



Behavioral and Clinical Characteristics and Outcomes of Treatment Among Older Patients Receiving Medical Care for HIV Infection in Iran

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Abstract

Background: Although the number of new HIV infections continues to decline in Iran, the number of HIV-infected patients aged ≥ 50 years continues to rise due to the introduction of new treatment and longer survival. The higher prevalence of medical comorbidities and treatment failure in this population is a critical challenge in HIV treatment. In the present study, prevalence of comorbidities, rate of response to treatment, and results of HIV drug resistance tests were explored in older patients.

Methods: A cross-sectional study was conducted at a tertiary referral HIV center in Tehran, Iran. The data for all the HIV-positive patients older than 50 years old were collected by reviewing their medical records within the last 15 years. Data included demographic and behavioral characteristics, immunologic and virologic response, rate of treatment failure, and HIV resistance.

Results: The records for 100 patients with a mean age of 62.5 (range 50-79) years were reviewed and analyzed. Medical comorbidities were observed in 20% of the patients, with HCV co-infection, diabetes mellitus, and neuropsychiatric impairments being the most common. Complete immunologic and virologic responses were respectively observed in 88 and 97% of patients. The treatment regimen was modified in 66 patients, with drug side effects being the reason in 63 patients (95.4%). HIV drug resistance tests showed a low rate of resistance ($<10\%$) to all drugs used in this population.

Conclusion: Our findings highlight the high prevalence of comorbidities in older HIV-positive individuals in Iran. A thorough endocrine and neuropsychiatric assessment at each visit is recommended for these patients. Access to an appropriate psychosocial support system will ensure earlier detection of HIV infection and comorbidities in the older population, and will undoubtedly improve the treatment outcome and quality of life among them.

Keywords: Aged, Comorbidity, HIV infections, Iran, Treatment a outcome

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Background

Iran faces the largest HIV epidemic in the Middle East (1). The official reports estimated a total of 75,700 People Living with HIV (PLWH) in 2014 though the real number may be much higher. Barriers to HIV-related research in the developing world, particularly in the Middle East, are manifold including cultural, political, and legal issues (2). In recent years, the introduction of Highly Active Antiretroviral Therapy (HAART) increased the survival of PLWH and with a tremendous decline in mortality, there is a growing population of older PLWH (3).

In addition to the rapidly increasing population of HIV-infected individuals aged ≥ 50 years, the proportion of newly infected individuals over the age of 50 has also increased in the past two decades (4). Despite the similar trend in the Iranian population, there is evidence that this age group may not be aware of their infection and delay diagnostic tests and treatment (5). Moreover, the strong stigma of HIV infection in the Middle East will undoubtedly hinder access to proper treatment in the most vulnerable populations such as older PLWH (6).

Although HIV mortality has dramatically decreased in older PLWH (3), the infection in older individuals is associated with a higher prevalence of comorbidities and related mortality along with reduced CD4 response to HAART (7-9). Studies suggest that even among well-managed PLWH over 50 years, the median survival is still remarkably lower than the younger population (3). There is no report on behavioral and clinical characteristics as well as treatment outcomes among older PLWH in Iran. Considering the HIV infection as a critical public health issue in Iran and the unique challenges of HIV treatment as well as HIV and aging in older PLWH, this study was conducted to extend the current knowledge on a cohort of older PLWH treated at a national HIV center by characterizing the comorbidities, behavioral risk factors, treatment adherence, and response to treatment among this population. It was hypothesized that the prevalence of medical comorbidities in this population is high and the rate of immunologic and virologic response to treatment would be lower in this age group.

Materials and Methods

Study setting

In a cross-sectional study, the medical records of 100

older PLWH who visited a tertiary referral HIV center in Tehran, were reviewed and the data on patient's sociodemographic characteristics, comorbidities, immunologic and virologic response, and treatment resistance were retrieved from March 2004 to February 2018. Patients were included in the study if they were HIV-seropositive on their 50th birthday. Patients with only one visit and those with incomplete records were excluded.

Variables

Sociodemographic variables included age, sex, body mass index (BMI), level of education, employment status, marital status, number of children, and length of time since HIV diagnosis. Behavioral variables were reported by patients and included smoking, drug use (injection and non-injection) for non-medical purposes, sexual preference and activity, and vaccination history.

Medical and clinical care variables included medical comorbidities, treatment status as indicated by documented ART prescription, the prescribed drug combination, adherence to the treatment protocol, immunologic response to treatment, adverse effects of the treatment, any change in drug regimen as well as the reason for the change, the most recent CD4 cell count (cells/mm^3), and complications of HIV infection including opportunistic infections. Only significant medical comorbidities were included in the study; co-infection with HCV, myocardial infarction, congestive heart failure, diabetes mellitus, hypertension, hemophilia, any tumor or malignancy, renal failure, psychiatric disorders, thyroid disease, lung disease, and dementia were the most important comorbidities.

Immunologic response to HAART was defined as the increase in CD4 cell count to more than $500 \text{ cells}/\text{mm}^3$. Virologic response was defined as the decrease in plasma level of HIV RNA to lower than $500 \text{ copies}/\text{ml}$. Both values were recorded at six months following the treatment initiation. The results of HIV drug resistance tests were also recorded.

Ethical considerations

The protocol of the present study was reviewed and approved by the Institutional Review Board (IRB) of Tehran University of Medical Sciences (Ethics

code: IR.TUMS.VCR.REC.1398.557). The medical records of patients were only used to retrieve the data on the variables analyzed in the present study. The information sheet and data file were stored as encrypted documents and were accessed only for the purpose of analysis in the current study. The identity information was not disclosed, neither collected in the present study.

Statistical analysis

The descriptive statistics were employed to describe the patient’s sociodemographic characteristics and the distribution of comorbidities as well as treatment regimen and outcome. SPSS software version 22.0 was used for statistical analysis.

Results

Table 1 summarizes the patients’ demographic and behavioral characteristics. One hundred patients with a mean age of 62.5 (range 50-79) years were included in the final analysis. Seventy-two patients (72%) were male and 28 were female. The proportion of patients infected via intravenous drug use (62%) was almost twice the proportion of sexually infected patients (32%). About half of the patients were married. Of the total study population, 68 reported receiving the pneumococcal vaccine according to the national guidelines, 65 influenza vaccine, 45 HBV vaccine, and 39 other vaccines.

Medical comorbidities

Table 2 represents the medical comorbidities of the study population. As it has been shown, HCV co-infection, psychiatric disorders, and diabetes mellitus with the equal number of four (4%) were the most prevalent comorbidities among older PLWH in this study. In total, 20 out of 100 patients were suffering from medical comorbidities.

Treatment, drug resistance, and outcome

Table 3 illustrates the initial treatment regimens for the patients. All patients were undergoing HAART treatment at their latest visit, per national guidelines. The immunologic and virologic response following six months of treatment were observed in 88 (88%) and 97 patients (97%), respectively. The initial drug regimen was modified in 66 patients (66%), with side

effects being the reason in 63 instances (95.4% of all regimen changes), and absence of virologic response in 3 cases (4.5%). Of 66 patients for whom the drug regimen was modified, EFV-3TC-TDF (16.6%) and TDF-3TC-ATV/r (13.6%) were the most common second-line drug combinations. . 3TC (Lamivudine), FTC (Emtricitabine), and NVP (Nevirapine) had the

Table1. Demographic and behavioral characteristics of the study population

	Number of patients *
Sex	
Male	72
Female	28
Marital status	
Single	9
Married	54
Divorced	19
Widowed	18
Mode of HIV transmission	
Sexual contact	32
Intravenous drug use	62
Blood products	6
Reason for HIV clinic visit	
Counseling	60
Opportunistic infections	9
Sexually-transmitted diseases	17
Referrals from other clinics	14
Household variables	
Living alone	11
HIV infected person in household	25

* Since the total number of patients is 100, the numbers reflect the percentage as well

Table 2. The distribution of medical comorbidities in the study population

Medical comorbidity	Number of patients *
HCV co-infection	4
Psychiatric disorders	4
Diabetes mellitus	4
Hypertension	2
Ischemic heart disease	1
Asthma	1
Hemophilia A	1
Chronic lymphoblastic leukemia	1
Thyroid disease	1
Chronic renal failure	1
Total	20

* Since the total number of patients is 100, the numbers reflect the percentage as well

Table 3. The distribution of HAART regimens for the study population

Drug regimen	Number of patients
EFV-3TC-TDF	44
EFV-3TC-AZT	36
RTV-DRV-TDF-3TC	3
TDF-3TC-DTG	3
ABC-3TC-EFV	3
NVP-3TC-d4T	2
FTC-DTG-TDF	2
AZT-3TC-NVP	2
ABC-3TC-DTG	1
AZT-3TC-DTG	1
AZT-3TC-ATV/r	1
AZT-3TC-NFV	1
LPV-3TC-AZT	1

EFV: Efavirenz, 3TC: Lamivudine, TDF: Tenofovir, AZT: Zidovudine, RTV: Ritonavir, DRV: Darunavir, DTG: Dolutegravir, ABC: Abacavir, NVP: Nevirapine, d4T: Stavudine, FTC: Emtricitabine, ATV/r: Atazanavir /Ritonavir, NFV: Nelfinavir, LPV: Lopinavir

highest resistance among HIV infected patients in this study.

Discussion

In the last two decades, the population of older PLWH has increased substantially worldwide and is expected to reach 21% of all PLWH by 2020 (10). The introduction of HAART in the 1990s and the significant increase in life expectancy and quality of life of PLWH is a major contributor to this global trend. Additionally, a larger proportion of the newly diagnosed PLWH are people older than 50 years (11). In Iran, the number of new HIV infections has been decreasing since 2009; however, this trend is not observed in age groups older than 50 years (12). To our knowledge, this is the first report in Iran that explored the demographic and socioeconomic characteristics and medical comorbidities in the older PLWH population. Moreover, the rates of virologic and immunologic responses to HAART and the rate of HIV resistance to commonly prescribed drugs were investigated in the study population.

Although the number of older PLWH could not be estimated in the present study owing to the nature of this study, the findings indicated that the global trend of the expanding population of older PLWH is also

occurring in Iran. The social stigma attached to HIV infection, especially in the Middle East countries with sensitive cultural and religious backgrounds, has been a major obstacle in the battle against HIV. Moreover, in older adults, the stigma of engaging in sex at old ages also exists (13). Therefore, a strong and well-oriented social support system is much needed in the management of HIV infection among this vulnerable population.

A high rate of medical comorbidities in older PLWH was observed with HCV co-infection, diabetes mellitus, and psychiatric disorders being the most common. Also, a low rate of adherence to vaccination recommended for older PLWH was found in our study population. The higher rate of comorbidities in the older PLWH has been reported in multiple studies (7,8,14-16). Rodriguez-Penney *et al* compared a group of young and old PLWH with a cohort of matched HIV-seronegative population (7); similar to our study, the prevalence of diabetes and neuropsychological impairments were significantly higher in the older PLWH. Therefore, higher risk-associated behavior, lower quality of life, lower socioeconomic status, and the side effects of HAART may have played a substantial role in replicating these findings. A thorough assessment of significant medical co-morbidities is recommended in all PLWH and is especially important in patients over the age of 50. Moreover, it is recommended to have a psychiatric evaluation at each visit, along with close cooperation with social workers and mental health professionals. High rates of virologic (97%) and immunologic response (88%) to HAART were found in older PLWH although the proposition about lower response rate of older patients to therapy is a matter of debate. Hasibi *et al* reported no significant difference in the mean increase of CD4 cell count between young and old PLWH populations in Iran (17). However, other studies have found a higher rate of treatment failure in patients ≥ 50 years old (9,18,19). Previous studies have found higher rates of treatment failure in patients with low adherence to HAART (20). Our study population appeared to be highly-motivated and highly-adherent to HAART, which may explain the high rate of response to treatment.

The initial HAART regimen was modified in 66 instances (66%), with only 3 (4.5%) being due to the

failure in virologic response. While side effects of HAART are well-known, and adjustments in the drug regimens are common due to side effects, it seems that older PLWH may have a higher rate of significant side effects requiring a change in the drug combination. A close monitoring system with an emphasis on the side effects of treatment is imperative in older PLWH.

A low rate of resistance to HAART was also found and all drugs had <10% of resistance in our study population. This is in line with previous reports on the Iranian HIV population (21,22). Lamivudine, Emtricitabine, and Nevirapine were found to have the highest resistance rate, which is also comparable to previous studies in Iran (22).

There were some shortcomings in the present study. First, the cross-sectional nature of our study precludes any conclusions on the epidemiology of HIV infection among those ≥ 50 years of age. Also, causality could not be inferred; for example, it was unclear whether the high rate of comorbidities is a result of HIV infection or old age. Second, a CD4 cell count of >500 cells/ mm^3 and a viral load of <500 copies/ ml were assumed as immunologic and virologic responses, respectively. Although the definition of these parameters is arbitrary, there is a trend of considering more strict criteria for response to treatment in the literature. However, due to the retrospective nature of our study, and some tests being performed almost fifteen years ago, aforementioned levels were considered as reasonable values to judge whether the patient has responded to the treatment or not. Third, all patients in our cohort were highly adherent to treatment and therefore may not be ideal representatives of the older PLWH regarding drug side effects and treatment resistance. Fourth, some of our records on non-HIV drugs taken by patients were not complete, and there may be some interactions between these drugs with

antiretroviral drugs and treatment outcomes. Fifth, all of our patients were on antiretroviral medications, and some of the comorbidities, particularly diabetes and renal disorders, could have been a complication of treatment. Lastly, only treatment responses during the 6 months following the initiation of HAART were collected. The long-term virologic and immunologic responses, therefore, cannot be inferred from this study.

Conclusion

Despite these limitations, our findings are of significant public health interest. Advances in treatment will continue to increase the population of older PLWH and the medical comorbidities and other influencing factors of treatment failure will undoubtedly complicate the management of HIV in this population. In this study, high rates of significant comorbidities were found among 100 HIV-seropositive patients aged ≥ 50 years. In addition, high rates of virologic and immunologic responses and a low rate of drug resistance were observed. Future studies may focus on the treatment of the comorbidities associated with older PLWH, screening and treatment of neuropsychological impairments, and the efficacy as well as the side effects of HAART in this population.

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Conflict of Interest

The authors declared no conflict of interests.

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