

ASSOCIATION BETWEEN CHRONIC KIDNEY DISEASE AND PLASMA HOMOCYSTEINE LEVEL - A HOSPITAL BASED STUDY

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Abstract

Background: CKD is defined as the presence of kidney damage, manifested by abnormal albumin excretion or decreased kidney function, quantified by measured or estimated glomerular filtration rate (GFR), that persists for more than 3 months. **Methods:** The hospital based cross-sectional study was conducted on 100 patients with CKD. Patients fell within the ages of 20 to 85 years and either were with stage 2–5 CKD. They were recruited from the outpatient clinic of the Division of general medicine govt. medical college, Bharatpur (Rajasthan). Patients' diagnoses and CKD staging were confirmed by an experienced Physician.

Results: Mean value of homocysteine level was 15.35 $\mu\text{mol/L}$ in stage 2-3 and 28.34 $\mu\text{mol/L}$ in stage 4-5 of CKD patients.

Conclusion: Level of homocysteine increased according to the stages of CKD.

Keywords: Homocysteine, GFR, CKD.

Introduction:

CKD is defined as the presence of kidney damage, manifested by abnormal albumin excretion or decreased kidney function, quantified by measured or estimated glomerular filtration rate (GFR), that persists for more than 3 months.¹

CKD, with its high prevalence, morbidity and mortality, is an important public health problem. With <3% of land mass, India hosts 17% of the Earth's population. Large numbers of patients below the poverty line, low gross domestic product, and low monetary allocations for health care have led to suboptimal outcomes. Moreover, CKD and other noncommunicable diseases have often been ignored in the face of persistent challenges from and competition for resources for communicable diseases and high infant and maternal mortality.²

Homocysteine (Hcy) is a thiol-containing amino acid that is derived from methionine. Methionine from dietary sources or from the breakdown of endogenous protein is converted to S-adenosyl methionine (SAM) by the enzyme SAM synthase. SAM is a major methyl group donor for various methylation reactions. When the methyl group is transferred by methyltransferases to respective

acceptors, SAM is converted to S-adenosylhomocysteine (SAH) and then subsequently hydrolyzed by SAH hydrolase to form Hcy and adenosine. Once formed, Hcy can be metabolized by two alternative pathways: remethylation (RM) and transsulfuration (TS).³

The tHcy level in patients with ESRD is 3-5 times higher than normal, and the prevalence of HHcy in this patient group is 85-100%. Almost every study has shown a highly significant positive correlation between the concentrations of creatinine and Hcy. GFR values estimated from serum creatinine or calculated creatinine clearance are consistently and inversely correlated with plasma Hcy levels. This relationship is a powerful indirect evidence that elevated Hcy levels in renal disease are intimately linked to kidney function.⁴

The close relationship between plasma Hcy and GFR suggests that Hcy is cleared from the body by urinary excretion after glomerular filtration, just like creatinine. It has been shown that kidney plays a major role in the maintenance of Hcy plasma homeostasis in rats.⁵ However, studies performed in humans have not shown the occurrence of any significant arteriovenous gradient of Hcy across this

organ ⁶. In hypertensive patients, the fractional extraction of Hcy across the kidney is positively related to renal plasma flow but not to GFR, indicating that in humans the removal of Hcy is less than it occurs in rodents, and that it is limited to conditions characterized by elevated renal blood flow. In addition, many studies showed that clinically stable renal transplant recipients have an excess prevalence of HHcy, suggesting that improvement of the GFR in these patients does not completely restore plasma Hcy to normal.⁷

Material and method

The hospital based cross-sectional study was conducted on 100 patients with CKD. Patients fell within the ages of 20 to 85 years and either were with stage 2–5 CKD [estimated glomerular filtration (eGFR) ≤ 89 mL/min/1.73 m²]. They were recruited from the outpatient clinic of the Division of general medicine govt. medical college, Bharatpur (Rajasthan). Patients’ diagnoses and CKD staging were confirmed by an experienced Physician.

Exclusion criteria included patients who were clinically unstable, pregnant, lactating, or having a history of liver disease, chronic inflammatory disease, cancer, or alcoholism.

Subjects’ age, gender, smoking, and drinking habits, along with their nutritional supplements were recorded. CKD patients’ height, weight, waist circumference, and systolic and diastolic blood pressure (SBP and DBP) were measured on an appointed day while patients receiving hemodialysis treatment were measured on an appointed day at a prehemodialysis session. Body mass index (BMI, kg/m²) was then calculated.

Blood samples taken after a period of fasting were drawn and collected in vacutainer tubes containing ethylenediaminetetraacetic acid as the anticoagulant. Serum or plasma was separated within 30 minutes after blood was collected and immediately measured or then frozen (-80°C) until analysis. Serum albumin, glucose, total cholesterol, creatinine, and blood urea nitrogen were measured using an automated biochemical analyzer. Homocysteine were quantified by high performance liquid chromatography using fluorescence detection.

Data analysis

Student’s T-test and Chi-square test were applied. Results were presented as mean ± SD or no. of

patients (percent); P value <0.05 defined statistical significant difference.

Results

Table 1: Demographic characteristics of patients with chronic kidney disease

Variable	Stage 2-3 CKD	Stage 4-5 CKD	p-value
Mean age ± SD(Yrs)	53.16±12.34	55.14±12.16	>0.05
Male: Female	38:12	37:13	>0.05
BMI(kg/mt ²)	23.34±2.41	24.12±2.87	>0.05
Waist circumference (Cm)	87.12±2.21	88.17±2.18	>0.05

Mean age of stage 2-3 CKD patients was 53.16 Yrs and stage 4-5 CKD patients was 55.14 Yrs. Male and female ratio in stage 2-3 CKD patients was 38:12 and in stage 4-5 CKD patients was 37:13.

Table 2: Homocysteine level

Variable	Stage 2-3 CKD	Stage 4-5 CKD	p-value
Homocysteine (µmol/L)	15.35±0.65	28.34±1.32	<0.05

Mean value of homocysteine level was 15.35 µmol/L in stage 2-3 and 28.34 µmol/L in stage 4-5 of CKD patients.

Discussion

Recently, disulfuramino acid homocysteine has gained much importance because of its role in vascular thrombosis and genesis of atherosclerosis. Studies have shown an increased prevalence of hyperhomocysteinemia in CKD patients and its association with cardiovascular morbidity and mortality. In the current study, we found that CKD patients had hyperhomocysteinemia correlating with other studies conducted elsewhere in the world and hyperhomocysteinemia was more prevalent as stages of CKD increases.

Menon V *et al*⁸ reported that hyperhomocysteinemia was prevalent in 56% Of CKD patients and hyperhomocysteinemia was partly amenable to treatment with vitamins in stages 3 and 4. Even though our study sample size was smaller, we found that hyperhomocysteinemia was more prevalent in the later stages of CKD. It was in accordance with the concept that as renal function deteriorates the homocysteine excretion decreases and its level increases in plasma.

Nair AP *et al*⁹ reported homocysteine level transiently decreased after a dialysis session but fell to normal range within two to three days to predialysis value.

We observed that the majority of patients with CKD had some ECG abnormality correlating well with the statement that cardiovascular morbidities are the most important cause of mortality in patients with CKD.¹⁰

Our main concern to evaluate for the presence or absence of hyperhomocysteinemia in CKD patients was to decrease the cardiovascular morbidity and mortality. So, its worthy to take measures to decrease homocysteine levels in patients with CKD. These findings should be considered understudies limitations. First, we could not exclude other genetic variations which might have influenced homocysteine level. Second, the exact correlation between decreased renal function and level of hyperhomocysteinemia could not be assessed due to the non-uniform distribution of sample size among CKD patients. Systematic reviews had reported the effect of B12 supplementation on decreasing homocysteine levels in patients with ESRDs when combined with folate supplementation.¹¹ But the levels of Vit B12 and folic acid, pyridoxine level could not be measured in the current study due to financial restriction.

Conclusion

Level of homocysteine increased according to the stages of CKD.

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