Ukrainian Journal of Nephrology and Dialysis
Scientific and Practical, Medical Journal

Founder:
- National Kidney Foundation of Ukraine

ISSN 2304-0238;
eISSN 2616-7352

Journal homepage: https://ukrjnd.com.ua

Research article

Md. Masudul Karim[1], Kazi Shahnoor Alam[2], A.H. Hamid Ahmed[1], Muhammad Nazrul Islam[1], Nowshin Taslima Hossain[3], Md. Rezaul Alam[1], Ferdous Jahan[1], Syed Fazlul Islam[1], Md. Kabir Hossain[1], Md. Farhad Hasan Chowdhury[4], Kanij Delara Akhter[1], A. K. M. Shahidur Rahman[1]

doi: 10.31450/ukrjnd.2(90).2026.04

Plasma PCSK9 and its correlation with serum lipid profile in patients undergoing peritoneal dialysis: A cross-sectional study

[1]Bangladesh Medical University, Dhaka, Bangladesh
[2]Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh
[3]Ahsania Mission Cancer and General Hospital, Uttara, Dhaka, Bangladesh
[4]Mugda Medical College & Hospital, Dhaka, Bangladesh

Citation: Karim MM, Alam KZ, Ahmed AHH, Islam MN, Hossain NT, Alam MR, et al. Plasma PCSK9 and its correlation with serum lipid profile in patients undergoing peritoneal dialysis: A cross-sectional study. Ukr J Nephrol Dialys. 2026;2(90):32-41. doi: 10.31450/ukrjnd.2(90).2026.04.

Abstract. *Peritoneal dialysis (PD) is a widely practiced treatment option for patients with chronic kidney disease (CKD). Patients undergoing PD have lipid abnormalities that pose a significant cardiovascular risk. Elevated Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) levels in these patients may worsen their lipid dysregulation. However, limited data are available on PCSK9 concentration in PD patients. The present study aimed to examine the correlation between plasma PCSK9 and serum lipid profile in patients on PD.*

Methods. In this cross-sectional study, a total of 160 participants were included following the selection criteria. Of them, 80 were CKD patients on PD (Group A) and rest 80 were apparently healthy subjects as controls (Group B). Fasting serum lipid profile, serum albumin, serum creatinine, urinary protein creatinine ratio (UPCR), and plasma PCSK9 levels of all participants were measured. Additionally, PD adequacy parameters (Kt/V urea, creatinine clearance, residual renal function, transport status) were recorded for PD patients.

Results. PD patients had significantly high levels of total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, and triglyceride (TG) compared to controls ($p<0.001$). PD patients exhibited a significantly elevated level of PCSK9 than controls ($p<0.001$). In PD patients, PCSK9 had a significant positive correlation with TC ($r= 0.713$, $p<0.001$) and LDL cholesterol ($r= 0.747$, $p<0.001$). TC (>200 mg/dL) and LDL cholesterol (>130 mg/dL) were significant predictors of elevated PCSK9 levels. A cut-off value of PCSK9 >125.3 ng/ml was significantly associated with dyslipidemia in PD patients, with a sensitivity and specificity were 85.0% and 87.5%.

Conclusions. Serum TC, LDL cholesterol, and TG levels are considerably higher in PD patients compared to healthy controls. Patients receiving peritoneal dialysis also had significantly elevated plasma PCSK9 levels. Plasma PCSK9 was positively associated with TC and LDL cholesterol. TC and LDL cholesterol were independent predictors of elevated plasma PCSK9 levels in patients undergoing peritoneal dialysis.

Key words: *chronic kidney disease, peritoneal dialysis, proprotein convertase 9, cholesterol, low-density lipoprotein, triglycerides, hypercholesterolemia.*

Article history:
Received March 15, 2026
Received in revised form April 26, 2026
Accepted April 26, 2026

Conflict of interest. The author declares no conflict of interest.

Correspondence should be addressed to Masudul Karim: masud15th@gmail.com

УДК: 616.6:616.381-089.819:[616.1-008.9:577.112.85]:616.153.922

Мд. Масудул Карім[1], Казі Шахнур Алам[2], А. Х. Хамід Ахмед[1], Мухаммад Назрул Іслам[1], Новшин Тасліма Хоссейн[3], Мд. Резаул Алам[1], Фердоус Джахан[1], Сайєд Фазлул Ісламі[1], Мд. Кабір Хоссейн[1], Мд. Фархад Хасан Чоудхурі[4], Канідж Делара Ахтер[1], А. К. М. Шахідур Рахман[1]

Плазмовий PCSK9 та його кореляція з ліпідним профілем пацієнтів, які лікуються перитонеальним діалізом: поперечне дослідження

[1]Бангладеський медичний університет, Дакка, Бангладеш
[2]Медичний коледж і лікарня імені сера Салімулли та Мітфордська лікарня, Дакка, Бангладеш
[3]Онкологічна та загальна лікарня Ahsania Mission, Уттара, Дакка, Бангладеш
[4]Медичний коледж і лікарня Мугда, Дакка, Бангладеш

Резюме. *Перитонеальний діаліз (ПД) є широко застосовуваним методом лікування пацієнтів з хронічною хворобою нирок (ХХН). У пацієнтів, які лікуються методом ПД, часто спостерігаються порушення ліпідного обміну, що підвищує серцево-судинний ризик. Підвищені рівні пропротеїнконвертази субтилізин/кексинового типу 9 (PCSK9) у цих пацієнтів можуть посилювати ліпідну дисрегуляцію. Однак дані щодо концентрації PCSK9 у ПД пацієнтів залишаються обмеженими. Метою цього дослідження було вивчити кореляцію між концентрацією PCSK9 і сироватковим ліпідним профілем у ПД пацієнтів.*

Методи. До цього поперечного дослідження було включено 160 учасників відповідно до критеріїв включення. З них, 80 були ПД пацієнтами (група А), а інші 80 – практично здоровими особами (група В). В усіх учасників визначали сироватковий ліпідний профіль натще, рівні сироваткового альбуміну й креатиніну, співвідношення білок/креатинін у сечі (UPCR), і рівень плазмового PCSK9. Додатково, у ПД пацієнтів визначали показники адекватності діалізу (Kt/V сечовини, кліренс креатиніну, залишкова функція нирок транспортний статус).

Результати. У ПД пацієнтів рівні загального холестерину (ЗХ), холестерину ліпопротеїнів низької щільності (ЛПНЩ) і тригліцеридів (ТГ) були достовірно вищими порівняно з контрольною групою ($p < 0,001$). У ПД пацієнтів також виявлено достовірно вищий рівень PCSK9 порівняно з контролем ($p < 0,001$). Концентрація PCSK9 у ПД пацієнтів мала статистично значущу позитивну кореляцію з ЗХ ($r = 0,713$; $p < 0,001$) та холестерином ЛПНЩ ($r = 0,747$; $p < 0,001$). ЗХ >200 мг/дл і холестерин ЛПНЩ >130 мг/дл були достовірними предикторами підвищених рівнів PCSK9. Порогове значення PCSK9 >125,3 нг/мл асоціювалось з дисліпідемією у ПД пацієнтів з чутливістю 85,0% і специфічністю 87,5%.

Висновки. Рівні сироваткового ЗХ, холестерину ЛПНЩ і ТГ є значно вищими у ПД пацієнтів порівняно зі здоровими особами контрольної групи. ПД пацієнти мали достовірно підвищені рівні плазмового PCSK9. PCSK9 позитивно асоціювався з ЗХ і холестерином ЛПНЩ. ЗХ і холестерин ЛПНЩ були незалежними предикторами підвищених рівнів плазмового PCSK9 у ПД пацієнтів.

Ключові слова: *хронічна хвороба нирок, перитонеальний діаліз, пропротеїнконвертаза 9, холестерин, ліпопротеїни низької щільності, тригліцериди, гіперхолестеринемія.*

Introduction. Peritoneal dialysis (PD) serves as a home-based treatment for end-stage kidney disease (ESKD), offering flexibility, preservation of residual kidney function, and better quality of life compared to in-center hemodialysis [1]. It accounts for approximately11% of global dialysis use [2]. Despite several advantages, a major metabolic side effect of PD is dyslipidemia, which has been predominantly considered as a cardiovascular risk [1, 3]. This population has a very high prevalence of dyslipidemia, which ranges from 18.1% to 91.7% [1]. The exact pathophysiology of abnormal synthesis of lipid components in PD patients is still unknown. Peritoneal protein losses of 1-2 g/l of drained dialysate, which results in hypoalbuminemia contributing to this abnormality [4]. Due to significant protein losses in peritoneal dialysate, patients with renal failure receiving PD have elevated serum levels of both total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol [5]. One conventional risk factor for cardiovascular events is dyslipidemia. Cardiovascular disease (CVD) continues to be the leading cause of death among patients using PD, with an incidence that is many times higher than that of the general population [3]. High levels of serum TC, LDL cholesterol, very low-density lipoprotein (VLDL) cholesterol, triglyceride (TG) and low levels of serum high-density lipo-

Masudul Karim:
masud15th@gmail.com

protein (HDL) cholesterol are all well-known risk factors of developing CVD [6]. Recently, serine protease proprotein convertase subtilisin/kexin type 9 (PCSK9) has been identified as the third gene linked to autosomal dominant hypercholesterolemia, alongside the well-established genes encoding the LDL- receptor (LDL-R) and apolipoprotein B (APOB). PCSK9 plays a crucial role in cholesterol metabolism by regulating the degradation of LDL receptors on the surface of hepatocytes [7].

The liver produces the majority of PCSK9. However, the kidney and intestine also produce smaller amounts [7]. PCSK9 binds to the LDL-R on the surface of hepatocytes, forming a complex that is then internalized and induces its breakdown via the lysosome metabolic pathway [8]. Through this mechanism, PCSK9 modulates the clearance of circulating LDL cholesterol from the bloodstream. Regardless of its enzymatic activity, PCSK9 functions as a chaperone that promotes the intracellular degradation of the LDL-R [9]. PCSK9 inhibits the LDL receptor's recycling to the cell membrane by promoting its degradation, which ultimately results in a posttranslational decrease in LDL receptor expression [10]. Indeed, a significant decrease in plasma LDL cholesterol is linked to a loss-of-function mutation of PCSK9 [11]. The discovery of PCSK9 has significantly advanced the understanding of lipid metabolism and has led to the development of PCSK9-targeted therapeutic agents, such as monoclonal antibodies that inhibit PCSK9 activity. The transcription factor known as sterol regulatory element binding protein 2 (SREBP-2) primarily regulates the expression of PCSK9, which is triggered when intracellular free cholesterol levels decrease and inhibited when they increase [12]. Numerous factors have a tendency to lower the concentration of free cholesterol in hepatocytes, which in turn encourages SREBP-2 activation and PCSK9 expression upregulation [12]. Acyl-coenzyme A cholesterol acyltransferase- 2 (ACAT-2; encoded by the SOAT2 gene) is the most important of them, as it catalyzes the esterification of free cholesterol [13]. Patients on PD have significantly higher serum TC and LDL cholesterol levels than most hemodialysis patients, typically whose values are within or below normal limits [14]. In this regard, lipid profiles of patients on PD are similar to those frequently observed in nephrotic syndrome patients [15]. Therefore, when statins are unable to control cholesterol levels effectively or cause harm to the muscles or liver, it might be necessary to explore alternative options. Patients receiving PD, PCSK9 inhibitors could be an effective and safe substitute for the treatment of dyslipidemia. Very few human studies have examined the association between PCSK9 and serum lipid profile in PD patients. Therefore, this **study aimed** to investigate the relationship between plasma PCSK9 and serum lipids in PD patients.

Patients and methods. *Study design and setting*. This cross-sectional study was carried out at the Department of Nephrology, National Institute of Kidney Diseases and Urology (NIKDU), Dhaka, Bangladesh, between August 2022 and February 2024. NIKDU is the only nationally dedicated tertiary referral center for kidney diseases in the country, receiving patients from all regions of Bangladesh. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethical Review Committee of NIKDU, Dhaka, Bangladesh (protocol number: NIKDU/ERC/2022/118). Written informed consent was obtained from all participants.

Study cohort. Adult patients with stage 5 CKD who had been receiving peritoneal dialysis for at least three months were enrolled using purposive sampling. Age-matched healthy adults were included as the control group. Participants were selected according to predefined inclusion and exclusion criteria.

Patients were recruited from the PD registry of the NIKDU. Patients were excluded if they had recent peritonitis within the previous four weeks, were receiving lipid-lowering therapy, had abnormal liver function, or were unwilling to participate. Additional exclusion criteria were active cancer, chronic liver disease, corticosteroid or other immunosuppressive therapy, and use of lipid-lowering medication.

Healthy controls were screened before inclusion. Their blood pressure, body mass index, random blood glucose, renal and liver function tests, and urine routine microscopic findings were assessed to confirm eligibility.

Study procedure. After participant selection, the study purpose, procedures, and possible risks and benefits were explained clearly. Blood pressure, height, and weight were measured, and body mass index was calculated. Relevant demographic, clinical, laboratory, and peritoneal dialysis-related data were recorded after clinical evaluation. PD-related data included dialysis duration, treatment-related history, PD fluid parameters, and other relevant information obtained from clinical records.

Blood sample collection and laboratory analysis. After overnight fasting, 6 ml of venous blood was collected from each participant using standard procedures. The sample was divided into two separate tubes for serum and plasma preparation. Serum and plasma were separated by centrifugation, properly labeled, and processed according to the study protocol. Serum samples were analyzed immediately, while plasma samples were stored at −20°C until PCSK9 measurement. All plasma samples were analyzed in the same batch.

Fasting serum lipid profile, serum albumin, serum creatinine, urinary protein-creatinine ratio (UPCR), and plasma PCSK9 levels were measured in all participants. In patients receiving peritoneal dialysis, PD adequacy parameters, including Kt/V urea, creatinine clearance, residual renal function, and peritoneal transport status, were also recorded.

Serum creatinine, albumin, and fasting lipid profile, including total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides, were measured using a fully automated biochemistry analyzer (Erba XL-

200). Peritoneal dialysis fluid urea, creatinine, and glucose levels, as well as the urinary protein-creatinine ratio, were also assessed. Plasma PCSK9 concentration was measured by enzyme immunoassay using the RD191473200R Human PCSK9 ELISA kit manufactured by BioVendor R&D, Czech Republic. All laboratory investigations were performed in the Department of Biochemistry laboratory at NIKDU, Sher-e-Bangla Nagar, Dhaka, Bangladesh.

Statistical analysis. All collected data were carefully checked for completeness, consistency and accuracy. Statistical analysis was performed using the Windows-based software Statistical Package for the Social Sciences (SPSS), version 26. Qualitative variables were presented as frequency and percentage, whereas quantitative variables were expressed as mean and standard deviation (M ± SD). The Unpaired t-test was used to compare the mean differences between two independent groups for continuous variables. The Chi-square test was applied to assess the association between categorical variables. Pearson's correlation coefficient test was performed to determine the strength and direction of correlation between continuous variables. In addition, multivariate logistic regression analysis was carried out to identify independent predictors after adjusting for potential confounding variables. A p-value of < 0.05 was considered statistically significant.

Results. *Participant flow and characteristics*. Initially, 190 patients receiving PD were screened from the NIKDU PD registry. After applying the eligibility criteria, patients were excluded for recent peritonitis within the previous four weeks, use of lipid-lowering medication, abnormal liver function tests, or unwillingness to participate. The final analysis included 160 participants. Of these, 80 were patients with chronic kidney disease on peritoneal dialysis (Group A), and 80 were apparently healthy age-matched controls (Group B).

Table 1 summarizes the demographic, clinical, and biochemical characteristics of the study participants.

Table 1

Characteristic of the study population

Variables	Patients on PD (n = 80)	Controls (n = 80)	p-value
	Mean±SD	Mean±SD	
Age (years)	63.32 ± 9.92	62.40 ±7 .66	0.464
Gender			
Male	36 (45%)	38 (47.5%)	0.751
Female	44 (55%)	42 (52.5%)	
BMI (kg/m2)	25.44 ± 4.64	23.83 ± 3.37	0.079
Hemoglobin (gm/dl)	10.20 ± 0.30	14.58 ± 1.34	<0.001
Etiologies of CKD among patients on PD			
Diabetes mellitus	62 (77.5%)	-	-
Hypertension	14 (17.5%)	-	-
Glomerulonephritis	4 (5%)	-	-
Biochemical findings			
Serum albumin (g/dl)	2.73 ± 0.77	4.68 ± 0.52	<0.001
Serum creatinine (mg/dl)	7.41 ± 2.52	0.92 ± 0.22	<0.001
UPCR	2.75 ± 1.48	0.20 ± 0.12	<0.001
Lipid profile (mg/dl)			
TC (Normal value: <200 mg/dl)	272.40 ± 82.59	149.53±30.35	<0.001
LDL cholesterol (Normal value: <130 mg/dl))	221.61 ± 106.94	120.50 ± 18.96	<0.001
TG (Normal value: <150 mg/dl)	272.86 ± 92.80	190.38 ± 28.13	<0.001
HDL cholesterol (Normal value: >40 mg/dl)	37.26 ±6.05	39.38 ± 7.65	0.117

p-values were obtained using the unpaired t-test and chi-square test, as appropriate; Abbreviations: BMI, body mass index; CKD, chronic kidney disease; PD, peritoneal dialysis; UPCR, urinary protein-creatinine ratio; TC, total cholesterol; LDL, low-density lipoprotein cholesterol; TG, triglycerides; HDL, high-density lipoprotein cholesterol.

The two groups were comparable in age, sex distribution, and BMI, indicating appropriate matching between patients receiving peritoneal dialysis and healthy controls. Among the PD patients, diabetes mellitus was the most common underlying cause of CKD, followed by hypertension and glomerulonephritis.

Compared with controls, PD patients had significantly lower hemoglobin and serum albumin levels. In contrast, serum creatinine and urinary protein-creatinine ratio were significantly higher in the PD group, consistent with advanced kidney disease and ongoing protein loss. Regarding lipid parameters, PD patients showed a more atherogenic lipid profile, with significantly higher total cholesterol, LDL cholesterol, and triglyceride levels than controls. However, HDL cholesterol did not differ significantly between the groups. These findings suggest that patients on PD had greater metabolic and nutritional disturbances than the control group (see Table 1).

Table 2 presents the clinical and dialysis-related characteristics of the patients receiving peritoneal dialysis.

Table 2

Clinical and dialysis-related characteristics of patients receiving PD (n= 80)

Characteristics	n (%)	Mean ± SD
Dialysis vintage		
<12 months	27 (33.75)	–
12–24 months	35 (43.75)	–
>24 months	18 (22.50)	–
Dialysis adequacy		
Peritoneal Kt/V urea per week	–	1.38 ± 0.33
Renal Kt/V urea per week	–	0.29 ± 0.43
Total Kt/V urea per week	–	1.67 ± 0.54
Peritoneal creatinine clearance per week	–	38.89 ± 13.35
Renal creatinine clearance per week	–	20.22 ± 22.94
Total creatinine clearance, L/week/1.73 m^2	–	59.11 ± 26.55
Residual kidney function, ml/min	–	3.11 ± 3.04
Peritoneal membrane transport status		
High transporter	18 (22.50)	–
High-average transporter	21 (26.25)	–
Low-average transporter	26 (32.50)	–
Low transporter	15 (18.75)	–

Abbreviations: *PD = Peritoneal dialysis, Kt/V urea = Indicate dialysis accuracy, RRF = Residual renal function*

Most patients had been on PD for 12–24 months, while smaller proportions had a dialysis vintage of less than 12 months or more than 24 months. Regarding dialysis adequacy, the mean total weekly Kt/V urea and total creatinine clearance reflected the combined contribution of peritoneal dialysis and residual kidney function. Residual kidney function was still present in the study population, although with considerable variability among patients. In terms of peritoneal membrane transport status, low-average transport was the most frequent pattern, followed by high-average, high, and low transport categories. Overall, these findings describe a clinically heterogeneous PD population with variable dialysis vintage, residual kidney function, and peritoneal transport characteristics.

Plasma PCSK9 levels and their association with lipid parameters. Patients receiving PD had significantly higher plasma PCSK9 levels than healthy controls ($p < 0.001$) (Fig. 1).

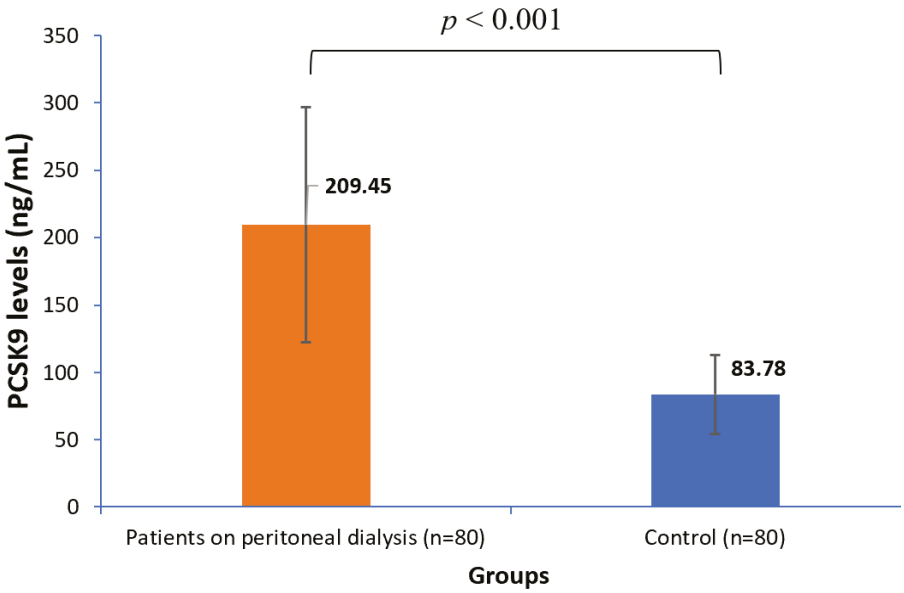

Fig. 1. Comparison of plasma PCSK9 levels between patients on PD and healthy controls. Abbreviations: PCSK9, proprotein convertase subtilisin/kexin type 9.

Among patients on PD, plasma PCSK9 showed a strong positive correlation with total cholesterol and LDL cholesterol. This means that higher PCSK9 levels were associated with higher TC and LDL cholesterol levels. No significant correlation was found between PCSK9 and triglycerides or HDL cholesterol in this group (Fig. 2).

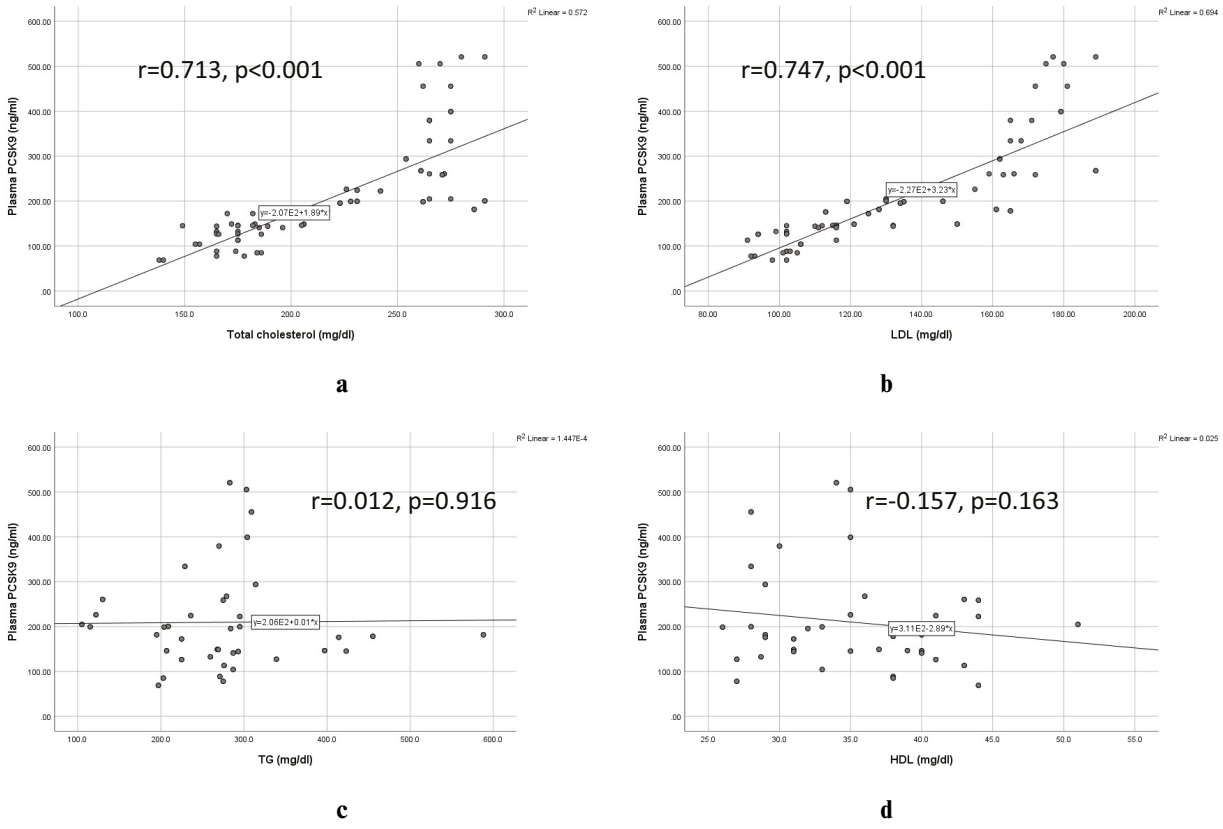

Fig. 2. Correlation between plasma PCSK9 and lipid parameters among patients on PD. (a) total cholesterol, (b) LDL cholesterol; (c) triglycerides; (d) HDL cholesterol.

Abbreviations: *PCSK9, proprotein convertase subtilisin/kexin type 9; LDL, low-density lipoprotein; TG, triglycerides; HDL, high-density lipoprotein.*

In the control group, plasma PCSK9 was not significantly correlated with any lipid parameter. The correlations with TC, LDL cholesterol, triglycerides, and HDL cholesterol were weak and not statistically significant (Table 3).

Table 3

Correlation between lipid parameters and plasma PCSK9 levels among healthy controls

Lipid parameter	r-value	p-value	95% CI lower limit	95% CI upper limit
Total cholesterol, mg/dl	0.193	0.086	−0.027	0.396
LDL cholesterol, mg/dl	0.140	0.215	−0.082	0.349
Triglycerides, mg/dl	−0.199	0.077	−0.401	0.022
HDL cholesterol, mg/dl	0.176	0.118	−0.045	0.381

Abbreviations: *PCSK9, proprotein convertase subtilisin/kexin type 9; CI, confidence interval; LDL, low-density lipoprotein; HDL, high-density lipoprotein.*

Multivariate linear regression analysis was performed to identify factors independently associated with plasma PCSK9 levels in patients on PD. Total cholesterol and LDL cholesterol remained significant independent predictors of PCSK9. In contrast, triglycerides, HDL cholesterol, total Kt/V urea, residual renal function, and peritoneal transport status were not significantly associated with PCSK9 levels. The model explained 75.0% of the variation in plasma PCSK9 levels ($R^2 = 0.750$) (Table 4).

Table 4

Multivariate linear regression analysis of factors associated with plasma PCSK9 levels among patients on peritoneal dialysis

Variable	β-value	Standard error	t-value	p-value
Total cholesterol	0.837	0.232	3.602	0.001
LDL cholesterol	2.205	0.361	6.115	<0.001
Triglycerides	−0.008	0.072	−0.105	0.917
HDL cholesterol	−3.737	2.598	−1.438	0.155
Total Kt/V urea	11.145	53.204	0.209	0.835
Residual renal function	−3.423	14.504	−0.236	0.814
Transport status	−59.171	102.243	−0.579	0.565

Model summary: $R^2 = 0.750$.

Abbreviations: *PCSK9, proprotein convertase subtilisin/kexin type 9; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Kt/V urea, dialysis adequacy index.*

ROC curve analysis showed that plasma PCSK9 had significant ability to predict dyslipidemia among patients on PD. The area under the curve was 0.914 (95% CI: 0.872–0.955; $p < 0.001$). At a cut-off value of >125.3 ng/ml, plasma PCSK9 had a sensitivity of 85.0%, specificity of 87.5%, and overall accuracy of 87.8% (Fig. 3).

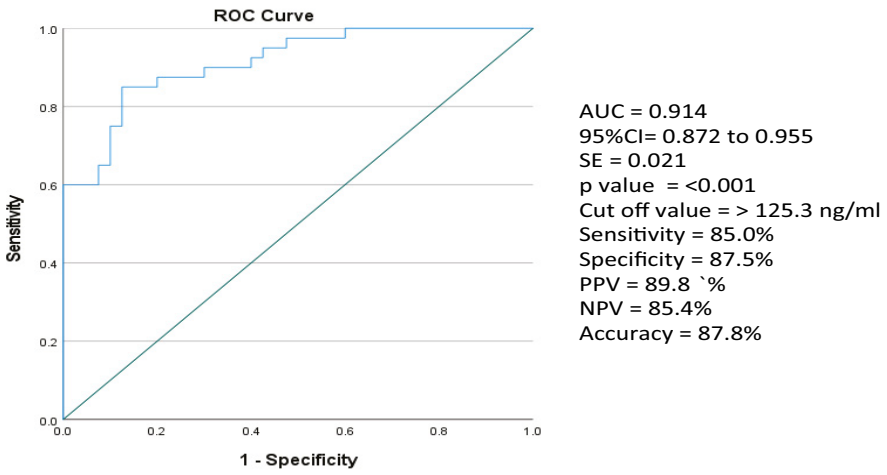

Fig. 3. ROC curve of plasma PCSK9 for predicting dyslipidemia among patients on PD.

Abbreviations: *ROC, receiver operating characteristic; PCSK9, proprotein convertase subtilisin/kexin type 9; PD, peritoneal dialysis.*

Discussion. This study revealed that PD patients have increased plasma PCSK9 levels and elevated total cholesterol, LDL cholesterol, and triglycerides as compared to controls. Among PD patients, plasma PCSK9 levels were positively correlated with total and LDL cholesterol but not with triglycerides and HDL cholesterol.

The main novelty of this study is the evaluation of plasma PCSK9 in relation to lipid parameters in patients on PD. Data on this association are still limited. The findings suggest that PCSK9 may be involved mainly in cholesterol-related lipid abnormalities in this population.

Several mechanisms may explain this association. Protein loss through the peritoneal membrane may act in a way similar to proteinuric kidney disease. Proteinuria affects hepatic PCSK9 binding and activity, leading to defects in LDL receptor function and enhanced LDL cholesterol [16]. This mechanism may partly explain elevated PCSK9 levels in the PD population and the link with atherogenic dyslipidemia. The potential role of inhibition of PCSK9 in patients with severe hypercholesterolemia related to nephrotic syndrome further supports this pathway [17].

Compared to controls, the PD population in this study had a significantly higher BMI, though the differences were not statistically significant. A high BMI among PD patients is a clinically important characteristic that has been related to a reduced technique survival, and to metabolic derangement and peritonitis [18, 19]. These PD patients also had a reduced hemoglobin level due to reasons such as iron deficiency, lack of erythropoietin stimulation, inflammation and other common factors [20]. Diabetes and hypertension were the etiology of CKD for the majority of patients in this cohort, as also documented globally [21].

Regarding dialysis-related parameters, this cohort reflects a heterogeneous group of PD patients. The dialysis vintage can affect technique survival, residual kidney function and the peritoneal membrane over time [22]. Total weekly Kt/V was not in a target of adequacy as it was close to the adequacy criteria of 1.7, which reflects that the PD adequacy was almost achieved [23]. The peritoneal transport profile of the patients also differed significantly since it affects the peritoneal solute and fluid removal [24]. The patients also have low serum albumin as a characteristic of CKD patients, and that may be correlated with inflammation, protein loss and malnutrition [25]. UPCR was also higher in PD patients, and chronic proteinuria has been established as the primary cause for protein losses, which are also associated with poor prognosis [26].

The results confirm that PD patients have dyslipidemia that includes significantly higher levels of total, LDL cholesterol, and triglycerides than healthy subjects. CKD and ESKD patients often have dyslipidemia [27]. Current lipid-lowering treatment has been proven to reduce cardiovascular events, though the dyslipidemia in CKD is complex and remains controversial [28].

Positive correlation of plasma PCSK9 levels with LDL cholesterol in PD patients is consistent with previously reported data that plasma PCSK9 levels are positively correlated with LDL cholesterol [29] and total cholesterol, and LDL cholesterol in diabetic patients [30]. PCSK9 also affects Apo B-100 metabolism and suggests its role in the handling of cholesterol-rich lipoproteins [31]. Data among CKD populations were not completely consistent, as a study in nondiabetic CKD patients documented different relations of PCSK9 with kidney function and lipid metabolism [32]. These differences could be explained by different dialysis modalities, inflammation level, residual kidney function, nutrition status, and drug exposure.

In multivariate regression analysis, it was observed that plasma PCSK9 level was associated with total and LDL cholesterol levels in PD patients. But, no statistically significant association was observed with triglycerides, HDL cholesterol, total Kt/V urea, residual renal function and transport status.

The ROC analysis shows that plasma PCSK9 levels have the ability to predict the existence of dyslipidemia in the population under PD. This analysis suggests that PCSK9 can be a useful predictor biomarker in the given cohort, but it has to be confirmed with further studies on a larger and prospective population.

Our study has several limitations. First, it was conducted in a single center, and thus, the findings cannot be extrapolated to other PD cohorts. Second, the number of patients involved is relatively small. Third, the cross-sectional design prevents a determination of causality. Thus, we could not establish high PCSK9 to be causal for the dyslipidemia or a consequence of metabolic changes. Fourth, we did not determine the long-term consequences. We could not ascertain if high PCSK9 can predict cardiovascular events, mortality, residual renal function progression or PD technique failure. Fifth, we did not analyse inflammatory markers, diet, dialysate glucose loading, and in-depth details of the medication regimen, which may influence both PCSK9 and lipid levels. Finally, PCSK9 was measured only once. Repeated measurements could provide better information about changes over time.

Conclusions. Patients receiving PD had higher plasma PCSK9 levels and a more atherogenic lipid profile than healthy controls. Plasma PCSK9 was positively associated with total cholesterol and LDL cholesterol, but not with triglycerides or HDL cholesterol. Total cholesterol and LDL cholesterol were independent predictors of plasma PCSK9.

These findings suggest a possible role of plasma PCSK9 in lipid abnormalities of PD patients and the potential use as a marker. Larger multicenter studies and follow-up will be important to confirm these findings.

Ethics approval and consent to participate. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethical Review Committee of NIKDU, Dhaka, Bangladesh (protocol number: NIKDU/ERC/2022/118).

Written informed consent was obtained from all participants.

Availability of data and materials. The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of interest. The authors declare that they have no competing interests.

Funding. No specific funding was received for this study.

Authors' contributions.

Md. Masudul Karim: contributed to the study conception, study design, dat collection and interpretation, manuscript drafting;

Kazi Shahnoor Alam, A.H. Hamid Ahmed, Muhammad Nazrul Islam, and Nowshin Taslima Hossain: data collection and record verification;

Md. Rezaul Alam and Ferdous Jahan: handled laboratory work and sample processing;

Syed Fazlul Islam, Md. Kabir Hossain, and Md. Farhad Hasan Chowdhury: data management and quality control;

Kanij Delara Akhter: statistical analysis and visualisation;

A. K. M. Shahidur Rahman: supervision, data interpretation, review and editing.

All authors critically reviewed the final version and approved it for submission.

Use of artificial intelligence. Artificial intelligence tools were used only to improve the language, grammar, and readability of the manuscript. They were not used to create data, analyze results, or make scientific conclusions. The authors reviewed the final manuscript and take full responsibility for its content.

References:

1. *Stepanova N.* Dyslipidemia in peritoneal dialysis: implications for peritoneal membrane function and patient outcomes. Biomedicines. 2024;12(10):2377. doi: 10.3390/biomedicines12102377.
2. *Jain AK, Blake P, Cordy P, Garg AX.* Global trends in rates of peritoneal dialysis. J Am Soc Nephrol. 2012;23(3):533-44. doi: 10.1681/ASN.2011060607.
3. *Prichard SS.* Management of hyperlipidemia in patients on peritoneal dialysis: current approaches. Kidney International. 2006;70:S115-7. doi: 10.1038/sj.ki.5001926.
4. *Shoji T, Nishizawa Y, Nishitani H, Yamakawa M, Morii H.* Roles of hypoalbuminemia and lipoprotein lipase on hyperlipoproteinemia in continuous ambulatory peritoneal dialysis. Metabolism. 1991;40(10):1002-8. doi: 10.1016/0026-0495(91)90120-l.
5. *Jin K, Park BS, Kim YW, Vaziri ND.* Plasma PCSK9 in nephrotic syndrome and in peritoneal dialysis: a cross-sectional study. Am J Kidney Dis. 2014;63(4):584-9. doi: 10.1053/j.ajkd.2013.10.042.
6. *Omran J, Al-Dadah A, Dellsperger KC.* Dyslipidemia in patients with chronic and end-stage kidney disease. Cardiorenal Med. 2013;3(3):165-77. doi: 10.1159/000351985.
7. *Seidah NG, Awan Z, Chrétien M, Mbikay M.* PCSK9: a key modulator of cardiovascular health. Circ Res. 2014;114(6):1022-36. doi: 10.1161/CIRCRESAHA.114.301621.
8. *Li J, Tumanut C, Gavigan JA, Huang WJ, Hampton EN, Tumanut R, et al.* Secreted PCSK9 promotes LDL receptor degradation independently of proteolytic activity. Biochem J. 2007;406(2):203-7. doi: 10.1042/BJ20070664.
9. *McNutt MC, Lagace TA, Horton JD.* Catalytic activity is not required for secreted PCSK9 to reduce low density lipoprotein receptors in HepG2 cells. J Biol Chem. 2007;282(29):20799-803. doi: 10.1074/jbc.C700095200.
10. *Maxwell KN, Breslow JL.* Adenoviral-mediated expression of Pcsk9 in mice results in a low-density lipoprotein receptor knockout phenotype. Proc Natl Acad Sci U S A. 2004;101(18):7100-5. doi: 10.1073/pnas.0402133101.
11. *Cohen JC, Boerwinkle E, Mosley Jr TH, Hobbs HH.* Sequence variations in PCSK9, low LDL, and protection against coronary heart disease. N Engl J Med. 2006;354(12):1264-72. doi: 10.1056/NEJMoa054013.
12. *Jeong HJ, Lee HS, Kim KS, Kim YK, Yoon D, Park SW.* Sterol-dependent regulation of proprotein convertase subtilisin/kexin type 9 expression by sterol-regulatory element binding protein-2. J Lipid Res. 2008;49(2):399-409. doi: 10.1194/jlr.M700443-JLR200.
13. *Chang TY, Li BL, Chang CC, Urano Y.* Acyl-coenzyme A: cholesterol acyltransferases. Am J Physiol Endocrinol Metab. 2009;297(1):E1-9. doi: 10.1152/ajpendo.90926.2008.
14. *Lluesa JH, López-Romero LC, Monzó JJ, Marugán MR, Boyano IV, Rodríguez-Espinosa D, et al.* Lipidic profiles of patients starting peritoneal dialysis suggest an increased cardiovascular risk beyond classical dyslipidemia biomarkers. Scientific Reports. 2022;12(1):16394. doi: 10.1038/s41598-022-20757-9.
15. *Vaziri ND.* Dyslipidemia of chronic renal failure: the nature, mechanisms, and potential consequences. Am J Physiol Renal Physiol. 2006;290(2):F262-72. doi: 10.1152/ajprenal.00099.2005.
16. *Shrestha P, Yazdani S, Viv s RR, El Masri R, Dam W, van de Sluis B, et al.* Proteinuria converts hepatic heparan sulfate to an effective proprotein convertase subtilisin kexin type 9 enzyme binding

partner. Kidney International. 2021;99(6):1369-81. doi: 10.1016/j.kint.2021.01.023.

17. *Jatem E, Lima J, Montoro B, Torres-Bondia F, Segarra A.* Efficacy and safety of PCSK9 inhibitors in hypercholesterolemia associated with refractory nephrotic syndrome. Kidney Int Rep. 2021;6(1):101-9. doi: 10.1016/j.ekir.2020.09.046.
18. *Prasad N, Sinha A, Gupta A, Sharma RK, Bhadauria D, Chandra A, et al.* Effect of body mass index on outcomes of peritoneal dialysis patients in India. Perit Dial Int. 2014;34(4):399-408. doi: 10.3747/pdi.2013.00056.
19. *McDonald SP, Collins JF, Rumpsfeld M, Johnson DW.* Obesity is a risk factor for peritonitis in the Australian and New Zealand peritoneal dialysis patient populations. Perit Dial Int. [Internet]. 2004;24(4):340-6. Available from: https://pubmed.ncbi.nlm.nih.gov/15335147/.
20. *Zeidan A, Bhandari S.* Anemia in Peritoneal Dialysis Patients; Iron Repletion, Current and Future Therapies. Perit Dial Int. 2017;37(1):6-13. doi: 10.3747/pdi.2016.00193.
21. *Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al.* Chronic kidney disease: global dimension and perspectives. The lancet. 2013;382(9888):260-72. doi: 10.1016/S0140-6736(13)60687-X.
22. *Davies SJ, Phillips L, Griffiths AM, Russell LH, Naish PF, Russell GI.* What really happens to people on long-term peritoneal dialysis?. Kidney Int. 1998;54(6):2207-17. doi: 10.1046/j.1523-1755.1998.00180.x.
23. *Gotch FA.* Urea kinetic modelling. Nephrol Dial Transplant. 1995;10(12):2378-9. doi: 10.1093/ndt/10.12.2378.
24. *Davies SJ, Brown B, Bryan J, Russell GI.* Clinical evaluation of the peritoneal equilibration test: a population-based study. Nephrol Dial Transplant. 1993;8(1):64-70. doi: 10.1093/oxfordjournals.ndt.a092275.
25. *Kaysen GA.* Serum albumin concentration in dialysis patients: Why does it remain resistant to therapy?: Management of comorbidities in kidney disease in the 21st century: Anemia and bone disease. Kidney Int Suppl. 2003;64:92-8. doi: 10.1046/j.1523-1755.64.s87.14.x.
26. *Kim HJ, Jung CY, Kim HW, Park JT, Yoo TH, Kang SW, et al.* Proteinuria Modifies the Relationship Between Urinary Sodium Excretion and Adverse Kidney Outcomes: Findings From KNOW-CKD. Kidney Int Rep. 2023;8(5):1022-1033. doi: 10.1016/j.ekir.2023.02.1078.
27. *Mikolasevic I, Žutelija M, Mavrinac V, Orlic L.* Dyslipidemia in patients with chronic kidney disease: etiology and management. Int J Nephrol Renovasc Dis. 2017;10:35-45. doi: 10.2147/IJNRD.S101808.
28. *Ruscica M, Ferri N, Santos RD, Sirtori CR, Corsini A.* Lipid lowering drugs: present status and future developments. Curr Atheroscler Rep. 2021;23(5):17. doi: 10.1007/s11883-021-00918-3.
29. *Alborn WE, Cao G, Careskey HE, Qian YW, Subramaniam DR, Davies J, et al.* Serum proprotein convertase subtilisin kexin type 9 is correlated directly with serum LDL cholesterol. Clin Chem. 2007;53(10):1814-9. doi: 10.1373/clinchem.2007.091280.
30. *Lambert G, Ancellin N, Charlton F, Comas D, Pilot J, Keech A, et al.* Plasma PCSK9 concentrations correlate with LDL and total cholesterol in diabetic patients and are decreased by fenofibrate treatment. Clin Chem. 2008;54(6):1038-45. doi: 10.1373/clinchem.2007.099747.
31. *Chan DC, Lambert G, Barrett PH, Rye KA, Ooi EM, Watts GF.* Plasma proprotein convertase subtilisin/kexin type 9: a marker of LDL apolipoprotein B-100 catabolism? Clinical chemistry. 2009;55(11):2049-52. doi: 10.1373/clinchem.2009.128645.
32. *Morena M, Le May C, Chenine L, Arnaud L, Dupuy AM, Pichelin M, et al.* Plasma PCSK9 concentrations during the course of nondiabetic chronic kidney disease: Relationship with glomerular filtration rate and lipid metabolism. J Clin Lipidol. 2017;11(1):87-93. doi: 10.1016/j.jacl.2016.10.005.