Comparative Study of Hscrp in Chronic Kidney Disease

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ABSTRACT

BACKGROUND: Chronic kidney disease (CKD) is a global threat to health mainly in developing countries because therapy is expensive and lifelong. Early detection of Chronic kidney disease (CKD) and its consequent complications can prevent its grave consequences. 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 an 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 levels 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 method 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 group. 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 kidneys. Nephrons are injured by toxic or immunological injury that may injure the glomerulus or the tubule or both together. Thus a significant reduction in functioning renal mass must have occurred much earlier than the onset of significant symptoms or any major biochemical alterations in blood (4). Renal failure is of two types acute renal failure and chronic renal failure. Chronic renal disease also known as chronic kidney disease (CKD) is progressive loss of function over a period of months or years through five stages. Each stage is a progression through a spectrum of abnormalities low and deteriorating Glomerular filtration rate (GFR), which is usually determined indirectly by the creatinine levels in the blood. The number of patients treated with dialysis or transplantation is progressively increasing from 3,40,000 in 1999 to 6,51,000 in 2010 (5). The most common causes of CKD are Diabetes mellitus and 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 and function, ultimately leading to ESRD (7). The pathophysiology of CKD involves initiating mechanisms specific to the underlying etiology, as well as a set of progressive mechanisms that are a common consequence following long term reduction of renal mass, irrespective of etiology. This reduction in renal mass causes structural 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 increased glomerular capillary pressure and flow. These short term adaptations eventually prove maladaptive because 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 maladaptive hypertrophy and sclerosis (8). CKD is identified when the GFR has been <60ml/min/1.73m² 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 an increase in progression of chronic kidney disease to end stage renal disease (ESRD). Haemodialysis 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 levels 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 his chronic kidney disease patients and accounts for 40-50% of all deaths in end stage renal disease patients. Mortality rates due to CVD are approximately 15 times higher in the ESRD population than in the general population. The Second National Healthy and Nutrition Examination Survey (NHANES II) showed that an estimated GFR of less than 70 ml/min/1.73m² was associated with a 68% increase in the risk of death from any cause and a 51% increase in the risk of death from CVD (9). In the Atherosclerosis Risk in the Communities study, an estimated GFR of 15-59 ml/min/1.73m² at baseline was associated with a 38% increase in the risk of CVD (10).

C- Reactive protein is an acute phase plasma protein produced by the liver and by adipocytes. It is a member 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 reactants. 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 up to 50,000 fold. It rises above normal limits within 6 hrs and peaks at 48 hrs. Its half life is constant and therefore its level is mainly determined by the rate of production (11). CRP binds to phosphorylcholine on microbes and helps in complement binding to foreign cells and enhances phagocytosis by macrophages. It also plays an important role in innate immunity. Patients with CKD and ESRD show elevated CRP levels in keeping with the underlying chronic inflammatory state. There 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 any previous history of cardiovascular disease with an acceptance precision level below 0.3 mg/L. Hs CRP assay is 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 College and department of General Medicine, Sri Venkateswara Ramarayan Ruia Government General Hospital, Tirupati. Total number of subjects selected were 80 who are in the age group of 35-65 yrs of age. Among them 45 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, and V based on their estimated GFR levels as per National Kidney Foundation K/DOQI.KDOQI CKD clinical practice 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 m² for ≥ 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 informed 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 sensitive CRP was estimated by using standard method on the same day of collection by Turbidimetric method, kit method 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 significance 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

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>CASES (n=45) Mean ± SD</th>
<th>CONTROLS (n=35) Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (mL/min/1.73m²)</td>
<td>22.22 ± 8.70</td>
<td>95.87 ± 7.43</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Hs CRP (mg/L)</td>
<td>26.08 ± 5.73</td>
<td>0.83 ± 0.15</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Fig I: Comparison of mean values of GFR (mL/min/1.73m²) and HsCRP (mg/L) in CKD cases and controls

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

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>STAGE III</th>
<th>STAGE IV</th>
<th>STAGE V</th>
<th>‘P’ VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR (mL/min/1.73m²)</td>
<td>33.40 ± 2.58</td>
<td>20.71 ± 3.69</td>
<td>11.03 ± 2.14</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Hs CRP (mg/L)</td>
<td>19.46 ± 2.31</td>
<td>26.96 ± 3.48</td>
<td>32.76 ± 3.24</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

* 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

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>CORRELATION COEFFICIENT (r)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hs CRP</td>
<td>Vs GFR</td>
<td>-0.969</td>
</tr>
</tbody>
</table>

* 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 have GFR less than 90 mL/min/1.73m². 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 studied.

GFR values of stage III are 30-59 mL/min/1.73m², stage IV are 15-29 mL/min/1.73m² and stage V are less than 15 mL/min/1.73m². 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 m².

The mean age of control group was 51.37 ± 5.78, stage III cases was 51.46 ± 7.70, stage IV cases was 57.59 ± 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 stage III group are in similar age group, stage IV and stage V are in similar age groups. As the age advances it may 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 –reactive protein (CRP). It is a good predictor of short term mortality and has become a routine test in dialysis units to warn of inflammation. The plasma levels of the prototypical acute phase protein CRP have been demonstrated 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 disease 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 group 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 session (15).Although CRP is one of the most sensitive acute phase reactants, it does not provide diagnostic specificity. CRP concentrations in plasma increase with inflammation and cardiovascular disease, but also increased levels of CRP are seen in surgical intervention, trauma, infections and neoplastic processes. Renal patients frequently 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 immediate 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 relationship between reduced GFR and Hs CRP levels which suggests that there is inflammatory activity in the CKD patients.

REFERENCES:


