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HIGH SENSITIVITY C-REACTIVE PROTEIN IN CHRONIC RENAL FAILURE WITH AND WITHOUT CARDIOVASCULAR COMPLICATIONS

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ABSTRACT

Introduction: Chronic renal failure patients are at greater risk of cardiovascular disease. Higher than expected cardiovascular morbidity and mortality in this population has been attributed to dyslipidaemia as well as inflammation. The causes of inflammation in chronic renal failure patients are multifactorial. Several markers were used for the detection of inflammatory reaction in patients with chronic renal disease. These markers can be used for the prediction of future cardiovascular events. Among the several parameters of inflammatory markers, serum, CRP is well known and its advantages for the detection of inflammation and its predictor ability has been evaluated in several studies. **Materials and methodology:** This work was done in department of Medicine at Government Rajaji Hospital, attached to the Madurai Medical College, Madurai in collaboration with departments of Nephrology and Cardiology. It is a cross sectional and analytical study. 42 newly detected CRF patients were included in the study along with 10 controls (normal individuals) and rest were cases which are newly detected CRF who satisfied the inclusion criteria were selected for the study. Patients with elevated blood urea levels, elevated serum Creatinine levels and Ultrasound abdomen showing medical renal disease were included in study. **Results and Conclusion:** The hs-CRP levels among CRF patients was independent of age, gender or serum creatinine levels. The hs-CRP levels was significantly elevated in CRF patients when compared to healthy controls. The hs-CRP levels were elevated significantly in those CRF patients with cardiovascular complications when compared with those without cardiovascular complications there by indicating that elevated hs-CRP is a marker of development of cardiovascular morbidity. The present study has brought out an association between elevated hs-CRP and degree of albuminuria, haemoglobin levels as well as cardiovascular morbidity. CRF patients with elevated hs-CRP should be adequately counselled regarding their proneness to develop cardiovascular complications.

KEYWORDS: Chronic renal failure, hs-CRP, Cardiovascular diseases.

INTRODUCTION

Cardiovascular disease is the leading cause of morbidity and mortality in patients with CRF (Chronic renal failure) at all stages. Previous studies has shown a rise in CVD (Cardiovascular disease) risk in CRF patients from 10 to 200 times depending on the stage of CRF, other risk factors and comorbid conditions. Between 30 to 45% of patients reaching ESRD (end stage renal disease), already have advanced cardiovascular complications which has been repeatedly proven by many studies. Thus the management of patients with CRF should stress prevention of cardiovascular complications as well as measures aimed at alleviating the progression and complications of CRF itself.[1] It is obvious that 'traditional risk factors, such as hypertension, chronic heart failure, dyslipidaemia, tobacco smoking and diabetes mellitus may influence the rise in cardiovascular mortality rate observed in these patients. However, based on recent research, it is evident that also other 'non-traditional', risk factors such as, chronic inflammation, oxidative stress may contribute to an increased cardiovascular mortality among dialysis patients.[2] Traditional risk factors are inadequate as predictors of cardiovascular mortality in CRF patients. Even though diabetes mellitus and smoking were strongly associated with CVD, neither serum total cholesterol nor systolic blood pressure was associated with coronary heart disease in these patients.[3] Hence it is prudent to look for other factors contributing to the morbidity and mortality in CRF patients. Recently CRP (C-reactive protein) has emerged as a more sensitive and specific indicator of an "acute phase" inflammatory mediator. Our study tries to evaluate the correlation of hs-CRP levels in CRF patients, particularly the CRF patients with cardiovascular complications. The available western reports concluded an association between elevated CRP levels and cardiovascular morbidity and mortality among CRF cases. It is likely that hs-CRP may be altered among

the CRF patients with cardiovascular diseases. However authenticated reports about this is very few in our geographical area and our presents study attempts to find out the same and its usefulness in clinical practice. Hence aim of our study is to estimate the hs-CRP levels in newly detected chronic renal failure patients and to identify variations in the hs-CRP level among CRF patients with and without cardiovascular complications. Also to find out the correlation between hs-CRP levels and albuminuria, haemoglobin levels as well as cardiovascular complications among CRF patients.

MATERIALS AND METHODOLOGY

This work was done in department of Medicine at Government Rajaji Hospital, attached to the Madurai Medical College, Madurai in collaboration with departments of Nephrology and Cardiology. It is a cross sectional and analytical study. This study was done from January 2005 to February 2006. Approval for the study was obtained from the ethical committee of Government Rajaji Hospital, Madurai. Prior informed consent was obtained from all patients included in the study. 42 newly detected CRF patients were included in the study along with 10 controls (normal individuals) and rest were cases which are newly detected CRF who satisfied the inclusion criteria were selected for the study. Patients with elevated blood urea levels, elevated serum Creatinine levels and Ultrasound abdomen showing medical renal disease were included in study. Patient with diabetes mellitus, Previous history of IHD, Acute & chronic liver diseases, Rheumatoid arthritis, documented connective tissue disorders, Previously diagnosed renal failure patients, smokers, fever within 1 week prior to admission, skin infections, Malignancy, children, pregnant women and patients on Immunosuppressive drug therapy were excluded from study.

We collected socio demographic data like age, sex and clinical data were collected. The study subjects were subjected to relevant investigations. Anaemia was identified. Systolic and diastolic blood pressures were measured. General and Systemic examination was done. Cardiovascular risk factors were assessed. Laboratory investigations like TC, DC, Hb%, Urine albumin, Urea & creatinine were done. Serum hs-CRP estimation was done by Nephalometry method. ECG, ECHO, and Ultra sonogram abdomen were also done. There were about 272 CRF patients diagnosed during the study period, of whom more than 65% were found to be diabetics. 13% were IHD patients. Analysis of data was done utilizing the software - Epidemiological Information Package 2002. Mean standard deviation and 'p' values were calculated using this package. Chi Square test was done were ever necessary to find out significance of relationship between both groups. Since the variances were not homogenous, Kruskal Wallis test (X^2 test) was used to find out the significance of difference.

RESULTS

In the present study 42 cases of CRF satisfied rigid selection criteria. Their age ranged from 23 years to 67 years and the mean ± S.D. was 48.6 ± 10.3 years. The mean age for the control group was 44. ±15.9 years. Among the CRF patients in this study 29 patients (69%) were found to be in the age group between 40 to 60 years. The patients did not differ statistically from the control with reference to age. In our study there were 28 male patients and 14 Females patients; the control group consisted of 5 males and 5 females. There was no statistical difference as for as the gender status of the study and control group.

Table 1: Blood parameters comparison between cases & controls.

Parameters	Cases		Controls	
	Mean	S.D	Mean	S.D
Blood sugar mg%	101.5	15.8	109.4	806
Urea mg%	143.8	46.1	35.3	2.8
Sr.Creatinine mg%	6.5	2.83	0.93	0.12
Hb. Gm%	8.75	1.31	13.6	0.4
C.R.P mg%	1.22	0.99	0.08	0.01
Sys. B.P mmHg	165.07	23.8	119	9.9
Dias. B.P.mmHg	104	13.3	77.2	5.5

The hs-CRP levels in the study group were significantly elevated when compared to the control group. Coming to creatinine level the mean level of study group was 6.5 ± 2.83 in comparison to control group which is 0.93 ± 0.12. The mean Hb% in this study group was 8.75 ± 1.31 gm% which was significantly lower than the control group - 13.6 ± 0.4 gm%. The CRP level varied from 0.10 - 3.02mg% in the study group whereas in the control group it varied from 0.07 - 1.1mg%. The mean CRP level in the study group was 1.22 ± 0.99. The mean CRP level in the control group was 0.08 ± 0.01. This was statistically significant. It was also found the CRP level was independent of serum creatinine.

Table 2: CRP levels in cases and controls.

	CRP Levels (mg /dl)				
	Range	**Mean**	**S.D.**	**'p' value**	**Significance**
Cases	0.10-3.02	1.22	0.99	0.0001	Significant
Controls	0.07-1.1	0.08	0.01		

Yet another indirect evidence of renal damage was the significant anaemia noted in the CRF patients. Of the 42 patients 36 (85.7%) had haemoglobin < 10gm% which was statistically significant. Among the CRF patients the mean CRP levels was 1.39 mg% ± 0.05 in those who were anaemic (haemoglobin <10gm %) which was statistically significant when compared with those without anaemia were 0.18mg% ± 0.97mg%. The CRP levels increased in direct proportion to the severity of albuminuria, which was statistically significant (0.018). Of the 42 CRF patients 15 had normal cardiac function on Echo whereas rest 27 patients had cardiac abnormalities in the form of LVH, Ischaemic changes, LV dysfunction and Pericardial Effusion.

Table 3: Hs-CRP level in comparison with CVD.

Cardiac Status	**Hs-CRP Levels**				
	Range	**Mean**	**S.D.**	**'p' value**	**Significance**
Without CVD	0.10-0.3	0.18	0.06	.0001	Significant
With CVD	0.13-3.02	1.96	0.45		

The mean CRP level in CRF patients without CVD was 0.18mg ± 0.06 (moderate cardiovascular risk 0.1 - 0.3mg/dL) and the mean CRP level in CRF patients with CVD was about 10 times higher, i.e., 1.96 ± 0.45. The statistical analysis was very much significant (p- 0.0001).

DISCUSSION

Despite the recent considerable improvements in Renal replacement therapy, cardiovascular disease still remains the main cause of morbidity and mortality in CRF patients 10. It is evident from recent studies[2,4,5] that the atherosclerotic process is accelerated in CRF patients. A number of 'non-traditional' risk factors for CVD, such as homocysteinemia, oxidative stress, vascular calcification, malnutrition and inflammation are commonly found in CRF patients. Evidence from experimental and clinical studies has shown that inflammation in general, and CRP specifically, may contribute directly to pathogenesis of atherosclerosis and its complications both in general community and in patients with CRF.[6] Recent studies[7,8,9] recognized that about 30-50% of predialysis, HD and PD (CRF) patients suffered from CVD and they had elevated CRP levels.

In the present study that the mean hsCRP level was 1.22 mg/dL in CRF patients which was significantly higher than the mean CRP level of the control group 0.08 mg/dL (<0.10 mg%). The mean CRP level of 1.22mg/dL in our CRF patients was definitely higher than the reference value of 0.3mg/dL for high cardiovascular risk (American Heart Association guidelines) 19. Elevated CRP as an independent risk factor for cardiovascular disorders was confirmed by various authors.[10,11] It was applicable to both men and women and across all age levels as well as to diverse populations. Elevated CRP levels in the present study was independent of age and gender. Thus the present observation of elevated hsCRP levels in CRF patients concurred with early published report.

The most significant process that correlates with inflammation is atherosclerotic CVD as evidenced by elevated CRP. Recent studies have established that the levels of pro-inflammatory cytokines such as IL-6 or acute phase proteins like CRP predict CVD.[11]

In the present study the echocardiographic evaluation revealed that out of the 42 CRF patients only 15 had normal cardiac function and 27 patients (64.3%) had cardiovascular abnormalities in the form of left ventricular hypertrophy, ischaemic changes (hypokinesia of wall/septum) LV dysfunction and pericardial effusion. The mean CRP level in CRF patients without CVD was 0.18 mg/dL whereas for CRF patients with CVD was 1.96 mg/dL which was significantly higher. An association between elevated CRP and CVD were shown by previous studies from different parts of the world.[12] In a recent updated meta-analysis including 2,557 cases, Danesh[3] et al reported that the combined risk ratio for coronary heart disease was 1.9 times higher in the patients who had the highest CRP. Elevated CRP has been shown to predict cardiovascular mortality by many previous authors.[9] The same conclusion was given by few previous researechers.[5,13]

Anaemia is commonly seen in CRF and its severity parallels roughly with the degree of renal failure.[14] Similar observations were made among CRF patient of the present study. It was found that 36 of the 42 CRF (85.7%) patients suffered from anaemia, which was statistically significant. The mean hsCRP levels of this anaemic CRF patients was 1.39mgldL which was very high (8 times higher) than the mean hs-CRP level of 0.18mgldL in CRF patients without anaemia. The severity of anaemia indirectly correlated with the severity of CRF. Interestingly it is to be noted here that anaemia per se does not influence CRP levels.

An attempt was made to find out whether any association exists between severity of albuminuria and serum levels

of hs-CRP. In the present study severity of albuminuria showed direct relation to severity of CRF. Of the 42 patients 20 had albuminuria of 1+, 17 had 2+ and 3 had 3+. The prevalence of albuminuria was (95.2%) in the CRP patients. And the mean CRP levels showed a linear relation with the degree of proteinuria, indirectly implicating the severity of CRF. The present study brought out significantly elevated hs-CRP levels in cases of CRF and association between hs-CRP and albuminuria, anaemia and cardiovascular complications, which were supported by an series of published literature from different parts of the world.

CONCLUSION

The hs-CRP levels among CRF patients was independent of age, gender or serum creatinine levels. The hs-CRP levels was significantly elevated in CRF patients when compared to healthy controls. The hs-CRP levels were elevated significantly in those CRF patients with cardiovascular complications when compared with those without cardiovascular complications there by indicating that elevated hs-CRP is a marker of development of cardiovascular morbidity. The present study has brought out an association between elevated hs-CRP and degree of albuminuria, haemoglobin levels as well as cardiovascular morbidity. CRF patients with elevated hs-CRP should be adequately counselled regarding their proneness to develop cardiovascular complications.

REFERENCES

1. Albert CM, Ma J, Rifa N et al: Prospective study of CRP, homocysteine and plasma lipid levels as predictors of sudden cardiac death. Circulation, 2002; 105: 2595.
2. Cheung AK, Sarnak MJ, YanG, Dwyer JT, Heyka RJ, Rocco MV et al: Atherosclerotic cardiovascular disease risks in chronic haemodialysis patients. Kidney Int., 2000; 58: 353-362.
3. Danesh J, Whincup P, Walker M et al. Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ, 2000; 321: 194-204.
4. Lindner A, Charra B, Sherrard DJ, Schribner BH: Accelerated atherosclerosis in prolonged maintenance haemodialysis. N Engl J Med., 1974; 290: 697-701.
5. Iseki K, Tozawa M, Yoshi S, Fukiyama K: Serum C-reactive and risk of death in chronic dialysis patients. Nephrol Dial Transplant, 1991; 14: 1956- 1960.
6. Pepys MB, The acute phase response and C-reactive protein, Oxford Textbook of Medicine, 4th edition, Vol II, 2003; 151-156.
7. Owen WF, Lowrie EG: C-reactive protein as an outcome predictor for maintenance haemodialysis patients. Kidney Int., 1998; 54: 627-636.
8. Yeun JY, Kaysen GA: Acute phase proteins and peritoneal dialysis:albumin loss are the main determinants of serum albumin and peritoneal dialysis patients. Am J Kidney Dis., 1997; 30: 923-927.
9. Zimmennann J, Herrlinger I, Precy A, Metzger T, Wanner C: Inflammation enhances cardiovascular risk and mortality in haemodialysis patients. Kidney Int., 1999; 55: 648-658.
10. Pradhan AD, Manson JE, Rossonw JE et al: Inflammatory biomarkers, hormone replacement therapy and incident coronary heart disease; prospective analysis from the women 's health initiative observational study. JAMA, 2002; 108: 647.
11. Braunwald E, Ridker PM, Libby P, Risk factors for atherothromboti c disease, Braunwald' s Heart Disease Elsevier and Saunders, Philadelphia, USA-ih edition, 2005; 939-958.
12. Stenvinkel P, Heimburger 0, Lindholm B, Kaysen GA, Bergstrom J: Are there two types of malnutrition in CRF? Evidence for relationships between malnutrition, inflammation and atherosclerosis (MIA syndrome). Nephrol. Dial Transplant, 2000; 15: 935-960.
13. Bergstorm J, Heinburger 0, Lindholm B, Qureshi AR: Elevated serum C- reactive protein is a strong predictor of increased mortality and low serum albumin in hemodialysis patients. JAm Soc Nephrol, 1995; 6: 573.
14. Malhotra K.K, Chronic renal failure, API Textbook of Medicine, Siddarth NS (Edi) India, 7'h edition, 2003; 695-699.