



Revista Colombiana de REUMATOLOGÍA

www.elsevier.es/rcreu



Original Investigation

Prevalence of Rheumatic Disease in a Cohort of Patients With Human Immunodeficiency Virus Infection[☆]

María Claudia Díaz,^a Julián Esteban Barahona-Correa,^b
Sebastián Felipe Sierra-Umaña,^c Luisa Fernanda Patiño-Unibio,^d
Mario Fernando Benavides-Solarte,^e Sandra Valderrama,^f
Daniel G. Fernández-Ávila,^{a,*} Juan Martín Gutiérrez^a

^a Unidad de Reumatología, Hospital Universitario San Ignacio-Pontificia Universidad Javeriana, Grupo Javeriano de Investigación en Enfermedades Reumáticas, Bogotá, Colombia

^b Facultad de Medicina, Pontificia Universidad Javeriana, Bogotá, Colombia

^c Centro Nacional de Endocrinología y Metabolismo (CENDEM), Bogotá, Colombia

^d Departamento de Medicina Interna, Hospital Universitario San Ignacio, Facultad de Medicina, Pontificia Universidad Javeriana, Bogotá, Colombia

^e Departamento de Reumatología, Universidad Nacional de Colombia, Bogotá, Colombia

^f Unidad de Infectología, Hospital Universitario San Ignacio-Pontificia Universidad Javeriana, Bogotá, Colombia

ARTICLE INFO

Article history:

Received 15 October 2014

Accepted 16 March 2015

Keywords:

Rheumatic diseases

Human immunodeficiency virus

Arthritis

ABSTRACT

Objective: To describe the prevalence of rheumatic diseases in a cohort of patients with HIV infection attending a university hospital, along with their demographic and clinical features.

Patients and methods: Cross-sectional study of 1712 outpatients with HIV infection treated at a university hospital between January 2005 and September 2013.

Results: There was a prevalence of rheumatic diseases of 5.2% (n=89) in the patients studied, with 76% being male patients. The mean age of onset was 45 ± 11 years. Fourteen patients had reactive arthritis (15%), 14 had osteoarthritis (15%), 10 had immune thrombocytopenic purpura (11%), and 53 had other conditions (59%). The mean time between HIV diagnosis and rheumatic condition onset was 73 ± 66 months. The most prevalent comorbidities were dyslipidemia in 12 patients (11%), hepatitis B in 19 (17%), lipodystrophy in 12 (11%), herpes zoster in 11 (10%) and hypothyroidism in 10 (9%).

[☆] Please cite this article as: Díaz MC, Barahona-Correa JE, Sierra-Umaña SF, Patiño-Unibio LF, Benavides-Solarte MF, Valderrama S, et al. Prevalencia de enfermedades reumáticas en una cohorte de pacientes con infección por virus de la inmunodeficiencia humana. Rev Colomb Reumatol. 2015. <http://dx.doi.org/10.1016/j.rcreu.2015.03.003>

*Corresponding author.

E-mail address: danielfernandezmd@gmail.com (D.G. Fernández-Ávila).

Conclusions: A description is presented on the rheumatic diseases found in a cohort of patients with HIV infection. As reported in previous series, reactive arthritis is the most frequent rheumatic condition along with osteoarthritis. This study shows a trend towards successful aging of HIV patients due to a better control of the disease with the use of antiretroviral therapy, but with an increasing prevalence of osteoarthritis.

© 2014 Asociación Colombiana de Reumatología. Published by Elsevier España, S.L.U.
All rights reserved.

Prevalencia de enfermedades reumáticas en una cohorte de pacientes con infección por virus de la inmunodeficiencia humana

R E S U M E N

Palabras clave:

Enfermedades reumáticas

Virus de inmunodeficiencia humana

Artritis

Objetivo: Describir la prevalencia de enfermedades reumáticas en una cohorte de pacientes con infección por VIH y sus características demográficas y clínicas.

Pacientes y métodos: Estudio descriptivo de corte transversal de una cohorte de 1.712 pacientes con infección por VIH, en un hospital universitario, seguidos desde enero del 2005 hasta septiembre del 2013.

Resultados: Se encontró una prevalencia de enfermedades reumáticas del 5,2% (n = 89 casos), el 24% de sexo femenino y el 76% de sexo masculino. Edad promedio \pm desviación estándar 45 ± 11 años. Las enfermedades encontradas fueron: artritis reactiva 15% (n = 14), artrosis 15% (n = 14), púrpura trombocitopénica inmune 11% (n = 10), otras 59% (n = 53). El tiempo promedio entre el diagnóstico de VIH y la condición reumática fue de 73 ± 66 meses. Dentro de las comorbilidades se encontraron: dislipidemia 39% (n = 43), hepatitis B 17% (n = 19), lipodistrofia 11% (n = 12), herpes zóster 10% (n = 11) e hipotiroidismo 9% (n = 10).

Conclusiones: Se presenta información respecto a las comorbilidades reumáticas en una cohorte de pacientes con infección por VIH. Como se ha documentado en otras series, la artritis reactiva fue la enfermedad reumática más frecuente junto con osteoartritis. Nuestro estudio evidencia una tendencia hacia el envejecimiento de los pacientes con VIH gracias a un mejor control de la enfermedad, con el uso de terapia antirretroviral, lo cual aumenta la prevalencia de osteoartritis.

© 2014 Asociación Colombiana de Reumatología. Publicado por Elsevier España, S.L.U.
Todos los derechos reservados.

Introduction

Since many years ago, the infection with human immunodeficiency virus (HIV) has become a pandemic, being estimated a prevalence of 35.3 million people infected worldwide for the year 2012.¹ In Colombia, it was estimated a prevalence of 0.52% persons infected with the HIV virus, with a total of 129,630 people infected by the year 2011.² With the emergence of the new highly effective antiretroviral therapies (HAART) it has been possible to increase the quantity and quality of life of patients with HIV infection; at the expense of the development of chronic and degenerative diseases, among which the rheumatic conditions take great importance. Several studies have shown that rheumatic manifestations in patients with HIV are frequent, however, the reported prevalence data are very variable, ranging between 9^{3,4} and 25%.³ We present below the information found in a cohort of patients treated at a university hospital in Colombia.

Patients and Methods

Descriptive cross-sectional study of a cohort of 1712 patients managed by the program of care for people with HIV infection, in the outpatient service of a third level of complexity university hospital in Bogota-Colombia, followed-up from January 2005 until September 2013. Only were characterized the patients referred by the service of infectious diseases to the rheumatology outpatient clinic due to any joint or muscle symptom.

In the study were included patients of both genders, older than 18 years, with HIV infection documented by Elisa and confirmed by Western Blot; a history of joint trauma that could explain osteoarticular symptoms was considered as a criterion of exclusion, however, no patient was excluded of the study for this reason. It was not kept a record of appointments scheduled or fulfilled by the patients referred to rheumatology, which might constitute a selection bias, however, since from the contractual point of view the hospital provides the totality of out-

patient and inpatient hospital services to this group of patients, it was considered that all the referred patients attended the rheumatology outpatient service of the institution.

The collection of the data under study of patients with HIV infection and diagnosed rheumatic condition was carried out in the rheumatology clinic through a form designed by the researcher with the variables of interest (age, gender, rheumatic condition, timing of the HIV infection and the rheumatic condition, antiretroviral treatment and comorbidities.) The data were analyzed with measures of central tendency, using frequencies, percentages, means, medians and averages with their respective standard deviation. Microsoft Excel was used for their analysis. The study was approved by the Ethics Committee of the San Ignacio University Hospital.

Results

For the period studied, of the 1712 patients infected with HIV, 80 patients were diagnosed with a rheumatic condition in the rheumatology outpatient service; 9 of them had double rheumatic condition, so the total number of events was 89. It was found a mean age \pm standard deviation of 45.4 ± 11 years for both genders. Of the patients with rheumatic comorbidity within the cohort, 61 were male (76.2%) and 19 were female (23.7%), with a similar distribution to that of the total cohort. All patients received antiretroviral treatment, 78 of them with 2 or more drugs (97.5%) and only 2 patients with monotherapy (2.5%) (Table 1).

19 different rheumatic conditions were diagnosed, being the most frequent: reactive arthritis 14 cases (15.7%), osteoarthritis 14 cases (15.7%), immune thrombocytopenic purpura 10 cases (11.2%), osteoporosis and fibromyalgia with 8 cases (8.9%) each (Table 2).

For the cohort of 1712 patients of the San Ignacio University Hospital with HIV infection, it was determined an overall prevalence of rheumatic diseases of 5.2%, being estimated a prevalence of 0.8% for reactive arthritis and osteoarthritis, 0.5% for immune thrombocytopenic purpura and 0.4% for fibromyalgia and osteoporosis, respectively. Sixty patients (75%) had at least one associated non-rheumatic comorbidity, the 20 remaining patients (25%) only had the rheumatic condition without other associated diseases. A total of 109 cases of non-rheumatic comorbidities were diagnosed, being the

most frequent: dyslipidemia with 43 cases (39.4%), infection with hepatitis B virus in 19 cases (17.4%), lipodystrophy in 12 cases (11%), herpes zoster infection in 11 cases (10%) and hypothyroidism in 10 patients (9.1%) (Table 3).

Nine patients had double rheumatic condition (11.2%), for a total of 89 rheumatic conditions diagnosed, of which 78 (87.6%) were diagnosed after the diagnosis of VIH infection, with a mean time between diagnoses of 79.4 ± 68.7 months. The diagnosis of the 11 remaining cases (12.3%) was established before

Table 2 – Prevalence of Rheumatic Conditions in 1,712 Patients Infected With HIV.

Rheumatic condition	Cases (n)	Percentage	Prevalence (%)
Arthrosis	14	15,73	0,82
Reactive arthritis	14	15,73	0,82
Immune thrombocytopenic purpura	10	11,24	0,58
Fibromyalgia	8	8,99	0,47
Osteoporosis	8	8,99	0,47
Gouty arthritis	6	6,74	0,35
Psoriasis	5	5,62	0,29
Rheumatoid arthritis	4	4,49	0,23
Raynaud's phenomenon	3	3,37	0,18
Spondyloarthritis	3	3,37	0,18
Vitiligo	3	3,37	0,18
Hip osteonecrosis	2	2,25	0,12
Systemic lupus erythematosus	2	2,25	0,12
Inflammatory myopathy	2	2,25	0,12
Juvenile idiopathic arthritis	1	1,12	0,06
Hyperuricemia	1	1,12	0,06
Ankylosing spondylitis	1	1,12	0,06
Primary vasculitis	1	1,12	0,06
Delayed hypersensitivity syndrome	1	1,12	0,06
Total rheumatic conditions	89		5,20

Percentage refers to the percentage of cases of each rheumatic disease within the group of patients with rheumatic comorbidity; prevalence calculated for the total cohort of patients with HIV.

Table 1 – Clinical and Demographic Features.

Features	HIV (n = 1,712) n (%)	HIV+ RC (n = 80) n (%)
Age (years) (mean \pm SD)	40 \pm 11	45.4 \pm 11
Gender		
Male	1,459 (85.2)	61 (76.2)
Female	253 (14.7)	19 (23.7)
Treatment		
Monotherapy	–	2 (2.50)
Polytherapy	–	78 (97.5)
RC: rheumatic condition.		

Table 3 – Non-rheumatic Comorbidities in Patients With Rheumatic Disease and HIV Infection.

Comorbidity	Number of cases	Percentage of cases
Dyslipidemia	43	39
Hepatitis B infection	19	17
Lipodystrophy	12	11
Herpes zoster infection	11	10
Hypothyroidism	10	9
Syphilis	6	6
Herpes simplex infection	5	5
Cytomegalovirus infection	3	3

the diagnosis of the HIV infection, with a mean time between diagnoses of 27.1 ± 45.2 months. The double rheumatic conditions were: reactive arthritis-fibromyalgia, spondyloarthritis-fibromyalgia, osteoarthritis-fibromyalgia, osteoporosis-fibromyalgia, osteoporosis-gouty arthritis, osteoporosis-osteoarthritis, osteoporosis-reactive arthritis, systemic lupus erythematosus-arthritis and reactive arthritis-osteoarthritis. In 2 of these patients, one of their rheumatic diagnoses was established before the diagnosis of HIV (patient n° 1 gouty arthritis before HIV and osteoporosis after HIV, and patient no. 2 osteoarthritis before HIV and systemic lupus erythematosus after HIV). The other rheumatic conditions were documented after the diagnosis of HIV.

Discussion

The HIV infection has been associated with a variety of rheumatic manifestations.⁵ Although acute rheumatic conditions such as reactive arthritis still show a high frequency; chronic osteoarticular diseases such as osteoarthritis have increased, probably due to the use of HAART, which has increased the life expectancy of patients with HIV.⁶⁻⁸

An overall prevalence of rheumatic manifestations of 5.2% was found in patients with HIV infection, being slightly lower than the value reported by Nguyen and Reveille, in 2009, with a prevalence of 9%.⁴ The present study makes evident the variety of rheumatic clinical expressions in patients with HIV infection, which could be associated with the different stages of the infection, the immunological stages specific to each patient, or be related to the immune reconstitution syndrome, as described previously in the literature.⁹

Regarding the most frequent diseases, previous studies^{4,10} reported a frequency of 5% of arthritis and arthralgias in patients with HIV infection, with a tendency to improve within 6 weeks after onset. In 2008, Yao et al. found, in a population of 888 patients with HIV infection, that the prevalence of arthropathies was 5.5%, being reactive arthritis one of the most frequent¹⁰; previously, septic and malignant complications were described more frequently,¹¹ however, our study shows 15.7% of cases of reactive arthritis among the rheumatic conditions found in this cohort, that could be related with the different infectious conditions to which such patients are exposed due to their immunosuppression status. 15.7% of osteoarthritis was documented among the rheumatic conditions identified, which, taking into account the directly proportional relationship between aging and frequency of this conditions, makes evident a trend towards the increase of the survival of these patients with the use of HAART and therefore, to the occurrence of more cases of osteoarthritis. The rheumatic conditions that occur in patients with HIV infection vary among different population groups, and therefore, genetic and environmental factors may be determinant in the presentation of the different rheumatic manifestations.^{12,13}

Additionally, other comorbidities were found in 75% of patients with HIV and associated rheumatic condition. Metabolic disorders and viral infections were the most frequent comorbidities; dyslipidemia (39.4%) was documented,

followed by cases of hepatitis B infection (17.4%). To explain the documented metabolic alteration, is well known the effect of HAART on the lipid metabolism, a fact that could explain this finding. It was found a remarkable frequency of hypothyroidism (9.1%), a disease that can have an autoimmune substratum, particularly in young patients such as those of our cohort. These findings recall the importance of the integrated management of these patients, always under a multidisciplinary approach that allows us to go beyond the antiretroviral treatment, allowing the identification of associated conditions that alter the patients' quality of life and generate a change in their morbidity and mortality profiles.

Among the limitations of our study we found the possibility of selection bias, because although contractually our hospital must guarantee the comprehensive care of the population that makes up the cohort and within this care is included the rheumatology consultation when it is necessary, some patients might not have attended the consultation with the rheumatologist; however, with the active follow-up performed by the nursing staff working in the HIV program to the orders of services that are delivered to patients, we consider that the possibility of loss of a significant number of patients in this way is unlikely.

Among the topics for future research, it is important to determine the influence of the different HAART regimes in the development of rheumatic conditions. Likewise, determining the antirheumatic management of the different conditions detected may be useful for the therapeutic approach of these patients. Additionally, the relation of infection and metabolic comorbidities in the development of the HIV-associated rheumatic pathology must be known more deeply.

Our work describes a population of HIV patients assessed on a regular basis at a university hospital and their comorbidities from the point of view of rheumatology, obtaining baseline information for future studies.

Conclusion

The present study describes the frequency of rheumatic comorbidities and within this population the non-rheumatic comorbidities in a cohort of patients with HIV infection, treated on an outpatient basis at a university hospital, with results that are close to those reported in other studies. Reactive arthritis and osteoarthritis were the most frequently encountered conditions; the first one correlates with the presence of acute infections in this type of patients due to their immunosuppression status; the second constitutes a novel report in the literature, which probably obeys to an increase in the average age of such patients, due to the effect of HAART on survival. Multidisciplinary treatment and follow-up are crucial for the detection and timely management of these and other associated conditions.

Ethical Considerations

This study was approved by the Ethics Committee of the San Ignacio University Hospital.

Ethical Disclosures

Protection of people and animals. The authors declare that the procedures followed were in accordance to the ethical standards of the responsible committee on human experimentation and according with the World Medical Association and the Declaration of Helsinki.

Data confidentiality. The authors state that they have followed the protocols of their workplace regarding the publication of patient data.

Right to privacy and informed consent. The authors state that patient data do not appear in this article.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgements

Service of infectious diseases of the San Ignacio University Hospital.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS. Global report: UNAIDS report on the global AIDS epidemic 2013. Geneva: Joint United Nations Programme on HIV/AIDS; 2013.
2. Ministerio de Salud y de Protección Social. Resumen de situación de la epidemia por VIH/SIDA en Colombia 1983-2011. República de Colombia. Mayo del 2012.
3. Solórzano A. Manifestaciones músculo esqueléticas en pacientes con VIH. Unidades de infectología, inmunología y reumatología-Complejo Hospitalario Universitario Ruiz y Páez. Julio 2005-julio 2006. Trabajo especial de grado de especialista. 2008.
4. Nguyen BY, Reveille JD. Rheumatic manifestations associated with HIV in the highly active antiretroviral therapy era. *Curr Opin Rheumatol*. 2009;21(4):404-10.
5. Reveille JD, Williams FM. Infection and musculoskeletal conditions: Rheumatologic complications of HIV infection. *Best Pract Res Clin Rheumatol*. 2006;20(6):1159-79.
6. Calabrese LH, Kirchner E, Shrestha R. Rheumatic complications of human immunodeficiency virus infection in the era of highly active antiretroviral therapy: Emergence of anew syndrome of immune reconstitution and changing patterns of disease. *Semin Arthritis Rheum*. 2005;35(3):166-74.
7. Zhang X, Li H, Li T, Zhang F, Han Y. Distinctive rheumatic manifestations in 98 patients with human immunodeficiency virus infection in China. *J Rheumatol*. 2007;34:1760-4.
8. Medina Rodríguez F. Rheumatic manifestations of human immunodeficiency virus infection. *Rheum Dis Clin North Am*. 2003;29(1):145-61.
9. Lawson E, Walker-Bone K. The changing spectrum of rheumatic disease in HIV infection. *Br Med Bull*. 2012;103(1):203-21.
10. Yao Q, Frank M, Glynn M, Altman RD. Rheumatic manifestations in HIV-1 infected in-patients and literature review. *Clin Exp Rheumatol*. 2008;26(5):799-806.
11. Márquez J, Restrepo CS, Candia L, Berman A, Espinoza LR. Human immunodeficiency virus-associated rheumatic disorders in the HAART era. *J Rheumatol*. 2004;31(4):741-6.
12. Vega K. Manifestaciones reumatológicas en pacientes infectados con VIH. *Acta Med Colomb*. 2010;35(1):15-20.
13. Patel N, Patel N, Espinoza LR. HIV infection and rheumatic diseases: The changing spectrum of clinical enigma. *Rheum Dis Clin North Am*. 2009;35(1):139-61.