IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
www.iosrphr.org Volume 5, Issue 7 (July 2015), PP. 08-12

Comparative Study of Hscrp in Chronic Kidney Disease

Dr. Sumanth kumar . B*, Dr. Shobharani.B
Department of Biochemistry , Sri venkateswara Medical college, Tirupati

ABSTRACT
BACKGROUND*: Chronic kidney disease (CKD) is a global threat to health mainly in developing countries be cause therapy is expensive and lifelong. over 1 million people worldwide are on dialysis or with a functioning gr aft. Early detection of Chronic kidney disease (CKD) and its consequent complications can prevent its grave c omplications . It causes not only significant morbidity but also it causes high mortality. Because of increase in i ncidence of Diabetes mellitus, hypertension, obesity and an aging population there is increase in progression of chronic kidney disease to end stage renal disease (ESRD). . Cardiovascular disease (CVD) is the major cause of mortality in haemodialysis patients and so it has become imperative to have a screening programme at all level s to detect CKD at an early stage and to initiate specific therapy to reduce the progression of renal disease and also the burden of ESRD (1). High sensitive C-Reactive protein (Hs CRP) assay is useful for sensitive detection of inflammatory state (2,3). This study aims at estimating Hs CRP as a marker of inflammation in CKD patients.*

AIM *: To study the variations of High sensitive C-Reactive protein in chronic kidney disease patients*
MATERIALS AND METHODS: Estimation of High sensitive C-Reactive protein by Turbidimetry method, kit me thod from Biosystems
RESULTS: *Mean and standard deviation of HsCRP in CKD cases obtained was* 26.08 ± 5.73 and in controls was 0.83 ± 0.15mg/L respectively
CONCLUSION: *The levels of Hs CRP were found to be elevated in patients with CKD compared to control gr oup. There was a significant relationship between reduced GFR and Hs CRP levels which suggests that there is inflammatory activity in the CKD patients*

I. INTRODUCTION

Renal failure is the consequence of the loss of homeostatic regulation which is maintained by the kidne ys. Nephrons are injured by toxic or immunological injury that may injure the glomerulus or the tubule or both t ogether. Thus a significant reduction in functioning renal mass must have occurred much earlier than the onset o f significant symptoms or any major biochemical alterations in blood (4). Renal failure is of two types acute ren al failure and chronic renal failure. Chronic renal disease also known as chronic kidney disease (CKD) is progre ssive loss of function over a period of months or years through five stages. Each stage is a progression through a n abnormally low and deteriorating Glomerular filtration rate (GFR), which is usually determined indirectly by t he creatinine levels in the blood. The number of patients treated with dialysis or transplantation is projected to in crease from 3,40,000 in 1999 to 6,51,000 in 2010 (5). The most common causes of CKD are Diabetes mellitus a nd hypertension, accounting for close to 70% of all CKD cases (6).

Chronic kidney disease is a pathophysiologic process that results in the attrition of nephron number an d also function, ultimately leading to ESRD (7). The pathophysiology of CKD involves initiating mechanisms s pecific to the underlying etiology, as well as a set of progressive mechanisms that are a common consequence fo llowing long term reduction of renal mass, irrespective of etiology. This reduction in renal mass causes structura l and functional hypertrophy of surviving nephrons. This compensatory hypertrophy is mediated by vasoactive molecules, cytokines and growth factors and is initially due to adaptive hyperfiltration, in turn mediated by incre ases in glomerular capillary pressure and flow . These short term adaptations eventually prove maladaptive beca use they predispose to sclerosis of the remaining viable nephron population. Increased intra renal activity of the renin-angiotensin axis appears to contribute to both the initial adaptive hyperfiltration and to the subsequent mal adaptive hypertrophy and sclerosis (8). CKD is identified when the GFR has been <60ml/min/1.73m^2 for at least 3 months (5, 8). It causes not only significant morbidity but also it causes high mortality. Because of increase in incidence of Diabetes mellitus, hypertension, obesity and an aging population there is increase in progression of chronic kidney disease to end stage renal disease (ESRD). Heamodialysis is successful in prolonging the life of ESRD patients. Even though there is high technical improvement still the annual mortality rate of patients with ESRD undergoing haemodialysis remains unacceptably high. Cardiovascular disease (CVD) is the major cause of mortality in haemodialysis patients and so it has become imperative to have a screening programme at all lev els to detect CKD at an early stage and to initiate specific therapy to reduce the progression of renal disease and also the burden of ESRD (1).

Cardiovascular disease has been found to be responsible for the majority of mortality and morbidity in t his chronic kidney disease patients and accounts for 40-50% of all deaths in end stage renal disease patients. Mo rtality rates due to CVD are approximately 15 times higher in the ESRD population than in the general populatio n. The Second National Healthy and Nutrition Examination Survey (NHANES II) showed that an estimated Glo merular Filtration Rate (GFR) of less than 70 ml/min/1.73m^2 was associated with a 68% increase in the risk of d eath from any cause and a 51% increase in the risk of death from CVD (9). In the Atherosclerosis Risk in the co mmunities study, an estimated GFR of 15-59 ml/min/1.73m^2 at baseline was associated with a 38% increase in t he risk of CVD (10).

C- Reactive protein is an acute phase plasma protein produced by the liver and by adipocytes. It is a m ember of the pentraxin family of proteins , it reacts with the C-polysaccharide of pneumococcus. The CRP gene is located on the first chromosome. CRP is a 224 residue protein with a monomer molar mass of 25106 Daltons. It is annular pentameric disc shaped protein. proteins with this type of configuration are known as pentraxins. As CRP levels rise during inflammatory processes it is considered as a member of the class of acute phase reactant s. This increment is due to a rise in the plasma concentration of IL-6 which is produced mainly by macrophages and adipocytes also. In acute inflammation like infection, CRP level rises upto 50,000 fold. It rises above norma l limits within 6 hrs and peaks at 48 hrs. Its half life is constant and therefore its level is mainly determined by th e rate of production (11). CRP binds to phosphorylcholine on microbes and helps in complement binding to fore ign cells and enhances phagocytosis by macrophages. It also plays an important role in innate immunity. Patient s with CKD and ESRD show elevated CRP levels in keeping with the underlying chronic inflammatory state. Th ere is a close correlation between changes in plasma levels of IL-6 and levels of CRP (12).

High sensitive CRP (Hs CRP) is the recent globular indicator of future vascular events in adults without an y previous history of cardiovascular disease with an acceptance precision level below 0.3 mg/L. Hs CRP assay i s useful for sensitive detection of inflammatory state (2,3).

II. MATERIALS AND METHODS:

The present study was carried out in the department of Biochemistry of Sri Venkateswara Medical Coll ege and department of General Medicine, Sri Venkateswara Ramnarayan Ruia Government General Hospital, Ti rupati . Total number of subjects selected were 80 who are in the age group of 35-65 yrs of age. Among them 4 5 subjects were diagnosed as chronic kidney disease patients in General Medicine department. The remaining 35 were selected as control group who are age and sex matched. Cases were divided into 3 groups stage III, IV, an d V based on their estimated GFR levels as per National Kidney Foundation K/DOQI.KDOQI CKD clinical pra ctice guidelines for chronic kidney disease(16) . Among the 45 cases stage III patients were 13, stage IV patients were 22 and stage V patients were 10 in number.

2.1 INCLUSION CRITERIA:

1. Males and females in the age group of 35 yr-65 yr who were diagnosed as Chronic kidney disease patients attending Department of Medicine, SVRRGGH are taken as cases.
2. Estimated GFR < 60 ml/min/1.73 m^2 for $\geq$ 3 months.
3. Age matched individuals without chronic kidney disease are selected as control group.

2.2 EXCLUSION CRITERIA:

1. Individuals of age under 35 yr and more than 65 yr are excluded from the study.
2. Patients with Acute kidney disorder attending Medicine department with sudden increase in serum creatinine levels due to varied etiology
3. Patients on dialysis

Fasting venous blood samples were collected under aseptic conditions from the study group after taking inform ed consent. Plain blood samples of total 10ml is drawn. Serum was separated after one hour by centrifugation at 1500 rpm and clear serum is transferred to separate aliquots and analysis was done on the same day. High sensit ive CRP was estimated by using standard method on the same day of collection by Turbidimetric method, kit m ethod from Biosystems in Semi Auto Analyser and GFR was estimated in both cases and controls by -

Cockcroft-Gault equation

Estimated creatinine clearance (ml/min) =

(140-age)×body weight (kg)/72×Pcr (mg/dl)

Multiply by 0.85 for women

2.3 STATISTICAL ANALYSIS

The data of these 2 parameters is compared between the cases and controls. The statistical analysis was done to calculate Mean, Standard deviation by Epi Info 7 and Microsoft excel 2007 version. Statistical significa nce level was taken as p-value <0.05

III. RESULTS

TABLE – I: MEAN AND SD VALUES OF BIOCHEMICAL PARAMETERS IN CASES (CKD PATIENTS) AND CONTROLS

PARAMETERS	CASES (n=45) Mean ± SD	CONTROLS (n=35) Mean ± SD	P value
GFR (mL/min/ 1.73m^2)	22.22 ± 8.70	95.87 ± 7.43	<0.001*
Hs CRP(mg/L)	26.08 ± 5.73	0.83 ± 0.15	<0.001*

* Significant

Fig I: Comparison of mean values of GFR (mL/min/1.73m$^{2)}$ and HsCRP (mg/L) in CKD cases and controls

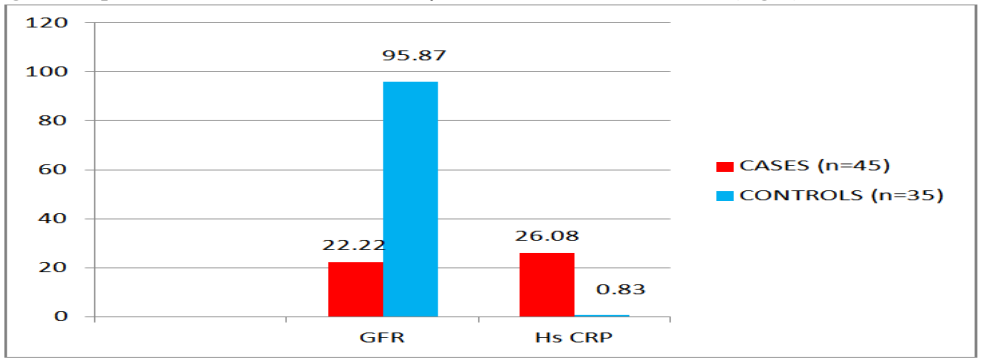


TABLE – II: MEAN AND SD VALUES OF BIOCHEMICAL PARAMETERS IN STAGE III, STAGE IV AND ST AGE V CKD PATIENTS

PARAMETERS	STAGE III	STAGE IV	STAGE V	'P' VALUE
GFR (mL/min/1.73m^2)	33.40 ± 2.58	20.71 ± 3.69	11.03 ± 2.14	< 0.001*
Hs CRP (mg/L)	19.46 ± 2.31	26.96 ± 3.48	32.76 ± 3.24	< 0.001*

* Statistically significant

Fig II: Comparison of mean values of GFR and HsCRP in stage III, IV, V CKD cases

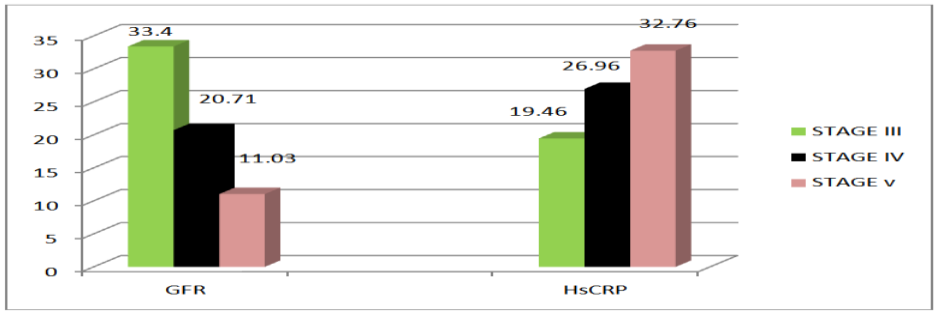
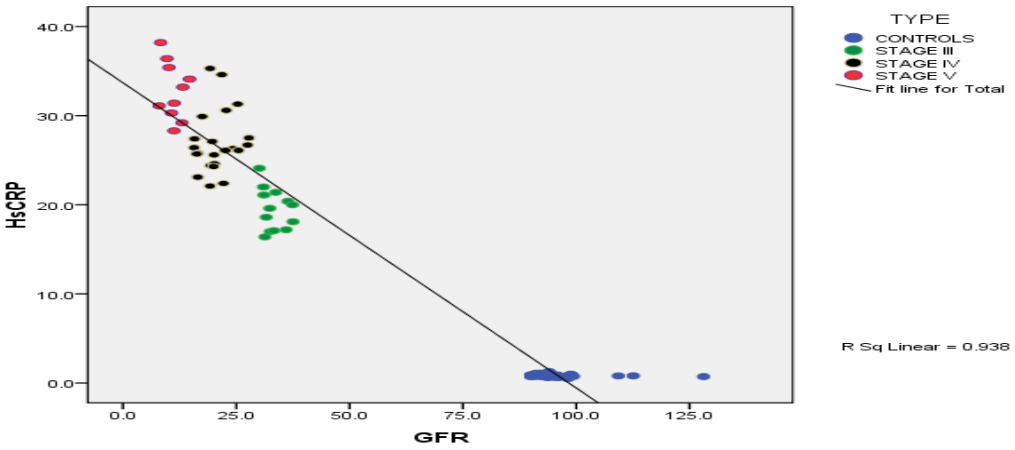


TABLE – III : PEARSON'S CORRELATION ANALYSIS BETWEEN GFR AND Hs CRP IN CKD PATIENTS

PARAMETERS	CORRELATION COEFFICIENT (r)	P value
Hs CRP Vs GFR	-0.969	<0.001*

* Significant



IV. DISCUSSION:

The results of the present study are discussed under two major groups.

1. Chronic kidney disease patients
2. Control group

4.1 CHRONIC KIDNEY DISEASE PATIENTS:

A total number of 45 cases of chronic kidney disease patients have been studied. All these subjects hav e GFR less than 90 mL/min/1.73m^2. This group has been divided into 3 stages as stage III, stage IV and stage V based on the GFR. A total number of 13 cases of stage III, 22 cases of stage IV and 10 cases of stage V were stu died.

GFR values of stage III are 30-59 mL/min/1.73m^2, stage IV are 15-29 mL/min/1.73m^2 and stage V are l ess than 15 mL/min/1.73m^2. The following observations were made.

4.2 CONTROL GROUP:

A total number of 35 subjects have been studied. All the subjects have GFR more than 90 mL/min/1.73 m^2.

The mean age of control group was 51.37 ± 5.78, stage III cases was 51.46 ± 7.70, stage IV cases was 5 7.59 ± 5.98, stage V cases was 57.1 ±5.82 and the mean age of total cases was 55.71 ± 6.91. Control group and s tage III group are in similar age group, stage IV and stage V are in similar age groups. As the age advances it ma y progress in stage from stage III to stage V.

The following observations were made with reference to various biochemical parameters.

4.3 HIGH SENSITIVE C –REACTIVE PROTEIN:

The gold standard among the microinflammatory markers for the measurement of inflammation is C –r eactive protein (CRP). It is a good predictor of short term mortality and has become a routine test in dialysis unit s to warn of inflammation. The plasma levels of the prototypical acute phase protein CRP have been demonstrat ed in numerous studies to be a powerful predictor of subsequent cardiovascular events and all cause mortality in the dialysis population. In our study we found the levels of Hs CRP were high in patients with chronic kidney di sease as compared to the controls. The mean and standard deviation (SD) of Hs CRP in the total cases was 26.08 ±5.73, in stage III was 19.46±2.31, in stage IV was 26.96±3.48, in stage V was 32.76±3.24 and in the control gr oup was 0.83±0.15. The values obtained were statistically significant, P value <0.001. In our study we found much higher values when compared to the previous studies by Ortega et al (13) which showed an increase in Hs CRP levels (8.3 ± 14.2mg/L) in pre dialysis patients. In another study by Menon et al (14) there was an increase in Hs CRP levels (2.2 mg/L) in pre dialysis patients.

Haubitz M et al by using a sensitive CRP assay showed a significant increase in 24 hrs after a dialysis s ession (15).Although CRP is one of the most sensitive acute phase reactants, it does not provide diagnostic speci ficity. CRP concentrations in plasma increase with inflammation and cardiovascular disease, but also increased l evels of CRP are seen in surgical intervention, trauma, infections and neoplastic processes. Renal patients freque ntly present with infections and risk factors that stimulate inflammation.

A significant negative correlation was found between Hs CRP and GFR (r= -0.969, P value <0.001).

Thus our present study on inflammatory marker in chronic kidney disease patients showed the presence of pro inflammatory state as evidenced by significant increase in Hs CRP concentration.

V. SUMMARY AND CONCLUSION:

Chronic kidney disease is a global problem which should be diagnosed at an early stage so that an immedi ate intervention can be undertaken and its progression to end stage renal failure can be curtailed. The levels of Hs CRP were found to be elevated in patients with CKD compared to control group. There was a significant rela tionship between reduced GFR and Hs CRP levels which suggests that there is inflammatory activity in the CK D patients.

REFERENCES:

[1]. Tsai Y, Lee C, Huang T, Cheng B. Inflammatory marker but not adipokine predicts mortality long term haemodialysis patients – Hindawi publishing corporation mediators of inflammation. 2007; 1-5.

[2]. Myers L, Christenson HM, Cushman M, Ballantyne M, Cooper R. National academy of clinical biochemistry laboratory medicine practice guidelines: emerging biomarkers for primary prevention of cardiovascular disease. *Clinical chemistry*. 2009; 55: 378-84.

[3]. Mora S, Musunuruand K, Blumenthal RS. The clinical utility of high sensitivity C-reactive protein in cardiovascular disease and the potential implication of Jupiter on current practice guidelines. *Clinical chemistry*. 2009; 55: 219-28.

[4]. Lamire E, Barsoom R. The burden of kidney disease. *Kidney international*. 2004; 1310.

[5]. Johnson CAJ, Levey AS, Coresh J, et al: Clinical practice guidelines for chronic kidney disease in adults: Part 1. Definition, disease stages, evaluation, treatment and risk factors. *Am Fam phys* 2004; 70(5): 869-76

[6]. Kidney-Failure-Symptoms. Causes of acute renal failure and chronic renal insufficiency. Found at: http://www.kidney –failure-symptoms.com. Accessed January 26, 2005.

[7]. Ferrone M: Pharmaceutical interventions in chronic kidney disease. *US Pharm* 2004; 11: HS34-45.

[8]. Kasper DL, Braunwald E, Fauci AS, et al: Harrison's internal medicine. New York, N.Y.McGraw-Hill, 2005: 1653-63.

[9]. Muntner p, He J, Hamm L, Loria C, Whetton PK. Renal insufficiency and subsequent death from cardiovascular disease. *J Am Soc Nephrol* 2002; 13: 745-53.

[10]. Manjunath G, Tighromart H, Ibrahim H. Level of kidney function as a risk factor for cardiovascular outcomes in the elders. *Kidney Int* 2003; 63: 1121-9.

[11]. Pepys MB, Hirschfield GM. "C-reactive protein: a critical update." *J. clinical investigations*. 2003; 111(12): 1805-12.

[12]. Zimmer man J, Herrlinger S, Pruy A, et al. Inflammation enhances cardiovascular risk and mortality in haemodialysis patients. *Kidney Int*. 1999; 54: 648-658.

[13]. Ortega O, Rodriguez I, Gallar P, et al. Significance of high C–reactive protein levels in predialysis patients. *Nephrol Dial Transplant* 2002; 17: 1105-9.

[14]. Menon V, Wang X, Green T, Beck GJ, Kusek JW, Marcovina SM. Relationship between C reactive protein, albumin, and cardiovascular disease in patients with chronic kidney disease. *Am J Kidney Dis* 2003; 42: 44-52.

[15]. Haubitz M, Brunkhorst R, Wrenger E, Froese P, Schulze M. chronic induction of C-reactive protein by haemodialysis, but not by peritoneal dialysis therapy. *Peritoneal Dialysis International*. 1996; 16: 158-62.

[16]. National Kidney Foundation K/DOQI.KDOQI CKD clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. National Kidney Foundation 2002. Found at: http://www.kidney.org. Accessed January 26, 2005.