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Correlates of Impaired Renal Function in Highly Active Antiretroviral Therapy (HAART) Naive HIV Infected Patients in Maiduguri, Nigeria

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Abstract - *Background :* Although renal function may be abnormal in as many as 30% of HIV -1 patients even in the era of highly active antiretroviral therapy, it may not be apparent at the initial stage and laboratory tests are needed to detect it. We determined the factors associated with impaired renal function in HIV infected patient initiating highly active antiretroviral therapy in North-eastern Nigeria. *Materials and Methods :* This was a retrospective study among HIV-1 infected patients that presented at infectious diseases clinic at the university of Maiduguri Teaching Hospital(UMTH) for care between July 2008- March 2009. Data were analysed for age, gender, weight, height, WHO clinical stage, HIV-1 RNA viral load, HBsAg and anti-HCV antibody status. Estimated glomerular filtration rate eGFR was calculated using the Cockcroft –Gault equation.

Keywords : *Highly active antiretroviral therapy, human immunodeficiency virus, correlates, serum creatinine.*

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Correlates of Impaired Renal Function in Highly Active Antiretroviral Therapy (HAART) Naive HIV Infected Patients in Maiduguri, Nigeria

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Materials and Methods : This was a retrospective study among HIV-1 infected patients that presented at infectious diseases clinic at the university of Maiduguri Teaching Hospital(UMTH) for care between July 2008- March 2009. Data were analysed for age, gender, weight, height, WHO clinical stage, HIV-1 RNA viral load, HBsAg and anti-HCV antibody status. Estimated glomerular filtration rate eGFR was calculated using the Cockcroft –Gault equation.

Results : A total of 415 participants with mean age of 43.65±9.70 (95% CI; 42.77 – 44.52), were considered for this study. Out of this 182 (43.6%) were males, with a mean age of 47.43±9.00, they were older than females with mean age of 40.54±9.08 ($p<0.05$). A total of 61(14.7%) had an eGFR<60mL/min, with disproportionately more males (17.0%vs 12.5%) having eGFR<60mL/min than females ($p<0.05$). On multivariate analysis, older age (≥50 years), anaemia (Hb<10g/dl), abnormal BMI (<18.5 kg/m² or >25.0 kg/m²) had significant associations with reduced GFR.

Conclusion : Older age, anaemia and abnormal weight are independently associated with risk of having impaired renal function in our cohort. We therefore recommend renal function tests to HIV infected patients at commencement of highly active antiretroviral therapy for effective and proper management.

Keywords : Highly active antiretroviral therapy, human immunodeficiency virus, correlates, serum creatinine.

I. Introduction

Despite the widespread use of highly active antiretroviral therapy (HAART), HIV disease remains associated with increased kidney disease risk (Phair and Palella,2011). Kidney disease is an often unrecognised problem as kidney function may be abnormal in up to 30% in HIV population (Gupta *et al.*,*2005*; Szczech*et al.*,2002). HIV-infected patients may undergo renal damage related to the HIV infection itself, to the presence of co-infection, arterial hypertension, diabetes or to the exposure to nephrotoxic drugs. Consequences of kidney disease in HIV-infected persons include increased risk of atherosclerosis and mortality, in addition immunosuppression that is known to be associated with development of opportunistic infections, malignancies and other organ diseases that affects kidney functions. (Choi A *et al.*,2010; Choi AI *et al.*,2010).

HIV-associated nephropathy (HIVAN) is traditionally the most common renal lesion affecting HIV-infected patients; it is the commonest cause of end stage renal disease (ESRD), often requiring renal replacement therapy. Although HIVAN has been documented in indigenous African patients, little is known about the prevalence or risk factors for renal disease in this population (Winston *et al.*, 1999; Cosgrove *et al.*, 2002; Szczech*et al.*,2004).

Kidney function can be measured by determining the glomerular filtration rate (GFR), the decrease in GFR has been shown to correlates with the severity of kidney disease. The Cockcroft-Gault equation, which estimates GFR using serum creatinine and anthropometric variables has been shown to predict renal function (Cockcroft and Gault,1976). The use of this equation in assessing GFR has been validated among black HIV positive patients (Chukwuonye,2007).

The aim of this study was to determine the factors associated with impaired renal function among the patients initiating highly active antiretroviral therapy.

II. Patients and Method

Design : Cross-sectional observational cohort study.

Study Area : The study was conducted in the Department of Medicine, University of Maiduguri Teaching Hospital, Borno State. This is a 500 bedded hospital designated as a Centre of Excellence for infectious diseases and provides primary, secondary and tertiary services for the North Eastern part of Nigeria. It also caters for the neighbouring Countries

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such as Cameroon, Niger and Chad Republics. Maiduguri the capital of Borno State is situated in the north eastern Nigeria and the largest settlement near the Lake Chad.

Study procedure : Cross-sectional data of 415 HIV positive patients were abstracted for the purpose of this study.

Variable abstracted included age, gender, weight and WHO clinical stage of HIV disease. Blood samples were collected for CD4 count using standardized flow cytometricCyflow machine (manufactured by Cytec, Partec, Germany 2005). While plasma HIV RNA levels was measured using freshly frozen specimen separated within 6 hours of phlebotomy utilizing the Amplicor HIV-1 Monitor Test, version 1.5 Manufactured by Roche® Germany, with a minimum cut off value of 200 copies per ml. Enzyme linked immunosorbentassay kits was used to detect the presence of HBsAg and HCV antibodies (DIA, PRO, DiagosticBioprobes Sri, via columella no 20128 milano-Italy).

The estimated Glomerular Filtration Rates (eGFRs) were calculated from serum creatinine measurements using the Cockcroft Gault equation (Cockroft and Gault, 1976; Chukwuonye, 2007) and graded according to the National Kidney Foundation grading (Leyvey*et al.*, 2003) of chronic kidney disease (CKD) as follows: Grade 1, 60-89mL/min; grade 2, 30-58mL/min, grade 3, 15-29mL/min; and grade 4, <15mL/min.

Ethical consideration : Permission was obtained from the University of Maiduguri Teaching Hospital (UMTH) Ethical Committee.

Statistical analysis : Data were analyzed using SPSS®, version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using Chi-square test, group means were compared the students t-test. Mann Whitney test was used to compare variables that did not follow normal distribution.

Factors associated with reduced eGFR (defined as <60mL/min) were tested for inclusion in a multivariate logistic regression model. A P-value of < 0.05 was considered statistically significant.

III. Results

a) Stratification of participants based on gender

A total of 415 HIV positive, highly active antiretroviral therapy (HAART) naive patients with mean age of 43.65±9.70 (95% CI; 42.77 – 44.52), were considered for this study. Out of this 182 (43.6%) participants were males, with a mean age of 47.43±9.00, they were older than their female counterpart that had a mean age of 40.54±9.08 (p<0.05). Female gender was associated with significantly low haemoglobin, viral load, and proportion with renal impairment (eGFR). Male cohort had significantly high proportion of participants infected with hepatitis B virus, while the body mass index and AIDS status between the males and females were not comparable as shown in Table 1.

b) Stratification of participants based on renal function

Categorization of the participants based on renal function indicated that 61(14.7%) had an eGFR<60mL/min, with disproportionately more males (17.0%vs 12.5%) having eGFR<60mL/min. The overall mean eGFR was 95.65±39.09 (95%CI;91.90 – 99.40), with males being more likely to have lower eGFR (males: 88.82±36.46, females 100.82 ± 39.34; p=0.002). Other variables associated with reduced eGFR (<60ml/min) in comparison with normal eGFR (≥60ml/min) includes; older age (eGFR<60ml/min:49.87±11.07, eGFR ≥ 60ml/min: 42.46±8.90; p = 0.000), low CD4 count (eGFR<60ml/min: 182.21±1105.46, eGFR≥ 60ml/min: 222.04±152.03; p = 0.013), low haemoglobin (eGFR<60ml/min: 10.19±2.31, eGFR ≥ 60ml/min: 11.60±2.05; p = 0.000), low Body mass index (eGFR<60ml/min: 20.70±3.9, eGFR ≥ 60ml/min: 22.77±4.48; p = 0.013). AIDS cohort were more likely to have renal impairement (eGFR<60ml/min) than participants that had no features of AIDS (16.5% vs11.9%) respectively. No difference was observed in viral load, platelets numbers and total white cell count parameters with respect to participants renal function (p>0.05) as depicted in Table 2.

c) Multivariate analysis of factors associated with reducedeGFR (eGFR<60ml/min)

On multivariate analysis, with younger age(<50 years), Hb≥10g/dl,WBC≥3X10^9/l, platelets≥150x10^9/l, HIV-1RNA≥100000copies/ml, no AIDS status, Normal BMI(18.5-25.0kg/m2) as a referent, it shows that older age (≥50 years), anaemia (Hb<10g/dl), abnormal BMI (<18.5kg/m^2 or >25.0 kg/m^2) had significant associations with reducedeGFR (eGFR<60ml/min) as shown in Table 3.

Table 1 : Characteristics of patients stratified by sex.

	Males(n=182)	Females (n=233)	P-value
Age (years)	47.43±9.00	40.54±9.08	0.000*
Mean Hb (g/dl)	11.90±2.10	10.88±2.06	0.000*
Mean WBC	5.20±2.46	5.09±1.89	0.611
Mean platelets	246.43±101.72	275.02±103.39	0.005*
Mean CD4 count(cells/μl)	201.87±149.22	224.36±150.69	0.112
Mean viral load log10 (copies/ml)	4.79±5.13	4.09±5.51	0.009
eGFR(mL/min)	88.82±36.46	100.82±39.34	0.002
e GFR grade			
≥ 90	77(42.3%)	136(58.4%)	0.002*
60-89	74(40.7%)	68(29.2%)	0.019
30-59	25(13.7%)	27(11.6%)	0.623
15-29	06(03.3%)	01(0.42%)	0.057
<15	0(0%)	01(0.004%)	-
Hepatitis C	-	03(1.3%)	-
Hepatitic B	30(16.5%)	28(12.0%)	0.000*
AIDS status			
yes	104(57.1%)	127(54.5%)	0.668
no	78(42.9%)	106(45.5%)	0.668
BMI	22.65±4.39	22.13±4.58	0.338

BMI (body mass index).
*Statistically significant.

Table 2 : Characteristics of patients stratified by reduced eGFR.

	(eGFR≥60mL/min) N=356	(eGFR<60ml/min) N=61	P-value
Age (years)	42.46±8.90	49.87±11.07	0.000*
Gender			
Male, no (%)	161(83.0%)	31(17.0%)	0.000*
Female, no (%)	104(87.5%)	29(12.5%)	0.000*
Mean Hb (g/dl)	11.60±2.05	10.19±2.31	0.000*
Mean WBC	5.05±1.93	5.68±2.90	0.115
Mean platelets	262.12±103.00	251.32±113.34	0.471
Mean CD4 count(cells/μl)	222.04±152.03	182.21±105.46	0.013*
Mean viral load log10 (copies/ml)	4.96±5.44	4.97±5.27	0.958
Hepatitis C	3	0	
Hepatitic B	48(13.5%)	10(16.4%)	0.000*
BMI	22.77±4.48	20.70±3.90	0.013*
AIDS status, no=231			
yes	193(83.5%)	38(16.5%)	0.000*
no	162(88.0%)	22(12.0%)	0.000*

BMI (body mass index).
*Statistically significant.

Table 3 : Multivariate analysis of correlates of reduced eGFR (< 60ml/min) among HIV-infected patients.

Variables	Odd ratio	95% confidence limits	P-value
Age (years)			
<50	Referent		
≥50	1.973	2.809 - 18.411	0.000
Gender			
Males	Referent		
Females	0.175	0.342 - 2.062	0.703
Haemoglobin			
≥10.00	Referent		
<10.00	1.310	0.095 - 0.766	0.014
White cell count			
≥3.00	Referent		
<3.00	0.374	0.229 - 2.063	0.504
Platelets count			
≥150	Referent		
<150	0.010	0.306 - 3.329	0.987
CD4 Count			
≥350	Referent		
<350	0.101	0.077 - 1.433	0.139
HIV-1 RNA			
≥100000	Referent		
<100000	0.157	0.312 – 4.392	0.816
AIDS Status			
no	Referent		
yes	0.573	0.701 - 4.486	0.226
BMI			
Normal (18.5-25.0)	Referent		
Abnormal weight	1.239	0.089 - 0.943	0.040

IV. Discussion

Our study examined the pattern of renal impairment and its associated factors among highly active anti retroviral naive HIV infected individuals. The prevalence of renal impairment as defined by an eGFR<60 ml/min/1.73m2 among HIV patients in our cohort was 14.7% similar to previous studies that reported a prevalence rate of 10 to 30% (Weiner *et al.*, 2002; Szczechet al., 2004; Winston *et al.*, 1979). It was however lower than prevalence rate of 53.3% reported in south south (Okafor*et al.*, 2011) and 23.8% determined in north central region (Agbajiet al., 2011), but higher than 7% reported by DART Trial group (Krawczyk*et al.*, 2004), 3% reported in California (Crum-Cianflone*et* al.,2010) and 3.5% in a predominantly Caucasian EuroSIDA cohort. (Mocroft*et al.*,2007).Discordance may be explained by study design, variations in patient population characteristicsincluding demographic characteristics, stage of HIV infection, and access to health care services. Of note, our population was relatively young (mean age 44 years), presented at late stage of the disease.Although somehow expected, this finding of prevalence of 14.7% in our cohort was worrisome for us. We used Cockcroft-Gaultequations to estimate glomerular filtration rate (eGFR), and since these equations can underestimate the actual GFR or creatinine clearance in patients with malnourishment or reduced muscle mass related to advance HIV, it is possible that the true prevalence of CKD in our cohorts is underestimated.

This study demonstrates older age, abnormal weight (under weight or over weight/obesity) and anaemia at presentation to be independent predictors of renal impairment in our cohort. Renal function is known to decline with age. Older age is an established risk factor for a decline in creatinine clearance in the general population (Davies and Shock, 1950). Similarly, older agehas been independently associated with renal function decline among HIV-infected subjects. (Mocroft*et al.*,2007; Cheung *et al.*, 2007).The preponderance of renal impairment in our male cohort may be related to significantly older male than female population.

The mean CD4 count of 222 cells/ul in patients with normal renal function was significantly higher than 182 cells/ul in our cohort with renal impairment. This is consistent with earlier studies that reported an association between impaired renal function in HIV infected patients with significantimmuno suppression, having CD4 cell count less than 200ul/L. Immunological AIDS (CD4 count <200ul/L) is known to be associated with development of opportunistic infections, malignancies and other organ diseases that affects kidney functions. (Winston *et al.*,1999; Szczech *et al.*, 2004; Winston *et al.*,2001; Krawczyk*et al.*,2004). CD4 cell had a protective role in the development of renal

diseases except acute tubular ischaemia (Wang *et al.*, 2005). Previous studies reported that in addition to CD4 cellcount of less than 200cells/ul, high viral load and proteinuria in HIV infected patients were othervariables that are associated with progressive renal impairment (Mulomaet *al.*, 2005; Chaparro *et al.*, 2009). However, Renal failure index (RFI) including HIVassociated nephropathy was recently reported in HIV patients with normal or mildly impaired immunestate with CD4 cell count above 200cells/ul and who usually were asymptomatic (Wang *et al.*, 2005; Ham *et al.*, 2006; Bourgoigni*et al.*, 2005).These information suggest that avoiding the occurrence of low CD4 cell counts, by early HIV diagnosis and treatment, may be important components of preventing future kidney disease among HIV patients; however further studies are needed to establish this preposition.

Reports from sub-Saharan Africa, indicated that the prevalence of decreased eGFR is high and varied substantially depending on the estimating method used (Chukwuonye,2007;Van Deventer *et al.*,2008;Eastwood *et al.*,2010). However the use of Cockcroft-Gault equations have been validated for use as it has been shown to predicts renal function in black HIV population (Chukwuonye, 2007). Renal dysfunction is an increasingly recognized non-AIDS–defining comorbidity among HIV-infected persons, with both HIV-associated nephropathy (HIVAN) and HIV-related ESRD disproportionately affecting black population (Choi *et al.*,2007;Lucas *et al.*, 2008). With the recent discovery of a locus on chromosome 22 that is associated with genetic susceptibility to HIVAN and other forms of CKD and ESRD among African-Americans (Kao *et al.*, 2008; Genovese *et al.*, 2010), there is increasing concern about the burden of HIV-related CKD in sub- Saharan Africa (Arendse*et al.*,2010). Available data suggest substantial regional variability in the prevalence of HIV-related CKD. The highest burden has been observed in West Africa, consistent with the predominant ancestry of the genetically susceptibleAfrican- American population (Emem*et al.*, 2008). With expanding access to ART across Africa, including the use of agents with nephrotoxic potential, screening of patients at commencement of ART to identify those with renal impairement is valuable. Also, early initiation of patients on ART in line with the new WHO guideline should be advocated to avoid AIDS related Kidney diseases.

V. Limitations

This study is limited in its retrospective design, with the greater proportion of HIV-infected with AIDS with advanced clinical disease, it implies that prevalence estimates derived from this study may not be generalizable to patients with early stage of HIV infection. In addition, we were limited by the use of a single serum creatinine, hence spurious results were not excluded. Finally, there was no assessment for protenuria; however, this was the standard of care in the centre at the time of this study.

References Références Referencias

1. Agbaji OO, Onu A, Agaba PE, Muazu MA, Falang KD, Idoko JA., 2011. Predictors of impaired renal function among HIV infected patients commencing highly active antiretroviral therapy in Jos, Nigeria. Niger Med J, 52:182-5.
2. Arendse CG, Wearne N, Okpechi IG, Swanepoel CR., 2010. The acute, the chronic and the news of HIV-related renal disease in Africa. Kidney Int 78: 239–245.
3. Bourgoigni J, Rao TKS, Roth D., 2005 Renal disease in patients with hepatitis and human immunodeficiency virus [HIV]. Atlas of the diseases of the kidney. On – lineedition.
4. Chaparro WA, Zilleruelo G, Riviera D., 2010. HIV nephropathy in children detected by quantitative proteinuria. 11th conf on retrovirus and opportunistic infections.Abst; 752: session 104.
5. Cheung CY, Wong KM, Lee MP, 2007. Prevalence of chronic kidney disease in ChineseHIV-infected patients.Nephrol Dialysis Transplant, 22:3186–3190.
6. Chukwuonye I, Comparison of the modification of diet in renal disease (MDRD) and Cockroft-Gault formula in HIV seropositive patients at Jos University Teaching Hospital, Jos. A dissertation submitted and approved in partial fulfilment of the requirement for the award of fellowship in internal medicine (Nephrology subunit): National Postgraduate Medical College of Nigeria; 2007.
7. Choi A, Scherzer R, Bacchetti P, Tien PC, Saag MS, Gibert CL, et al. Cystatin C, albuminuria, and 5-year all-cause mortality in HIV-infected persons. Am J Kidney Dis 2010; 56:872–882.
8. Choi AI, Li Y, Deeks SG, Grunfeld C, Volberding PA, Shlipak MG. Association between kidney function and albuminuria with cardiovascular events in HIV-infected persons. Circulation 2010; 121:651–658.
9. Choi AI, Rodriguez RA, Bacchetti P, Bertenthal D, Volberding PA, 2007. Racial Differences in End-Stage Renal Disease Rates in HIV Infection versus Diabetes. J Am SocNephrol, 18: 2968–2974.
10. Cockcroft D, Gault M, 1976. Prediction of creatinine clearance from serum creatinine. Nephron, 16:31-41.
11. Cosgrove CJ Abu-Alfa AK, Perazella MA, 2002. Observations on HIV-associated renal disease in the era of highly active antiretroviral therapy. Am J Med Sci, 323:102–6.
12. Crum-Cianflone N, Ganesan A, Teneza-Mora N, Riddle M, Medina S, Barahona andBrodine S, 2010. Prevalence and Factors Associated with Renal Dysfunction Among HIV-Infected Patients

AIDS PATIENT CARE and STDs Volume 24, Number 6, Davies DF, Shock NW,1950. Age changes in glomerular filtration rate, effective renal Plasmaflow, and tubular excretory capacity in adult males. J Clin Invest, 1, 29:496–507.

13. Eastwood JB, Kerry SM, Plange-Rhule J, Micah FB, Antwi S, 2010. Assessment of GFR by four methods in adults in Ashanti, Ghana: the need for an eGFR equation for lean African populations. Nephrol Dial Transplant 25: 2178–2187.
14. Emem CP, Arogundade F, Sanusi A,Adelusola K, Wokoma F, 2008. Renal disease in HIV-seropositive patients in Nigeria: an assessment of prevalence, clinical features and risk factors. Nephrol Dial Transplant 23: 741–746.
15. Genovese G, Friedman DJ, Ross MD, Lecordier L, Uzureau P, 2010. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. Science 329: 841–845.
16. Gupta SK, Eustace JA, Winston JA, Boydstun II, Ahuja TS, Rodriguez RA, 2005.
17. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America.Clin Infect Dis,40:1559–1585.
18. Ham TM, Naicker S, Ramdial PK, Assoung AG, 2006. A cross sectional study of HIV seropositivepatients with varying degrees of proteinuria in South Africa. *Kidney Int*, 69:2243 – 50.
19. Kao WH, Klag MJ, Meoni LA, Reich D, Berthier-Schaad Y, 2008. MYH9 isassociated withnondiabetic end-stage renal disease in African Americans. NatGenet 40: 1185–1192.
20. Krawczyk CS, Holmberg SD, Moorman AC, Gardner LI, McGwinjnr G for HIV out patient group, 2004. Factors associated with chronic renal failure in HIV-infected ambulatory patients. AIDS, 18:2171-8.
21. Levey A, Coresh J, Balk E, Kausz A, Levin A, Staffes M, 2003. National Kidney Foundation Practice Guildelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Ann Intern Med, 139:137-47.
22. Lucas GM, Lau B, Atta MG, Fine DM, Keruly J, 2008. Chronic Kidney Disease Incidence, and Progression to End-Stage Renal Disease, in HIV Infected Individuals: A Tale of Two Races. J Infect Dis 197: 1548–1557.
23. Mocroft A, Kirk O, Gatell J, 2007. Chronic renal failure among HIV-infected patients. AIDS, 21:1119–1127.
24. MulomaE, OwumoOng'or W, Sidlee J, 2005. Renal disease in an ART naïve HIV infectedpopulation in western Kenya. IAS conf HIV pathog Treat: Abst MOPE 11.6c23.
25. Okafor UH, Unuigbe EI, Ojogwu LI, Oviasu E, Wokoma FS, 2011. Renal disease in HIV infected patients at University of Benin Teaching Hospital in Nigeria African Health Sciences Vol 11 Special Issue 1 August.
26. Phair J, PalellaF , 2011. Renal disease in HIV-infected individuals.CurrOpin HIV AIDS 2011.
27. Szczech LA, Gange SJ, van der Horst C, Bartlett JA, Young M, Cohen MH, 2002.
28. Predictors of proteinuria and renal failure among women with HIV infection. Kidney Int, 61:195–202.
29. Szczech LA, Gupta SK, Habash R, 2004. The clinical epidemiology and course of the spectrum of renal diseases associated with HIV infection.KidneyInt, 66:1145–52.
30. Van Deventer HE, George JA,Paiker JE, Becker PJ, Katz IJ, 2008. Estimating glomerular filtration rate in black South Africans by use of the modification of diet in renal disease and Cockcroft-Gault equations. ClinChem 54: 1197–1202.
31. Wang Y, Feng X, Bao S, 2005. Depletion of CD4 (+) T cells aggravates glomerular and interstitial injury in murine adriamycin nephropathy. Kidney International, 67, (S96–S100);1523-1755.
32. Weiner NJ, Goodman JW, Kimmel PL, 2002. The HIV associated renal diseases; current insight intopathogenesis and treatment. *Kidney Int*, 63:1618-1631.
33. Winston JA, Bruggeman LA, Ross MD, 2001. Nephropathy and establishment of a renal reservoir of HIV type 1 during primary infection. *NEJM* , 344(26): 1979 – 83.
34. Winston JA, Klotman ME, Klotman PE,1999. HIV-associated nephropathy is a late, not early, manifestation of HIV-1 infection. Kidney Int, 55:1036–40.