How to Cite:
Sadaria, R. G., Vasava, S. N., & Gosai, D. (2022). Estimation of serum homocysteine & lipid profile in chronic kidney disease patients. *International Journal of Health Sciences*, *6*(S5), 5476–5482. https://doi.org/10.53730/ijhs.v6nS5.11136

Estimation of serum homocysteine & lipid profile in chronic kidney disease patients

Roshni G. Sadaria
Associate Professor, Department of Biochemistry, Smt. B.K. Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University), Piparia, Vadodara, Gujarat, India.

Smita N. Vasava
Assistant Professor, Department of Biochemistry, Smt. B.K. Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University), Piparia, Vadodara, Gujarat, India.
Corresponding author email: smita15051987@gmail.com

Devanshi Gosai
Assistant Professor, Department of Pathology, Smt. B.K. Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be University), Piparia, Vadodara, Gujarat, India.

***Abstract*---**Background: Chronic kidney disease (CKD) is a deterioration of renal function, which results from diminished effective functioning of renal tissue. CKD is associated with dyslipidemia associating hypertriglyceridemia, elevated LDL cholesterol, an accumulation of apolipoprotein B (Apo B) containing lipoproteins, increased concentrations of lipoprotein(a) particles, and low HDL levels. Homocystein is considered as a risk or pathogenic factor in the progression of CKD which has been considered globally as a serious health issue. Aim & Objective: To estimate and compare the levels of serum homocysteine & lipid profile between chronic kidney disease patients and healthy individuals. Materials & Methods: The present case control study was conducted at Dhiraj General hospital, Piparia, Vadodara, Gujarat, India in which 100 age and sex matched subjects were enrolled, out of which 50 were cases of CKD patients and 50 were controls. Approximately 5 ml of fasting blood sample was drawn from the each person with aseptic precautions. Serum was separated which was used for the estimation of serum homocysteine, lipid profile, serum creatinine and blood urea. Results: mean Serum Homocysteine, Triglyceride, VLDL-C, urea and creatinine levels found to be significantly higher in cases than controls($p<0.001$) & mean serum levels of HDL-C in cases were significantly lower than controls ($p<0.01$). Conclusion: We found in our study that dyslipidemia and

Manuscript submitted: 27 Feb 2022, Manuscript revised: 9 April 2022, Accepted for publication: 18 June 2022

hyperhomocysteinemia is seen in >70 % of CKD cases. We recommend early evaluation of CKD patients for cardiovascular risk using homocysteine levels and lipid profile abnormalities.

***Keywords*---**Chronic Kidney Disease, Homocysteine, Lipid Profile.

Introduction

Chronic kidney disease (CKD) is a deterioration of renal function, which results from diminished effective functioning of renal tissue. The kidneys serve several essential roles in humans, not only filtering the blood and excreting waste products but also playing a crucial role in regulatory functions such as maintaining blood pressure, water balance, electrolyte levels and acid–base balance. The kidneys also play a major role in degradation of proteins as well as producing hormones affecting red blood cells production and mineral turnover (1). Chronic kidney disease (CKD) is defined as abnormalities in kidney structure or function that are present for more than 3 months and have health implications. The disease is classified on the basis of cause and category of glomerular filtration rate (GFR) (G1 to G5) and albuminuria (A1 to A3) (2).

Chronic renal failure is often associated with dyslipoproteinemia, high levels of cholesterol and triglycerides, as well as a decrease in the polyunsaturated fatty acids. Each of these abnormalities has been identified as an independent risk factor for atherosclerosis (3). CKD is associated with dyslipidemia associating hypertriglyceridemia, elevated LDL cholesterol, an accumulation of apolipoprotein B (Apo B) containing lipoproteins, increased concentrations of lipoprotein(a) particles, and low HDL levels (4).

Homocysteine (Hcy) is a thiol-containing amino acid formed in the metabolic conversion of methionine to cysteine. Hcy undergoes either to be metabolized to cysteine by trans-sulfuration or converted back to methionine through re-methylation (5). Hcy is considered as a risk or pathogenic factor in the progression of CKD which has been considered globally as a serious health issue (6). Hyperhomocysteinemia, the state of elevated plasma Hcy levels, is very common among patients with chronic renal insufficiency (defined as the range of kidney function below normal but above that requiring renal replacement therapy) and occurs almost uniformly in the end-stage renal disease (ESRD) population (7). Anurag et al. in their study, concluded that serum homocysteine level were significantly increased on both the chronic renal failure patient either in dialysis or without dialysis condition but it was noted that serum homocysteine level were more elevated in patients of renal failure on dialysis compared to without dialysis renal patients. Serum homocysteine is positively correlated with serum cholesterol, Serum Triglycerides, Serum LDL and negatively with serum HDL and eGFR. No significant correlation with VLDL (1). On these bases, this study is designed to estimate and compare the levels of serum homocysteine & lipid profile between chronic kidney disease patients and healthy individuals.

Materials and Methods

The present case control study was conducted at Dhiraj General hospital, Piparia, Vadodara, Gujarat, India in which 100 age and sex matched subjects were enrolled, out of which 50 were cases of CKD patients and 50 were controls. Study was conducted from July 2019 to Dec 2019.

Case Groups: - Diagnosed cases of Chronic Kidney Disease
Controls:-Age and Sex matched Normal healthy Individual in and around the Dhiraj Hospital is termed as controls.

Inclusion criteria:

- CKD patients who are willing to participate
- Both male and female subjects with age group 18-70 years.

Exclusion criteria:

- Not willing to participate in study
- Acute Renal Failure
- Cardiovascular disorders
- Thyroid disorders, liver diseases.
- Patients who are on drugs like steroids, lipid lowering drugs.

Sample Collection & Processing

Written Informed consent was taken in person's respective language. Performa was available for the filling of biodata such as age and gender, clinical examination findings and investigations. Approximately 5 ml of fasting blood sample was drawn from the each person with aseptic precautions. Plain vacutainer was used for blood collection. Then it was centrifuged for 15 min. at 3000 RPM. Serum was separated which was used for the estimation of serum homocysteine, lipid profile, serum creatinine and blood urea.

Methodology

Serum Homocysteine estimation was done by enzymatic method. Serum Total cholesterol and Serum Triglyceride estimation was done by Cholesterol oxidase peroxidase & Glycerophosphate oxidase (GPO) end point method respectively. HDL-C was estimated using HDL direct reagent based on modified polyvinyl sulfonic acid (PVS) and Polyethylene-glycol-methyl ether (PEGME) coupled classic precipitation method. Serum VLDL and LDL was calculated by Friedewalds formula. Serum Creatinine was estimated by enzymatic method. Blood urea was estimated by urease method. All the parameters was performed on EM-200 fully auto chemistry analyzer.

Ethical Approval

Ethical Approval was taken from the institutional Ethical committee.

Statistical analysis

Data were presented as Mean and SD values. Comparisons between cases and controls were performed using the Independent student t- test. A p-value less

than 0.05 ($p < 0.05$) was considered as statistical significant. Medcalc software was used for statistical analysis.

Results

Results are presented as Mean ± SD. The mean distribution of biochemical parameters in the cases and controls are depicted in Table 1. There was no significant difference in age between the two groups.

Table 1: shows comparison of Homocysteine, Lipid profile and other biochemical parameters in cases and controls. Values are expressed as means ±SD

Parameters	Group –I (Cases)	Group-II (Controls)	P-Value
Age (Years)	47.44±14.88	42.92±11.99	0.0978
Homocysteine(umol/l)	23.88±10.91	8.60±2.46	<0.001
Cholesterol (mg/dl)	163.10±45.11	150.22±25.28	0.0813
Triglyceride(mg/dl)	156.48±68.18	115±19.15	<0.001
HDL-C(mg/dl)	45.00±4.49	47.40±3.12	<0.01
LDL-C(mg/dl)	86.80±44.36	79.62±25.02	0.32
VLDL-C(mg/dl)	31.29±13.63	23.19±3.83	<0.001
Urea(mg/dl)	178.24±59.43	26.46±8.79	<0.0001
Creatinine(mg/dl)	11.80±5.72	0.81±0.16	<0.0001

Table 2: shows prevalence of hyperhomocysteinemia and dyslipidemia.

Parameters	Group –I (Total Cases - 50)	Group-II (Total Controls - 50)
Hyperhomocysteinemia No.(%)	40 (80%)	0
Dyslipidemia No.(%)	37 (74%)	05(10%)

Table 1 shows mean Serum Homocysteine, Triglyceride, VLDL-C, urea and creatinine levels found to be significantly higher in cases than controls($p<0.001$) & mean serum levels of HDL-C in cases were significantly lower than controls ($p<0.01$).

Table 2 shows prevalence of hyperhomocysteinemia and lipid abnormalities in cases and controls. According to our study, 80% of cases have hyperhomocysteinemia and 74% cases have dyslipidemia.

Discussion

Cardiovascular disease (CVD) is the leading cause of mortality in Chronic kidney disease (CKD) patients. Therefore, early determination and management of the risk factors for CVD in CKD patients play an important role to develop more

effective screening and treatment strategies to decrease cardiovascular mortality and morbidity in CKD patients (4).

Renal dysfunction is also associated with many perturbations in lipoprotein metabolism leading to dyslipidemia and accumulation of atherogenic particles. CKD is associated with dyslipidemia associating hypertriglyceridemia, elevated LDL cholesterol and low HDL levels (4). In CKD, urinary protein loss stimulates an increased LDL synthesis by the liver. It is likely that proteinuria with the resultant hypoalbuminemia leads to an upregulation of 3-hydroxy-3-methylglutaryl CoA reductase with a consequent hypercholesterolemia. Conversely, low HDL with a poor maturation of HDL-3 to cholesterol-rich HDL-2 is due to acquired lecithin-cholesterol acyltransferase deficiency secondary to abnormal urinary losses of this enzyme. Impaired clearance of chylomicrons and VLDL has emerged as the dominant factor for the increased serum triglyceride concentration. Lipoprotein lipase (LPL) is the rate-limiting step in lipolysis of chylomicrons and VLDL. LPL binds to heparan sulfate proteoglycans on the cell surface of endothelium. In proteinuric renal diseases, a downregulation of LPL protein abundance and enzymatic activity was found. These events are largely responsible for profound abnormalities in lipoprotein metabolism in chronic renal failure's rendering these lipoproteins more atherogenic (8).

The close relationship between plasma homocysteine and GFR suggests that homocysteine is cleared from the body by urinary excretion after glomerular filtration, just like creatinine. However, the amount of homocysteine in the urine is minimal (about 6 µmol/day). From a normal GFR of 180 L/day and a free homocysteine concentration of 3 µmol/l, it can be calculated that 99% of the filtered homocysteine is reabsorbed (9).

Hhcy (Hyperhomocysteinemia) exerts its pathogenic action on the main processes involved in the progression of vascular damage already enhanced in CKD patients. Hhcy induces oxidative stress and antagonizes the vasodilator properties of NO (Nitric oxide) by the formation of S-nitrosohomocysteine, thus leading to endothelial dysfunction. Following oxidative injury, endothelial cells produce various cytokines participating in inflammatory reactions. The link between Hcy and inflammatory factors seems to be the activated transcription factor, nuclear factor-kappa B. Hhcy activates metalloproteinases and induces collagen synthesis, leading to the reduction of vascular elasticity. Hcy was proven to promote the proliferation of smooth muscle cells leading to several interactions with platelets, clotting factors, and lipids, and indeed might contribute to the scavenger receptor-mediated uptake of oxidized-LDL by macrophages resulting in foam cell formation in atherosclerosis. These pathways end to amplify the atherosclerotic process and the inflammatory state present in CKD (10).

In our study, prevalence of lipid abnormalities and homocysteine levels were studied in cases and control. We found 80% cases has hyperhomocysteinemia and 74% cases has dyslipidemia. Also we have compared Homocysteine, Lipid profile and other biochemical parameters in cases and controls. In our study, mean Serum Homocysteine, Triglyceride, VLDL-C, urea and creatinine levels found to be significantly higher in cases than controls($p<0.001$) & mean serum levels of HDL-C in cases were significantly lower than controls ($p<0.01$). These

findings are consistent with the study done by Ajay kumar katiyar et al (11). Study done by Adejumo OA et al also found dyslipidemia in CKD especially in females and older CKD patients (12). Dr Sarita H Patel et al also found in their study that Total cholesterol and LDL was significantly raised in patients of CKD compared to controls The triglycerides were elevated. However, the statistical analysis showed that it was not significant (13). Findings of the study done by Yadav V et al showed that serum homocysteine levels were elevated in CKD. A positive correlation of serum homocysteine with serum creatinine and a negative correlation with serum albumin indicates that increase in serum homocysteine is associated with the progressive decline of kidney functions (14).

Conclusion

We found in our study that dyslipidemia and hyperhomocysteinemia is seen in >70 % of CKD cases. CKD is associated with dyslipidemia associating hypertriglyceridemia, elevated LDL cholesterol and low HDL levels. We recommend early evaluation of CKD patients for cardiovascular risk using homocysteine levels and lipid profile abnormalities. Further studies are required to see correlations between lipid profile and homocysteine levels in CKD patients.

References

1. Kesarwani A, Asegaonkar SB, Jha A. Study of Serum homocysteine and lipid profile parameters in patients of chronic renal failure. Int J Health Sci Res. 2017; 7(8):142-49.
2. Markus Kettelar, Geoffrey A Block, et al. Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder: Synopsis of the Kidney Disease: Improving Global Outcomes 2017 Clinical Practice Guideline Update. Clinical Guidelines, March 2018. https://doi.org/10.7326/M17-2640.
3. Nelva T de Gómez, Ana M Giammona, et al. Variations in the lipid profile of patients with chronic renal failure treated with pyridoxine. Lipids in the health and disease.2003; 2(7):1-6.
4. Mustafa C. Bulbul, Tuncay Dagel, et al. Disorders of Lipid Metabolism in Chronic Kidney Disease. Blood Purif. 2018;46:144–52.
5. Hatem K. Amin, Mohamed-I Kotb El-Sayed & Ola F. Leheta. Homocysteine as a predictive biomarker in early diagnosis of renal failure susceptibility and prognostic diagnosis for end stages renal disease. Renal Failure.2016;38(8),1267-75, DOI:10.1080/0886022X.2016.1209382
6. Azmi MA, et al. Determination of Homocysteine and Lipid Profile Level in the Blood of Chronic Kidney Disease Patients with and without Hemodialysis in Comparison to Normal Healthy Individuals. J Urol Nephrol. 2018, 3(4): 000150.
7. Allon n. Friedman, Andrew g. Bostom, et al. The Kidney and Homocysteine Metabolism. J Am Soc Nephrol. 2001; 12: 2181–9.
8. Roberto Trevisan, Alessandro R. Dodesini, et al. Lipids and Renal Disease. JASN. April 2006, 17 (4 suppl 2) S145-S147.
9. Coen van Guldener. Why is homocysteine elevated in renal failure and what can be expected from homocysteine-lowering? Nephrology Dialysis Transplantation. 2006; 21(5):1161–66.

10. Cianciolo G.,De Pascalis A, et al. Folic Acid and Homocysteine in Chronic Kidney Disease and Cardiovascular Disease Progression: Which Comes First. Cardiorenal Med. 2017;7:255-66.
11. Ajay Kumar Katiyar1, S. K. Katiyar. Study of lipid profile and homocysteine levels in cases of chronic kidney disease. Journal of Evolution of Medical and Dental Sciences. 2014; 3(26):7135-42.
12. Diniari, N. K. S., & Aryani, L. N. A. (2022). Characteristics and pharmacological treatment options of delirium patients treated at Sanglah Central General Hospital. International Journal of Health & Medical Sciences, 5(1), 37-43. https://doi.org/10.21744/ijhms.v5n1.1835
13. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. International Journal of Health Sciences, 6(1), i-v. https://doi.org/10.53730/ijhs.v6n1.5949
14. Adejumo OA, Okaka EI, Ojogwu LI. Lipid profile in pre-dialysis chronic kidney disease patients in southern Nigeria. Ghana Med J. 2016;50(1):44-9. doi:10.4314/gmj.v50i1.7
15. *Dr Sarita H Patel, Dr Milav Bhavsar, et al.* Study of Lipid profile in chronic kidney disease patients. Journal of Medical Science and Clinical Research. April 2019; 07(04): DOI: https://dx.doi.org/10.18535/jmscr/v7i4.113
16. Vandana Yadav, Vivek Prakash, et al. Study of serum homocysteine level in patients with chronic kidney disease and its association with renal function and serum albumin. Int J Res Med Sci. June 2020; 08(06):2195-8.