Prevalence of chronic kidney disease in Chinese HIV-infected patients

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Abstract

Background. To evaluate the prevalence of chronic kidney disease (CKD) in Chinese HIV-infected population.

Methods. This was a cross-sectional point prevalence study. All Chinese HIV-infected patients who were followed up in a tertiary referral center in Hong Kong were recruited. Spot urine was saved for each patient to calculate urine protein-to-creatinine ratio (urine P/Cr). Those with urine P/Cr > 0.3 would have 24-h urine collection to determine the exact amount of proteinuria. Glomerular filtration rate (GFR) was estimated using MDRD formula. CKD was defined as GFR <60 ml/min/1.73 m2 and/or urine P/Cr > 0.3. Baseline demographic and clinical data were extracted from patients’ records.

Results. In total 322 patients were recruited. The mean age was 45.2 ± 11.7 years. The duration of follow up was 6.0 ± 4.0 years. There were 264 male and 58 female patients. The prevalence of hypertension, diabetes mellitus and CKD were 7.4%, 10.6% and 16.8%, respectively. Eighteen patients (5.6%) had GFR <60 ml/min/1.73 m2 while 44 patients (13.7%) had spot urine P/Cr > 0.3. Among those with urine P/Cr > 0.3, 38 patients had 24-h urine collection. Using univariate analysis, CKD was found to be significantly (P < 0.05) associated with age, hypertension, diabetes, use of indinavir, lower CD4 count and peak viral load. Multivariate logistic regression revealed older age (P < 0.001), lower CD4 count (P = 0.02) and use of indinavir therapy (P = 0.04) were associated with development of CKD.

Conclusion. CKD is prevalent in Chinese HIV-infected patients. Patients with CKD were more likely to be older, associated with use of indinavir and CD4 nadir less than 100 cells/μl.

Keywords: chronic kidney disease; human immunodeficiency virus; proteinuria

Introduction

Human immunodeficiency virus (HIV)-infected patients can develop different types of chronic kidney disease (CKD). The most common histological finding of renal biopsy is HIV-associated nephropathy (HIVAN). HIVAN is now the third most common cause of end stage renal failure (ESRF) (after diabetes mellitus and hypertension) in African-Americans aged 20–64 years [1]. With the improved survival after the use of highly active antiretroviral therapy (HAART) in HIV-infected patients, there are increasing reports of development of CKD and ESRF in this population [2]. The presence of proteinuria and elevated serum creatinine levels are positively associated with an increased risk of death (adjusted relative risk, 2.5) and higher hospitalization rates (adjusted relative risk, 1.5) [3,4]. With the possibility of improved outcomes in these patients using glucocorticoids, angiotensin-converting enzyme inhibitors and HAART, it is desirable to identify those who are at high risks of developing CKD.

According to the World Health Organization definition, the HIV prevalence in Hong Kong is low. It is estimated that there are about 3000 HIV-infected patients in this territory [5]. The indications of initiation of HAART include (i) symptomatic HIV disease, (ii) CD4 cell count <200 cells/μl, (iii) asymptomatic and CD4 cell count 200–350 cells/μl (CD4 cell count in decreasing trend with high viral load). However, there is lack of data showing the basic epidemiology of CKD in Chinese patients. In this study, we screened for the presence of CKD and evaluated its prevalence in our Chinese HIV-infected population. We also determined the clinical variables that would predict the development of CKD.
Methods

This was a cross-sectional point prevalence study. All Chinese HIV-infected patients who were followed up in the out-patient clinic of the Queen Elizabeth Hospital, the tertiary referral centre in Hong Kong, were recruited into the study. Patients who developed ESRF and received dialysis were excluded.

The study was performed in accordance with the Declaration of Helsinki. The protocol was approved by our local ethical committee. Informed and written consent were obtained. All patients were assessed for existing kidney disease with a screening urine analysis for proteinuria and a calculated estimate of glomerular filtration rate (GFR). CKD was defined as GFR <60 ml/min/1.73 m² and/or proteinuria more than 3 months. Spot urine was saved for each patient to calculate the urine protein-to-creatinine ratio (urine P/Cr). Those patients with urine P/Cr > 0.3 would have 24-h urine collection to determine the exact amount of proteinuria. GFR was calculated using the simplified modification of diet in renal disease (MDRD) equation [6]. Basic demographic and clinical variables were extracted from patients’ records. Indinavir and tenofovir therapy were identified for those taking indinavir or tenofovir, respectively, for at least 1 month.

The demographic and clinical variables were compared between the group of patients who did and did not develop CKD. Student’s t-test, Pearson’s χ² test or Fisher’s exact test was used where appropriate. Associations between the clinical variables and the development of CKD were estimated using both univariate and multivariate logistic regression analyses. The multivariate model incorporated a backward and stepwise elimination method using variables with a P-value of <0.25 from the univariate analysis. Odds ratios (OR) and 95% confidence intervals (95% CI) were also obtained. All analyses were performed using SPSS version 14 (Chicago, USA). A P-value of <0.05 was considered to be statistically significant.

Results

A total of 322 patients were recruited. The patients were diagnosed with HIV infection between 1 January 1985 and 30 June 2005. The duration of follow up was 6.0 ± 4.0 years. The baseline demographic data and clinical variables are shown in Table 1. The mean age was 45.2 ± 11.7 years. There were 264 male and 58 female patients. The body mass index (BMI) was 21.78 ± 3.07 kg/m². Three hundred and one patients (93.5%) received HAART. Among them, 107 patients had received indinavir therapy before while 17 patients had a history of tenofovir therapy. Six patients had a history of both indinavir and tenofovir therapy. The mean CD4 nadir was 102 ± 117 cells/μl (median: 50 cells/μl and range: 1–711 cells/μl). On the other hand, the mean peak viral load was 141 730 ± 159 990 copies/ml (median 78 650 copies/ml and range: 30–853 100 copies/ml). The prevalence of hypertension and diabetes mellitus was 7.4% and 10.6%, respectively. The mean GFR was 90 ± 21 ml/min/1.73 m². Eighteen patients (5.6%) had GFR less than 60 ml/min/1.73 m² while 44 patients (13.7%) had spot urine P/Cr > 0.3. Eight patients had both reduced GFR and proteinuria. The prevalence of CKD was 16.8%. Among those patients with urine P/Cr > 0.3, 38 patients had 24-h urine collection. One of the 38 patients (2.6%) had proteinuria more than 2 g per day. This patient had a long history of diabetes mellitus with nephrotic range of proteinuria. Clinically the cause was attributed to diabetic nephropathy. Four patients (10.5%) had proteinuria between 1 and 2 grams per day; and 33 patients (86.8%) had <1 g of proteinuria per day. The median 24-h urine total protein was 0.19 g per day (range: 0.05–5.73 g per day). The amount of 24-h urine total protein are categorized into subgroups, and the median and range are shown in Table 2.

CKD was found to be significantly (P < 0.05) associated with age, hypertension, diabetes mellitus, use of indinavir therapy and lower CD4 count (both absolute and <100 cells/μl) and peak viral load ≥100 000 copies/ml. There was no significant association between CKD and hepatitis status or use of tenofovir therapy (Table 1). Multivariate logistic regression revealed older age (OR 1.1, 95% CI 1.0–1.1, P < 0.001), CD4 nadir <100 cells/μl (OR 3.6, 95% CI 1.2–10.5, P = 0.02) and use of indinavir therapy (OR 6.1, 95% CI 1.7–57.6, P = 0.04) was associated with development of CKD.

The mean GFR of patients with a history of indinavir therapy was 83 ± 24 ml/min/1.73 m² while the mean GFR of those without a history of indinavir therapy was 94 ± 18 ml/min/1.73 m². The difference between them was statistically highly significant (P < 0.001).

Discussion

This is the first study evaluating the prevalence of CKD and proteinuria in a Chinese HIV-infected population. Different criteria for classification of CKD were used in different studies. The criteria used in our study were based on the definition defined by the National Kidney Foundation, i.e. GFR <60 ml/min/1.73 m² and/or proteinuria more than 3 months [7]. Abnormal kidney function may not be recognized among patients who have lower relative muscle mass using serum creatinine level alone. Equations adjusting for surrogates of muscle mass (e.g. age, weight, race and sex), therefore, provide a more sensitive estimation of true renal function. However, all these equations have not been validated for the HIV-infected population. There is no absolutely preferred equation to use consistently among HIV-infected patients. In our study, estimated GFR was calculated using simplified MDRD formula because it is generally preferred in staging CKD purpose [8]. Although limited data suggest that the equation may overestimate GFR in the Chinese population, there is still a lack of widely accepted formula for the estimation of GFR in our population. Moreover, spot urine was collected from each patient to measure the
urine protein-to-creatinine ratio. These quantitative urine measurements of abnormal glomerular function are accurate, correlate with 24-h urine measurements and avoid the inconvenience of and difficulty in the collection of timed urine specimens in clinical practice [9]. The BMI of our patients were comparable with our general population. As our patients had a good nutritional state and a normal serum albumin level, concerns that estimated GFR and urine P/Cr ratio being compromised by a patient’s cachexic state are not well founded.

It is well established that HIVAN is the predominant renal manifestation in HIV-infected patients of African-American descent. However, it is not common in other racial groups [10–12]. In an Ethiopian population, the clinical definition used for HIVAN was proteinuria >2 g per day in an HIV-seropositive patient without other predisposing factors for renal damage [13]. None of our patients fulfilled the criteria. This shows that HIVAN is extremely rare in our population. However, lack of histological data may raise the concern that some cases of renal insufficiency can still be unrecognized HIVAN.

Different risk factors associated with the development of CKD were identified in African-American patients. However, there was no such data concerning the Chinese population in literature. In this study, we evaluated different risk factors for CKD in our HIV-infected patients. We found that patients with CKD were more likely to be older, associated with use of indinavir and CD4 nadir <100 cells/μl.

Many studies showed that low CD4 cell count is a risk factor for CKD [14,15]. However, few studies have assessed viral load as a risk factor for CKD despite

<table>
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<tr>
<th>Subgroup of proteinuria (g/day)</th>
<th>Number of patients (n = 38)</th>
<th>Median of proteinuria (g/day)</th>
<th>Range of proteinuria (g/day)</th>
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<tr>
<td>&lt;1</td>
<td>33</td>
<td>0.17</td>
<td>0.05–0.69</td>
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<td>1–2</td>
<td>4</td>
<td>1.41</td>
<td>1.13–1.85</td>
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<tr>
<td>&gt;2</td>
<td>1</td>
<td>5.73</td>
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Table 2. Median and range of proteinuria in each subgroup

Values expressed as mean ± SD or number (percentage).

*Pearson’s χ² test, †Student’s t-test.
Prevalence of CKD in Chinese HIV patients

evidence of a direct pathogenic role of HIV [16]. In a study by Krawczyk et al. [17] the highest ever viral load was found to be statistically significant only in univariate analyses but not in multivariate analyses. In this study, higher peak viral load was also significantly associated with development of CKD only in univariate analyses. This may be explained by the possibility that viral load may not be a sensitive risk indicator for CKD when patients are already advanced in their HIV disease and have initiated HAART. This was supported by another study in which the viral load was associated with declining creatinine clearance only during early visits, where few had started antiretroviral therapy [3].

Several studies have reported the beneficial prognostic effects of HAART on renal diseases, including non-HIVAN [18,19]. However, the individual effects of specific antiretroviral agents are not shown. The need of prolonged use of HAART makes long-term toxicity an important issue. Indinavir is a commonly used protease inhibitor with known renal adverse effects. In our study, we found that use of indinavir was significantly associated with development of CKD in both univariate and multivariate analyses (OR 6.1). Moreover, we also showed that the renal function was significantly better in patients without a history of indinavir therapy. Nephrolithiasis and crystalluria are the most common serious adverse effects of indinavir. Patients receiving indinavir may have progressive elevation of serum creatinine [20]. Most urologic symptoms and elevations in serum creatinine levels normalize within weeks after discontinuation of indinavir. However, irreversible renal toxicity has been reported [21]. It has been shown that indinavir can cause vasoconstriction and reduce renal blood flow [22]. Tenofovir is a nucleotide reverse-transcriptase inhibitor known to be associated with renal tubular damage. In general, the tubular dysfunction is reversible after withdrawal of tenofovir [23], although persistent renal damage with impairment of renal function has been reported [24]. However, in all randomized, double-blinded studies, tenofovir had been demonstrated to have a renal safety profile similar to that of other combination therapies and to have an overall low potential for nephrotoxicity [25–27]. In our study, the lack of association between CKD and use of tenofovir might also be related to the small number of patients.

Conclusion

Although HIVAN is uncommon in the Chinese population, CKD occurs in 16.8% of Chinese HIV-infected patients. Those patients who are older, have a history of indinavir therapy and CD4 nadir <100 cells/μl are more likely to develop CKD. However, renal biopsy is required to determine the spectrum of renal diseases in our HIV-infected population.

Conflict of interest statement. None declared.

References


Received for publication: 25.10.06
Accepted in revised form: 8.5.07