



## SERUM HSCRP AS A PREDICTOR OF CARDIO VASCULAR DISEASE IN CHRONIC KIDNEY DISEASE

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### ABSTRACT

**Background:** CKD is a global public health problem along with serious complications like ESRD, CVD and Premature Death. Serum hs-CRP is a strong predictor of cardiovascular mortality in CKD patients. Hence in this study hsCRP was estimated in patients with different stages of CKD and the relationship between serum hsCRP and estimated GFR was analyzed.

**Aim:** To estimate serum hsCRP in patients with CKD and to compare them with healthy controls.

**Results:** In this study we observed a significantly higher levels of hsCRP in cases when compared to controls [mean value: cases  $4.5432 \pm 2.9689$ ; controls  $0.5360 \pm 0.2343$ , Pvalue < 0.05]. As the renal function declined, we observed a progressive increase in the serum hsCRP levels.

**Conclusion:** Life style modification and therapeutic intervention should be taken as soon as a diagnosis of CKD is made to reduce the cardiovascular risk

**KEYWORDS :** Chronic kidney disease; hsCRP; CVD

Chronic Kidney Disease (CKD) is composed of a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive deterioration in Glomerular Filtration Rate (GFR) (Chawla & Kimmel, 2012). CKD is defined as kidney damage or GFR < 60ml/min/1.73m<sup>2</sup> for a minimum of 3 months irrespective of the cause (Conditions, 2008). The GFR is defined as the rate of plasma flow filtered across the glomerular basement membrane (Blantz & Wilson, 1976). CKD is a global public health problem along with serious complications like End Stage Renal Disease (ESRD), Cardio Vascular Disease (CVD) and Premature Death (Couser, Remuzzi, Mendis, & Tonelli, 2011). Cardiovascular disease (CVD) constitutes of about 40% of hospitalization and 50% of mortality in CKD patients at all stages – (Shah & Dumler, 2008). Mortality rate due to CVD is about 10–20 times higher in patients with end stage renal disease (ESRD) than the general population (Control & Prevention, 2010).

Not only the traditional cardiovascular risk factors such as Diabetes Mellitus (DM), Hypertension (HT), Smoking and Dyslipidemia but also the nontraditional risk factors such as Inflammation, Endothelial dysfunction, Insulin resistance are the reason for the high cardiovascular risk of CKD patients (Meshkani & Adeli, 2009). Among these non traditional factors inflammation has been associated with the increased cardiovascular event rates and mortality risk in CKD patients. Chronic kidney disease is a chronic inflammatory state due to the factors like uremic toxins, infection, oxidative stress, and dialysis related factors – (Sundaram, Palaneeswari, Nagarajan, Devi, & Jagdeeshwaran, 2014). There is a gradual deterioration of renal function in CKD may also lead onto accumulation of uremic toxins which in turn stimulate inflammation and result in atherosclerosis. Because of the reduced renal function in CKD patients, there will be accumulation of these inflammatory cytokines. The causes of inflammation among patients with CKD are complex and multifactorial. Serum hs-CRP is a strong predictor of cardiovascular mortality in CKD patients. C-reactive protein is an acute phase reactant that comes from the protein family known as pentraxin. It is synthesized by the liver in response to inflammatory cytokines like interleukin-1, interleukin-6, tumour necrosis factor-alpha released from macrophages and adipocytes (Adejumo, Okaka, Okwuonu, Iyawe, & Odujoko, 2016). C-reactive protein levels of <1 mg/L, 1 to 3 mg/L, and >3 mg/L correspond to low, moderate, and high-risk groups for future cardiovascular events (Pearson et al., 2003). Therefore CKD patients with a high cardiovascular risk can be identified by doing serum hsCRP assay and these high risk group can be closely followed up and

monitored. Aggressive cardiovascular risk factor modification can be instituted before they develop cardiovascular disease.

Hence in the present study the serum level of hsCRP was estimated in patients with different stages of CKD and the relationship between serum hsCRP and estimated GFR was analyzed.

### AIMS AND OBJECTIVES

#### AIM:

To estimate the levels of serum hsCRP in patients with CKD and to compare them with healthy controls.

#### OBJECTIVES:

1. To study the relationship of serum hsCRP with estimated GFR

### MATERIALS AND METHODS

The study was conducted at Thanjavur Medical College Hospital, Thanjavur after getting approval from the ethical committee. 50 patients of known CKD (25 males and 25 females) were selected as cases from the outpatients and wards of the Department of Nephrology. 50 age and gender matched healthy individuals were selected as controls.

### INCLUSION CRITERIA

- Patients with established diagnosis of CKD.
- Age > 18 years.

### EXCLUSION CRITERIA

- Acute/chronic inflammatory diseases
- Previous history of Coronary Artery Bypass Graft surgery.
- Patients on lipid lowering drugs.
- Acute kidney injury.
- Patients on immuno therapy.
- Previous history of cerebrovascular diseases.
- Patients who underwent renal transplantation.
- Nephrotic syndrome.

Informed consent was obtained from all subjects prior to the study. Under aseptic precautions, 5ml of venous blood sample was collected after an overnight fasting of 12 hours from all subjects. After retraction of the clot, samples were centrifuged at 2000rpm for 15 minutes for separation of serum.

### ANALYSIS OF BLOOD SAMPLES

The serum collected above was used for the estimation of the following parameters.

**A. ESTIMATED PARAMETERS**

1. Serum hsCRP Turbidimetric Immunoassay.
2. Blood Urea Urease –Glutamate Dehydrogenase (GLDH) Method.
3. S.Creatinine Modified Jaffe's method.

**B. CALCULATED PARAMETERS**

1. Creatinine clearance was calculated using CKD-EPI formula

**ESTIMATION OF SERUM hs-CRP:**

**METHOD:**

Turbidimetric Immuno Assay

**PRINCIPLE:**

Serum C-reactive protein causes agglutination of the latex particles washed with Antihuman C-reactive protein. The latex agglutination is proportional to the concentration of CRP and can be measured by turbidimetry.

**RESULTS**

A total of 100 subjects were selected as the study group for the present study. This includes 50 cases with CKD and 50 healthy controls.

Levels of serum Creatinine, hs CRP and blood Urea, were estimated for all the samples of the study group. Estimated GFR was calculated from CKD-EPI formula.

**STATISTICAL ANALYSIS**

- Student's t-test was used for the statistical analysis of data.
- The datas were expressed in terms of mean and standard deviation.
- p' value less than 0.05 was taken as the significant value.

**RESULTS**

**Table 1 COMPARISON OF BLOOD UREA, SERUM CREATININE AND CREATININE CLEARANCE IN THE STUDY GROUP**

PARAMETERS	GROUPS	MEAN	SD	STATISTICAL INFERENCE
B.Urea(mg/dl)	Cases(n=50)	94.36	26.33	t=19.00 P<0.05 significant
	Control(n=50)	23.04	3.33	
Creatinine(mg/dl)	Cases(n=50)	2.87	2.05	t=6.999 P<0.05 significant
	Control(n=50)	0.83	0.10	
Ccr(ml/min)	Cases(n=50)	35.91	23.51	t=17.363 P<0.05 significant
	Control(n=50)	98.78	10.10	

Blood urea and Serum Creatinine were found to be significantly higher in cases and Ccr was significantly lower in the cases than controls (p<0.05, significant).

**Table 2 COMPARISON OF SERUM hsCRP IN THE STUDY GROUP**

PARAMETERS	GROUPS	MEAN	SD	STATISTICAL INFERENCE
s.hsCRP(mg/L)	Controls(n=50)	0.53	0.23	t=9.514; P<0.05 Not significant
	Cases(n=50)	5.54	2.96	

From this table it is obvious that hsCRP level was significantly higher in the cases than controls (p<0.05, significant).

**Table 3 COMPARISON OF hs CRP IN RELATION TO Ccr IN CASES**

Ccr (ml/min)	hsCRP(mg/L)		STATISTICAL INFERENCE
	MEAN	SD	
60-90 (n=14)	1.56	0.58	F=43.09; P<0.05 Significant
30-59 (n=12)	2.88	0.90	
15-29 (n=12)	6.73	2.20	
<15 (n=12)	7.48	2.05	

This table represents the comparison of serum hsCRP levels in the study group in relation to Ccr. We observed a significant progressive increase in the hs CRP value in the cases as the renal function

declined ( p<0.05).serum hs CRP level is increased in all stages of CKD and there is a gradual increase of hs CRP from stage 2 to stage 5.

**DISCUSSION**

In the present study we observed a significantly higher levels of serum hsCRP in CKD cases when compared to controls [mean value: cases 4.5432 ± 2.9689; controls 0.5360 ± 0.2343, Pvalue < 0.05].As the renal function declined, we observed a progressive increase in the serum hsCRP levels. These results of the present study are in accordance with that of the previous studies suggesting a global pro-atherogenic inflammatory activation occurs even in early stages of CKD.C-reactive protein has been reported as a highly valuable predictor of cardiovascular risk in CKD patients. Its level is associated with carotid intima media thickness in CKD patients.

**CONCLUSION**

Serum hs CRP in CKD patients can serve as a biomarker to estimate cardiovascular risk. Life style modification and therapeutic intervention should be taken as soon as a diagnosis of CKD is made irrespective of the stage to reduce the cardiovascular risk and to decrease the mortality rate and premature death in CKD patients

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