Original Article

A Comparative Study of the Effect of Anaemia on Lipid Levels in Patients with Chronic Kidney Disease in Tertiary Care Hospital of Bihar

Dr. Anil Kumar[1], *Dr. Deepak Kumar[2], Dr. Md Abunasar[3], Dr. Shambhu Kumar[4]

1. Tutor (Senior Resident), Department of Biochemistry, Government Medical College, Bettiah, Paschim Champaran, Bihar, India.
2. Tutor (Senior Resident), Department of Pharmacology, Government Medical College, Bettiah, Paschim Champaran, Bihar, India.
3. Professor and HOD, Department of Biochemistry, Government Medical College, Bettiah, Paschim Champaran, Bihar, India.
4. Associate Professor and HOD, Department of Pharmacology, Government Medical College, Bettiah, Paschim Champaran, Bihar, India.

***Corresponding author's E-mail:** deepak.dk58@gmail.com

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ABSTRACT

Background: CKD has become a significant public health issue, having a global occurrence of approximately 8-16%. Numerous epidemiological studies have shown a correlation between elevated iron levels in the body and a heightened susceptibility to coronary heart disease. The primary risk factor identified is elevated cholesterol levels. This study was done to compare lipid profile between patients of CKD with moderate to severe anaemia versus patients with mild or no anaemia in tertiary care hospital of eastern India.

Methods: Consecutive sampling was done to enrol 50 patients of CKD with normal haemoglobin or mild anaemia (Hb ≥ 11 g/dl) [CONTROL] and 50 patients with moderate or severe anaemia (Hb<11 g/dl) [CASES] using WHO haemoglobin cutoffs. Comparisons of continuous data such as TC, LDL, VLDL, TG, HDL age, and disease duration were performed using unpaired t-tests.

Results: Total cholesterol, LDL, TG, VLDL were significantly elevated in patients with mild or no anaemia as compared to patients with moderate or severe anaemia. Serum HDL levels in patients with moderate to severe anaemia (36.08 ± 4.93) was significantly lower as compared to patients with mild or no anaemia (40.03 ± 5.35).

Conclusion: Greater level of dyslipidaemia in CKD patients with higher degree of anaemia was evidenced by reduced level of HDL. However, this dyslipidaemia could be masked by haemodilution in anaemia as marked by reduced total cholesterol in patients with higher degree of anaemia.

Keywords: Anaemia, Chronic Kidney Disease, Lipid Profile, Dyslipidaemia.

INTRODUCTION

Chronic Kidney disease (CKD) is a medical disorder characterized by the progressive deterioration of kidney function lasting for more than three months.[1,2] CKD has become a significant public health issue, having a global occurrence of approximately 8-16% and over 10 percent prevalence among adults in the US.[3-5]

Lacking a national registration, the prevalence of CKD within India has not been clearly established. Yet, the projected incidence of CKD in India is as high as 785 individuals / million people.[6] CKD advances steadily toward end-stage renal disease (ESRD)", often accompanied by significant "cardiovascular morbidity and mortality." Indeed, patients with CKD have a higher likelihood of mortality due to coronary diseases compared to those with ESRD. [7]

Multiple recently published research suggests that dyslipidaemia in patients with CKD may play an active role in the advancement of "cardiovascular disease (CVD)" as well as the decline of renal function. [6] CVD is the primary cause of death in CKD patients, and its occurrence is greatly increased in individuals undergoing haemodialysis.[8, 9]

Dyslipidaemia is a recognized risk factor for CVD in the wider population. However, there is a need to further investigate and record the associated risk factors of dyslipidaemia in the course of CKD.

Anaemia is the prevailing nutritional illness in India, yet there are a lot causes associated with anaemia. Several research publications have documented the positive impact of anaemia on lipid profile. Effect of anaemia type on lipid level reduction is negligible. The decline in levels of cholesterol in the blood is not caused by a targeted reduction of any one lipoprotein family. Rather, it is seen that there is an associated reduction in each of the major lipoprotein families. It is noteworthy that the drop in serum lipids among anaemic individuals may reduce the likelihood of developing CAD, a condition that claims the lives of so many Indians each. The precise process by which anemia leads to a decrease in blood lipid levels remains unclear. The observed phenomena may be attributed towards the dilution effect, heightened cholesterol use by rapidly dividing cells, diminished liver oxygenation resulting in lower endogenous cholesterol production, elevated levels of GM-CSM, as well as ultimately, "the receptor-mediated uptake of LDL" facilitated by bone marrow. Correction of anaemia leads to normalisation of the lipid profile. [10]

Previous research indicates that overweight or obese individuals experience a lesser degree of anaemia compared to those with normal body weight. [11, 12]

Conversely, another study's results suggest that anaemia is linked to a higher likelihood of long-term problems from cardiovascular disease and mortality, particularly in those who are obese. [13]

Numerous epidemiological studies have shown a correlation between elevated iron levels in the body and a heightened susceptibility to coronary heart disease. The primary risk factor identified is elevated cholesterol levels.[14, 15] Notably, whereas the correlation between iron consumption and serum lipid levels has been shown in studies on animals, this correlation has not been thoroughly investigated in people. [16-18]

This study was done to compare lipid profile between patients of CKD with moderate to severe anaemia versus patients with mild or no anaemia in tertiary care hospital of eastern India.

MATERIALS AND METHODS

This was an observational and prospective study conducted on patients with CKD in a tertiary care centre of eastern India. The anticipated risk to the CKD patients due to study intervention was less than minimal, so the study was "exempted from full review of institutional ethic committee." The study was conducted under the "principle of Good Clinical Practice and declaration of Helsinki." The study duration was from January 2024 to June 2024.

Sample Size

Consecutive sampling was done to enrol 50 patients of CKD with normal haemoglobin or mild anaemia (Hb ≥ 11 g/dl) [CONTROL] and 50 patients with moderate or severe anaemia (Hb<11 g/dl) [CASES] using WHO haemoglobin cutoffs.[19]

Inclusion Criteria

Patients of age between 18-65 years of either gender with diagnosis of stage 3-5 CKD (eGFR<60 ml /min / 1.73m^2).

Exclusion Criteria

Exclusion criteria for our research included metabolic diseases, a history of cigarette and alcohol use, overweight individuals (BMI more than 25 kg/m^2), patients on drug for dyslipidaemia.

A measured volume of two millilitres of venous blood was collected in a plain vial following an obligatory fasting period of 8 hours for further analysis. Haemoglobin levels were determined using the colorimetric technique. The "total cholesterol (TC), high-density lipoprotein (HDL), and triglycerides (TGs)" were estimated using the "Autopak cholesterol kit on the Technicon RA-XT tools, manufactured by Bayer in Germany." Value of "very low-density lipoprotein (VLDL)" was determined by applying the formula "VLDL = TGs/5." The calculation of "LDL-cholesterol (LDL-C)" was performed using "Friedewald's equation. LDL = TGs - [(TGs/5) + HDL] milligrams per decilitre."

Statistical Analysis

Statistical analysis was done using Microsoft Excel 2010 and Graph Pad 8.4.3 software. The data obtained were presented in tabular form and calculations of percentages, means, and standard deviations (SD) of the parameters were performed. Comparisons of continuous data such as TC, LDL, VLDL, TG, HDL age, and disease duration were performed using unpaired t-tests. Other outcome measures and baseline parameters such as gender were expressed as percentages and ratios and compared using chi-square test. A P-value less than 0.05 was taken as a measure of significance.

RESULTS

Table 1: Comparison of Baseline Demographic and Clinical Characteristics between Cases (Moderate or Severe Anaemia) and Controls (Mild or No Anaemia)

Parameters	Case (N = 50)	Control (N = 50)	P-Value
Age in Years (Mean ± SD)	55.34 ± 12.62	57.28 ± 11.79	0.11*
Gender (n)			0.69**
Male	30	27	
Female	20	23	
Duration of CKD in Years (Mean ± SD)	2.03 ± 0.98	2.11 ± 0.66	0.63*
BMI in kg/m^2	23.21 ± 2.45	23.07 ± 2.23	0.76*

*Unpaired t test **Fisher's Exact Test

Most of the patients were males of age group 50-60 years with 1-3 years of duration of CKD. There was no significant deference between Cases (Moderate or Severe Anaemia) and Controls (Mild or No Anaemia) with respect to age, gender, duration of CKD.

Table 2: Comparison of Total Cholesterol between Cases (Moderate or Severe Anaemia) and Controls (Mild or No Anaemia)

	Case	Control
Number of Patients (N)	50	50
Mean Total Cholesterol in mg/dl	193.88	216.49
Standard Deviation (SD)	16.25	19.60
Difference in Mean	-22.6100	
95% CI of Difference	-29.7553 to -15.4647	
P Value (One Way ANOVA)	<0.0001	

Table 3: Comparison of LDL between Cases (Moderate or Severe Anaemia) and Controls (Mild or No Anaemia)

	Case	Control
Number of Patients (N)	50	50
Mean LDL in mg/dl	101.79	119.93
Standard Deviation (SD)	11.77	13.41
Difference in Mean	-18.14	
95% CI of Difference	-23.1475 to -13.1325	
P Value (One Way ANOVA)	<0.0001	

Table 4: Comparison of HDL between Cases (Moderate or Severe Anaemia) and Controls (Mild or No Anaemia)

	Case	Control
Number of Patients (N)	50	50
Mean HDL in mg/dl	40.03	36.08
Standard Deviation (SD)	5.35	4.93
Difference in Mean	3.9500	
95% CI of Difference	1.9083 to 5.9917	
P Value (One Way ANOVA)	0.0002	

Table 5: Comparison of Triglyceride and VLDL between Cases (Moderate or Severe Anaemia) and Controls (Mild or No Anaemia)

Parameters	Case N = 50	Control N = 50	P-Value
Triglyceride in mg/dl (Mean ± SD)	195.76 ± 19.12	237.33 ± 21.39	<0.0001
VLDL in mg/dl (Mean ± SD)	40.73 ± 3.54	49.43 ± 7.52	<0.0001

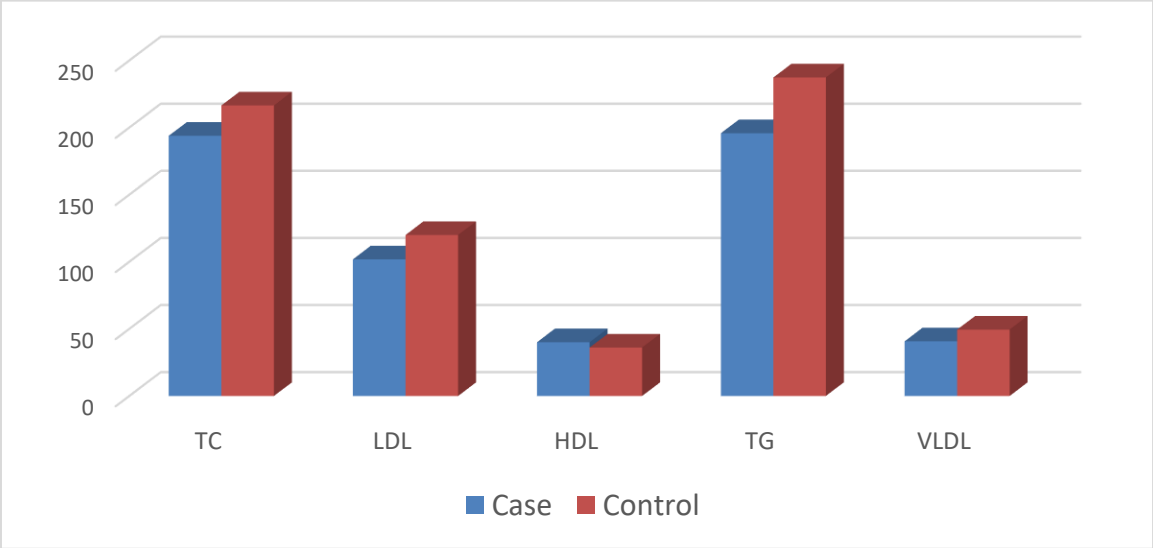

Figure 1: Comparison of Lipid Profile

Total cholesterol, LDL, TG, VLDL were significantly elevated in patients with mild or no anaemia as compared to patients with moderate or severe anaemia. Serum HDL levels in patients with moderate to severe anaemia (36.08 ± 4.93) was significantly lower as compared to patients with mild or no anaemia (40.03 ± 5.35).

DISCUSSION

A precise mechanism behind the correlation between anaemia with lipid profile remains unclear. The generally acknowledged processes include the effect of dilution (with an increase in serum volume in cases of anaemia), reduced production of cholesterol by the liver, higher use by cells undergoing proliferation, and improved elimination by GM-CSF.[20]

Anaemia accompanied by hypocholesterolaemia can arise from several processes, such as plasma dilution, heightened erythropoiesis leading to higher cholesterol requirements, stimulation of the macrophage systems causing cytokine release, and enhanced cholesterol uptake by "the reticuloendothelial system." Anaemia may therefore safeguard the lipid profile, so reducing the incidence of CAD. [21]

Anaemia is a medical disorder characterised by insufficient numbers of RBCs or inadequate levels of haemoglobin (Hb) within them. Insufficient or distorted RBCs with inadequate Hb levels will result in a diminished ability of the circulatory system to transport oxygen to the tissues of the body.[22]

Confounding variables have the potential to introduce bias and alter the findings of our study. Through multivariate analysis, specifically categorized evaluation for energy expenditure, Ece et al. noticed no correlation among the lipid profile along with the occurrence of anaemia. This suggests that energy levels, perhaps as a confounding variable, have a significant impact on the lipid profile and therefore contribute to the development of atherogenic status.[23] The present investigation found no statistically significant association between BMI and the kind as well as degree of anaemia.

Consistent with our study findings, Chowta et al. reported a notable decrease in lipoprotein levels (LDL and VLDL) among anaemic patients in comparison with nonanemic patients. This decrease was directly related to the degree of anaemia and not influenced by the specific type of anaemia.[24]

The present study did not investigate the impact of iron therapy on the association between anaemia with the lipid profile. The subsequent investigations examined the impact of iron supplementation on lipid metabolism and produced findings that were remarkably contradictory.

An improvement in the lipid profile resulting from anaemia was observed by Özdemir et al.[25] Investigators noted a substantial increase in both total as well as LDL-C levels following anaemia therapy, although these values remained lower than those of the controls.[25] Shirvani et al. found that the average levels of serum TG, cholesterol, and low-density lipoprotein (LDL) in older individuals with anaemia were notably lower than those in healthy individuals without anaemia. [26] This suggests an early preventive impact against coronary artery disease.

A study by Aboromia et al. found a negative adverse impact of anaemia on the lipid profile. Their observation revealed that the administration of iron resulted in a notable elevation in haemoglobin levels and a reduction in lipid markers including total cholesterol, triglycerides, low-density lipoproteins, and very low-density lipoprotein levels. They hypothesized substantial advantageous alterations in the lipid profile by the administration of iron treatment to anaemic patients.[27] In their study, Miri-Aliabad et al. noted a little elevation in TG and LDL levels among individuals with iron deficient anaemia, however this elevation was not statistically significant.[28]

Most investigations indicated that TG as well as lipoproteins were responsive to anemia and, with treatment, could be more easily restored to normal levels. Verma and colleagues reported that the levels of TGs and VLDL-C were considerably increased in individuals with iron deficient anaemia.[29]

Our analysis revealed that all lipid parameters exhibited an atherogenic profile, with the exception of HDL-C. Nandyala et al. reported that HDL levels were notably lower in the iron deficient anaemia group in comparison to the controls. However, after iron therapy, HDL levels significantly rose in comparison to the pretreatment levels. Their observation revealed that the levels of TC, TG, LDL, as well as VLDL were markedly increased in individuals with iron deficient anaemia. However, after receiving iron treatment, the levels of TG and VLDL were dramatically decreased.[30]

An underlying process contributing to low HDL levels is the tendency of CKD patients to display reduced levels of "apolipoprotein AI and AII." Reduced "lecithin-cholesterol acyltransferase (LCAT) activity" and enhanced cholesterol ester activity promote the migration of cholesterol esters from high-density lipoprotein (HDL) to lipoproteins that contain triglycerides (TG), effectively lowering HDL cholesterol levels. Furthermore, the lower HDL protective ability over oxidative stress in haemodialysis may be attributed to the decreased reverse cholesterol transfer.

CONCLUSION

Greater level of dyslipidaemia in CKD patients with higher degree of anaemia was evidenced by reduced level of HDL. However, this dyslipidaemia could be masked by haemodilution in anaemia as marked by reduced total cholesterol in patients with higher degree of anaemia. Clinician should correlate the degree of anaemia with serum lipid levels while making diagnosis of dyslipidaemia so that this potential risk factor cardiovascular mortality and morbidity in CKD patients would get proper attention and subsequent pharmacotherapy.

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REFERENCES

1. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. Lancet. 2016;389:1238–1252.
2. Wickramasinghe MP, Perera DM, Kahandawaarachchi KA. Dietary prediction for patients with chronic kidney disease (CKD) by considering blood potassium level using machine learning algorithms. 2017 IEEE Life Sciences Conference (LSC) 2018:300–303.
3. Pandya V, Rao A, Chaudhary K. Lipid abnormalities in kidney disease and management strategies. World J Nephrol. 2015;4:83–91.
4. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382:260–272.
5. Saini M, Vamne A, Kumar V, Chandel MS. The Study of Pattern of Lipid Profile in Chronic Kidney Disease Patients on Conservative Management and Hemodialysis: A Comparative Study. Cureus. 2022 Jan 23;14(1):e21506. doi: 10.7759/cureus.21506. PMID: 35223282; PMCID: PMC8863557.
6. Brosnahan G, Fraer M. Chronic kidney disease: whom to screen and how to treat, part 1: definition, epidemiology, and laboratory testing. South Med J. 2010;103:140–146.

7. Abraham G, Moorthy AV, Aggarwal V. Chronic kidney disease: a silent epidemic in Indian subcontinent--strategies for management. J Indian Med Assoc. 2006;104:689–691.
8. Zoccali C, Vanholder R, Massy ZA, et al. The systemic nature of CKD. Nat Rev Nephrol. 2017;13:344–358.
9. Gowdak LH, Arantes RL, de Paula FJ, Krieger EM, De Lima JJ. Underuse of American College of Cardiology/American Heart Association Guidelines in hemodialysis patients. Ren Fail. 2007;29:559–565.
10. Vetrivel S, Ganesan C, Kannan VP. A study of lipid profile in anemia patients- Case-control study in Indian patients done in Thanjavur Medical College, Tamil Nadu. J. Evid. Based Med. Healthc. 2017;4(67):3989-4000. DOI: 10.18410/jebmh/2017/798
11. Qin Y, Melse-Boonstra A, Pan X, et al. Anemia in relation to body mass index and waist circumference among Chinese women. Nutr J. 2013;12:10.
12. Ausk KJ, Ioannou GN. Is obesity associated with anemia of chronic disease? Obesity (Silver Spring) 2008;16:2356–61.
13. Winther SA, Finer N, Sharma A, Trop-Pedersen C, Anderson C. Association of anemia with the risk factor of cardiovascular adverse events in overweight/obese patients. Int J Obes. 2014;38:432–7.
14. Avila F, Echeverría G, Pérez D, et al. Serum ferritin is associated with metabolic syndrome and red meat consumption. Oxid Med Cell Longev. 2015;2015:769739.
15. Guglielmi V, D'Adamo M, Bellia A, et al. Iron status in obesity: An independent association with metabolic parameters and effect of weight loss. Nutr Metab Cardiovasc Dis. 2015;25:541–7.
16. Bristow-Craig HE, Strain JJ, Welch RW. Iron status, blood lipids and endogenous antioxidants in response to dietary iron level in male and female rats. Int J Vit Nutr Res. 1994;64:324–9.
17. Verma U, Shankar N, Madhu SV, et al. Relationship between iron deficiency anaemia and serum lipid levels in Indian adults. J Indian Med Assoc. 2010;108:555–8.
18. Ahmed U, Latham PS, Oates PS. Interactions between hepatic iron and lipid metabolism with possible relevance to steatohepatitis. World J Gastroenterol. 2012;18:4651–8.
19. Guideline on haemoglobin cutoffs to define anaemia in individuals and populations [Internet]. www.who.int. Available from: https://www.who.int/publications/i/item/9789240088542
20. Bataju M, Bhattarai B, Niraula A, Priyadarshinee A, Gautam S. Study of correlation between iron deficiency anaemia and serum lipid profile in a tertiary care center Nepal Med J. 2021;4:446–9
21. Ahmed U, Latham PS, Oates PS. Interactions between hepatic iron and lipid metabolism with possible relevance to steatohepatitis World J Gastroenterol. 2012;18:4651
22. Domenica Cappellini M, Motta I. Anaemia in clinical practice-definition and classification: Does hemoglobin change with aging? Semin Hematol. 2015;52:261–9.
23. Ece A, Yigitoglulu MR, Vurgun N, GÜven H, İşcan A. Serum lipid and lipoprotein profile in children with iron deficiency anaemia Pediatr Int. 1999;41:168–73.
24. Chowta N, Reddy S, Chowta M, Shet A, Achappa B, Madi D. Lipid profile in anaemia: Is there any correlation? Ann Trop Med Public Health. 2017;10
25. Özdemir A, Sevinç C, Selamet U, Türkmen F. The relationship between iron deficiency anaemia and lipid metabolism in premenopausal women Am J Med Sci. 2007;334:331–3.
26. Shirvani M, Sadeghi MV, Hosseini SR, Bijani A, Ghadimi R. Does serum lipid profile differ in anaemia and non-anemic older subjects? Caspian J Intern Med. 2017;8:305-11.
27. Aboromia MMM, El-Sherbeny AA, El-Hady EAA. Iron-deficiency anaemia as a risk factor for dyslipidemia in Egyptian patients Egypt J Haematol. 2019;44:14-9.
28. Miri-Aliabad G, Dashipour A, Khajeh A, Shahmoradzade M. Correlation between serum lipid profile and iron deficiency anaemia in children in southeast of Iran Iran J Blood Cancer. 2017;9:112–5.
29. Verma U, Shankar N, Madhu SV, Tandon OP, Madan N, Verma N. Relationship between iron deficiency anaemia and serum lipid levels in Indian adults J Indian Med Assoc. 2010;108:555–8 562.
30. Nandyala V, Gandiah P, Karthik RS, Sivarajappa P, Indira G, Krishna Prasad T. A study of lipid profile in iron deficiency anaemia Int J Recent Trends Sci Technol. 2013;9:258–66.