ORIGINAL RESEARCH

Correlation Between Homocysteine and Lipid Parameters in Patients with End-Stage Renal Disease

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Abstract

Introduction. Chronic kidney insufficiency presents a progressive decline in renal function. Long-term hemodialysis treatments lead to biochemical parameter imbalances like an altered level of homocysteine (Hcy). Hcy can contribute to oxidative stress and endothelial damage, which promotes the accumulation of low-density lipoprotein (LDL) cholesterol and the development of atherosclerosis. It can also affect lipoprotein metabolism and trigger inflammatory processes that alter the lipid profile, especially increasing triglycerides and lowering high-density lipoprotein (HDL) cholesterol.

Methods. This cross-sectional, clinical and descriptive-analytical study included 83 patients, 40 patients on hemodialysis, and 43 subjects in healthy control group.

Results. The hemodialysis group had significantly higher Hcy values compared to the control group of seemingly healthy subjects ($p<0.05$). The control group had significantly higher values of total cholesterol, LDL and very low-density lipoprotein (VLDL) compared to the hemodialysis patients ($p<0.05$). There was non significant correlation between Hcy and lipid parameters in the hemodialysis group, neither in the control group.

Conclusion. Patients undergoing hemodialysis had significantly higher total homocysteine levels compared to the control group. However, total homocysteine did not demonstrate an association with lipid status parameters in either the hemodialysis patients or the healthy subjects.

Keywords: homocysteine, hemodialysis, cholesterol, triglycerides, metabolism.

INTRODUCTION

End-stage renal disease (ESRD) represents the final stage of chronic kidney disease (CKD) and is associated with high cardiovascular morbidity and mortality (1). Cardiovascular disease is the leading cause of death in this population and is driven by both traditional and non-traditional risk factors, including hyperhomocysteinemia and dyslipidemia (2).

Homocysteine, a sulfur-containing amino acid generated during methionine metabolism, is normally remethylated or transsulfu-

rated in a vitamin B-dependent pathway (3, 4). In patients with ESRD, homocysteine clearance is impaired due to reduced renal function, leading to elevated plasma levels – a condition known as hyperhomocysteinemia (4). Elevated homocysteine has been associated with endothelial dysfunction, oxidative stress, and vascular inflammation, all contributing to development of atherosclerosis (5).

Dyslipidemia in ESRD differs from that seen in the general population. It is often characterized by elevated triglycerides (TG), reduced high-density lipoprotein (HDL), and altered low-density lipoprotein (LDL) (6). The uremic milieu affects hepatic and lipoprotein metabolism, contributing to abnormal lipid profiles and increased cardiovascular risk (7).

Although homocysteine and dyslipidemia are independently linked to cardiovascular risk in ESRD, the relationship between them remains unclear. Some studies suggest homocysteine may influence lipid metabolism via oxidative mechanisms or inflammation, while others find no such association (7, 8). Exploring this relationship is crucial for understanding the interplay of modifiable risk factors in ESRD. Therefore, this study aimed to assess differences in homocysteine and lipid parameters between hemodialysis patients and healthy controls, and investigate the correlation between homocysteine levels and lipid profiles in examined groups.

MATERIALS AND METHODS

Patients and Study Design

This study was designed as a cross-sectional, clinical and descriptive-comparative study, including 83 subjects of both genders 34-78 years old. The subjects were divided into two groups: patients with end-stage renal disease on hemodialysis treatment (n=40) and a control group (apparently healthy subjects) (n=43). Inclusion criteria for study participants were: patients ≥ 18 years, patients with end-stage renal disease who were on hemodialysis treatment for more than six months; each patient included in the study had a comprehensive and systematically maintained medical history, and laboratory test results; healthy individuals of both genders who have no medical history or laboratory findings indicating kidney or liver disease; voluntary consent to participate in the study and willingness to cooperate; provided written informed consent to participate in the study. Exclusion criteria from the study were: patients who were on hemodialysis treatment for less than six months, individuals with severe malnutrition with albumin levels below 25 g/L, individuals with confirmed acute or chronic infections or malignant diseases, pregnant women, patients without complete medical documentation and individuals taking medications that affect blood lipid concentrations. All participants provided written informed consent to take part in the study, in accordance with the Declaration of Helsinki and with the approval of the Ethics Committee of the Clinical Center of the University of Sarajevo.

Methods

All biochemical analyses were conducted in the laboratories of the Clinic for Biochemistry and Laboratory Medicine,Clinical Center University of Sarajevo. For patients on hemodialysis, blood samples were taken before the hemodialysis procedure. Biochemical laboratory analyses, including measurements of total cholesterol, triglycerides, HDL, LDL and homocysteine, were conducted using an automated analyzer (Abbott Laboratories, Illinois, United States).

The following reference intervals were applied, as per standard clinical laboratory practice: total cholesterol: ≤ 5.0 mmol/L, triglycerides: ≤ 1.7 mmol/L, HDL: ≥ 1.2 mmol/L, LDL: ≤ 2.6 mmol/L, homocysteine: 5.0 – 15.0 μmol/L.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics software. Descriptive statistics were applied to monitor parameters. The Shapiro-Wilk test was utilized to evaluate data normality, and the Mann-Whitney U test was applied for comparisons between two independent

groups. Relationships between homocysteine and lipid parameters were tested using Spearman's correlation tests. A p-value<0.05 was considered statistically significant.

RESULTS

The study included 83 participants of both sexes, aged between 36 and 78. Testing the age differences between the two examined groups resulted in a p-value of 0.746, indicating that there is no difference in age between the two groups.

The values of total homocysteine, one of the key parameters in this study, were compared between the two predefined groups. The Mann-Whitney test results for homocysteine showed a p-value of $p < 0.001$, indicating a significant difference in homocysteine levels between the two groups of participants.

Table 1. Comparison of Total Homocysteine Levels Between Hemodialysis Patients and the Control Group

	HD (n=40)	CG (n=43)	p-value
Homocysteine (μmol/L)	25.60 (20.5-34.2)	11.43 (10.0-14.2)	**<0.001***

Median values with interquartile range, HD - Hemodialysis patients, CG - Control group, μmol/L – micromoles per liter

The results of the comparison of lipid parameter variables between hemodialysis patients and the control group are presented in Table 2. While comparing mean values of total cholesterol, LDH and HDL significant difference is observed between the two examined groups.

Table 2. Lipid Profile Comparison Between Hemodialysis Patients and the Control Group

Parameter	HD	CG	P Value
Cholesterol (mmol/L)	4.31 ± 1.07	6.06 ± 0.88	**<0.001***
LDL (mmol/L)	2.66 ± 0.99	4.12 ± 1.10	**<0.001***
HDL (mmol/L)	0.87 (0.73-1.03)	1.09 (0.93-1.32)	**<0.001***
TG (mmol/L)	1.62 (1.04-2.14)	1.785 (1.25-3.00)	0.082
VLDL (mmol/L)	0.74 (0.47-0.99)	0.94 (0.55-1.29)	0.035

HD - Hemodialysis, CG - Control group, LDL - Low-density lipoprotein, HDL - High-density lipoprotein, VLDL - Very low-density lipoprotein, TG - Triglycerides, mmol/L – millimoles per liter.

The correlation analysis of total homocysteine and lipid profile parameters in hemodialysis patients and the control group showed that none of the obtained values reached significance ($p > 0.05$).

Table 3. Relationship Between Total Homocysteine and Lipid Profile Parameters in Hemodialysis Patients and the Control Group

Parameter	HD ρ	P value	CD ρ	P value
HDL	-.001	0.993	-.152	0.349
Cholesterol	-.047	0.765	.134	0.410
LDL	.015	0.923	.161	0.321
VLDL	-.272	0.078	.077	0.635
TG	.016	0.083	.055	0.321

HD - Hemodialysis patients, CD - Control group, HDL - High-density lipoprotein, LDL - Low-density lipoprotein, VLDL - Very low-density lipoprotein, TG - Triglycerides.

DISCUSSION

Our results demonstrated a significantly higher level of homocysteine in hemodialysis patients compared to the control group (median 25.60 μmol/L vs. 11.43 μmol/L, $p < 0.001$), consistent with previous findings that identify hyperhomocysteinemia as a prevalent abnormality in ESRD (4, 5). Impaired renal function in these patients results in reduced clearance and metabolic processing of homocysteine, making its elevation a hallmark of uremia (18).

Despite markedly different homocysteine levels, no significant correlations were found between homocysteine and any lipid parameters, including total cholesterol, LDL, HDL, VLDL, or triglycerides. This is in line with studies that have failed to demonstrate a consistent relationship between homocysteine and lipid levels in patients with renal diseases (9, 10). The absence of significant correlation suggests that while both homocysteine and dyslipidemia are prevalent in ESRD, they may act through independent pathophysiological mechanisms in contributing to cardiovascular disease (19).

Interestingly, our study also identified significant differences in lipid parameters between groups. Hemodialysis patients showed

significantly lower levels of total cholesterol, LDL, and HDL (all $p < 0.001$), a pattern typical in ESRD, attributed to chronic inflammation, protein-energy wasting, and altered lipoprotein metabolism (6, 7). VLDL levels were modestly lower ($p = 0.035$), and triglycerides did not differ significantly, highlighting inter-individual variability influenced by factors such as dialysis adequacy, nutrition, and medication (11).

Although a weak negative correlation between homocysteine and VLDL (rho = -0.272, $p = 0.078$) was observed in the hemodialysis group, it did not reach statistical significance. The lack of association may also reflect confounding effects of inflammation or vitamin deficiencies, both of which are common in ESRD and can independently influence homocysteine and lipid profiles (12).

It is also worth noting that interventions aimed at lowering homocysteine, such as folic acid and vitamin B supplementation, have shown variable effects on cardiovascular outcomes, particularly in patients with CKD or ESRD. While these treatments can reduce homocysteine levels, large randomized trials have failed to demonstrate consistent cardiovascular benefit (13, 14). Therefore, the clinical relevance of homocysteine-lowering therapy in ESRD remains debated. Furthermore, our study confirms the high prevalence of hyperhomocysteinemia and dyslipidemia in ESRD patients. However, the absence of significant correlations between these parameters suggests that their roles in cardiovascular risk may be independent (15-19). Prevention strategies of cardiovascular disaeses in ESRD patients must be aggressive, individualized, and multidisciplinary due to the unique cardiovascular risks associated with kidney failure and dialysis.

Further large-scale and longitudinal studies are warranted to explore the mechanistic links and clinical implications of these findings.

CONCLUSION

Hemodialysis patients had significantly higher total homocysteine values compared to the control group. Control group patients had significantly higher total and LDL cholesterol values compared to hemodialysis patients. However, a negative correlation trend was observed between homocysteine and total, HDL, and LDL cholesterol in hemodialysis patients. Given the lack of a significant correlation between homocysteine levels and lipid parameters, it is not possible to definitively conclude that elevated homocysteine concentration holds substantial clinical importance in the evaluation of lipid profile values.

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