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RESEARCH ARTICLE

STUDY OF PREVALENCE OF HYPERHOMOCYSTEINEMIA IN CHRONIC KIDNEY DISEASE PATIENTS AT TERTIARY CARE HOSPITAL IN NORTHWEST MAHARASHTRA

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Abstract

Introduction-Chronic Kidney Disease is growing problem across all over world and India as well. Chronic kidney disease encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate(GFR).The risk for cardiovascular disease (CVD) morbidity and mortality remains high in all stages of CKD, including in patients with hemodialysis. More patients with CKD die of CVD than of the progression of kidney failure.The increase of homocysteine level, referred as hyperhomocysteinemia, is highly prevalent in CKD patients and associated with an increased risk of CVD complications. Proposed mechanisms for hyperhomocysteinemia in kidney failure is due to reduced clearance of total plasma homocysteine (tHcy) secondary to defective kidney and/or extra kidney metabolism of tHcy and deficiencies of folate, vitamin B12, and pyridoxal 5-phosphate (PLP).

Aim-To study Serum Homocysteine levels in patients with Chronic kidney disease and to estimate Serum Homocysteine levels in different stages of Chronic kidney disease.

Materials And Methods- All the patients presenting with clinical, biochemical and ultrasound kidney evidence of chronic kidney disease in department of medicine at tertiary care centre in northern Maharashtra. Normal plasma homocysteine level was considered to be below 15 umol/litre.

Results- A study of 54 patients with Chronic Kidney disease of both sex were taken as sample. Of the 54 patients 38 were males and 16 were females .36 patients were in age range of 41-60 . 32 patients were in stage 5 CKD , 14 were in stage 4 CKD , 8 were in stage 3 CKD. Hyperhomocysteinemia was observed in 78 % of CKD patients. Serum Homocysteinemia levels were maximum in patients with higher grade of CKD. The association between decreased GFR and increase in serum homocysteine levels was found to be statistically significant. (p<0.05).

Conclusion-Study concludes that hyperhomocysteinemia is highly prevalent in CKD patients. Homocysteine is commonly considered as

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toxicthrombogenic amino acid which causes atherosclerosis and cardiovascular diseases. Mortality due to cardiovascular diseases is high in CKD. Hence early screening and treatment for Hyperhomocysteinemia should be done in CKD to prevent cardiovascular diseases.

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Introduction:-

-Chronic Kidney Disease is growing problem across all over world and India as well.

-Chronic kidney disease encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate(GFR).¹

-The term chronic renal disease applies to the process of continuing significant irreversible reduction in nephron number and typically corresponds to CKD stages 3-5.¹

-The Kidney Disease Improving Global Outcome (KDIGO) defines Chronic Kidney Disease as-

1) Kidney damage for >3 month ,as defined by structural or functional abnormalities of the kidney, with or without decreased GFR , manifest by either, pathological abnormalities or markers of kidney damage,including abnormalities in the composition of the blood or urine or abnormalities in imaging tests.

2) GFR <60 ml/min/1.73m² for >3 month,with or without kidney damage.

-The risk for cardiovascular disease (CVD) morbidity and mortality remains high in all stages of CKD,²including in patients with hemodialysis.^{3,4} More patients with CKD die of CVD than of the progression of kidney failure.⁵

-The increase of homocysteine level, referred as hyperhomocysteinemia, is highly prevalent in CKD patients⁶ and associated with an increased risk of CVD complications.⁷⁻⁹

-Underlying mechanism for hyperhomocysteinemia in kidney failure is reduced clearance of total plasma homocysteine (tHcy) secondary to defective kidney and/or extra kidney metabolism of tHcy and deficiencies of folate, vitamin B12, and pyridoxal 5-phosphate (PLP).^{10,11}

-Folic acid, vitamin B6, and B12 are essential cofactors in homocysteine-methionine metabolism. Therefore, low vitamin B availability (B6, B12 and folic acid) causes impaired remethylation of homocysteine to methionine and leads to homocysteine accumulation.¹²

-Vitamin deficiency (including vitamin B1, B6, B12, and folic acid) are common in people with advanced renal failure who do not take nutritional supplements.^{13,14} This factor thought to be one of the reasons of the high prevalence of hyperhomocysteinemia in CKD patients.

Materials And Methods:-

- **Study Design-**An Observational Cross-Sectional Study.
- **Source of data-** All the patients presenting with clinical, biochemical and ultrasound kidney evidence of chronic kidney disease in Department of Medicine at Tertiary Care Centre in Northwest Maharashtra.
- **Participant size-** Minimum of 54 patients were included in this study.
- **Data Collection-** All patients of chronic kidney disease after fulfilling inclusion and exclusion criteria were enrolled in this study. Total 54patients were included in the study. Patients with diagnosed chronic kidney disease with USG showing bilateral shrunken kidney/loss of corticomedullary differentiation or biochemically elevated blood urea, serum creatinine for more than 3 months were included.

- According to Kidney Disease Improving Global Outcome¹ (KDIGO) classification of chronic kidney disease is as follows-

GFR categories : -	GFR
G1 – Normal or high	≥ 90
G2 – Mildly decreased	60-89
G3a – Mildly to Moderately decreased	45-59
G3b – Moderately to Severely decreased	30- 44
G4 – Severely decreased	15-29
G5 – Kidney Failure	< 15

 eGFR calculated by – Modification of Diet in Renal Disease Study
 -Estimated GFR = 1.86 x [Pcr]^{-1.54} x (age)^{-0.203}
 -Multiply by 0.742 for women
 -Multiply by 1.21 for African Americans.
- After routine informed consent from patients, serum homocysteine and renal function test samples were sent and GFR (Glomerular Filtration Rate) was calculated.
- Statistical analysis were performed using Chi- Squared test and results interpreted.

Aim:-

- 1) To Study serum homocysteine levels in patients with Chronic Kidney Disease.
- 2) To Estimate serum homocysteine levels in different stages of Chronic Kidney Disease.

Inclusion Criteria-

All those patients above 18 years of age diagnosed with Chronic Kidney Disease during the period June 2021 to October 2022 were included.

Exclusion Criteria-

1. Patients who are smokers and alcoholics.
2. Patients who are known case of chronic liver disease and acute kidney injury.
3. Patients on drugs like Anticonvulsant agents (Phenytoin, Carbamazepine), Folate antagonist (Methotrexate).

Results:-

Total of 54 cases of CKD (Chronic Kidney Disease), admitted to the hospital at Tertiary Care Hospital in Northwest Maharashtra from June 2021- Oct 2022 were studied.

Table 1:- Gender wise distribution of patients:

Gender	No. of patients (N)	Percentage (%)
Male	38	70.37
Female	16	29.63
Total	54	100

Male predilection was found in our study with 38 (70.37%) male patients suffering from CKD while 16 (29.62%) females suffered from the disease.

Table 2:-Age wise distribution of patients:

Age groups (Years)	No. of patients (N)	Percentage (%)
21-30	2	3.70
31-40	4	7.40
41-50	14	25.92
51-60	22	40.74
>60	12	22.22
TOTAL	54	100

-Of the 54 patients of chronic kidney disease selected, majority of patients were in age group between 41 to 60 years. From this table it is obvious that as age increases the incidences and prevalences of people suffering from chronic kidney disease increases.

-As age increases, the no of functioning nephron decreases leading to chronic kidney disease.

Table 3:- Frequency distribution of CKD Stages:

CKD stages	No. of patients (N)	Percentage (%)
Stage III	8	14.81
Stage IV	14	25.93
Stage V	32	59.26
Total	54	100

-Staging of CKD according to creatinine clearance and glomerular filtration rate as calculated by Cockcroft-Gault formula.

- Of the patients selected majority of patients were in CKD stage 4 and 5 constituting around 85 percentage.

Table 4:- Frequency distribution based on result of Hyperhomocysteinemia:

SEX	TOTAL PATIENTS	NORMAL HCY	HYPER HCY	% HYPER HCY
MALE	38	9	29	76
FEMALE	16	3	13	81
Total	54	12	42	

Of the 54 patients in the study, 42 patients found to be having elevated serum homocysteine values constituting around 78%.

Table 5:- CKD Stage and Elevated SrHomocysteine level:

CKD STAGE	TOTAL PATIENTS	NORMAL HCY	HYPER HCY	% HYPER HCY
STAGE I	8	5	3	37.5
STAGE II	14	4	10	71.4
STAGE III	32	3	29	90.6
TOTAL	54	12	42	P-value=0.0043

Chi-Squared test applied. P-value =0.0043 Statistically significant.

If P-value <0.05, it is significant.

-If we compare plasma homocysteine level with corresponding glomerular filtration rate and stage of CKD, it shows that as patient deteriorates to next lower level of chronic kidney disease, incidence of hyperhomocysteinemia increases.

-A significant association was noticed between CKD grades and serum homocysteine levels of patients (P=0.0043). Elevation of SrHomocysteine was seen with progression of CKD grades.

-Here in this study we observed that in stage 4 and stage 5 of chronic kidney disease incidence of hyperhomocysteinemia was 71.4% and 90.6% respectively.

Table 6:- Serum Homocysteine and GFR Correlation:

Sr HCY	GFR < 15 Total no N=32	GFR < 15 %	GFR 15- 29 Total No n= 14	GFR 15- 29 %	GFR 30- 59 Total No n= 8	GFR 30- 59 %	Total No n= 54	Total %
NORMAL	3	9.37	4	28.57	5	62.5	12	22.22

HCY								
HYPERTHYREOIDISM	29	90.32	10	71.42	3	37.5	42	77.77
								P=0.0043

Chi- Square test applied. P-value= 0.0043 Statistically significant.

If p-value <0.05, it is significant.

-A significant decrease in GFR was seen in patients with hyperhomocysteinemia as compared to patients with normal serum homocysteine levels (P<0.0043). As GFR decreased, a rise in serum homocysteine was seen. Thus as kidney functioning deteriorated, serum homocysteine levels increased and result was found statistically significant. P<0.0043.

Discussion:-

1. Hyperhomocysteinemia is defined as homocysteine level higher than 15µmol/L. The prevalence of chronic kidney disease in Indian population is much more.
2. Patients with CKD are very much susceptible to cardiovascular system involvement related morbidity and mortality.
3. As recent studies have shown an increased prevalence of hyperhomocysteinemia in CKD patients, so we tried to conduct a study on this.
4. In present study, 38 were male patients and 16 were female patients. Majority (66.66%) 36 patients in present study belonged to age group 41-60 years followed by patient aged more than 60 years (22.22%). This finding was similar with study conducted by Prakash S et al¹⁵ concluded the higher prevalence of CKD in the elderly.
5. 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.
6. Similar results were observed by Yadav V et al.¹⁶ in a study to estimate serum Homocysteine in CKD patients and its association with renal function and serum albumin in patients with CKD.
7. In present study, majority patients (59.25%) were classified as CKD stage V. A rise in patients with hyperhomocysteinemia was seen with progression of CKD grades. A significant decrease in GFR (P=0.0043) was seen in patients with hyperhomocysteinemia as compared to patients with normal serum homocysteine levels.
8. Ciancolo, et al. (2017)¹⁷ stated hyperhomocysteinemia occurs in about 85% of CKD patients because of impaired renal metabolism and reduced renal excretion. This statement is in concordance with Long and Nie (2016)¹⁸. Homocysteine level in patients with end-stage of renal disease (ESRD) is 3 to 5 times higher than normal and the prevalence of hyperhomocysteinemia in this patient group is 85-100%.
9. In present study we found that 78% of CKD patients were having hyperhomocysteinemia correlating with other studies conducted elsewhere in the world and hyperhomocysteinemia was more prevalent as stages of CKD increases.
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.

Conclusion:-

1. The Study concludes that hyperhomocysteinemia is highly prevalent in CKD patients.
2. Hyperhomocysteinemia was observed in 78% of patients with CKD. Prevalence of hyperhomocysteinemia was more in End stages of CKD (stage 3, 4 &5).
3. Homocysteine is commonly considered as toxic thrombogenic amino acid which causes atherosclerosis and cardiovascular diseases. Mortality due to cardiovascular diseases is high in CKD. Hence early screening and treatment for Hyperhomocysteine should be done in CKD to prevent cardiovascular diseases.

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