

Clinical Spectrum of Rheumatologic Manifestations in HIV Patients: A Study from Southern India

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ABSTRACT

Introduction: HIV infection is a common disease in India and a variety of rheumatological manifestations are known to occur in HIV Infection. Rheumatological manifestations are significant cause of morbidity in these patients.

Aim: To study the clinical spectrum and prevalence of rheumatologic manifestations in HIV patients.

Materials and Methods: Patients with HIV 1 and 2 attending the Infectious disease outpatient department of Medical College Hospital, Thiruvananthapuram during the study period (March 2009 to March 2010) were assessed by clinical examination and with relevant laboratory investigations, to diagnose the rheumatological manifestation. Based on the clinical manifestations and investigations a rheumatological diagnosis was made. Patients with diabetes mellitus, hypothyroidism and other pre-diagnosed rheumatologic illness were excluded from the study. Statistical analyses were done using SPSS IBM Statistics 17.0 version and chi-square test.

Results: Out of 385 patients, 161 (41.8%) of HIV patients were in the 30-39 years age group. Male and female were 225 (58.4%) and 160 (41.6%) respectively. A total of 276 (71.7%) patients

were receiving antiretroviral therapy (ART). Disease duration of 1-5 year in 174 (45.19%), <1 year in 135 (35.06%) and rest had more than 5 years of disease. A total of 97 (25.2%) of HIV patients had rheumatological manifestations. HIV Arthralgia was the most common manifestation affecting 34 patients (35.1%) of the population with rheumatological manifestations. Knee joint was the most common joint which was involved. The other manifestations noted along with percentage were Myalgia/muscle ache in 18 patients (18.6%), inflammatory back pain in 14 patients (14.4%), soft Tissue Rheumatism in 12 patients (12.4%), undifferentiated spondyloarthritis in 11 patients (11.3%), fibromyalgia in 9 patients (9.3%), HIV wasting in 7 patients (7.2%), HIV arthritis in 4 patients (4.1%) and psoas abscess (3.1%). Each of plantar fasciitis, psoriatic Nail changes, pyomyositis, painful articular syndrome, erythema nodosum and episcleritis constituted about 2.1% each of the rheumatological manifestations. Degenerative joint disease constituted 17.5% of the rheumatological manifestations. One patient had evidence of tuberculosis of the spine.

Conclusion: The rheumatological manifestations are common in HIV Infected patients. HIV arthralgia, myalgia and undifferentiated spondyloarthritis are the common manifestations.

Keywords: Antiretroviral therapy, Arthritis, Spondyloarthritis

INTRODUCTION

India has the third largest HIV epidemic in the world. In 2016, HIV prevalence in India was estimated 0.3% [1]. The estimated adult HIV prevalence in India was 0.34%. HIV infection is quite common in Kerala, with an estimated adult prevalence of 0.26 % in 2016. The prevalence seems to be small when compared to other middle income countries but due to India's huge population, it equates to a large number of people living with HIV [2]. The estimated adult HIV prevalence in India was 0.34%. HIV infection is quite common in Kerala, India, with an estimated adult prevalence of 0.26 % in 2016 [1]. Besides its well known signs and symptoms, HIV infection can have a wide spectrum of musculoskeletal manifestations. The first report of rheumatological manifestation of HIV infection was mentioned by Winchester R et al., from New York in their case series of 13 patients [3]. Rheumatic manifestations can develop during any stage of the clinical course of HIV infection but usually in the later period. The commonly described rheumatic manifestations in HIV infection include arthralgia, HIV associated arthritis, painful articular syndrome, soft tissue rheumatism, reactive arthritis, undifferentiated spondyloarthritis, septic arthritis, osteomyelitis, HIV related myalgia, polymyositis, Dermatomyositis, Diffuse Infiltrative Lymphocytic Syndrome (DILS), vasculitis like syndromes have also been described [4,5].

Most of these syndromes were initially described in patients with Acquired Immunodeficiency Syndrome (AIDS), which made it difficult to ascertain if these diseases were truly associated with HIV or they are merely a causal co-occurrence, detected because

of increased awareness of symptoms during the follow-up of HIV infected patients [4,5].

The prevalence of musculoskeletal manifestations in HIV has been varied in different studies [5,6]. Prospective studies have shown a high prevalence of rheumatic complaints in 30-40% of HIV infected patients, with arthralgia the most common manifestations in 25-40% of patients [6,7]. A study by Zhang X et al., has shown rheumatic manifestations in 54.08% HIV patients [6]. There has been a scarcity of studies looking at the prevalence and characteristics' of rheumatic manifestations from India. A study conducted by Kutty Krishnan K et al., in which 29 HIV patients with some musculoskeletal problems were evaluated, showed very high rates of Spondyloarthritis (44.8%) [7].

Since HIV infection is very common problem in India, studies are needed to record the prevalence and spectrum of musculoskeletal manifestations in HIV patients. Till the date of study, no studies were available in Kerala to explore this area. This study can help us in bridging this small gap and enhance these areas. Hence, the present study was conducted with the aim to find the prevalence and the clinical spectrum of musculoskeletal manifestations in HIV infected patients attending the Infectious disease and the ART clinic in medical college, Thiruvananthapuram, Kerala, India.

MATERIALS AND METHODS

This was a descriptive study of Clinical Spectrum of Musculoskeletal Manifestations in HIV Patients. A total of 385 patients were studied.

HIV infected patients attending the Infectious disease and the ART clinic of medical college, Thiruvananthapuram, during the study period of March 2009 to March 2010 was included. Patients with Diabetes mellitus, hypothyroidism and previously diagnosed rheumatological illness were excluded from study.

The sample size was calculated based on a study done in India by Kutty Krishnan K et al., [7]. The prevalence of arthritis was nearly 60%, spondyloarthropathy was 44%, HIV associated arthralgia 19.8%. Assuming an average prevalence of rheumatological manifestations in HIV Patients to be 20% based on the previous studies [5,6], the sample size was taken as 385.

A total of 385 HIV infected patients attending the General Medicine outpatient department during the study period were included in the study after taking informed consent of the patients. Ethical committee clearance was taken IEC NO:01/12/2009/MCT. The patients' demographic details, the duration of musculoskeletal complaints (if any) was noted, the patient were to mark the site of pain/swelling in the mannequin provided in the performa, tenderness (if any) would be carefully marked in the mannequin. If arthritis was present the type of arthritis was marked. Back pain if present the possible nature (inflammatory/non inflammatory) was determined. A detailed joint evaluation was done to detect any joint swelling/tenderness and restriction in the range of movement of various joints.

STATISTICAL ANALYSIS

The assimilated data were used to study the clinical spectrum of musculoskeletal manifestations in the selected patients, the percentage of each of these manifestations and the prevalence of musculoskeletal manifestations in the study population. IBM SPSS Statistics version 17.0 was used for statistical analysis.

RESULTS

As shown in [Table/Fig-1], Out of 385 patients, 161 (41.8%) HIV patients were in the 30-39 year age group, There were 143 (37.1%) patients in the 40-49 age group. A total of 225 (58.4%) of patients with HIV infection were males and 160 (41.6%) were females.

Age distribution	Percentage %	Number
Less than 30	9.4	36
30-39	41.8	161
40-49	37.1	143
Above 50	11.7	45
Sex		
Male	58.4	225
Female	41.6	160
ART		
Yes	71.7	276
No	28.3	109
Musculoskeletal abnormality		
Present	25.2	97
Absent	74.8	288

[Table/Fig-1]: Demographic details of subjects.

A total of 276 (71.7%) patients were receiving ART, 109 patients were not on ART. Disease duration of less than one year in 135 (35.06%) patients, 1-5 year was seen in 174 (45.19%); while 76 (19.74%) patients had a disease duration of greater than five years.

The [Table/Fig-2] was shown the list of rheumatological manifestations seen in the study. A total of 97 (25.2%) HIV patients had some musculoskeletal abnormalities. Of total patients, 34 (8.8%) had HIV arthralgia while 34 patients (35.1%) of the affected HIV patients with Rheumatological manifestations had HIV arthralgia. Knee joint was the most commonly affected joint (94.1%) followed by hip shoulder wrist and elbow joint.

Rheumatological manifestation	Percentage of cases (%) / Number of cases
HIV arthralgia	35.1/34
Myalgia	18.6/18
Inflammatory back pain	14.4/14
Soft tissue rheumatism	12.4/12
Undifferentiated spondyloarthropathy	11.3/11
Fibromyalgia	9.3/9
HIV wasting	7.2/7
HIV arthritis	4.1/4
Psoas abscess	3.1/3
Plantar fasciitis	2.1/2
Pyomyositis	2.1/2
Psoriatic nail changes	2.1/2
Painful articular syndrome	2.1/2
Erythema nodosum and episcleritis	2.1/2
Miscellaneous (Degenerative spine/joint)	17.5/17
Potts spine	0.26/1

[Table/Fig-2]: Shows relative frequency of Rheumatological Manifestations in HIV patients.

Myalgia/muscle ache occurred in 18 patients (4.7%) and constituted 18.6% of the musculoskeletal symptoms. 14 (3.6%) patients of the total sample had Inflammatory Back Pain (IBP), while 14.4% of the musculoskeletal abnormalities was comprised by IBP. Twelve patients (3.1%) of HIV patients from the sample was having soft tissue rheumatism, shoulder area was most commonly involved followed by tennis elbow in 3 patients. Eleven patients (2%) had spondyloarthropathy and it constituted about 11.3% of the musculoskeletal manifestations found. All the cases of spondyloarthropathy seen were of the undifferentiated type. Nine patients (2.3%) from the total sample had fibromyalgia seven patients (1.8%) from the sample had HIV wasting, while it constituted 7.2% of the total musculoskeletal complaints detected. Four patients (1%) of the sample had HIV arthritis, and 17 patients (4.4%) of the sample had evidence of degenerative disease. Mechanical back pain was commoner 12.4%, degenerative joint disease was seen in 8.2% of the affected patients.

Three (3.1%) patients of 97 patients had evidence of Tubercular psoas abscess. Similarly out of 97 patients two patient (2.1%) each had evidence of plantar fasciitis, psoriatic nail changes, pyomyositis (*Staphylococcus aureus* related), painful articular syndrome, erythema nodosum and episcleritis. One patient had evidence of tuberculosis of the spine which resolved after treatment.

DISCUSSION

In the present study, most common musculoskeletal manifestation seen was HIV associated arthralgia. Myalgia was the next common symptom 4.7%. Inflammatory back pain was quite common but spondyloarthropathy was relatively less common. Undifferentiated spondyloarthropathy was the only spondyloarthropathy seen.

Mechanical back pain and degenerative joint disease was quite common and was also seen in a younger population infected with HIV. HIV arthritis was not very common musculoskeletal problem in the studied population. There were no cases of Vasculitis or diffuse infiltrative lymphoproliferative syndrome.

The incidence of rheumatic manifestations in HIV infection is about 4-71.3% cases in different studies [5-8]. Incidence depends on various factors like the stage of the disease and use of antiretroviral therapy. Musculoskeletal involvements and was found to be much more common in HIV patients than the HIV negative population [7-9]. Mechanisms of musculoskeletal involvement may be related directly due to the virus, opportunistic infections, non-infectious HIV related complications like medication induced or related to malignancies, or

Manifestations	USA (n=101)	Spain (n=556)	Argentina (n=102)	Delhi (n=102)	Chennai (n=29)	Present study Kerala (n=385)	Darjeeling (n=300)
HIV Arthralgia	34	1.6	26	11.7	17.2	35.1	26.7
HIV Arthritis	12	0.4	5	-	13.8	4.1	-
Undifferentiated Spondyloarthropathy	0	0.2	22	1.96	17.2	11.3	0.7
Septic Arthritis	-	-	-	0.98	3.4	-	2.3
Pyomyositis	-	-	-	-	3.4	2.1	0.7
Psoriatic arthropathy	2	0.4	1.1	0.98	0.34	2.1	-
Reactive Arthritis	10	0.4	11.2	1.96	17.2	-	2.3
Vasculitis	0.9	0.4	-	2.9	10.4	-	0.3
DILS	2	-	3	-	-	-	-

[Table/Fig-3]: Comparison of clinical manifestations in various studies [7,16,17,18].

unrelated rheumatologic disorders whose course have been altered by HIV related effect on the immunity of the host [10-12].

A range of rheumatic manifestations are known to occur related to HIV infection like arthralgia, body aches, rheumatoid arthritis, Systemic Lupus Erythematosus (SLE), HIV associated arthritis, reactive arthritis, painful articular syndrome, undifferentiated spondyloarthropathies, fibromyalgia, gouty arthritis, avascular bone necrosis, infections like pyomyositis, septic arthritis and osteomyelitis. Inflammatory muscle diseases have also been seen. Sjogren's syndrome, Diffuse Infiltrative Lymphocytosis Syndrome (DILS), vasculitis and Kaposi's sarcoma are uncommon manifestations [10].

The paradox seen in HIV infection is disease like DILS, reactive arthritis and inflammatory myopathies are occurring even in the presence of immunodeficient state while some disorders like rheumatoid arthritis and SLE have been known to improve in the face of the CD4 lymphocyte depletion [10].

Rheumatic manifestations can be due to direct effect of the HIV infection or related to the immune response generated by the host in relation to the infection which is mediated by the intact CD 8 cell component of the immune system. Introduction of ART has led to reduced rates of rheumatic manifestations like inflammatory arthritis and connective tissue diseases in patients with HIV infection. However, Arthralgia and myalgia has remained the commonest rheumatic manifestations in HIV patients in both Pre and Post-ART era [13-15].

The overall prevalence of musculoskeletal manifestations i.e., 25.2%, was comparable to the various studies [5-8] available, HIV associated arthralgia was the commonest symptom in all these studies. Indian studies in south India [7] had shown a high prevalence of spondyloarthropathy which was not seen in this study, [Table/Fig-3] shows the prevalence of various rheumatological manifestations seen in studies worldwide.

HIV arthritis was less prevalent compared to the other studies from India and Spain, USA and Argentina [7, 16-18]. Degenerative disease was commoner in the studied HIV positive patients. Conditions like vasculitis and diffuse infiltrative lymphoproliferative syndrome was not at all seen in the study population.

LIMITATION

Lack of control arm in the study and that it was not population-based.

CONCLUSION

Rheumatological manifestations are commonly seen in HIV Infected patients. HIV arthralgia, myalgia and undifferentiated spondyloarthropathy are the common manifestations of the disease.

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