ORIGINAL ARTICLE

Effect of diabetes and oxidative stress on plasma CCL23 levels in patients with severe chronic kidney disease

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KEY WORDS

CCL23, chronic kidney disease, diabetes, inflammation, oxidative stress

ABSTRACT

INTRODUCTION CCL23 is a new CC chemokine involved in leukocyte trafficking and inflammatory diseases. Inflammation, oxidative stress, and diabetes are common in patients with chronic kidney disease (CKD), particularly in those with cardiovascular disease (CVD).

OBJECTIVES The aim of this study was to evaluate CCL23 concentrations in patients with CKD and to identify the factors affecting its plasma level.

PATIENTS AND METHODS CCL23 levels, inflammatory markers (high-sensitivity C-reactive protein, interleukin 6, and tumor necrosis factor α) and oxidative stress markers (neopterin and Cu/Zn superoxide dismutase [Cu/Zn SOD]) were measured in the plasma of patients with mild-to-moderate CKD (group A) and severe CKD (group B) both with and without diabetes and in controls.

RESULTS CCL23 concentrations were higher in group B, particularly in patients with diabetes compared with controls (P <0.001) and group A (P <0.01). The inflammatory markers were increased in CKD patients but they were not correlated with CCL23 levels. In contrast, there were associations between CCL23 and oxidative stress markers and kidney function. The presence of diabetes, Cu/Zn SOD, and percentage of lymphocytes were found to be independent factors affecting CCL23 concentrations in the whole CKD group. In patients without diabetes, only Cu/Zn SOD was independently associated with CCL23.

CONCLUSIONS CCL23 levels were increased in patients with severe CKD and were strongly correlated with kidney function. The coexistence of diabetes and oxidative stress independently affected CCL23 levels, while the presence of CVD and inflammation had no impact on its concentrations.

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INTRODUCTION Recent studies have reported that low estimated glomerular filtration rate (eGFR) is associated with higher risk of cardiovascular disease (CVD).[1,2] In patients with chronic kidney disease (CKD), this cardiovascular risk is related partly to a high prevalence of traditional risk factors for atherogenesis, but, most likely, also to the action of nontraditional risk factors specific to CKD, such as enhanced inflammation, oxidative stress, or advanced glycation end products.[3-5]

Atherosclerosis is a chronic inflammatory process mediated through several families of diverse cytokines and growth factors.[6] Among them, CC chemokines, produced by cells engaged in atherosclerotic process, exacerbate vascular inflammatory responses, which leads to the formation of fatty streak lesions and promotes plaque rupture.[7]

CCL23 (also known as myeloid progenitor inhibitory factor 1 [MPIF1] or macrophage inflammatory protein 3 [MIP3]) is a new member of the CC chemokine family, which demonstrates a chemotactic activity for monocytes/macrophages, dendritic cells, lymphocytes, and endothelial cells.[8,9] It has been shown that CCL23 upregulates inflammatory cytokines such as tumor necrosis factor α (TNF-α) and monocyte chemoattractant protein 1 (MCP-1/CCL2) in human monocytes.[10] Circulating CCL23 levels have

TABLE 1 Biochemical and clinical characteristics of healthy controls and patients with mild-to-moderate (group A) and severe (group B) chronic kidney disease both with and without diabetes

Variable	Controls	Group A	Group B	
			without diabetes	with diabetes
sex, male/female	15/11	10/8	4/9	6/3
age, y	49.0 ±7.0	40.0 ±12.0	56.8 ±13.6	61.11 ±15.0[a,e]
BMI, kg/m^2	26.8 ±4.6	25.9 ±4.4	24.1 ±4.2	25.82 ±9.15
eGFR, ml/min/1.73 m^2	114.9 ±8.8	78.5 ±20.2[a]	16.6 ±10.1[c,f]	21.7 ±9.2[c,f]
hemoglobin, mmol/l	8.8 ±0.8	8.6 ±1.0	6.3 ±1.2[c,e]	6.6 ±0.4[c,e]
white blood cells, × 10^9/l	5.9 ±1.0	6.7 ±1.8	6.7 ±2.5	6.4 ±2.3
neutrophils, %	58.8 ±6.4	53.9 ±9.1	65.9 ±13.0[d]	53.1 ±14.5
lymphocytes, %	33.0 ±5.5	36.0 ±8.0	22.6 ±9.9 [b,f]	26.1 ±11.3[a,e]
total cholesterol, mmol/l	4.9 ±0.8	5.7 ±2.3	5.2 ±1.0	4.4 ±1.1
triglycerides, mmol/l	0.8 (0.4–1.7)	2.4 (0.7–7.0)[c]	1.9 (0.8–5.3)[c,d]	1.6 (0.7–5.4)[b,e]
total protein, g/l	67.8 ±4.3	59.1 ±13.3	63.1 ±11.0	58.3 ±13.2
albumin, µmol/l	643 ±203	416 ±130[c]	472 ±111[c]	507 ±110[b]
creatinine, µmol/l	86.6 (56.6–124.0)	91.1 (69.0–133.0)	460.0 (115.0–822.0)[c,f]	390.6 (160.9–533.4)[c,f]
urea, mmol/l	5.5 ±1.3	6.0 ±2.5	23.1 ±7.5[c,f]	21.6 ±6.4[c,f]
glucose, mmol/l	4.9 ±0.8	5.3 ±1.2	4.8 ±1.0	6.1 ±1.6[a,g]
SBP, mmHg	128.3 ±11.3	129.4. ±9.0	128.3 ±13.6	135.7 ±10.0
DBP, mmHg	83.3 ±8.8	84.8 ±9.8	86.7 ±6.9	87.8 ±5.1
smokers	3 (12)	3 (15)	6 (19)	1 (11)
cardiovascular disease	–	3 (15)	15 (47)[e]	7 (78)[f,h]
angiotensin-converting enzyme inhibitors	–	11 (62)	13 (41)	6 (67)[g]
calcium channel antagonists	–	6 (31)	20 (63)[d]	7 (78)[e]
β-blockers	–	7 (38)	14 (44)	4 (44)
α-blockers	–	0 (0)	2 (7)	2 (22)[d]
nitrates	–	0 (0)	2 (7)	1 (11)

Data are shown as mean ± standard deviation, median (range), or number (percentage).

a $P<0.05$ **b** $P<0.01$ **c** $P<0.001$ controls vs. patients
d $P<0.05$ **e** $P<0.01$ **f** $P<0.001$ group A vs. group B
g $P<0.05$ **h** $P<0.01$ nondiabetic vs. diabetic patients

Abbreviations: BMI – body mass index, DBP – diastolic blood pressure, eGFR – estimated glomerular filtration rate, SBP – systolic blood pressure, WBC – white blood cells

been associated with inflammatory disease (such as rheumatoid arthritis and systemic sclerosis) and with atherosclerotic markers (aortic wall thickness and aortic plaque burden).[11-13] Moreover, Kim et al.[14] showed that plasma CCL23 levels were higher in atherosclerotic patients than in normal subjects, and that expression of this cytokine at the mRNA level was significantly higher in human atherosclerotic lesions than in normal arteries; they also explained the mechanisms by which CCL23 mediates the development of atherosclerosis.

In previous studies, we demonstrated that other CC chemokines, MCP-1/CCL2 and MIP-1β/CCL4, are associated with increased oxidative stress and carotid atherosclerosis in patients on hemodialysis[15,16] and peritoneal dialysis.[17] However, CCL23 has not been previously studied in patients with kidney diseases. Thus, the aim of the present study was to evaluate plasma CCL23 concentrations in CKD patients and to identify the potenial factors affecting its circulating level in these patients. Considering the results of the previous studies,[11-17] the possible associations between plasma CCL23 levels and oxidative stress markers (Cu/Zn superoxide dismutase [Cu/Zn SOD] and neopterin) inflammatory markers: high-sensitivity C-reactive protein (hs-CRP), interleukin 6 (IL-6), and TNF-α were also determined. Moreover, we examined whether CCL23 levels could be associated with the presence of diabetes or cardiovascular complications in these patients.

PATIENTS AND METHODS Fifty adult patients with CKD and 26 healthy subjects (controls) participated in the study. Patients were divided into 2 groups: group A included 18 subjects with mild-to-moderate CKD (GFR category from G1 to G3a), and group B included 32 subjects with severe CKD (GFR category from G3b to G5), according to a recent definition of CKD proposed by the Kidney Disease: Improving Global Outcomes foundation.[18] All patients were clinically

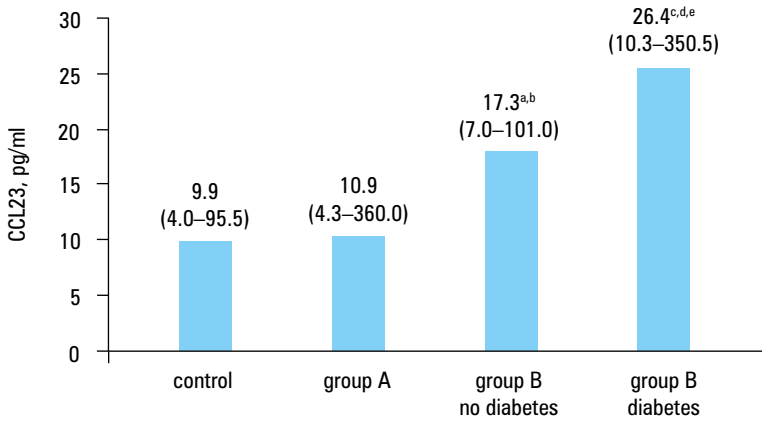

FIGURE 1 CCL23 levels in healthy controls and in patients with mild-to-moderate chronic kidney disease (CKD, group A) and with severe CKD (group B) with and without diabetes

a $P < 0.01$ **b** $P < 0.05$

c $P < 0.001$ controls vs. patients **d** $P < 0.01$ group A vs. group B

e $P < 0.05$ group B without diabetes vs. group B with diabetes

stable and none of them received immunosuppressive treatment, lipid-lowering agents, nonsteroidal anti-inflammatory drugs, recombinant human erythropoietin, or antioxidants at the time of the study. Patients with elevated aminotransferase levels, hepatitis B or C seropositivity, and thrombotic complications were excluded. CKD was attributed to glomerulonephritis in 24 cases, interstitial nephritis in 3, polycystic kidney disease in 10, hypertensive nephropathy in 4, and type 2 diabetes in 9. CVD was defined as a medical history of myocardial infarction, ischemic stroke, coronary revascularization procedures, angina pectoris, typical changes on coronary angiograms, typical ischemic changes on electrocardiogram, peripheral artery surgery, intermittent claudication, or pain at rest. Twenty-five patients (50%) had a history of CVD. Body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters. eGFR was calculated using the Modification of Diet in Renal Disease study formula.[19]

Twenty-six healthy subjects who were receiving no drugs or vitamin supplements at the time of the study volunteered as control subjects. The study was conducted in accordance with the Declaration of Helsinki (1985 amendment) and was approved by the Ethics Committee of the Medical University of Bialystok, Białystok, Poland. The informed consent was obtained from each participant.

Biochemical and clinical characteristics of CKD patients and healthy controls are shown in TABLE 1. Healthy controls were well-matched in terms of sex, BMI, and smoker status with patients. However, patients with diabetes were older than controls and patients with mild-to-moderate CKD (group A). Compared with controls, patients from group A had higher triglyceride and lower albumin levels. The largest differences in biochemical parameters were observed between controls and patients with severe CKD (group B), who had higher levels of triglycerides, creatinine, urea and glucose, while lower levels of hemoglobin, percentage of lymphocytes, and albumin. Compared with group A, group B had lower levels of eGFR, hemoglobin, lymphocytes, and triglycerides, but higher levels of neutrophils, creatinine, and urea. Moreover, diabetic patients had higher glucose levels than those without diabetes and controls. Regarding the clinical status, the prevalence of CVD was higher in group B, particularly in patients with diabetes, than in group A. Moreover, group B of CKD patients received more calcium channel antagonists as the antihypertensive therapy in comparison with group A.

Laboratory measurements Blood samples from CKD patients and controls were taken from the antecubital vein under fasting conditions. Citrated-plasma samples were prepared using the conventional method, aliquoted, and stored at –30°C until the assay.

Plasma CCL23 levels were measured by an enzyme-linked immunosorbent assay (ELISA) using the CLIA Kit for Myeloid Progenitor Inhibitory Factor 1 (MPIF1) (Uscn Life Science Inc., Wuhan, China). Plasma hs-CRP and IL-6 levels were measured by high-sensitivity ELISA kits (Imuclone CRP [hs] ELISA, American Diagnostica Inc, Greenwich, Connecticut, United States, and human IL-6 HS ELISA, Bender MedSystems GmbH, Vienna, Austria, respectively). The levels of TNF-α and SOD were determined by human TNF-α and human Cu/Zn SOD ELISA kits from Bender MedSystems. Plasma neopterin levels were determined by Neopterin ELISA kit from Demeditec Diagnostics GmbH, Kiel, Germany. Biochemical and hematological parameters were determined by routine laboratory techniques using automated analyzers.

Statistical analysis The Shapiro–Wilk test for normality was used for data distribution analysis. The normally distributed data were expressed as mean ± standard deviation. The non-Gaussian data were presented as median (full range), depending on their distribution. Multiple group comparisons were performed by 1-way analysis of variance, and significant differences between the groups were assessed by the Tukey–Kramer test, nonparametric Mann–Whitney test, or unpaired t test with Welch correction. Univariate correlations between the variables were calculated by the Spearman rank correlation. The Pearson χ^2 test was used to compare frequency distributions. Stepwise multiple regression analysis was performed to determine which variables could predict CCL23. A 2-tailed P value of less than 0.05 was considered statistically significant. All analyses were performed using the Statistica v. 9 software (StatSoft, Tulsa, Oklahoma, United States).

RESULTS As shown in FIGURE 1, patients with severe CKD (group B) had higher CCL23 concentrations

TABLE 2 Plasma inflammatory and oxidative stress markers in healthy controls and patients with mild-to-moderate (group A) and severe (group B) chronic kidney disease (CKD) both with and without diabetes

	Controls	Group A	Group B	
			without diabetes	with diabetes
hs-CRP, µg/ml	0.56 (0.10–7.24)	1.24 (0.10–4.71)[a]	5.24 (0.10–94.00)[c,d]	5.61 (0.4–9.8)[c,d]
hs-IL-6, pg/ml	0.92 (0.25–3.67)	27.48 (5.00–49.80)[c]	18.54 (5.05–45.72)[c]	19.10 (3.64–28.68)[c]
TNF-α, pg/ml	1.12 (0.15–2.55)	89.25 (58.30–238.00)[c]	76.40 (40.50–241.00)[c]	83.40 (44.00–119.50)[c]
neopterin, nmol/l	5.66 (0.22–12.93)	10.78 (5.06–16.34)[a]	30.28 (5.77–72.21)[c,d]	35.51 (13.79–87.71)[c,d]
Cu/Zn SOD, ng/ml	53.85 ±19.25	42.15 ±15.93	82.25 ±36.24[b,d]	82.67 ±34.94[b,d]

Data are shown as mean ± standard deviation or median (range) depending on their normal or skewed distribution.

a $P < 0.05$ **b** $P < 0.01$ **c** $P < 0.001$ controls vs. patients
d $P < 0.001$ group A vs. group B

Abbreviations: Cu/Zn SOD – Cu/Zn superoxide dismutase, hs-CRP – high-sensitivity C-reactive protein, hs-IL-6 – high-sensitivity interleukin 6, TNF-α – tumor necrosis factor α

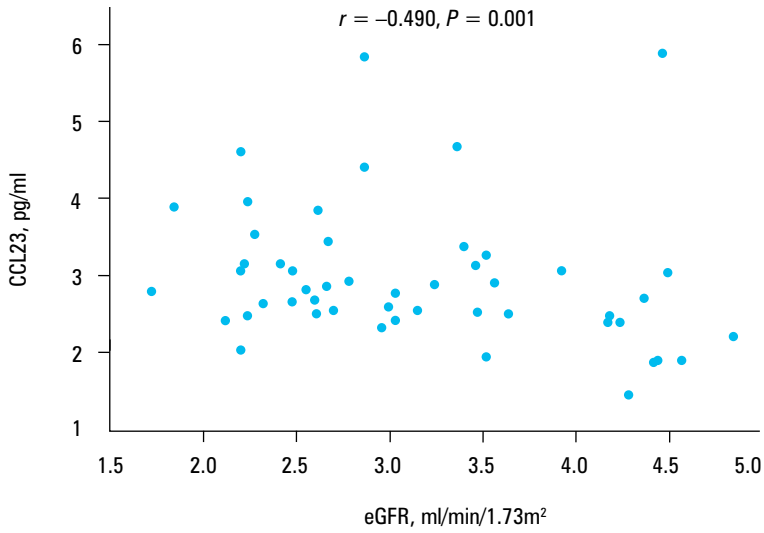

FIGURE 2 Association between CCL23 and estimated glomerular filtration rate (eGFR)

compared with healthy controls and patients with mild-to-moderate CKD (group A). Those concentrations were even higher in patients with severe CKD and diabetes.

As shown in TABLE 2, the inflammatory parameters were significantly higher in CKD patients, particularly in those with severe CKD compared with controls. Neopterin levels, which were measured in 32 subjects, were also significantly elevated in CKD patients, especially in those from group B compared with healthy volunteers. A significant increase in Cu/Zn SOD was observed only in group B compared with healthy controls and group A. However, the presence of diabetes had no effect on the inflammatory and oxidative stress markers in patients with severe CKD.

Plasma CCL23 levels in the whole CKD group were significantly associated with the markers of impaired kidney function: eGFR (FIGURE 2) and creatinine and urea concentrations ($r = 0.44$ and $r = 0.51$, respectively; both, $P < 0.001$). FIGURE 3 demonstrates strong positive correlations between CCL23 and Cu/Zn SOD neopterin concentrations. We also observed a strong positive correlation between Cu/Zn SOD and neopterin ($r = 0.38$; $P = 0.03$), and those parameters were also strongly correlated with the markers of kidney function. In contrast, there were no associations between CCL23 and inflammatory markers: hs-CRP, hs-IL-6, and TNF-α ($r = 0.19$, $r = –0.002$, and $r = 0.153$, respectively; all, $P > 0.05$). There were strong correlations between hs-IL-6 and TNF-α ($r = 0.64$; $P < 0.0001$), but those cytokines were not correlated with hs-CRP levels. Moreover, those 3 inflammatory markers were not correlated either with the markers of kidney function or with Cu/Zn SOD and neopterin levels. Regarding other biochemical parameters, CCL23 levels were inversely associated with hemoglobin ($r = –0.40$; $P = 0.002$), white blood cell (WBC) count ($r = –0.30$; $P = 0.04$), and percentage of lymphocytes in WBC ($r = –0.31$; $P = 0.03$).

We observed a tendency to an inverse association between CCL23 and age in controls ($r = –0.49$; $P = 0.054$).

Median plasma CCL23 levels were not affected by sex, BMI, smoking status, and the type of antihypertensive drugs in patients with CKD. There was a positive but not significant correlation between CCL23 levels and age of CKD patients ($r = 0.25$; $P = 0.06$). Positive correlations were observed between CCL23 levels and systolic and diastolic blood pressures ($r = 0.32$ and $r = 0.33$, respectively; both, $P < 0.05$). To establish whether CCL23 levels could be associated with the presence of cardiovascular complications, we focused on patients with severe CKD (group B), of whom 54% had CVD. However, the majority of patients with CVD also had diabetes, which could additionally increase CCL23 levels. Therefore, patients with diabetes were excluded from the study. However, there was no difference in CCL23 levels between CKD patients with and without CVD (16.00 [7.69–82.14 pg/ml] vs. 18.66 [6.95–100.89 pg/ml], $P = 0.71$ by unpaired t test with Welch correction).

Multiple stepwise regression analysis with CCL23 as dependent variable To examine the combined effect of the factors affecting plasma CCL23 levels

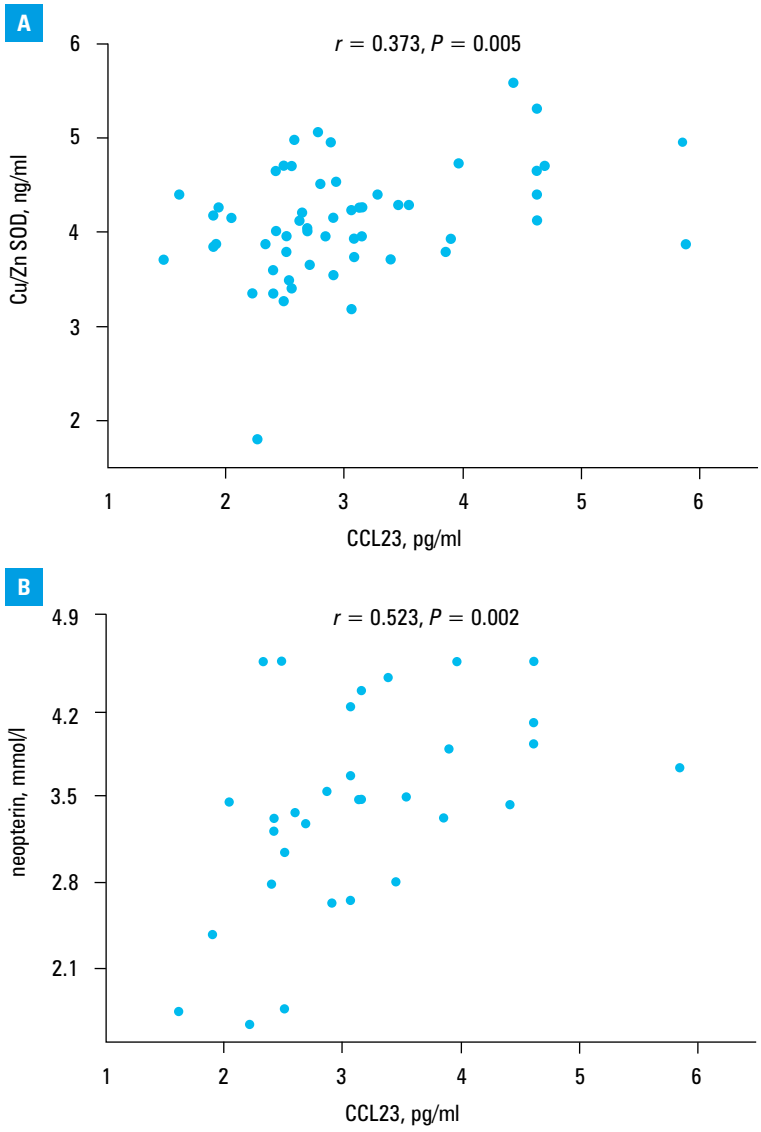

FIGURE 3 Associations between CCL23 and Cu/Zn superoxide dismutase (Cu/Zn SOD) (**A**) and neopterin (**B**) levels in the whole study group

in patients with CKD, multiple regression analysis was performed on the basis of the results of Spearman rank correlation in all patients with CKD (groups A and B) as well as in a subgroup of patients with CKD and without diabetes (**TABLE 3**). The presence of diabetes, Cu/Zn SOD levels, and the percentage of lymphocytes in WBC were found to be significant independent factors affecting plasma CCL23 concentrations in the whole CKD group (r^2 for the model = 0.573). In the case of CKD patients without diabetes, only Cu/Zn SOD levels were significantly independently associated with CCL23 levels (r^2 for the model = 0.456).

DISCUSSION This is the first study to report elevated plasma CCL23 levels in patients with CKD. We assessed patients with different stages of CKD but only patients with severe CKD showed increased CCL23 levels. Moreover, even higher CCL23 levels were observed in patients with severe CKD and diabetes. Strong associations were also found between CCL23 levels and the markers of kidney function. In addition, we demonstrated that CCL23 levels were not associated with common inflammatory markers, but were strongly associated with oxidative stress markers. Finally, the multiple regression analyses confirmed that the presence of diabetes, Cu/Zn SOD levels, and the percentage of lymphocytes in WBC were independent factors affecting plasma CCL23 concentrations in the whole CKD group, whereas Cu/Zn SOD levels proved to be an independent predictor significantly associated with CCL23 concentrations in CKD patients without diabetes.

In the present study, the strong correlations between CCL23 levels and kidney function markers could suggest that elevated CCL23 levels might result from its accumulation in the plasma in severe CKD. However, there were no differences in eGFR values between patients from group B with and without diabetes. Because patients with diabetes had significantly higher CCL23 levels than those without, it seems impossible that impaired kidney function alone can be responsible for increased concentrations of this chemokine. Recently, diabetes has been the most common cause of end-stage renal disease requiring dialysis,[20] and various factors of the diabetic milieu can induce renal expression of CC chemokines and other inflammatory molecules, thus mediating the macrophage responses that ultimately cause renal injury.[21] Until now, no studies have examined plasma CCL23 levels either in diabetes or diabetic nephropathy. The results of the present study have shown for the first time that the presence of diabetes can independently affect plasma CCL23 concentrations in patients with severe CKD.

One of the objectives of the present study was to establish whether CCL23 could be associated with inflammation in CKD patients. For this reason, we measured common inflammatory markers such as hs-CRP, hs-IL-6, and TNF-α, and examined their associations with CCL23. Although there was no relationship between CCL23 and any of the above markers, we cannot exclude that CCL23 could reflect other aspects of the inflammatory process than the common markers of inflammation. CRP is secreted mainly by hepatocytes owing to an increase in IL-6 levels.[22] CCL23 was identified in the aortic endothelium,[23] monocytes and macrophages, and/or foam cells from atherosclerotic lesions.[13,14] This suggests the different origin of these markers, which may be clinically important.

In patients with CKD, the balance between pro- and antioxidant capacities is shifted towards a state of increased oxidative stress.[24] Several intracellular and extracellular antioxidant systems have evolved to inactivate free radicals and avoid tissue damage. SOD serves as an antioxidant enzyme responsible for superoxide removal, and its increase may represent a compensatory response to oxidative stress.[25] The plasma level of the cytosol isoform SOD (Cu/Zn SOD) has been reported as a useful oxidative stress marker in uremic patients in our previous study[26] and in a study by Washio et al.[27] In the present study,

TABLE 3 Variables predicting CCL23 levels in all patients with chronic kidney disease (groups A and B) and in patients with chronic kidney disease and without diabetes

Groups A + B				Groups A + B without diabetes			
independent variables	regression coefficient	standard error	*P* value	independent variables	regression coefficient	standard error	*P* value
presence of diabetes	0.5	0.1	0.003	–	–	–	–
Cu/Zn SOD	0. 5	0.1	0.002	Cu/Zn SOD	0.6	0.2	0.01
lymphocytes	–0.4	0.1	0.007	lymphocytes	–0.3	0.2	0.06
SBP	0.3	0.1	0.07	creatinine	0.3	0.2	0.1

Groups A+B: multiple r for variables in the model = 0.801; multiple r^2 = 0.641; adjusted r^2 = 0.573; P <0.0001

Groups A+B without diabetes: multiple r for variables in the model = 0.736; multiple r^2 = 0.542; adjusted r^2 = 0.456; P <0.0001

Abbreviations: see TABLES 1 and 2

we observed a strong positive association between CCL23 and Cu/Zn SOD levels, both in univariate and multiple regression analyses. These data confirmed that increased oxidative stress is, apart from diabetes, a significant independent predictor of CCL23 in CKD patients. This finding is in accordance with the study by Kim et al.[14] who demonstrated that oxidative stress markedly enhanced CCL23 production and release by human TPH-1 macrophages.

Another new observation of the present study is that CCL23 strongly correlated with neopterin levels in the whole CKD group. Neopterin is a marker related to immune response.[28] The interferon-γ-activated monocytes/macrophages produce high levels of neopterin and also reactive oxygen species due to the immune activation.[29] Thus, neopterin may be used as a marker of both immune system activation and oxidative stress.[28,29] In this study, neopterin was correlated with Cu/Zn SOD but not with the inflammatory markers. However, the multiple regression analysis did not confirm neopterin as an independent factor associated with CCL23 levels in CKD patients. Thus, it seems possible that both neopterin and CCL23 may be released from the same source—monocytes and macrophages activated in patients with CKD.[30]

The third independent factor significantly associated with the CCL23 concentration in the whole CKD group was low percentage of lymphocytes in peripheral WBC, which was observed in patients with severe CKD. The study by Litjens et al.[31] showed that already in moderate CKD (GFR between 30 and 59 ml/min/1.73 m^2), the lymphocyte compartment was decreased in relation to a further loss of renal function. The inverse association between CCL23 levels and the percentage of lymphocytes observed in this study is difficult to explain at present. However, in the previous work of Pernice et al.,[32] lymphopenia in patients with end-stage renal disease was strictly related to dysregulation in programmed cell death caused by oxidative stress. In the current study, we also observed an inverse correlation between the percentage of lymphocytes and Cu/Zn SOD. Thus, it is possible that oxidative stress may be a common link between the increased CCL23 production on the one hand and lymphopenia on the other.

Finally, we wanted to examine whether CCL23 levels could be associated with cardiovascular complications in CKD patients. CCL23 levels were compared between patients with and without CVD, who had severe CKD without diabetes. There was no difference in CCL23 levels between those 2 groups, suggesting that the presence of CVD had no effect on the CCL23 concentration.

Our study has several limitations. The cross-sectional design did not confirm that there was any cause-and-effect relationship between the studied parameters. In addition, the studied group was relatively small, and it would be important to confirm the results in a larger cohort.

In conclusion, CCL23 levels were increased in patients with severe CKD, which was strongly related to kidney function. The median levels of this chemokine were not affected by sex, age, BMI, smoking status, and the type of antihypertensive drugs. The presence of diabetes was a significant independent factor for increased CCL23 levels, while the prevalence of CVD had no impact on its concentration. Moreover, there were no associations between CCL23 and the common indicators of inflammation, while there were significant independent associations between this chemokine and oxidative stress in CKD patients both with and without diabetes.

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ARTYKUŁ ORYGINALNY

Wpływ cukrzycy i stresu oksydacyjnego na stężenie CCL23 w osoczu pacjentów z zaawansowaną przewlekłą chorobą nerek

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SŁOWA KLUCZOWE

CCL23, cukrzyca, przewlekła choroba nerek, stan zapalny, stres oksydacyjny

STRESZCZENIE

WPROWADZENIE CCL23 jest nową CC-chemokiną uczestniczącą w migracji leukocytów i powstawaniu chorób na podłożu zapalnym. Stan zapalny, stres oksydacyjny i cukrzyca powszechnie występują u pacjentów z przewlekłą chorobą nerek (PChN), zwłaszcza u osób z towarzyszącą chorobą sercowo-naczyniową (ChSN).

CELE Celem badania było oznaczenie stężenia CCL23 w grupie pacjentów z PChN oraz zidentyfikowanie czynników mających wpływ na jej osoczowe stężenie.

PACJENCI I METODY Stężenia CCL23, markerów stanu zapalnego (białka C-reaktywnego oznaczonego metodą o wysokiej czułości, interleukiny-6, czynnika martwicy nowotworu α) oraz wskaźników stresu oksydacyjnego (neopteryny i zależnej od jonów Cu i Zn dysmutazy ponadtlenkowej [Cu/Zn *superoxide dismutase* – Cu/Zn SOD]) zostały zmierzone w osoczu pacjentów z łagodną i umiarkowaną PChN (grupa A) oraz z zaawansowaną PChN (grupa B), zarówno z cukrzycą, jak i bez niej, oraz w grupie kontrolnej.

WYNIKI Stężenia CCL23 były większe w grupie B, zwłaszcza wśród pacjentów z cukrzycą, w porównaniu z grupą kontrolną ($p < 0{,}001$) i grupą A ($p < 0.01$). Wskaźniki stanu zapalnego były podwyższone u pacjentów z CKD, ale nie korelowały ze stężeniem CCL23. Zależności wystąpiły natomiast pomiędzy stężeniem CCL23 a wskaźnikami stresu oksydacyjnego i czynności nerek. Obecność cukrzycy, Cu/Zn SOD i odsetek limfocytów okazały się niezależnymi czynnikami związanymi ze stężeniem CCL23 w całej grupie pacjentów z PChN. W grupie pacjentów bez cukrzycy jedynie Cu/Zn SOD były niezależnie związane ze stężeniem CCL23.

WNIOSKI Stężenie CCL23 było podwyższone u pacjentów z zaawansowaną PChN i silnie korelowało ze stopniem upośledzenia czynności nerek. Współistnienie cukrzycy i stresu oksydacyjnego w sposób niezależny wpływało na stężenie CCL23, podczas gdy obecność ChSN i stan zapalny nie korelowały ze zmianami jej stężenia.

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