Cutaneous Manifestations In HIV Positive Paediatric Patients
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Citation

Abstract
Background: Over the past decade Human Immunodeficiency Virus (HIV) infection has emerged as a major cause of severe illness and death in childhood in the United States and throughout the world. CD4 cell count and CD8 cell percentage are key markers for determining disease progress and the risk for opportunistic infection (OI) in HIV-infected patients.

Objectives: This study was carried out to analyze the cutaneous manifestations in HIV positive paediatric patients and to correlate their pattern and severity with CD4 count.

Material and Methods: This was a hospital based study wherein all HIV positive patients in the paediatric age group were screened for cutaneous manifestations over a period of two years, CD4 counts were estimated and their severity and atypical presentations were correlated with the CD4 counts.

Results: Out of the 104 children included in this study, 93 had cutaneous manifestations. Transplacental was the commonest mode of transmission. There was a significant risk of Grade III malnutrition (p=0.03). Dermatological manifestations were present in all with CD4 count less than 200. The highest mean CD4 count was for bacterial infections and the lowest was for oral candidiasis. The mean CD4 count for fungal infection, oral candidiasis and xerosis were statistically significant (p=0.001, 0.002, 0.025 respectively)

Conclusion: This study shows that the prevalence of mucocutaneous manifestations increases with advanced immunosuppression in pediatric age group and help in early recognition of the infection.

Keywords: Cutaneous manifestations, Paediatric HIV

Introduction
Despite recent, improved access to antiretroviral treatment (ART) and care in many regions of the world, more than 35 million people now live with HIV/AIDS out of which 3.3 million of them are under the age of 15 years. In 2012, an estimated 2.3 million people were newly infected with HIV wherein 260,000 were under the age of 15 years.¹ The first case of AIDS in a child was reported to the Centers for Disease Control (CDC) in 1982. Over the past decade, this disease, caused by infection with human immunodeficiency virus (HIV), has emerged as a major cause of severe illness and death in childhood in the United States and throughout the world.²

Cutaneous manifestations of HIV infection in children include a wide variety of infectious, inflammatory disorders and rarely neoplasms. These disorders tend to be more severe, persistent and resistant to treatment.³ Majority of children with HIV infection develop some form of mucocutaneous disease during the course of their illness. In some children, cutaneous disease may
be the presenting symptom of HIV-related illness. CD4 cell count and CD4 cell percentage are key markers for determining disease progress and the risk for opportunistic infection (OI) in HIV-infected patients.

The present study is aimed to assess the pattern and severity of cutaneous disease in HIV/AIDS children in relation to CD4 count.

Methodology
The study population included all HIV positive patients in the paediatric age group attending or referred to the Outpatient Department of Dermatology, Kasturba Medical College Attavar and Wenlock District Hospital, Mangalore over a period of 25 months from August 2006 to September 2008. A total of 104 confirmed cases of HIV infection were comprehensively evaluated and screened for cutaneous manifestations after taking an informed consent. A detailed history pertaining to HIV infection, associated systemic complaints, the mode of onset and evolution of lesions were taken. Details of treatment, including ART and prophylaxis for OI were also noted. Routine investigations, blood chemistry, CD4, CD8 counts and CD4:CD8 ratios were estimated. Tzanck smear, KOH preparation, fungal culture and pus for culture and sensitivity were done when indicated.

All patients were followed up monthly for 6 months for a repeat complete cutaneous and systemic examination.

Results
A total of 104 patients with HIV infection/AIDS were screened for cutaneous manifestations. Cutaneous manifestations were seen in 93/104 (89.4%), 68 (65.4%) patients being males and 36 (34.6%) being females (Table 1). The mean age in our study was 8.27 years SD ± 3.4. In this study, 11 children were asymptomatic (category N), 16 children were in category A, 29 in category B, and 48 in category C as per CDC classification.

In 100 (96.15%) the mode of transmission was transplacental. Both the parents were HIV positive in 100/104 (96.15%). Both parents were HIV negative in 2/104 (1.9%) cases who had received blood transfusion for ITP and fracture femur respectively and the HIV status of both parents were not known in 2(1.9%) cases.

Table 1: Age and sex distribution of the children screened

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>13</td>
<td>5</td>
<td>18 (17.30%)</td>
</tr>
<tr>
<td>5-8</td>
<td>22</td>
<td>13</td>
<td>35 (33.65%)</td>
</tr>
<tr>
<td>9-12</td>
<td>25</td>
<td>15</td>
<td>40 (38.46%)</td>
</tr>
<tr>
<td>13-18</td>
<td>8</td>
<td>3</td>
<td>11 (10.57%)</td>
</tr>
<tr>
<td>Total</td>
<td>68(65.38%)</td>
<td>36(34.62%)</td>
<td>104</td>
</tr>
</tbody>
</table>

40 (38.46%) patients were in the 9-12 years age group, the youngest patient being 2 years old, while the eldest 13 years (Table 1). Past history of tuberculosis was noted in 36 (34.6%). Pneumocystis jiroveci pneumonia (PCP) was present in 15.4% and Cryptosporidial diarrhea in 9.6%. Recurrent scabies and herpes zoster (HZ) were present in 4.8% and 1.9% respectively.

Tuberculosis (TB) was the most common opportunistic infection, present in 36 (34.6%) patients. Commonest form of TB was pulmonary in 28/36 (77.7%) patients, followed by lymphadenitis in 8/36 (22.2%).

Treatment history revealed 58 (55.8%) patients were on Antiretroviral therapy (ART), 20 (19.2%) were on anti-TB treatment and 30 (28.84%) were on PCP prophylaxis.

Table 2: Comparison of CD4 counts in patients with and without ART

<table>
<thead>
<tr>
<th>CD4 count</th>
<th>ART (+)</th>
<th>ART (-)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td>40 (68.96%)</td>
<td>1 (2.38%)</td>
<td>41</td>
</tr>
<tr>
<td>200-500</td>
<td>16(27.58%)</td>
<td>22 (52.3%)</td>
<td>38</td>
</tr>
<tr>
<td>&gt;500</td>
<td>2 (3.44%)</td>
<td>19 (45.2%)</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>58 (100%)</td>
<td>42 (100%)</td>
<td>100</td>
</tr>
</tbody>
</table>
General physical examination revealed lymphadenopathy in 32 (30.76%) patients, among whom 59.3% of patients had generalized lymphadenopathy. Only cervical lymph nodes were enlarged in 31.25% and inguinal nodes were enlarged in 9.37%. Among 19 patients having generalized lymphadenopathy, 12 (63.15%) had CD4 count less than 200. Pallor was present in 41 (39.42%) patients, 21 (51.21%) had CD4 count less than 200. Clubbing was present in 2 (1.9%) patients, both with CD4 count less than 200.

Grade I malnutrition was seen in 28.8% patients, 21.2% showed Grade II and 18.3% showed Grade III malnutrition (p value 0.03). In this study, CD4 count was available for 100 patients out of 104.

**Table 3: Anthropometric evaluation for presence of Malnutrition & Stunting**

<table>
<thead>
<tr>
<th>Malnutrition</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Total n-104</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 (28.8%)</td>
<td>22 (21.2%)</td>
<td>19 (18.32%)</td>
<td>71 (68.27%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stunting</th>
<th>First degree</th>
<th>Second degree</th>
<th>Third degree</th>
<th>Total n-104</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>32 (30.8%)</td>
<td>19 (18.3%)</td>
<td>17 (16.3%)</td>
<td>68 (65.38%)</td>
</tr>
</tbody>
</table>

Dermatologic manifestations were present in 89.4% of patients in this study. All the patients with CD4 count below 200 showed cutaneous manifestations (Table 4).

**Table 4: CD4 count in relation with the presence or absence of dermatological manifestation**

<table>
<thead>
<tr>
<th>CD4 count</th>
<th>Dermatologic Manifestations</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td></td>
<td>41 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>200-500</td>
<td></td>
<td>37 (97.37%)</td>
<td>1 (2.63%)</td>
</tr>
<tr>
<td>&gt;500</td>
<td></td>
<td>15 (71.43%)</td>
<td>6 (28.57%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>93</td>
<td>7</td>
</tr>
</tbody>
</table>

A total of 11 (10.57%) patients presented with bacterial infections (Table 5), 7 of whom had folliculitis, of which 2 had CD4 count less than 200. Impetigo was present in 3 patients; one of them had CD4 count less than 200. Ecthyma was present in 1 patient with CD4 count between 200-500.

Viral infections were seen in 23 (22.11%) patients (Table 5). A total of 15 (14.4%) patients had Molluscum Contagiosum (MC), of which 40% had CD4 count below 200 and 4 patients had MC on face alone. Two patients had a giant MC surrounded by multiple small lesions on the face. HZ was present in 3 (2.9%) patients aged 11 and 12 years and verruca vulgaris (VV) in 5 (4.8%) patients.

A total of 36 (34.61%) patients presented with fungal infections (Table 5). Candidiasis (oral and cutaneous) was present in 29.8% patients out of whom 18 (58.06%) patients had CD4 count below 200 (p value 0.024). Tinea versicolor was present in 4 (3.8%) patients (p value .001) and tinea cruris in 0.9% patient. Onychomycosis was seen in 4.8% patients.

Scabies was present in 21.2% patients of whom 50% had CD4 count below 200 (Table 5). Recurrent scabies was seen in 5 patients as they were staying together in an ashram.

Among the Non-infectious dermatosis, xerosis was present in 15.4% and 50% of them had a CD4 count of less than 200, which was statistically significant (p value 0.025) (Table 5). Seborrheic dermatitis (SD) was present in 7.7% patients, and 50% had CD4 count less than 200. Drug reactions were present in 4.8% patients of whom 3 patients presented with maculopapular rash to cotrimoxazole and 2 patients presented with Steven Johnson Syndrome (SJS) to Nevirapine and Cotrimoxazole. All the 5 patients had CD4 count between 200-500. Papular urticaria was present in 4.8% patients and 80% of them had CD4 count less than 200. Acquired ichthyosis
with rhomboidal scales was present in 1.9% patients and both of them had CD4 count less than 200. The CD4 count in the single eczema craquelé patient was less than 200.

Oral lesions were present in 28.84% patients. Pseudomembranous candidiasis was present in 28 (26.9%) patients, 61% of them has CD4 count less than 200 and 39% has CD4 count between 200-500 (p value 0.002) (Table 5).

Nail changes were present in 13.46% patients. Commonest was melanonychia in 5.8% patients, followed by onychomycosis in 4.8% patients. Beaus line was seen in 3 (2.9%) patients.

**Mean CD4 count and dermatologic manifestations**

The mean CD4 count in patients with bacterial infections was 398.55 and in patients with oral candidiasis (OC) was 214.9. The mean CD4 count for fungal infections, OC and xerosis (223.38) was statistically significant.

**Table 5:** Correlation of Dermatological manifestations with Mean CD4 count

<table>
<thead>
<tr>
<th>Dermatological manifestations</th>
<th>Mean CD4 count</th>
<th>Standard Deviation</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial infection (n=11)</td>
<td>398.55</td>
<td>200.5</td>
<td>NS</td>
</tr>
<tr>
<td>Viral infection (n=23)</td>
<td>280.61</td>
<td>200.9</td>
<td>NS</td>
</tr>
<tr>
<td>Fungal infection (n=36)</td>
<td>288.64</td>
<td>220</td>
<td>.001</td>
</tr>
<tr>
<td>Scabies (n=22)</td>
<td>297.64</td>
<td>189.1</td>
<td>NS</td>
</tr>
<tr>
<td>Seborrheic dermatitis (n=8)</td>
<td>371.00</td>
<td>238.9</td>
<td>NS</td>
</tr>
<tr>
<td>Xerosis (n=16)</td>
<td>223.38</td>
<td>118.5</td>
<td>.025</td>
</tr>
<tr>
<td>Drug reaction (n=5)</td>
<td>233.40</td>
<td>39.469</td>
<td>NS</td>
</tr>
<tr>
<td>OC (n=28)</td>
<td>214.9</td>
<td>135.9</td>
<td>.002</td>
</tr>
<tr>
<td>Onychomycosis (n=5)</td>
<td>301.6</td>
<td>197</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Discussion**

The study group comprised of 68 males and 36 females amongst whom majority (38.46%) belonged to the age group 9-12 years. The commonest mode of acquiring the infection was transplacental transmission accounting for 96.15% and 1.9% by blood transfusion and 1.9% unknown similar to earlier studies. 

The commonest systemic OI was TB accounting for 34.6% patients. Verghese VP et al in their study accounted for 15.3% TB of which 14% had pulmonary and 1.3% had miliary TB. In this study, pulmonary TB was seen in 77.7% patients and 22.2% had TB lymphadenitis. The high percentage may be correlated to the low CD4 count (<200) in 41% of our patients. 

PCP was the other systemic OI, seen in 15.4% of patients. In a study by Verghese VP et al only 8% had PCP. Cryptosporidial diarrhea was present in 9.6% of patients in our study in comparison to 30% in the same study.

**Cutaneous Manifestations**

In this study 89.4% of patients had cutaneous manifestations. Seoane R et al reported an incidence of 56% among 210 patients included in his study. El Hachem M et al reported an incidence of 97% among 166 seropositive children.

In this study 10.5% patients had bacterial infections. Folliculitis was the commonest (63.6%), followed by impetigo (27.2%) and eczema (9%). The incidence of bacterial infection was 18% in a study by Straka BF et al and 8% in a study by Lim W et al. The highest mean CD4 count was for bacterial infection (398), and this can be considered as an early cutaneous marker for HIV/AIDS.

Viral infections in this study accounted for 23/104 (22.11%). Lim W et al reported an incidence of 38% in their study among 21 HIV infected patients. MC was the commonest viral infection
seen in 14.4% patients in this study, similar to other similar studies. The lesions responded to multiple crotchetery sessions. HZ was present in 2.8% and VV in 4.8% of patients. This is similar to the other study, where HZ was seen in 2.2% and VV in 1.1%. The mean CD4 count for viral infection was 280.61.

Fungal infections was found in 34.6% patients. Lim W et al reported an incidence of 69% in their study among 21 HIV infected children. The commonest fungal infection in this study was candidiasis (oral and cutaneous) found in 31 (29.8%) patients. Prose NS reported an incidence of 48% to 85% in his study. Fifty eight percent of patients with candidiasis had CD4 count below 200. The occurrence of candidiasis in patients having CD4 count less than 200 was statistically significant (p value 0.002). OC was seen in 26.9% and cutaneous candidiasis in 2.8% similar to other studies. The mean CD4 count for OC was as low as 214.9 (p value 0.002) and thus can be considered as a marker for advanced immunosuppression.

Tinea versicolor was seen in 3.8% patients, and all of them had CD4 count more than 500 compared to an incidence of 2% in an earlier study of 210 HIV infected children. The occurrence of tinea versicolor in patients having CD4 count above 500 was statistically significant (p value 0.000).

Onychomycosis was seen in 4.8% patients. All the patients had proximal subungual onychomycosis and had CD4 count between 200-500. The mean CD4 count for onychomycosis is 301.6.

Tinea cruris was seen 0.9% patient, who had a CD4 count between 200-500.

Scabies was present in 21.2% patients and 50% of them had CD4 count less than 200. Five patients had recurrent scabies as they were staying together in a care centre out of which two had extensive lesions which was higher compared to earlier similar studies. The mean CD4 count for scabies was 297.6.

Seborrhic dermatitis was present in 7.7% patients compared to 20% and 38% in earlier studies. The commonest site of involvement was scalp, followed by retroauricular area. CD4 count was less than 200 in 50% patients. The mean CD4 count for SD was 371.

Xerosis was seen in 15.4% patients in our study. Lim W et al reported an incidence of 8% in their study. Fifty percent of our patients had CD4 count less than 200 (p value 0.025) which is statistically significant. The mean CD4 count for xerosis was as low as 223.3 and can be considered as another marker of advanced immunosuppression. Acquired ichthyosis was seen in 1.9% patients who had CD4 count below 200.

Drug reactions were present in 4.8% in our study. Three patients presented with maculopapular rash due to co-trimoxazole and 2 patients presented with SJS due to nevirapine and co-trimoxazole. All 5 patients had CD4 count between 200-500 and the mean CD4 count was 233.40. In a study by Lim W et al, 8% of patients had drug reactions to co-trimoxazole and in a study by Straka BF et al 16% of 50 patients had drug reactions to co-trimoxazole and nevirapine.

Papular urticaria was present in 4.8% patients and 80% of them had CD4 count less than 200 which was lower compared to other similar study.

**CD4 count and dermatologic manifestations**

Dermatologic manifestations were present in all 41 the patients with CD4 count below 200 and in 35.5% of patients with CD4 count between 200-500. Dermatologic manifestations were present only in 14.4% of patients with CD4 count above 500. This shows that the prevalence of
mucocutaneous disease increases with decreasing CD4 count. In a study by Wananukal S et al, prevalence of mucocutaneous disease in the groups that had severe, moderate and no evidence of immunosuppression was found to be 62%, 43% and 20% respectively.\textsuperscript{12}

Conclusion
The highest mean CD4 count was for bacterial infection. The mean CD4 count for xerosis (p value 0.025) and OC (p value 0.002) was the lowest. So, these two can be considered as markers of advanced immunosuppression. Thus this study shows that the prevalence of mucocutaneous manifestations increases with advanced immunosuppression in pediatric age group and help in early recognition of the infection.

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References