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Original Article

To study C reactive protein as an inflammatory marker in pre and post dialysis patients of chronic kidney disease with diabetes and hypertension

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ABSTRACT

Background: Chronic kidney disease encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney functions and a progressive decline in glomerular filtration rate. The present study was planned to assess C reactive protein as an inflammatory marker in pre and post dialysis patients of chronic kidney disease with diabetes and hypertension. **Materials & Methods:** The study included one hundred patients attending OPD and indoor medical wards of Guru Nanak Dev Hospital, Amritsar. The patients were subjected to detailed history and clinical examination and other investigations. Information regarding age and sex distribution, clinical diagnosis was collected. Biochemical testing for serum creatinine was performed in the Biochemistry department of Guru Nanak Dev Hospital. In a secondary analysis, C- reactive protein relation to albuminuria [defined as an urinary albumin-to-creatinine ratio (UACR) of > 30 mg/g on spot or 24-hour urine collection] was considered. Estimation of blood urea was done by Berthelot method. Serum creatinine was measured by Jaffe's method The data was collected systematically and analysed statistically according to the standard statistical methods. **Results:** Mean pre-dialysis CRP was found to be 3.10 mg/L.Mean post-dialysis CRP was found to be 3.36 mg/L. Significant results were obtained while comparing the mean pre-dialysis and post-dialysis CRP levels. **Conclusion:** CRP value increases after dialysis, suggesting increased systemic inflammatory process which is a risk factor for cardiovascular morbidity and mortality.

Key Words: Chronic kidney disease, C Reactive proteins.

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INTRODUCTION

Chronic kidney disease encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney functions and a progressive decline in glomerular filtration rate. It is defined as progressive loss in kidney function as either kidney damage or a decreased glomerular filtration rate of less than 60 ml/min/1.73 m^2 for at least 3 months.[1]

Dialysis is an artificial replacement of kidney functions. It is performed in renal failure cases, those who have ESRD. It is usually done in Chronic Kidney Disease when the glomerular filtration rate falls below 15 ml/min/1.73m^2. This procedure may be responsible for the development of oxidative stress, due to an imbalance between the overproduction of reactive oxygen species and reduced defense mechanism of the body. Oxidative stress disrupts the normal functioning of the cell.[2]

In recent years,hemodialysis has been successful in extending life span of renal patients and is effective in correcting the metabolic abnormalities that contributes to morbidity in hemodialysis patients. Factors like dialysis membrane, purity of dialysis water and dietary limitations make CKD patients on dialysis more susceptible to oxidative stress and inflammation.[3-5]

Hence under the light of above obtained data, it is worthwhile to determine the alterations of oxidant-antioxidant status and vascular inflammation in pre and post dialysis patients of Chronic Kidney Disease. For this we planned the present study to assess C reactive protein as an inflammatory marker in pre and post dialysis patients of chronic kidney disease with diabetes and hypertension.

MATERIAL & METHODS

The study included one hundred patients attending OPD and indoor medical wards of Guru Nanak Dev Hospital, Amritsar. This study was undertaken after approval of the Institutional Ethics Committee, Government Medical College, Amritsar. Written informed consent was obtained in vernacular language for

their inclusion. The patients were subjected to detailed history and clinical examination and other investigations. Information regarding age and sex distribution, clinical diagnosis was collected. The data was analyzed statistically.

Chronic Kidney Disease has been defined according to the criteria.[1]

Kidney damage for greater than or equal to 3 months as defined by structural or functional abnormalities of the kidney, manifested by either

- Pathological abnormalities
- Glomerular filtration rate less than 15ml/min/1.73m^2 with our without kidney damage

MEASUREMENT OF RENAL FUNCTION:

Biochemical testing for serum creatinine was performed in the Biochemistry department of Guru Nanak Dev Hospital. The primary measure of renal function is glomerular filtration rate, as calculated by the Modification of Diet and Renal Disease (MDRD) equation. In a secondary analysis, C- reactive protein relation to albuminuria [defined as an urinary albumin-to-creatinine ratio (UACR) of > 30 mg/g on spot or 24-hour urine collection] was considered.

Glomerular filtration rate was calculated using Cockroft Gault equation which is:

$$eGFR = \frac{(140 - \text{age}) \times \text{body weight in kilograms}}{72 \times \text{serum creatinine in mg/dl}} \times (0.85 \text{ for women})$$

MEASUREMENT OF C- REACTIVE PROTEIN:

C-reactive protein was measured in the Biochemistry department of Guru Nanak Dev Hospital. C-reactive protein test was done by Nephelometry. The test gives results in 25 minutes with sensitivity down to 0.04mg/L.

Estimation of blood urea was done by Berthelot method. Serum creatinine was measured by Jaffe's method

STATISTICAL ANALYSIS

The data was collected systematically and analysed statistically according to the standard statistical methods. SPSS software was used for assessment of level of significance. Paired t- test was used for analysis. P value of less than 0.05 was taken as significant.

RESULT

The table 1 shows the distribution of subjects according to gender. The number of male subjects was found to be 57 (57%) and number of female was found to be 43 (43%). The table 2 shows the mean age of the patients of the present study. The mean age was found to be 57.57 with SD value of 8.88. The minimum age was 45 years whereas maximum age was 85 years. The table 3 shows the age wise distribution of patients and their respective mean CRP pre-dialysis. The mean CRP pre dialysis in the age group of 40-50 years, 51-60 years, 61-70 years and more than 70 years was 3.09, 3.17, 3.01, 3.32 respectively.

The table 4 show the age wise distribution of patients and their respective mean CRP post dialysis. The mean CRP post dialysis in the age group of 40-50 years, 51-60 years, 61-70 years and more than 70 years was 3.33, 3.44, 3.27, 3.57 respectively. The table 5 shows the comparison of CRP pre-dialysis and post-dialysis. The Mean CRP (mg/L) in Pre-dialysis was found to be 3.10 with SD (mg/L) value of 0.38 whereas the Mean CRP (mg/L) in Post-dialysis was found to be 3.36 with SD (mg/L) value of 0.37.

Table 1: Gender wise distribution of patients

Gender	Number of subjects	Percentage
Males	57	57
Females	43	43
Total	100	100

Table 2: Mean age of the patients of the present study

Parameter	Value
Mean age (years)	57.57
SD	8.88
Minimum	45
Maximum	85

Table 3: Age wise distribution of the mean CRP pre-dialysis

Age Group(in years)	Mean CRP Pre Dialysis
40-50	3.09
51-60	3.17
61-70	3.01
>70	3.32

Table 4: Age wise distribution of the mean CRP post-dialysis

Age Group(in years)	Mean CRP Post Dialysis
40-50	3.33
51-60	3.44
61-70	3.27
>70	3.57

Table 5: Comparison of CRP pre-dialysis and post-dialysis

Parameter	Pre-dialysis	Post-dialysis	Test statistic	p- value
Mean CRP (mg/L)	3.10	3.36	5050	0.000
SD (mg/L)	0.38	0.37		

DISCUSSION

The study included 100 patients attending OPD and indoor medical wards of Guru Nanak Dev Hospital, Amritsar. Mean age of the patients of the present study was 57.57 years. Our results were in concordance with the results obtained by previous authors who also reported similar findings in their respective studies. In the study conducted by Lee Je et al and Adejumo et al, mean age of the patients was reported to be 51 years and 49.09 years respectively.[6, 7]

57 percent of the patients of the present study were males while remaining 43 percent were females. Our results were in concordance with the results obtained by Lee JE et al, who reported that 68 percent of the patients of their study group were males. However; contrasting results have been reported by Braga FLM et al, who have reported female preponderance in their study.[6, 8]

Mean CRP pre-dialysis was found to be 3.11 mg/l while mean CRP post-dialysis was found to be 3.36 mg/l.Significant results were obtained while comparing the mean CRP values pre-dialysis and post-dialysis.Similar results were reported in the study of Ugonabo MC et al who also observed similar findings. The slight increase in the mean level of post-dialysis of the first session (though not significant, P>0/05) in their study correspond to that by Reyes et al. This increase cannot be strongly accepted because both the pre- and post-dialysis of the first session showed significant difference when compared together (P>0.05).[9- 11]

In present study, results were in concordance with the results obtained by EL-Attar HA et al who observed a significant increase in sensitive CRP in patients on hemodialysis when compared to both controls and patients on non-dialytic therapy with CKD.[12]

Although our study shows that the level of CRP is increased in CKD, there are still some controversies in the level of CRP in pre- and post-dialysis. Dahaba and Rehak, (2003) reported that there was no significant difference between CRP plasma concentrations before and after three successive sessions of haemodialysis.[13]

. In the present study the number of patients with IHD was found to be 14 (14.0%). The number of patients with LVH with LAD were found to be 46 (46.0%) whereas with NORMAL SINUS RHYTHM were found to be 28 (28.0%). The number of patients with TALL T WAVES was found to be 12 (12.0%). Shafi S et al studied the ECG abnormalities in patients with CKD. It was a cross-sectional study done between ages of 20-80 years with CKD not previously on renal replacement therapy who were admitted to nephrology ward at a tertiary care facility over a 6-month period. Overall 78.4% of all CKD patients have one or more ECG abnormality. Left ventricular hypertrophy (40%), Q waves (27.2%), ST segment elevation or depression (23.4%), prolonged QRS duration (19.2%), tachycardia (17.6%) and left atrial enlargement (17.6%) were the most common abnormalities.[14]

Our study showed that the number of patients with Microcytic Hypochromic Anemia were33.0%, whereas the number of patients with Normocytic Normochromic Anemia was65.0%. The numbers of patients with Normocytic Normochromic picture with microcytes were found to be 2.0%.ArjunChakravarti et al studied the haematological profile in CKD patients undergoing dialysis and showed a 100% prevalence of anemiain patients on hemodialysis. It was predominantly of the normocytic normochromic type, suggesting EPO deficiency as the primary cause. However, in some cases, the presence of abnormal cells such as fragmented RBCs, pencil cells and macro-ovalocytes suggest other contributory factors, such as hemolysis, iron deficiency or folate/vitamin B12 deficiency.[15]

Mahmood HAM et al showed the incidence of pleural effusion in CKD and ESRD patients was 80.8%, followed by Pyopneumothorax then Pneumothorax[16]. Our study showed that the percentage of patients with Bilateral pleural effusion were 10%, whereas patients with Left sided pleural effusion were found to be 18%. The percentage of Right side pleural effusion were found to be 10%

Other studies have also shown that higher CRP concentrations are related to reduce kidney cortex width and reduced renal cortex width is related to increase blood pressure. Hence, CRP may be a marker of kidney inflammation with increased scarring in the kidney cortex, which may then relate to blood pressure.[17-21]

Adejumo OA, in their study, also reported a significant association between some lipid parameters and CRP levels. Serum CRP correlated positively, in their study, with serum TG and negatively with serum HDL-C.[50] The Atherogenic index of plasma(AIP) has been

reported to have higher sensitivity compared to other lipid ratios in estimating atherogenic index and predicting cardiovascular events in both CKD and non-CKD patients. These associations therefore, strengthen the fact that CRP is associated with increased cardiovascular event risk in CKD patients.[22-24]

Dialysis is a state of chronic inflammation. Stimuli that lead to the development of chronic inflammatory state are infections, repeated exposure to dialysis filters and auto-oxidation products. As a result of these processes, the levels of C-reactive protein (CRP) increase in the body. CRP is considered a significant risk factor for the development of CVD and the most important predictor of cardiovascular mortality in patients with the end-stage renal disease. Although it has been shown that interleukin 6 (IL-6) is a stronger predictor of above mortality than CRP, but determination of CRP levels is more reliable and cost-effective in everyday practice.[22-24]

Multiple factors responsible for inflammation in post dialysis patients include exposure to endotoxin contained in dialysate, generation of complement fractions as a result of plasma protein-membrane contact, back filtration of contaminated dialysate to the blood compartment and direct contact of blood cells with the dialysis membrane.[25,26]

Thus it can be concluded that CRP is an important inflammatory marker in CKD patients and its value increases in post dialysis patients.

CONCLUSION

There is high prevalence of C - reactive protein in CKD patients with diabetes and hypertension with end stage renal disease.CRP value increases after dialysis, suggesting increased systemic inflammatory process which is a risk factor for cardiovascular morbidity and mortality.

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