

The profile of the dermatoses in children with the HIV virus at the Fundação de Medicina Tropical do Amazonas*

Perfil das dermatoses em crianças portadoras do vírus HIV na Fundação de Medicina Tropical do Amazonas

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Abstract: **BACKGROUND:** The Acquired Immunodeficiency Syndrome (AIDS) constitutes a sub-epidemic in Brazil. Due to the increasing number of women infected by the virus, the vertical transmission increased substantially, and due to the lack of adequate prophylactic treatment, many children are infected and show manifestations of the disease in early ages. Multiple systems are affected by the HIV virus, and the skin is often the first organ to be involved.

OBJECTIVES: The objective of this study is to analyze the clinic, dermatological and epidemiological profiles of children carriers of the virus in the City of Manaus aiming at identifying the most frequent dermatoses that affect these children and try to relate these dermatoses to the immunologic deterioration.

METHODS: A study was conducted where children carriers of the HIV virus from the Fundação Alfredo da Matta and Fundação de Medicina Tropical were studied from March 2007 to July 2008. These children were submitted to dermatological and laboratorial exams such as viral load dosage and CD4+ and CD8+ counts.

RESULTS: During the study period, 70 HIV + children were examined; all of them had AIDS and had been contaminated by vertical transmission. The average number of dermatoses by children was 1.73, and 95.5% had at least one dermatosis during the study period. The most frequent manifestations were atopic dermatitis (22.9%), childhood prurigo (20%) and warts (18,6%).

CONCLUSIONS: Children with HIV/AIDS have more skin disorders than children without HIV/AIDS. There was no statistical difference between the children in the group using ARVT and the group that wasn't using it.

Keywords: Disabled children; HIV; Minors; Skin diseases

RESUMO: **FUNDAMENTOS:** A Síndrome da Imunodeficiência Adquirida (AIDS) tem se configurado como uma sub-epidemia no Brasil, devido ao crescente número de mulheres infectadas pelo vírus, a transmissão vertical aumentou significativamente, e devido à falta de tratamento profilático adequado, muitas crianças são infectadas e convivem com as manifestações da doença precocemente. Múltiplos são os sistemas acometidos pelo vírus HIV, sendo a pele muitas vezes o primeiro órgão acometido.

OBJETIVOS: O estudo teve por objetivo analisar o perfil clínico-dermatológico e imunológico das crianças portadoras do vírus HIV na cidade de Manaus com a finalidade de identificar as dermatoses mais frequentes que as acometem e relacioná-las com a deterioração de seu sistema imunológico.

MÉTODOS: Realizou-se um estudo onde foram acompanhadas entre março de 2007 a julho de 2008, crianças portadoras do vírus HIV atendidas na Fundação de Medicina Tropical do Amazonas. Estas foram submetidas a exame dermatológico e a exames laboratoriais como dosagem de carga viral, CD4+, CD8+.

RESULTADOS: Durante o período estudado, foram atendidas 70 crianças HIV+, todas já apresentavam AIDS e tinham sido contaminadas por transmissão vertical. A média de dermatose por criança foi de 1,73 sendo que 95,5% apresentaram pelo menos uma dermatose. As manifestações mais frequentes foram: dermatite atópica (22,9%), prurigo estrófulo (20%) e verruga (18,6%).

CONCLUSÃO: As crianças com HIV/AIDS apresentaram mais dermatoses do que as crianças sem HIV/AIDS. Não houve diferença estatística em relação às dermatoses entre o grupo de crianças que estava em uso de Terapia antiretroviral (TARV) e o que não estava.

Palavras-chave: Crianças com deficiência; Dermatopatias; HIV; Menores de idade

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INTRODUCTION

The vertical transmission is responsible for 80 to 90% of the cases of AIDS in children in Brazil and throughout the world, and the progression of the disease in mothers has been associated with a decrease in the number of CD4⁺ lymphocytes and a high viral load, which is one of the main risk factors for the increase of vertical transmission.¹ In Brazil, from the total of more than 474 thousand confirmed cases, 160 thousand are women. According to a study conducted in 2004 in a sample of parturient women aged 15 to 49 years from all regions of Brazil, the prevalence rate of parturients with HIV was 0,42%, which corresponds to approximately 13 thousand infected parturients.²

The infection by the HIV in children differs from the infection in adults in terms of the transmission, the natural course of the viral dynamics, the maturation of the immune system and the clinical manifestations. At birth the viral load is usually low (less than 10.000 copies/ml) and then it slowly increases over the next 2 months of life to values around 100.000 copies/ml and only slowly decreases after the age of 4 to 5 years. The high viral load in children is associated with the somatic development of the lymphatic system and the inability of the immune system, still immature, to prepare a HIV-specific response.³

The skin is the organ most frequently affected in patients with HIV/AIDS; the prevalence of dermatological problems can reach up to 92%, and they are sometimes the first sign of infection by the virus. Many of the dermatoses that affect people with the HIV also develop in the non-infected population, the differences in their presentation can be minimal while the patient is still immune competent; however, with the decline of the immune system, the dermatoses become more frequent, severe, recurrent and refractory to conventional therapy.⁴

Children infected by the HIV can develop a variety of mucocutaneous manifestations like skin infections, tumors and inflammatory diseases, and they tend to be less responsive to conventional treatment. The disease most frequently found are candidiasis, dermatophytosis, herpes simplex, herpes zoster and a variety of bacterial dermatoses, as well as pharmacodermia due to the institution of antiretroviral therapy.⁵⁻⁷ Amongst the inflammatory dermatoses seborrheic dermatitis, pyoderma gangrenosum and vasculitis are included. Besides, severe seborrheic dermatitis, vasculitis and drug eruption can represent the first manifestation of infection by the HIV.⁸

In Manaus, during the present study period the pediatric population was 122 HIV+ children and most of them were followed at the Fundação de Medicina Tropical do Amazonas (FMT-AM).

The objective of this study was to analyse the clinical, immunologic and epidemiologic characteristics of the children carrying the HIV virus followed at the FMT-AM (reference centre for HIV positive children in the Amazonas).

MATERIAL AND METHODS

A descriptive, observational, cross-sectional study, with an analytic component, was conducted in all children under the age of 13 carrying the HIV virus who were being followed at the pediatric infectious diseases outpatients' clinic, during the period of March 2007 to July 2008. Only one indigenous child was excluded from the study. A total of 70 children from Manaus and the country Amazonas were assessed, and they went through a detailed dermatological examination; standard attendance cards were used, and they contained the personal details of the child and guardians, demographic and clinical data like the type of transmission, medication used, etc, and they underwent dermatological examination.

Results from complementary tests like complete blood count, CD4 and TCD8 T lymphocytes and viral load count were taken from each child's medical chart, according to the routine of the service. The patients were classified into categories according to clinical and immunological criteria, based on the system of classification of immune suppression in children with the HIV from the Centre for Disease Control (CDC) presented on charts 1 and 2.⁹

The data collected was entered into an Excel spreadsheet and analysed in the Epi-Info Windows version. A description of the observed frequencies was conducted and the statistical test χ^2 for the association among clinical and immunological variables was applied.

RESULTS

A total of 124 consultations were conducted during the study period, and some children were examined more than once due to the development of a new dermatosis. All of them were exposed to the HIV by vertical transmission and already had AIDS. Durante the study one child died with a pneumopathy.

There were 39 (55,7%) female children and 31 (44,3%) male. The children's age range varied from 1 to 12 years, with an average age of 7 (SD=3,2). In relation to housing 45 (69,2%) amongst the 65 who provided this data, resided in their own home and 20 (30,8%) did not. In terms of the type of house, 42 (65,6%) lived in a brick house, 15 (23,4%) in timber houses and 7 (10,9%) in mixed type houses, from a total of 64 children from whom we had this data. From the total of 70 patients 18 (26,5%) were housed

at the Casa Vhida (and institution that offers support to children with HIV) at the time of the study, 50 (73,5%) were living with relatives and for two we did not have this data. Amongst the 70 children, 17,1% were offspring from a deceased mother and 8,5% from a deceased father; 2,8% had been abandoned by the mother and 8,5% abandoned by the father.

With the exception of the children who were institutionalized or unaccompanied by a parent at the time of consultation, we collected data regarding parents' schooling and their income; the family total income from 72,2% of them was around two minimum wages. In terms of the educational level of the children's parents who were accompanied by a mother or father, from the ones we obtained this data most completed between years 5 to 8 of fundamental school. Only 3% of the mothers and 4% of the fathers had started tertiary studies. Amongst the minors studied, 44 were at school age (from 6 years old); from four of them we did not obtain information regarding schooling and from the remaining 40 the situation was as follows: 72% were between levels 1 and 4 of fundamental school, 13% children were between years 5 and 8 and 15% were being alphabetized. A biggest proportion of the children studied (33%) had moderate clinical symptoms and severe immunologic abnormalities (B3), followed by the category B2 and a small number were part of the C1 classification as shown on table 1.

In terms of treatment, 20 children (28,6%) were not using antiretroviral therapy because they did not fit the criteria for the initiation of the ARVT in children, while 50 (71,4%) were using it. As for the prophylaxis against *Pneumocystis jiroveci*, 49 patients (70%) amongst the 70 studied were using trimethoprim - sulfamethoxazole, while 21(30%) were not using it. Medication was prescribed to all children who presented with a dermatological manifestation, according to the pathology identified and whenever available for distribution at the institution. Amongst the 50 children under ARVT, 44 (88%) were using three ARV medications, 4 used only 2 ARVs and 2 were

using 4 ARV medications. Amongst the 70 children assessed, 67 (95,7%) had at least one dermatosis during the study period and from the 3(4,3%) children without dermatosis only one was not using ARVT and was classified as B2.

The average number of dermatoses per child examined was 1,73. Table 2 shows the distribution of the dermatoses grouped according to their etiology; from the grouped categories, 8,6% were from bacterial origin, 11,4% fungal, 28,6% were viral and 42,9% were allergic manifestations; 29 disease were grouped in the other dermatoses category and they included acne, seborrheic dermatitis, follicular keratosis, miliaria, dyshidrosis, aphtha, livedo reticularis, insect bites, scars, residual hypochromias and mucous cyst. In the children on the age range from 1 to 5 years with a severe immunological profile (CD4<500) there was a predominance of dermatoses from bacterial origin (50% of the cases), and no viral, fungal or allergic dermatosis, while in those with a moderate profile (CD4 from 500 to 1000) the allergic diseases predominated, followed by the ones of viral etiology, and the others were equally represented. As for those children with mild alterations (CD4>1000), there was a predominance of allergic diseases (50%) followed by viral ones and dermatozoonoses (16,7% each), fungal and pharmacodermia (8,3% each) (Table 3). There was no case of bacterial disease in this group.

On the 'others' category the following dermatoses were included: scars, residual hypochromias, aphtha, miliaria, follicular keratosis, seborrheic dermatitis, mucous cyst, dyshidrosis, and livedo reticularis.

It was not possible to apply the statistical tests due to x² restrictions.

There was the same prevalence of dermatoses from both allergic and viral etiologies (50% of the cases) in children aged between 6 and 12 years with a severe immunological profile (CD4<200) and there was no case of bacterial dermatosis or dermatozoonosis, and the fungal ones represented 25% in this group. In those with moderate immunological deficiency (CD4 from 200 to 499) no viral disease or der-

CHART 1: Immunological categories based on the age and TCD4+ cells count

Immunological categories	Child Age		
	Under 12 months	1-5 years	6-12 years
	µl	µl	µl
No evidence of supression	≥1500	≥1000	≥500
Moderate supression	750-1499	500-900	200-499
Severe supression	< 750	< 500	< 200

Source: Center for Disease Control and Prevention (CDC), 1994.

CHART 2: Clinical and immunological classification of the children with the HIV virus

Immunological Categories	Clinical Categories			
	N - No signs/ symptoms	A - mild signs/ symptoms	B - moderate signs/ symptoms	B -severe signs/ symptoms
No evidence of suppression	N1	A1	B1	C1
Moderate suppression	N2	A2	B2	C2
Severe suppression	N3	A3	B3	C3

Source: Center for Disease Control and Prevention (CDC), 1994.

matoozoonosis was observed, and the remaining dermatoses had the same frequency. In children with mild immunological alteration ($CD4 \geq 500$) there was a predominance of allergic dermatoses (46,2%), followed by viral ones (38,5%) and dermatoozoonoses (19,2%) as shown (Table 4).

It was not possible to apply the statistical tests due to χ^2 restrictions.

Among the children making use of the ARVT the allergic processes were the most frequent (46%), followed by viral (32%), fungal (12%), and bacterial diseases and dermatoozoonoses (10% each), as well as 4% of pharmacodermia (from the 3 children who had it, one was due to the use of trimethoprim – sulfamethoxazole, another to ceftriaxone and the third to the ARV Efavirenz). In the children who were not receiving ARVT we also found a higher frequency of allergic conditions (30%), equally followed by viral (20%), and fungal diseases and dermatoozoonoses with 8% each, 6% bacterial diseases and 3% had pharmacodermia (Table 5).

DISCUSSION

On the present study, as in other studies conducted with children with HIV/AIDS, we found a high prevalence of dermatological manifestations, 67% of the children presented with at least one dermatosis. CARVALHO et al. Found 82,5% e WANANUKUL et al. found a 51,6% prevalence.^{5,8}

The most common group of dermatoses in the children assessed was the allergic (42,9%), a group which included atopic dermatitis (22,9%) and childhood prurigo (20%). According to Cestari et al in: AZULAY, (2006), AIDS can aggravate the cases of atopic dermatitis however, all the cases of AD found had mild manifestations. It is also known that after the start of the ARVT there is a somewhat accelerated control of the viral replication and a slower and progressive increase of the $TCD4+$ and, depending on their recovery, latent immunological disturbances can become apparent, as it is the case of AD.¹⁰ Childhood prurigo was present in 52,5% of the cases on the study by CARVALHO et al. (2003) and it was more frequent in patients from the mild and moderate immunological categories which, according to the author, is due to the fact that the dermatosis needs a partially intact immune system to occur. Our results were similar on the age range of 1 to 5 years however, on the range of 6 to 12 years the occurrence of prurigo was higher in children with immunological classification 3, representing 25% of the patients with $CD4 < 200$.⁸

Most works conducted in HIV+ children on the literature quotes candidiasis as the most frequent dermatosis, with percentages of 56% as found by HACHEN et al, (1998) and 33% by WANANUKUL et al. 1999. On the present study the occurrence of such dermatosis was null, which could be due to the fact that it affects most frequently newborns, an age range

TABLE 1: Clinical-immunological classification of the children studied

Classification	fi (n=70)	%
A1	6	8,6
A2	3	4,3
A3	2	2,9
B1	9	12,9
B2	20	28,6
B3	24	34,3
C1	1	1,4
C3	5	7,1

TABLE 2: Distribution of the dermatoses according to etiology

Classification	fi (n=70)	%
Category	fi	%
Viral	20	28,6
Fungal	8	11,4
Bacterial	6	8,6
Dermatoozoonosis	8	11,4
Allergic	30	42,9
Pharmacodermia	3	4,3
Others	29	41,4

TABLE 3: Relationship between immunological category and dermatoses found in children in the age range of 1 to 5 years

CD ₄₊ Age range 6-12 years	<200 n=8		200 - 499 n=8		≥500 n=26	
	Frequency	%	Frequency	%	Frequency	%
Dermatozoonosis	-	-	1	8,3	2	16,7
Bacterial	1	50	1	8,3	-	-
Fungal	-	-	1	8,3	1	8,3
Viral	-	-	2	16,7	2	16,7
Pharmacodermia	-	-	1	8,3	1	8,3
Allergic	-	-	6	50	6	50
Others	2	100	6	50	4	33,3

not contemplated in this study, or to the fact that the children were followed by a relatively short period, whereas in works such as the one from HACHEN et al. (1998), 85 children with HIV were followed by 5 years, with a registered prevalence of 93%, which suggests that at some point during the follow up of these patients such infection will develop; or to the fact that it affects children who are extremely immunosuppressed before the start of the ARVT or those whose scheme fails.^{5,6,11}

The second most common group of dermatoses was the one of viral etiology, where the common wart and the molluscum contagiosum were the main ones, with 18,6% and 10% respectively, followed by the herpes simplex (2,9%) and zoster (1,4%) (Table 6). The warts always presented as multiple lesions, more frequently on the hands and the periungual region, and they had a slow response to treatment with liquid nitrogen (recommended for this population). The prevalence of warts found in the present study was higher than the one found in the general population, where the estimate is around 10%; when we take into consideration the adult population with HIV, the percentage is around 5 to 30%. In children with HIV, HACHEN et al. (1998) found a prevalence of 8% and

the lesions were also multiple and recalcitrant.¹¹ CARVALHO et al, (2003) in Brazil does not quote warts among the dermatoses found in his study.⁸ Molluscum contagiosum is a dermatosis with a prevalence that varies between 5 to 8% in children with HIV; in the present study we had a prevalence of 10%, with one case of gigantic molluscum contagiosum confirmed after skin biopsy and histopathological examination. The child with this atypical presentation was on the moderate immunological category.

Seborrheic dermatitis is frequently found in adult patients with HIV/AIDS and, according to PORRO et al. (2000), it can reach up to 85% of the patients.⁴ In our sample the prevalence of such dermatosis was well smaller than the one found in adults, affecting only 8,6% of the children studied. Similar results were found by other authors in studies conducted with children where EL HACHEN et al. (1998) found 6%, CARVALHO et al. (2003) 17,5% and LIM et al. (1990) registered a prevalence of 38% of seborrheic dermatitis.^{8,11,12}

Onychomycosis, a rare disease in childhood, was found in two twin sisters who presented with moderate immunological disturbance. Contrary to what happens in adult patients with HIV/AIDS who

TABLE 4: Relationship between the immunological category and dermatoses found in children with HIV/AIDS in the age range of 6 to 12 years

CD ₄₊ Age range 6-12 years	<200 n=8		200 - 499 n=8		≥500 n=26	
	Frequency	%	Frequency	%	Frequency	%
Dermatozoonosis	-	-	-	-	5	19,2
Bacterial	-	-	2	25	2	7,7
Fungal	2	25	2	25	2	7,7
Viral	4	50	2	25	10	38,5
Pharmacodermia	1	12,5	-	-	-	-
Allergic	4	50	2	25	12	46,2
Others	4	50	2	25	9	34,6

TABLE 5: Relationship between the use of ARVT and the presence of dermatoses range of 6 to 12 years

Dermatoses (n=70)	Present (n=50)		Absent (n=20)		Total	p
	Frequency	%	Frequency	%		
Dermatozoonosis	5	10	3	5	8	0,859
Bacterial	5	10	1	5	6	0,839
Fungal	6	12	2	25	8	0,859
Viral	16	32	4	20	20	0,477
Pharmacodermia	2	4	1	5	3	0,641
Allergic	23	46	7	35	30	0,567

TABLE 6: Distribution of the most frequently found dermatoses

Dermatosis	fi	%
Contact dermatitis	5	7,1
Seborrheic dermatitis	6	8,6
Superficial mycoses	8	11,4
Allergic manifestations	16	22,9
Scabies	6	8,6
Pharmacodermia	3	4,3
Herpes simplex	2	2,9
Herpes zoster	2	1,4
Larva migrans	1	1,4
Molluscum Contagiosum	7	10
Pediculosis	2	2,9
Pyodermatitis	6	8,6
Childhood prurigo	14	20
Common warts	13	18,6

present with multiple affected nails, the disease in the twins was found only in one nail on the left finger. Mycological examination and culture were requested for the two minors and performed for only one of them. The material collected evidenced the presence of septate and branched hyphae and the causative dermatophyte could not be identified on the culture. The disease regressed in both children without any treatment 3 months after the first consultation, which is considered atypical as onychomycosis are usually difficult to treat and cure in immunosuppressed patients and their immunological profile did not change during this period; on the contrary, one of the children died and the last CD4 value was 76. The prevalence of onychomycosis registered in children with HIV/AIDS by El HACHEN et al. (1998) was 5% and by WANANUKUL et al. (2003) 3%, represented by 2 children who had severe immunosuppression.^{5,11} According to the literature onychomycosis affects around 3% of healthy adults up to 55 years, and it tends to increase with age and is rare in childhood.⁹ YAMADDA et al. (2000), in a study performed with the aim of assessing the mycoses that

affect adults with HIV, found onychomycosis in 32,3% of the adults.¹³ In a study conducted in France, CRI-BIER et al. (1998) analyzed the nails of adult patients with HIV and they found the presence of onychomycosis in 1/3 of the cases and they suggest that it might be associated with worsening of the immunosuppression, as they observed a high rate of the disease in patients at the terminal stage.¹⁴

Herpes zoster is also a disease frequently found in adults with HIV, and it is considered an early marker of AIDS; in children, however, it has a smaller prevalence. CARVALHO et al. (2003) in a study conducted in Brazil in children with AIDS had an incidence of 2,5%.⁸ On the present study we had only one case of herpes zoster, which developed on the same child who had onychomycosis, giant molluscum contagiosum and a progressive decline of the levels of TCD4 lymphocytes, with fatal progression due to the infectious disease, which lead us to infer that such manifestations can possible indicate a bad prognosis for children with AIDS.

On the present study we did not see statistical differences in relation to the dermatoses found in the groups who made use of ARVT and the ones who did not.

CONCLUSIONS

On the present study, the predominant immunological classification of the children seen was severe and moderate, in terms of the clinical classification. The most frequent dermatoses were atopic manifestations followed by common warts and childhood prurigo.

The children who had severe immune suppression and moderate to severe clinical manifestations presented with dermatoses hardly found in the pediatric population without HIV, like onychomycosis, herpes zoster and giant molluscum contagiosum.

There was no statistical significance in terms of the frequency of the dermatoses between the ones in use of ARVT and the ones not using it. □

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