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Serum C-Reactive Protein in chronic kidney disease patients undergoing hemodialysis and correlation with dialytic age

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Abstract. Mortality in CKD patients undergoing hemodialysis considerably high. Previous study showed that mortality in patients undergoing hemodialysis was strongly correlated with chronic inflammation. The current study examined whether the serum c-reative protein concentration (hsCRP) changed from pre- to post-dialysis. In addition, the current study also investigated the correlation between dialysis age and hsCRP in chronic kidney disease patients undergoing hemodialysis. The study was a case-series study of 30 patients with hemodialysis. The patients were devided into three group based on dialysis age. Hemodialysis had been undergone for 4 hours, using *hemoflow F8HPS*, polysulfone synthetic dialysis membrane, and bicarbonate dialysis fluid. The primary outcome was serum concentration of high-sensitivity C-reactive protein (hsCRP), which was assessed in the pre-and-post dialysis, measured using *chemiluminescent method*. Dialysis does increased the hsCRP post-dialysis. It resulted in significant ($p < 0.05$) increment of serum hsCRP concentration, pre-dialysis 1.04 ± 0.90 mg/L compared to post-dialysis mean value 1.84 ± 2.01 mg/dL. There was no significant difference among serum hsCRP concentration mean value among group of dialysis age. The correlations between various measurement of serum hsCRP concentration and dialysis age were statistically insignificant.

1. Introduction

Chronic kidney disease (CKD) is a current global health issue with estimated global prevalence between 11 to 13% [1]. CKD leads to a gradual decline of kidney function, with renal replacement therapy eventually demanded to substitute the function of the kidneys. The rate of decline in kidney function differs among patients, and the initiation of renal replacement therapy relies on the presence of symptoms related to kidney failure [2]. A decline in the glomerular filtration rate to less than 30 mL/min/1.73 m2 is associated with severely decreased kidney function, described as stage four CKD, and preparation for renal replacement therapy is recommended [3-4]. The modalities of renal replacement therapy comprise transplantation, peritoneal dialysis, and hemodialysis, with 85% of patients with terminal stage of CKD in 53 countries undergoing hemodialysis [5].

Mortality among patients with hemodialysis is considerably high, in part due to the cardiovascular complications [6]. Several studies suggest that cardiovascular-related mortality among patients with hemodialysis was associated with chronic inflammation [7-9]. Inflammation during hemodialysis may

occur in some manners. Bio-incompatibility between dialyzer and blood, the endotoxin in dialysis fluid, access-related infections, and the glucose degradation products have been contributed to the inflammation responses during hemodialysis [10]. A study reports that about 35–65% of CKD patients undergoing haemodialysis exhibit the signs of inflammation, considering the prevalence in patients before dialysis is lower [11].

High-sensitivity C-reactive protein (hsCRP) is a well-known marker of systemic inflammation. Some epidemiologic studies have revealed that hsCRP may independently predicts vascular risk and may provide prognostic information [12-13]. In contrast to several other parameters that also constitute biological aspects of inflammation, hsCRP measurement is standardized and commonly available [14]. A study reports that postdialysis increment of hsCRP is associated with increased mortality among patients with hemodialysis [15]. The aim of current study was to determine the effect of hemodialysis on pre-to-post dialysis changes of serum c-reative protein concentration (hsCRP), a well-known marker of systemic inflammation. In addition, the current study also identified the correlation between dialysis age and serum hsCRP concentration among chronic kidney disease patients undergoing hemodialysis.

2. Methods

The subjects were consecutively recruited from chronic kidney disease (CKD) patients who regularly attended the session of hemodialysis in Hemodialysis Unit of Mohammad Hoesin General Hospital Palembang. The prospective subjects were 25-60 years old and having hemodialysis session for at least 2 times. Patients with liver function disorders, lupus nephritis, and acute infection manifestations were excluded from the study. Patients were selected from a pool of 108 patients.

Dialysis age was determined by clinical records. Dialysis age was group into less than three months, between three and twelve months, and more than one year. Prior to hemodialysis, blood was taken via venipuncture to measure complete blood count and hsCRP. hsCRP was also measured four hours after hemodialysis. Hemodialysis had been undergone for 4 hours, using *hemoflow F8HPS,* polysulfone synthetic dialysis membrane, and bicarbonate dialysis fluid (all products were Nipro's, Akita, Japan). hsCRP was measured based on a blood specimens and was determined by *chemiluminescent method* (hsCRP, Cat.No,LKCRP1, Siemens Diagnostics).

Normal distribution of data was deduced with Shapiro-Wilk test. Kruskal Wallis non-parametric test and one-way ANOVA were used to compare data among more than two groups. Pearson correlation test was used to determine the correlation between variable. P-values of less than 0.05 were considered to be significant. Statistical analysis was performed using *SPSS 22.0 for Windows*.

3. Results

There were 30 patients recruited in total for the analysis of the study. General characteristics of patients were shown in Table 1. Mean of the patients' body mass index was normoweight range. Most of the patients were between 51-years-old and 60-years-old. There were 17 females and 13 males. The commonest etiology was hypertension. Hemoglobin, serum ureum, serum creatinine, random blood glucose, serum natrium, serum potassium, serum albumin, SGOT, and SGPT were normally distributed.

The measurements of hsCRP were shown in table 2. Hemodialysis resulted in significant (p<0.05) increment of serum hsCRP concentration, pre-dialysis 1.04±0.90 mg/L compared to post-dialysis mean value 1.84±2.01 mg/dL. There was no significant difference among serum hsCRP concentration mean value among group of dialysis age.

The correlations between various measurement of serum hsCRP concentration and dialysis age were shown in table 3. Prehemodialytic, posthemodialytic, and pre-to-post hemodialytic hsCRP value were having insignifancant negative correlation toward dialytic age. Pre-to-post hemodialytic hsCRP changes percentage was having insignificant weak positive correlation toward dialytic age.

4. Discussions

CRP has been popular as one of acute phase proteins and used as a biomarker of inflammation in clinical settings. CRP is synthesized in liver, mostly induced by interleukin-6. It is produced during acute phase response to infection or other inflammatory episodes [16]. An in vitro study showed that CRP activates the expression of adhesion molecules in human monocytes that involved in

inflammation [17]. CRP also contributes in scavenge processes of cell debris, conducting classical pathway of complement system [18]. The measurement of hsCRP has been suggested to be important biomarker in the initiation and progression of atherosclerosis [19]. Some studies have revealed that chronic hsCRP elevation of the vascular endothelium has a pivotal role in the development of cerebral and cardiac vascular disease, mainly in patients with chronic hemodialysis [20-22]. Since cerebral and cardiac vascular disease were main cause of death in patients with hemodialysis, hsCRP have been established as a useful tool in predicting mortality in hemodialysis.

Table 1. General characteristics of the subjects.

Characteristics	Total (n=30)	Median Value (min-max)	Mean±SD
Age (years)			
≤30	3(10%)		
31 - 40	6(20%)		
41 – 50	9(30%)		
51 – 60	12(40%)		
Sex			
Male	13(43.3%)		
Female	17(56.7%)		
Body Mass Index (kg/m^2)			21.79±3.51
Duration on HD (months)		10(1-58)	
<3	10(33.3%)		
3-12	10(33.3%)		
>12	10(33.3%)		
Cause of HD			
Hypertension	19(63.3%)		
Diabetes Mellitus	5(16.7%)		
Renal Infection	3(10%)		
Gout Nephropathy	1(3.33%)		
Renal Cyst	1(3.33%)		
Obstructive Nepropathy	1(3.33%)		
Hemoglobin (g/dL)			8.27±1.14
Leucocytes (cell/mm^3)[a]		7150(4200-10500)	
Trombocytes (/mm^3)[a]		185000(111000-431000)	
Serum Ureum (mg/dL)			140.83±52.36
Serum Creatinine (mg/dL)			11.81±4.15
Random Blood Glucose (mg/dL)			130.23±64.29
Serum Natrium (mEq/L)[a]		143(133-149)	
Serum Potassium (mEq/L)			4.69±0.73
Serum Albumin (mg/dL)			3.85±0.42
SGOT (µgL)			22±11.01
SGPT (µgL)			23.47±15.21

[a] Shapiro-Wilk test for normality <0.05

Table 2. Serum hsCRP concentration profile in subjects.

Duration on HD	n (%)	Prehemodialysis hsCRP		Posthemodialysis hsCRP	
		Mean(mg/dL)	p value	Mean(mg/dL)	p value
<3 months	10(33.%)	1.09±0.49		1.75±1.07	
3-12 months	10(33.%)	1.16±1.25	0.224[a]	1.60±1.30	0.254[a]
>12 months	10(33.%)	0.85±0.89		2.17±3.15	
All Subjects	30(100%)	1.04±0.90		1.84±2.01	0.008[b]

[a]Kruskal-Wallis Test among three group, [b]Dependent t-test for pre-to-post hemodialysis mean value

In current study, there was significant increment in four hours postdialysis serum hsCRP concentration compared to predialysis value. The similar finding was also found in other study conducted by Nagane et al [23], in spite of the increament of hsCRP was relatively small compared to the study conducted in European [24]. Previous study showed that the prevalence of chronic inflammation in American and European patients were considerably higher than Asians [24]. The genetic factors was hypothesized to be taken the role.

The current study showed that there was no significant correlation between dialysis age and serum hsCRP concentration among chronic kidney disease patients undergoing hemodialysis. This finding may relate to the theory that CRP concentrated optimally after 24 hours [25]. Serial monitoring of CRP may be used to in determining the magnitude of inflammation in patients undergoing hemodialysis.

Table 3. The correlation between dialysis age and various measurements values of hsCRP.

Measurement Values of hsCRP	Duration on Hemodialysis	
	r	p
Prehemodialytic hsCRP	-0.227[a]	0.228
Posthemodialytic hsCRP	-0.134 [a]	0.481
Pre-to-post hemodialytic hsCRP changes	-0.059 [a]	0.769
Pre-to-post hemodialytic hsCRP changes percentage	0.029 [a]	0.945

[a]Pearson Correlation Test

5. Conclusion
In conclusion, dialysis increased the hsCRP post-dialysis significantly. The current study shows that there was no significant correlation between dialysis age and hsCRP.

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