Patient-Reported Noninfectious Comorbidities in Chinese HIV-Infected Patients: The Gaps Among Self-Awareness, Diagnosis, and Prevalence

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Abstract

Background: This study was performed to investigate the gaps among patient-reported data, physician-reported data, and laboratory test data in human immunodeficiency virus (HIV)-infected patients and to detect potential risk factors for the awareness gap.

Methods: We included patients from 38 hospitals in China. Patient-reported data, physician-reported data, and laboratory test data on four typical noninfectious comorbidities (NICMs) (osteoporosis, kidney disease, neuropsychiatric comorbidities, and atherosclerotic cardiovascular disease (ASCVD)) were collected. We compared differences in and consistency of these types of data and investigated the associations between baseline characteristics and the awareness gap between patients and physicians.

Results: This study included 1390 patients. The difference between the diagnosis rate and laboratory test positivity rate for all NICMs was significant. Patient-reported data on the three NICMs other than kidney disease were significantly different from the diagnosis rates. The agreement between patients and physicians for all NICMs was poor. The region, infection stage, hospital level, sex, and age influenced the awareness gap between patients and physicians.

Conclusions: Our findings suggest that NICMs in HIV-infected patients in China are underestimated; gaps among patient awareness of disease exist, the clinical diagnosis rate, and the actual prevalence; patient characteristics influence the awareness gap between patients and physicians.

Background

The prevalence of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), which is a complex chronic disease, still imposes a considerable burden on the medical system, especially in developing countries ^{1–3}. The growing HIV-infected population is still a challenge for the Chinese medical system ⁴. The incidence of HIV infection in China increased to 4.2 per 100 000 individuals in 2017 from 0.23 per 100 000 in 2004 ⁵. In addition, the HIV-infected population is also living longer, and the number of middle-aged and older people who are newly infected with HIV is rising rapidly ^{6,7}.

The introduction of combination antiretroviral therapy (ART) has contributed substantially to the reductions in morbidity and mortality associated with HIV infection ^{8,9}. Despite the increased life expectancy, mortality remains 3- to 15-fold higher in HIV-infected people than in the general population ^{9,10}. Together with the increased life expectancy of HIV-positive patients and the expansion of the elderly HIV-infected population, long-term treatment toxicity and old age-associated comorbid conditions have become more prevalent in these patients ^{11–13}. In addition, the progression of HIV infection may exacerbate or cause comorbidities. Although diseases caused by immunodeficiency contribute some to the excess mortality observed in the HIV-infected population, noninfectious comorbidities (NICMs) lead to more than half of the deaths among HIV-infected patients who undergo ART ^{14,15}. Renal failure,

osteoporosis, neuropsychiatric comorbidities, and cardiovascular disease (CVD) are representative NICMS among HIV-infected patients, as these conditions have relatively high prevalences in HIV-infected patients^{8, 15–17}.

Research is needed to determine whether these comorbidities are underestimated among HIV populations. Insufficient awareness on the part of both doctors and patients may lead to the underestimation of NICMs and the absence of related diagnosis and treatment, which in turn may lead to increased mortality and decreased patient quality of life^{10, 18}. In addition, this kind of research is particularly lacking in the Asian HIV-infected population. Therefore, research focusing on the differences among the patient awareness, clinical diagnosis, and prevalence of NICMs based on national survey data of HIV-infected patients is needed to fill this gap. To better understand the NICM awareness gap and the associated risk factors, this cross-sectional study was conducted. This study explored the gap between patient-reported data and physician-reported data and the gap between the clinical diagnosis rate and laboratory test positivity rate.

Methods

Study Design And Participants

A national survey was conducted in 38 hospitals. In total, 139 physicians from the departments of infectious diseases in these hospitals were selected; then, ten patients seen by each physician were selected randomly. The inclusion criteria for the patients were as follows: (1) use of ART and (2) ability to understand and complete the questionnaire (including four self-assessment scales for osteoporosis, depression, anxiety, and sleep disorders). The questionnaire used in this survey included baseline information and information on comorbid conditions, and it was completed by both the physician and the patient. The questionnaire was paper-based, and the involved doctors interviewed their own patients and completed the questionnaire based on the interview. This study was evaluated and approved by the ethics committee of Shanghai Public Health Clinical Center. Written informed consent was obtained from all patients and doctors before the survey began.

Noninfectious Comorbidities

Four classes of common noninfectious comorbidities, namely, osteoporosis, kidney disease, neuropsychiatric comorbidities, and atherosclerotic cardiovascular disease (ASCVD), were investigated in this study. Patient-reported data, physician-reported data, and laboratory test data on the above four groups of diseases were collected via the questionnaire, and we further summarized them into 12 binary variables. Details are as follows:

Osteoporosis

The patient self-reported osteoporosis risk was measured by the IOF Osteoporosis Risk Check ^{19, 20}. Physician-reported osteoporosis was measured by the diagnosis records regarding osteoporosis and related diseases. The laboratory indicator (gold standard) of osteoporosis was bone mineral density in the lumbar spine and hip (within the last 6 to 12 months).

Kidney diseases

Self-reported kidney disease was indicated by the patient-reported chronic kidney disease stage. The physician-reported metric was the diagnostic record for kidney diseases. The laboratory indicators of kidney disease were the blood urea nitrogen and creatinine levels. ^{21–23}

Neuropsychiatric comorbidities

The neuropsychiatric comorbidities measured in this survey were anxiety, depression, and sleep disorders ^{24, 25}. Self-reported neuropsychiatric comorbidities were measured by the Chinese versions of three self-rated scales for anxiety ²⁶, depression ²⁷, and sleep disorders ²⁸. Physician-reported neuropsychiatric comorbidities were obtained from the diagnostic records of the above neuropsychiatric comorbidities.

ASCVD

The self-reported ASCVD risk was determined by the patient-reported ASCVD risk factors. Physician-reported ASCVD was obtained from the diagnostic records of cardiovascular diseases. The laboratory indicator for ASCVD was the 10-year risk of ASCVD, calculated based on blood pressure, diabetes history, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) ^{29, 30}.

Statistical analysis

R language (version 3.6.2) was used for all analyses. Proportions or mean values and standard deviations were used for the descriptive analysis of the baseline characteristics. Comparisons between two groups were made using chi-square tests (a 2-tailed probability value of 0.05 was considered significant). The consistency of the two measurements for the same disease was determined with Cohen's kappa coefficient ³¹. An awareness gap was defined by an inconsistency in the information reported by physicians and patients regarding noninfectious comorbidities. Multiple logistic regression analysis was applied to detect potential associations between background characteristics and awareness gaps. The associations were considered statistically significant at the $P < 0.05$ level.

Results

Baseline characteristics

There were 139 physicians and 1390 HIV-infected patients who eventually participated in the survey. As shown in Table 1, nearly half of the participants were from the eastern region of China (45.3%), followed

by the western region (38.8%); the lowest proportion of participants was from the central region (15.8%). A total of 95.0% of the participants were from tertiary hospitals. The average age of the patients was 48.8 (13.8) years old. Most patients were male (79.9%). The average body mass index of patients was 22.2 kg/m² (3.6). More than half of the patients were in the clinical latency stage (59.2%); 40.4% of patients were in the AIDS stage; and only 0.4% of patients were in the acute HIV infection stage. More than half of the patients were on urban employee basic medical insurance (62.1%); 21.4% of patients were on the new rural cooperative medical scheme; 16.5% of patients were self-funded; and only 0.2% of patients were on commercial insurance. A total of 97.6% of the patients were included in the Integrated AIDS Information System.

Table 1
Baseline characteristics of enrolled doctors and patients, china

Characteristics	% or Mean (Standard Deviation)
Doctor (n = 139)	
Region	
East	45.3
Central	15.8
West	38.8
Hospital Level	
Tertiary	95.0
Others	5.0
Patients (n = 1390)	
Age, years	48.8 (13.8)
Sex	
Male	79.9
Female	20.1
BMI	22.2 (3.6)
Stages of HIV Infection	
Acute HIV Infection	0.4
Clinical Latency	59.2
AIDS	40.4
Medical Insurance	
Urban Employee Basic Medical Insurance	62.1
New Rural Cooperative Medical Scheme	21.4
Self-Funded	16.5
Commercial Insurance	0.2
Included in "Integrated AIDS Information System"	97.6

Comparison And Consistency In Different Nicms

Figure 1 shows a comparison among patient-reported results, physician-reported results, and laboratory indicators. The proportion of patients with self-reported existing osteoporosis disease risks was 83.6%, and the physician diagnosis rate was only 0.7%. Only 37 patients underwent a bone density test, and the proportion of those patients who had osteoporosis was 16.2%. There was a significant difference between patient-reported disease risk and the diagnosis rate ($P < 0.001$); the difference between the diagnosis rate and laboratory test results was also significant ($P < 0.001$). The proportion of patients who reported kidney diseases was 3.8%; the physician-reported diagnosis rate was 5.4%; and the rate of positivity on laboratory tests was 11.3%. The difference between the patient-reported disease risk and the physician-reported diagnosis rate for kidney diseases was nonsignificant ($P = 0.052$), while the difference between the diagnosis rate and the laboratory test results was significant ($P < 0.001$). The proportion of patients who reported neuropsychiatric comorbidities was 66.0%, and the diagnosis rate was 16.0%. No related laboratory test indexes for neuropsychiatric comorbidities were investigated in this study. There was a significant difference between the patient-reported disease risk and physician-reported diagnosis rate ($P < 0.001$). The proportion of patients who reported ASCVD was 25.7%; the diagnosis rate was 4.2%; and the rate of positivity on laboratory tests was 42.3%. The patient-reported disease risk for ASCVD was significantly different from the physician-reported diagnosis rate ($P < 0.0001$), and the difference between the diagnosis rate and the laboratory test results for ASCVD was also significant ($P < 0.001$). In addition, the differences among patient-reported results, physician-reported results, and laboratory indicators for osteoporosis, kidney diseases and ASCVD were all significant (all $P < 0.001$).

To assess the interrater reliability of the patient-reported results and the physician-reported clinical diagnosis results for the same disease, we also calculated the Kappa statistic (as shown in Table 2). We found that the patient-reported results and physician-reported results were more similar for kidney disease than for the other three groups of diseases; while the percentage agreement was the same, the percentage agreement that would occur 'by chance' was significantly larger for kidney disease (0.395 compared to 0.001, 0.170, and 0.075). However, according to Landis and Koch³¹, these results showed that the agreement between patients and physicians with regard to all four diseases was poor. The agreement with regard to osteoporosis, neuropsychiatric comorbidities, and ASCVD was slight, and the agreement with regard to kidney diseases was fair.

Table 2
Cohen's kappa coefficient for comorbidities

Cohen's Kappa Coefficient for Comorbidities									
Comorbidity		Osteoporosis		Kidney Disease		Neuropsychiatric Comorbidities		ASCVD	
Patient-Reported Results									
		Yes	No	Yes	No	Yes	No	Yes	No
Physician-Reported Diagnosis	Yes	9	1	27	48	218	4	29	30
	No	1153	227	26	1289	697	471	318	1003
Cohen's Kappa		0.001		0.395		0.170		0.075	

Potential Risk Factors And Nicm Awareness Gaps

Table 3 shows the results for the associations between potential risk factors and the awareness gap between patients and physicians for the four NICMs included in this study based on the results of multiple logistic regressions. Patients from the central and western regions were more likely to report results that were inconsistent with those reported by their physician than were patients from the eastern region with regard to osteoporosis (odds ratio (OR) = 1.96, 95% confidence interval (CI): 1.25, 3.07; OR 3.45, 95% CI: 2.41, 4.95; respectively) and neuropsychiatric comorbidities (OR = 2.69, 95% CI: 1.89, 3.81; OR = 2.12, 95% CI: 1.66, 2.71; respectively). Patients from tertiary hospitals were less likely to report information that was inconsistent with that reported by their physicians with regard to neuropsychiatric comorbidities (OR = 0.48, 95% CI: 0.20, 0.89). Old age (age $\geq$ 60) increased the risk of awareness gaps with regard to osteoporosis (OR = 2.37, 95% CI: 1.53, 3.67), kidney disease (OR = 3.71, 95% CI: 2.32, 5.93) and ASCVD (OR = 3.11, 95% CI: 2.36, 4.10). Male patients were less likely to report information that was inconsistent this that reported by their physicians with regard to kidney diseases (OR = 0.48, 95% CI: 0.29, 0.79). Patients with acute HIV infections and those in the clinical latency stage were less likely to report results that were inconsistent with those of their physician compared with patients with AIDS with regard to kidney diseases (OR = 0.04, 95% CI: 0.01, 0.16; OR = 0.04, 95% CI: 0.01, 0.18; respectively) and ASCVD (OR = 0.34, 95% CI: 0.14, 0.86; OR = 0.34, 95% CI: 0.13, 0.86; respectively). Additionally, inclusion in the “Integrated AIDS Information System” was a protective factor against an awareness gap with regard to ASCVD (OR = 0.43, 95% CI: 0.22, 0.86).

Table 3

Multiple logistic regression analysis of risk factors for nicms awareness gaps between doctors and patients

Characteristics (n = 1390)	Osteoporosis		Kidney Disease		Neuropsychiatric Comorbidities		ASCVD	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Region (East as reference)								
Central	1.96 ^{**}	1.25, 3.07	0.95	0.43, 2.06	2.69 ^{***}	1.89, 3.81	0.72	0.48, 1.07
West	3.45 ^{***}	2.41, 4.95	1.47	0.89, 2.43	2.12 ^{***}	1.66, 2.71	0.81	0.61, 1.07
Tertiary Hospital	0.49	0.20, 1.23	3.50	0.87, 14.01	0.48 ^{**}	0.20, 0.89	1.33	0.70, 2.51
Old Age (Age ≥ 60 years)	2.37 ^{***}	1.53, 3.67	3.71 ^{***}	2.32, 5.93	0.97	1.53, 1.27	3.11 ^{***}	2.36, 4.10
Male	1.00	0.68, 1.47	0.48 ^{**}	0.29, 0.79	0.78	0.68, 1.03	1.27	0.92, 1.76
Overweight (BMI ≥ 24 kg/m ²)	1.30	0.92, 1.82	1.50	0.90, 2.51	0.96	0.92, 1.24	1.28	0.97, 1.70
Stages of HIV Infection (AIDS as reference)								
Acute HIV Infection	2.54	0.83, 7.83	0.04 ^{***}	0.01, 0.16	1.26	0.83, 3.08	0.34 [*]	0.14, 0.86
Clinical Latency	2.67	0.86, 8.27	0.04 ^{***}	0.01, 0.18	1.35	0.86, 3.32	0.34 [*]	0.13, 0.86
With Any Medical Insurance	1.20	0.84, 1.71	0.84	0.45, 1.57	0.86	0.84, 1.16	1.17	0.83, 1.66
Included in "Integrated AIDS Information System"	1.63	0.75, 3.55	0.42	0.14, 1.24	1.86	0.75, 3.65	0.43 [*]	0.22, 0.86
* <i>P</i> < 0.05; ** <i>P</i> < 0.01; *** <i>P</i> < 0.001.								
***: <i>P</i> < 0.001								

Discussion

The prevalence of HIV/AIDS still imposes a substantial burden on the Chinese medical system because it is a complex chronic disease, and the HIV-infected population is still increasing. With aging and the

increasing life expectancy of the HIV-positive population, as well as the rapidly increasing number of newly infected middle-aged and older adults, the toxicity associated with long-term treatment and old age-associated comorbidities are becoming more prevalent in patients. There have been few relevant studies on the awareness of NICMs and the gaps among the self-awareness of diseases, the diagnosis rate, and the prevalence according to laboratory indicators in HIV-infected patients, especially in the Chinese population. Therefore, to provide evidence to support clinical work, we conducted this study. In this study, patient-reported data, physician-reported data (the diagnosis of related diseases), and laboratory test results were compared. We found that the patient-reported risks of osteoporosis, neuropsychiatric comorbidities, and ASCVD were significantly different from the diagnosis rates; the difference between the patient-reported disease risk and diagnosis rate for kidney disease was nonsignificant. The differences between the diagnosis rate and rate of positivity on laboratory tests for all four groups of diseases were statistically significant. The differences among the above three disease assessment methods for all four groups of diseases were also statistically significant. In addition, we also assessed the interrater reliability of the patient-reported results and the physician-reported clinical diagnoses for the same diseases. We found that the agreement between patients and physicians with regard to all of the above four diseases was poor ($\kappa < 0.400$). The agreement with regard to osteoporosis, neuropsychiatric comorbidities, and ASCVD was slight, and the agreement with regard to kidney diseases was fair.

To further analyze the findings we obtained and place them in context, we reviewed the prevalence of NICMs in the HIV-infected population in China and provided further interpretation. A limited number of studies have focused on osteoporosis in HIV-infected Chinese patients. Hsieh et al.³² conducted a multicenter study with 263 HIV-infected patients in China, and they found that 10.7% of patients reported a fracture history (though the majority of the cases were linked to trauma). Guo et al.³³ observed lower bone mineral density in HIV-infected patients than in noninfected controls. In this study, we found a high self-reported risk (83.6%) of osteoporosis in our sample, and the rate of a positive identification of osteoporosis in the patients who underwent a bone density test was 16.2%. However, the diagnosis rate was only 0.7%. This result may be due to the physicians' lack of awareness of this group of diseases, which stems from the fact that osteoporosis is usually not significant or fatal when it occurs. This may also explain the extremely low proportion of patients in our sample who underwent bone density tests, which in turn further reduced the rate of diagnosis of osteoporosis.

The incidence of chronic kidney disease is high in Chinese HIV-infected patients. A cross-sectional study with HIV-infected ART-naïve patients reported a prevalence of 16.1%³⁴, and another cross-sectional study with 322 Chinese patients reported a prevalence of 16.8%³⁵. In our sample, the prevalence of kidney diseases was lower than but relatively close to the prevalence in the general Chinese population (10.8% (10.2–11.3))²¹. This difference may be related to the fact that compared with this study, the studies mentioned above were based on relatively small samples from large tertiary hospitals. As a result, the patients in their sample may have had more severe disease and have undergone ART for a longer time than a nationally representative sample. We also noticed that the self-report rate and diagnostic rate for

kidney disease were relatively low, which may indicate that kidney disease is underdiagnosed in HIV-infected patients.

We used depression, sleep disorders, and anxiety to assess neuropsychiatric comorbidities in our patients. In previous studies, the prevalence of neuropsychiatric comorbidities has usually been assessed by patient self-reported scales, and the results of those studies were consistent with those of this study (66.0%)^{36–38}. However, in clinical practice, the rate of diagnosis of neuropsychiatric comorbidities is much lower. In this study, we found that only 16.0% of patients were diagnosed with neuropsychiatric comorbidities. This may be attributed to physicians' insufficient recognition of disease symptoms and the shortage of psychiatrists.

The prevalence of ASCVD in HIV-infected patients was 20.41% according to a meta-analysis of real-life data³⁹, which is close to the patient-reported prevalence in this study (25.7%); however, we did not find much information on the prevalence of ASCVD specifically in Chinese HIV-positive patients. As the physician-reported ASCVD metric reflected diagnosed cardiovascular disease, the proportion was lower than the patient-reported result (4.2% vs. 25.7%). Moreover, the low diagnosis rate of ASCVD and the rate of positive laboratory test results of nearly 50% can be attributed to misclassification. More details are described in the limitations section.

We also identified several potential risk factors for NICM awareness gaps. We found that receiving treatment in hospitals in the eastern region was a protective factor against awareness gaps between patients and physicians with regard to osteoporosis and neuropsychiatric comorbidities, while receiving treatment in tertiary hospitals was a protective factor against awareness gaps with regard to neuropsychiatric comorbidities. This may be due to the greater amount of medical resources in the eastern region and tertiary hospitals (including but not limited to the number of specialists and testing equipment). Old age (age ≥ 60) was a risk factor for awareness gaps with regard to osteoporosis, kidney disease and ASCVD. This may be related to the increased prevalence of these diseases with increasing age. Patients with acute HIV infections and in the clinical latency stage were less likely to report results that were inconsistent with those reported by their physician than patients with AIDS with regard to kidney diseases and ASCVD. This may be related to the side effects of long-term ART in AIDS patients.

There are several limitations of our study. First, the hospitals included in this study were selected and not randomly sampled (though the patients were selected randomly). In our sample, the proportion of patients from the central region was slightly lower than the proportions of patients from the other regions, and this sample was not nationally represented. However, compared with current published studies on NICMs in Chinese HIV-infected patients (for example,^{38,40,41}), the sample in our study was larger and was drawn from all regions of the country, suggesting that our sample is relatively more representative of HIV-infected patients in China. Second, there was a significant difference in the measurement standards for ASCVD between physician-reported data and the laboratory test results. The physician-reported data on ASCVD were the records of the diagnosis of cardiovascular diseases. In contrast, a positive laboratory test result indicated a moderate or greater 10-year ASCVD risk (which included existing cardiovascular

diseases and additional ASCVD risk). Despite these limitations, this study has some implications for clinical work.

Conclusion

Generally, NICMs in Chinese HIV-infected patients were underestimated. HIV-infected patients are usually treated in the department of infectious diseases, and infectious disease specialists may not identify these common noninfectious comorbidities in a timely manner or provide the appropriate treatment to the patients. Therefore, it is important for infectious disease specialists to pay more attention to possible noninfectious comorbid conditions. In addition, patient self-reported scales can be introduced for the primary screening of osteoporosis and neuropsychiatric comorbidities. In addition, using a multidisciplinary team to treat HIV patients could be a reasonable solution to this issue. In this way, doctors would be likely to identify comorbidities earlier and adjust the treatment plan of patients as soon as possible.

Our findings suggest that NICMs in HIV-infected patients in China are underestimated, and there are gaps among patient awareness of disease, the clinical diagnosis rate, and the actual prevalence. The awareness gap between patients and physicians is influenced by patient characteristics.

Abbreviations

AIDS: Acquired immune deficiency syndrome; ART: Antiretroviral therapy; ASCVD: Atherosclerotic cardiovascular disease; CI: Confidence interval; CVD: Cardiovascular disease; HDL-C: High-density lipoprotein cholesterol; HIV: Human immunodeficiency virus; LDL-C: Low-density lipoprotein cholesterol; NICMs: Noninfectious comorbidities; OR: Odds ratio; TC: Total cholesterol

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with Declaration of Helsinki and ethically approved by the Ethics Committee of Shanghai Public Health Clinical Center. Written informed consent was obtained from all patients and doctors before the survey began.

Consent for publication

Not applicable.

Availability of data and materials

All the data supporting our findings are contained within this article.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

The project was completed by the HIV Comorbidity Management Working Group. All authors contributed substantively to this study and article. Hongzhou Lu was the leader of the project and was responsible for project development, and Jun Chen contributed to the data analysis and manuscript writing.

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Figures

Figure 1

The comparison among patient-reported results, physician-reported results, and laboratory indicators. ***: $P < 0.001$