since 2018, and diagnosed of periodontal disease were selected. As of November 2021, 923 participants, with full data including hematologic factors were studied.

Results: From 923 KT patients, 30 were diagnosed with periodontal disease. Fasting glucose levels were higher in patients with periodontal disease, while total bilirubin levels were lower. When divided by fasting glucose levels, high glucose level showed increase of periodontal disease with odds ratio (OR) of 1.031 (95% confidence interval (CI) 1.004-1.060). After adjusting for confounders, results were significant with OR 1.032 (95% CI 1.004-1.061).

Conclusions: Our study have shown that KT patients, of whom uremic toxin clearance has been revolted, are yet at risk of periodontitis by other factors, such as high blood glucose levels.

Background

Kidney transplantation (KT) is a treatment for patients with end stage renal disease (ESRD), which improves survival rate and enhances quality of life. [1, 2]. Number of ESRD patients of whom have under gone kidney transplant is ever growing, with more than 2,000 transplantation cases each year since 2016 [3].

Along with increase in transplant, so did side effects of immunosuppressants, including infection, fractures, and malignancy [4, 5]. Oral complication includes gingival enlargement in patients treated with cyclosporine A, which is present in 25–81% of the patients [6]. Other complications include oral candidiasis, saburral -tongue, and Kaposi sarcoma [7–9]. More half of KT patients suffer from one or more oral lesions [8]. Therefore, good oral hygiene and routine care is necessary to reduce patients` burden.

Various factors are reported to be associated with periodontal inflammation. Systemic conditions, such as cardiovascular disease and stroke have been reported to be associated with periodontal inflammation [10, 11]. Other factors include diabetes, oxidative stress, and ESRD [12–14].

To date, no research has been performed to understand factors associated to periodontal disease development in KT patients. Therefore, we compared hematologic factors between patients with and without periodontal disease to suggest methods of improving KT patients` oral health.

Methods

Study population

The study participants were patients who visited Dongsan Hospital, Daegu, Korea, since 2018. All of the patients diagnosed of periodontal disease were selected. As of November 2021, 934 patients had undergone kidney transplantation.

From 934 patients, patients without laboratory data, including aspartate transaminase (AST), alanine transferase (ALT), and fasting glucose levels were excluded from the study. As result, 923 patients were used for the study, of whom 30 were diagnosed of periodontal disease. This study was conducted with the approval of Institutional Review Board of Dongsan Hospital, Keimyung University in Korea (IRB No. DSMC 2022-03-006). The study was carried out in accordance with the Declaration of Helsinki and with the term of local legislation.

Data Collection

Laboratory data were collected from blood samples, which were collected after 8 hours of overnight fasting. All of the samples were analyzed on the same day. BUN, creatinine, albumin, total bilirubin, fasting glucose, white blood cell, red blood cell, hemoglobin, platelet, AST, ALT, alkaline phosphatase (ALP), inorganic phosphorus, calcium, total protein, and estimated glomerular filtration rate (eGFR) were obtained by Cobas 8000 c702 (Roche Diagnostics System, Switzerland).

Definition Of Renal Functions And Periodontitis

eGFR was obtained by CKD-EPI equation, of which the validity was studied elsewhere [15]. Diabetes was defined as fasting glucose of 126 or higher.

Periodontitis was diagnosed based on residual bone level in panoramic views, according to study of Machado et al [16].

Statistical analysis

Participants were studied according to diagnosis of periodontal disease. Laboratory data and other confounders were compared between each group, using one-way analysis of variance for continuous variables and chi-square test for categorical variables. Results were shown as mean \pm standard deviation (SD) for continuous variables.

Odds Ratio (OR) and 95% confidence interval (CI) was used to study the relationship between diabetes and periodontal disease. The analyses were adjusted for confounders, which were significantly associated in the analysis, or were profoundly known confounders in other literatures. In Model 1, no

confounders were adjusted. In Model 2, age, gender, smoking, AST, ALT, albumin, and eGFR were adjusted. A p value of < 0.05 was used to indicate statistical significance. All of the analyses were performed by R version 3.5.1 (<http://www.r-project.org>).

Results

A total of 923 KT patients were used for the study, of 30 were also diagnosed with periodontal disease. The general characteristics of the participants, divided by periodontal disease are shown in Table 1. Fasting glucose levels were higher in patients with periodontal disease, while total bilirubin levels were lower. There were no significant differences in age, gender, smoking and other hematologic factors.

Table 1
Baseline Characteristics of the Participants by Gingivitis

	Gingivitis (n = 30)	Normal (n = 893)	p
Age,y	56.47 ± 11.07	55.72 ± 11.11	0.719
Men, n(%)	18 (60.00%)	537 (60.13%)	1
Smoking, n(%)	3 (10.00%)	37 (4.14%)	0.274
BUN	26.60 ± 16.96	22.90 ± 14.71	0.178
Creatinine	2.08 ± 2.07	1.47 ± 1.26	0.118
AST	20.90 ± 10.56	31.24 ± 241.54	0.214
ALT	19.43 ± 19.45	21.49 ± 79.00	0.643
ALP	81.90 ± 27.62	80.40 ± 43.43	0.777
IP	3.37 ± 0.98	3.34 ± 0.92	0.851
Albumin	4.26 ± 0.38	4.26 ± 0.47	0.959
Total Protein	6.78 ± 0.46	6.69 ± 0.64	0.298
Total Bilirubin	0.51 ± 0.32	0.67 ± 0.59	0.01
WBC	6.50 ± 2.05	7.32 ± 2.81	0.042
RBC	4.13 ± 0.87	4.37 ± 0.81	0.121
Hb	12.40 ± 2.08	13.13 ± 2.37	0.092
Hct	37.75 ± 6.09	39.89 ± 6.88	0.092
Platelet	214.87 ± 65.52	220.24 ± 66.64	0.664
Calcium	9.48 ± 0.67	9.53 ± 0.77	0.729
Glucose	134.93 ± 53.86	116.36 ± 47.44	0.036
eGFR	55.76 ± 28.39	63.56 ± 24.46	0.088
ALT, alanine transferase; ALP, alkaline phosphatase; AST, aspartate transaminase; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; Hct, hematocrit; IP, inorganic phosphorus; RBC, red blood cell; WBC, white blood cell.			
Data were expressed as mean ± standard deviation for continuous variables and n(%) for categorical variables.			

Location Of Table

Table 2 shows association between fasting glucose, divided by 126mg/dL. Compared to low glucose level, high glucose level showed increase of periodontal disease with OR of 1.031 (95% CI 1.004–1.060). After adjusting for confounders, results were significant with OR 1.032 (95% CI 1.004–1.061).

Table 2
Odds Ratios of Gingivitis according to Diabetes

	Model 1		Model 2	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Diabetes	1.031 (1.004–1.060)	< 0.05	1.032 (1.004–1.061)	< 0.05

Model 1: not adjusted; Model 2: adjusted for age, gender, smoking, aspartate transaminase, alanine transferase, albumin and estimated glomerular filtration rate.

CI, confidence interval; OR, odds ratio.

Discussion

Our study has shown that high fasting glucose levels are associated with periodontal disease in KT patients. The results were consistent after adjusting for confounding factors.

ESRD is characterized by structural changes in renal system, causing uremia by reducing filtration abilities [17]. Uremia causes various systemic abnormalities, including cardiovascular disease, metabolic abnormalities, and infection due to leukocyte dysfunction [18]. Furthermore, uremia is cause of several dental problems, including xerostomy, uremic stomatitis, and dental calculus formation [19]. Periodontal disease is also linked to ESRD, according to several studies [20–22]. Therefore, current study aimed to assess risk factors associated with periodontal disease in ESRD patients, of whom have undergone KT.

To date, association between periodontal disease and transplantation have not been studied. However, several factors have been reported to be associated with periodontal inflammation in KT patients. Smoking, diabetes and cardiovascular disease have been reported to be associated with periodontal inflammation [10, 12, 23]. Another factor, eGFR was not significant in our study [14]. Especially, diabetes is suspected to increase susceptibility of disease via altering gingival flora, and increase in oxidative stress [15, 24]. This might have caused association of glucose and periodontal disease in transplantation in our study.

Our study was cross-sectional study, lacking follow up. Therefore, long term effect of glucose levels on periodontal disease are yet to be studied. Furthermore, as data was collected retrospectively, additional survey data, such as oral hygiene and care are absent. Further studies should be performed to adjust its effects.

Our study has shown that KT patients, of whom uremic toxin clearance has been revolted, are yet at risk of periodontitis by other factors, such as high blood glucose levels.

Conclusion

Our study has shown that KT patients, of whom uremic toxin clearance has been revolted, are yet at risk of periodontitis by other factors, such as high blood glucose levels.

Abbreviations

ALT: Alanine transferase

AST: Aspartate transaminase

CI: Confidence interval

eGFR: Estimated glomerular filtration rate

ESRD: End stage renal disease

KT: Kidney transplantation

OR: Odds Ratio

SD: Standard deviation

Declarations

Ethics declarations

This study was conducted with the approval of Institutional Review Board of Dongsan Hospital, Keimyung University in Korea (IRB No. DSMC 2022-03-006).

Informed consent was waived by the board due to its retrospective nature, and the data was acquired without personal id or information.

The study was carried out in accordance with the Declaration of Helsinki and with the term of local legislation.

Consent for publication

Not applicable.

Availability of data and materials

All of the data used in this study is not publicly available, but are available from the corresponding author on reasonable request.

Competing interests

Authors declare no conflict of interest

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No funding was involved in current study.

Authors` s contributions

Shin Young-Min contributed to study design, data collection, and preparation of manuscript.

Kwang Ho Mun contributed to study design, data analysis, data interpretation, preparation of manuscript and literature analysis/research.

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