Published in final edited form as:

J Assoc Nurses AIDS Care. 2010 ; 21(1): 16. doi:10.1016/j.jana.2009.07.005.

Ignoring the Obvious Missing Piece of Chronic Kidney Disease in HIV: Cigarette Smoking

María José Míguez-Burbano, MD, PhD [Associate Professor],

Department of Health Promotion and Disease Prevention, Robert Stempel College of Public Health and Social Work and College of Medicine and School of Medicine, Florida International University, Miami, FL

Christina Wyatt, MD [Assistant Professor],

Division of Nephrology, Mount Sinai Medical Center, New York, NY

John E. Lewis, PhD [Assistant Professor],

Department of Psychiatry and Behavioral Sciences, University of Miami School of Medicine, Miami, FL

Allan Rodríguez, MD [Associate Professor], and

Department of Medicine, University of Miami School of Medicine, Miami, FL

Robert Duncan, PhD [Professor]

Department of Epidemiology, University of Miami School of Medicine, Miami, FL

Abstract

The impact of tobacco use on the development of chronic kidney disease (CKD) in people living with HIV (PLWH) has been overlooked, despite remarkably higher rates of smoking in these individuals. We examined the association between smoking and the risk of CKD in a case-controlled study that included 75 PLWH with CKD and 461 PLWH consecutively admitted to the hospital for other causes. Significant differences in gender, race/ethnicity, hypertension, hepatitis B, CD4 cell counts, and smoking between cases and controls were found, suggesting that these variables may be risk factors for CKD. In logistic regression analyses, smoking (OR = 1.97, $p = 0.003$), hypertension (OR = 2), and African ancestry, particularly for Black Caribbeans (OR = 2.6), were independent factors associated with CKD. Moreover, the results pointed to a dose-response relationship between packs smoked per day and CKD. Smoking was found to contribute a significant risk for CKD in our subjects.

Keywords

AIDS; chronic kidney disease; HIV; race/ethnicity; renal disease

Combination antiretroviral therapy (ART) has had a significant impact on the course of HIV disease (Connick, 2001; Zeller, Caumes, Bossi, Bricaire, & Katlama, 2002). With the decline of opportunistic infections, however, other conditions such as liver and kidney diseases have emerged as threats to the lives of people living with HIV (PLWH; Moroni & Antinori, 2003). PLWH are at risk for the development of a variety of acute and chronic kidney diseases (CKD).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Kidney damage is postulated to result from the cytopathic effects of HIV gene products, immune dysfunction, opportunistic infections, malignancies, and HIV-related medications (D'Agati & Appel, 1997; Kimmel, Barisoni, & Kopp, 2003; Kopp & Winkler, 2003; Laradi, Mallet, Beaufils, Allouache, & Martinez, 1998; Mazbar, Schoenfeld, & Humphreys, 1990; Mocroft, Kirk, & Gatell, 2007; Praditpornsilpa et al., 1999; Ross & Klotman, 2002; Szczech, 2001; Wyatt, 2007; Wyatt & Klotman, 2006). Even though studies have reported improvements in the course of HIV-associated nephropathy with ART (Kimmel et al., 2003; Moroni & Antinori, 2003), data are inconclusive regarding the impact of combination ART on other forms of CKD (Mocroft et al., 2007; Wyatt & Klotman, 2006). Of concern, the prevalence of end-stage renal disease among HIV-infected individuals is estimated to rise exponentially during the next 10 years (Szczech, 2001). Although the prevalence of smoking in PLWH has been estimated to be between 44–88%, or 2–4 times higher than that in the general population, the impact of smoking on the development of CKD in PLWH has not yet been evaluated (Laradi et al., 1998; Mazbar et al., 1990; Mocroft et al., 2007; Praditpornsilpa et al., 1999; Wyatt, 2007). The first evidence that smoking was a risk factor for renal disease was published in 1978 (Dales, Friedman, Siegelau, Seltzer, & Ury, 1978). Since then, several studies have documented that smoking is nephrotoxic in patients with renal disease of diverse origins (Krimholtz, Thomas, & Viberti, 2000; Molander et al., 2000; Orth, Stockmann, & Conradt, 1998; Stengel, Couchod, Lenee, & Hemon, 2000). In light of the high prevalence of smoking in PLWH, we investigated the effect of smoking as a risk factor for CKD in a diverse population of PLWH.

Subjects and Methods

Sampling

All HIV-infected patients consecutively hospitalized at Jackson Memorial Hospital in Miami, Florida, between 2003 and 2004 were eligible for enrollment in the study. Following admission, patients ($n = 553$) were contacted and fully informed about the study. Those who were stable, expressed willingness to participate (97%; 536/553), and provided a written informed consent and a medical release were enrolled. The institutional review board at University of Miami Miller School of Medicine approved the study.

The baseline examination for each participant included the use of standardized research questionnaires regarding tobacco, alcohol, and drug use; past and present medical history; physical examination; and laboratory testing. Comprehensive hospital discharge summaries, laboratory values (BUN, creatinine, 24-hour urine collection, and biopsy), imaging tests, and treatment data were collected from medical records, from the day of admission and up to a year thereafter, by three experienced HIV clinicians/researchers.

Definition of Cases

According to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines (National Kidney Foundation [NKF], 2008a), CKD was defined as structural or functional abnormalities of the kidney for more than 3 months, with or without decreased glomerular filtration rate ($\text{GFR} < 60 \text{ ml/min/1.73 m}^2$), manifested by pathologic abnormalities or markers of kidney damage, including abnormalities in the composition of the blood or urine or in imaging tests (Levey et al., 2003, NKF, 2008a). The definition of CKD used in this study relied on data from the time of hospital admission plus a 3-month window period. In subjects with abnormal kidney function, we abstracted additional clinical and laboratory data before hospitalization and up to the hospital discharge follow-up visit to confirm persistent kidney damage or decreased GFR. The GFR was calculated using the four variables in the Modification of Diet in Renal Disease (MDRD) equation (Levey et al., 2003; NKF, 2008b). As illustrated in Table 1, the GFR was used to classify the stage of CKD of each patient according to the K/

DOQI Clinical Practice Guidelines (Levey et al., 2003). The requirement for dialysis during the hospital admission was determined based on procedure code.

HIV-infected patients, hospitalized for causes other than a renal disease, were enrolled in the study as controls. Subjects with any abnormality indicating renal compromise (i.e., acute renal disease or urinary tract infection) and those who were diagnosed with CKD at any other point of the follow-up (i.e., 6- or 12-month visits) were excluded from these analyses.

Tobacco Exposure

Information on smoking (cigarettes, cigars, and pipes) were collected at baseline using research questionnaires and included: duration of smoking (years); the estimated number of cigarettes, cigars, and/or pipes per day; and the age at which participants began smoking. Participants were categorized as *non-smokers* if they reported never having smoked at all. An *ever smoker* was defined as anyone who had at some time smoked at least one cigarette, cigar, or pipe per week for at least 3 months. An *ex-smoker* was defined as an individual who had stopped smoking for at least 1 year prior to the interview. *Current smokers* were those who reported present, regular cigarette smoking. The frequency of smoking was based on number of packs per day, packs per year, and the following numerical scale: 0 = *never*, 1 = *current smoker*, and 2 = *past smoker*.

Other Risk Factors

To investigate risk factors associated with CKD, potentially confounding variables were measured and categorized on all participants. Each was first analyzed as a continuous variable, and then dichotomized to facilitate analyses. Participants were defined as hypertensive if they fulfilled at least one of the following conditions: (a) hypertension was included in the discharge medical records as a clinical diagnosis, (b) the mean blood pressure met criteria for the clinical diagnosis of hypertension (systolic pressure of > 140 mm Hg or a diastolic pressure of > 90 mm Hg), or (c) blood pressure medication was prescribed to control blood pressure.

Race/ethnicity was divided into four categories: (a) non-Hispanic White, (b) Hispanic White, (c) African American, or (d) Black Caribbean (non-Hispanic Black). A subject was defined as diabetic if the participant had a history of diabetes, a fasting glucose ≥ 126 mg/dL or reported a regular use of hypoglycemic agents or insulin. Finally, blood was drawn to obtain hepatitis B and C serology and categorize as positive or negative.

Statistical Analyses

Data were analyzed using SAS 8.1 and SPSS 15. Associations between the main variables of interest were examined with Pearson's correlation coefficient analyses. Multivariate regression analysis was used to describe the associations between CKD and cigarette smoking, while controlling for all variables that were statistically significant in the univariate analyses.

Results

Sociodemographic Characteristics

With an overall participation rate of 97%, 536 HIV-infected participants were enrolled in the study. CKD was diagnosed in 14% of participants ($n = 75$), and 10% met the CKD diagnosis criteria at the time of enrollment, based on GFR estimates obtained before and during the initial hospitalization. In another 4% of participants, the diagnosis of CKD was confirmed at the first follow-up visit 1–2 months after hospital discharge. Table 2 shows baseline characteristics of the study population stratified by the presence or absence of CKD. CKD participants were more likely to be men (OR = 2, 95% CI: 1.03–3.11; $p = 0.04$), African Americans or Black Caribbeans ($p = 0.01$), and tended to have lower hemoglobin and serum albumin levels.

Stage of CKD and Risk Factors

GFR levels below 60 ml/min/1.73m² were evident in 86% ($n = 65$) of participants with CKD. Based on the K/DOQI guidelines for CKD staging, 4% of the CKD cases had stage 1 CKD, 31% stage 2, 30% stage 3, and 35% had stage 4–5 CKD. Participants with CKD had a mean serum creatinine value (6.6 ± 5.8 mg/dL vs. 0.89 ± 0.4 mg/dL, $p = 0.0001$) and BUN levels significantly higher than the value for control participants (49.8 ± 27.5 mg/dl vs. 13.1 ± 8.5 mg/dl, $p = 0.001$).

Cigarette Smoking and CKD

Fifty-three percent of the non-CKD participants reported current smoking behavior at baseline. Sixty-nine percent of those with CKD reported being current smokers, with an additional 11% indicating former use. Univariate analyses indicated that hospitalized participants with CKD were twice as likely as those without CKD to be current smokers (OR = 2.2, 95% CI: 1–3.03; $p = 0.04$). Among the current smokers, 40% were heavy smokers (> 20 cigarettes/day), 3% were moderate smokers (10–19 cigarettes/day), and 57% were light smokers (< 10 cigarettes/day). Not only did many participants continue to smoke after CKD diagnosis, 38% of them smoked more than 1 pack per day. Even those participants who, during the follow-ups (12 months), required dialysis, smoking was not discontinued. Accordingly, the mean packs per year were significantly higher in CKD participants compared to those without CKD (12.7 ± 0.9 vs. 8.8 ± 1.3 , $p = 0.01$). Non-Hispanic White participants were more likely to report current smoking compared to Black Caribbeans, most of whom were non-smokers ($p = 0.001$). Black Caribbeans were 12 times less likely than African Americans and 7 times less likely than Hispanics to report smoking.

Compared to non-smokers, current smokers had significantly higher BUN (19.9 ± 2 vs. 15.8 ± 1.1 mg/dL, $p = 0.03$). Smokers also tended to have higher serum creatinine levels (0.9 ± 0.7 vs. 0.8 ± 0.2 mg/dL, $p = 0.06$). This relationship remained significant among participants with CKD, with higher BUN (54 ± 4.5 vs. 37 ± 6.5 mg/dL, $p = 0.04$) and creatinine levels (6.8 ± 0.8 vs. 4.5 ± 2.5 mg/dL, $p = 0.05$) in current smokers compared to non-smokers.

A total of 84 participants had a diagnosis of hypertension, of these approximately two thirds were smokers and the remaining 35% were non-smokers. Comparison of blood pressure in smokers and non-smokers revealed significantly higher mean diastolic measurements in smokers versus non-smokers (73.6 ± 13.9 vs. 70.9 ± 15.3 mmHg, $p = 0.04$) and slightly higher systolic measurements in smokers compared to non-smokers (125 ± 22 vs. 119.7 ± 23). A similar trend was observed when patients with CKD were analyzed separately. Of relevance, these findings were significant despite the fact that participants were under strict medical control and receiving antihypertensive medications.

Univariate analyses indicated that even 1–2 packs/year significantly increased the risk of developing CKD among HIV-infected participants (OR = 1.57, 95% CI: 1–2.53, $p = 0.05$). Of interest, past use of any amount of packs per year did not seem to increase the risk (OR = 1.1, 95% CI: 0.2 – 4.7, $p = 0.8$).

Confounding Variables

Well-established risk factors for CKD were analyzed by study groups and are shown in Table 3. CD4 counts tended to be lower in participants with CKD. After controlling for hepatitis co-infection, date of HIV diagnosis, and use of combination ART, Black Caribbeans had lower CD4 counts (81 ± 12 cells/mm³) than African Americans (139.5 ± 9.8 , $p = 0.002$), Hispanics (171.8 ± 25.9 , $p = 0.002$), and Whites (162.8 ± 37 , $p = 0.01$). No significant differences in HIV viral load were noted by race-ethnicity.

The prevalence of diabetes ($n = 2$), other systemic diseases (cancer, $n = 2$), and hepatitis C virus co-infection was similar in both groups, while hepatitis B virus co-infection (27% vs. 14%) and hypertension (33% vs. 11%) were more prevalent among participants with CKD. No correlations with GFR or stage of CKD were evident.

Univariate analyses indicated that participants with hypertension were twice as likely to be hospitalized with CKD (95% CI: 1.8–3.5, $p = 0.005$). Prevalence of hypertension was higher in African Americans (21.7%) than in Black Caribbeans (13%) and Hispanics (17%). No cases were observed among non-Hispanic Whites ($p = 0.05$). Resting systolic blood pressure was significantly higher in Black Caribbeans than in Whites (123.3 ± 27.9 vs. 113.3 ± 17 mm Hg, $p = 0.05$).

Sixty-nine percent of the participants with CKD and 60% of the control group were not on combination ART at the time of study enrollment. Twenty-nine percent of those with CKD and 35% of the control group were using co-trimoxazole and/or other prophylaxis. Among the participants, time from CKD diagnosis to dialysis ($n = 38$) was longer in ART-treated (11.9 ± 9 months) than in untreated individuals (9 ± 8 months, $p = 0.2$), but was not significantly different. No other beneficial effects of combination ART were observed in level of BUN, GFR, severity of the disease, or the presence of proteinuria.

Adjusted Analyses

In multivariate logistic regression, current cigarette smoking (packs/day), Black race (both African Americans and Black Caribbeans), and hypertension remained independently associated with CKD after adjusting for gender, combination ART use, CDC stage of HIV disease, and HIV viral load. As illustrated in Table 4, smokers were 3 times more likely than non-smokers to be hospitalized with CKD (95% CI: 1.4–5.6, $p = 0.005$). CD4 cell counts, combination ART, viral load, and gender were no longer independently associated with CKD in the final model.

The number of packs smoked/day strongly influenced the risk of CKD. Participants who had smoked 1 pack/day had a 59% increased risk (OR=1.59, 95% CI: 1.00, 2.41, $p = 0.05$) compared to never-smokers, and a threefold increased risk was observed in participants who reported the use of more than 2 packs/day (OR = 3.29, 95% CI: 1.33, 8.10, $p = 0.003$). Of interest, when analyses of risk were performed in packs/year, rather than packs/day, instead of a linear curve we observed an inverted U shape distribution (See Figure 1).

Discussion

The current investigation is the first large study to demonstrate that cigarette smoking is a major modifiable risk factor for CKD in PLWH. Although several studies in the general population have documented that smoking contributes to the risk of CKD, this fact has been neglected in HIV even though cigarette smoking is widespread in PLWH (Krimholtz et al., 2000; Míguez-Burbano, Rodriguez, Hadrigan, Azor, & Shor-Posner, 2004; Molander et al., 2000; Orth et al., 1998; Stengel et al., 2000; Wesson, 2003). The magnitude of the association between smoking and CKD, its independence from traditional CKD risk factors, and evidence of a dose-response relationship suggest that these findings are less likely to be due to chance. In agreement with previous studies, our data also demonstrated an adverse relationship between smoking and blood pressure, suggesting a potential biologic mechanism by which smoking could contribute to kidney damage (Narkiewicz et al., 1998; Stengel et al., 2000; Wesson, 2003). Other potential mechanisms have been proposed, including intense sympathetic nervous system excitation and increased concentrations of catecholamines and cytokines (Stengel et al., 2000).

In the inverse U-shaped relationship between packs/year being smoked and CKD, the ascending leg of the U-shaped risk function could be attributed to recent heavy smoking, while the descending leg is probably reflecting more years of low to middle smoking and those who stopped smoking, and subsequently avoided almost all of the excess risk that they would otherwise have suffered. Future studies are needed to identify the mechanisms by which smoking contributes to the development of CKD in the setting of HIV infection.

Our data, in accord with previous epidemiological studies, reveal a high prevalence of CKD among participants of African ancestry (Bourgoignie, Sreepada Rao, & Roth, 1999; Feehally, 2003; Kopp & Winkler 2003; Kimmel et al., 2003; McClellan & Flanders, 2003; Moroni & Antinori 2003; Ross & Klotman 2002; Szczech, 2001; U.S. Renal Data System, 2007). Nonetheless, our study is novel in suggesting that Black Caribbeans, despite being less likely to be cigarette smokers, may be at higher risk of developing CKD than any other group including African Americans. Although Black Caribbeans have been a lesser-studied ethnic group, and studies comparing African Americans and Black Caribbeans are lacking, Black Caribbeans seem to be particularly susceptible to diabetes, hepatitis C, and cardiovascular disease; factors associated with CKD (Cantor, Kimmel, & Bosch, 1991; Feehally, 2003; Haffner, 1998; Kimball, Elswick, & Shiffman, 2001; McClellan & Flanders, 2003; Tillin, Forouhi, McKeigue, & Chaturvedi, 2005; U.S. Renal Data System, 2007). Previous studies have also found that age-adjusted albumin excretion rates are significantly higher in Black Caribbeans with CKD (Tillin et al., 2005). Consistent with previous reports, most of the participants with CKD in the current study were in advanced stages of HIV disease (D'Agati & Appel, 1997), and Black Caribbeans in our study exhibited significantly lower CD4 counts than any other group. While this may partially explain our findings, CD4 values were not independently associated with CKD after adjusting for other factors. Combination ART use was similar across the groups, and according to other researchers, the impact of combination ART was limited to a non-significant prolongation of renal survival among participants with CKD (Ahuja, Borucki, & Grady, 2003). Nonetheless, additional studies are needed in light of a recent study suggesting that combination ART interruptions may increase the risk of renal damage (Mocroft et al., 2009).

A number of limitations must be acknowledged. Our findings are limited to hospitalized patients and may represent a more aggressive clinical course of HIV and kidney diseases. Clinical controls with cancers, cardiovascular disease, or chronic obstructive pulmonary disease may have high rates of smoking, minimizing the chance of detecting an association between smoking and CKD. A small number of participants with acute kidney injury that had not resolved at the time of the first follow-up visit may have been misclassified as having CKD. Nonetheless, the diagnostic criteria employed in this study were consistent with accepted practice guidelines. In addition, approximately 5% of participants had a discharge diagnosis of acute kidney injury, but did not meet the study criteria for CKD because the kidney function had recovered by the first follow-up visit, or they were lost to follow-up within 3 months of the first documented GFR < 60 ml/min/1.73m². This type of misclassification could affect the magnitude of the observed associations between CKD and smoking, race, and hypertension. Finally, a significant proportion of the study participants were not receiving treatment at the time of admission, probably associated with poor adherence to prescribed regimens or problems with obtaining the prescribed medications (no insurance, poverty, illegal status), thus additional studies may be required.

Conclusion

The present findings have a number of important clinical and public health implications. First, current guidelines recommend screening for CKD at the time of HIV diagnosis in all patients, with annual screening in individuals at increased risk for CKD (NKF, 2008). These guidelines

do not currently include cigarette smoking as a marker of increased risk, although smoking cessation is encouraged in patients diagnosed with CKD because of the increased risk of cardiovascular disease. By virtue of its long-lasting renal, vascular, and immune deleterious effects, our findings suggest, although not absolutely, that one of every three observed CKD cases in PLWH might not have occurred if the person had not smoked. Secondly, the former smokers did not exhibit a significantly increased risk of developing CKD, further supporting the urgent need for smoking cessation interventions and education campaigns designed to specifically target PLWH. Our data also illustrated that CKD patients were often diagnosed in late stages of CKD, suggesting that annual tobacco screening for PLWH and follow-up with CKD screening among active smokers may be cost-effective. Finally, the lack of any change in smoking behaviors in PLWH who initiated dialysis documented the need to implement treatment to modify smoking behaviors in CKD patients.

Acknowledgments

We want to thank Sonya Hadrigan for editorial assistance. The grant was funded by the Florida Health Department Tobacco Grant (BM023 MJM) and analyzed thanks to the support of NIAAA (3R01AA017405-02S1 MJM).

References

- Ahuja TS, Borucki M, Grady J. Highly active antiretroviral therapy improves survival of HIV-infected hemodialysis patients. *American Journal of Kidney Disease* 2003;36:574–580.
- Bourgoignie, JJ.; Sreepada Rao, TK.; Roth, D. Renal disease in patients infected with hepatitis and human immunodeficiency virus. 1999 [Retrieved January 27, 2008]. from: <http://www.kidneyatlas.org/book4/adk4-07.pdf>
- Cantor ES, Kimmel PL, Bosch JP. Effect of race on expression of acquired immunodeficiency syndrome-associated nephropathy. *Archives of Internal Medicine* 1991;151:125–128. [PubMed: 1985586]
- Connick E. Immune reconstitution in HIV-1-infected individuals treated with potent antiretroviral therapy. *Journal of Investigative Dermatology* 2001;6:212–218. [PubMed: 11924830]
- D'Agati V, Appel GB. HIV infection and the kidney. *Journal of the American Society of Nephrology* 1997;8:138–152. [PubMed: 9013459]
- Dales LG, Friedman GD, Siegelaub AB, Seltzer CC, Ury HK. Cigarette smoking habits and urine characteristics: Urinalysis abnormalities are more common in smokers, but the reasons are unclear. *Nephron* 1978;20:167–170. [PubMed: 628498]
- Feehally J. Ethnicity and renal disease: Questions and challenges. *Clinical Medicine* 2003;3:578–582. [PubMed: 14703041]
- Haffner SM. Epidemiology of type 2 diabetes: Risk factors. *Diabetes Care* 1998;21:C3–C6. [PubMed: 9850478]
- Kimball P, Elswick RK, Shiffman M. Ethnicity and cytokine production gauge response of patients with hepatitis C to interferon-alpha therapy. *Journal of Medical Virology* 2001;65:510–516. [PubMed: 11596086]
- Kimmel PL, Barisoni L, Kopp JB. Pathogenesis and treatment of HIV-associated renal diseases: Lessons from clinical and animal studies, molecular pathologic correlations and genetic investigations. *Annals of Internal Medicine* 2003;139:214–226. [PubMed: 12899589]
- Kopp JB, Winkler C. HIV-associated nephropathy in African Americans. *Kidney International* 2003;83:S43–S49. [PubMed: 12864874]
- Krimholtz M, Thomas S, Viberti G. Cigarette smoking and diabetic nephropathy. *Contributions to Nephrology* 2000;130:85–93. [PubMed: 10892554]
- Laradi A, Mallet A, Beaufile H, Allouache M, Martinez F. HIV-associated nephropathy: Outcome and prognosis factors. Groupe d'Etudes Nephrologiques d'Ile de France. *Journal of the American Society of Nephrology* 1998;9:2327–2335. [PubMed: 9848787]
- Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, classification, and stratification. *Annals of Internal Medicine* 2003;139:137–147. [PubMed: 12859163]

- Mazbar SA, Schoenfeld PY, Humphreys MH. Renal involvement in patients infected with HIV: Experience at San Francisco General Hospital. *Kidney International* 1990;37:1325–1332. [PubMed: 2345428]
- McClellan WM, Flanders WD. Risk factors for progressive chronic kidney disease. *Journal of the American Society of Nephrology* 2003;14:S65–S70. [PubMed: 12819305]
- Míguez-Burbano, MJ.; Rodríguez, A.; Hadrigan, S.; Azor, C.; Shor-Posner, G. Renal disease in HIV-infected subjects: The deleterious effect of smoking. XV International AIDS Conference, Bangkok; Bangkok, Thailand. 2004. Abst. #17370
- Mocroft A, Kirk O, Gatell J. EuroSIDA Study Group. Chronic renal failure among HIV-1 infected patients. *AIDS* 2007;21:1119–1127. [PubMed: 17502722]
- Mocroft A, Wyatt C, Szczech L, Neuhaus J, El-Sadr W, Tracy R, et al. Interruption of antiretroviral therapy is associated with increased plasma cystatin C. *AIDS* 2009;23(1):71–82. [PubMed: 19050388]
- Molander L, Hansson A, Lunell E, Alaintalo L, Hoffmann M, Larsson R. Pharmacokinetics of nicotine in kidney failure. *Clinical Pharmacology and Therapeutics* 2000;68:250–260. [PubMed: 11014406]
- Moroni M, Antinori S. HIV and direct damage of organs: Disease spectrum before and during the highly active antiretroviral therapy era. *AIDS* 2003;17:S51–S64. [PubMed: 12870531]
- Narkiewicz K, van de Borne PJ, Hausberg M, Cooley RL, Winniford MD, Davison DE, et al. Cigarette smoking increases sympathetic outflow in humans. *Circulation* 1998;98:528–534. [PubMed: 9714109]
- National Kidney Foundation. Educational program about kidney disease in patients with HIV. 2008a [Retrieved January 27, 2008]. from: <http://www.kidney.org/news/newsroom/newsitem.cfm?id=92&&cid=68>
- National Kidney Foundation. GFR calculator. 2008b [Retrieved January 27, 2008]. from: http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm
- Orth SR, Stockmann A, Conradt C. Smoking as a risk factor for end-stage renal failure in men with primary renal disease. *Kidney International* 1998;54:926–931. [PubMed: 9734618]
- Praditpornsilpa K, Napathorn S, Yenrudi S, Wankrairo P, Tungsaga K, Sitprija V. Renal pathology and HIV infection in Thailand. *American Journal of Kidney Disease* 1999;33:282–286.
- Ross MJ, Klotman PE. Recent progress in HIV-associated nephropathy. *Journal of the American Society of Nephrology* 2002;13:2997–3004. [PubMed: 12444220]
- Stengel B, Couchod C, Lenee S, Hemon D. Age, blood pressure and smoking effect on chronic renal failure in primary glomerular nephropathies. *Kidney International* 2000;57:2519–2526. [PubMed: 10844621]
- Szczech LA. Recent developments and current issues in HIV-related renal. 2001 May 10; from <http://www.medscape.com/viewarticle/408276>.
- Tillin T, Forouhi N, McKeigue P, Chaturvedi N. Microalbuminuria and coronary heart disease risk in an ethnically diverse UK population: A prospective cohort study. *Journal of the American Society of Nephrology* 2005;16:3702–3710. [PubMed: 16207830]
- U.S. Renal Data System. USRDS Annual Data Report: Atlas of end-stage renal disease in the United States. *American Journal of Kidney Disease* 2007;51:S1–S320.
- Wesson DE. The relationship of cigarette smoking to end-stage renal disease. *Seminars in Nephrology* 2003;23:317–322. [PubMed: 12838500]
- Wyatt CM, Klotman PE. Antiretroviral therapy and the kidney: Balancing benefit and risk in patients with HIV infection. *Expert Opinion on Drug Safety* 2006;5:275–287. [PubMed: 16503748]
- Wyatt CM. Chronic Kidney Disease in HIV infection: An urban epidemic. *AIDS* 2007;21:2101–2103. [PubMed: 17885301]
- Zeller VE, Caumes P, Bossi F, Bricaire F, Katlama C. Current clinical aspects of HIV/AIDS. *Presse Med* 2002;31:74–79. [PubMed: 11850990]

* Statistically Significant

Figure 1.
Risk of Developing Chronic Kidney Disease by Packs

Table 1

CKD Definition and Stages of Chronic Kidney Disease (CKD)*

Stage	Description	GFR (mL/min/1.73 m ²)
1	Kidney Damage with normal or ↑ GFR	≥90
2	Kidney Damage with mild ↓ GFR	60 – 89
3	Moderate ↓ GFR	30 – 59
4	Severe ↓ GFR	15 – 29
5	Kidney failure	< 15

GFR = glomerular filtration rate

* CKD is defined as either kidney damage or GFR < 60 mL/min/1.73 m² for ≥ 3 months

Table 2

Study Group Characteristics

Variables	CKD <i>N</i> = 75 mean ± SD or percent	Non-CKD <i>N</i> = 461 mean ± SD or percent	<i>p</i> value
Age (years)	41.6 ± 8	42.1 ± 8.8	NS
Gender			
• Men (<i>n</i> = 306)	69%	55%	0.04
• Women (<i>n</i> = 230)	31%	45%	
Race/Ethnicity			
• African Americans	57%	62%	0.01
• Black Caribbeans	29%	16%	
• Hispanics	14%	17%	
• Caucasians	0%	4%	
• Asian	0	1%	
Substance Use			
• Alcohol users	36%	44%	NS
• Marijuana	25%	20%	
• Crack/cocaine	22%	32%	
• Heroin	1%	3%	
Number of Years Diagnosed with HIV	7.7 ± 6	7.2 ± 5.6	NS
CD4 Cell Counts/mm³	106 ± 99	187 ± 140	0.07
> 200 CD4/mm³	16%	24%	
HIV Viral Load copies/mL	212,999 ± 45,905	237,835 ± 23,112	NS
Albumin g/dl	3.1 ± 0.8	3.4 ± 0.7	0.006
Triglycerides mg/dl	298.7 ± 194	165 ± 62	NS
Cholesterol mg/dl	183.4 ± 119	169.2 ± 48	NS
Hemoglobin g/dl	10.0 ± 2.6	12.2 ± 8.5	0.06

CKD = chronic kidney disease

Table 3

Distribution of Risk Factors for CKD

Variables	CKD <i>N</i> = 75	Non-CKD <i>N</i> = 461
Cigarette smoking		
Current	69%	53%
Former	11%	9%
High Blood Pressure	33%	11%
Hepatitis		
B	27%	14%
C	15%	13%
CD4 < 200 cell counts/mm³	84%	75%
Diabetes	4%	1%

CKD = chronic kidney disease

Table 4

Odds Ratios for CKD

MODEL	UNIVARIATE OR	95% CI	MULTIVARIATE OR	95% CI	<i>p</i> Value
Cigarette Smoking	1.9	1 – 3.03	3	1.4 – 5.6	0.005
Black Caribbean	2.6	1.1 – 6.4	2.2	1.2 – 3.9	0.005
African American	1.9	1.1–4.4	1.8	1–3.7	0.04
Hypertension	2	1.7 – 3.5	2.4	1.7 – 3.5	0.0001
Male	1.6	1.0 – 3.1			NS
Hepatitis B	1.8	1.0 – 3.4			0.06

CKD = chronic kidney disease