

Musculoskeletal and rheumatological disorders in HIV infection: Experience in a tertiary referral center

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Abstract

Background: Musculoskeletal involvement in human immunodeficiency virus (HIV) infected patients are important disease manifestations, responsible for increased morbidity and also decreased quality of life. **Objectives:** To study the spectrum of different musculoskeletal involvement in HIV infected patients and its impact on quality of life. **Patients and Methods:** Three hundred ($n = 300$) HIV-1 reactive patients were evaluated in respect to different musculoskeletal involvement including the quality of life from January 2010 to January 2011. **Results:** Male to female ratio was 11:1 with a mean age of 35 (± 6.4) years and mean duration of the disease was 3 (± 1.54) years. Majority of cases were truck drivers, motel workers, and jewelry workers. Musculoskeletal disorders were observed in a total of 190 cases (63.33%). The spectrum of musculoskeletal involvement was: Body ache in 140 (46.7%), arthralgia in 80 (26.7%), mechanical low back pain in 25 (8.3%), osteoporosis in 20 (6.7%), painful articular syndrome in 10 (3.3%), hypertrophic osteoarthropathy in two (0.7%), pyomyositis in two (0.7%), osteomyelitis in one (0.3%), and avascular bone necrosis in one patient (0.3%). Rheumatologic disorders associated were: Reactive arthritis in seven (2.3%), fibromyalgia in four (1.3%), septic arthritis in three (1%), acute gout in three (1%), spondyloarthropathy in two (0.7%), rheumatoid arthritis in two (0.7%), dermatomyositis in one (0.3%), and systemic lupus erythematosus (SLE) in one patient (0.3%). But HIV associated arthritis and diffuse infiltrative lymphocytosis syndrome (DILS) were not detected. Most of the patients had decreased quality of life. **Conclusions:** Musculoskeletal involvement was common in HIV patients causing increased morbidity, so early detection and timely intervention is essential to improve quality of life.

Key words: Human immunodeficiency virus infection, musculoskeletal disorder, quality of life

INTRODUCTION

Human immunodeficiency virus (HIV) infection is pandemic nowadays and India harbors the second highest number of people with HIV/acquired immunodeficiency syndrome (AIDS) infection.^[1]

Besides the opportunistic infections, various musculoskeletal disorders in HIV infected patients are of great concern, not only for the treating physicians but also for the rheumatologists because of its diagnostic dilemma. With the introduction of highly active antiretroviral therapy (HAART) in 1995, life span of HIV patients had been prolonged, but there is subsequent emergence of various newer musculoskeletal disorders causing increased morbidity. The incidence of rheumatic manifestations in HIV infection was reported in about 4 to 71.3% cases in different studies depending on the stage of the disease/musculoskeletal involvements and was reported to be much more prevalent in HIV

Access this article online

Quick Response Code:



Website:

www.ijstd.org

DOI:

10.4103/0253-7184.120542

How to cite this article:

Kole AK, Roy R, Kole DC. Musculoskeletal and rheumatological disorders in HIV infection: Experience in a tertiary referral center. Indian J Sex Transm Dis 2013;34:107-12.

patients than the HIV negative population.^[2,3] Though musculoskeletal disorders are not always related to the HIV infection, these may be either the direct effect of the virus, opportunistic infections, noninfectious HIV complications (malignancy, drug toxicities), or unrelated rheumatologic disorders whose course have been altered by HIV infection on the immune system.^[4-6] Musculoskeletal manifestations, though common in late stages, can occur at any stage, even may precede the diagnosis of HIV infection and many atypical manifestations may be present. Some of the risk factors (unsafe sexual practices and intravenous drug use) associated with HIV infection are shared with risk of developing certain rheumatic diseases. The spectrum of rheumatic manifestations in HIV infection include body ache, arthralgia, painful articular syndrome, reactive arthritis, HIV-associated arthritis, rheumatoid arthritis, undifferentiated spondyloarthropathy, systemic lupus erythematosus (SLE), fibromyalgia, septic arthritis, acute gout, avascular bone necrosis, osteoporosis, osteomyelitis, hypertrophic osteoarthropathy, polymyositis, dermatomyositis, pyomyositis, Sjogren's syndrome, diffuse infiltrative lymphocytosis syndrome (DILS), vasculitis, Kaposi's sarcoma, and lymphoma. But a great paradox in HIV infection is that certain rheumatic diseases such as DILS, reactive arthritis, Reiter's syndrome, and inflammatory myopathy are occurring in the face of immunodeficiency; whereas diseases like rheumatoid arthritis and SLE have been reported as improving in the face of the CD4 lymphocyte depletion.^[7] Another important issue is difficulty in differentiating HIV infection from SLE which may also present with oral ulceration, alopecia, arthritis, fever, sicca syndrome, or neuropathy with false positive test for HIV antibody.^[8] In the post HAART era, certain changes in musculoskeletal disorders were observed; decreasing prevalence of spondyloarthropathy and DILS and on other side increasing incidence of newer disorders such as osteopenia, osteonecrosis, and infective lesions. Moreover, with the immune restoration following HAART, certain inflammatory and autoimmune diseases (SLE, rheumatoid arthritis, and polymyositis) may exacerbate or even may develop de novo.^[9] Musculoskeletal disorders in HIV infected patients greatly influence the quality of life in respect to physical, mental, social, and economic ground.^[10] Early diagnosis and effective management, sometimes in consultation with a rheumatologist will reduce the morbidity and improve the overall quality of life.

The objectives of this study were to evaluate the different musculoskeletal involvement in HIV infected patients and its impact on quality of life.

PATIENTS AND METHODS

This was a cross-sectional observational study done in a tertiary referral hospital, Darjeeling, India from January 2010 to January 2011. A total of 300 HIV patients were enrolled for this study excluding recent history of trauma to joints, known diabetes or hypothyroidism, muscle weakness within 6 weeks of initiation of HAART therapy (probably zidovudine induced), and evaluated regarding the quality of life in respect to different musculoskeletal involvement (SF-36 questionnaire). Laboratory investigations including blood biochemistry, CD4 count, rheumatoid factor with titer, antinuclear antibody (ANA) with titer, anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibodies, anti-neutrophil cytoplasmic antibodies (ANCA), X-ray/ultrasonography/magnetic resonance imaging (MRI) of different joints, bone mineral density, electromyography- nerve conduction velocity (EMG-NCV) study, joint fluid analysis, and muscle biopsy were done.

RESULTS

Male to female ratio was 11:1 and the mean age was 35 (± 6.4) years. Majority of them were truck drivers (70, 23.3%), motel workers (45, 15%), jewellery workers (40, 13.3%), prisoners (35, 11.7%), businessmen (30, 10%) [Table 1]. The major routes of transmission enquired were: Heterosexual practices in 220 (73.3%), intravenous drug use in 50 (16.7%), and blood/blood product transfusion in 15 (5%) [Table 2]. Mean duration of the disease

Table 1: Occupations of human immunodeficiency virus patients

Occupations	Number of patient (%)
Truck drivers	70 (24)
Motel workers	45 (16)
Jewelry worker	40 (14)
Prisoner	35 (12)
Businessmen	30 (10)
Farmer	25 (9)
Housewives	20 (7)
College students	15 (5)
Children	10 (3)

Table 2: Different routes of transmission observed in this study

Routes of transmission	Number of patients (%)
Heterosexual	220 (73)
Intravenous drug user	50 (17)
Blood transfusion related	15 (5)
Vertical transmission	6 (2)
Unknown	9 (3)

observed was 3 (± 1.54) years and mean CD4 count of $127 \pm 28.3/\text{mm}^3$. A total of 238 patients were on HAART therapy currently, whereas 62 patients were not on HAART (among them 40 patients had never taken HAART and 22 patients stopped taking HAART). As per the World Health Organization (WHO) clinical staging, eight patients (2.7%) were in stage 1, 60 patients (20%) were in stage 2, whereas 160 patients (53.3%) were in stage 3 and 72 patients (24%) were in stage 4. Rheumatic manifestations in different combinations were observed in a total of 190 cases (63.33%) and the spectrum of involvement observed were body ache in 140 cases (46.7%), arthralgia in 80 (26.7%), mechanical low back pain in 25 (8.3%), osteoporosis in 20 (6.7%), osteoarthritis [Figure 1] in 18 (6%), painful articular syndrome in 10 (3.3%), hypertrophic osteoarthropathy in 2 (0.7%), pyomyositis in two (0.7%), osteomyelitis [Figure 2] in one (0.3%), and avascular necrosis of bone involving right femoral head in a patient (0.3%) on HAART who presented with severe pain in right

hip region [Table 3]. The rheumatologic disorders associated were reactive arthritis [Figures 3 and 4]

Table 3: Spectrum of different musculoskeletal manifestations in respect to HAART therapy[#]

Musculoskeletal disorder	Patients on HAART (238)	Patients without HAART (62)	P value	Total no. of patients
Myalgia	116	24	0.2	140
Arthralgia	58	22	0.1	80
Low back pain (mechanical)	21	4	0.8	25
Osteoporosis	13	7	0.15	20
Painful articular syndrome	7	3	0.44	10
Hypertrophic osteoarthropathy	2	-	1.0	2
Pyomyositis	2	-	1.0	2
Osteomyelitis	1	-	1.0	1
Avascular bone necrosis	1	-	1.0	1

[#]Sometimes present in combinations. HAART=Highly active antiretroviral therapy



Figure 1: Osteoarthritis with effusion involving left knee joint in a HIV patient



Figure 2: Osteomyelitis in a HIV patient involving ankle joint



Figure 3: Reactive arthritis in a human immunodeficiency virus patient involving left ankle, erythema nodosum involving both shin bone



Figure 4: Reactive arthritis in a HIV patient with bilateral knee joint effusion

in seven cases (2.3%), fibromyalgia in four (1.3%), septic arthritis [Figure 5] in three (1%), acute gout in three (1%), spondyloarthropathy in two (0.7%), rheumatoid arthritis [Figures 6 and 7] in two (0.7%), and adhesive capsulitis [Figure 8] in one patient [Table 4]. Regarding the quality of life, HIV patients having musculoskeletal involvement had poor physical health in contrast to other HIV patients without musculoskeletal involvement (39.2 ± 4.3 vs 40.2 ± 4.7 , $P = 0.0153$), whereas the mean mental health in both the above group were 38.1 ± 2.9 and 38.8 ± 3.3 ($P = 0.0556$), respectively. The laboratory investigation revealed positive rheumatoid factor in five patients, ANA in two patients and hepatitis B surface antigen in 10 patients. Synovial fluid aspiration was done in a total of eight patients, three of them revealed high leukocyte count ($>50,000$ cells/mm³) suggestive of septic arthritis. Ultrasound and MRI of different joints done in a total of 15 patients and avascular necrosis of right femoral neck was detected in one patient.

DISCUSSION

In this study, rheumatic manifestations were observed in a total of 63.33% of HIV patients corroborating with a study from Thailand (55%), whereas this was reported in only 31.5% in a study from Iran.^[11,12] The high prevalence of musculoskeletal involvement was probably due to a large number of HIV cases detected in advanced stages from different states of northeast India. Myalgia was the commonest symptom present in 46% patients and arthralgia involving knee, shoulder, and elbow were also frequent complaints and observed in about 26% of HIV patients requiring frequent analgesics for relief. The most distressing musculoskeletal disorders were mechanical low back pain and painful articular syndrome for which they required frequent outpatient visits and also frequent absence from their work. Reactive arthritis was detected only in 2.3% of HIV patients corroborating with other Indian studies and the mode of transmission was mainly heterosexual



Figure 5: Septic arthritis in a HIV patient involving left knee joint



Figure 6: Rheumatoid arthritis with deformity in a HIV patient



Figure 7: Rheumatoid arthritis without deformity in a HIV patient



Figure 8: Adhesive capsulitis in a HIV patient involving right shoulder joint

in contrast to western population where this was reported in 5-10% cases and mostly were homosexual.^[13-17] Fibromyalgia was diagnosed in 1.3% of HIV patients in this study though this was the common musculoskeletal disorder reported from western population.^[18] Septic arthritis involving the ankle and knee joints were observed in 1% of HIV patients and most of them were intravenous drug users. Spondyloarthropathy was seen in 0.7% of cases in this study corroborating with other Indian studies and also a study from China; and all these patients required biologics (infliximab) to control the disease activity and was significantly observed in

patients without HAART ($P = 0.004$) [Table 5].^[13,14] SLE was diagnosed in one female HIV patient who had a low CD4 count ($112/\text{mm}^3$) but developed flare (increased disease activity) after initiation of HAART. DILS, specific for HIV infection, was reported with a high percentage (11.22%) in a study from China, but not detected in this study as well as other Indian studies.^[19] It had been observed that HIV patients of stage 2 had suffered predominantly from arthralgia, spondyloarthropathy, and rheumatoid arthritis; whereas patients with stage 3 disease had suffered predominantly from body ache and mechanical low back pain, but patients with stage 4 disease had suffered predominantly from septic arthritis, osteomyelitis, and pyomyositis [Table 6]. Another important observation was that patients on prolonged HAART therapy developed osteoporosis (6.7%) and osteonecrosis (0.3%), possibly due to the metabolic effects of the antiretroviral drugs though there is no controlled study to prove this association [Table 3].^[20] Most of the patients in this study had history of frequent outpatient visit or hospital admission due to incapacitating pain due to musculoskeletal disorders in addition to opportunistic infections hampering their day-to-day activities, resulting in long absence from work. Moreover, it had been observed that majority of the HIV patients in this study were from lower socioeconomic group and were also the earning members of their families, resulting in economic crisis.

The major challenges for a physician practicing in HIV endemic area include not only recognizing HIV

Table 4: Spectrum of different rheumatological disorders in respect to HAART therapy

Rheumatological disorder	Patients on HAART	Patients without HAART	P value	Total no. of patients
Osteoarthritis	13	5	0.54	18
Reactive arthritis	3	4	0.03	7
Fibromyalgia	2	2	0.19	4
Acute gout	3	-	1.0	3
Septic arthritis	3	-	1.0	3
Spondyloarthropathy	-	2	0.004*	2
Rheumatoid arthritis	1	1	0.37	2
Dermatomyositis	1	-	1.0	1
Sjogren's syndrome	-	1	0.21	1
SLE	1	-	1.0	1
Vasculitis	1	-	1.0	1
Adhesive capsulitis	1	-	1.0	1

*Statistically significant HAART=Highly active antiretroviral therapy; SLE=Systemic lupus erythematosus

Table 5: Spectrum of different rheumatologic disorders in HIV patients and comparison to other Indian studies (% of cases)

Rheumatologic disorders	kutty Krishnan, et al., ^[15] (Chennai) India (n=29)	Achuthan and Uppal ^[14] (Delhi) India (n=102)	Azami et al., ^[12] (Tehran) Iran (n=200)	Present study (Darjeeling) India (n=300)
Reactive arthritis	17.2	1.96	-	2.3
Fibromyalgia	-	-	-	1.3
Acute gout	-	-	-	1
Septic arthritis	3.4	0.98	-	1
Spondyloarthropathy	24.1	1.96	4	0.7
Rheumatoid arthritis	-	-	0.5	0.7
Dermatomyositis/polymyositis	-	-	0.5	0.3
Sjogren's syndrome	-	-	-	0.3
SLE	-	-	-	0.3
HIV associated arthralgia	17.2	11.7	2	26.7
Pyomyositis	3.4	-	0.5	0.7
HIV associated arthritis	13.8	-	0.5	-
Psoriatic arthritis	3.4	0.98	-	-
Vasculitis	10.4	2.9	-	0.3
Painful articular syndrome	-	-	-	3.3
DILS	-	-	-	-

HIV=Human immunodeficiency virus; SLE=Systemic lupus erythematosus; DILS=Diffuse infiltrative lymphocytosis syndrome

Table 6: Musculoskeletal involvement in different stages of HIV infection

	Stage 1	Stage 2	Stage 3	Stage 4
Body ache	3	24	70	43
Arthralgia	2	40	23	15
Low back pain (mechanical)	3	2	12	8
Osteoporosis	-	3	5	12
Painful articular syndrome	-	3	2	5
Hypertrophic osteoarthropathy	-	-	1	1
Pyomyositis	-	-	-	2
Osteomyelitis	-	-	-	1
Avascular bone necrosis	-	-	-	1
Osteoarthritis	3	9	5	1
Reactive arthritis	-	5	2	-
Fibromyalgia	-	2	1	1
Acute gout	-	-	1	2
Septic arthritis	-	-	-	3
Spondyloarthropathy	-	2	-	-
Rheumatoid arthritis	1	1	-	-
Dermatomyositis	-	1	-	-
Sjogren's syndrome	-	1	-	-
SLE	-	1	-	-
Vasculitis	-	1	-	-
Adhesive capsulitis	1	-	-	-

HIV=Human immunodeficiency virus; SLE=Systemic lupus erythematosus

infection associated rheumatic disorders but also distinguishing them from classic rheumatic diseases like rheumatoid arthritis, SLE, spondyloarthropathy, and vasculitis. So an aggressive multidisciplinary approach to early detection and timely intervention of these disorders, sometimes in consultation with a rheumatologist are all essential for effective management and to improve the quality of life. Moreover a well-balanced diet and exercise program in addition to HAART therapy may be the best way to maintain good health in these groups of patients.

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Source of Support: Nil. Conflict of Interest: None declared.