ORIGINAL ARTICLE

Risk factors for chronic kidney disease do not influence the serum levels of asymmetric dimethylarginine in HIV-1-infected patients without significant renal disease

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KEY WORDS

antiretroviral therapy, asymmetric dimethylarginine, chronic kidney disease, HIV-1 infection

ABSTRACT

INTRODUCTION Chronic kidney disease (CKD) is one of the consequences of human immunodeficiency virus-1 (HIV-1) infection. The disease increases the risk of progression to acquired immunodeficiency syndrome and death and complicates antiretroviral therapy. The prevalence of CKD in HIV-1-infected patients is difficult to estimate and depends on the diagnostic criteria for CKD.

OBJECTIVES The aim of the study was to evaluate the usefulness of a single measurement of serum asymmetric dimethylarginine (ADMA) levels in the diagnosis of kidney damage in patients infected with HIV-1.

PATIENTS AND METHODS The study included 119 HIV-1-infected individuals (88 males [74%]), both on antiretroviral treatment and treatment-naive, with a negative history of kidney disease, and 31 healthy volunteers. We analyzed demographic characteristics as well as data on concomitant diseases, antiretroviral regimen, serum ADMA concentrations, parameters of renal function, $CD4^+$ cell count, and HIV-1 viral load.

RESULTS No significant impairment of renal function was observed. Mean serum ADMA levels in all HIV-1-infected patients, as well as in treatment-naive patients and treated patients, were significantly higher ($P < 0.0001$; $P = 0.0001$; $P < 0.0001$; respectively) compared with those in the control group. The difference between treatment-naive and treated HIV-1-infected patients was nonsignificant. ADMA levels were not correlated with the mean duration of antiretroviral therapy, antiretroviral drugs used, or other risk factors for CKD.

CONCLUSIONS A single measurement of ADMA levels is not useful for the diagnosis of CKD in patients without significant renal pathology or as an indicator of kidney damage related to antiretroviral therapy. The significance of repeated measurements of ADMA levels in renal function assessment requires further research.

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INTRODUCTION Wide access to effective combined antiretroviral therapy (cART) and increasingly better virological and immunological control of human immunodeficiency virus 1 (HIV-1) infection results in continuous improvement of the prognosis for survival of HIV-1-infected individuals. Therefore, increasing attention is directed towards prevention and treatment of comorbidities and minimizing the side effects of antiretroviral drugs.

The first reports of kidney disease in patients with acquired immunodeficiency syndrome (AIDS) caused by HIV-1 date back to the mid-1980s.[1-3] It was proved then for the first time that HIV-1 can infect epithelial cells of the kidney.[4] Later, it was shown that there are many other

infectious agents that can affect the course of renal disease, also in patients infected with HIV-1. These are hepatitis C and B viruses (HCV, HBV), parvovirus B19, cytomegalovirus, Ebstein–Barr virus, BK virus, *Cryptococcus neoformans*, *Mycobacterium tuberculosis*, and other opportunistic infections, as well as nephrotoxic drugs.[5,6] The risk of chronic kidney disease (CKD) is associated with age, hypertension, diabetes, lower T CD4$^+$ cell count, higher HIV viral load, and proteinuria.[7-10] CKD increases the risk of progression to AIDS and death as well as the risk of side effects of antiretroviral therapy with protease inhibitors (PI).[11]

The prevalence of renal disease in HIV-1-infected patients is difficult to estimate and depends on the diagnostic criteria for CKD. Moreover, the clinical importance of the diagnosis of CKD, particularly at its early stages, is still unclear.[12] Therefore, data on CKD from various studies are not uniform. The differences may result from the use of different formulas for glomerular filtration rate (GFR) estimation or from including proteinuria and albuminuria into diagnostic criteria or not.

The measurement of serum creatinine levels, namely, the most commonly used method for the assessment of renal function, has insufficient sensitivity and specificity. GFR estimation can be affected by numerous factors that influence plasma levels of creatinine and its synthesis, tubular secretion, as well as by the various factors affecting the course of laboratory testing.[13] The aim is to select the best formula that would most accurately estimate GFR for all stages of CKD, in acute kidney injury and healthy kidneys, in all groups of patients, regardless of the type of kidney problem and associated diseases. In everyday practice, the most common formulas used for GFR estimation are those based on endogenous substances: creatinine and, recently, also on cystatin C. Experts of Kidney Disease: Improving Global Outcomes recommend the measurement of cystatin C levels and, on this basis, the determination of estimated GFR (eGFR) in patients whose GFR calculated using creatinine is in the limit range for the diagnosis of CKD (45–59 ml/min/1.73 m^2).[13]

Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide (NO) synthesis. NO is the most potent endogenous vasodilatator and, due to its anti-inflammatory and antithrombotic potential, also endogenous antiatherogenic factor.[14] Elevated levels of ADMA were observed in numerous studies in patients with CKD, even at stage 1 of the disease.[15-19] In contrast, there have been no studies on the use of ADMA in the diagnosis of CKD in HIV-1-infected patients. This marker has been studied in HIV-1-infected patients mainly in the context of cardiovascular disease and its diagnosis.[20-26]

Due to the complex pathology of HIV-1 infection, which is associated with a higher number of kidney-damaging agents than that occuring in the general population, it is important to determine the prevalence of renal damage in HIV-1-infected population inhabiting a given region, as well as the most optimal early diagnosis of renal changes. This could have a positive impact on early intervention, closer monitoring of renal function, and adjusting antiretroviral therapy and treatment of comorbidities to kidney function.

The aim of this study was to evaluate the prevalence of abnormal kidney function in patients infected with HIV-1 in the population of Lower Silesia, the administrative region of Poland, as well as to evaluate the usefulness of ADMA in the diagnosis of kidney damage in this patient group. We also studied the effect of some antiretroviral drugs on the parameters of renal function.

PATIENTS AND METHODS The study was approved by the Bioethical Committee of the Wroclaw Medical University, Wrocław, Poland (No. of consent: KB-237/2011). All study participants gave written informed consent to participate in the study.

The study group consisted of 119 people infected with HIV-1, both on antiretroviral treatment and treatment-naive, with a negative history of kidney disease. The control group included 31 HIV-negative volunteers from the Lower Silesia region, matched for age and sex. All participants were Caucasians, older than 18 years of age. In the study group, there were 88 men (74%) and 31 women (26%), aged from 23 to 68 years (mean age, 40 ±9.5 years), and in the control group, there were 21 men (68%) and 10 women (32%), aged from 23 to 58 years (mean age, 40.1 ±8.9 years). All HIV-1-infected patients belonged to the clinical category A of the Center for Disease Control and Prevention criteria from 1993.

The exclusion criteria were as follows: diabetes, uncontrolled hypertension, thyroid disease, rheumatoid arthritis treated with corticosteroids, malignancy, fever, acute bacterial, viral, or fungal infection, current AIDS-defining disease, HBV infection (patients with detectable HBs antigen in serum), any other known inflammatory states potentially influencing ADMA levels, a past episode of acute renal failure, and use of any illicit drugs.

Data concerning the course of HIV infection, smoking status, and concomitant diseases (HCV infections, hypertension, hyperlipidemia, hyperuricemia, and nephrolithiasis) were collected. Hypertension was defined as previous diagnosis and use of antihypertensive medications, because uncontrolled hypertension was the exclusion criterion. Dyslipidemia was defined as any of the following: total cholesterol and low-density lipoprotein (LDL) cholesterol levels above the upper normal range, triglyceride level above the upper normal range, and high-density lipoprotein (HDL) cholesterol below the lower normal range.

The serum ADMA concentration was measured using an enzyme-linked immunosorbent assay (DLD Diagnostics GMBH, Hamburg, Germany). The sensitivity of the method was 0.05 mmol/l. HIV-1 viral load was determined by a real-time polymerase chain reaction assay (COBAS TaqMan HIV-1 Test v. 2.0, Roche Diagnostics, Basel,

TABLE 1 Characteristics of the study group

Parameter		HIV-1-infected individuals			Controls (n = 31)	*P* value	
		total (n = 119)	untreated (n = 21)	treated with cART (n = 98)		HIV-1--infected group vs controls	untreated vs treated groups
patients, n (%)		119 (100)	21 (17.6)	98 (82.4)	31 (100)		
Caucasian race		119 (100)	21 (100)	98 (100)	31 (100)		
males, n (%)		88 (74)	18 (85.7)	70 (71.4)	21 (68)	NS	NS[a]
age, y, mean ± SD (range)		40 ±9.5 (23–68)	35.5 ±8 (26–56)	41 ±9.6 (24–68)	40.1 ±8.9 (23–68)	NS	0.037[b]
$CD4^+$ count, cells/µl, mean ± SD		545 ±243	476 ±206	560 ±249	NA		NS[c]
CDC category of HIV-1 infection, n (%)	1	64 (54.7)	26 (50)	10 (47.6)	NA		NS[a]
	2	49 (41.9)	23 (44.2)	10 (47.6)			
	3	4 (3.4)	3 (5.8)	1 (4.8)			
HIV-1 viral load, n (%)	undetectable (<34 copies/ml)	77 (64.7)	0	41 (77.4)	NA		<0.0001[a]
	detectable	42 (35.3)	21 (100)	12 (22.6)			
intravenous drug user, n (%)		47 (40.9)	3 (14.3)	44 (46.8)	0		0.009[a]
BMI, kg/m^2, mean ± SD		23.76 ±0.32	23.52 ±0.78	23.81 ±0.36	25.92 ±0.64	0.003[c]	NS[b]
smoking status, n (%)	never smoking	19 (16.8)	5 (25)	14 (15.1)	31 (100)		<0.0001[a]
	past smokers	25 (22.1)	1 (0.05)	24 (25.8)	0		
	current smokers	69 (61.1)	14 (70)	55 (59.1)	0		
concurrent diseases							
hypertension, n (%)		13 (11)	1 (4.8)	12 (12.2)	1 (3.2)	NS	NS[a]
dyslipidemia, n (%)		89 (74.8)	16 (90.4)	73 (74.5)	24 (77.4)	NS	NS[a]
hyperuricemia, n (%)		11 (9.2)	3 (14.3)	9 (9.2)	6 (19.4)	NS	NS[a]
HCV infection, n (%)		47 (39.5)	2 (9.5)	45 (45.9)	0 (0)		0.002[a]
basic inflammatory markers							
CRP, mg/dl, median (IQR)		1.1 (0.0–2.1)	1.3 (1.0–2.3)	0.5 (0.0–1.9)	1.0 (1.0–1.5)	NS[d]	NS[e]
WBC, $10^9/l$, mean ±SD		5.57 ±0.15	5.00 ±0.7	5.69 0.17	5.94 ±0.3	NS[c]	NS[b]

a χ^2 test, **b** Newman–Keuls test, **c** *t* test, **d** Kruskal–Wallis test, **e** Mann–Whitney test

Abbreviations: cART, combined antiretroviral therapy; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CRP, C-reactive protein; HCV, hepatitis C virus; HIV-1, human immunodeficiency virus 1; IQR, interquartile range; NA, not applicable; NS, not significant; WBC, white blood cell

Switzerland). The isolation of HIV-RNA was performed using System Viral Nucleic Acid Kit (Roche Diagnostics). The $CD4^+$ T cell count was determined by flow cytometry using FacsCount Becton Dickinson system (BD Biosciences, San Jose, California, United States). Other tests were performed with standard methods used in routine diagnostic workup.

Statistical analysis The groups were tested for normal distribution. Mean values were compared by the analysis of variance with the *t* test and post-hoc Newman–Keuls test. For nonnormal distribution, nonparametric Kruskal–Wallis test, Mann–Whitney test, and χ^2 test were used. For the analysis of ADMA levels, Mann–Whitney test with Bonferroni correction was used. The dependence of the variables was assessed using the Pearson correlation coefficient *r*. The *P* values of less than 0.05 were considered statistically significant. Calculations were performed using Statistica 10.0 software for Windows (StatSoft Inc., Tulsa, Oklahoma, United States).

RESULTS The characteristics of the study and control groups are presented in **TABLE 1**. Among HIV-1-infected patients, 98 were treated with standard cART. The schedules were as follows: 65 patients were treated with 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and ritonavir-boosted PI (PI/r); 25 patients, with 2 NRTIs and nonnucleoside reverse transcriptase inhibitor (NNRTI); 3 patients, with 2 NRTIs and integrase inhibitor; 3 patients, with PI/r and integrase inhibitor; and 2 patients, with PI/r only.

All patients with diagnosed hypertension from the study and control groups were successfully treated with antihypertensive medications. No individual was treated with potentially anti-inflammatory medications, including acetylsalicylic acid, other nonsteroid anti-inflammatory drugs, or statins.

TABLE 2 Mean values of estimated glomerular filtration rate (according to the CKD-EPI$_{creat}$ formula)

Parameter	HIV-1-infected individuals			Controls	*P* value	
	total (n = 119)	untreated (n = 21)	treated with cART (n = 98)	(n = 31)	HIV-1-infected group vs controls	untreated vs treated groups
eGFR, ml/min/1.73m^2, mean ±SD	105.0847 ±15.64941	114.53 ±9.42	103.014 ±16.2	99.6721 ±15.41513	NS	0.003

Abbreviations: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; others, see TABLE 1

TABLE 3 Asymmetric dimethylarginine levels according to antiretroviral therapy

Parameter	HIV-1 infected individuals								Controls (n = 31)
	total (n = 119)	untreated (n = 21)	treated with cART						
			total (n = 98)[a]	TDF (n = 53)	PI/r (n = 70)	TDF+PI/r (n = 37)	ATV/r (n = 21)	LPV/r (n = 26)	
ADMA, µmol/l, median (IQR)	0.6 (0.5–0.71)	0.64 (0.53–0.77)	0.59 (0.5–0.7)	0.59 (0.5–0.7)	0.61 (0.51–0.7)	0.61 (0.5–0.7)	0.61 (0.5–0.64)	0.63 (0.51–0.8)	0.42 (0.41–0.5)

a The total number of patients treated with listed drugs is larger than that of the total group because the subgroups of patients were partially overlapping.

Abbreviations: ADMA, asymmetric dimethylarginine; ATV/r, ritonavir-boosted atazanavir; LPV/r, ritonavir-boosted lopinavir; PI/r, ritonavir-boosted protease inhibitor; TDF, tenofovir; others, see TABLE 1

The values of eGFR calculated according to the CKD-EPI$_{creat}$ in the study and control groups are presented in TABLE 2. The highest values of GFR were observed in cART-naive patients and the lowest values—in the control group. Significant differences were observed between treatment-naive patients and those on cART (P = 0.003) and between treatment-naive patients and controls (P = 0.001). After adjustment for age, the differences in eGFR between the treatment-naive and treated groups showed borderline significance (P = 0.051). The difference in eGFR between all HIV-1-infected patients and controls was not significant (P = 0.21).

Impaired renal function (eGFR below 60 ml/min/1.73 m^2) was observed only in 1 HIV-1-infected patient and in no control individuals. ADMA levels in the study group are presented in TABLE 3. HIV-1-infected patients were divided according to the cART status. Additionally, the treated patients were divided into subgroups according to the use of potentially nephrotoxic antiretroviral drugs (tenofovir [TDF], PI/r, with, separately, atazanavir [ATV] and lopinavir [LPV]).

Serum ADMA levels in HIV-1-infected patients were significantly higher than those in the control group (P <0.0001). The significant differences were also noted between treatment-naive HIV-1-infected patients and controls (P <0.0001) and between treated individuals and controls (P <0.0001). Among HIV-1-infected individuals, ADMA levels were higher in treatment-naive patients than in patients on cART; however, the difference was not significant (P = 0.14). Adjustment for significantly different variables: age, smoking status, HCV infection, and intravenous drug use did not influence the results.

We observed significant effects of potentially nephrotoxic antiretroviral drugs on increasing ADMA levels compared with controls: TDF, P = 0.0001; any PI/r, P <0.0001; TDF with PI/r, P = 0.0002; ATV/r, P = 0.005; LPV/r, P <0.0001 (FIGURES 1–5). There were no significant differences in ADMA levels between patients treated with different potentially nephrotoxic drugs and those treated with the cART regimens without these drugs. ADMA levels and eGFR values were not correlated with the antiretroviral drug used (TDF, PI/r, TDF + PI/r). Serum ADMA levels were also not correlated with the mean duration of cART.

In 8 HIV-1-infected individuals, proteinuria was observed. Mean serum ADMA levels were higher in the group with proteinuria compared with individuals with normal urinalysis (0.708 vs 0.601). This difference showed borderline significance (P = 0.054).

The effect of HIV infection-related factors on ADMA level was also analyzed. No significant differences in ADMA levels were noted according to either current CD4$^+$ T cell count, CD4$^+$ nadir, or HIV-1 viral load in treatment-naive patients and suboptimally treated patients (with detectable viral load despite treatment). Coinfection with HCV also did not affect ADMA levels. There were no significant differences related to a HIV-1 transmission route. The highest ADMA levels were observed in current smokers, and the lowest levels were noted in never-smokers; however, this difference was not significant. Other nonsignificant parameters included sex, age, body mass index (BMI), concomitant conditions (arterial hypertension and nephrolithiasis), white blood cell count, and C-reactive protein level.

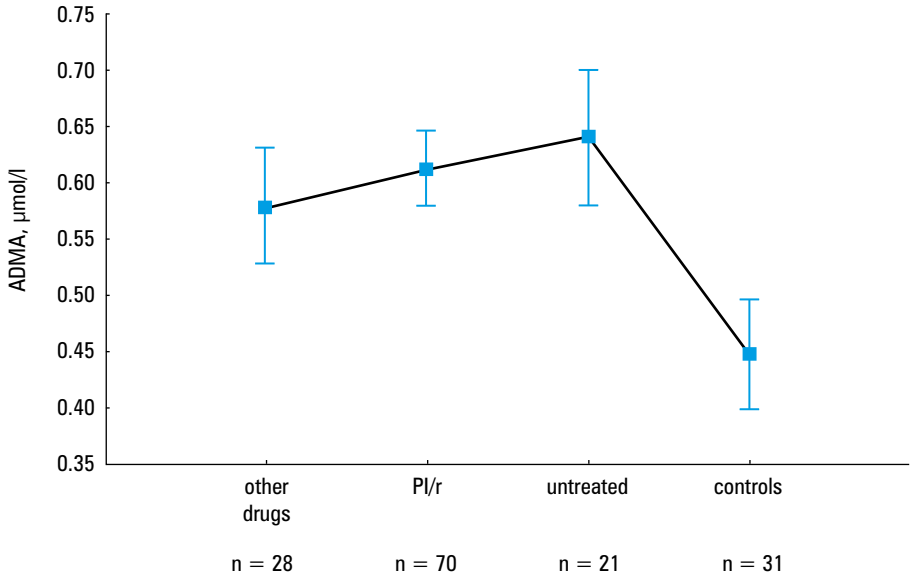

FIGURE 1 Serum asymmetric dimethylarginine (ADMA) levels in patients treated with ritonavir-boosted protease inhibitors (PI/r), treated with other drugs, utreated individuals, and controls ($P < 0.0001$)

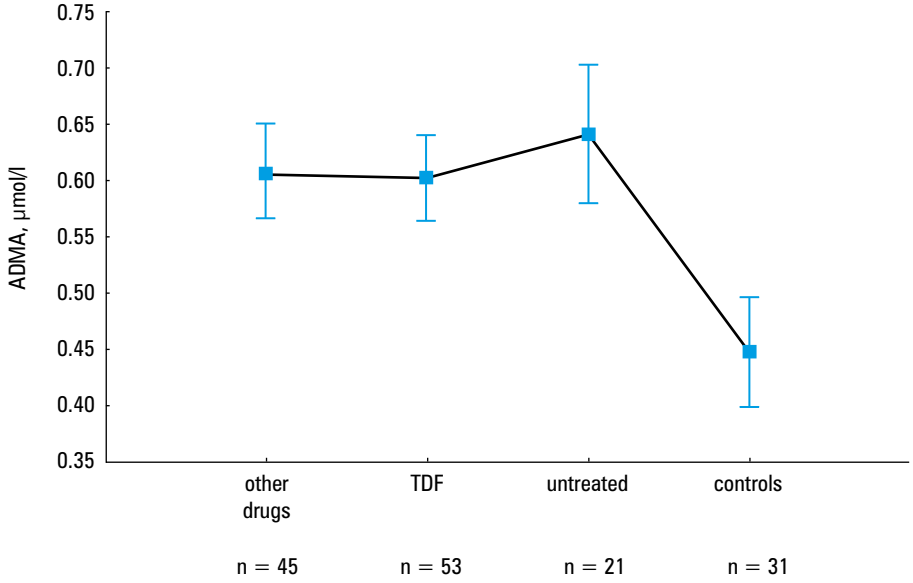

FIGURE 2 Serum asymmetric dimethylarginine (ADMA) levels in patients treated with tenofovir (TDF), treated with other drugs, untreated individuals, and controls ($P = 0.0001$)

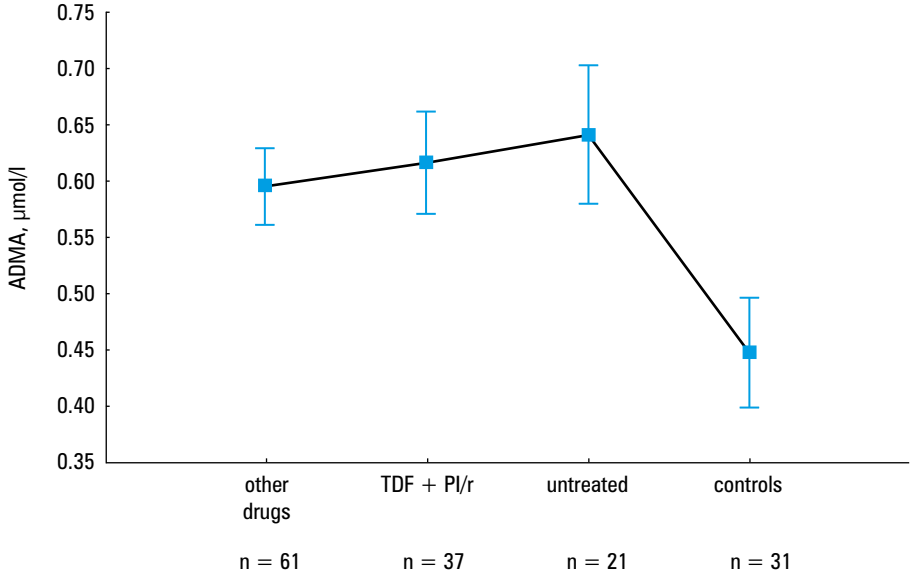

FIGURE 3 Serum asymmetric dimethylarginine (ADMA) levels in patients treated with tenofovir (TDF) and ritonavir-boosted protease inhibitor (PI/r), treated with other drugs, untreated individuals, and controls ($P = 0.0002$)

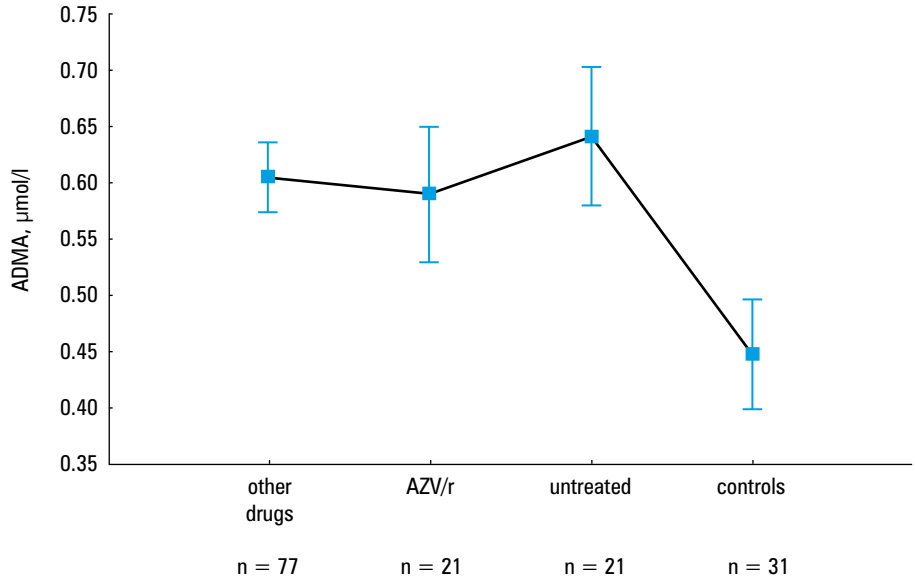

FIGURE 4 Serum asymmetric dimethylarginine (ADMA) levels in patients treated with ritonavir-boosted atazanavir (AZV/r), treated with other drugs, untreated individuals, and controls ($P = 0.005$)

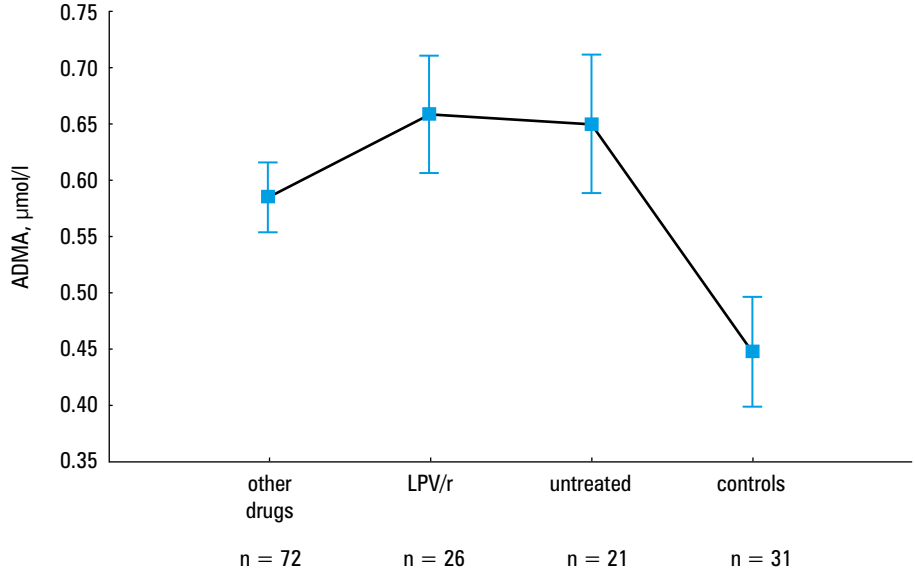

FIGURE 5 Serum asymmetric dimethylarginine (ADMA) levels in patients treated with ritonavir-boosted lopinavir (LPV/r), treated with other drugs, untreated individuals, and controls ($P < 0.0001$)

DISCUSSION CKD is currently one of the most important causes of morbidity and mortality among so called non-AIDS diseases in HIV-infected patients,[27,28] ranking the fourth after malignancies, cardiovascular diseases, and liver diseases, according to the EuroSIDA study.[28] The extent of the problem is not fully understood in the population of Polish HIV-1-infected patients. Among patients infected with HIV-1 in Poland, there is still a large group of drug users (many currently inactive).[29] The drugs used by them were prepared by themselves with poppy and contained various contaminations, the type and amount of which could not be determined. A large percentage of HIV-positive patients in Poland is coinfected with HCV or HBV (or both). The socioeconomic status of these patients is often low, which affects their lifestyle, diet, and treatment, similarly as in the report of Ganesan et al[30] in different populations.

The age of patients included in our study ranged from 23 to 68 years. This is the typical age for the population of people infected with HIV-1 in Poland.[29] Immunological results and HIV-1 viral loads did not differ from the data reported by other Polish centers [31-33] treating people with HIV infection.

ADMA plays an important role in the pathogenesis and progression of CKD and cardiovascular diseases, and this role is related to endothelial function. ADMA works by inhibiting the synthesis of NO. As an inhibitor of NO, ADMA impairs vasodilatation of capillaries. Impaired blood flow through the renal tubular capillaries causes hypoxia within the tubules and renal parenchyma,[34] which results in renal fibrosis.[35,36] ADMA is a marker of renal impairment, independent from GFR, proteinuria, hemoglobin, and homocysteine levels.[37] Thus, ADMA allows an objective assessment of renal function. Research on ADMA is conducted in 2 directions: to assess its usefulness as a diagnostic tool and to develop drugs lowering its concentrations, thereby inhibiting its pathogenic effect on endothelial function.[34]

Given the numerous publications on the diagnostic role of ADMA in renal diseases, we studied it in patients infected with HIV-1, who have multiple risk factors of impaired kidney function. We did not demonstrate any significant relationship between ADMA levels and age, BMI, history of intravenous drug use, smoking, or hypertension, although other authors demonstrated a correlation between ADMA levels and hypertension.[35,38] HCV coinfection was noted in 39.5% of patients in the study group. This coinfection was acquired primarily by intravenous drug use. The proportion of HCV-positive patients also did not differ from data obtained in other regions of Poland. Our data showed no effect of HCV coinfection on ADMA levels.

In our study, we did not find any correlation between serum ADMA levels and eGFR in patients on cART and treatment-naive patients. Moreover, we did not find differences in the concentration of ADMA in patients with eGFR values above and below 90 ml/min/1.73 m^2, but we did not identify any similar analyses in the available literature to confirm the latter results. Also, we did not observe a relationship between the concentration of ADMA and severity of albuminuria. In contrast, there were significantly higher levels of ADMA among persons infected with HIV-1, treated and untreated with cART, compared with the control group, regardless of the type of antiretroviral therapy.

It seems that it is not the antiretroviral drugs but the presence of HIV-1 infection itself that affects the concentration of ADMA. Hudson et al[39] and Jang et al[24] showed that HIV-infected people had significantly higher levels of ADMA compared with uninfected individuals. On the other hand, Kurz et al[23,40] and Baker et al[20] proved that the concentration of ADMA decreased on cART and correlated with a decrease in the levels of immune activation markers. Most publications concerning ADMA and HIV infection underline the impairment of endothelial function as a result of chronic inflammation. This impairment results in the development of subclinical atherosclerosis[24] and primary pulmonary hypertension.[21] It is believed that the accumulation of ADMA as a result of chronic immune activation is associated with a predisposition to atherosclerosis.[22]

It is known that antiretroviral drugs, mainly PIs, are responsible for the development of lipodystrophy syndrome.[5] In this syndrome, body fat distribution disorders, metabolic disorders such as hyperlipidemia, insulin resistance, and glucose intolerance are present and can lead to the development of accelerated atherosclerosis.[5,41,42] On the other hand, ADMA is involved in the pathogenesis of atherosclerosis.[20,22-24] In the literature, there are few reports on ADMA in patients infected with HIV-1 treated with PIs or other antiretroviral drugs. The development of atherosclerosis in people infected with HIV-1 is a complex process. The primary consideration is the virus that causes chronic inflammation, in which ADMA is also involved. On the other hand, antiretroviral drugs cause metabolic abnormalities associated with lipodystrophy syndrome. Our results point out to chronic inflammation, independently from suppression of HIV-1 replication, as the etiological factor of atherosclerosis. We should also keep in mind the microreplication of HIV-1, undetectable with routine molecular tests, which could have an impact on the higher levels of ADMA in patients on effective cART. Perhaps the determination of ADMA levels in HIV-infected patients could have prognostic value in the assessment of atherosclerosis and its consequences, including for the kidneys.

As mentioned above, Kurtz et al[23] and Baker et al[20] showed a decrease in the concentration of ADMA as a result of antiretroviral treatment, and explained this phenomenon by the reduction of chronic immune activation and inflammation. However, they did not analyze ADMA levels in relation to the different classes of antiretroviral drugs, including PIs. It would be interesting to compare ADMA concentrations before treatment and during antiretroviral therapy with the use of certain classes of drugs. It might enable a determination of the practical value of this marker in the decision making process as to whether change the antiretroviral drug for the drug that efficiently inhibits immune activation. Such studies, however, as well as those examining the significance of ADMA as a marker of various degrees of renal dysfunction, require a large cohort of patients and the involvement of many HIV and AIDS centers.

In summary, ADMA levels are useful in the assessment of chronic inflammation (in HIV-1-infected patients on cART and treatment-naive patients) and, indirectly, of the function of renal circulation. A single measurement of ADMA levels does not have a diagnostic value for identifying certain risk factors for CKD in patients without advanced renal pathology or as an indicator of cART-related kidney damage. The diagnostic value of repeated measurements of ADMA requires further research.

Study limitations Our study has several limitations. The study group was relatively small, and our analysis did not include the parameters of chronic immune activation and microinflammation. Data were obtained at 1 timepoint, without follow-up, so we could not show the dynamics of ADMA levels.

Contribution statement BK conceived the idea for the study. AS-P and BK contributed to the design of the research. AS-P, AS, MZ, and BK were involved in data collection. AS-P, AS, KM, and BK analyzed and interpreted the data. All authors edited and approved the final version of the manuscript.

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ARTYKUŁ ORYGINALNY

Czynniki ryzyka przewlekłej choroby nerek nie wpływają na stężenie asymetrycznej dimetyloargininy w surowicy u osób zakażonych HIV-1 bez istotnej choroby nerek

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SŁOWA KLUCZOWE

asymetryczna dimetyloarginina, przewlekła choroba nerek, terapia antyretrowirusowa, zakażenie HIV-1

STRESZCZENIE

WPROWADZENIE Przewlekła choroba nerek (*chronic kidney disease* – CKD) stanowi jedną z konsekwencji zakażenia HIV-1 (*human immunodeficiency virus 1* – HIV-1). Jej wystąpienie zwiększa ryzyko progresji do AIDS i zgonu oraz utrudnia prowadzenie terapii antyretrowirusowej. Częstość występowania CKD u osób zakażonych HIV-1 jest trudna do oszacowania oraz zależy od zastosowanych kryteriów rozpoznania CKD.
CELE Celem badania była ocena przydatności pojedynczego pomiaru stężenia asymetrycznej dimetyloargininy (ADMA) w surowicy do diagnostyki uszkodzenia nerek u pacjentów zakażonych HIV-1.
PACJENCI I METODY Do badania włączono 119 osób zakażonych HIV-1 (88 mężczyzn [74%]), leczonych i nieleczonych antyretrowirusowo, bez choroby nerek w wywiadzie, oraz 31 zdrowych ochotników. Przeanalizowano dane demograficzne oraz dane dotyczące chorób towarzyszących i leczenia antyretrowirusowego, a także stężenie ADMA w surowicy, parametry funkcji nerek, liczbę komórek $CD4^+$ i wiremię HIV-1.
WYNIKI Nie stwierdzono istotnego upośledzenia funkcji nerek. Średnie wartości ADMA w surowicy były istotnie wyższe u wszystkich pacjentów zakażonych HIV-1 oraz u pacjentów nieleczonych i leczonych antyretrowirusowo (odpowiednio $p < 0{,}0001$; $p = 0{,}0001$; $p < 0{,}0001$) w porównaniu z grupą kontrolną. Pomiędzy leczonymi i nieleczonymi pacjentami zakażonymi HIV-1 różnica była nieistotna. Stężenie ADMA nie korelowało ze średnim czasem terapii antyretrowirusowej, stosowanymi lekami antyretrowirusowymi ani występowaniem innych czynników ryzyka CKD.
WNIOSKI Pojedynczy pomiar stężenia ADMA nie jest przydatny do rozpoznania przewlekłej choroby nerek u pacjentów bez istotnej patologii nerek ani jako wskaźnik uszkodzenia nerek związanego z terapią antyretrowirusową. Znaczenie powtarzanych pomiarów stężenia ADMA w ocenie funkcji nerek wymaga dalszych badań.

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