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The Socio-demographic and Quality of Life of People Living with HIV (PLHIV) Presenting with Cutaneous Manifestation: A Cross-Sectional Study in the Department of Dermatology, Sarawak General Hospital

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Abstract

Background

People living with Human Immunodeficiency Virus (PLHIV) are living longer with the advent of highly active antiviral therapy (HAART). Aside from extending the life span, quality of life is vital in PLHIV management. However, there is a paucity of data on the cutaneous manifestations in PLHIV on HAART. The objective of this study is to ascertain the prevalence of cutaneous manifestations, effect on daily lives, and relation to CD4 levels.

Methods

This is a prospective cross-sectional study comparing 2 groups of PLHIV patients on HAART and not on HAART therapy done from March 2020 to November 2020.

Results

A total of 259 patients were recruited in this study with a mean age of 40 years. There were 216 (83.4%) male and 43 (16.6 %) female. Men having sex with men accounts for 49%. The most common cutaneous disorder was post-inflammatory pigmentation (20.4%). Infective dermatoses were 43 (6.7%), and cutaneous malignancy 3 (0.6%). Mean DLQI in PLHIV on HAART were 2, as compared to PLHIV not on HAART which scored 3. Bidayuh ethnicity accounts for 30% of adverse drug reactions with Bactrim being the most common drug.

Conclusion

There is a high prevalence of dermatoses in PLHIV. HAART increases the CD4 count of patients thereby reducing the risk of opportunistic infection and related disorders. However, it did not reduce the cutaneous manifestations in PLHIV, as HAART itself may increase the risk of adverse cutaneous drug reactions. DLQI is not the best tool to assess quality of life.

Key words: *Human Immunodeficiency Virus, quality of life, cutaneous manifestation*

Introduction

Human Immunodeficiency Virus (HIV) is a multifaceted burden of modern society. The march on awareness and control of HIV infections resulted in a successful reduction in the number of new infections and deaths. However, there is a continuous increase in the number of people living with HIV (PLHIV) globally. In 2019, Malaysia recorded a total of 87 000 HIV cases, of which 5 600 are newly

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diagnosed with 2 600 deaths from HIV.[1]

HIV was first described in 1981 in light of 5 cases of Pneumocystis carinii pneumonia (PCP) among previously healthy young men. There is no cure but a lifelong manageable therapy. Highly Active Antiviral Therapy (HAART) inhibits HIV proliferation hence suppresses the viral load and leads to improvement of CD4 function. Due to the nature of persistent viral reservoir, complete eradication is not possible with current therapy.[2] HAART extends the life span of people living with HIV (PLHIV) and sustains the nation's powerhouse as this infection predominates in young to middle-aged adults.[3] The focus on the quality of life in PLHIV is emerging in the literature across the world as researches for cure are underway.

The prevalence of cutaneous manifestations in acute HIV-infected patients is greater than 90%.[4] They range from subtle to severe impairment in the quality of life. On the contrary, data on mucocutaneous disorder in chronic HIV infection is lacking. These data are crucial to aid in understanding and improving the quality of life in PLHIV.

This study aims to determine the prevalence of dermatoses with its impact on the quality of life and to determine the correlation between various factors (demographic, HAART, severity of immunosuppression) in PLHIV.

Materials and Methods

This is a prospective, cross-sectional study conducted on adult HIV-infected patients from March to November 2020 (8 months). Patients were recruited from the HAART Clinic of Sarawak General Hospital, a tertiary referral center in East Malaysia.

Approval from the Medical Research and Ethics Committee was obtained before the commencement of this study (NMRR approval code: NMRR-19-3446-52216). Consented subjects were examined, notes reviewed and then subjected to Dermatology Life Quality Index (DLQI) questionnaire.

DLQI is a user-friendly validated tool used to assess impact of skin diseases on the quality of life. In this study, validated DLQI both in Bahasa Melayu and English language were used. It consists of 10 questions concerning patients' perception on different aspect of daily living in the past weeks. The DLQI is calculated by adding the score of each question, resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. Impact on the quality of life is as follow;

- 0 – 1 no effect at all on patient's life
- 2 – 5 small effects on patient's life
- 6 – 10 moderate effects on patient's life
- 11 – 20 very large effect on patient's life
- 21 – 30 extremely large effect on patient's life.

Cases that required further management will be referred to the Dermatology Department of Sarawak General Hospital. Stable HAART is defined as the duration of HAART treatment for more than 1 year.[5]

Data on demographic, dermatological diagnosis, and characteristics were recorded and analyzed using SPSS Version 21. Descriptive statistics were presented as counts and percentages for categorical variables. Fisher's exact test was used for analysis of dermatoses comparing HAART treated and HAART not treated group as the data collected were of small sample size and non-parametric distribution. Statistical significance was set at $p<0.05$. As for the correlation analysis, Spearmann's rho method analysis was used data.

Results

A total of 261 patients were seen in HAART Clinic. Out of these, 1 patient declined to participate while another patient had false-positive result of HIV. This resulted in a final sample size of 259. Among the study population, 13.1% required dermatology referral, 35.9% were given a prescription, and 1.1% had skin biopsy done. Demographic characteristics are shown in Table 1.

Table 1. Characteristics of the study population

Characteristics	n	%
Age	40.7±12.68 (18-87)	
18-29	61	23.6
30-39	76	29.3
40-49	61	23.6
>50	61	23.6
Gender		
Male	216	83.4
Female	43	16.6
Ethnicity		
Malay	82	31.7
Bidayuh	62	23.9
Chinese	58	22.4
Iban	47	18.1
Others	3	1.2
Indian	2	0.8
Kayan	2	0.8
Melanau	1	0.4
Kelabit	1	0.4
Kenyah	1	0.4
Education		
None	1	0.4
Primary	40	15.4
Secondary	132	51
Tertiary	86	33.2
Marital status		
Single	172	66.4
Married	77	29.7
Divorced	9	3.5
Widowed	1	0.4
Occupation		
White collar	39	15.1
Blue collar	131	50.6
Housewife	11	4.2
Unemployed	78	30.1
Mode of Transmission		
Homosexual	105	40.5
Heterosexual	96	37.1
Bisexual	23	8.9
Unknown	20	7.7
IVDU usage	12	4.6
Vertical	3	1.2
CD4		
>500	68	26.3
200-499	115	44.4
<200	74	28.6
Not available	2	0.8
Viral load		
<200 copies/ml	197	76.1
>200 copies/ml	35	13.5
Not available	27	10.4
On HAART treatment		
No	38	14.7
Yes	221	85.3
Duration on HAART		
<1 years	57	25.8
>1 years	164	74.2

Table 2. Comorbidities in PLHIV

Comorbidities		n	%
Before HIV diagnosis		68	26.3
After HIV diagnosis		45	17.4
Non-infective			**83.2**
	Dyslipidaemia	26	15
	Hypertension	25	14.5
	Atopic Diseases	24	13.9
	Diabetes mellitus	18	10.4
	Chronic Kidney Disease	6	3.5
	Psychiatry disorders	5	2.9
	Gastritis	5	2.9
	Adrenal insufficiency	4	2.3
	G6PD	3	1.7
	Malignancy	3	1.7
	Ischemic heart disease	3	1.7
	Seizure	3	1.7
	Stroke	2	1.2
	Gout	2	1.2
	Pregnant	1	0.6
	Liver cirrhosis	1	0.6
	Anaemia	1	0.6
	Others	16	9.2
Infective			**16.8**
	Syphilis	31	17.9
	Tuberculosis	20	11.6
	Hepatitis C	5	2.9
	Hepatitis C and Syphilis	4	2.3
	Hepatitis B and Tuberculosis	4	2.3
	Hepatitis B	3	1.7
	Hepatitis C and Tuberculosis	3	1.7
	Tuberculosis and Syphilis	3	1.7
	Hepatitis B and Hepatitis C	2	1.2
	Hepatitis B and Syphilis	1	0.6

The mean age in this study population was 40.1 years (ranging from 18 to 87 years). The

mean age of HIV diagnosis was 35.7 years. There were 216 (83.4%) males and 43 (16.6 %) females, with a ratio of male to female being 5 to 1. Eighty-two subjects are Malay (31.7%), followed by Bidayuh (23.9%), Chinese (22.4%), Iban (18.1%) and foreigners (1.2 %).

The literacy rate was high (99.6%), of which 51% PLHIV had secondary school education, and 33.2% had tertiary education, meanwhile only one subject did not have any formal education. Hence the corresponding DLQI was obtained via assistance. There is a great role for designing interactive questionnaires for low-literate persons. Majority of the participants were single (66.4 %), whereas only 29.7% of the subjects were married. Blue-collar workers recorded the highest distribution which accounts for 50.6%, whereas unemployment was 30 %. Sexual transmission was the most common mode of infection. Homosexuality accounted for 40.5 percent, followed by heterosexuality (37.1%), IVDU (4.6%), and vertical transmission (1.2%).

The mean CD4 count was 362 cells/m³ with 74 participants (28.6%) who had CD4 level below 200 cells/mm³. There were 85.3% of participants who were on HAART treatment with the mean duration of 2.9 years (ranges up to 18 years from the initiation of treatment). In addition, prior HIV diagnosis, 26.3% had pre-existing comorbidity, where else 17.4 % developed new comorbidity after HIV diagnosis. Non-infective comorbidities in this study population were dyslipidemia 15%, hypertension 14.5%, diabetes mellitus 10.4%, atopic diseases 13.9%, psychiatry disorders 2.9% and others (Table 2). Infective comorbidities account for 16.8% of the participants which include syphilis 17.9%, tuberculosis 11.6 %, hepatitis C 2.9%, and hepatitis B 1.7%, while the remainder is attributed to mixed infection.

The overall prevalence of cutaneous manifestations in PLHIV was 90.7%, whereas for PLHIV on HAART was 78.9%. In this study, 64.9% of PLHIV had more than 1 type of cutaneous diagnosis. Two types of dermatoses were the highest, accounting for 92 participants (41.6%). The highest number of dermatoses were 6 (0.9 %) (Table 3). In this study, stable PLHIV on HAART with CD4 more than 200 cells/mm³ accounts for 64.7%, where as, CD4 less than 200 cells/mm³ were 9.5%. A total of 481 dermatoses were found in 259 patients. Table 4. As high as 48.6% participants in this study complained of pruritus, whereas aesthetic concerns were 29.5 %, scaly skin 18.6%, and pain 3.2%.

The types of dermatoses were divided into infective 8.1%, non-infective 87.9%, malignant 0.6%, and drug-induced adverse events 1%. In comparison between HAART-treated and untreated ones, drug-induced maculopapular eruption was statistically significant ($p = 0.01$). Table 4.

The negative correlation coefficient between the severity of immunosuppression with DLQI was not statistically significant (Spearman's rho correlation coefficient, $p = -0.23$). There was an extremely large effect on the quality of life in PLHIV with severe immunosuppression (Table 5). Untreated HIV participants had a mean DLQI of 3, meanwhile treated HIV participants had a mean DLQI of 2. However, there was no statistically significant difference in DLQI between the treated and untreated group.

Table 3. Number of dermatoses in the study population in correlation with CD4 and duration of HAART

Duration HAART	CD4, cells/mm³	Number of dermatoses, n						
		0	1	2	3	4	5	6
< 1 years	>500	2	1	2	1	0	0	0
	201-499	3	7	7	6	1	0	0
	<200	1	4	15	5	1	1	0
> 1 years	>500	7	14	23	11	4	1	0
	201-499	9	25	36	9	2	1	1
	<200	0	5	9	3	3	0	1

Table 4. Distribution of dermatosis in PLHIV on HAART and without HAART

Dermatosis	Not on HAART, n (%)	On HAART, n (%)	*p-value*
	N=68	N=413	
Infective dermatosis			
Fungal			
Tinea coporis	1(1.5)	9(2.1)	*0.98*
Tinea pedis	0	9(2.1)	*0.36*
Tinea Cruris	2(2.9)	3(0.7)	*0.16*
Tinea capitis	1(1.5)	1(0.2)	*0.27*
Onychomychosis	0	2(1.5)	*0.10*
Bacterial			
Impetigo	1(1.5)	1(0.2)	*0.27*
Ecthyma	0	1(0.2)	*0.98*
Syphilis	0	1(0.2)	*0.98*
Viral			
Genital warts	3(4.4)	6(1.5)	*0.13*
Non genital warts	2(2.9)	2(4.9)	*0.10*
Herpes zoster	1(1.5)	2(4.9)	*0.31*
Molluscum contagiosum	0	2(4.9)	*0.97*
Parasites			
	0	0	*NA*
Non infective Dermatosis			
Inflammatory disorder			
Post inflammatory pigmentation	15(22.1)	83(20.1)	*0.86*
Xerosis	9(13.2)	70(16.9)	*0.45*
Folliculitis	5(7.4)	25(6.1)	*0.78*
Eczema	2(2.9)	22(5.3)	*0.55*
Contact dermatitis	0	19(4.6)	*0.09*
Seborrheic Dermatitis	4(5.9)	12(2.9)	*0.23*
Acne vulgaris	2(2.9)	7(1.7)	*0.62*
Psoriasis	2(2.9)	5(1.2)	*0.27*
Nail pitting	1(1.5)	4(1)	*0.55*
Chronic spontaneous urticaria	0	4(1)	*0.92*
Livedo reticularis	1(1.5)	2(0.5)	*0.14*
Stasis eczema	0	2(0.5)	*0.93*
Cheilitis	0	1(0.2)	*0.97*
Prurigo nodularis	0	1(0.2)	*0.97*
Ulcer	0	1(0.2)	*0.97*
Post Infective desquamation	1(1.5)	0	*0.15*
Thrombophlebitis	1(1.5)	0	*0.15*
Pruritic papular eruption	0	0	*NA*
Oral lesions	0	0	*NA*
Non-inflammatory disorder			

Scars	2(2.9)	24(5.8)	*0.39*
Tattoo	3(4.4)	16(3.9)	*0.75*
Melanonychia	3(4.4)	15(3.6)	*0.73*
Chronic paronychia	1(1.5)	14(3.4)	*0.71*
Scabs	0	9(2.2)	*0.36*
Subungual hematoma	1(1.5)	1(0.2)	*0.27*
Sebaceous cyst	0	1(0.2)	*0.98*
Scrotal angioma	0	1(0.2)	*0.98*
Acanthosis nigrican	0	1(0.2)	*0.98*
Striae	0	1(0.2)	*0.98*
Lipoid atrophy	0	1(0.2)	*0.98*
Lipoma	0	1(0.2)	*0.98*
Tophi	0	1(0.2)	*0.98*
Delusional parasitosis	0	1(0.2)	*0.98*
Ganglion cyst	0	1(0.2)	*0.98*
Degenerative disorder			
Deformed nail	0	8(1.9)	*0.61*
Seborrheic keratosis	0	4(1)	*0.90*
Cherry angioma	0	3(0.7)	*0.95*
Alopecia	0	3(0.7)	*0.95*
Skin tag	0	3(0.7)	*0.95*
Callus	0	2(0.5)	*0.97*
Guttate hypomelanosis	0	1(0.2)	*0.99*
Malignant			
Kaposi Sarcoma	1(1.5)	2(0.5)	*0.38*
Squamous cell carcinoma	0	0	*NA*
Basal cell Carcinoma	0	0	*NA*
Melanoma	0	0	*NA*
Drugs adverse event			
Maculopapular lesion	3(4.4)	1(0.2)	*0.011*
Acne	0	1(0.2)	*0.98*

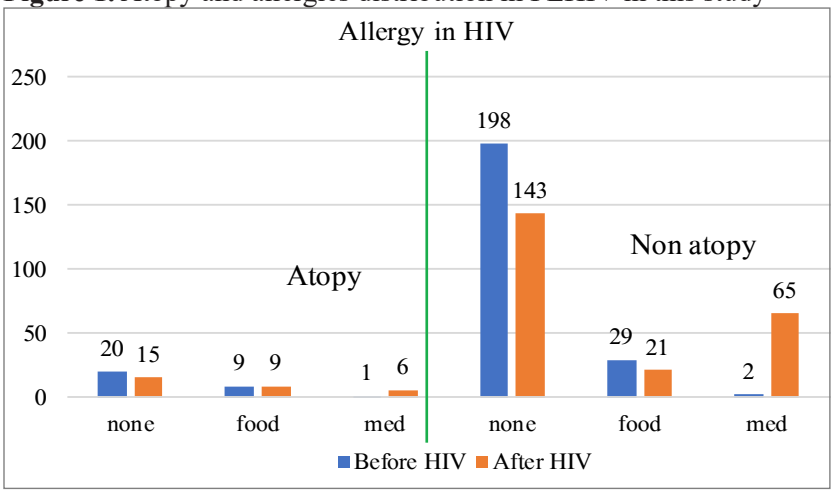
NA: not available as the statistic analysis is unable to perform for the comparison to obtain p-value
p-value is obtain from Fisher exact test
**One patient may have multiple mucocutaneous manifestations; the percentage reported is based on total patients in each group*

Table 5. Correlations of severity of immunosuppression with DLQI in PLHIV

CD4, cells/mm³	DLQI, n (%)				
	No effect	**Small effect**	**Moderate effect**	**Very Large effect**	**Extremely Large effect**
>500	57(22.2)	9(3.5)	2(0.8)	0	0
200-499	79(30.8)	25(9.8)	9(23.5)	1(0.4)	1(0.4)
<200	41(16)	20(7.8)	10(3.9)	1(0.4)	2(0.8)

Spearmann's rho corelation shows negative corelation with insignificant p =0.224

Figure 1. Atopy and allergies distribution in PLHIV in this study



None: no allergy; Food: allergy to food; Med: allergy to medication

A quarter of the allergies (25.1%) in PLHIV were attributed to medication. In non-atopy arm, 143 participants (55%) remain allergy-free after initiation of HAART (Figure 1). Allergy incidents before and after HIV diagnosis were 41(16%) and 101(39.3%) respectively. However, these differences were not statistically significant. (Table 6).

Table 6. Overview of DLQI scores in this study

DLQI Severity	DLQI score	n	%
No effect	0	125	48.3
	1	53	20.5
Small effect	2	29	11.2
	3	11	4.2
	4	8	3.1
	5	7	2.7
Moderate effect	6	5	1.9
	7	7	2.7
	8	3	1.2
	9	3	1.2
	10	3	1.2
Very large effect	11	1	0.4
	15	1	0.4
Very large effect	22	1	0.4
	24	1	0.4
	25	1	0.4

A total of 91 participants had adverse drug event. Despite the Malay race having the highest prevalence of PLHIV in this study, Bidayuh ethnicity had the most frequent adverse drug reactions (30.8%). Bactrim accounts for the highest incidence 64.8%, followed by HAART 12.1%, dapsone 8.8%, antibiotics 7.7 %, and others 6.7%. (Table 7).

Table 7. Distribution of adverse drug event based on ethnicity in PLHIV in Sarawak

Ethnic\ Drugs	Bactrim	Dapsone	HAART	Antibiotics	Others
Bidayuh	19	4	2	2	1
Chinese	11	1	2	1	1
Iban	13	1	4	3	2
Malay	13	2	3	1	2
Indian	1	0	0	0	0
Other	1	0	0	0	0
Kelabit	1	0	0	0	0
Melanau	0	0	0	0	0
Kayan	0	0	0	0	0
Kenyah	0	0	0	0	0

Discussion

HIV infection is complex and multifactorial. The male gender, compounded by homosexual practice, raises the risks of HIV infection. This is consistent with our local[6] and international studies.[7-8] Anal intercourse is associated with a higher rate of infection due to biological factors as compared to vaginal intercourse. However, in other parts of the world, females are the predominant gender.[9-10] This is supported by literatures on the differences in HIV acquisition by gender[11] and pathophysiology of sex and hormone levels with inflammation induced by the microbiome.[12-13]

Adults, young to middle-aged are the most often infected group. This study majority of PLHIV is in between 18 to 39 years old. This is supplemented by our national HIV data in 2018 which shows that 67 % prevalence of HIV infection occurs in those who are 20 to 39 years old. Data from CDC US in 2019 states that, the rate of HIV infection was highest for persons aged 25–34. Curiosity and the drive to be unique are probably the key factors to the rate of infection in this region. Additionally, social media, population density, adaptive change in urbanisation and information accessibility could be the other contributing factors.

Comorbidities observed in stable HIV were mainly non-infective, where as in acute HIV infection, infective disorders predominate.[14] Significant metabolic disorders in this population are attributed to HAART itself and the other conventional risk factors such as diet, lifestyles, and genetic predispositions. Once PLHIV is stable, clinicians are left with another hurdle to manage the arising comorbidity and focus on the quality of life.

This study recorded 74.2% of stable PLHIV on HAART. In this group, the number of diseases is expected to reduce because of improved immune systems. On the contrary, the number of dermatoses observed have increased. Non-HIV related cutaneous malignancy was not observed in this study despite the older HIV-infected population. Kaposi sarcoma with an incident of 1.2% was the only cutaneous malignancy observed. It is associated with men who have sex with men (MSM) practice. Usage of saliva as a lubricant was postulated to be the main principle of transmission as the viral load of Kaposi sarcoma in the semen is substantially low.[15] Also called human herpesvirus-8, has since been shown to be the etiologic agent for several other tumors and diseases, including primary effusion lymphoma (PEL Half of the Kaposi sarcoma in this study failed to achieve complete resolution despite being stable HAART, which is consistent with the previous research.[16] These findings can be explained by immune deviation instead of normalising immune function due to HAART via persistent HIV replication in memory T lymphocytes despite optimal HIV virus control.[17] There were no statistically significant differences between cutaneous manifestations in a treated and untreated patient in this study ($p = 0.357$). As PLHIV are surviving longer, degenerative cutaneous disorders are more apparent in our study. However, more comparison data is required to conclude this finding.

The occurrence of genital warts was higher in PLHIV not on HAART, as compared to those on HAART. High-risk Human Papillomavirus (HPV) types commonly affect the anogenital and the oral cavity.[18] Prolonged life span in stable HAART group predisposes to oncogenic transformation.[19] HAART had not been shown to reduce incidents of HPV-related cervical diseases in women living with HIV.[20] The impact of HAART on cervical cancer, however, remains uncertain. The objective of this review is to summarize the last ten years of registry-based and clinical research into the impact of HAART on human papillomavirus Census from Human Papillomavirus and Related Diseases Report Malaysia recorded significant HPV-related cervical cancer in the high-risk type of HPV in the non-HIV population. Data on HPV related cancer in the treated HIV population in this region is lacking. HPV vaccination have since been included in the national vaccination scheme for 13-year-old girls in schools since 2012. Data on the effective regime of HPV vaccination in PLHIV is lacking,[21] hence more trials are needed before implementation in the national health scheme.

Impact on living due to cutaneous manifestation was highest in the stable HIV with higher CD4 levels. This is due to a higher number of dermatosis and demand on quality of life as a struggle to blend into stigmatised society towards HIV. However, a lower mean DLQI score compare to a recent study, could be explained by different expectations of the quality of life in different urban populations; Johor (East Malaysia)[22] and Kuching, Sarawak (West Malaysia). Furthermore, population

with lower socioeconomic status are more ignorant of the non-life-threatening nature of the cutaneous manifestation, resulting in an underrepresentation of the actual situation. Despite 85.3% of PLHIV are on HAART in Kuching which is higher than the national statistics record of 48%, the unemployment rate is significant at 30% in contrast to local unemployment rates of 15% (2018, Sarawak statistics). This result is also observed in France where the unemployment rate in PLHIV is 15.9% as compare to 6.1% in the population in 2011.[23] unemploymet has increased among people living with HIV. Employment is one of the important defining factors on the quality of life. The high unemployment rate in the background of high literacy rate is the result of social stigma, discriminatory policies prohibitive laws and ultimately, the lack of societal support. Another factor with great impact on the quality of living is the side effect of HAART which is statistically significant in this study. Due to the nature of this study, no severe cutaneous adverse reactions syndrome (SCARS) was reported as most SCARS would necessitate inpatient treatment.

The limitation of this study is the small sample size and the absence of data from suburban areas. Covid-19 pandemic has a significant implication on both the quality and quantity of the data collected in this study.

Conclusion

There is a shift in the mode of transmission from intravenous to sexual route and from infective to non-infective disorders in PLHIV. Ultimately, our findings revealed that, despite the introduction of HAART, the number of cutaneous manifestations in HIV patients have not significantly reduced. Quality of living in PLHIV is best defined by unemployment rate and ADR rather than DLQI scoring due to the socioeconomic factors. As we embark on our quest to cure HIV and raise the standard of living of those living with HIV, we will constantly face new challenges. A comprehensive registry and awareness are needed to provide a clearer picture to redefine management guidelines.

Conflict of Interest Declaration

The authors have no conflict of interest to declare. There is no affiliation or significant financial involvement in any organisation or entity with direct financial interest in the subject matter or materials discussed in the manuscript.

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