

## Original Research Article

# Study of serum homocysteine level in patients with chronic kidney disease and its association with renal function and serum albumin

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## ABSTRACT

**Background:** Chronic kidney disease (CKD) includes irreversible destruction of nephrons leading to progressive decline in glomerular filtration rate. A preferential defect in Homocysteine disposal could hypothetically occur in CKD and subsequently lead to hyperhomocysteinemia. Understanding the status of Homocysteine and other parameters in CKD is useful in the management of the disease. Objective of the study is to estimate serum Homocysteine in CKD patients and its association with renal function and serum albumin in patients with CKD.

**Methods:** The study design involves hospital based observational comparative study. The study was conducted in Department of Biochemistry in association with Department of Nephrology of Mahatma Gandhi Medical College and Hospital, Jaipur between May 2017 to June 2018. 100 diagnosed patients of CKD, visiting the Outpatient Department of Nephrology were enrolled as cases for the study. Patients having cardiovascular disease, Chronic liver disease, Age more than 60 years and pregnant females were excluded from study. The control group consists of 100 age and sex matched healthy individuals.

**Results:** The mean serum creatinine levels of case and control group were  $7.50 \pm 3.74$  mg% and  $0.83 \pm 0.22$  mg% respectively. The mean of serum homocysteine levels of subject group was  $27.35 \pm 12.52$   $\mu\text{mol/L}$  while the mean serum homocysteine levels of control group was  $11.06 \pm 3.52$   $\mu\text{mol/L}$ . The serum homocysteine levels were significantly higher in the CKD patient group. The serum level of albumin in CKD patients and control group were  $2.86 \pm 0.86$  g/dl and  $4.10 \pm 0.58$  g/dl respectively. A positive correlation was found between serum creatinine and serum homocysteine levels. A negative correlation between serum homocysteine and serum albumin was found.

**Conclusions:** Findings of the present study exhibit that serum homocysteine levels are elevated in CKD in comparison to healthy controls and it is positively correlated with serum creatinine level.

**Keywords:** Albumin, Jaipur, Amino acid, Chronic kidney disease, Homocysteine

## INTRODUCTION

Chronic kidney disease (CKD) is characterized by chronic irreversible destruction of kidney tissues. It is a worldwide public health problem with an increasing incidence and prevalence. Current evidence suggests diabetes and hypertension to be the major causes of kidney diseases worldwide.<sup>1</sup> Homocysteine is a sulphur containing intermediary amino acid which is derived by the demethylation of methionine. The primary source of

methionine is animal protein.<sup>2</sup> The normal range of Homocysteine is 5 to 15  $\mu\text{mol/L}$ .<sup>3,4</sup> It is cleared from the body by urinary excretion after glomerular filtration. However, the amount of Homocysteine in the urine is minimal. From a normal Glomerular Filtration Rate (GFR) of 180 L/day, it is estimated that 99% of the filtered Homocysteine is reabsorbed.<sup>5</sup>

Homocysteine transsulphuration and remethylation occurs in human kidney tissue, indicating that its metabolism is

possible. Studies in the rat have shown that Homocysteine is taken up and metabolized by the kidney.<sup>6</sup> Arteriovenous distribution in Homocysteine concentration across the kidney is however debated.<sup>7,8</sup> A preferential defect in Homocysteine disposal could hypothetically occur in CKD and subsequently lead to hyperhomocysteinemia. For the above theory, however, there is no supportive evidence. Further loss of renal amino acid metabolism in CKD does not always predict the consequences on plasma concentration.<sup>9</sup>

Hyperhomocysteinemia may be due to genetic insufficiencies of the enzymes needed for its metabolism, nutritional deficiencies in vitamin cofactors, or other circumstances such as drugs and medical conditions. Similarly, low intake and plasma concentrations of folate and vitamins B<sub>6</sub> and B<sub>12</sub> have been associated with increased plasma Homocysteine levels. Recently, hyperhomocysteinemia has been linked to CKD.<sup>10</sup> Understanding the status of Homocysteine and other parameters in CKD stages is useful in the management of the disease. The present study was planned to study the Homocysteine levels in patients with CKD.

## METHODS

This prospective observational study was conducted in Department of Biochemistry in association with Department of Nephrology of Mahatma Gandhi Medical College and Hospital, Jaipur from May 2017 to June 2018. 100 Patients diagnosed for CKD, visiting the Outpatient Department of Nephrology fulfilling the inclusion criteria were enrolled for the study. Age and sex matched 100 healthy subjects constituted the control group. The study was conducted after seeking approval from Institutional Ethical Committee (IEC). Written informed consent was obtained from all participants before enrollment into the study.

### Inclusion criteria

- Patients diagnosed with chronic kidney disease.
- Patient who are willing to participate.

### Exclusion criteria

- Patients of Chronic liver disease.
- Pregnant women.
- Patients of Cardiovascular disease.
- Patients age more than 60 yrs.

Serum urea, creatinine, homocysteine levels were measured using Vitros 4600 in all study subjects. The results obtained were presented as mean±SD. All parameters analyzed were compared between case and control groups by applying student's t-test. Pearson's correlation was further applied between serum levels of homocysteine, albumin, and creatinine in CKD subjects. p value ≤0.05 was considered as statistically significant.

## RESULTS

Authors enrolled 100 patients (69 male and 31 females) of diagnosed cases of chronic kidney disease and 100 (68 male and 32 females) healthy individuals as control group. Males were found to be more prone to CKD as compared to that of females. Mean age of patients and controls were 45.30 and 46.56 years respectively. The mean age in subject and control group was comparable.

In this study authors compared Renal Functions of cases and controls by measuring serum urea and serum creatinine. Serum urea level of case and control groups were 131.89±77.42 mg% and 26.28±7.07 mg% respectively.

The mean serum creatinine levels of case group was 7.50±3.74 mg% and of control group was 0.83±0.22 mg%. The mean of both urea and creatinine levels were significantly higher in cases as compared to control group.

In this study authors observed that the mean serum level of homocysteine in subject group was 27.35±12.52 µmol/L while the mean serum level of homocysteine in control group was 11.06±3.52 µmol/L. The serum homocysteine levels were significantly higher in the CKD patient group (Table.1).

**Table 1: Comparison of serum homocysteine level between case and control groups.**

| Group   | No of cases | S. Homocysteine (µmol/L) (Mean±SD) | t-value | p-value |
|---------|-------------|------------------------------------|---------|---------|
| Case    | 100         | 27.35±12.52                        | -12.526 | 0.000   |
| Control | 100         | 11.06±3.52                         |         |         |

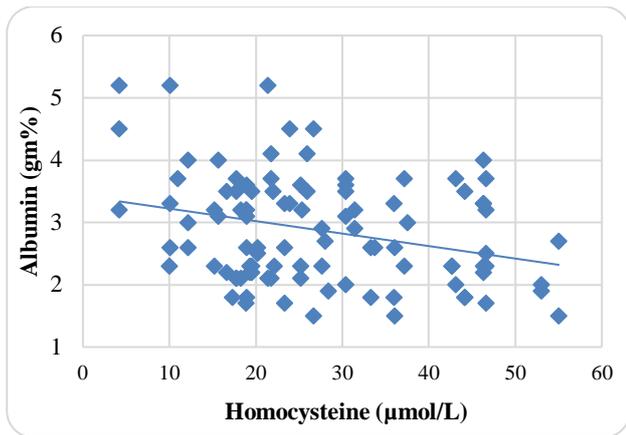
On comparing the serum level of albumin in CKD patient and control groups authors found those were 2.86±0.86 g/dl and 4.10±0.58 g/dl respectively (Table.2).

**Table 2: Comparison of serum albumin level between case and control groups.**

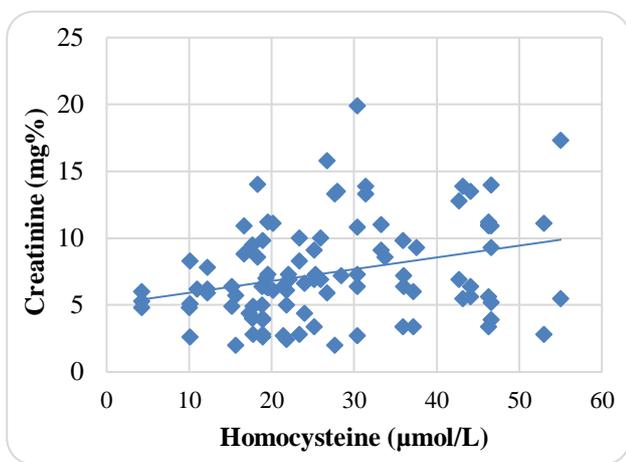
| Group   | No of cases | S. Albumin (g/dl) (Mean±SD) | t-value | p-value |
|---------|-------------|-----------------------------|---------|---------|
| Case    | 100         | 2.86±0.86                   | 11.954  | 0.000   |
| Control | 100         | 4.10±0.58                   |         |         |

A negative correlation was observed between serum levels of homocysteine and albumin with correlation coefficient of -0.291 (p=0.003) (Figure.1).

Correlation coefficient of serum homocysteine v/s serum creatinine was +0.301 (p=0.008). So positive correlation found between serum creatinine and serum homocysteine levels (Figure 2).



**Figure 1: Correlation between serum values of homocysteine and albumin.**



**Figure 2: Correlation between serum values of homocysteine and creatinine.**

**DISCUSSION**

CKD, also called as chronic renal disease, is progressive decline in kidney function over a period of months or years. Symptoms of CKD are nonspecific and it is diagnosed as a result of screening of high-risk individuals, example as those having hypertension, diabetes mellitus.<sup>11,12</sup>

Kidney function tests include measuring serum levels of urea and creatinine. The major pathway of nitrogen excretion is in the form of urea. It is synthesized in the liver, released into the blood, and cleared by the kidneys. Creatinine is a waste product of muscle metabolism and its precursor is creatine. Creatinine is excreted by glomerular filtration and it is minimally reabsorbed. So by measuring creatinine clearance authors can estimate GFR. Creatinine levels may be normal in the early stages of CKD.<sup>11</sup>

In the present study the mean age of control and patient group was comparable with no significant variation. This finding was in contrast with study conducted by Prakash

S et al, concluded the higher prevalence of CKD in the elderly reflects the presence of a variety of different risk factors like diabetes and hypertension in older individuals.<sup>13</sup> However high rates of CKD in the elderly may also occur because of an age associated decline in kidney function that is not explained by other known factors.<sup>13</sup>

In the present study, sex distribution among the CKD and control group was almost similar. Mean sex distribution of subject group showed higher incidence of CKD in male than female. That was in contrast with study conducted by Idan Goldberg et al, proposed that the prevalence of CKD tends to be higher in women, whereas the disease in men is more severe which is associated with the influence of sex hormones on several biological processes involve in kidney injury.<sup>14</sup>

On comparing the renal profile in control and CKD group of patients it was observed that serum urea and creatinine were significantly higher in CKD group as compared to control group.

Inflammation of nephron occurs in CKD which further affects filtration capacity of glomerulus. This leads to albuminuria, finally causing hypoalbuminemia.<sup>15</sup> It was observed in present study that mean albumin level of control group was  $4.10 \pm 0.58$  g/dl while the mean albumin level of subject group was  $2.86 \pm 0.86$  g/dl. Serum albumin was significantly lower in the CKD patients. Study conducted by Guest S et al, reported that the development of hypoalbuminemia in CKD patient has been associated as a part of acute phase response and certain non-nutritional factors such as inflammation, volume status and comorbidities.<sup>15,16</sup>

The mean of Serum Homocysteine levels of control group was  $11.06 \pm 3.52$  µmol/L while the mean homocysteine levels of subject group was  $27.35 \pm 12.52$  µmol/L. The serum homocysteine levels were significantly higher in the CKD patient group. Li J et al, reported that the kidney function is critical for Hcy clearance, and hyperhomocysteinemia occurs frequently in patients with renal failure.<sup>17</sup> Friedman AN et al, concluded that the hyperhomocysteinemia of renal disease is primarily attributable to reduced renal clearance and intrarenal metabolism.<sup>18</sup>

The present study shows a positive correlation of Homocysteine with serum creatinine and a negative correlation of serum Homocysteine with serum albumin which clearly depicts hyperhomocysteinemia and hypoalbuminaemia as comorbid conditions and a potent risk factor of cardiovascular disease in CKD subjects.

**CONCLUSION**

Findings of the present study exhibit that serum homocysteine levels are elevated in CKD. A positive correlation of serum homocysteine with serum creatinine

and a negative correlation with serum albumin indicates that increase in serum homocysteine is associated with the progressive decline of kidney functions. In other words, elevated homocysteine in CKD patients indicates progression of disease. The study recommends screening of chronic kidney disease patients for serum Homocysteine.

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