Section: General Medicine

Original Research Article

ESTIMATION OF PLASMA HOMOCYSTEINE LEVEL IN CHRONIC KIDNEY DISEASE PATIENTS WITH AND WITHOUT DIALYSIS

Maulik Patel[1], R C Bidri[2]

[1]Final year Postgraduate Student, Department of General Medicine, Shri BM Patil Medical College and Research Centre, Vijayapura, Karnataka, India.
[2]Professor & Unit Chief, Department of General Medicine, Shri BM Patil Medical College and Research Centre, Vijayapura, Karnataka, India.

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Corresponding Author:
Dr. Maulik Patel,
Email: maulik2mvp@gmail.com

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Abstract

Background: Chronic kidney disease (CKD) is the gradual and progressive loss of filtration capacity of the kidney and loss of the nephron by various underlying mechanisms. Reduced homocysteine excretion by diseased kidneys and altered homocysteine metabolism in uremic conditions are the main causes of hyperhomocysteinemia in chronic kidney disease (CKD). The objective is to study Plasma Homocysteine levels in patients with chronic kidney disease with and without dialysis. **Materials and Methods:** This cross-sectional study was conducted among patients diagnosed with CKD who were admitted to Shri B M Patil Medical College, Hospital and Research Center, Vijayapura. The patients who met the inclusion and exclusion criteria were selected for the study. and their fasting plasma Homocysteine levels were measured. **Result:** Out of 110 Chronic Kidney Disease (CKD) patients, 66 patients were male and 44 were female and 71% of CKD patients had diabetes mellitus, 61 patients (55%) were on hemodialysis, and 62% had hypertension. Hyperhomocysteinemia was detected in 58% of CKD patients. Among the 63 patients with hyperhomocysteinemia,50 patients had mild hyperhomocysteinemia and 13 patients had moderate hyperhomocysteinemia. Out of 110 patients, 40 patients - 36.36% had cardiovascular and cerebrovascular events; among the majority of cases, about 80% were cardiovascular, and 20% of patients had cerebrovascular events. **Conclusion:** End-stage renal disease patients had an increased prevalence of Hyperhomocysteinemia. Chronic kidney disease Patients with declining kidney function, especially in advanced stages, with no significant impact of dialysis on serum homocysteine level, primarily due to its inadequate clearance, inadequate dialysate composition, vitamin deficiencies, and increased oxidative stress because of frequent dialysis. So management through monitoring and vitamin supplementation is crucial to reducing cardiovascular risks and improving patient outcomes, particularly in those with lower GFR.

INTRODUCTION

"Chronic kidney disease (CKD) is defined as a persistent estimated glomerular filtration rate (eGFR) <60 mL/(min·1.73m2), albuminuria (albumin/ creatinine ratio [UACR] ≥30 mg/g), or other markers of kidney damage for at least 3 months".[1]

Chronic kidney disease is an age-related risk factor with different morbidities affecting many people, with a progressive reduction in glomerular filtration rate (GFR).

Retention of fluid leads to hypervolemia and fluid shifting to the extravascular compartment, resulting in bilateral pedal edema, acute pulmonary edema, and other symptoms, as well as the retention of uremic toxins.[1]

Chronic kidney disease causes numerous systemic abnormalities. In chronic kidney disease patients, the major cause of increased morbidity and mortality is cardiovascular system involvement. Many factors have been identified as increasing susceptibility to cardiac vascular disease and death in people with chronic kidney disease. Hyperhomocysteinemia is one of the causes of CKD.

Reduced homocysteine excretion by diseased kidneys and altered homocysteine metabolism in uremic conditions are the main causes of hyperhomocysteinemia in chronic kidney disease (CKD).[1] Numerous ongoing studies have demonstrated a strong negative connection and link between increased homocysteine levels and decreased glomerular filtration rate. There are several studies to determine if cardiovascular mortality will

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be reduced in CKD patients with lower homocysteine levels.
So, in this study, we investigated the relationship and correlation between decreasing renal function and a rise in homocysteine levels.

MATERIALS AND METHODS

This Cross-sectional study was conducted among Patients diagnosed with CKD were admitted to Shri B M Patil Medical College, Hospital and Research Center, Vijayapura. The patients who fulfilled the inclusion criteria and exclusion criteria were taken up for the study; demographic data, history, and systemic examination were recorded. The duration of the study was 18 Months.

Inclusion Criteria

Age >18 years, male and female
eGFR<60 mL/min/1.73 m2

Exclusion Criteria

Acute kidney injury
Current Alcoholics
Chronic Liver disease
Pregnancy

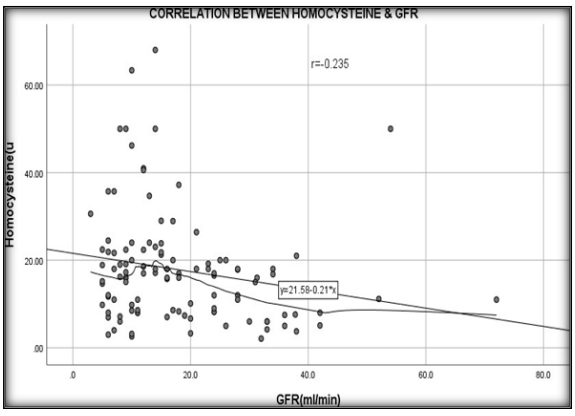
Calculation of Sample Size: With the anticipated Proportion of chronic kidney disease patients, 17% (1) 110 patients would be needed for the investigation, with a 95% confidence level and 7% absolute precision.
Formula used,
n=z2 p*q
Where Z= Z statistic at α level of significance d2= Absolute error
P= Proportion rate
q= 100-p
Size of 110 patients with 95%level of confidence and 7% absolute precision.

Statistical analysis: The data obtained was entered into a Microsoft Excel sheet, and statistical analysis was performed using the statistical package for the JMP SAS 16 Software. Information displayed as Mean ±SD or Median and Interquartile rage, percentages, numbers, and charts. The Independent t-test is used to compare regularly distributed continuous variables across two groups, and the Whitney U test is used to compare non-normally distributed variables. Categorical variables were compared using the Chi-square test. Comparison of eGFR of homocysteine concentration will be analyzed using ANOVA test with post hoc. Odd's Ratio and 95% CI having CKD patients compared with their plasma homocysteine levels. Statistics are considered significant when P is less than 0.05. Every statistical test was run with two tails.

RESULTS

A total of 110 chronic kidney disease patients who were chosen between the 50–70 age range. The age group of less than 40 years old accounted for the least number of patients (15.5%).

The incidence and prevalence of individuals with chronic renal disease rise with age. Chronic kidney disease is caused by a decline in the number of functional nephrons as age increases. Out of 110 patients of CKD 60% are male and 40% are female. The study included 66 males and 44 females.
In this study 71% of CKD patients have diabetes mellitus and 29% of patients have no diabetes mellitus.
Out of 110 patients, 62% of CKD patients have hypertension.
Out of the 110 patients with chronic kidney disease selected, 61 patients (55%) are on hemodialysis, and 49 patients (45%) are not on dialysis.
In Table 5 out of the 110 patients in the research, 63 patients were found to have increased plasma homocysteine values, comprising approximately 58%.
Majority of patients with hyperhomocysteinemia are classified as having mild hyperhomocysteinemia. Among the 63 patients with hyperhomocysteinemia, 50 patiens had mild hyperhomocysteinemia. 13 patients had moderate hyperhomocysteinemia.
Majority of patients fall into the "< 15.0" – G5 category, indicating that a significant portion (50.0%) of the patients have severely impaired kidney function. The "15.0 - 28.9" category represents about 36 patients around one-third (32.7%) of the observations, indicating a moderate impairment of kidney function.
Data is categorised into five age groups: <= 40, 41 - 50, 51 - 60, 61 - 70, and 71+ years. Each age group has a distribution of patients across Normal, Mild, and Moderate levels of Homocysteine.
The distribution of Homocysteine levels varies across different age groups, with generally higher percentages of patients having mild and moderate levels as age increases.



There is no significant statistical association between Age and Homocysteine levels in this study This suggests that age alone may not be a strong predictor of Homocysteine levels when considering this specific population. Clinical implications would involve continuing to monitor Homocysteine levels across age groups to manage cardiovascular risk factors associated with elevated Homocysteine.

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Table 8 shows patients on dialysis show higher percentages of Mild (68.0% vs. 32.0%) and Moderate (69.2% vs. 30.8%) Homocysteine levels compared to those not on dialysis

This table indicate that the incidence of hyperhomocysteinemia in stages 4 and 5 of chronic renal disease was 61% and 64%, respectively.

Hyperhomocysteinemia was prevalent in 32% of patients with stage 3 chronic renal disease. Patients with low GFR (< 60 ml/min/1.73m²) have increased rates of Mild and Moderate Homocysteine levels compared to higher GFR categories. This may indicate that as kidney function declines (lower GFR), there is a trend towards higher Homocysteine levels.

In our study Out of 110 CKD patients in the study, 36.36% (40 patients) had either cardiovascular or cerebrovascular events. Among these 40 patients, the majority (about 80%) suffered from cardiovascular events (e.g., heart attacks, coronary artery disease), while the remaining 20% had cerebrovascular events (e.g., strokes, transient ischemic attacks).

This graph 10 indicate that as kidney function declines (lower GFR), there is a trend towards higher Homocysteine levels lower GFR categories (G4 and G3) show a higher prevalence of Hyperhomocysteinemia, potentially reflecting a higher metabolic oxidative stress associated with reduced kidney function.

Table 1: Distribution of age.

Age(Years)	No. of patients	Percentage
<= 40	17	15.5
41 - 50	22	20.0
51 - 60	19	17.3
61 - 70	34	30.9
71+	18	16.4
Total	110	100.0

Table 2: CKD Patients with Diabetes and Hypertension

Diabetes	No. of patients	Percentage
Present	78	70.09
Absent	32	29.1
Total	110	100.0

Table 3: CKD Patients with Diabetes and Hypertension

Hypertension	No. of patients	Percentage
Present	68	61.81
Absent	42	38.18
Total	110	100.0

Table 4: Patients with chronic kidney disease and Dialysis

Dialysis	No. of patients	Percentage
Present	78	70.09
Absent	32	29.1
Total	110	100.0

Table 5: Serum Homocystiene In CKD Patients

Serum homocystine levels	Number of patients	Percentage
< 14.80	47	42.7
14.80 – 29.99	50	45.5
30.00 +	13	11.8
Total	110	100

Table 6: Distribution of patients with eGFR.

KDIGO- GRADE	eGFRmL/min/1.73 m2	PATIENTS	PERCENT
G5	< 15.0	55	50.0
G4	15.0 - 28.9	36	32.7
G3	29.0+	19	17.3
	Total	110	100.0

Table 7: Age-wise distribution with severity of serum homocysteine

Age(Years)	Serum Homocysteine			
	Normal	Mild	Moderate	Total
<= 40	10	6	1	17
	21.3%	12.0%	7.7%	15.5%
41 - 50	10	9	3	22
	21.3%	18.0%	23.1%	20.0%
51 - 60	8	8	3	19
	17.0%	16.0%	23.1%	17.3%
61 - 70	11	18	5	34

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	23.4%	36.0%	38.5%	30.9%
71+	8	9	1	18
Total	17.0%	18.0%	7.7%	16.4%
	47	50	13	110

Table 8: Homocysteine Distribution on Dialysis Status

Serum Homocysteine						**Total**
Normal				**Mild**	**Moderate**	
Dialysis status	Not on Dialysis	Patients	29	16	4	49
		% Homocysteine	61.70%	32.00%	30.80%	44.50%
	On Dialysis	Patients	18	34	9	61
		% Homocysteine	38.30%	68.00%	69.20%	55.50%
Total		Patients	47	50	13	110
		% Homocysteine	100.00%	100.00%	100.00%	100.00%

Table 9: Stage of CKD and elevated homocysteine level

Serum Homocysteine						
			Normal	**Mild**	**Moderate**	**Total**
GFR(ml/min/1.73m2	G5	Patients	20	24	11	55
		% Homocysteine	42.6%	48.0%	84.6%	50.0%
	G4	Patients	14	21	1	36
		% Homocysteine	29.8%	42.0%	7.7%	32.7%
	G3	Patients	13	5	1	19
		% Homocysteine	27.7%	10.0%	7.7%	17.3%
Total		Patients	47	50	13	110
		% Homocysteine	100.0%	100.0%	100.0%	100.0%

DISCUSSION

Homocysteine, a sulfur amino acid, has recently received a lot of attention due to its role in vascular thrombosis and atherosclerosis progression. Chronic renal illness is extremely common in the general population. Patients with CKD are more susceptible to cardiovascular system involvement-related morbidity and mortality.

We held a study to investigate the increased prevalence of Hyperhomocysteinemia in CKD patients, as reported in recent studies. Recent research and publications reveal that chronic renal disease is linked to hyperhomocysteinemia, which adds significantly to cardiovascular morbidity and mortality.

Eytan Cohen, Ili Margalit conducted Cross sectional analysis on 17,010 subjects between 2000–2014. "Significant variations were identified between the four quartiles of homocysteine concentrations and estimated glomerular filtration rate (eGFR), with higher homocysteine concentrations resulting in lower eGFR ($p < 0.0001$)." [2]

Ninomiya et al. "conducted the first population-based cohort study of 1,477 Japanese people living in the community who did not have chronic kidney disease. After 5 years of follow-up, age-adjusted rates of CKD were 2.2% in the low tertile (≤ 8.3 μ M), 5.4% in the middle tertile (8.3-10.5 μ M), and 8.6% in the high tertile (≥ 10.6 μ M) of tHcy levels for men and 3.3, 6.0, and 6.9% for women."[3]

Mohamed K., Al-Obaidi et al. studied "consecutive individuals with acute myocardial infarction (MI) (n = 205) and unstable angina pectoris (UAP) (n = 18) and measured homocysteine using high-performance liquid chromatography (HPLC). Homocysteine levels were substantially higher in cTnT positive than cTnT negative individuals, 13.8 (11.7-15.3) versus 10.3 (9.4-11.3)mol/liter, respectively, p >0.002.[4]

Anoop Kumar, Preeti Sharma et al.conducted a "cross-sectional investigation Between December 2017 and May 2018 on 172 participants, including 100 non-diabetic MI patients and 72 seemingly healthy controls with no history of diabetes or MI. Homocysteine levels were abnormal in 98% of the troponin-T positive group and just 18.06% of the troponin-T negative group. The difference was statistically significant ($p < 0.0001$)." [5]

Mildred E. Francis, Paul W. Eggers, et al. "studied serum homocysteine concentrations (umol/L) from the National Health and Nutrition Examination Survey (NHANES) from 1991 to 1994. The adjusted odds ratios for elevated homocysteine risk were 9 to 11 times higher in persons with the lowest GFRest levels."[6]

Our study found that 58% of CKD patients had hyperhomocysteinemia, which is consistent with other research studies. The prevalence of hyperhomocysteinemia increased as the stage of CKD increased. Even though our study sample size was small, we discovered Hyperhomocysteinemia was more common in the late stages of CKD. It was consistent with the idea that as renal function deteriorated Homocysteine excretion reduced as plasma levels increased. We found in the study that even if the patient was on dialysis, this had no effect on the elevation of homocysteine levels.

Homocysteine levels vary by age group, with older patients having higher percentages of hyperhomocysteinemia up to Mild to Moderate levels.

There is no significant statistical relationship between age and homocysteine levels in this study. This suggests that age not alone may not be a reliable predictor of Homocysteine levels in this particular

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population. Clinical implications include continuing to monitor homocysteine levels across age groups in order to manage cardiovascular risk factors associated with elevated homocysteine.

In our study, in those having hyperhomocysteinemia with a Standard Deviation(SD) of 12.80733, the majority fell in the group of mild hyperhomocysteinemia. Out of the 63 patients with hyperhomocysteinemia, 1. 50 patiens had mild hyperhomocysteinemia. 2. 13 patients had moderate hyperhomocysteinemia.

We discovered that the majority of CKD patients had some comorbidities. Among them, the most common are diabetes and hypertension disorders. In our study, Compared to other CKD patients than with comorbidities like DM and HTN, they had higher levels of serum HCY level. This confirms the assumption that cardiovascular morbidities are the primary cause of death in CKD patients.

Our primary goal in determining the presence or absence of hyperhomocysteinemia in CKD patients was to reduce cardiovascular morbidity and mortality. Thus, it is worthwhile to take steps to reduce homocysteine levels in CKD patients.

We noticed that the incidence of hyperhomocysteinemia in stage 4 and stage 5 of chronic renal disease was 61% and 64%, respectively. As kidney function declines (lower GFR), there is a trend towards higher Homocysteine levels. Lower GFR categories (G4 and G3) show a higher prevalence of Hyperhomocysteinemia, potentially reflecting a higher metabolic oxidative stress associated with reduced kidney function.

In our study Out of 110 CKD patients in the study, 36.36% (40 patients) experienced either cardiovascular or cerebrovascular events. Among these 40 patients, the majority (about 80%) suffered from cardiovascular events (e.g., heart attacks, coronary artery disease), while the remaining 20% had cerebrovascular events (e.g., strokes, transient ischemic attacks).

This indicates that CKD patients in the study had a high risk of cardiovascular complications, which are well-known to be the leading cause of death in CKD patients.

Hyperhomocysteinemia was present in 78% of patients who experienced cardiovascular events and in all of the patients who experienced cerebrovascular events.

This strong correlation suggests that elevated homocysteine levels may play a significant role in the development of these complications. Homocysteine is known to damage blood vessels, promote clot formation.

Understanding the relationship between GFR and Homocysteine levels can help Monitoring and managing Homocysteine levels can be an important aspect of comprehensive care for patients with kidney disease, especially those with reduced GFRs and making treatment strategies aimed at reducing cardiovascular risk factors and improving overall outcomes.

CONCLUSION

Hyperhomocysteinemia was detected in 58% of CKD patients. Hyperhomocysteinemia was highly prevalent in the end stages of CKD (stages 3, 4, and 5). Homocysteine levels were elevated in both CKD patients without dialysis and those who received intermittent hemodialysis. Out of 110 patients, 40 patients - 36.36% had cardiovascular and cerebrovascular events; among the majority of cases, about 80% were cardiovascular, and 20% of patients had cerebrovascular events. Hyperhomocysteinemia was found in 78% of patients who were noted with cardiovascular events and all the patients with cerebrovascular events. Chronic kidney disease Patients with declining kidney function, especially in advanced stages, with no significant impact of dialysis on serum homocysteine level, so management through monitoring and vitamin supplementation is crucial to reducing cardiovascular risks and improving patient outcomes, particularly in those with lower GFR.

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