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Rheumatologic Manifestations Among HIV-positive Patients, Tehran, Iran

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ABSTRACT

Background: Due to the increase of HIV patients' survival, rheumatologic symptoms associated with HIV such as septic arthritis, psoriatic arthritis and other manifestations have increased. Also, diseases such as Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) can be intensified during AIDS.
Objectives: The aim of this cross-sectional study was to evaluate the prevalence and nature of rheumatologic manifestations in HIV positive patients, Tehran, Iran.
Materials and Methods: This cross-sectional investigation was done on 200 HIV infected patients from 2009 to 2010. Demographic characteristics (age and sex), the route of HIV transmission and the duration of infection, existence of any concurrent infection such as hepatitis B (HBV) and hepatitis C (HCV) infections, last CD4 count, regimen and duration of the anti-retroviral therapy, presence of any musculoskeletal manifestation and joint disease and their quantity and quality were obtained. Patients were also examined by a clinician and information was recorded via checklists. Data were analyzed using SPSS software and reported as means and percentages.
Results: Two hundred HIV patients including 153 male and 47 female participated in the study. Sixty three patients (31.5%) had musculoskeletal manifestations. The most prevalent complaints were arthralgia in 25 patients (39.7%), myalgia in seven patients (11.1%) and unspecified spondyloarthritis in four patients (6.3%). Also, a borderline association was observed between HBV-HIV co-infection and presence of musculoskeletal findings ($P = 0.047$).
Conclusions: Considering the high prevalence of rheumatologic manifestations in patients with HIV/AIDS and its probable relation to the quality of life of patients, there is a pressing need for evaluating patients in this regard, especially among patients who are receiving highly active anti-retroviral therapy (HAART) and experience better clinical responses.

Keywords: HIV Infections; Rheumatology; Prevalence

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Implication for health policy/practice/research/medical education:
This study is the first to assess the prevalence of rheumatologic manifestations among Iranian HIV infected patients and thus provides the grounds for further research in this area with regard to the impact of such manifestations on the quality of life and general well-being of Iranian HIV patients.

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1. Background

Since the first description of patients with human immunodeficiency virus (HIV) infection, over 60 million people have been affected (1-3). By targeting CD4+ cells, the subsequent immune-suppression results in the development of further opportunistic infections and malignancies, which may be associated with clinical manifestations of almost every organ system.

It has been previously stated that HIV infection is associated with various rheumatologic manifestations such as rheumatoid arthritis (RA) and systemic lupus erythematous (SLE) (4). Psoriasis, reactive arthritis and Diffuse Infiltrative Lymphocytosis Syndrome (DILS) also occur in HIV-infected patients, with a higher prevalence in compare to general population. Unexplained arthralgia and myalgia were also reported in about 5% of HIV patients (5-7).

The first reports of rheumatologic signs and symptoms in HIV-positive patients were in 1980s and since then, the spectrum of rheumatologic conditions associated with HIV/AIDS has substantially extended, especially after the introduction of Highly Active Anti-retroviral Therapy (HAART) (5). Some previous studies also showed that the subsequent loss of immune competence in HIV infection can cause autoimmune and inflammatory diseases (8-10). However, data regarding the national epidemiology of such manifestations among Iranian HIV-positive patients remains unidentified.

2. Objectives

In this cross-sectional study, we sought to determine the nature and prevalence of rheumatologic findings in HIV-positive patients, Tehran, Iran.

3. Materials and Methods

This cross-sectional study was performed on 200 HIV-positive patients referred to the voluntary counseling and testing center (VCT) of Imam Khomeini hospital during 2009-2010, Tehran, Iran. HIV infection was diagnosed by positive enzyme-linked immunosorbant assay (ELISA) for HIV antibodies and then to confirm the positive test, a western blot was performed as well. The institutional review board (IRB) of Tehran university of medical sciences approved the study protocol. Also, informed consent was obtained from all the patients. Patients with musculoskeletal manifestations which were basically not related to HIV such as degenerative joint disorder (DJD), flexor muscle contracture associated with hemophilia and traumatic bone fractures, septic arthritis and patients with defined joint diseases such as gout in addition to patients who had ceased using opioids and patients who were not interested to participate in the study were excluded. A total number of 200 patients who met the inclusion criteria were sequentially recruited in our study.

Data regarding age, sex, route of HIV acquisition, duration of the infection, existence of any other contemporaneous infection such as hepatitis B (HBV) or hepatitis C (HCV) infections, last CD4 count, regimen and period of taking anti-retroviral treatment and presence of musculoskeletal and rheumatologic manifestations were collected. Also, all the patients underwent physical examination in order to identify further rheumatologic conditions. Patients were also asked to explain the quality and quantity of any present rheumatologic condition. In some cases, related laboratory tests and radiographic imaging were done.

Data were analyzed and reported as means and percentages. Data were analyzed using Statistical Package of Social Software (SPSS, version 17). $P < 0.05$ was considered statistically significant.

4. Results

Among the 200 HIV-positive patients that entered the study, 153 (76.5 %) were male and 47 (23.5%) were female. The average age of patients was 36.5 ± 9.5 years. One hundred and nineteen (59.5%) of cases were married and 81 (40.5%) were single. There was a significant difference between males and females in marrital status ($P < 0.001$). Most of the patients (56%) were infected via injection drug use (IDU). Fifty nine people (29.5%) were infected through sexual intercourse and 12 of them (6%) from blood transfusion. In three patients (1.5%) infection was transmitted through an infected mother and in 14 patients (7%) the route of transmission was unspecified. The mean of last CD4 count was 272 ± 194.1 cells/microlitr. The average duration of the infection was 3.8 ± 3.9 years. From 200 cases, 144 (72%) of patients were receiving HAART. Additionally, 118 patients (59%) were co-infected with HCV and 17 (8.5%) patients were co-infected with HBV. Twelve patients (6%) were HIV-HBV-HCV co-infected. One hundred thirty two patients (66%) had a positive history of drug abuse from which 128 patients (83%) were male.

In the current study among 200 subjects, 63 (31.5%) patients had musculoskeletal manifestations and 137 (68.5%) patients reported no musculoskeletal complaint. The average period of the musculoskeletal manifestations was 1.36 ± 1.70 years. Among the 63 patients with musculoskeletal manifestations, 47 patients were male (30.7% of male patients) and 16 patients were female (34% of female patients). Also, the distribution of rheumatologic findings was not significantly different among male and female patients ($P > 0.05$), considering that 47 patients (74.6% of patients with musculoskeletal findings) were male and 16 patients (25.4% of patients with musculoskeletal findings) were female. Among the 63 patients with musculoskeletal findings, 43 patients (68.3%) were receiving HAART and 20 patients (31.7%) were not receiving HAART which yielded a non-significant relation ($P > 0.05$). Moreover, among the 137 patients that had no musculoskeletal finding, 101 patients (73.7%) were receiving HAART which was not statistically significant. From the total of 200 patients, 11 (5.5%) patients had a positive family history for

rheumatologic illnesses such as RA; however the association between positive family history and rheumatologic manifestations was not significant. The details of the rheumatologic manifestations are shown in *Table 1*.

Table 1. Rheumatologic Manifestations in HIV-positive Patients Referred to the Voluntary Counseling and Testing Center, Imam Khomeini Hospital, Tehran, Iran

Manifestations	Numbers of Patients	Percentage
Arthralgia	25	12.5
Myalgia	7	3.5
Spondiloarthropaty	4	2
Bone Pain	2	1
HIV-associated Arthritis	2	1
PathologicBone Fractures	1	0.5
Polymyalgia Rheumatica (PMR)	1	0.5
Probable Polymyositis	1	0.5
Rachitis	1	0.5
Myasthenia Gravis (MS)	1	0.5
Rheumatoid Arthritis(RA)	1	0.5
Hypothyroidism	1	0.5
Reynauds' Phenomenon	1	0.5
Non-inflammatory Myopathy	1	0.5

Among all cases, three people complained of septic arthritis, however such diagnosis was not established by any physician, and 11 people had musculoskeletal findings which were not related to HIV. From the total of 118 HIV-HCV co-infected patients, 39 patients (33.1%) had musculoskeletal findings that was not statistically significant; however, there was a borderline association between HBV-HIV co-infection and presence of musculoskeletal findings, hence 9 HBV-HIV co-infected patients (52.9%) reported positive musculoskeletal findings (P = 0.047). There was no relation between cigarette smoking as well as drug abuse and positive rheumatologic findings. Moreover, the mean CD4 count in 63 patients with musculoskeletal findings was 295.9 ± 227 cell/microlitr; however, it was 260.9 ± 176.8 cells/microlitr among the remaining 137 patients. The association between positive musculoskeletal findings and CD4 count was also not significant.

5. Discussion

In the current study, 31.5% of the study population complained of musculoskeletal conditions. Arthralgia was the most prevalent complaint, followed by myalgia and spondiloarthropathy. The prevalence of musculoskeletal manifestations in patients with HIV infection has been reported from 7% to 16% in various studies (11-14). The first reports of HIV-associated rheumatologic conditions were in the mid-1980s, with polymyositis, vasculitis, reactive arthritis and HIV-associated Sjogren's syndrome (or the diffuse infiltrative lymphocytosis syndrome, or DILS) (10, 15, 16). By 1988, it was reported that a wide spectrum of rheumatologic diseases are associated with HIV infection (17). It should be noted that most of our study population were infected via IDU and therefore, unspecified arthralgia or myalgia could have been more reported among this group of patients. Nevertheless, arthralgia and myalgia comprise a prominent clinical feature of the acute retroviral syndrome.

Most of the rheumatologic diseases associated with HIV infection such as reactive arthritis and polymyositis are typically similar to that of non-HIV patients; however, DILS and HIV-associated arthritis may possess specific clinical features among HIV patients (17). There are also quite rare reports of RA and SLE, even in the presence of active HIV viral infection (18). Nonetheless, HIV infection may alter the epidemiology of certain rheumatologic conditions as well. For example, the prevalence of unspecified spondiloarthropathies increased in Sub-Saharan Africa –where the prevalence of HLA B27 allele is less than other parts of the world-after the epidemics of HIV infection in such regions. Also, considering that immune reactions play an important role in many of such diseases, the consequences of CD4 decline among such patients is possibly responsible for the different epidemiology of rheumatologic conditions. In this regard, the prevalence of such conditions might be associated with CD4 count, considering that some findings are more prevalent among patients who are receiving HAART and experience better clinical responses. However, we did not find any significant association between rheumatologic manifestations and CD4 count and we reported only one case with RA; though the prevalence of RA might have been more among patients who receive HAART and experience significant CD4 increase and immune reactivation (5). On

the other hand, in diseases such as psoriasis, reactive arthritis and DILS which might be the first manifestations of AIDS in HIV infected patients, CD8+ T cells are predominant. Therefore, the consensus is that the progressive reduction of CD4+ cells in HIV patients, decreases/increases the prevalence of various rheumatologic conditions in compare to general population. On the contrary, we were not able to find a significant association between rheumatologic conditions and last CD4 count of patients as well as rheumatologic conditions and receiving HAART.

This study has several limitations: first, the correlations between certain demographic characteristics of patients as well as the route of HIV transmission and rheumatologic manifestations were not assessed. For example, majority of our patients had contracted the infection via IDU, and thus one could anticipate a more prevalence of arthralgia and myalgia among such patients. Thereby, we suggest performing future studies which assess the aforesaid correlations in addition to considering the detailed drug history and quality of life of patients. Moreover, data regarding rheumatologic manifestations of HIV patients from other VCTs in other cities should be collected to further characterize the national epidemiology of rheumatologic conditions of Iranian HIV patients.

This study was the first to report the prevalence of rheumatologic conditions among Iranian HIV patients. In conclusion, we showed that the prevalence of rheumatologic conditions could be as high as 30% among these patients, highlighting the needs for assessing HIV patients with regard to their musculoskeletal findings. It is noteworthy that many HIV patients in Iran are primarily being assessed for other clinical conditions (i.e. co-infections, malignancies) and thus their musculoskeletal manifestations remain unidentified. Regarding that musculoskeletal finding could be the primary manifestation of the acute retroviral syndrome- especially where HIV is prevalent- clinicians should consider the nature and quality of such findings among patients and assess them by means of probable immune-suppression under favorable clinical settings. Additionally, many rheumatologic manifestations have been related to the extensive use of HAART (17). Therefore, evolution of any rheumatologic conditions such as arthralgia, rhabdomyolysis and osteonecrosis should be considered for any patient who is receiving HAART.

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Authors' Contribiution

AA designed the study protocol; SRN, HEK and AA conducted the study and collected data. SS performed the statistical analysis. KP and SLS drafted the manuscript. All authors were involved in finalizing and amendment of the article.

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