ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 11 | November - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MUCO-CUTANEOUS MANIFESTATIONS IN HIV INFECTED CHILDREN AND ITS CORRELATION WITH THE CD4 COUNT

Dermatology

Dr Meetu Singh Senior Resident, Department of Pediatrics, ABVIMS & Dr RML Hospital, New Delhi.
Dr Alok Hemal Professor, Department of Pediatrics, ABVIMS & Dr RML Hospital, New Delhi.
Dr Ruchi Bhatt Senior Resident, Department of Pediatrics, ABVIMS & Dr RML Hospital, New Delhi.
Dr Zeeshan Ahmed* Senior Resident, Department of Pediatrics, ABVIMS & Dr RML Hospital, New Delhi.
*Corresponding Author

ABSTRACT

Background
Dermatological manifestations increase both in frequency and severity with the progression of HIV and thus can serve as important markers of disease progression. Early recognition of such dermatological manifestations is important for an early diagnosis and also to assess the prognosis of HIV infection

Objective
The objective was to determine the cutaneous manifestations among HIV children and its correlation to clinical staging and the level of immunosuppression.

Material And Methods
The study was a cross sectional study conducted in the Department of Pediatrics, Dr. RML Hospital, New Delhi. The study population included all the HIV infected children. A total of 102 study participants were recruited. Absolute counts of CD4,CD8 and ratio of CD4/CD8 and Tzanck smear, KOH preparation, and skin scrapings was done. Chi square tests and independent t test was applied. P value of <0.05 is considered to be significant.

Results
The age of study participants ranged from one and half years to 17 years with a mean(SD) of
10.54 (± 11). The median age was 3.58. Males were 73.5% and females were 26.5%. Most of the patients were in WHO stage I. Prevalence of mucocutaneous manifestation was 16.7%. Lower mean CD4 counts and lower total leucocyte counts were associated with higher incidence of mucocutaneous lesions. (p value <0.05)

Conclusion
The prevalence of muco cutaneous manifestation increases with decline in CD4 count. Hence muco cutaneous manifestations can be taken as the marker of deteriorating immune status of patients.

KEYWORDS

mucocutaneous manifestation, CD4 counts, HIV, children

INTRODUCTION

Human immunodeficiency virus (HIV) infection in children is becoming a common occurrence. In 2012, approximately 35.3 million people are living with HIV globally, of these 3.4 million are less than 15 years old.[1] There were about 1.8 million deaths from AIDS in 2010[2]. In India an estimated 2.5 million people were newly infected with HIV, wherein 2,60,000 were under age 15 year.[3] The prevalence is about 0.3% [4] and the chief mode of HIV transmission to children in India is through the vertical route[5].

The dermatological manifestations increase both in frequency and severity with the progression of HIV and decline in CD4+ cell counts and thus can serve as important markers of disease progression especially in countries with poor resources.[6]

Clinical manifestation can thus help in correlating with the patient's immune status. The occurrence and pattern of cutaneous manifestation in HIV infected children was determined to understand the relationship between CD4 cell count and various cutaneous disorders[7].Thus an early recognition of such features is important for an early diagnosis and also to assess the prognosis of HIV infection[8].

Data regarding the muco cutaneous manifestations of HIV infection in pediatric population is available mainly from western literature. Some data from other nations are very limited and are mainly from adult cases. Extrapolating from adult cases was difficult because prevalence and pattern of cutaneous lesions varies among children and adults.[7] There is paucity of studies on cutaneous manifestations in pediatric population infected with HIV in India, which can serve as clinical indicator of immunity.[9]

Thus this study was undertaken to determine the cutaneous manifestations among HIV children and its correlation to clinical staging and the level of immunosuppresion.

MATERIALAND METHODS

Study Setting:
The study was a cross sectional study conducted in the Department of Pediatrics, Dr. RML Hospital, New Delhi

Study Duration: The study was conducted from November 2015 To March 2019

Study Population :
The study population included all the HIV infected children attending the pediatric HIV clinic during the study period. HIV positive children between 18months to 18 years were included in the study and were screened for presence of skin diseases. A total of 102 study participants were recruited.

Data Collection Procedure:
An informed consent was obtained from parents or guardians for the enrolment in the study. A complete dermatological screening of the scalp, face, oral mucosa, neck, trunk, genitalia and extremities was performed in each patient following which dermatologist opinion was taken. After detailed history and examination Complete blood count (Hb, TLC, DLC, Platelet count) and biochemical investigations (B.Urea, Sr.Creatnine,Sr. Electrolytes, Sr. Protiens, Sr. Bilirubin, SGOT, SGPT). Complete blood count and biochemical investigation was done by automated analyser. CD4, CD8 counts and CD4:CD8 ratio were assessed. The estimation of $CD4^+$, $CD8^+$ T lymphocytes and CD4 /CD8 was done by FACS (Fluorescent Activated Cell Sorter) count system. The software identifies T-lymphocyte subpopulations and correlates with the absolute count and provide absolute counts of CD4,CD8and ratio of CD4/CD8 [10].

Skin Procedures
Appropriate laboratory investigations like Tzanck smear, KOH preparation, and skin scrapings was done.

Tzanck Smear [11]
Using a blunt scalpel blade, gently deroof the lesion was done. In skin

scrapings, lesion was gently scraped with sterile blade, transferred to glass slide and was viewed under microscope. The specimen was allowed it to dry in the air and the specimen was fixed with preservative.

KOH Mount [12]

Skin, nail, or hair samples were collected from the infected area on the patient. For skin samples, a scalpel or edge of a glass slide was used to gently scrape skin scales from the infected area. For hair samples, a forceps was used to remove hair shafts and follicles from the infected site. The scrapings were placed directly onto a microscope slide and were covered with 10% or 20% potassium hydroxide. The slide was left to stand until clear, normally between five and fifteen minutes, in order to dissolve skin cells, hair, and debris. To enhance clearing dimethyl sulfoxide was added to the slide. To make the fungi easier to see lactophenol cotton blue stain was be added. The slide was gently heated to speed up the action of the KOH. Adding calcofluor-white stain to the slide caused the fungi to become fluorescent, making them easier to identify under a fluorescent microscope.

Statistical Analysis: Data was entered and analysed with statistical software- Statistical Package for Social Sciences (SPSS IBM) version 21.0. The qualitative variables are described in proportions and quantitative variables in mean, and standard deviation. Required tests of significance was applied. P value of <0.05 is considered to be significant.

RESULTS

The age of study participants ranged from one and half years to 17 years with a mean(SD) of 10.54 (± 11). The median age was 3.58. Out of 102 patients, majority of patients 39 (52%) were males and 14 (51.8%) were females in the age group of 10-15 years. In the age group of 5-10 years 25 (33.3%) were males and 8(29.6%) were females . In the age group of 18months -5years 6 (8.0%) and 4(14.8%) were males and females respectively. In patients more than 15 years, 5 (6.6%) were males and 1 (3.7%) was females. Most of the patients were in WHO stage I. Out of which majority of 53(51.96%) patients were in the age group 10-15 years where as 31(30.39 %) were in 5-10 years age group. Further 10 (9.8%) patients were in the age group of 18months to 5 years and 5(4.9%) patients were more than 15 years of age group. One patient each had in WHO stage II and III in the 5-10 years age group. One patient in the age group 10-15years was in WHO stage IV. (table 1)

Table 1 Profile Of Study Participants.(n=102)

S.No.	Variables	N(%)
1.	**Age group**	
	18 months- 5 years	10(9.8)
	6- 10 years	33(32.3)
	11- 15 years	53(51.9)
	>15 years	6(5.8)
2.	**Sex**	
	Male	75(73.5)
	Female	27(26.5)
3.	**Route of acquisition**	
	Perinatal	99(97.1)
	Injection	2(2)
	Blood transfusion	1()
4.	**WHO clinical staging**	
	I	97(97.08)
	II	1(0.8)
	III	1(0.8)
	IV	1(0.8)
5.	**Immunological staging**	
	None/Not significant	73(71.9)
	Mild	15(14.1)
	Advanced	8(7.9)
	Severe	6(5.9)
6.	**CD4 count**	
	>500	73(71.9)
	350-499	15(14.1)
	200-349	8(7.9)
	<200	6(5.9)

In our study out of 102 patients, 17 patients were found to have muco cutaneous manifestations. Hence the prevalence of muco cutaneous manifestation was 16.7% among the study population.

Table 2: Distribution Of Types Of Mucocutanoeus Manifestation In Our Study. (n=17)

I) Infectious Dermatoses	No. Of cases	Percentage(%)	
a) Bacterial	1) Folliculitis Decalvans	1	5.9
	2) Acne	1	5.9
	3) Folliculitis	1	5.9
	4) Pyoderma	1	5.9
b) Viral	1) Ptyriasis rosea	1	5.9
	2) Viral exanthema	1	5.9
	3) Molluscum	1	5.9
c) Fungal	1) Oral thrush	1	5.9
	2) Tenia corporis	1	5.9
d) Parasitic	1) Scabies	4	23.5
II Non- infectious Dermatoses			
1) Intertrigo	1	5.9	
2) Nummular dermatitis	1	5.9	
3) Ulcer	1	5.9	
4) Atopy	1	5.9	

In our study majority of patients (13) had infectious dermatoses. In the bacterial infection one patient each had folliculitis decalvans, acne, folliculitis and pyoderma. Molluscum, viral exanthema, ptyriasis rosea were present in one paitent each among the viral group. Among the fungal infection one patient had oral thrush and one patient had tenia corporis. 4 patients had scabies infection. Intertrigo, Nummular dermatitis, ulcer and atopy were in one patient each in non infectious dermatoses group. (table 2)

Chi square test was applied to find any association between mucocutaneous lesion and variables such as age group, sex, WHO staging, CD4 count and immunological staging. It was observed that males, perinatal transmission had higher prevalence of mucocutaneous lesions. Lower mean CD4 counts and lower total leucocyte counts were associated with higher incidence of mucocutaneous lesions. This was found to be statistically significant. (table 3 & table 4)

Table 3 Association Of Mucocutaneous Manifestations With Selected Variables. (n=102)

S. No.	variables	Mucocutaneous lesion		P value
		No N(%)	Yes N(%)	
1.	Age group			
	18months - 5years	8(9.4)	2(11.7)	
	5 - 10 years	26 (30.5)	7 (41.1)	0.940
	10 - 15 years	46(54.1)	7 (41.1)	
	>15 years	5 (5.8)	1 (5.8)	
2.	Sex			
	Male	64(75.2)	11(64.7)	0.366
	Female	21(24.8)	6(35.2)	
3.	WHO staging			
	I	84(98.8)	15(88.2)	
	II	0	1(5.8)	0.071
	III	0	1(5.8)	
	IV	1(1.2)	0	
4.	CD4 count			
	>500	65(76.4)	8 (47)	
	350-499	11(12.9)	4 (23.5)	0.101
	200-349	6(7)	2 (11.8)	
	<200	3(3.5)	3 (5.8)	
5.	Immunological staging			
	None	65(76.5)	8(47)	
	Mild	11(12.9)	4(23.5)	0.101
	Advanced	6(7)	2(11.7)	
	Severe	3(3.5)	3(17.6)	
6.	Route of acquisition of HIV			
	Perinatal	83(97.6)	16(94.1)	
	Injection	1(1.2)	1(5.8)	0.571
	Blood transfusion	1(1.2)	0	

7.	Treatment history			
	HAART	81 (98.7)	15 (88.2)	
	HAART + septran	2 (2.3)	2 (11.2)	0.299
	HAART + septran + ATT	1(1.2)	0	
	Pre ART	1(1.2)	0	

Table 4 Association Of Mucocutaneous Manifestations With Blood Parameters. (n=102)

Variables	Muco cutaneous manifestations	P Value					
	No	Yes					
	Mean ± SD	Median	Min - max	Mean ± SD	Median	Min – max	
Hb	11.00 ± 1.32	11.00	6.1 - 14.6	10.61 ± 3.71	10.70	8.4 - 15.0	0.226
TLC	6452.04 ± 2290.25	6000.00	990 - 17000	5465.00 ± 1231.19	5350.00	3200 – 8000	0.040
PLATELET	2.67 ± 0.71	2.50	1.2 - 4.4	2.35 ± 0.74	2.45	1.1 -3.7	0.136
B.UREA	22.25 ± 8.60	22.00	10 - 74	20.00 ± 4.68	21.00	12 – 29	0.390
S.CREAT	0.47 ± 0.15	0.40	0.3 -1.0	0.43 ± 0.09	0.40	0.3 - 0.6	0.526
SGOT	31.49 ± 13.28	28.00	10 - 83	32.00 ± 9.14	28.50	22 – 56	0.539
SGPT	32.14 ± 13.96	30.00	15 - 112	26.00 ± 5.14	25.50	15 – 35	0.029
CD4 COUNT	692.35 ± 337.44	668.00	86 - 2074	486.81 ± 243.69	496.00	136 – 1194	0.004

Independent T Test Applied.

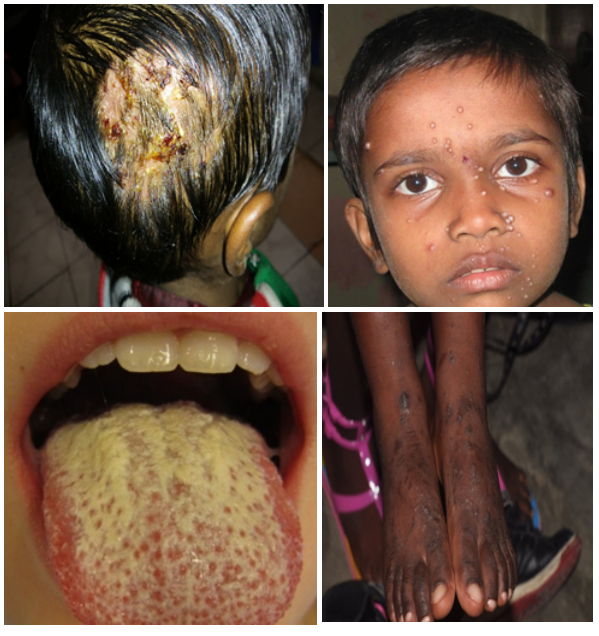

Figure 1 Images Of Skin Lesions- Folliculitis Decalvans, Molluscum Contagiosum, Oral Thrush And Scabies.

DISCUSSION

Introduction of HAART therapy and better control of opportunistic infection has led to the dramatically increased survival of HIV infected children. Muco cutaneous manifestations are common among HIV positive patients and serve as clinical indicator of immunity [6]. In the present study, children between the age of 18 months to 18 years were screened. The mean age was 10.54 ± 3.58 years in our study. In a study by Kondreddy[3] et al, mean age of children was 8.27± 3.4 years. Endayehu et al[7] studied muco cutaneous manifestation among the children of age group 0 to 14 years with the mean age of 9.3 ± 3.5 years. Whereas Wananukul[11] et al had mean age of 46.9 months and 38.6 months respectively in their studies. Hence the mean age was higher in our study group as compared to other studies.

In our study majority 73.5% were male patients whereas only 26.5% were females. Study conducted by Millembe[12] et al also has male predominance with 52% males and 48% females. Majority of patients (65.4%) were males with 34.6% females in the study by Kondreddy[3] et al. Study by Sebhat[15] et al also has male patients (51.7%) more than female population. On the other hand, predominant population is female (51.5%) in the study by Endayehu[6] et al with 48.5% males. Also female patients (55%) were more as compared to male patients (45%) in the study by Wananukul[11] et al also had female (61%) predominance in their study.

The prevalence of Muco cutaneous manifestation in our study is found to be 16.7 % which is lower as compared to most of previous studies. Millembe[12] et al conducted cross sectional descriptive study in 347 HIV positive children and reported prevalence of muco cutaneous manifestation to be 85% while Kondreddy et al [3] and Endayehu[6] et al reported prevalence to be 89.4% and 72.6% respectively. Wananukul S et al[11] and Sebhat[15] et al also found prevalence of mucocutaneous manifestations to be 52% and 46.1%.

In our study 50% of patients with CD4 count less than 200 were found to have muco cutaneous manifestation. 26.6% and 25% of patients with CD4 count between 350-499 and 200-349 had muco cutaneous manifestation respectively. While only 10.9% of patients with CD4 count more than 500 had muco cutaneous manifestation. There by suggesting muco cutaneous manifestation were more common with decline in CD4 count. Similar inferences were projected by the study conducted by Endayehu[6] et al, in which they found that 100 % of patients with CD4 count less than 200 had muco cutaneous manifestation. 97.37% of patients with CD4 count between 200-500 had muco cutaneous manifestatation and 71.43 % patients withCD4 count more than 500 had muco cutaneous manifestations. Krishnam[16] et al in their study concluded that there is inverse relationship between CD4 count and the incidence and severity of skin diseases in patients with HIV/AIDS.

In our study maximum (50%) patients with severe immunological suppression had muco cutaneous manifestations while 26.6% and 25% of patients with mild and moderate immuno suppression had muco cutaneous manifestation. Whereas only 10.9% of patients with no immunological suppression had muco cutaneous manifestation. Similar results were found in the study by Endeyehu[6] et al in which 100% of patients with severe immunological suppression had muco cutaneous manifestation while 70% of patients with moderate and 48.3% of patients with no immono suppression had muco cutaneous manifestation. Millembe[12] et al found 97%, 84.5% and 71.5% of patients had muco cutaneous manifestation among the patients with severe, moderate and no immunological suppression respectively. Kondreddy[3] et al in their study concluded prevalence of muco cutaneous manifestion increases with advanced immunosuppression.

CONCLUSION

The present study found 16.7% prevalence of mucocutaneous manifestation among HIV positive children. Low prevalence is attributed to higher CD4 count in patients on HAART,lesser number of patients in WHO stage III and IV and lesser number of patients in severe and advanced immunological suppression. The prevalence of muco cutaneous manifestation increases with decline in CD4 count. Hence muco cutaneous manifestations can be taken as the marker of deteriorating immune status of patients. In our study we found CD4 cut off of 621 below which maximum number of muco cutaneous were found. However, further studies are required to clearly delineate the natural course of muco cutaneous manifestation and its correlation to CD4 count. There is also a need for well-designed studies with sufficiently large sample size to asses various muco cutaneous manifestation among HIV positive children.

REFERENCES

1. UNAIDS report on the global AIDS epidemic 2013 [Internet]. 2016 [cited 24 May 2016].http://www.unaids.org/en/media/unaids/contentassets/documents/document/2013/GARPR_2013_guidelines_en.pdf
2. Chigwedere P, Seage G, Gruskin S, Lee T, Essex M. Estimating the Lost Benefits of Antiretroviral Drug Use in South Africa. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2008;49(4):410-415.
3. Kondreddy B, Kuruvila M, Ullal KR, Bhat K. Cutaneous manifestation in HIV positive pediatric patients.NJDVL2014;12(1): 14 -19.
4. Sidibe M. Antiretrovirals for Prevention: Realizing the Potential. Closing Commentary by the Executive Director of UNAIDS. CHR. 2011;9(6):470-472.
5. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. June 2013.http://www.who.int/hiv/pub/guidelines/arv2013/download/en/index.html.Accessed May 9, 2019
6. Vasudevan B, Sagar A, Bahal A, Mohanty A. Cutaneous manifestations of HIV—a detailed study of morphological variants, markers of advanced disease, and the changing spectrum. Medical Journal Armed Forces India. 2012;68(1):20-27.
7. Endayehu Y, Mekasha A, Daba F. The pattern of muco cutaneous disorders in HIV infected children attending care and treatment in TikurAnbesa specialised hospital, Addis Abzbz, Ethopia. BMC Dermatology. 2013; 13:12.
8. Raju P, Rao G, Ramani T. Skin disease: clinical indicator of immune status in human immunodeficiency virus (HIV) infection. International Journal of Dermatology. 2005;44(8):646-649.
9. Panaya M F, Magonda Y M, Massawe A W.The pattern of Mucocutaneous disorders in HIV –infected children attending care and the treatment centres in Dar es Salaam, Tanzania.BMC Public Health. 2009; 9:234-5.
10. Julius M, Masuda T, Herzenberg L. Demonstration That Antigen-Binding Cells Are Precursors of Antibody-Producing Cells After Purification with a Fluorescence-Activated Cell Sorter. Proceedings of the National Academy of Sciences. 1972;69(7):1934-1938.
11. Singh A, Preiksaitis J, Romanowski B. The Laboratory Diagnosis of Herpes Simplex Virus Infections. Canadian Journal of Infectious Diseases and Medical Microbiology. 2005;16(2):92-98.
12. Smalls S, Fischbach F. A Manual of Laboratory Diagnostic Tests. The American Journal of Nursing. 1982;82(2):334.
13. Wananukul S, Tawatchal D, Chitansu O, Thisyakom, USA. Mucocutaneous findings in paediatrics AIDS related to degree of immunosuppression.British Journal of Dermatology.2005Aug; 153(2) :382-9
14. Panaya M F, Magonda Y M, Massawe A W. The pattern of Mucocutaneous disorders in HIV –infected children attending care and the treatment centres in Dar es Salaam, Tanzania.BMC Public Health. 2009; 9:234-5.
15. Sebhat A, Amsalu S. Clinical Manifestations of HIV/AIDS in Children in Northwest Ethiopia.Ethiop.J.HealthDev.2005; 19(1).
16. Raju PVK, Rao GR, Ramani TV, Vandana S. Skin disease clinical indicator of immune status in human immunodeficiency virus infection. International Journal of Dermatology.2005Aug; 44(8): 646-9.