http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 14 (10): 595-599, 2011
ISSN 1028-8880 / DOI: 10.3923/pjbs.2011.595.599

Evaluation of Serum C-reactive Protein Level and its Related Factors in Hemodialysis Patients in Sari, Iran

[1]Afshin Gholipour Baradari, [2]Amir Emami Zeydi, [3]Fatemeh Espahbodi and [4]Soheyla Shahmohammadi
[1]Department of Anesthesiology and Critical Care, Faculty of Medicine,
Mazandaran University of Medical Sciences, Sari, Iran
[2]MSc of Critical Care Nursing, Mazandaran University of Medical Sciences, Sari, Iran
[3]Department of Nephrology, Mazandaran University of Medical Sciences, Sari, Iran
[4]CRNA, Mazandaran University of Medical Sciences, Sari, Iran

Abstract: Chronic inflammation, as reflected by increased level of acute phase protein such as C-reactive Protein (CRP) is highly prevalent in hemodialysis patients. CRP is a strong predictor of overall and cardiovascular mortality and morbidity in hemodialysis patients. This research was conducted to determine the C-reactive Protein (CRP) levels and its correlation to demographic and clinical characteristics and Laboratory values in hemodialysis patients in Sari, Iran. In a cross sectional study, 147 hemodialysis patients were studied. Patients' demographic and clinical data were recorded and also serum CRP, Cholesterol, Albumin, Phosphorous, Calcium, Hemoglobin and Hematocrit levels were measured. Overall, the mean CRP concentration was 15.8 mg L^{-1}. With considering to the different cutoff point (5, 6.2, 10 mg L^{-1}) for CRP level, 107 patients (72.8%) had CRP level >5 mg L^{-1}, 99 patients (67.3%) had CRP level>6.2 mg L^{-1} and 77 patients (52.4%) had CRP level >10 mg L^{-1}. The CRP levels greater than 6.2, had a direct statistically significant correlation with duration of hemodialysis and phosphorus level ($p = 0.01$). Also, CRP levels above 10 mg L^{-1} had a direct statistically significant correlation with age and phosphorus levels ($p = 0.02$). According to the prevalence of high CRP level and it's correlation with age, duration of hemodialysis and phosphorus level in hemodialysis patients, CRP level should be screened in this group of patients routinely because of its prognostic importance.

Key words: C-reactive protein, inflammation, phosphorus, end stage renal disease, dialysis, hemodialysis

INTRODUCTION

The number of patients with End Stage Renal Disease (ESRD) increases rapidly (Kalantar-zadeh *et al*., 2003). In spite of the noticeable improvement in dialysis technology and patients care (Pecoits-Filho *et al*., 2002), unacceptably the mortality rate of hemodialysis patients has remained high (Ortega *et al*., 2002). Cardiovascular Disease (CVD) remains the major cause of morbidity and mortality in ESRD patients (Nasri *et al*., 2006a), accounting for approximately half of all death in these patients (Zimmermann *et al*., 1999). Although, the prevalence of classic and traditional cardiovascular risk factors such as hypertension, hypercholesteremia, etc. is high in this population, it cannot fully explain this increased incidence of cardiovascular disease (Selim *et al*., 2006). Therefore, the focus of research has shift on newer cardiovascular risk factors in these patients such as chronic inflammation. Chronic inflammation, as reflected by increased level of acute phase protein such as CRP (Korevaar *et al*., 2004) is highly prevalent in hemodialysis patients. CRP is an acute-phase protein (Al-Hamdan *et al*., 2009) and a Well-known indicator (Avram *et al*., 2005) and a sensitive marker of underlying inflammation (Ducloux *et al*., 2002). CRP is a strong predictor of overall and cardiovascular mortality and morbidity in hemodialysis patients (Racki *et al*., 2006; Korevaar *et al*., 2004). Chronic inflammation may lead to adverse consequences such as decline in appetite, increased rate of protein depletion in skeletal muscle and other tissues, muscle and fat wasting, hypercatabolism, endothelial damage and atherosclerosis (Kalantar-zadeh *et al*., 2003). Therefore, monitoring of the inflammatory status of hemodialysis patients is generally recommended (Hung *et al*., 2008) and measurement of CRP may faster determine risk of death in chronic dialysis patients (Iseki *et al*., 1999). Considering the importance of inflammatory factors, especially CRP, in hemodialysis patients, this research has done, as a basis for subsequent studies.

Corresponding Author: Amir Emami Zeydi, MSc of Critical Care Nursing, Faculty of Nursing and Midwifery, Mazandaran University of Medical Sciences, P.O. Box 481675793, Sari, Iran
Tel: 0098 1512267342-5, 00989111510004 Fax: 0098 1512268915

Hence, the objective of present study was to evaluate serum C-reactive protein (CRP) level and its correlation to demographic and clinical characteristics and Laboratory values in hemodialysis patients in Sari, north of Iran.

MATERIALS AND METHODS

In February 2011, in a cross-sectional study from two hemodialysis centers (Imam Khomeini and Fatemeh Zahra Hospitals), 147 hemodialysis patients, aged between 20-70 years, were studied. All included patients were on chronic hemodialysis for minimum of six months and clinically stable without any obvious active inflammatory state or infectious disease. Patients with history of renal transplantation, overt cardiovascular, liver and autoimmune disease or malignancy were excluded. Also, patients who had a history of vitamin C, alcohol, oil fish and immunosuppressive drugs consumption during 2 months prior to the study were excluded. Dialysis was performed three times a week, 3.5-4 h session and the bicarbonate-based dialysate was used for all patients. Demographic and clinical characteristics of patients were obtained from interview and chart reviews. Approval from Mazandaran University of medical sciences Ethics Committee and informed written consent from patients obtained. At the beginning of the hemodialysis session, 10 mL of blood sample was drawn from venous end of Arteriovenous (AV) fistula for measuring of CRP, Cholesterol, Albumin, Phosphorous, Calcium, Hemoglobin and Hematocrit level. Serum CRP concentration was measured by Nephelometric method (Nycocard, England, Norway). Phosphorus level was measured with Pars azmoon company kit and photometric technique by BT 3000 and serum calcium was measured with ortho-cresolphthalein Complexone (o-CPC). Serum cholesterol and albumin levels were measured by standard kits. Hemoglobin and Hematocrit level was measured with cell counter.

Statistical analysis: Statistical analysis was performed with SPSS version 17 statistical software package. Data were collected and then, analyzed by chi-square, paired t test and fisher statistical tests. Statistical correlations were assessed using bivariate correlation test. The $p<0.05$ has been considered as statistically significant level.

RESULTS

A total of 147 hemodialysis patients were studied. The mean age of patients was 60.38±13.5 years, ranging from 25 to 70 years. The mean duration of hemodialysis was 38.82 months (range from 6 to 214 months). The mean of BMI (Body Mass Index) in patients was 24.62 (95% CI characteristics of the patients are shown in Table 1. 23.77 to 25.47). The demographic and clinical Overall, the mean CRP concentration was 15.8 mg L^{-1} (95% CI: 13.7 to 17.9). Female patients had higher CRP value than men; however the difference was not statistically significant. Overall laboratory values are shown in Table 2. With considering the different cutoff point for CRP level (5, 6.2, 10 mg L^{-1}), 107 patients (72.8%) had CRP level>5 mg L^{-1}, 99 patients (67.3%) had CRP level>6.2 mg L^{-1} and 77 patients (52.4%) had CRP level> 10 mg L^{-1} (Table 3). CRP levels greater than 5 mg L^{-1}, as a cutoff point, didn't have statistically significant correlation with any of the demographics, clinical and laboratories parameters. Relationship between CRP levels greater than 6.2, as a cutoff point, with duration of hemodialysis and phosphorus level was statistically significant. So, higher phosphorus level [in CRP<6.2= 5.5±1.7 and in CRP>6.2= 6.3±1.8 mg dL^{-1} ($p = 0.01$)] and more time being on hemodialysis [in CRP<6.2 = 27.9 and in CRP>6.2 = 44.1 months ($p=0.02$)] has been associated with higher CRP levels. Also, considering CRP cutoff point above 10 mg L^{-1} had a direct statistically significant correlation with age and phosphorus levels. So that the mean age of patients with CRP levels lower than 10 mg L^{-1} was equal

Table 1: Frequency distribution of patient's demographic and clinical characteristics

Characteristics	No.	Percentage
Gender		
Male	74	50.3
Female	73	49.7
Marital status		
Single	8	5.4
Married	139	94.6
Smoking		
Yes	14	9.5
No	133	90.5
Cause of renal failure		
Diabetes	60	40.8
Hypertension	69	46.9
Other causes	18	12.3
Shift of dialysis		
Fixed day	38	25.8
Fixed evening	2	1.4
Fixed night	19	12.9
Mixed	88	59.9

Table 2: Laboratory values in hemodialysis patients (mean and 95% confidence interval)

Test	Overall (n = 147)
Cholesterol (mg dL^{-1})	149 (145 to 152)
CRP	15.8 (13.7 to 17.9)
Albumin (mg dL^{-1})	4.22 (4.16 to 4.29)
Phosphorous (mg dL^{-1})	6.07 (5.77 to 6.37)
Calcium (mg dL^{-1})	8.46 (8.32 to 8.69)
Hematocrit	30.6 (29.7 to 31.5)
Hemoglobin	9.80 (9.51 to 10.08)

Table 3: Frequency distribution of patients with considering different CRP cutoff point

CRP cutoff point	No.	Percentage
>5 mg L^{-1}	107	72.8
>6.2 mg L^{-1}	99	67.3
>10 mg L^{-1}	77	52.4

Table 4: The relationship between different cutoff point of CRP with some demographic and clinical characteristic

Characteristics	CRP	No.	Mean	SD	SEM	p-value (between groups)
Age	≤5	40	59.90	13.04784	2.06304	0.79
	>5	107	60.5607	13.72244	1.32660	
	≤6.2	48	59.9375	13.17865	1.90217	0.783
	>6.2	99	60.596	13.71571	1.37848	
	≤10	70	57.80	14.00269	1.67364	0.027
	>10	77	62.7273	12.66640	1.44347	
Duration of hemodialysis	≤5	40	30.35	37.35042	5.90562	0.15
	>5	107	41.9907	45.49881	4.39854	
	≤6.2	48	27.9375	34.71857	5.01119	0.020
	>6.2	99	44.101	46.58643	4.68211	
	≤10	70	36.10	46.23386	5.52600	0.472
	>10	77	41.2987	41.24767	4.70061	
Phosphorus	≤5	40	05.665	1.71293	0.27084	0.10
	>5	107	06.2236	1.88314	0.18205	
	≤6.2	48	05.5583	1.71586	0.24766	0.019
	>6.2	99	06.3204	1.86882	0.18782	
	≤10	70	05.7429	1.64269	0.19634	0.039
	>10	77	06.3704	1.98276	0.22596	

to 57.8 and in patients with higher CRP levels was equal to 62.7 years ($p = 0.02$). In addition in patients with CRP levels lower and higher than 10 mg L^{-1}, the mean blood phosphorus level was 5.7 and 6.3 mg dL^{-1}, respectively ($p = 0.03$) (Table 4). Moreover, a significant correlation between CRP greater than 10 mg L^{-1} and fixed night shift of hemodialysis was found ($p = 0.04$). No significant correlation between BMI, cholesterol, albumin, hemoglobin, hematocrit, calcium level and CRP was found ($p>0.05$).

DISCUSSION

With considering to the different cutoff point (5, 6.2, 10 mg L^{-1}) for CRP level in hemodialysis patients (Racki *et al*., 2006; Hung *et al*., 2008; Iseki *et al*., 1999), results of the present study showed that a significant proportion of hemodialysis patients had elevated level of CRP. Indeed 72.8% of patients had CRP level over the upper limit of normal human subjects (5 mg L^{-1}), 67.3% had CRP level>6.2 mg L^{-1} and 52.4% had CRP level>10 mg L^{-1}. In view of the fact that hemodialysis procedure itself contributes to the inflammatory response (Yao *et al*., 2004), chronic inflammation may be one of the causes of increased mortality and morbidity in this population (Yilmaz, 2007), especially because of its association to atherogenesis and cardiovascular events which account for approximately 50% of the death in dialysis patients (Collins *et al*., 2003). Several studies have confirmed that inflammation, as reflected by elevated level of CRP, is a significant independent predictor of mortality in dialysis patients (Yeun *et al*., 2000; Wanner and Metzger, 2002). Korevaar *et al*. (2004) identified that CRP level itself and an increase in CRP level during a dialysis session are independently associated with an increased mortality risk in hemodialysis patients. In a study conducted by Racki *et al*. (2006), the CRP cutoff point of 6.2 mg L^{-1} was predictive of increased mortality in patients with ESRD. Finding of present study showed that more than two-third of patients had CRP concentration above 6.2 mg L^{-1}. In another study that performed by Iseki *et al*. (1999) they used 10 mg L^{-1} as their cutoff values in dialysis patients. With considering 10 mg L^{-1} as a CRP cutoff in hemodialysis patients, 52.4% of our patients have CRP higher than 10 mg L^{-1}. This indicates the high incidence of inflammation in this patients. Razeghi *et al*. (2008) observed that in 41% of hemodialysis patients, CRP was higher than 10 mg L^{-1}. In a study by Hung *et al*. (2008) the mean of CRP was 14.3 mg L^{-1} and 53% of patients had CRP level>5 mg L^{-1}. Increase of 1 mg L^{-1} in CRP level was associated with 9% increasing in mortality risk (Korevaar *et al*., 2004). Iseki *et al*. (1999) showed a 3.5 times higher mortality risk in hemodialysis patients with CRP level greater than 5 mg L^{-1} after 5 years of follow up. In all studies with different CRP cutoff points, patients with CRP values above chosen cutoff point were at increased risk of overall and cardiovascular mortality. Also, in dialysis patients high CRP level predict lower serum albumin concentration and lower serum Hemoglobin (Hb) level with poor response to EPO (Ortega *et al*., 2002). Teruel *et al*. (2005) found an inverse correlation between CRP and serum albumin and Hb level in hemodialysis patients. Also, in another study in hemodialysis patients, an inverse correlation of Mean Platelet Volume (MPV) with serum CRP level was seen (Nasri *et al*., 2006b).

In this study, CRP levels above 6.2 had a direct statistically significant correlation with duration of hemodialysis and phosphorus level. CRP levels greater than 10 mg L^{-1} have significant relation with age and

phosphorus levels ($p<0.05$). But no significant correlation between CRP and BMI, cholesterol, albumin, hemoglobin, hematocrit and calcium levels was found ($p>0.05$). On the other hand, studies have reported increased risk of cardiac disease with high CRP levels without a decrease in albumin levels. Therefore, in the presence of normal albumin levels, CRP levels may increase (Razeghi *et al*., 2008). Absence of a significant correlation between CRP and albumin in the present study was compatible with the study of Nascimento *et al*. (2004) which observed no significant correlation between CRP and serum albumin level in hemodialysis patients. Also, in another study that conducted on hemodialysis patients, no significant association between serum CRP and serum albumin was seen (Baradaran and Hamid, 2005). Hung *et al*. (2008) observed a direct relationship between serum phosphorus and CRP in a cohort study In another study, Calo *et al*. (2011) showed that in dialysis patients, CRP reduction can lead to decrease in phosphorus level.

CONCLUSION

The results of this study demonstrate that the prevalence of inflammation among the hemodialysis patients is high and CRP level greater than 6.2 and 10 mg L^{-1} (as a cutoff point), have correlation with age, duration of hemodialysis and phosphorus level in these patients. Considering that even a single determination of CRP level is predictive of poor prognosis in hemodialysis patients, regular checking of CRP may be helpful to tailor appropriate management strategy.

ACKNOWLEDGMENTS

The authors thank of all the participants and the staff of Imam Khomeini and Fatemeh Zahra dialyze centers for their efficient and kind collaboration.

REFERENCES

Al-Hamdan, A.A., R.H. Al-Huthail, M.A. Alsaif, A.M. Al-Othman, M.N. Al-Muammer *et al*., 2009. The effect of weight reduction diet on C-reactive protein level in obese-adult subjects. J. Med. Sci., 9: 17-23.

Avram, M.M., P.A. Fein, M. Paluch, T. Schloth and J. Chattopadhyay, 2005. Association between C-reactive protein and clinical outcomes in peritoneal dialysis patients. Adv. Peritoneal Dialysis, 21: 154-158.

Baradaran, A. and N. Hamid, 2005. Association of serum c-reactive protein (CRP) with some nutritional parameters of maintenance hemodialysis patients. Pak. J. Nutr., 4: 175-182.

Calo, L.A., V. Savica, A. Piccoli, M. Fusaro, A. D'Angelo and P.A. Davis, 2011. Reduction of hyperphosphatemia is related with the reduction of c-reactive protein in dialysis patients. Study in sevelamer-resistant dialysis patients treated with chitosan chewing gum as salivary phosphate binder. Renal. Failure., 33: 11-14.

Collins, A.J., S. Li, D.T. Gilbertson, J. Liu, S.C. Chen and C.A. Herzog, 2003. Chronic kidney disease and cardiovascular disease in the Medicare population. Kidney. Int., 64: S24-S31.

Ducloux, D., C. Bresson-Vautrin, M. Kribs, A. Abdelfatah and J.M. Chalopin, 2002. C-reactive protein and cardiovascular disease in peritoneal dialysis patients. Kidney. Int., 62: 1417-1422.

Hung, A., L. Pupim, C. Yu, A. Shintani and E. Siew *et al*., 2008. Determinants of C-reactive protein in chronic hemodialysis patients: Relevance of dialysis catheter utilization. Hemodialysis. Int., 12: 236-243.

Iseki, K., M. Tozawa, S. Yoshi and K. Fukiyama, 1999. Serum C-reactive Protein (CRP) and risk of death in chronic dialysis patients. Nephrol. Dial. Transplant., 14: 1956-1960.

Kalantar-zadeh, K., T.A. lkizler, G. Block, M.M. Avram and J.D. Kopple, 2003. Malnutrition-inflamation complex syndrome in dialysis patients: Cause and consequences. Am. J. Kidney. Dis., 42: 864-881.

Korevaar, J.C., J.G. van Manen, F.W. Dekker, D.R. de Waart, E.W. Boeschoten and R.T. Krediet, 2004. Effect of an increase in C-reactive protein level during a hemodialysis session on mortality. J. Am. Soc. Nephrol., 15: 2916-2922.

Nascimento, M.M., R. Pecoits-Filho, A.R. Qureshi, S.Y. Hayashi and R.C. Manfro *et al*., 2004. The prognostic impact of fluctuating levels of C-reactive proteins in Brazilian haemodialysis patients: A prospective study. Nephrol. Dial. Transplant., 19: 2803-2809.

Nasri, H., S. Shirani and A. Baradaran, 2006a. Association of platelet count and mean platelet volume with serum C-reactive protein in regular hemodialysis patients. Asian J. Cell Biol., 1: 59-64.

Nasri, H., S. Shirani and A. Baradaran, 2006b. Pulmonary artery pressure in maintenance hemodialysis patients. Pak. J. Biol. Sci., 9: 107-110.

Ortega, O., I. Rodriguez, P. Gallar, A. Carreno and M. Ortiz *et al*., 2002. Significance of high C-reactive protein levels in pre-dialysis patients. Nephrol. Dial. Transplant., 17: 1105-1109.

Pecoits-Filho, R., P. Barany, B. Lindholm, O. Heimburger and P. Stenvinkel, 2002. Interleukin-6 is an independent predictor of mortality in patients starting dialysis treatment. Nephrol. Dial. Transplant., 17: 1684-1688.

Racki, S., L. Zaputovic, Z. Mavric, B. Vujicic and S. Dvornik, 2006. C-reactive protein is a strong predictor of mortality in hemodialysis patients. Renal. Fail., 28: 427-433.

Razeghi, E., H. Omati, S. Maziar, P. Khashayar and M. Mahdavi-Mazeh, 2008. Chronic inflammation increases risk in hemodialysis patients. Saudi. J. Kidney. Dis. Trans., 19: 785-789.

Selim, G., O. Stojceva-Taneva, k. Zafirovska, A. Sikole, S. Gelev *et al*., 2006. Inflamation predicts all-cause and cardiovascular mortality in haemodialysis patients. Biol. Med. Sci., 27: 133-144.

Teruel, J.L., R. Marcen, J. Ocana, M. Fernandez-Lucas, M. Rivera, G. Tabernero and J. Ortuno, 2005. Clinical significance of C-Reactive protein in patients on hemodialysis: A longitudinal study. Nephron. Clin. Prac., 100: 140-145.

Wanner, C. and T. Metzger, 2002. C-reactive protein a marker for all-cause and cardiovascular mortality in hemodialysis patients. Nephrol. Dial. Transplant., 17: 29-32.

Yao, Q., B. Lindholm and P. Stenvinkel, 2004. Inflammation as a cause of malnutrition, atherosclerotic cardiovascular disease and poor outcome in hemodialysis patients. Hemodialysis. Int., 8: 118-129.

Yeun, J.Y., R.A. Levine, V. Mantadilok and G.A. Kaysen, 2000. C-Reactive protein predicts all-cause and cardiovascular mortality in hemodialysis patients. Am. J. Kidney Dis., 35: 469-476.

Yilmaz, M.I., 2007. The causes of the inflammation and possible therapeutic options in dialysis patients. Gulhane Med. J., 49: 271-276.

Zimmermann, J., S. Herrlinger, A. Pruy, T. Metzger and C. Wanner, 1999. Inflamation enhances cardiovascular risk and mortality in hemodialysis patients. Kidney. Int., 55: 648-658.