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To study Plasma homocysteine levels in chronic kidney disease

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Abstract
Background: Numerous factors contribute to the widespread prevalence of chronic kidney disease (CKD). Hyperhomocysteinemia has been linked to increased cardiovascular morbidity and mortality, and it has been reported that chronic renal disease is a leading cause of this condition.
Material and Methods: This was a prospective, single-center study that was carried out at the Department of General Medicine, Annali Medical College and Hospital, Chennai, Tamil Nadu. It was done by the departments of general medicine and nephrology. The study took place over eight months, from February 2013 to February 2014. 40 patients with chronic kidney disease who were admitted to Annali Medical College and Hospital, Chennai, Tamil Nadu and hospital met the standards for inclusion and exclusion.
Observations and Results: Thirty-seven of the 40 cases were men, while 13 were women. There were 34 patients between the ages of 41 and 60. There were 36 patients at Stage 5, 11 at Stage 4, and 3 at Stage 3 of chronic kidney disease. Seventy-eight percent of CKD patients were found to have hyperhomocysteinemia. Hyperhomocysteinemia was mild in 94.87% of the sample. Patients with end-stage renal illness were more likely to have elevated homocysteine levels.
Conclusion: Patients on dialysis and those who are not did not differ significantly in their levels of hyperhomocysteinemia. Patients with CKD frequently suffer from hyperhomocysteinemia.

Keywords: Chronic renal disease, homocysteine, and hyperhomocysteinemia

Introduction
Chronic kidney disease is a prevalent morbidity associated with age and various risk factors. It is characterized by a progressive decline in kidney function, primarily caused by the loss of nephrons. This decline leads to a reduced ability to excrete metabolic waste products from the body, resulting in their accumulation. Consequently, a range of symptoms arises due to fluid retention and extravasation, including pedal edema, acute pulmonary edema, and other signs of volume overload. Additionally, the retention of uremic toxins contributes to further signs and symptoms [1, 2].
The kidneys are essential organs within the human body. The kidneys are located in the posterior position, behind the peritoneum, on both sides of the vertebral column [3]. The superior border of the 12th dorsal vertebra marks their superior position, while their inferior position is located at the 3rd lumbar vertebra. Furthermore, their left side is positioned somewhat superior to the right side. The left side is often slightly longer and smaller than the right side, and it is situated in closer proximity to the median plane. The dimensions of a typical kidney are around 3cm in the anteroposterior direction, 11cm in length, and 6 cm in width. The average weight of the human kidney is said to be 150 grams in males and 135 grams in females. The nephrons serve as the functional units of the kidneys. The structure comprises of the renal tubule and its corresponding glomerulus. It has been observed that the number of nephrons in each human kidney is estimated to be around 1 million [4, 5]. Various varieties of nephrons exist.

There exist nephrons within the cortex as well as nephrons within the Juxtamedullary region. The nephrons located in the cortex possess a somewhat shorter loop of Henle, whereas the nephrons situated in the juxtamedullary area exhibit a longer loop of Henle. According to existing research, it has been shown that around 15% of nephrons in the human body are classified as juxtamedullary nephrons [6].

Chronic renal disease is associated with a variety of systemic disorders. Cardiovascular system involvement is widely recognized as a prominent contributor to morbidity and mortality among individuals with chronic renal disease. Several potential factors have been hypothesized to contribute to the heightened vulnerability to heart disorders and mortality resulting from cardiac diseases in individuals with chronic renal disease. One of the conditions that might occur in individuals with chronic renal disease is hyperhomocysteinemia [7, 8].

Hyperhomocysteinemia arises from a variety of etiological factors. The primary factors contributing to hyperhomocysteinemia in chronic kidney disease (CKD) include reduced elimination of homocysteine by the impaired kidney and altered homocysteine metabolism within the uremic environment. Numerous studies have demonstrated a substantial relationship and inverse correlation between the decline in Glomerular filtration rate and the elevation of homocysteine levels. Numerous current studies are being conducted to investigate the potential impact of reducing homocysteine levels on cardiovascular morbidity and mortality in people with chronic kidney disease (CKD). This study aims to investigate the potential link and correlation between a decline in renal function and an elevation in homocysteine levels [9-11].

The primary objectives of this study were to investigate the homocysteine levels in individuals diagnosed with chronic kidney disease and to examine the potential link and correlation between the decline in renal function and the elevation of homocysteine levels in patients with chronic kidney disease.

Materials and Methods

This was a prospective, single-center study that was carried out at the Annali Medical College and Hospital, Chennai, Tamil Nadu. It was done by the departments of general medicine and nephrology. The study took place over eight months, from February 2013 to February 2014. 40 patients with chronic kidney disease who were admitted to Annali Medical College and Hospital, Chennai, Tamil Nadu and hospital met the standards for inclusion and exclusion.

Inclusion Criteria

- Individuals with elevated serum creatinine and blood urea
- Individuals whose abdominal ultrasounds reveal signs of chronic renal disease

Exclusion Criteria

- Individuals who currently abuse alcohol
- Individuals with documented chronic liver disease
- Individuals with diabetic mellitus

Study Method

This study includes a sample of 40 individuals diagnosed with chronic renal disease who have been admitted to Thanjavur Medical College for symptoms associated with the condition or for other medical reasons. Demographic attributes such as age, gender, body weight, height, and residential address were recorded. The patients were surveyed regarding the existence of a family history of chronic kidney disease, whether they were having dialysis for the condition, the presence or absence of diabetes mellitus, systemic hypertension, chronic liver disease, smoking habits, or alcohol usage. The general and systematic examinations were conducted.

Observation and Results

Among the cohort of 40 individuals diagnosed with chronic renal disease, a significant proportion of patients fell between the age range of 41 to 60 years. The data shown in the table clearly indicates a positive correlation between age and the occurrence and prevalence of chronic renal disease. However, due to the restricted sample size, it is not possible to determine the exact prevalence rates among different age groups. As individuals age, there is a decline in the number of functional nephrons, which contributes to the development of chronic kidney disease (as shown in Table 1).

Table 1: Patient age distribution

Sr. No.	Age	Number of patients
1.	<20	2
2.	21-30	3
3.	31-40	3
4.	41-50	12
5.	51-60	12
6.	>60	08

Patient distribution by sex

Among the participants included in the study, 28 individuals were identified as male, while 12 individuals were identified as female, as indicated in Table 2.

Table 2: Patient distribution by sex

Sr. No.	Gender	Number	Percent
1.	Males	28	70%
2.	Females	12	30%

Cockcroft-gault method for CKD staging based on creatinine clearance and glomerular filtration rate

The majority of patients recruited for this study were in stages 4 and 5 of chronic kidney disease, comprising approximately 94% of the total sample (Table 3).

Table 3: CKD based on glomerular filtration rate and creatinine clearance

Sr. No.	Number of patients
1.	1
2.	2
3.	1
4.	2
5.	20
6.	14

Hyperhomocysteinemia

Among the cohort of 40 participants included in the study, it was observed that around 78% exhibited high plasma Homocysteine levels, as indicated in Table 4.

Table 4: Hyperhomocysteinemia

Sr. No.	Sex	Total number	Normal HCY	Hyper HCY
1.	Males	28	20	08
2.	Females	12	10	02

ECG result in patients with elevated homocysteine and normal CKD

It was noticed that a significant proportion of patients exhibited aberrant electrocardiograph readings, suggesting that a majority of individuals with Chronic Kidney Disease also experienced various cardiac ailments. This observation underscores the prominent role of cardiovascular disorders as primary contributors to morbidity and mortality among CKD patients. The majority of individuals exhibited left ventricular hypertrophy, maybe attributable to the heightened prevalence of hypertension among patients diagnosed with chronic renal disease. Out of the cohort of 40 patients included in the study, 27 individuals exhibited aberrant electrocardiograph readings, accounting for 94% of the sample. Among those diagnosed with hyperhomocysteinemia, only three individuals were observed to exhibit a normal electrocardiogram reading. The remaining individuals exhibited abnormal electrocardiogram readings.

Discussion

In recent times, there has been a significant increase in the significance attributed to the disulfur amino acid homocysteine, mostly due to its involvement in arterial thrombosis and the development of atherosclerosis. Chronic kidney disease exhibits a high prevalence within the general population. Individuals diagnosed with chronic kidney disease exhibit a heightened vulnerability to experiencing adverse cardiovascular events, which can significantly impact their overall health and increase the risk of mortality. Recent investigations have indicated a higher occurrence of hyperhomocysteinemia in patients with chronic kidney disease [12, 13].

Recent literature and online publications have demonstrated a correlation between chronic renal disease and hyperhomocysteinemia, which has been found to substantially contribute to both cardiovascular morbidity and death.

In a study conducted by Menon *et al*., it was observed that hyperhomocysteinemia was discovered to be widespread in 56% of the chronic kidney disease patients included in their research. Furthermore, the study indicated that the condition of hyperhomocysteinemia may be partially improved with the administration of vitamins in stages 3 and 4 of CKD [14, 15]. This study revealed that a significant proportion of patients with chronic kidney disease exhibited hyperhomocysteinemia, aligning with previous research conducted globally. Furthermore, the prevalence of hyperhomocysteinemia was observed to increase as CKD advanced through its phases. Despite the limited size of our study sample, we observed a higher prevalence of hyperhomocysteinemia in the advanced stages of chronic kidney disease. The observed phenomenon can be explained by the correlation between declining renal function and a decrease in the excretion of homocysteine, resulting in an increase in its concentration within the plasma [16-18].

The study observed that the elevation of homocysteine levels in patients was not influenced by the administration of dialysis. This finding contradicts previous literature reviews which suggested that homocysteine levels tend to temporarily decrease after a dialysis session, but return to pre-dialysis values within two to three days. It was discovered that a significant proportion of patients diagnosed with chronic kidney disease exhibited various types of electrocardiogram abnormalities. This finding is consistent with the assertion that cardiovascular complications are the primary contributors to death in individuals with CKD, as indicated by previous studies [19, 20]. The primary objective of our study was to assess the presence or absence of hyperhomocysteinemia in patients with chronic kidney disease in order to mitigate the risk of cardiovascular morbidity and death. Therefore, it is advisable to implement interventions aimed at reducing homocysteine levels in individuals diagnosed with chronic kidney disease [21-23].

Efforts were made to mitigate the influence of confounding variables such as diabetes, smoking, chronic alcoholism, and chronic liver disease, all of which have been identified as independent factors linked with hyperhomocysteinemia [24]. The available evidence on the sexual difference in hyperhomocysteinemia is inconclusive due to variations in sample size and sex proportion. The potential influence of further genetic variants on homocysteine levels must be disregarded. Due to cost constraints, the measurement of Vit B12 and Folic acid levels, as well as Pyridoxine levels, in patients with CKD was not feasible [25-27].

The levels of Vitamin B12 and Folic acid in patients with Chronic Kidney Disease are higher in order to address the condition of hyperhomocysteinemia, in comparison to those who do not have CKD. It is recommended to administer higher doses of vitamins as a supplement in order to address hyperhomocysteinemia in patients with chronic kidney disease, with the aim of reducing the risk of cardiovascular morbidity and death. Additional research is needed to investigate the occurrence and prevalence of hyperhomocysteinemia in patients with Chronic Kidney Disease through studies that involve a larger sample size and measure vitamin levels. Furthermore, genetic studies should be conducted to gain a more comprehensive understanding of this condition. Large cohort studies are also necessary to establish a precise correlation between hyperhomocysteinemia and cardiovascular morbidity and mortality. It is imperative to develop treatment strategies that aim to reduce hyperhomocysteinemia in order to mitigate the risk of cardiovascular morbidity and mortality [28-30].

Conclusion

A prevalence rate of 78% was reported for hyperhomocysteinemia among individuals diagnosed with chronic kidney disease. The occurrence of hyperhomocysteinemia was shown to be higher in individuals with end-stage chronic kidney disease. Elevated levels of homocysteine were observed in individuals with chronic kidney disease who did not undergo dialysis, as well as in those who received intermittent hemodialysis or peritoneal dialysis. The study revealed that a majority of patients diagnosed with chronic kidney disease exhibited mild hyperhomocysteinemia, while a smaller proportion displayed moderate hyperhomocysteinemia. Notably, none of the patients exhibited severe hyperhomocysteinemia. Despite the detection of hyperhomocysteinemia in 78% of the individuals under investigation, it is imperative to conduct more research with a larger sample size and the exclusion of other risk factors associated with hyperhomocysteinemia in

order to substantiate these findings.

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Conflict of Interest: None

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