Impact of HIV infection in dermatomycosis. Cases and controls study

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ABSTRACT

Background: In the population of HIV-infected patients, superficial mycoses may have different clinical manifestations, evolution and etiology from those found in the non-HIV population. **Objectives**: To describe superficial lesions of fungal etiology in HIV-infected patients and compare them with a control group. **Materials and methods:** 79 patients (25 HIV positive and 54 controls) were evaluated. A card was prepared with data: age, sex, description and location of the lesion, evolution time and previous treatment. Samples of skin and lines of lesions with suspected fungal etiology were taken and a mycological study was performed. **Results:** A slightly significant difference was observed between HIV reactive patients with respect to the control group in the number of cases of foot Tinea unguium. The clinical presentation of intertrigo was more observed in the group of HIV positive patients. **Conclusions:** Superficial mycoses are more common infections in HIV reactive patients, with mixed clinical presentations and the difference in CD4 count between the HIV population in successful ARV treatment does not modify the clinical presentation of dermatophytosis.

KEYWORDS

Dermatomycoses, Human Immunodeficiency Virus, Epidemiology

Impacto de la infección por VIH en la dermatomicosis. Estudio de casos y controles

RESUMEN

Introducción: En la población de pacientes infectados por VIH las micosis superficiales pueden tener manifestaciones clínicas, evolución y etiología diferentes de las halladas en la población sin esta condición. **Objetivos**: Analizar las lesiones superficiales de etiología micótica en pacientes infectados por VIH en relación a un grupo control. **Materiales y métodos**: Se evaluaron 79 pacientes (25 VIH positivos y 54 con-

troles). Se analizaton variables demográficas, topografía de la lesión, tiempo de evolución, carga viral, CD4 y tratamiento previo. **Resultados**: Se tomaron muestras por raspado de las lesiones con y se realizò estudio micológico de las mismas Se observó una diferencia levemente significativa entre pacientes VIH reactivos con respecto al grupo control en el número de casos de Tinea unguium de pies. La presentación clínica de intertrigo fue más observada en el grupo de pacientes VIH positivos. **Conclusiones**: Las micosis superficiales son infecciones más comunes en los pacientes VIH reactivos, con presentaciones clínicas mixtas y los diferentes valores de LTCD4 entre la población VIH en tratamiento ARV exitoso no modifica la presentación clínica de las dermatofitosis.

PALABRAS CLAVE

Dermatomicosis, Infecciones por HIV

INTRODUCTION

The disease caused by the Human Immunodeficiency Virus (HIV) causes a diminution of the host's immune response that leads to the onset of opportunistic infections, secondary neoplasms and neurological complications (1)

HIV-infected patients have a marked decrease in the number of Langerhans cells, TCD4 lymphocytes (LT CD4), Natural Killer cells, macrophages and monocytes, and lower activity of Langerhans cells (2, 4) has been reported. In this population we find opportunistic diseases such as superficial mycosis, which may have different clinical manifestations, evolution and etiology than those found in the population without HIV infection so it is very important to make a correct diagnosis to avoid treatment failures (5,6). The number of patients with HIV and Acquired Immunodeficiency Syndrome (AIDS) who will develops some form of manifestation or infection of the skin, varies according to different publications between 40 and 95% (2.3).

The main etiological agents of dermatomycosis are filamentous fungi (dermatophytes) belonging to the genera *Trichophyton, Microsporum* and *Epidermophyton*, in addition there are mycosis produced by yeast belonging to the genera *Candida, Malassezia* and *Trichosporon* (7).

There are several clinical manifestations of dermatophytosis and they depend on factors such as the species of dermatophyte involved, the size of the inoculum, the anatomical location and the host's immune state.

In patients with HIV infection, dermatophyte infections can be extensive, multiple with compromise of the limbs of the body, several nails, that respond poorly to treatment (8).).

This mycosis may predispose to other skin infections as they cause a disruption of the mucous skin barrier. (8) Therefore in HIV patients rapid diagnosis and correct treatment, are essential to prevent the onset of other infections.

Dermatophytosis can occur at any time during HIV infection, but most cases of extensive or atypical lesions have been reported in patients with severe immunosuppression with LTCD4+ count below 100 cells/mm3 (8.9). Proximal white onychomycosis is very rare in the general population, but is described as a sign of HIV virus infection (8). Antiretroviral therapy or the use of systemic antifungals for the prophylaxis of opportunistic infections may also influence the onset of atypical forms of these mycosis. (9).

The objective of this work is to describe superficial lesions of fungal etiology in HIV-infected patients and compare them with a control group.

MATERIALS AND METHODS

STUDY DESIGN

An observational case and control study was performed. The confidentiality of patients' personal data was maintained in accordance with the National Law on the Protection of Personal Data (No. 25.326).

Patients of both sexes and any age participated. The variables studied were age, gender, location of the lesion, time of evolution and prior treatment. Of the HIV infected population the LT CD4 count and viral load (copies/ml) were also recorded. The data collected was encoded and uploaded to a prospective database.

PROCEDURES

Skin, nails and hairs samples were taken of lesions with suspected mycotic etiology by scraping with sterile scalpel. The scales collected between sterile slides were processed for mycological study that included direct microscopic examination with 20% potassium hydroxide and culture in Saboureaud Agar and Lactrimel Agar, incubated at 28◦C for 21 days with and without chloramphenicol. Fungal identification of positive cultures was performed by: a) macromorphological description of color and texture of colonies and micromorphological analysis by dissociation with lactophenol blue and microscopic observation, and b) matrix -assisted lasser desorption/ ionization time-of-flight mass spectrometry (MALDI-TOF MS, VITEK® 2 Systems, BioMerieux).

STATISTICAL ANALYSES

Pearson chi square, Fisher's Exact Test, and Student t-test were performed for the statistical analysis. IBM-SPSS v25 Software was used.

RESULTS

A total of 79 patients, 25 with prior diagnosis of HIV and 54 controls were analysed. The characteristics of the population studied are shown in Table 1 and 2. A slightly significant difference was observed between HIV reactive patients (17/25) from the control group (47/54) in the number of cases of Tinea unguium of feet (p 0.048). (Graph1) With regard to clinical presentation the intertrigo was most observed in the group of HIV patients (5/25) with a significant difference (p.0 .002) where 5 patients presented it out of a total of 25. No patients in the control group had intertrigo. (Graph2) Significant differences (p= ,000) were found between the viral load of HIV-positive associated with the presence of intertrigo (5/25) (Graph4) Respect to microbiological diagnosis, a significant difference was observed with respect to direct microscopic examinations of samples between HIV-positive and negative patients(Graph3).Patients in the control group had positive directs in all cases, filaments were observed in 47 cases and in 7 yeasts, while in the HIV group only 14 of 25 samples were positive, 12 with dermatophytes and 2 with yeast. The most frequently isolated agent was *Trichophyton rubrum* in both groups.

DISCUSSION

The most common dermatophytes in patients with HIV, *Trichophyton rubrum* and *T. mentagrophytes* are the same as those affecting the general population. In HIV patients, *Trichophyton rubrum* is responsible for infection in the skin of lower limbs, interdigital spaces and in the proximal part of the affected nails (11). In our study, patients had mixed infections, tinea pedis and intertrigue in greater proportion than seronegative patients. This prevalence of mixed infections in HIV-positive patients has already been described in other papers (11). There were not found any no dermatophyte fungi although they were found in other researches, in which the presence of hyaline fungi of the genera *Scopulariopsis* spp. *Aspergillus* spp., *Acremonium* spp. , *Fusarium* spp .and *Scytalidium* spp were detected in nail injuries (12). We also didn t find lesions compatible with Majocci granuloma, (11) a dermatophytosis caused by *Trichophyton* pp species. This could be explained by why Majocci granuloma is more common to observe in non-HIV immunosuppressed patients. The clinical course and incidence of dermatophytosis in HIV patients can be modified with the use of ARV treatment and fungal therapy (10), our work shows that although many had ARV treatment with undetectable viral loads, HIV patients had significant differences from clinical presentation compared to seronegatives. Some authors show that more than 30% of HIV patients have onychomycosis that develops with a CD4 account of approximately 450 mm3(2). Reactive HIV patients have a diminution of the cellular immune response that facilitates local fungal invasion, hence the lesions can look more atypical, extensive and severe compared to the group of HIV-negative patients (10). Immunosuppression would allow the uncontrolled multiplication of dermatophytes, with clinical samples observing large

numbers of filaments and arthroconids. Our results correspond to a population that was not in the AIDS category according to the classification of the Center for Disease Control and Prevention (CDC) at the time of sampling

We consider that in the future could be necessary to evaluate other factors related to the appearance of dermatoffices in both populations, such as obesity, basic treatments, comorbidities: diabetes, use of corticosteroids.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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STROBE STATEMENT—CHECKLIST OF ITEMS THAT SHOULD BE INCLUDED IN REPORTS OF ***CASE-CONTROL STUDIES***

	Item No	Recommendation	Page No
Title and abstract	1	(***a***) Indicate the study's design with a commonly used term in the title or the abstract	
		(***b***) Provide in the abstract an informative and balanced summary of what was done and what was found	
		Introduction	
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	
		Methods	
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	
Participants	6	(***a***) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		(***b***) For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(***a***) Describe all statistical methods, including those used to control for confounding	
		(***b***) Describe any methods used to examine subgroups and interactions	
		(***c***) Explain how missing data were addressed	
		(***d***) If applicable, explain how matching of cases and controls was addressed	
		(***e***) Describe any sensitivity analyses	
		Results	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	

	Item No	Recommendation	Page No
Main results	16	(***a***) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (***b***) Report category boundaries when continuous variables were categorized (***c***) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
		Discussion	
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	
		Other information	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*GIVE INFORMATION SEPARATELY FOR CASES AND CONTROLS.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

TABLE 1: CHARACTERISTICS OF THE POPULATION STUDIED DEMOGRAPHICS AND CLINICAL PRESENTATIONS

	Controls	Patients HIV+
GENDER		
Male	25 (46%)	15 (60%
Female	29 (54%)	10 (40%)
LOCATION		
Tinea pedis	6 (11.11%)	6 (24%)
Tinea ungeum (hands)	11 (20,37%)	7 (28%)
Tinea ungeum (feet)	47 (87,03%)	18 (72%)
Tinea interdigitalis (intertrigo feet)	0 (100%)	5(20%)
Tinea capitis	1 (1.85%)	0 (0 %)
Tinea corporis	0	2 (8%)
Clynic in onychomycosis		
Onicolisis	6 (11.11%)	13 (52%)
Onychodistrophy	12 (22,22%)	0
Leuconiquia	2 (3,70%)	2 (7.6%)
Hyperkeratosis	12 (22,22%)	28 (96%)

Perionixis	1 (1.85%)	0
Antifungal treatment	15 (27,7%)	0

TABLE2 CHARACTERISTICS OF THE HIV POPULATION

LT CD4	
>200 mm3	20 (80%)
<200 mm3	5 (20 %)
Viral load (number of copies/ml)	
< 40	16 (64%)
≥ 40	9 (36%)

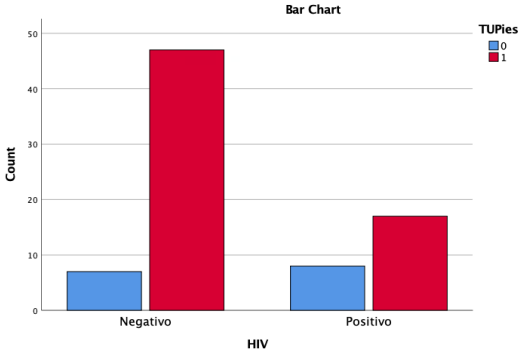

FIGURE 1: COMPARISON OF THE NUMBER OF PATIENTS WITH TINEA UNGEUM IN HIV POSITIVE AND CONTROL GROUPS (0: NO PRESENTATION, 1: WITH PRESENTATION)

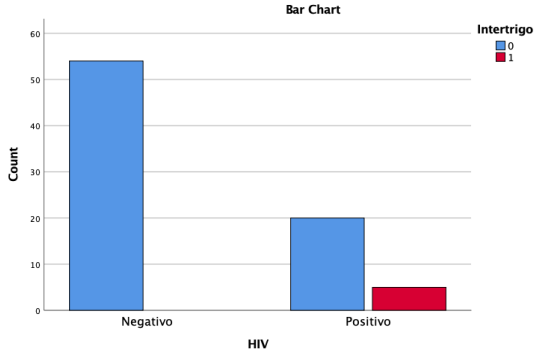

FIGURE 2: COMPARISON OF THE NUMBER OF PATIENTS WITH INTERTRIGO IN HIV POSITIVE AND CONTROL GROUPS (0: NO PRESENTATION, 1: WITH PRESENTATION)

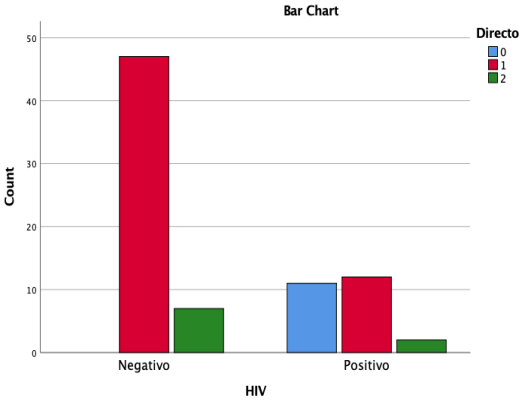

FIGURE 3: RESULTS OF DIRECT MICROSCOPIC EXAMINATIONS OF CLINICAL SAMPLES IN HIV AND NON-HIV PATIENTS (0= NEGATIVE 1: FILAMENT 2) YEAST)

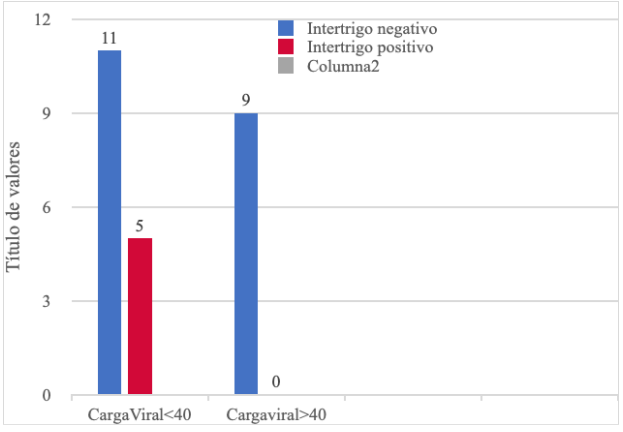

GRÁFICO 4: RELACIÓN ENTRE INTERTRIGO Y CARGAS VIRALES EN EL GRUPO VIH POSITIVO (0=SIN PRESENTACIÓN 1= CON PRESENTACIÓN)