



HOMOCYSTEINE LEVELS IN PATIENTS RISK OF DIABETES WITH AND WITHOUT CHRONIC KIDNEY DISEASE

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ABSTRACT

CKD (Chronic Kidney Disease) is famous to cause hyperhomocysteinemia which contributes to extended cardiovascular morbidity and mortalities. Thus, present study has a look at aimed to determine the homocysteine stage in patients with chronic kidney disease. Seventy patients with CKD have been recruited within this examined, and their fasting plasma homocysteine levels was measured. Normal plasma homocysteine level became considered to be below 15 $\mu\text{mol/litre}$. Out of 140 patients with CKD (Males: 114, Females: 26 mean age 35-60), 104 patients had stage 5 CKD. Hyperhomocysteinemia turned into discovered in 74.2% of CKD patients. 25.7% had moderate hyperhomocysteinemia. End-level renal diseases patients had extended occurrence of hyperhomocysteinemia. There is no massive difference in hyperhomocysteinemia levels between patients undergoing dialysis and without dialysis. Hyperhomocysteinemia is a particularly prevalent condition seen in CKD patients.

Key words: Homocysteine, Chronic Kidney Disease, Hyperhomocysteinemia.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a serious public health issue, and is now the third-leading cause of disease-related mortality worldwide. In 2017, approximately 451 million adults aged between 18 and 99 years suffer from diabetes, and this number is predicted to increase to 629 million by 2045. Chronic kidney disease (CKD) is a severe scientific and public health challenge globally. [1] In India, it's been currently anticipated that the age-adjusted occurrence price of End-Stage Renal Disease (ESRD) to be 229 in keeping with million populations, and also 100,000 new patients enter renal alternative programs annually. [2] CKD is related to age-associated renal function decline elevated in hypertension, diabetes, weight problems and primary renal problems. [3] Cardiovascular disorder (CVD) is the number one cause of morbidity and mortality where CKD is appeared as an accelerator of

CVD risk and an independent risk thing for CVD activities. [4] Homocysteine has been implicated as a capacity danger factor for cardiovascular sickness that is the primary motive of morbidity and mortality in sufferers with CKD. [5] A moderate increase of plasma total homocysteine occurs inside the early tiers of CKD and will increase as renal function decreases, indicating the crucial role of the kidney on homocysteine metabolism. [6] Hyperhomocysteinaemia, defined as a plasma overall homocysteine level of 12 $\mu\text{mol/l}$, happens already at a GFR of about 60 ml/min and whilst ESRD has been reached, the superiority of hyperhomocysteinaemia is eighty five–a hundred%. [7, 8]

Many research are ongoing to discover whether decreasing homocysteine in CKD patients will lower cardiovascular

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morbidity and mortality. [9] Even though many studies have shown widespread affiliation and a poor correlation between the lower in Glomerular filtration fee and increase in homocysteine level. [10] There is a restricted range of studies inside the Indian context. Therefore, the modern look at turned into achieved with an aim to discover the homocysteine degree in sufferers with chronic kidney sickness and to locate its affiliation and correlation with reduced renal feature.

Material and Methods:

The present study turned into a single targeted observational study performed in Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry, for a period of 10 months. Ethics approval for patient recruitment and statistics evaluation changed into received from the Institutional Review Board. Inclusion criteria have been patients with extended blood urea, serum creatinine and displaying feature of CKD in ultrasound stomach. Patients with acute kidney injury, liver diseases and diabetics. In present study smokers /alcohol customers have been excluded. A general of 140 sufferers with chronic kidney disorder within the health center were recruited after obtaining the consent. Information about medical records, circle of relatives’ history, contemporary medicine, and records of dialysis of individuals turned into accrued via self-report questionnaire. Investigations blanketed assessment of blood urea, serum creatinine, electrocardiograph, plasma homocysteine, GFR were measured by using fluorescein polarization, immunoassay. Statistical analyses were finished using the SPSS statistical software program SPSS-11.5. Student’s t-check and chi-square check had been used to examine imply values and percentages respectively.

Results:

Along with the study population, the majority of the participants were in the age group of 51-60 (42%) years, and males 114 (74%) with the mean age of 73.12±19.152 years. The mean weight of the study population was 57.81±11.4 kg. The mean serum urea and creatinine values were 117.12±36.83 mg/dl, 9.41±9.40 mg/dl respectively. The serum homocysteine level was 21.2±8.31 µmol/l.

The compared between plasma homocysteine level along with glomerular filtration rate. The stage of chronic kidney disease it suggests that as affected person deteriorates to next lower degree of CKD prevalence of hype discovered that during stage 4 and five of persistent kidney disorder occurrence of hyperhomocysteinemia have been 33.3% and 58.3% respectively. We located that the majority of sufferers have been having atypical electrocardiograph indicating the bulk of patients with Chronic kidney disorder had a few them cardiac illnesses. Out of 140 patients decided on for the take a look at 86 patients had abnormal electrocardiograph constituting 89.5% In people with hyper homo cysteinemia best one found to have regular ECG All others had been having odd ECG.

The total population majority of patients, 96(68.5%) were in CKD stage 5. In our study in those having hyperhomocysteinemia majority are falling in the group of mild hyperhomocysteinemia. Of the 90% patients with hyperhomocysteinemia, 126 patients were in the group of mild hyperhomocysteinemia. Seven were found to have moderate hyperhomocysteinemia.

Table: 1 Baseline characteristics of study participants (n=70)

Parameter	Summary
Gender	
Male	114(81.4%)
female	26(18.5%)
Weight(in kgs)	58.74±15.145
Dialysis	20(14.2%)
Smoking	18(12.8%)
Alcohol	16(11.4%)
Clinical characteristics	
Serum urea	116.12±36.102
Serum creatinine	9.41±9.40
GRF	15.7±6.86
Homocysteine	21.2±8.31
Co-morbidities	
Diabetes mellitus	0
SysHT	96(68.5%)

Table2: stages CKD and ECG with normal and increased homocysteine level

Homocysteine level		
Stages of CKD	Normal(44)	Abnormal(96)
3	6(13.6%)	8(8.3%)
4	16(36.3%)	32(33.3%)
5	22(50%)	56(58.3%)
ECG		
NORMAL	2(4.5%)	10(10.4%)
ABNORMAL	42(95.4%)	86(89.5%)

Table3: Based on CKD stage and hyperhomocysteinemia

Stage of CKD	Number of patients (%)
Stage0	0
Stage1	0
Stage2	0
Stage3	10(7.1%)
Stage4	34(34%)
Stage5	96(68.5%)
Hyperhomocysteinemia	
Mild (15 -30 umol/lite)	126(90.0%)
Moderate (31- 100 umol/litre)	14(10.0%)
Severe (> 100 umol/litre)	

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Discussion:

Homocysteine (Hcy) is a sulfur-containing amino acid formed by the demethylation of methionine; it is an emerging risk factor for diabetic nephropathy and cardiovascular disease that has gradually elicited the interest of researchers. Newly, disulfuramino acid homocysteine has gained much significance because of its role in vascular thrombosis and genesis of atherosclerosis. These studies have shown an increased prevalence of

hyperhomocysteinemia in CKD patients and its involvement with cardiovascular morbidity and mortality. In the recent study, we establish that 87% of CKD patients had hyperhomocysteinemia similar with other studies conducted somewhere else in the world and hyperhomocysteinemia was more ubiquitous as stages of CKD increases. It is also possible that tHcy may be a risk factor for progression of kidney disease and thereby promote the development of CVD. In support of this hypothesis, in a population-based cohort, tHcy was found to be a predictor of the development of microalbuminuria in nondiabetic individuals, and this relationship was independent of GFR.

Menon *et al* showed that hyperhomocysteinemia was prevalent in 56% Of CKD patients and hyperhomocysteinemia was partly amenable to treatment with vitamins in stages 3 and 4. [11] Although our take a look at pattern length turned into smaller, we found that hyperhomocysteinemia was extra regularly occurring inside the later stages of CKD due to renal function deteriorates the homocysteine excretion decreases and its degree more in plasma. Our study notices that during dialysis condition, it was not affecting the homocysteine level elevation. On the other hand, Nair *et al* results shown homocysteine level transiently decreased after a dialysis session but fell to normal range within two to three days to predialysis value. [12]

Homocysteine may be a marker for severity of kidney disease rather than a mediator for the development of CVD, in patients with CKD stages 3 to 4. Prior studies demonstrating an association between tHcy and CVD risk

may have been confounded by their less precise measurements of GFR. This is a relatively healthy CKD population; however, this makes it an ideal population to assess a potentially independent effect of tHcy on mortality in the absence of powerful confounders such as diabetes and preexisting CVD.

We determined that the majority of sufferers with CKD had some ECG abnormality correlating with the declaration that cardiovascular morbidities are the most vital purpose of mortality in patients with CKD. (Subbiah AK, Chhabra YK et al., 2016) Our major challenge to assess for the presence or absence of hyperhomocysteinemia in CKD patients became to decrease the cardiovascular morbidity and mortality. So, it's worthy to take measures to decrease homocysteine levels in sufferers with CKD. These findings need to be taken into consideration under studies barriers. First, we couldn't exclude different genetic versions which may have inspired homocysteine stage. Second, the precise correlation between decreased renal function and stage of hyperhomocysteinemia couldn't be assessed due to the non-uniform distribution of sample length amongst CKD patients.

Systematic reviews had reported the effect of B12 supplementation on decreasing homocysteine levels in patients with ESRDs when combined with folate supplementation. [13] although the levels of Vit B12 and folic acid, pyridoxine level could not be measured in the present study due to financial restriction. Plasma Hcy levels are influenced by environmental and genetic factors, as well as by age, sex, duration of diabetes, smoking habits, body mass index, metabolic control, creatinine

REFERENCE:

1. Long Y, Nie J. Homocysteine in Renal Injury. *Kidney Dis (Basel)*. 2(2), 2016, 80-7.
2. Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SR, Acharya VN, et al. Epidemiology and risk factors of chronic kidney disease in India - results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. *BMC Nephrol*. 14, 2013, 114.
3. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJ, Mann JF, et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet*. 382(9889), 2013, 339-52.
4. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalisation. *N Engl J Med*. 351(13), 2004, 1296-305.
5. Nerbass FB, Draibe SA, Feiten SF, Chiarello PG, Vannucchi H, Cuppari L. Homocysteine and its determinants in non dialysed chronic kidney disease patients. *J Am Diet Assoc*. 106(2), 2006, 267-70.
6. Busch M, Göbert A, Franke S, Ott U, Gerth J, Müller A, et al. Vitamin B₆ Metabolism in Chronic Kidney Disease – Relation to Transsulfuration, Advanced Glycation and Cardiovascular Disease. *Nephron Clinical Practice*. 114(1), 2010, c38-c46.
7. Veldman BAJ, Vervoort G, Blom H, Smits P. Reduced plasma total homocysteine concentrations in Type 1 diabetes mellitus is determined by increased renal clearance. *Diabetic Medicine*. 22(3), 2005, 301-5.
8. van Guldener C. Why is homocysteine elevated in renal failure and what can be expected from homocysteine-lowering? *Nephrology Dialysis Transplantation*. 21(5), 2006, 1161-6.
9. Subbiah AK, Chhabra YK, Mahajan S. Cardiovascular disease in patients with chronic kidney disease: a neglected subgroup. *Heart Asia*. 8(2), 2016, 56-61.
10. Cheng Y, Kong FZ, Dong XF, Xu QR, Gui Q, Wang W, et al. Influence of renal function on the association between homocysteine level and risk of ischemic stroke. *Am J Transl Res*. 9(10), 2017, 4553-63.

clearance, impaired renal function, vitamin status, and blood pressure. The kidney has an important function in maintaining Hcy levels. The enzyme MTHFR is active in the kidney, and impairment of renal function can lead to hyperhomocysteinemia. Hcy may be a potential useful biomarker in assessing the microvascular risk in diabetes, and hyperhomocysteinemia is a potential risk factor for Diabetic Retinopathy.

Conclusion:

Homocysteine Level is increased consistent to the stages of CKD. Hyperhomocysteinemia appears to be linked with increased cardiovascular disease risk between patients with CKD. In view of the study findings further large-scale longitudinal studies are recommended to explore further this association. Attempts must be taken by physician in identifying CKD patients with high homocysteine level owing to its improved susceptibility to cardiovascular risk.

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Conflicts Of Interest

The authors declare no conflict of interest.

11. Menon V, Wang X, Greene T, Beck GJ, Kusek JW, Selhub J, *et al.* Homocysteine in chronic kidney disease: Effect of low protein diet and repletion with B vitamins. *Kidney Int.* 67(4), 2005, 1539-46.
12. Nair AP, Nemirovsky D, Kim M, Geer EB, Farkouh ME, Winston J *et al.* Elevated homocysteine levels in patients with end-stage renal disease. *Mt Sinai J Med.* 72(6), 2005, 365-73.
13. Amini M, Khosravi M, Baradaran HR, Atlasi R. Vitamin B12 supplementation in end-stage renal diseases: a systematic review. *Med J Islam Repub Iran.* 29, 2015, 167.