Crosstalk between Periodontitis and Chronic kidney disease

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Abstract

Introduction*: Poor oral health in chronic kidney disease patients is an important contributory factor in atherosclerosis, protein energy wasting, systemic infection, and inflammation. In developing countries oral health care is neglected among chronic kidney disease patients. Therefore, the objective of this study is to establish the relationship between periodontitis and chronic kidney disease by measuring serum interleukin-6 and serum procalcitonin.*

Material and method: *It was a prospective study that was conducted in department of medicine at MLN Medical College India from July 2021 to June 2022 in which 50 chronic kidney patient was included on the basis of inclusion and exclusion criteria . Blood sample was taken and send for serum interleukin-6, serum procalcitonin, serum creatinine and other investigations. Clinical periodontal examination was performed and classify it by using CDC-AAP classification.*

Result*: Out of 50 patients, periodontal evaluation was done,40 patient had periodontitis changes which was considered as case and 10 patient had no periodontitis changes considered as control .The percentage of chronic kidney disease stage 5 (80%) is higher overall in both cases and control. We found that periodontitis changes were more associated with higher stages of chronic kidney disease. The mean (±SD) interleukin-6 of cases was found to be 394.41±699.07 and control was 10.34±7.35, the overall mean of interleukin -6 is found to be 317.60±642.70,that was significant (p value=0.001). Similarly mean of serum procalcitonin of cases was found to be 18.44±23.97 and control was 1.48±1.18, the overall mean of serum procalcitonin 15.05±22.46, that was significant (P value<0.001).Serum interleukin-6 (p value=<0.001) and serum procalcitonin (p value=0.005) wasfound to significant with respect to periodontal status. In intragroup comparison between mild and severe periodontitis, serum interleukin-6 and serum procalcitonin were found to be statistically significant with p value (<0.001&= 0.006).*

Conclusion*: Therefore, our study revealed that periodontitis is important risk factor of chronic kidney disease patients that was explained by our markers interleukin-6 and serum procalcitonin as they are statistically significant in chronic kidney disease with periodontitis patient. So these marker may be used as prognostic marker in chronic kidney disease with periodontitis for predicting outcome of these patients.*

Keywords: *chronic kidney disease, stages , severity , serum interleukin-6, serum procalcitonin.*

I. Introduction

Chronic kidney disease (CKD) is a worldwide health problem, with adverse outcome of cardiovascular disease and premature death. It has become evident that inflammation plays an important role in the pathogenesis of arthrosclerosis complication. CKD patient also has an increased risk of arthrosclerosis complication. In line with this, dental problems can be important source of systemic inflammation. Periodontitis(PO) is a highly prevalent disease, affecting around 50% of the population [1]. Investigations on trends of prevalence based on the estimates from the Global Burden of Disease study found that in 2019, there were 1.1 billion prevalent cases of severe PO worldwide [2]. PO is a chronic microbially-induced inflammation of the supporting tissues of the tooth that results in loss of periodontal attachment, alveolar bone, and finally of the tooth [3].CKD patients have associated periodontitis arising from the disease process or the effect of therapy or both. Untreated periodontitis may deteriorate the clinical presentation and prognosis, there are clinical and radiological changes in the mouth in CKD patients .[4]

As CKD progresses, the prevalence of PO increases, being more important in advanced stages [5,6] when compared to earlier stages of CKD [7,8].CKD and PO might have common pathophysiologic mechanisms, based on increased inflammatory state, impaired immune clearance, increased bacteraemia and other factors such as xerostomia, gingival hypertrophy, or uremic milieu. As such, in a recent analysis data from a prospective study

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(RIISC) (Renal Impairment in Secondary Care) with longitudinal data on PO, kidney function, and oxidative stress available, structural equation modelling was used to test causal assumptions between PO and kidney function. This study was positive in that 10% increase in periodontal inflammation resulted in a 3.0% decrease in renal function and a 10% decrease in renal function resulted in a 25% increase in PO, and the common denominator is thought to be oxidative stress. Inflammation and bacteraemia play an important role in causing various complications in CKD patient and inflammatory markers such as C‑ protein, serum il-6 and bacteraemia marker such as serum procalcitonin are sensitive and independent predictors of outcomes in CKD patient. Periodontitis could result in stimulation of cytokine and sepsis. With 2 exceptions out of 8 reported studies, CRP was significantly elevated in CKD patients with PO [9]. Few studies who mainly evaluated the relationship of CRP and ESR with ckd and periodontitis that was not very significant, so we evaluated the serum IL -6 and serum procalcitonin because these marker is more specific to inflammation and bacteraemia. The objective of this study is to establish the relationship between periodontitis and chronic kidney disease patients by measuringserum Il-6 and serum procalcitonin.

II.   Material and Method

This prospective study comprised of patients visited to nephrology department from July 2021 to June 2022 at SRN Hospital Prayagraj. All adults (age>18 years), male and female patients, were recruited after informed consent.

Study Design: Prospective observational case control study.

Study location:This was a tertiary care teaching hospital-based study done in Department of Medicine, at Swaroop Rani Nehru Hospital, MLN medical college, Prayagraj, Uttar Pradesh.

Study Duration: July 2021 to June 2022

Sample size: 50

Patient Selection: A total of 50 patients (both male and female) with CKD who visited the nephrology department of MLN Medical College, Prayagraj, Uttar Pradesh, India from July 2021 to June 2022 were selected.

Inclusion Criteria:
- All adults (age>18 years), male and female patients, were recruited after Informed Consent.
- Already diagnosed CKD patient
- Patients diagnosed CKD during hospital stay were observed, and these were our patient..

Exclusion Criteria:
- Individual who underwent periodontal therapy
- Malignancy, HIV, Hepatitis
- Upper respiratory tract infections
- Pregnant and lactating women.
- Other systemic infection like AKI and Pancreatitis

Study Procedure
- Medical history taken and clinical examination was done.

- Define CKD & its stages by measuring eGFR and USG abdomen.

- Blood samples for serum procalcitonin and serum interleukin 6 were collected within 8 h of admission to ICU aseptically via venipuncture.

- Clinical examination of mouth done by two dental surgeon by using Mouth mirror and by using the periodontal probe measure the periodontitis changes.

- During oral examination by using the periodontal probe we measure the Pocket depth of teeth in which the maximum measurement of pocket Depth was taken and similarly we measure clinical loss of attachment and Maximum measurement considered.

- After taking all measurements we classify the periodontal status of the patient by using CDC-AAP classification

- Serum Urea and serum Creatinine were measured. Patients diagnosed CKD during hospital stay were observed, and those were our cases.

- After that on the basis of periodontal status we divided all CKD patient into two groups: CASES:CKD with periodontitis and those CKD who did not had periodontitis changes consider as CONTROL:CKD without periodontitis.

Data collection and statistical analysis: The data was collected on a semistructured questionnaire. Records of all the test. Reports were maintained. All observation were made under direct supervisior, categorical variables were presented in number and percentage (%) and continuous variables were presented as mean and SD. Quantitative variables were compared using Mann Whitney U test /unpaired T test as appropriate Between two groups. Qualitative variables were compared using Chi-Square test And Fischer exact test as appropriate. To measure the strength of association between two scale parameters using spearman correlation coefficient as appropriate. A P value of< 0.05 was considerely statistically significant. The Data was entered in MS Excel spreadsheet and analysis was done using statistical package for Social Science version 23.0

Ethical considerations –

1. The protocol of the thesis was approved by the ethical committee **(Registration No ECR/922/Inst./UP/2017 issued under Rule 122DD/of the Drugs & Cosmetics Rule 1945)** of MLN Medical College, Prayagraj, Uttar-Pradesh India.

2. All participants were told about the purpose of the study along with informed written consent.

3. No pressure was exerted on subjects for participation in the study.

4. Confidentiality and privacy was ensured at all stages of the study period.

5. The subjects were free to leave the study at any time and no reasons for the same were asked. They were not debarred from getting any medical services from the hospital even if they refused to participate in the study.

6. The data collected was used for the study purpose only.

III. Result

Out of 50 CKD patients, 40 patients showed the changes of periodontitis were taken as cases, where as 10 patients had no findings suggestive of periodontitis were taken as controls.

Table 1 and Fig. 1 reveals that In Cases the percentage of Stage 5, Stage 4 and Stage 3 are 80.0%, 15.0% and 5.0% respectively. In controls the percentage of Stage 5, Stage 4 and Stage 3are 80.0%, 00.0% and 20.0% respectively. It shows an insignificant difference between the groups (p value = 0.153).

Table 1 : Distribution of CKD stages based on their groups.

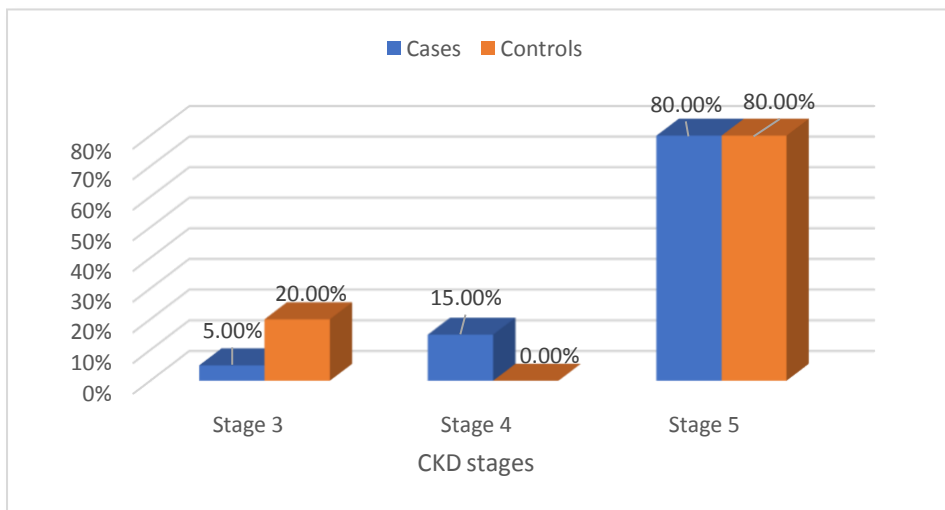| CKD stages	Groups						χ2 value (df)	p-value
	Cases		Controls		Total			
	N	%	N	%	N	%		
Stage 3	2	5.0%	2	20.0%	4	8.0%	3.75 (2)	0.153
Stage 4	6	15.0%	0	.0%	6	12.0%		
Stage 5	32	80.0%	8	80.0%	40	80.0%		

Fig. 1 : Bar graph showing the frequency of different stages ofCKD in cases and control.

Table 2: Distribution of inflammatory markers based on their groups.

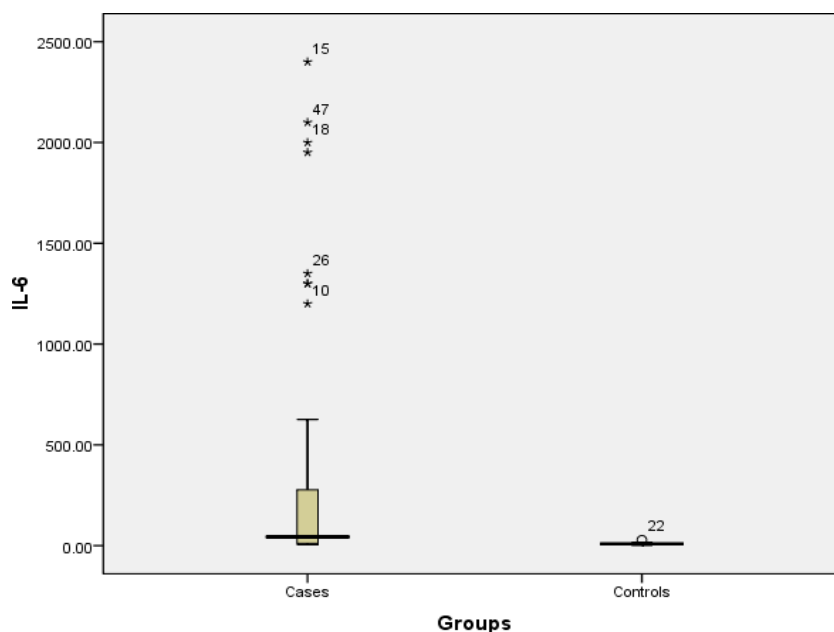|	Groups						Mann Whitney U test	
	Cases		Controls		Total		Z value	p-value
	Mean	SD	Mean	SD	Mean	SD		
IL-6	394.41	699.07	10.34	7.35	317.60	642.70	-3.250	**0.001**
Serum procalcitonin	18.44	23.97	1.48	1.18	15.05	22.46	-3.799	**<0.001**

Fig. 2.1: Box & Whisker diagram showing the mean & standard deviation ofIL-6 in cases & control.

The classification of different inflammatory markers of both groups based on their mean (±SD) is summarized in Table 2. The mean(±SD) IL-6 of cases is found to be 394.41 ± 699.07 and controls is 10.34 ± 7.35, the overall mean(±SD) of IL-6 is found to be 317.60 ± 642.70. There is a significant difference found in both groups (p value = 0.001). (Fig. 2.1)
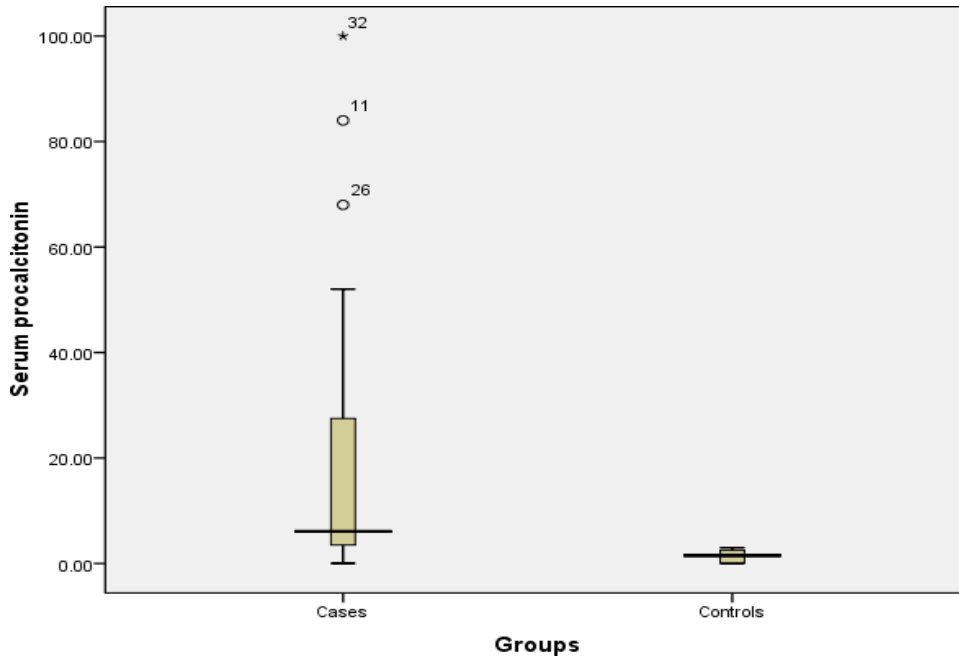

Fig:2.2Box & Whisker diagram showing the mean & standard deviation of Serum procalcitonin in cases& control.

The mean(±SD) serum procalcitonin of cases is found to be 18.44 ± 23.97 and controls is 1.48 ± 1.18, the overall mean(±SD) of serum procalcitonin is found to be 15.05 ± 22.46 There is a significant difference found in both groups (p value < 0.001). (Fig. 2.2)

Table 3 : Relation between inflammatory markers and periodontal status.

	Periodontal status						ANOVA test	
	Mild		Moderate		Severe		F value	p-value
	Mean	SD	Mean	SD	Mean	SD		
IL-6	14.89	11.40	572.11	809.13	915.49	865.70	12.28	**<0.001**
Serum procalcitonin	7.11	15.72	21.02	29.17	31.52	22.01	5.86	**0.005**
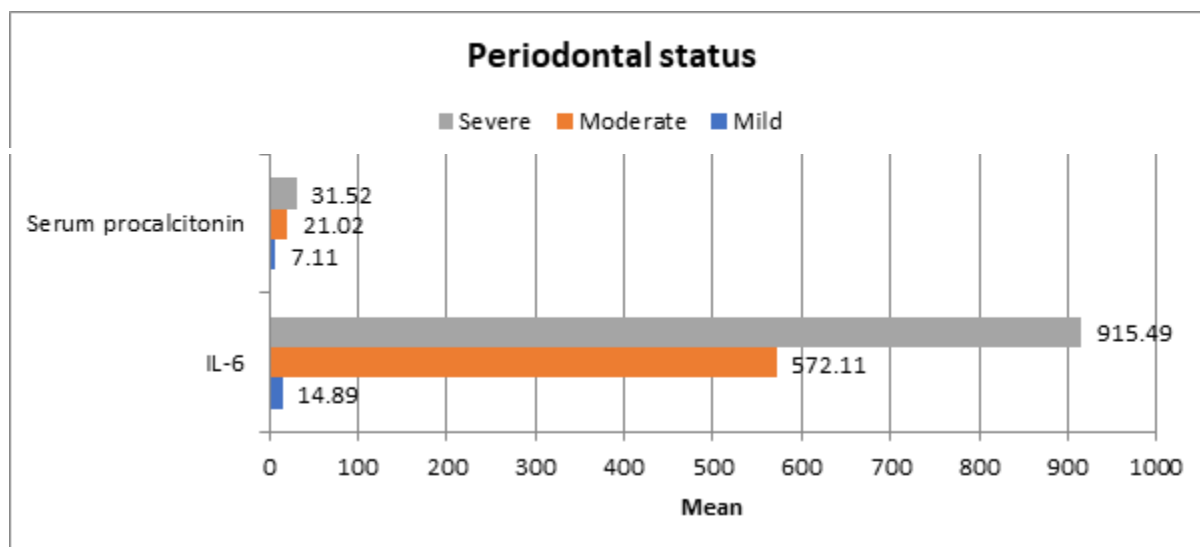
Fig. 3: Bar graph showing the mean of inflammatory markers with respect severity of periodontitis status in cases.

The distribution of different inflammatory markers with periodontal status of the he study population has been depicted in Table 03 and fig 03. The mean($\pm$SD) interleukin-6 of mild periodontitis patients is found to be 14.89 $\pm$ 11.40; for moderate periodontitis patients is 572.11 $\pm$ 809.13; and for severe periodontitis patients was 915.49 $\pm$ 865.70. There is a significant difference found between interleukin-6 with periodontal status (p value = <0.001). It can be concluded that the mean serum procalcitonin of the patients increase with the respective grouping of patients with mild, moderate, and severe periodontitis. The change in the mean is significant (p value= 0.005)

Table 4: shows the intra-group comparison of periodontal status with different Inflammatory markers.

	Periodontal status					
	Mild vs Moderate		Mild vs Severe		Moderate vs Severe	
	Mean diff.	p-value	Mean diff.	p-value	Mean diff.	p-value
IL-6	-557.22	**0.013**	-900.61	**<0.001**	-343.38	0.311
Serum procalcitonin	-13.91	0.146	-24.41	**0.006**	-10.50	0.476

In the study of mild versus moderate, it is depicted that interleukin-6 were found significantly differ; p values are 0.013 .When mild versus severe cases comparison was carried out, all the inflammatory markers including interleukin-6 and serum procalcitonin were found to be statically significant with p values equal to <0.001 and 0.006.(table:4)

IV.   Discussion

CKD and periodontitis, these two pathological conditions have been independent of each other.[10 ,11]. However, recent findings demonstrated a bidirectional relationship between CKD and periodontitis. Moreover, clinical trials and cross-sectional studies suggested an association between CKD and the severity periodontal problems[12,13,14]. Earlier studies explained that CKD and peridontitis both had underlying inflammatory process but these studies did not had proper explanation in this regard may be due to lack of inflammatory markers .Therefore, we designed this study to evaluate of such inflammatory markers which can measured the affect of periodontitis in chronic kidney disease patients and may be used as important biomarkers for the monitoring .In our study we found that serum interleukin-6 and serum procalcitonin both are statistically significant(p value=0.001& p value<0.001 respectively) in CKD with periodontitis patient .These markers were more significant in higher stages of CKD as severity of periodontitis increased. Due to lack of literature we are unable to compare this data so in this regard our study is unique. Therefore, our study is first one from our country in which we found that these marker are statistically significant in chronic kidney disease with periodontitis so this explained that periodontitis is directly affect the prognosis of ckd patient .Hence serum interleukin-6 and serum procalcitonin may be used as prognostic marker in management of periodontitis in ckd patient which indirectly improve the quality of life.

V.   Conclusion

This study provides a useful approach to the future management of CKD patients, focusing on the importance of monitoring oral hygiene by using theses marker serum interleukin-6 and serum procalcitonin as prognostic marker which has often been neglected. Periodontal therapy should be part of the treatment in retarding the progression of CKD patients in the future. More studies should be performed to further enhance our knowledge in this research area to support the study findings.

Limitations

The limitation of this study is that our sample size was small.

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Abbreviations

CKD   –   Chronic Kidney Disease

IL-6   –   Interleukin -6

Serum PCT   –   Serum procalcitonin

PO   –   Periodontitis

Mild P   –   Mild Periodontitis

Moderate P   –   Moderate Periodontitis

Severe P–   Severe Periodontitis