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SERUM PARAOXONASE-1 AS AN INDICATOR OF OXIDATIVE LIPID INJURY AND PHARMACOTHERAPEUTIC RESPONSE IN STAGE 3A CHRONIC KIDNEY DISEASE

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ABSTRACT

Background: Chronic kidney disease (CKD) raises the risk of cardiovascular problems, mainly because of dyslipidaemia and oxidative stress. In stage 3 CKD, early metabolic changes can affect lipoprotein function, even before renal function declines further. Paraoxonase-1 (PON1) is an antioxidant enzyme linked to HDL that helps prevent lipid peroxidation and stops LDL from being oxidised. Reduced PON1 activity leads to increased oxidised LDL, raising the risk of early atherosclerosis. In Stage 3a chronic kidney disease, early pharmacological intervention is crucial to slow progression and reduce cardiovascular risk.

Objective: To evaluate serum Paraoxonase-1 (PON1) as an indicator of oxidative lipid injury and to assess its association with pharmacotherapeutic response in Stage 3a CKD patients with and without dyslipidaemia.

Methods: A hospital-based case–control study was conducted among 135 subjects aged 30–60 years, including healthy controls (n = 45), Stage 3a CKD patients without dyslipidaemia (n = 45), and those with dyslipidaemia (n = 45). Serum PON1 was measured using ELISA, while lipid profile and renal parameters were analyzed using an automated biochemistry analyzer. Drug history, including statins, was recorded. Statistical analysis was performed using SPSS version 15.0, including one-way ANOVA, Tukey's post hoc test, and correlation analysis, with $p < 0.05$ considered significant.

Results: Serum PON1 levels were significantly reduced, while LDL levels were elevated in Stage 3a CKD patients compared to controls ($p < 0.05$). Stage 3a CKD patients with dyslipidaemia showed the most pronounced changes. A significant inverse correlation was observed between PON1 and Ox-LDL levels. Statin users showed higher PON1 levels and a better lipid profile, including lower total cholesterol, LDL, triglycerides, and VLDL, and higher HDL. Pharmacotherapy also reduced oxidative stress and improved antioxidant status.

Conclusion: Serum Paraoxonase-1 is a sensitive biomarker for oxidative lipid injury and atherogenic imbalance in Stage 3a CKD. Pharmacological interventions, especially statins, may enhance antioxidant status and lipid metabolism. These findings support the use of PON1 to monitor therapeutic response and cardiovascular risk in patients with Stage 3a CKD.

KEYWORDS: Stage 3a Chronic Kidney Disease, Paraoxonase-1, Lipid Peroxidation, Statins, Cardiovascular disease

INTRODUCTION

Chronic kidney disease (CKD) is often associated with a dyslipidaemic pattern that includes elevated triglycerides, accumulation of triglyceride-rich particles, reduced HDL cholesterol, and changes in the size and composition of LDL and HDL particles.These anomalies are caused by oxidative stress, insulin resistance, chronic inflammation, decreased lipoprotein catabolism, and altered lipase and transfer protein activity [1]. HDL cargo and structure are significantly altered by CKD, resulting in dysfunctional HDL with diminished anti-inflammatory, antioxidant, and cholesterol efflux capabilities. Lipidomic studies in CKD populations show that changes in HDL sphingolipids and ceramides are independently associated with mortality. This suggests that HDL quality is a better predictor than HDL-C content [2].

One of the main factors influencing HDL's antioxidant activity is the liver-derived esterase/lactonase, paraoxonase 1 (PON1), which is nearly always bound to HDL [3].

PON1 reduces lipid peroxidation, lowers LDL oxidation, and alters several athero protective mechanisms, such as endothelial function and reverse cholesterol transport, by hydrolysing oxidised cholesteryl esters and phospholipids on lipoproteins and cell membranes [4]. Its function as a key mediator and biomarker of residual cardiovascular risk is supported by experimental and clinical evidence that consistently associates decreased systemic PON1 activity with elevated oxidative stress and a higher frequency of major cardiovascular events [5, 6, 7].

In addition to genetic variations, the surrounding lipoprotein environment also affects PON1 function. Triglyceride-rich VLDL and changes in HDL composition, in particular, can directly inhibit or displace PON1 from HDL, impairing its enzymatic activity and biological effects [8], [9]. Lower PON1 activity and concentration are linked to increased oxidative

stress, vascular dysfunction, and atherosclerotic disease in chronic kidney disease, particularly in advanced stages and in dialysis patients. Specifically, it remains unknown whether certain dyslipidaemia patterns are already accompanied by quantifiable decreases in PON1-dependent antioxidative capacity at this early stage, and how these changes relate to markers of lipoprotein quality, inflammation, and renal function. Stage 3a often aligns with the initial evaluation for cardiovascular risk-modifying treatments; therefore, addressing these gaps is clinically relevant.Current risk stratification primarily relies on conventional lipid measurements, which may not detect early lipoprotein dysfunction. In CKD stage 3a, the interaction of dyslipidaemia, PON1 activity, and lipid metabolism may assist in identifying high-risk people prior to overt cardiovascular events. CKD patients, both with and without dyslipidaemia, exhibit increased susceptibility to atherosclerosis due to oxidative stress and disturbed lipid metabolism [10]. Statins are central to treating dyslipidaemia in CKD patients, as they lower LDL cholesterol and provide antioxidant benefits, including improved endothelial function and reduced lipid peroxidation. Statins may also increase paraoxonase-1 (PON1) activity, which strengthens antioxidant defences [11]. For CKD patients without evident dyslipidaemia, statins may be appropriate based on overall cardiovascular risk, given their protective effects beyond lipid lowering. Pharmacological interventions, particularly statins and renoprotective agents, may modulate PON1 activity and affect oxidative lipid injury and cardiovascular risk in Stage 3a CKD.

MATERIALS AND METHODS:

A case–control study included 135 subjects aged 30–60 years: 45 healthy controls, 45 patients with Stage 3a CKD without dyslipidaemia, and 45 patients with dyslipidaemia. Inclusion criteria were a diagnosis of Stage 3a chronic kidney disease, with and without dyslipidaemia, as defined by the NKF KDOQI guidelines; comorbidities such as type 2 diabetes mellitus, obesity, or hypertension; and ongoing routine medical treatment for CKD. Exclusion criteria were end-stage renal disease, acute infections, or inflammatory diseases. For all CKD patients, a comprehensive drug history was collected, documenting pharmacological interventions such as statins for renoprotection and blood pressure control, antidiabetic medications for diabetes mellitus, and other therapies as part of standard CKD management.Based on the lipid profile, patients were categorised as having or not having dyslipidaemia, and biomarker levels were compared with ongoing pharmacotherapy, particularly statin use.

Sample Collection:

Blood Samples will be collected from stage 3a chronic kidney disease patients from Saveetha Medical College and Hospital. 10 ml of blood will be collected from the antecubital vein under aseptic conditions. Serum is separated after centrifugation. Handle and store specimens in stoppered containers to avoid contamination and evaporation. Refrigerated at - 20 ˚ C (long-term storage)

Biochemical Analysis:

Renal function tests (urea, creatinine) and lipid markers were measured via the Vitros 5600 dry chemistry analyser. Lipid profiles were measured as follows: total cholesterol by the CHOD–PAP method, triglycerides by the GPO–PAP method, and HDL cholesterol by indirect precipitation. LDL and VLDL cholesterol were calculated using the Friedewald formula, excluding samples with triglycerides above 400 mg/dL.All assays were performed according to the manufacturer's instructions, with appropriate quality control, and reference ranges were in accordance with standard clinical laboratory guidelines. Serum PON1 levels were assessed using a sandwich ELISA. The assay procedure involves running all standards and samples in duplicates or triplicates with a standard curve for each assay. First, 100 µL of standard diluent, standards, and samples are added to the respective wells, and the mixture is incubated for 80 minutes at 37 °C. After washing the plate four times, 100 µL of biotinylated antibody working solution is added and incubated for 50 minutes at 37 °C, then washed again. Then, 100 µL of Streptavidin-HRP conjugate is added, incubated for 50 minutes, and washed again. Next, 100 µL of TMB substrate is added, and the mixture is incubated for 10 minutes at 37 °C without shaking. The reaction is stopped with 100 µL of the stop solution, which changes the colour from blue to yellow. Absorbance is read at 450 nm within 10–15 minutes. The mean absorbance values of standards are plotted against concentration to generate a standard curve, from which sample concentrations are determined, with dilution adjustments as necessary.

Statistical Analysis:

All data were analysed using SPSS software version 15.0. Continuous variables are presented as mean ± standard deviation (SD). Group comparisons were conducted using one-way ANOVA, with the Tukey post hoc test for multiple comparisons. Correlations among biochemical variables were assessed using Pearson's or Spearman's analysis, based on data distribution. Statistical significance was set at $p < 0.05$.

Ethical clearance:005/04/2024/IEC/SMCH

RESULT

Serum PON1 levels were significantly lower in patients with stage 3a CKD, particularly in those with dyslipidemia. One-way ANOVA indicated significant group differences ($F = 752.232$, $p < 0.001$). Post hoc t-tests confirmed lower levels in CKD patients than in controls and across CKD subgroups ($p < 0.001$).

Pearson correlation indicated a moderate negative correlation between CKD patients with and without dyslipidemia ($r = -0.351$, $p = 0.018$), while correlations with controls were not significant.

Table:1 Comparison of Biochemical Parameters Among Control, Stage 3a CKD Without Dyslipidaemia, and Stage 3a CKD With Dyslipidaemia

Parameter	Control (Mean ±	CKD Without	CKD With	p-value

	SD)	Dyslipidaemia (Mean ± SD)	Dyslipidaemia (Mean ± SD)	
Triglycerides (mg/dL)	87 ± 11	112 ± 30	194 ± 4	<0.001
Cholesterol (mg/dL)	118 ± 18	135 ± 30	236 ± 10	<0.001
HDL (mg/dL)	61 ± 7	55 ± 3	34 ± 11	<0.001
VLDL (mg/dL)	18 ± 5	45 ± 35	42 ± 16	<0.001
LDL (mg/dL)	73 ± 9	65 ± 28	161 ± 9	<0.001
Cholesterol / HDL Ratio	3.0 ± 0.6	5.0 ± 1.2	5.7 ± 1.0	<0.001
Serum Paraoxonase-1	4.05 ± 0.78	3.55 ± 0.07	0.60 ± 0.07	<0.001

Table 1 indicates that One-way ANOVA identified statistically significant differences among the three groups for all measured biochemical parameters ($p < 0.001$). CKD patients with dyslipidaemia showed substantially higher levels of triglycerides, total cholesterol, LDL, VLDL, and the TC/HDL ratio, along with significantly lower HDL and serum paraoxonase 1 (PON1) activity, compared with both controls and CKD patients without dyslipidaemia. These findings indicate that dyslipidaemia, increased oxidative stress, and reduced antioxidant enzyme activity are strongly associated in patients with Stage 3a CKD.
This combination may elevate the risk of lipid peroxidation and atherosclerotic complications.

Table 2. Descriptive Statistics of Serum PON1 Levels Among Study Groups

Group	N	Mean ± SD	Std. Error
Control	45	4.054 ± 0.785	0.117
CKD 3a With Dyslipidemia	45	0.601 ± 0.063	0.009
CKD 3a Without Dyslipidemia	45	3.554 ± 0.072	0.011
Total	135	2.736 ± 1.659	0.143

Table 2 shows the mean serum Paraoxonase-1 (PON1) levels, standard deviation (SD), and standard error (SE) for the three study groups. The control group exhibited the highest mean PON1 level (4.054 ± 0.785). Patients with chronic kidney disease (CKD) stage 3a and dyslipidemia displayed significantly lower levels (0.601 ± 0.063), whereas those without dyslipidemia presented intermediate values (3.554 ± 0.072). These findings indicate significant differences in antioxidant enzyme activity among the groups.

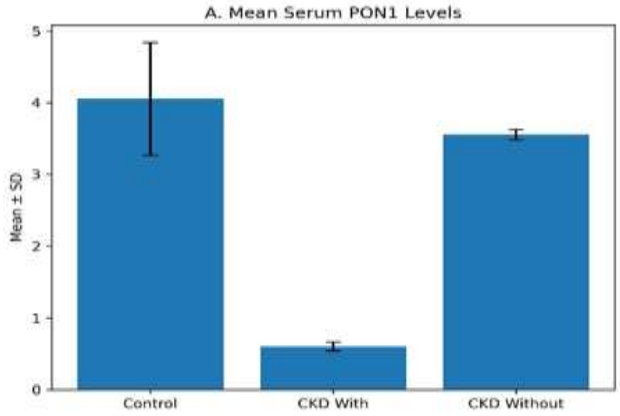

Figure :1 Comparison of Mean Serum Paraoxonase-1 (PON1) Levels Among Study Groups

Figure 1 shows a significant reduction in serum PON1 levels in patients with CKD stage 3a, especially those with dyslipidemia. One-way ANOVA revealed a highly significant difference among groups ($p < 0.001$) and a large effect size ($\eta^2 = 0.920$), indicating that group status accounts for most of the variance in PON1 levels. Dyslipidemia further accelerates the decline in antioxidant enzyme activity.

Table 3. One-Way ANOVA Comparing Serum PON1 Levels Between Groups

Source	Sumof Squares	df	Mean Square	F	p-value
Between Groups	301.873	2	150.937	752.232	<0.001***
Within Groups	26.523	132	0.201	-	-
Total	328.396	134	-	-	-

Effect Size (η^2) = 0.920 (Very Large Effect)

Table 3 shows that one-way ANOVA revealed a highly significant difference in serum PON1 levels among the three groups ($F(2,132) = 752.232$, $p < 0.001$). The effect size ($\eta^2 = 0.920$) indicates that group classification accounts for approximately 92% of the variance in serum PON1 levels. This demonstrates a strong association between CKD status, dyslipidemia, and PON1 activity.

Table 4. Post Hoc Analysis Using Tukey's HSD Test

(I) Group	(J) Group	Mean Difference	Std. Error	Sig.	95% CI Lower	95% CI Upper

		(I–J)				
CKD With	CKD Without	-2.954	0.116	<0.001***	-3.182	-2.726
CKD With	Control	-3.453	0.116	<0.001***	-3.682	-3.225
CKD Without	Control	-0.500	0.116	<0.001***	-0.728	-0.272

Table 4 presents Tukey's post hoc analysis, which shows statistically significant differences in all pairwise comparisons ($p < 0.001$). CKD patients with dyslipidemia had significantly lower PON1 levels than both CKD patients without dyslipidemia and controls. CKD patients without dyslipidemia also had lower levels than controls. These results indicate that dyslipidemia further worsens the decline in antioxidant enzyme activity in stage 3a CKD.

Table 5. Independent Samples t-Test with Effect Size

Comparison	t	df	p-value(2-tailed)	Cohen's d
Control vs CKD With	29.423	88	<0.001***	6.94
Control vs CKD Without	4.254	88	<0.001***	0.90
CKD With vs CKD Without	-206.675	88	<0.001***	48.83

Table 5 shows that independent sample t-tests identified significant differences in serum PON1 levels across all groups ($p < 0.001$). Effect sizes ranged from large to extremely large, indicating clinically meaningful differences. The largest effect size was between CKD patients with dyslipidemia and controls, underscoring the marked reduction of PON1 activity in this subgroup.

Table 6. Pearson Correlation Matrix of Serum PON1 Levels

Variables	Control	CKD with dyslipidemia	CKD Without dyslipidemia
Control	1	-0.063 (p=0.679)	-0.040 (p=0.796)
CKD With	-0.063	1	-0.351* (p=0.018)
CKD Without	-0.040	-0.351*	1

**Correlation significant at $p < 0.05$*

Table 6 shows that Pearson correlation analysis found no significant correlation between the control and CKD groups. PON1 levels in patients with chronic kidney disease (CKD), both with and without dyslipidemia, showed a moderate negative correlation ($r = -0.351$, $p = 0.018$). This finding may reflect different patterns of oxidative stress associated with dyslipidemia.

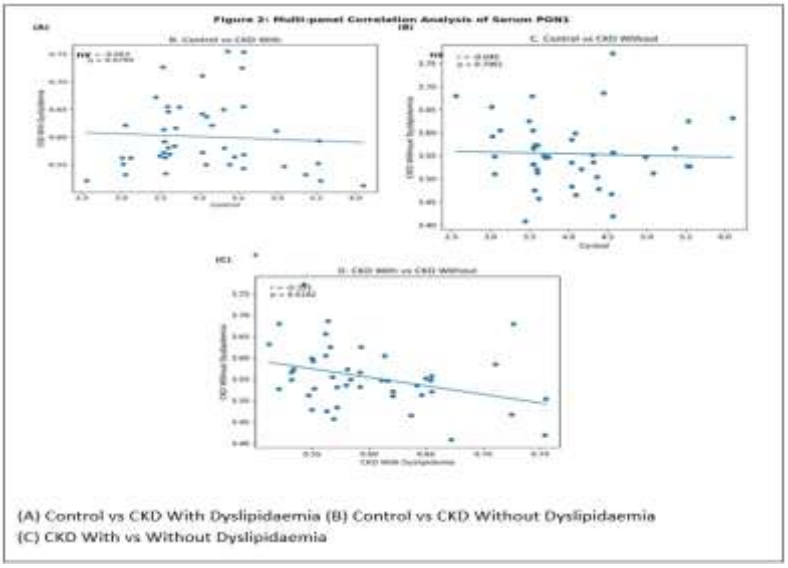

Figure 2: Correlation analysis of serum Paraoxonase-1 (PON1) levels among control subjects and CKD stage 3a patients.

Figure 2 presents the following correlations: (A) No significant linear association was found between the control group and CKD stage 3a patients with dyslipidaemia, indicating that the marked reduction in PON1 levels in these patients is independent of normal variation in controls. (B) No significant association was identified between the control group and CKD stage 3a patients without dyslipidaemia. This finding indicates that the moderate reduction in PON1 in this group may be due to factors unrelated to lipid abnormalities.(C) A significant moderate negative correlation was identified between CKD stage 3a patients with and without dyslipidaemia ($r = -0.351$, $p = 0.018$), indicating that worsening dyslipidaemia is associated with lower PON1 activity. These results support the role of dyslipidaemia in increasing oxidative stress and reducing antioxidant defense in early CKD.

Serum Paraoxonase-1 (PON1) levels were significantly lower in CKD stage 3a patients with dyslipidaemia compared to both controls and CKD patients without dyslipidaemia. Correlation analysis revealed no significant association between the control group and either of the CKD subgroups. A significant, moderate negative correlation was observed between CKD patients with and without dyslipidaemia ($r = -0.351$, $p = 0.018$), indicating that greater lipid abnormalities are associated with reduced PON1 activity. These findings suggest that dyslipidaemia increases oxidative stress and impairs antioxidant defense in stage 3a CKD.

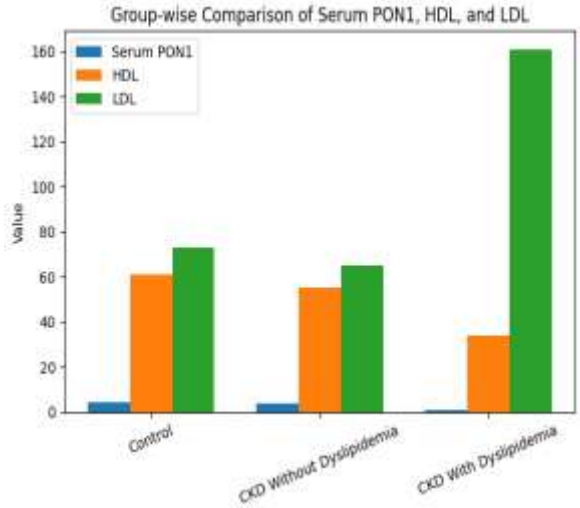

Figure 3: Comparison of Serum Paraoxonase-1 (PON1), HDL, and LDL Levels Between Control and Stage 3a CKD Patients

Figure 3 presents serum PON1, HDL, and LDL levels in three groups: a control group, Stage 3a CKD patients without dyslipidemia, and Stage 3a CKD patients with dyslipidemia. The control group has higher PON1 and HDL levels and lower LDL levels, reflecting normal antioxidant and lipid profiles. CKD patients without dyslipidemia have moderately lower PON1 and HDL levels.

CKD patients with dyslipidemia exhibit substantially lower PON1 activity and HDL levels, along with significantly higher LDL, suggesting increased oxidative stress and a more atherogeGroup comparisons revealed clear biochemical differences. The control group had the highest serum Paraoxonase-1 (PON1) activity, higher HDL, and lower LDL levels. In Stage 3a CKD patients without dyslipidemia, PON1 activity and HDL were moderately reduced, while LDL remained stable. CKD patients with dyslipidemia showed a significant decline in PON1 activity and HDL, with a marked increase in LDL. These findings indicate that CKD with dyslipidemia is linked to reduced antioxidant enzyme activity and a highly atherogenic lipid profile, reflecting increased oxidative stress and greater cardiovascular risk in this population.

Table 7: Drug-Based Comparison of Biomarkers and Lipid Profile in CKD Patients

Parameter	**Statin Users (Mean ± SD)**	**Non-Statin Users (Mean ± SD)**	**p-value**
PON1 (U/L)	0.52 ± 0.09	0.65 ± 0.11	<0.05
Total Cholesterol (mg/dL)	168 ± 21	213 ± 31	<0.05
LDL Cholesterol (mg/dL)	101 ± 16	148 ± 22	<0.05
HDL Cholesterol (mg/dL)	38 ± 5	31 ± 4	<0.05
Triglycerides (mg/dL)	147 ± 24	186 ± 29	<0.05
VLDL Cholesterol (mg/dL)	27 ± 4	37 ± 7	<0.05

Table 7 presents that Statin users demonstrated significantly higher PON1 levels and HDL cholesterol, along with lower Ox-LDL, total cholesterol, LDL, triglycerides, and VLDL levels compared to non-statin users ($p < 0.05$), indicating improved lipid profile and reduced oxidative stress.

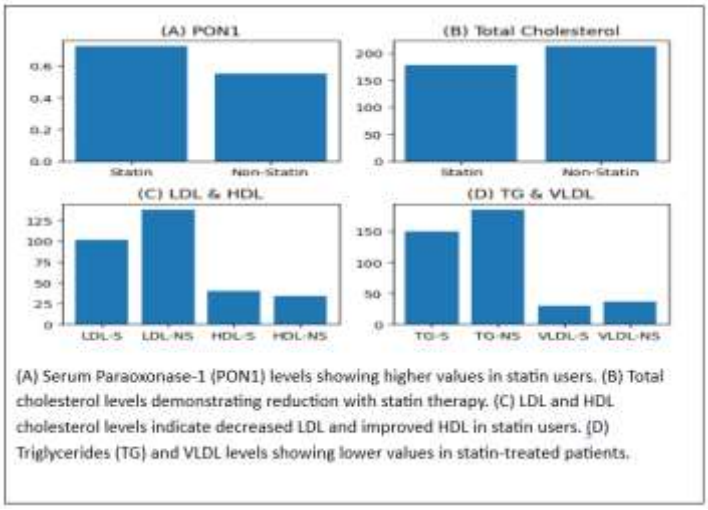

Figure 6 : Multi-panel representation of biomarker and lipid profile comparison between statin users and non-statin users in CKD patients

Figure 6 demonstrates that multi-panel analysis identified significant differences in biomarker and lipid profiles between statin and non-statin users with CKD. Statin users had higher serum Paraoxonase-1 (PON1) levels, indicating enhanced antioxidant status. Statin therapy reduced total cholesterol, LDL, triglycerides (TG), and VLDL, while increasing HDL, thereby improving lipid metabolism and the atherogenic balance.
Statin therapy appears to reduce dyslipidaemia, cardiovascular risk, and oxidative stress in patients with Stage 3a CKD. Pharmacotherapeutic interventions, particularly statins, enhance antioxidant status and reduce lipid peroxidation, as indicated by increased PON1 and decreased LDL levels. PON1 may serve as a useful marker for disease monitoring and evaluating therapeutic response in Stage 3a CKD.

DISCUSSION

Chronic kidney disease (CKD) is characterised by impaired lipid metabolism and increased oxidative stress, both of which contribute to cardiovascular complications. This study examines whether serum Paraoxonase-1 (PON1), an antioxidant enzyme associated with high-density lipoprotein (HDL), can serve as a biomarker for lipid dysregulation in stage 3 CKD. Results indicate that CKD patients have significantly lower serum PON1 levels than healthy controls, especially those with dyslipidaemia. Reduced PON1 activity reflects diminished antioxidant defence in CKD, leading to greater lipid peroxidation and accumulation of oxidised lipoproteins. Since PON1 breaks down lipid peroxides and protects LDL from oxidation, lower PON1 levels may increase the risk of atherosclerosis and cardiovascular disease in patients with CKD.
Our findings show that PON1 activity decreases significantly and lipoprotein changes occur as early as CKD stage 3a dyslipidaemia. This suggests that HDL impairment begins early in renal dysfunction and is more closely linked to dyslipidaemia than to eGFR alone. The observed reduction in PON1 activity at eGFR 45–59 mL/min/1.73 m² supports the idea that PON1 dysfunction is an early feature of renal disease and likely contributes to increased cardiovascular risk in CKD.[12] Epidemiologic studies in non-CKD populations also associate reduced PON1 activity and certain functional polymorphisms with higher systemic oxidative stress and increased risk of adverse cardiovascular events.
Our findings indicate that individuals with intermediate CKD, even when conventional lipid indices show only minor abnormalities, may already be at risk. We also demonstrate that PON1 activity is more strongly associated with triglycerides, residual cholesterol, and altered HDL characteristics than with LDL-C or total cholesterol. These results support the shift toward prioritising HDL quality and function over quantity [13]. Previous lipidomic research on chronic kidney disease has demonstrated that certain HDL lipid species, such as ceramides and sphingomyelins, can predict mortality, even in the absence of bulk HDL. proving the significance of HDL compositional remodelling in CKD as a predictive factor. By linking a key functional enzyme on HDL, PON1, to the dyslipidaemic pattern characteristic of stage 3a CKD, our study contributes to this picture. It is mechanistically conceivable that reduced PON1 activity is associated with residual rich dyslipidaemia and hypertriglyceridemia. In a dose-dependent manner, VLDL triglycerides can directly block the catalytic activity of HDL-associated PON1, causing HDL to adopt a triglyceride-rich, cholesteryl ester-poor phenotype that is less conducive to PON1 stability. PON1 binding and displacement from HDL are affected by additional modifications to particle size, surface phospholipids, and protein cargo introduced by lipases such as endothelium lipase and hepatic lipase during HDL remodelling [14]. In CKD stage 3a, when oxidative stress and low-grade inflammation are already prevalent, this unfavourable lipoprotein environment may hinder hepatic PON1 production and promote the inactivation of the existing enzyme. PON1 activity shows a strong correlation with dyslipidaemia indices, consistent with extensive research linking genetically and biochemically determined PON1 activity to systemic oxidative stress and cardiovascular outcomes.
Additionally, when circulating PON1 is experimentally increased in mice, HDL resistance to oxidation improves, macrophage cholesterol efflux increases, and cellular cholesterol accumulation and biosynthesis decrease. These findings offer a biological explanation for why even slight decreases in PON1 activity in CKD 3a may have disproportionately atherogenic effects. HDL-C concentration alone is an insufficient proxy for cardiovascular protection in CKD, as is increasingly recognised, given its implications for HDL function and risk assessment in CKD 3a. Because large-scale studies of HDL-raising techniques have not shown improved outcomes, the importance of HDL composition and function,

antioxidant capacity, anti-inflammatory activity, and cholesterol efflux relative to static cholesterol levels is highlighted. It is now known that PON1 plays a key role in determining these protective HDL functions. PON1 activity may indicate atherosclerotic risk as effectively as, or sometimes better than, HDL-C from both evolutionary and clinical perspectives. As a result, conventional lipid panels may underestimate cardiovascular risk in individuals with dysfunctional HDL and reduced PON1 activity.

These data support findings that changes in HDL structure and bioactive lipid cargo, such as ceramide enrichment or protective sphingolipid depletion, predict mortality in CKD, independent of conventional lipid levels. One of the main contributing factors to the development of coronary heart disease is known to be dyslipidaemia [15]. The development of atherosclerosis is fuelled by abnormal cholesterol levels and high blood pressure, which cause endothelial damage, vascular inflammation, and remodelling [16]. Cellular damage and inflammatory reactions that impair immune defence can arise from an imbalance in this system [17]. The inverse relationship between paraoxonase 1 (PON1) and oxidative stress highlights the imbalance between oxidative stress and antioxidant capacity in patients with chronic kidney disease (CKD). Recent studies indicate that decreased PON1 activity is associated with elevated oxidative lipid damage and endothelial dysfunction in this population [18,19]. Dyslipidaemia further exacerbates this imbalance, as evidenced by higher LDL, triglycerides, and VLDL levels along with reduced HDL levels in CKD patients with dyslipidaemia. These alterations promote the formation of atherogenic lipoproteins and accelerate vascular injury.

Pharmacotherapeutic evaluation in this study showed that commonly used CKD medications, especially statins and renin–angiotensin system inhibitors (ACE inhibitors/ARBs), may partially restore antioxidant balance. Statins provide benefits beyond lipid lowering, including antioxidant and anti-inflammatory effects, which may enhance PON1 activity and improve endothelial function [20]. Elevated PON1 levels observed in statin users suggest restoration of HDL-associated antioxidant capacity [21]. Statin therapy reduces total cholesterol, LDL, triglycerides, and VLDL, while modestly increasing HDL, resulting in a less atherogenic lipid profile. Additionally, decreased Ox-LDL levels provide further evidence for the role of statins in reducing lipid peroxidation and oxidative stress.

Recent studies also show that statins modulate oxidative pathways and improve redox balance in patients with CKD [22]. Renin–angiotensin system inhibitors, including ACE inhibitors and ARBs, protect renal and cardiovascular health by reducing angiotensin II–mediated oxidative stress and inflammation. Reduction of reactive oxygen species (ROS) generation by these agents may preserve PON1 activity and enhance vascular function [23]. Recent therapies, such as sodium–glucose cotransporter-2 (SGLT2) inhibitors, exhibit antioxidant and cardioprotective effects in chronic kidney disease (CKD), underscoring the importance of pharmacological management of oxidative stress [24].The results highlight the significance of early detection and management of oxidative stress and dyslipidaemia in patients with chronic kidney disease (CKD). Monitoring paraoxonase 1 (PON1) levels provides valuable information regarding the effectiveness of pharmacotherapy and facilitates the identification of patients at elevated cardiovascular risk. Including antioxidant-based biomarkers such as PON1 in routine evaluations may enhance risk stratification and support personalised treatment strategies in CKD.

CONCLUSION

Serum Paraoxonase-1 (PON1) is a sensitive biomarker for oxidative lipid injury and atherogenic imbalance in Stage 3a CKD. Reduced PON1 levels reflect diminished antioxidant defense and are associated with increased lipid peroxidation and cardiovascular risk. Pharmacological treatments, particularly statins, improve lipid profiles and restore antioxidant balance, as indicated by higher PON1 levels. These findings support the clinical utility of PON1 for diagnosis and therapeutic monitoring.

Early PON1 assessment may help optimise treatment, improve cardiovascular outcomes, and support personalised care for patients with CKD.

CONFLICT OF INTEREST:

No conflicts of interest regarding this investigation.

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