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Original Article

Prevalence of renal impairment among HIV positive patients hospitalized in the first hospital of China medical university

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Abstract: Background: HIV positive patients are at high risk of kidney disease, end-stage renal disease and renal death. We aimed to evaluate the prevalence and risk factors of renal impairment among HIV positive patients hospitalized in The First Hospital of China Medical University. Methods: We did a retrospective study of in-patient samples of Chinese HIV positive patients. Estimated glomerular filtration rate (eGFR) was calculated by creatinine and cystatin C based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPIscr-cys) equation. Urine protein was measured by spot urine dipstick examination, and urine protein ≥1+ was defined as proteinuria. Risk factors for renal impairment were assessed by multivariate logistic regression. Results: In total, 306 patients were included in this study. There were 15 female and 291 male patients. The mean age was 39.91±11.63 years. The weight was 59.69±10.67 kg. The mean CD4 T cell count was 101.47±163.76/μl (median: 37/μl and range: 1-1428/μl). The mean eGFR CKD-EPIscr-cys was 97.58±19.68 ml/min/1.73 m^2. Ten (3.26%) patients had eGFR <60 ml/min/1.73 m^2, nine (2.94%) patients had proteinuria ≥1+ and 2 patients had both eGFR <60 ml/min/1.73 m^2 and proteinuria ≥1+. Using multivariate regression analysis, renal impairment was significantly correlated with age (OR 2.294, 95% CI 1.490-3.533, P=0.000) and highly active antiretroviral therapy (HAART) (OR 0.173, 95% CI 0.036-0.838, P=0.029). Conclusions: The prevalence of renal impairment among Chinese hospitalized HIV positive patients was 5.56% (17/306). Older age was a risk factor for renal impairment and HAART showed a beneficial effect on renal function.

Keywords: Renal impairment, HIV, cystatin C and creatinine based Chronic Kidney Disease Epidemiology Collaboration equation, highly active antiretroviral therapy

Introduction

Until October 2015, an estimated 575000 people were living with HIV infection in China. Nowadays, the introduction of highly active antiretroviral therapy (HAART) dramatically changes the HIV infection from a fatal disease to a chronic controlled condition, improving the survival of HIV positive patients [1]. As their life span prolonged, chronic morbidities needs more concern.

In recent 10 years, chronic kidney disease becomes one of the leading public health problems. Chronic kidney disease is highly prevalent in developing countries [2, 3]. A cross-sectional survey of a nationally representative sample of Chinese adults showed the overall prevalence of chronic kidney disease was 10.8% [4]. Compared with the general population, HIV positive patients are at high risk of chronic kidney disease [5], end-stage renal disease and renal death [6, 7]. As for the prevalence of renal impairment in Chinese HIV positive patients, there are several cohort studies [8-10]. To evaluate the renal function, they used Modification of Diet in Renal Disease (MDRD) equation to calculate the estimated glomerular filtration rate (eGFR). However, recent studies demonstrated that compared with MDRD, creatinine and cystatin C based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPIscr-cys) equation appeared to be more accurate especially in HIV positive individuals [11]. Moreover, CKD-EPIscr-cys equation also showed a better capability to evaluate eGFR in Chinese ethnic [12]. Thus we

Table 1. Baseline demographic and clinical variables of HIV positive patients hospitalized in The First Hospital of China Medical University

Clinical variable	eGFR ≥60 ml/min/1.73 m^2 n=289	eGFR <60 ml/min/1.73 m^2 or proteinuria ≥1+ n=17	*P*-value
Sex			0.85
Male	275 (95.2)	16 (94.1)	
Female	14 (4.8)	1 (5.9)	
Age (years)	39.33±11.11	49.71±15.76	0.016*
Weight (kg)	59.81±10.45	57.76±10.93	0.463
Hypertension			0.012*
Yes	12 (4.2)	3 (17.6)	
No	277 (95.8)	14 (82.4)	
Diabetes Mellitus			0.114
Yes	11 (3.8)	2 (11.8)	
No	278 (96.2)	15 (88.2)	
Hepatitis B			0.576
Yes	29 (10.0)	1 (5.9)	
No	260 (90.0)	16 (94.1)	
Hepatitis C			0.308
Yes	6 (2.1)	1 (5.9)	
No	283 (97.9)	16 (94.1)	
Opportunistic infection			0.911
Yes	241 (83.4)	14 (82.4)	
No	48 (16.6)	3 (17.6)	
CD4 T cell count (cells/ul)	98.75±163.99	118.47±135.01	0.627
CD4 T cell count			0.732
≥100	210 (72.7)	4 (23.5)	
<100	79 (27.3)	13 (76.5)	
WHO Clinical Stage			0.849
1-2	46 (15.92)	3 (17.65)	
3-4	243 (84.08)	14 (82.35)	
Use of HAART			0.059
Yes	98 (33.9)	2 (11.8)	
No	191 (66.1)	5 (88.2)	
Use of tenofovir			0.165
Yes	56 (19.4)	1 (5.9)	
No	233 (80.6)	16 (94.1)	

Values are expressed as mean ± SD or number (percentage). *represent significant difference between two groups.

employed CKD-EPIscr-cys equation to assess the eGFR of Chinese HIV positive patients.

This study aimed to evaluate the renal function in the hospitalized HIV positive patients in The First Hospital of China Medical University by CKD-EPIscr-cys equation and to determine the possible risk factors associated with the renal impairment.

Patients and methods

This was a retrospective study. The study population comprised of HIV seropositive patients aged 16 years and above hospitalized in The First Hospital of China Medical University from 1st November 2010 to 30th August 2016. The clinical and demographic data were extracted from the patients' electronic medical records. Patients with acute renal failure, urinary tract infection or obstruction, past history of kidney disease, pregnant patients or patients without baseline creatinine and cystatin C measurements were excluded. 306 HIV seropositive patients who met the study criteria and presented within the study period were included in the study. The Human Research Ethics Committee of The First Hospital of China Medical University approved the study (Certificate number: 2016-211-2).

The following baseline demographic and clinical variables were assessed at the time of initial evaluation for all patients: age, sex, weight, blood pressure, presumed duration of HIV seropositive based on known dates of first HIV test, World Health Organization (WHO) HIV/AIDS clinical stage, presence of diabetes mellitus, hypertension, chronic infection with either hepatitis B or C virus, opportunistic infection, initiation of HAART and the regimen, serum creatinine and cystatin C, urine protein and total blood CD4 T cell count. HAART and TDF therapy were identified respectively for at least 1 month. Serum creatinine was measured in μmol/l. The eGFR was calculated by the CKD-EPIscr-cys equation [13].

To determine the possible risk factors associated with renal impairment, patients were divided into two groups as eGFR ≥60 ml/min/1.73 m^2 and eGFR <60 ml/min/1.73 m^2 or urine protein ≥1+. The demographic and clinical variables were compared between these two gro-

Table 2. Multivariate logistic regression analysis of risk factors for renal impairment in HIV positive patients hospitalized in The First Hospital of China Medical University

Characteristics of patients	OR (95%)	*P*-value
Age (per 10 year increase)	2.294 (1.490-3.533)	0.000*
Initiation of HAART	0.173 (0.036-0.838)	0.029*

*represent significant difference between two groups.

ups. Categorical variables were analyzed using χ^2 test, and continuous variables were analyzed by student's t test (for normally distributed variables). Correlations between the clinical variables and renal impairment were analyzed by both univariate and multivariate logistic regression. The multivariate model incorporated a backward and stepwise elimination method using variables with a *P*-value of <0.25 from the univariate analysis. Odd ratios (OR) and 95% confidence intervals (95% CI) were also obtained. All analyses were performed using SPSS 18.0 (Chicago, IL, USA). A *P*-value <0.05 was considered statistically significant.

Results

Demographics and clinical features

In total, 306 patients were included in this study. The patients were diagnosed with HIV infection between October 2002 and August 2016. The baseline demographic data and clinical variables are shown in **Table 1**. There were 15 female and 291 male patients. The mean age was 39.91±11.63 years. The weight was 59.69±10.67 kg. The mean CD4 T cell count was 101.47±163.76/μl (median: 37/μl and range: 1-1428/μl). The mean creatinine was 62.93 ±23.67 μmol/l and mean cystatin C was 1.08 ±0.32 mg/l. 103 patients received HAART, and the HAART drugs used in this study were lamivudine (3TC), zidovudine (AZT), stavudine (D4T), nevirapine (NVP), efavirenz (EFV), disoproxil fumarate (TDF) and lopinavir/ritonavir (LPV/r). 56 patients received TDF-based treatment. The mean duration of HAART and TDF therapy was 10.88±17.38 months (range: 1-96 months) and 7.40±10.32 months (range: 1-48 months) respectively. The overall prevalence of opportunistic infection was 83.33% and prevalence of pneumocystis jiroveci pneumonia, tuberculosis, candidiasis and cryptococcal meningitis was 42.14% (132/306), 37.58% (115/306), 23.53% (72/306) and 5.56% (17/306) respectively. The prevalence of hypertension and diabetes mellitus was 4.90% (15/306) and 4.25% (13/306) respectively. The prevalence of HBV and HCV infection was 9.80% (30/306) and 2.61% (8/306). The mean eGFR was 97.58±19.68 ml/min/1.73 m^2. Ten (3.26%) patients had eGFR <60 ml/min/1.73 m^2, nine (2.94%) patients had proteinuria ≥1+ and 2 patients had both eGFR <60 ml/min/1.73 m^2 and proteinuria ≥1+. The prevalence of renal impairment as eGFR <60 ml/min/1.73 m^2 and/or proteinuria ≥1+ was 5.56% (17/306).

Rask factors

Age and presence of hypertension were found significantly different between two groups in the univariate analysis (*P*=0.016 and *P*=0.012 respectively). Using multivariate regression analysis, renal impairment was significantly correlated with age (OR 2.294, 95% CI 1.490-3.533, *P*=0.000) and HARRT (OR 0.173, 95% CI 0.036-0.838, *P*=0.029) (**Table 2**).

Discussion

Here we report the prevalence of renal impairment in Chinese HIV positive patients hospitalized in The First Hospital of China Medical University by evaluating eGFR with CKD-EPIscrcys equation. The prevalence of renal impairment with eGFR less than 60 ml/min/1.73 m^2 was 3.27%, and the prevalence of proteinuria was 2.94%. The renal impairment was correlated with age, and HAART showed beneficial effect on renal function.

In this study, the patient population was hospital in-patient, most of whom were in malnutrition and with muscle wasting diseases as pneumocystis jiroveci pneumonia, tuberculosis, candidiasis and cryptococcal meningitis. Less muscle mass and lower dietary could lead to less creatinine generation. For patients with lower body mass, creatinine based equation is less accurate which may overestimate eGFR. Cystatin C production is independent of muscle mass and dietary influences, and the cystatin C based prediction equation are therefore potentially not subjected to the limitations of creatinine based equations [14]. Hence the cystatin C based formula seems more suitable for the patients enrolled in this study. However, the cystatin C-only based equations do not perform

better than creatinine-only based equations [13]. So in this study, to calculate eGFR, CKD-EPIscr-cys equation was employed which further demonstrated more accurate than either MDRD or Cockcroft-Gault equation in HIV positive patients and in Chinese patients with chronic kidney diseases [11, 12].

Compared with the former studies, the prevalence of renal impairment in our study was lower. This discrepancy might come from: First, the equation chosen in the former studies to calculate eGFR was MDRD. Moving from MDRD to CKD-EPIscr-cys would decrease the prevalence of CKD [15]. Second, our study is regional. The First Hospital of China Medical University is a tertiary hospital localized in northeast China, of which over 90% patients come from north area of China. As for the different geographical regions, the prevalence of low eGFR and albuminuria differs [4]. Third, in our study the lower prevalence of renal impairment was partly due to the lower prevalence of proteinuria (2.94%) as compared with Cao's (12.2%) [9] and Cheung's (13.7%) studies [8]. In the present study, the initial routine urine check showed 31 of 306 (10.13%) patients had proteinuria as evidenced by urine protein ≥1+. However, 15 of them were febrile when proteinuria was evaluated. In our clinical practice, all urine samples from patients with proteinuria were tested at least twice at different time points and at last only nine samples with persistent pathological proteinuria evidenced by repeated measurements were considered positive.

By multivariable analysis, we found that the renal impairment was associated with older age which was consistent with other studies. Moreover, initiation of HAART showed beneficial effect on renal function. This could be explained by its effective inhibition of viral load. Viral load has been identified as risk factor for renal impairment [9, 16], and sustained suppression of viral replication can have direct beneficial effect on renal function [17]. Nowadays, TDF is a first-line treatment of HIV infection and was used in 54.37% HAART regimens in the present study likewise the conditions in other countries [18, 19]. Even though cases of acute kidney injury (AKI), proximal tubular dysfunction and CKD induced by TDF have been frequently reported [20], no significant correlation was found between TDF treatment and renal impairment in present study, which could demonstrate the renal safety of TDF treatment in HIV positive patients. However, lack of association between TDF treatment and renal impairment might also relate to the short term usage. In our study, the mean time of TDF treatment was 7.4 months with the longest treatment of 48 months. Renal safety of long-term TDF treatment needs further investigation in our patient population.

There are several limitations in this study. First, this is a retrospective study which does not allow us to collect kidney markers over a period of three months as normally required for the final CKD diagnosis [21]. However, there are also some studies investigating renal impairment use one-time-only evaluation of eGFR [22]. Second, evaluation of proteinuria might be not accurate just defined as protein urine ≥1+ by spot urine dipstick examination. Spot urine protein-to-creatinine and spot urine albumin-to-creatinine should be monitored among patients with proteinuria. Third, it is better to confirm the beneficial effect of HAART initiation on renal function by measuring HIV viral load. However, due to the high expense, viral load measurement was not performed in all patients. Fourth, inflammation is one of the factors that might affect serum cystatin C level other than GFR [23]. Most patients in this study were with inflammatory diseases as pneumocystis jiroveci pneumonia, tuberculosis and other opportunistic infections. The association between inflammation and serum cystatin C level would lead to systemic bias of eGFR CKD-EPIscr-cys in this patient population, which needs further investigation.

Conclusion

This study revealed that 5.56% hospitalized Chinese HIV positive patients were with impaired renal function evaluated by eGFR CKD-EPIscr-cys equation. The renal impairment was found to be correlated with older age and HAART showed a beneficial effect on renal function. Thus the study highlighted the importance of monitoring renal function especially for elderly patients and emphasized the early initiation of HAART for patients with low CD4 T cell count and high risk of renal impairment.

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Disclosure of conflict of interest

None.

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