Original Article

Prevalence of pruritic papular eruption among HIV patients: A cross-sectional study

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Abstract

Introduction: Pruritic papular eruption (PPE) remains as one of the most common cutaneous manifestations in HIV-infected patients. Proper knowledge about understanding the risk factors associated with this disease may help to decrease the prevalence of PPE. **Objective:** The present study was conducted to determine the prevalence of PPE in HIV-infected patients and to correlate between the severity of PPE and individual CD4 count. **Materials and Methods:** This was a cross-sectional study, conducted in Palakkad Antiretroviral Therapy Centre, Kerala, between March 2017 and April 2017. A total of 100 HIV patients with evidence of multiple itchy skin lesions of 1-month duration were included in the study. Severity of lesion was evaluated using an objective "rash severity scale" for PPE. Data were coded and analyzed. **Results:** Prevalence of PPE was 11.35% in our study. The mean age of the study population was 41.17 ± 12. Male-to-female ratio was 1:2. In our study, 97% of the patients were giving history of mosquito bite. Most of the patients (40%) had moderate type of PPE. In our study, majority (86%) had a CD4 count of more than 200, and the incidence of PPE was more frequently seen in patients with CD4 count more than 200 cells which was statistically significant. **Conclusion:** PPEs are unique dermatosis, which is having a devastating impact on the quality of life, stigmatizing them in their communities. Thus, recognizing those lesions helps in allowing better treatment of this distressing condition.

Key words: CD4 count, HIV/AIDS, pruritic papular eruption

INTRODUCTION

"Pruritic papular eruption" (PPE) of HIV is a major cause of morbidity in AIDS patients. It is characterized by chronic pruritus and symmetric papular eruptions on the extensor surfaces of the extremities, trunk, and face with sparing of the palms and soles. PPE is one of the most common conditions in HIV-infected population living in tropics, with a reported prevalence of 11%–46%.[1-5]

The exact etiology of PPE is unknown but might be an altered and exaggerated immune response to arthropod antigens.[3] Immune dysregulation is of paramount importance in the development of PPE lesions. PPEs are regarded as the WHO clinical Stage II for infants and children.[6] PPEs manifest in advanced immunosuppressive stage in majority of the cases, but they may appear as an initial cutaneous disease with high CD4 count.[7] Information about the relationship between PPE and HIV/AIDS in India is limited.

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The purpose of the study is to introduce "PPE" in HIV-infected individuals as a marker of immune status for field-based settings in developing countries like India and to identify potential risk factors for PPE in HIV-positive patients. The fact that PPE can be readily detected by a trained clinician in a standardized, objective fashion without any complicated or expensive diagnostic technique has increased their utility.

Objectives

The objective of the study was to determine the prevalence of PPE in HIV-infected patients and to correlate between the severity of PPE and individual CD4 count.

MATERIALS AND METHODS

This was a cross-sectional study conducted in antiretroviral therapy (ART) Centre, Palakkad, Kerala, after getting approval from the ethical committee of our institution and also from the National AIDS control organization (NACO). The study population included all the HIV patients who attended the ART center with evidence of multiple papular or nodular lesions of 1-month duration during the study period of March 2017–April 2017. Those patients who had other itchy conditions were excluded from the study.

Written informed consent was obtained from the participants. Baseline information regarding demographic features, high-risk behavior, route of transmission, duration of the disease, and history of ART were collected from all the individuals on a pretested structured questionnaire. Duration of PPE, environmental, and other types of exposure were also recorded. The previous CD4 counts of each patient (maximum of 6 months) were recorded from the patient's medical records.

Proper dermatological examination was done in natural light and severity of lesion was evaluated using an objective "rash severity scale" for PPE that was used by Farsani *et al.*[8] in their study. Lesions that were limited to either the upper or lower extremities were described as "mild." When both the upper and lower extremities were involved, the rash was categorized as "moderate" disease. A "severe" rash included lesions present on the extremities as well as the trunk. Lesions present all over the body, including the face, were defined as "very severe." All the findings were recorded in a pro forma for analysis and interpretation of data.

Data were entered and analyzed using SPSS Version 16 (SPSS, Inc., Chicago, IL, USA). Fisher's exact test was carried out to find the association between variables. Level of significance was estimated with 95% confidence intervals and $P < 0.05$.

RESULTS

During the study period of March 2017–April 2017, a total of 100 HIV-positive patients who presented to the ART center with pruritic cutaneous eruption of more than 1-month duration with clinical features suggestive of PPE were included in the study. This represented 11.35% of all patients screened ($n = 898$ patients) during this time period. The following observations were made in our study.

Of 100 patients, majority of the study participants were more than 46 years (40%). Twenty-nine percent of the study population were in the age group of 33–40 years and 18% were in the age group of 33–40 years, whereas 8% were in the age group of <18 years. Only 3% were in the age group of 26–32 years and 2% in the age group of 19–25 years. The mean age of the study population was 41.17 ± 12. In our study, 33 patients (33%) were male, while 67 patients (67%) were female. There was a female preponderance, and the male-to-female ratio was 1:2. About 84% of the study population was literate, whereas 16% were illiterates.

In our study, majority (66%) had the working time during morning hours, whereas only 1% was working in the evening hours. Rest (33%) of the study population was unemployed. Among the patients, 48% were working outdoor, 19% were working indoor, and 33% were unemployed. Ninety-seven percent of the patients were giving history of mosquito bite, whereas only 3% were there without that history. Most of the patients (94%) were using repellant coils against mosquito bite and 2% were using topical insect repellents, whereas 4% were not taking any prevention against mosquito bite.

About 93% of the study population were on ART and 7% were not on ART. In our study population, 33 patients (33%) were on treatment ART for more than 5 years, 22% on treatment between 3 and 5 years, 20% on treatment <1 year, and 18% on treatment between 1 and 3 years. Seven patients (7%) were not on treatment. The mean duration of treatment was 44.72 ± 35.5 months. Fifty-one percent of patients were of more than 5 years after diagnosis, 18% of patients were of <1 year after diagnosis, 14% of patients were in between 3 and 5 years after diagnosis and 16%

of patients were in between 1 and 3 years after diagnosis.

About 93% of patients were in the WHO Stage II and 7% of patients were in the WHO Stage III. Fourteen percent of the patients had CD4+ count of <200, 34% had CD4+ between 200 and 500, and 52% had >500 CD4+ counts [Table 1]. It was observed that more number of patients had CD4+ count of >500 cells/mm^3.

In our study, 60% of patients had PPE for more than 3 months duration, 15% had PPE for 1 month duration, 13% had PPE between the duration of 1 and 2 months, and 12% had PPE between the duration of 2 and 3 months [Table 2]. In our study, majority (40%) had moderate PPE which involves both the upper limbs and lower limbs [Figure 1]. Mild PPE was seen in 38% involving either the upper limb or lower limb [Figure 2]. Thirteen percent had severe PPE which involves face [Figure 3] along with upper and lower limbs. Very severe PPE was seen in nine patients which involves the face, trunk, and upper and lower extremities [Table 3]. Majority (86%) of the patients had a CD4 count of more than 200 and the incidence of PPE was more frequently seen in patients with CD4 count more than 200 cells which was statistically significant (P = 0.036). In the study population of CD4 more than 200 cells, 36% had moderate PPE, 35% had mild PPE, 10% had severe PPE, and 5% had very severe PPE. In patients with CD4 <200, moderate and very severe PPE was seen in 4% of patients each, and mild and severe grades were seen in 3% of patients each. The strength of association between PPE and CD4 count was done by Fisher's test and P = 0.036 which is statistically significant [Table 4].

DISCUSSION

In 1981, when the first reports about HIV/AIDS were published in medical literature, cutaneous diseases

Table 1: Distribution of the population according to CD4+ count groups

CD4 count	Frequency (%)
0-200	14 (14)
200-500	34 (34)
>500	52 (52)

Table 2: Duration of pruritic papular eruption

Duration of PPE (months)	Frequency (%)
1	15 (15)
1-2	13 (13)
2-3	12 (12)
>3	60 (60)

PPE=Pruritic papular eruption

Table 3: Grading of pruritic papular eruption

Grading of PPE	Frequency (%)
Mild	38 (38)
Moderate	40 (40)
Severe	13 (13)
Very severe	9 (9)

PPE=Pruritic papular eruption

Table 4: Correlation between CD4 count and pruritic papular eruption

Grading of PPE	CD4 count		Total number of patients
	<200	>200	
Mild	3	35	38
Moderate	4	36	40
Severe	3	10	13
Very severe	4	5	9
Total	14	86	100

Fisher's exact calculated value=8.565; P=0.036. PPE=Pruritic papular eruption

Figure 1: Papules over upper limbs in a Grade II pruritic papular eruption patient

Figure 2: Papules over lower limbs in a Grade I pruritic papular eruption patient

played an important role in the clinical diagnosis of AIDS. Kaposi's sarcoma in young homosexual men was the first symptom that made HIV/AIDS a visible disease.[9] Even though many studies are in the direction to throw light over the PPE in HIV infected individuals, the pathophysiology of PPE is not completely understood so far. Nevertheless, it remains the most common cutaneous manifestation in HIV-infected patients.[10]

Prevalence

The prevalence of PPE was found to be 11.35% among the HIV-infected patients in our study, whereas in Farsani *et al.* (2.9%)[8] and Kumarasamy *et al.* (7.7%)[11] showed the low prevalence of PPE in their study. However, Singh *et al.* (22.5%),[12] Sharma *et al.* (35.8%),[13] Lowe *et al.* (42%),[14] Shittu *et al.* (33.9%),[15] and Thompson *et al.* (32%)[16] showed the high prevalence of PPE in their study [Table 5].

These substantial differences in the prevalence of HIV-related PPE may be explained by many factors such as (i) inclusion of histopathologically confirmed cases in certain studies; (ii) lifestyle, access to health-care ART, and the level of immune suppression influence the development of PPE in patients with HIV infection; and (iii) recruitment of an appropriate study population is a crucial point in any study design. Different populations, clinical settings used for evaluation of clinical stage, distribution of risk groups, race and socioeconomic status are the major confounding factors.

Figure 3: Papules over face in a Grade IV pruritic papular eruption patient

Mosquito bites and pruritic papular eruption

Majority of PPE patients observed by Resneck *et al.*[3] gave positive histories of exposure to insect bites and especially mosquitoes. This observation makes arthropod bites a likely etiology for PPE. In our study also, most of our patients (97%) gave history of recent mosquito bites, and this could probably explain mosquito bites as the etiology of PPE. The symmetry, plurality, and distribution of lesions on exposed body areas may possibly reflect the frequency of arthropod bites or a systemic response to these bites as interleukin-2 levels have been found to be low in PPE.[17] Nevertheless, the etiology of PPE remains controversial.

Correlation between CD4 count and pruritic papular eruption

In our study, PPE was more commonly seen in individuals (86%) who had CD4 count more than 200 cells/cu.mm, and it is statistically significant. This may be partly explained by the fact that PPE is a hypersensitivity reaction to arthropod bites which needs some sort of immunity for its development.

As per Lakshmi *et al.*, PPE's usually manifest in advanced immunosuppressive stage in majority of the cases, but they may appear as an initial cutaneous disease with high CD4 count.[7] Liautaud *et al.* had observed in their study intensely pruritic eruptions as the first markers of HIV in 79% patients, and the eruptions appeared a mean of 8 months before the diagnosis of either Kaposi's sarcoma or opportunistic infection, thus acting as the indicators of advancing immunosuppression.[1] In some studies, they have been shown to be highly

Table 5: Prevalence of pruritic papular eruption in HIV-positive patients from comparable studies done elsewhere

Researcher	Study population	Year	Sample	Prevalence (%)
Our study	Salem, South India	2016-17	100 (898)	11.35
Farsani *et al.*[8]	Chennai, India	2008	52 (1466)	2.9
Kumarasamy *et al.*[11]	Chennai, India	2003	833	7.7
Singh *et al.*[12]	Chhattisgarh, India	2009	-	22.5
Sharma *et al.*[13]	India	2007	-	35.8
Lowe *et al.*[14]	Zimbabwe	2010	139	42
Shittu *et al.*[15]	Nigeria	2009	160	33.9
Thompson *et al.*[16]	Jamaica	2003	286	32

predictive markers of severe immune suppression and disease progression, but the specificity of PPE to the level of immunosuppression was never assessed. Like that our study also not able to correlate the CD4 counts with severity of PPE rash. Using the rash severity scale, the severity of skin rash was not significantly associated with the CD4 count. This implies that we cannot use rash distribution or severity as an indicator of CD4 count.

PPE is seen more commonly among patients on highly active antiretroviral therapy (HAART) probably occurring as part of an immune reconstitution syndrome.[18] If this is the case, then the PPE prevalence may increase when our patients start taking HAART. More studies to this direction are warranted. In our study, majority of the patients (93%) were on HAART. We did not suspect IRIS in the patients of this study even though majority of the patients were receiving HAART because a rapid increase in CD4 cell counts was not detected. Through the ability of HAART to reconstitute the immune system, there have undoubtedly been significant changes in the nature and prevalence of skin disorders affecting the HIV-infected population.[19]

Clinical diagnosis alone is not optimal in cases of PPE and confirmation by biopsy is encouraged which is the limitation of our study. Numerous authors have reported the pathologic findings in PPE with much inconsistency. Resneck *et al*.[3] noted that in early PPE, findings resembled arthropod bites, showing dense superficial and deep perivascular and interstitial infiltrate of lymphocytes and eosinophils often extending into the subcutis and associated with epidermal hyperplasia, and in some cases, a punctum. Hevia *et al*.[20] found a superficial and mid-dermal mixed perivascular and perifollicular infiltrate of lymphocytes and eosinophils with variable degrees of follicular damage.

PPE is a marker of advancing immunosuppression in HIV and has a major impact on the quality of life of the patient and should thus be recognized early and promptly treated. PPE is one of the mucocutaneous manifestations which play a major role in diagnosing HIV infection in countries where serologic testing is not available or affordable. Treatment of PPE remains notoriously difficult. There are no randomized controlled studies to prove us, regarding the best treatment options for PPE. As the etiology is not definitively known, the therapy is directed toward symptoms, predominantly pruritus which is often severe and unresponsive to traditional antipruritic measures. No formal studies have been reported, and treatment successes or failures are purely anecdotal. Treatments have included potent topical corticosteroids, used alone or in combination with oral antihistamines, oral antibiotics, emollients, antipruritic lotions, antifungal creams, and antiscabies treatments.[20,21] Ishii *et al*.[22] demonstrated UVB phototherapy to be effective in the treatment of PPE. Resneck *et al*.[3] present anecdotal reports of PPE improving with the initiation of antiretroviral medication.

CONCLUSION

PPEs are a unique dermatosis among the spectrum of cutaneous lesions in HIV-infected patients. Both from a medical and a cosmetic point of view, it has a devastating impact on the quality of life of the affected patient, stigmatizing them in their communities. Thus, recognizing those lesions helps in allowing better treatment of this distressing condition. Immune dysregulation is of paramount important factor in the development of PPE. Further large-scale, multicentric studies correlating the natural history of PPE with immunological markers and prognostic indicators for HIV disease may be helpful. Genetic polymorphisms may also be an area of future study to explain why certain HIV-positive patients develop PPE while others do not.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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