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Pain Among Ambulatory HIV/AIDS Patients: Multicenter Study of Prevalence, Intensity, Associated Factors, and Effect

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Abstract: **This study aimed to determine the prevalence, intensity, associated factors, and effect of pain among ambulatory HIV/AIDS patients. Three-hundred two adult ambulatory HIV/AIDS patients were consecutively recruited from HIV/AIDS outpatient clinics at 2 teaching hospitals in Uganda. The presence and intensity of pain were self-reported using the Brief Pain Inventory (BPI); symptom data were collected using the Memorial Symptom Assessment Scale (MSAS-SF); and quality of life (QOL) was assessed using the Medical Outcome Scale-HIV. Forty-seven percent reported pain in the 7 days prior to the survey and pain was a symptom at the time of diagnosis for 68%. On the 0 to 10 numeric scale, 53% reported mild pain (1–4 rating), 20% reported moderate pain (5–6 rating) while 27% reported severe pain (7–10 rating). Gender was not associated with pain intensity, but reduced functional performance, increasing number of symptoms, advanced HIV disease , physical symptom distress (MSAS-SF), and number of health comorbidities were significantly associated with pain intensity ($P < .04$). Increasing pain intensity was associated with greater functional ability impairment (BPI functional interference index) and poorer QOL. Pain is a common symptom among ambulatory HIV/AIDS patients and has a debilitating effect on QOL. There is a significant unmet need for pain relief in the population.**

Perspective: ***This article discusses the characteristics and effect of pain on function and QOL in East African patients. It also contributes information on characteristics of HIV/AIDS adult patients in the East Africa demonstrating the aspects in which pain is similar across different cultures.***

Key words: *HIV, pain rating, pain interference, function, quality of life.*

Sub-Saharan Africa remains the region most heavily affected by the Human Immunodeficiency Virus (HIV) epidemic, accounting for 69% (ie, 22.5 million) of the global disease burden and 72% (ie, 1.3 million) of acquired immune deficiency syndrome (AIDS) deaths in 2009.[61]

A high prevalence of burdensome physical and psychological symptoms has been reported at all stages of HIV infection.[26,53,62,64,66] Pain is also experienced throughout the HIV disease trajectory, with severe pain experienced by 80 to 98% of those with advanced HIV.[4,43,57]

Recent studies show that antiretroviral therapy (ART) has not eliminated the need for effective pain and symptom control, given that problems (sometimes treatment related) persist.[16,21,23] Studies to establish potential correlates of the presence of pain in HIV have shown that the number of HIV-associated symptoms, disease stage,[52] and use of ART are associated with pain prevalence.[2,6,55] Moreover, disturbances in physical, psychological, and social functioning have been found to be greater in patients experiencing pain compared to pain-free patients.

Despite the increased attention paid to pain treatment, few data are available concerning the frequency and severity of pain in HIV in Africa. Existing literature on the continent has been based on specific populations, has rarely used outcome measures, has often focused solely on patients with advanced disease or specifically

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on neuropathic pain, and used differing criteria for determining the presence of pain, rendering data interpretation problematic.[3]

Several studies have demonstrated the adverse impact of pain on patient well-being.[44,45,50] However, the vast majority of studies that have investigated HIV-related pain have been conducted in economically developed countries and on patient cohorts consisting predominantly of males, Caucasians, men who have sex with men, and intravenous drug users.[2,25,55] These cohorts limit the generalizability of these studies. In addition, there has been conflicting evidence on the association between ART and presence of pain. Some studies have found that use of ART is not associated with presence of pain,[3,30] while others have associated use of ART with reduced risk of having pain.[21] In addition, the relationship between gender and pain is ambiguous. Some studies have found gender to be associated with presence and intensity of pain[3,5,20] while other are at odds with this finding.[17,36] The divergent findings may be due to sample variations in sample composition and/or pain assessment including use of unstandaridized measures and small convenience samples.

Consequently, given these existing research limitations, coupled with the subjective nature of pain and the potential mediating role of ethnicity, culture, and gender in pain perception,[17,20,29,34] this study sought to examine the three-day period prevalence of pain among ambulatory HIV/AIDS patients in 2 clinical HIV outpatient sites in Uganda, further explore the association between use of ART and pain presence as well its intensity, and assess the association between pain, function, and quality of life (QOL). The authors hypothesized that there would be no association between gender and presence or intensity of pain because gender differences are not necessarily confined to HIV-related pain but rather differences in psychological and social factors between the men and women based on their settings.[8,60]

Methods

Design and Study Setting

This was a cross-sectional patient self-report study conducted in Uganda at 2 HIV/AIDS outpatient clinics, 1 in a rural and 1 in an urban setting.[19,24]

Sample Size Estimation

For the descriptive component of the study (ie, aimed at establishing the prevalence of pain in adult ambulatory HIV/AIDS patients), the statistical concepts of power and null hypothesis did not apply.[28] Instead, an average expected pain prevalence of 35% was used for sample size computation based on estimates from previous studies conducted with similar populations.[5,17,36,57] Using the Kish[33] formula for prevalence studies, with a 95% confidence interval and a proportion of 35%, a sample size of 302 patients was derived.

For the analytical component of the study, power calculations for sample size using EPI INFO 6.04 with a 5% level of significance and 80% power were used. The calculations produced sample sizes ranging from 290 to 299 for testing associations between the presence of pain and the clinical variables of disease stage, number of symptoms, use of ART, functional performance, and recent CD4+T-cell count, and the sociodemographic variables of age, gender, and marital status. Therefore, the sample size of 302 calculated for pain prevalence was additionally sufficient for the analytical component of the study.

Recruitment, Sampling and Ethics

Participants were consecutively recruited into the study on each clinic day if they met the following inclusion criteria: adult patients (at least 18 years old); a confirmed and documented HIV diagnosis; and with sufficient physical and cognitive ability to participate in interviews. Individuals were excluded if they could not comprehend any of the 3 commonly used languages of English, Luganda, and Runyakitara. In those instances where a patient did not meet the inclusion criteria, the next patient who met the inclusion criteria was invited into the study.

The information sheets, consent forms, and study tools (with the latter discussed below) used with study participants were forward- and back-translated from the source language (ie, English) to the 2 common local languages of Runyakitara and Luganda by indigenous clinical research teams. These teams were trained in instrument translation by an academic clinical psychologist and an academic researcher. Inconsistencies were resolved through discussion and consultation with the instruments' developers and linguistic experts.

Written informed consent was obtained from all participants, with the study reviewed and approved by the Mulago Hospital Ethics Review Committee and Mbarara University Faculty of Medicine Research Ethics Committee.

Where respondents were literate, questionnaires were completed individually, with trained health workers offering clarification where necessary. For study patients who could not read and write, questions were read out aloud and patients were requested to select the answer that best represented their position. After each interview, a site-based, trained senior medical professional crosschecked each questionnaire for completeness. Patient responses were not challenged but rather the process was intended to ensure data completeness, assuming that omissions were not a deliberate patient choice. To avoid re-enrollment, self-report by clients was enhanced by the recording of patients' individual clinic numbers and lists referred to each time a new client presented at the clinics.

Data Collection

Sociodemographic and Clinical Data

Data on sociodemographic characteristics (age, gender, marital status, and religion) were obtained by self-report. Data on disease and treatment (including time since HIV diagnosis, use of ART, CD4+T-cell count and

WHO clinical stage) were obtained from the most recent laboratory and clinician report in the subject's medical records. The WHO clinical staging system for HIV/AIDS was developed in 1990 and emphasizes the use of clinical parameters to guide clinical decision-making in the management of HIV/AIDS patients.[67] The system classifies HIV disease on the basis of clinical manifestations that can be recognized and treated by clinicians in diverse settings, including resource-constrained ones, and by clinicians with varying levels of HIV expertise and training.[68]

Additional information on the number of comorbid conditions (including general medical comorbidities, such as diabetes, hypertension, and dementia, as well as opportunistic infections, such as tuberculosis, cryptococcal meningitis, hepatitis B, and malignancies) was separately extracted from patients' medical files. Having an AIDS diagnosis was defined as having a CD4+ T-cell count below 200 cells/mm^3 or having had an AIDS-defining illness.[7] Additionally, 4 validated data collection tools were used: the Karnofsky Performance status score (KPS); the Brief Pain Inventory (BPI); the Memorial Symptom Assessment Scale (short form) (MSAS-SF); and the Medical Outcome Scale-HIV(MOS-HIV).

The Karnofsky Performance Status Score (KPS)

This is an observer-rated scale used to report a patient's level of physical functioning ability.[31] Patients are rated on a scale of 0 to 100, with 0 corresponding to no functioning ability (ie, death) and 100 corresponding to complete, independent functioning. The KPS scale is a validated tool that has been widely used in patients with terminal illnesses,[31,32,42] In this study, patients' functional performance was rated by health workers who have been trained in using the KPS to classify patients according to their functional impairment using the KPS definitions rating (%) criteria.[31]

Brief Pain Inventory (BPI)

The BPI is a self-report measure that includes valid scales of pain intensity and pain-related interference with various domains of functioning.[11,15] The instrument has been well validated in cancer populations,[14,15,54] has been validated in South Africa,[41] and has been used to characterize pain in HIV patients.[5]

Using a 7-day reference period, pain intensity "on average", "at its worst," "at its least," and "pain right now" are measured on separate 11-point (ie, 0–10) numerical scales. Two surveys that compared these numerical scores with ratings of functional interference concluded that a score of 1 to 4 corresponds to "mild pain," 5 to 6 "moderate pain," and 7 to 10 "severe pain."[11,12,54] Similar ratings are used to estimate the degree to which pain interferes with 7 aspects of functioning (ie, general activity, mood, walking ability, sleep, work, relations with others, and enjoyment of life).[12] These 7 scales can be summed to generate an overall index of functional interference due to pain.[5,14] Patients are also asked to estimate the degree to which their pain was relieved by pain intervention using a percent scale.[15] The BPI also collects information on patient perceptions about the potential causes of their pain.

Patients who did not report having pain in the previous 7 days answered the first 10 questions only. These questions capture information on sociodemographic data, time since diagnosis, whether the patient ever experienced pain due to HIV/AIDS, whether pain was 1 of the patient's symptoms at their first diagnosis, and whether the patient has had any surgery in the preceding month. Patients reporting pain in the 7 days prior to the survey were further interviewed on pain sites and pain intensity, medications received for pain, relief received from the medications, and description of the pain and its interference on different domains of the patient's function.

Memorial Symptom Assessment Scale-Short Form (MSAS-SF)

The MSAS-SF is a patient-rated symptom assessment tool commonly used in HIV-infected populations that records the presence and burden of 28 physical symptoms and 4 psychological symptoms in the 7 days prior to an assessment.[9,47] The MSAS-SF has been widely used in describing symptom experience in HIV/AIDS patients and in African settings.[63,66]

Each physical symptom experienced by the patient was scored for the level of distress it caused on a 5-point (ie, 0 to 4) Likert scale (ie, "not at all," "a little bit," "somewhat," "quite a bit," and "very much"). The burden of psychological symptoms was scored on a scale of 0 to 4 (corresponding to "not at all," "rarely," "occasionally," "frequently," and "almost constantly"). These scores are added and a mean taken to calculate the MSAS-SF subscales. The first subscale, the global distress index (GDI), is calculated on the basis of 10 items; namely, 6 physical symptoms and 4 psychological items.[9,46] Each physical symptom was scored according to the level of discomfort experienced. While psychological symptoms are scored based on their frequency of occurrence, subscale indices are computed from the mean burden ratings. The second subscale (MSAS-PHYS) consists of 12 physical symptoms.[9,47] The third subscale (MSAS-PSYCH) consists of 6 psychological symptoms. Where the physical symptom distress subscale was used in the analysis as a variable in relation to pain, the pain item was excluded to avoid multicolinearity.

The Medical Outcome Scale-HIV (MOS-HIV)

Developed in the USA, the MOS-HIV is the most widely used HIV-targeted questionnaire for QOL.[70] The tool has been adapted and validated in Uganda and found to be a valid and reliable QOL measure in HIV patients for all domains.[37] The 35 MOS-HIV items contribute to 8 multi-item subscales (ie, health perceptions, physical function, role function, cognitive function, pain, mental health, energy/fatigue, and health distress) and 2 single-item subscales (ie, social function and QOL).

Scoring of the MOS-HIV is achieved by summing and linear transforming the raw scores of the 35 individual

items into 10 dimension scores that range from 0 to 100, with a high score indicating better functioning. Summary scores for all domains were calculated by weighting each subscale score with standard coefficients, then aggregating the weighted scores across subscales, which were also scored out of 100.[70] Physical and mental health summary scores can also be calculated.[49] QOL is viewed as a comprehensive subjective evaluation of life as a whole.[10] In the conceptual model of QOL, the patient's perception of the impact of symptoms extends beyond the reporting of symptom severity into more abstract concepts like that included in the meaning of QOL (eg, health transition and cognitive functioning).[10] This model, however, limits the questioning of impact to the patient's impressions of the impact of specific symptoms or symptom clusters.[10] Against the latter background, it has further been noted that a conceptual connection between symptom reduction and changes in QOL has led to an argument that it may be useful to explore both symptoms and QOL as patient-reported outcomes.[10,18] The authors therefore chose to include both a symptom and QOL measure in assessing the effect of pain on patient-reported outcomes.

Data Management and Analysis

Data were double entered into a predesigned EpiData database with conditional checks for internal consistency. Two rounds of data entry were conducted by 2 different people, followed by a validation exercise. Identified discrepancies were corrected by the manual checking of questionnaires, with results revalidated until the 2 datasets were identical. Data were analyzed using STATA version 9.0 (StataCorp LP, College Station, TX).

Descriptive statistics were used to summarize the demographic and clinical characteristics of the sample. Frequency distributions were calculated for overall sample and pain intensity profiles. Prevalence of pain was obtained by calculating the percentage of respondents who reported having had pain in the last 7 days, as defined by the BPI. The outcome of pain intensity has been categorized into 3 groups: 0–3, "no pain/mild pain;" 4–6, "moderate pain;" and 7–10, "severe pain" using the worst pain scores.[54] Differences between the pain intensity profiles in the 3 groups of no pain/mild pain, moderate pain, and severe pain in demographic and clinical characteristics, as well as in symptom severity scores, were evaluated using the chi-square test (χ^2) for categorical variables and analysis of variance was used for continuous variables. A stringent *P* value cutoff point of .03 was used for statistical significance because of the multiple tests conducted.[59] The total number of symptoms experienced, global distress, physical distress, and psychological distress indices, with respect to the pain intensity profiles, were compared using the F-test.

To establish the functional correlates of pain intensity, correlation analysis was performed, with the continuous dependent variables of functional performance, age, number of symptoms, most recent CD4+ T-cell count, time since diagnosis, physical symptom distress, and psychological distress. A cutoff correlation coefficient of .5 was adopted to suggest a reasonable linear relationship between the independent variables and pain intensity.[40]

To assess the relationship between the pain-intensity profiles and continuous variables, single variable multinomial logistic regression analysis was performed. Only those independent variables with a *P* value of less than .2 in the univariate and bivariate analyses were entered into the multivariate multinomial logistic regression model.[1] Variables entered were; time since diagnosis, most recent CD4+T, WHO clinical staging, cell count, psychological symptom distress, number of symptoms, and number of other health comorbidities.

Multinomial logistic regression analysis was further used to assess the relationship between pain intensity and several sociodemographic and clinical variables. A cutoff *P*-value of .05 was adopted for statistical significance and the chi-square was used to assess the goodness of fit of the model and the pseudo R squared for the variance in the dependent variable explained by the independent variables.

Results

Sample Characteristics

A total of 302 adult ambulatory HIV/AIDS patients participated in the study (with 200 recruited from Mbarara and 102 from Mulago, figures proportionate to the number of patient populations served by each site). Table 1 shows the characteristics of the whole sample, which was largely female (64.2%). The female participants were younger than the males, with an average age of 35 years (interquartile range [IQR]: 30–40), compared to an average male patients age of 40 years (IQR: 33–47). The whole sample mean age was 37 years (IQR: 31–43). Two hundred and twenty four (74.2%) of the study participants were on ART at the time of the study. Of the 279 study participants with information on the most recent CD4+ T-cell count, 75 (26.9%) had counts below 200, 147 (52.7%) were between 201 and 499, and 57 (20.4%) had counts of 500+. The mean functional performance for the whole sample was 89.9 (SD = 14.6; range 40–100), indicating independent functional ability.

Pain Characteristics

A total of 143 participants (47%) indicated the presence of pain in the 7 days prior to the survey on the BPI. The most common pain sites were: chest (21.7%), back (20.3%), head (19.6%), abdomen (15.4%), and legs (7.7%). Of the 15 words used to describe the quality of pain, the terms sharp (60.6%), aching (54.2%), miserable (50.7%), exhausting (43.7%), and penetrating (43%) were most common. On the 0 to 10 numeric rating scale, the mean ratings for pain "on average," "at its least," and "at its worst" were 5.01 (SD = 1.72), 4.41 (SD = 1.72), and 7.23 (SD = 1.91), respectively. The highest pain interference was on general activity (6.57; SD = 2.39) followed by normal work (5.90; SD = 2.74) and walking ability (5.63; SD = 3.10). The 2 lowest scores for pain interference were relationship with others (3.20;

Table 1. Baseline Characteristics for the Total Samples and Differences in Characteristics Between the Pain Groups

Characteristic	Total N = 302	No Pain/Mild N = 167	Moderate N = 48	Severe N = 87	Statistical Test P-values Chi-Square for Categorical Variables and F Test for Continuous Variables
Gender		N (%)	N (%)	N (%)	
Female	194 (64.2)	112 (57.7)	29 (15.0)	53 (27.3)	1.303,
Male	108 (35.8)	55 (50.9)	19 (17.6)	34 (31.5)	$P = .521$
Religion					
Anglican	166 (55.0)	91 (54.8)	25 (15.1)	50 (30.1)	
Catholic	75 (24.8)	41 (54.7)	16 (21.3)	18 (24)	3.362,
Moslem	38 (12.6)	21 (55.3)	5 (13.2)	12 (31.6)	$P = .762$
Other	23 (7.6)	14 (60.9)	2 (8.7)	7 (30.4)	
Marital status					
Single	30 (9.9)	16 (53.3)	1 (3.33)	13 (43.3)	
Married	142 (47.0)	79 (55.6)	26 (18.3)	37 (26.1)	7.665,
Widowed	70 (23.2)	40 (57.1)	13 (18.6)	17 (24.3)	$P = .264$
Separated	60 (19.9)	32 (53.3)	8 (13.3)	20 (33.3)	
Education					
None	37 (12.3)	25 (67.6)	7 (18.9)	5 (13.5)	
Primary	117 (38.7)	62 (53.0)	17 (14.5)	38 (32.5)	7.202,
Secondary	100 (33.1)	50 (50.0)	18 (18)	32 (32)	$P = .303$
Diploma/degree	48 (15.9)	30 (62.5)	6 (12.5)	12 (25)	
Age					
18–35	133 (44.0)	76 (57.1)	19 (14.3)	38 (28.6)	.537,
36+	169 (56.0)	91 (53.9)	29 (17.2)	49 (29.0)	$P = .764$
WHO clinical stage					
1	16 (5.3)	9 (56.3)	2 (12.5)	5 (31.3)	
2	69 (22.9)	42 (60.9)	16 (23.2)	11 (15.9)	25.56,
3	164 (54.3)	98 (59.8)	24 (14.6)	42 (25.6)	$P \leq .001$*
4	53 (17.6)	18 (34.0)	6 (11.3)	29 (54.7)	
Use of ART					
Yes	224 (74.2)	122 (54.5)	31 (13.8)	71 (31.7)	4.925,
No	78 (25.8)	45 (57.7)	17 (21.8)	16 (20.5)	$P = .085$
Most recent CD4+ T cell count cells/mm^3†					
<200 cells per mm^3	75 (26.9)	35 (46.7)	5 (6.7)	35 (46.7)	
201–499 cells per mm^3	147 (52.7)	88 (59.9)	26 (17.7)	33 (22.5)	22.922,
500+ cells per mm^3	57 (20.4)	30 (52.6)	16 (28.1)	11 (19.3)	$P < .001$*
Time since HIV diagnosis in months (mean, SD)	52 (49.0)	54 (53)	38 (40)	55 (45)	2.40, $P = .092$
Number of symptoms (mean and SD)	12.49 (5.9)	9.79 (3.19)	12.44 (4.07)	17.71 (7.11)	78.75, $P < .0001$*
Functional performance (mean and SD)	89.90 (14.6)	97 (6)	92 (7)	75 (18)	115.27, $P < .0001$*
Mean number of comorbid health problems	1.3 (1.0)	.38 (.47)	.41 (.22)	1.7 (.75)	21.8, $P < .001$*
Global distress Index subscale	1.293 (.683)	1.062 (.43)	1.159 (.44)	1.812 (.89)	46.37, $P < .001$*
MSAS physical symptom distress subscale	.748 (.626)	.527 (.31)	.648 (.33)	1.23 (.893)	48.0, $P < .001$*
MSAS Psychological distress subscale	1.295 (.81)	1.007 (.48)	1.062 (.49)	1.973 (1.033)	59.76, $P < .001$*

*Statistically significant *P* values.
†23 missing values.

SD = 3.30) and sleep (4.13; SD = 3.89). On the BPI broad domain of pain interference scores, pain interference was highest on the activity domain (6.03; SD = 2.47) and lowest on the mood domain (4.61; SD = 2.82). The majority of respondents (62.9%; n = 190) also noted that pain was 1 of their symptoms at the time of their HIV diagnosis.

Approximately 14% attributed their pain to the effects of HIV-related therapies, 34% attributed it to HIV/AIDS, while 57% thought the pain was attributed to a medical condition unrelated to their primary disease. Those patients who gave the latter response most commonly mentioned the following as the cause of pain: meningitis, pulmonary tuberculosis, somatitis, cancer, lymphadenopathy, post-toxoplasmosis headache, malaria, and chronic pelvic inflammatory disease, the latter reported by females.

Of the 143 patients who reported pain in the last 7 days, 142 reported pain on the day of the survey, and of these, 53% reported mild pain, 20% moderate pain, and 27% severe pain. Fifty-three percent of those with pain on the BPI reported being on step 1 analgesics, 28% on step 2 analgesics, 16% on step 3 analgesics, and 3% not on any pain medication. Pain treatments or medications provided a mean relief of 68% (SD 21, range 6–100, IQR: 60–80%), with higher scores indicating

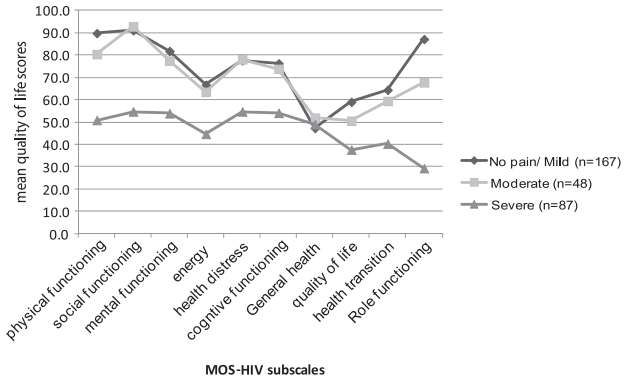

Figure 1. Comparing quality of life scores across no pain/mild pain, moderate pain, and severe pain groups.

better relief. Fifty-seven percent of patients in pain reported needing a stronger type of pain medication.

Differences in Demographic and Clinical Characteristics

As Table 1 shows, no differences were reported between the no/mild pain, moderate, and severe pain groups on any of the sociodemographic characteristics at the bivariate level of analysis. Patients in WHO clinical stage 4 were more likely to report pain (χ^2 = 13.02, P = .004). No differences were reported between the 3 pain groups (no pain/mild pain, moderate pain, and severe pain) on other clinical characteristics.

Differences in Symptom Prevalence and Distress Scores

The MSAS-SF scores revealed an average of 12.4 symptoms (SD = 5.616, range 4–30). The most prevalent symptoms were worry (94.4%), feeling sad (91.7%),) and nervousness (75.2%). On the MSAS-SF, patients reporting severe pain reported the highest scores on all MSAS-SF symptom distress subscales Table 1. Patients who reported severe pain also reported the highest mean number of symptoms (F = 78.75, P < .001), more comorbid health problems (F = 21.8, P < .001), and the lowest functional performance (F = 115.27, P < .0001).

Differences in QOL Scores

Fig 1 shows the differences in QOL scores for the 3 pain severity groups: "no pain/ mild," "moderate pain," and "severe pain." The 3 groups had quite similar scores on the general health domain but significantly different scores on the domains of physical and role function.

Factors Associated With Pain Intensity

Only variables associated with pain intensity at a statistical significance level of .2 were considered for further analysis; age, gender, highest level of education, and marital status were therefore excluded. As Table 2 shows, a unit increase in the number of symptoms was associated with a 30% increased relative risk of experiencing moderate pain relative to no pain, and associated with a 30% increased relative risk of experiencing severe pain relative to no/mild pain (P < .001) given that other variables in the model are constant. Increasing functional performance was associated with a 14% reduction in the relative risk of experiencing moderate pain

Table 2. Factors Associated With Pain Intensity

	Single Multinomial Regression Results		Multivariate Multinomial Regression Results	
Pain Outcome	RRR	P-value	RRR	P-value
Moderate pain				
Age	1.02	.310		
Gender				
Male	1.33	.394		
Female	1.00			
CD4+ T cell Count				
<=200	1.00		1.00	
201–499	2.07	.168	2.51	.121
500+	3.73	.021*	4.31	.024*
WHO stage				
1&2	1.00			
3	.69	.305	.51	.124
4	.94	.917	.60	.446
Use of ARVs				
No	1.00			
Yes	.67	.255		
MSAS global distress index	1.53	.205		
MSAS physical distress index	2.35	.042*	.44	.04*
MSAS psychological distress index	1.24	.501	.51	.153
Functional performance	.89	<.001*	.86	<.001*
Number of symptoms	1.19	<.001*	1.30	.001*
Number of other comorbid conditions	1.21	.003*	1.71	.002*
Severe pain				
Age	.99	.689		
Gender				
Female	1.00			
Male	1.31	.330		
CD4+ T cell Count				
<=200	1.00		1.00	
201–499	.38	.002*	1.44	.523
500+	.37	.018*	2.1	.259
WHO stage				
1&2	1.00		1.00	
3	1.37	.360	.84	.733
4	5.14	<.001*	.49	.357
Use of ARVs				
No	1.00			
Yes	1.64	.132		
MSAS global distress index	6.50	<.001*	2.45	.379
MSAS physical distress index	10.48	<.001*	.31	.003*
MSAS psychological distress index	5.85	<.001*	1.53	.369
Functional performance	.80	<.001*	.77	<.001*
Number of symptoms	1.38	<.001*	1.30	.003*
Number of other comorbid conditions	2.1	.029*	3.01	.001*

NOTE. No/mild pain is the reference category only; variables significant at .2 at bivariate were entered into the multivariate model.
*Significant P values.

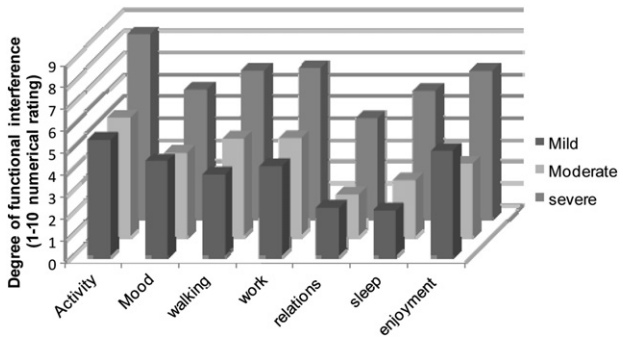

Figure 2. Relationship between pain intensity and domains of the pain-related functional interference (n = 143).

relative to no/mild pain, and a 23% reduction in the relative risk of experiencing severe pain relative to no/mild pain. The MSAS–SF physical subscale was associated with an increasing relative risk of experiencing moderate pain or severe pain relative to no/mild pain. CD4+ T cell count greater than 200 was associated a reduced relative risk of experiencing severe pain relative to no pain/mild pain and WHO clinical stage 4 was associated with an increased relative risk of experiencing severe pain relative to no pain/mild pain. With these variables in the final prediction equation, no other variables significantly improved the overall model fit. The chi square value of the final model was 207.6 with a P value < .001 and the model explained 37% of the variance in factors associated with pain intensity.

Functional Correlates of Pain Intensity

Pain intensity "on average" significantly correlated with functional performance (n = 143, r = −.659, P = <.001). There was also significant correlation between pain intensity on average and pain-related interference (n = 143, r = .624, P = < .001). Pain intensity was classified into "mild" (rating of 1–4), "moderate" (5–6), and "severe" (7–10) categories using BPI pain on worst pain ratings.[53] Fig 2 demonstrates the relationship between pain interference items on the BPI and pain intensity. Patients with "mild pain" reported average pain interference scores ranging from 2.12 to 5.37, and pain interfered most with activity (mean = 5.37, SD = 2.0). Patients with "moderate pain" reported slightly higher levels of interference across most functional domains as compared to the latter (range 1.95–5.48); even in this instance, pain interfered most with activity (mean 5.48, SD = 2.0). Patients with "severe pain" reported pain interference across all domains of functioning (range 4.56–8.41). For this subgroup, pain interfered most with general activity (mean 8.41, SD = 2.1), work (mean 6.89, SD = 2.8), walking (6.75, SD = 3.0), and enjoyment (6.75, SD = 3.1).

Discussion

We assessed pain prevalence, intensity, and their correlates in 2 HIV centers in Uganda. Our sample was similar to previous HIV/AIDS samples in the African settings in terms of its sociodemographic characteristics.[32,42,66]

A proportion (47%) experienced pain in the 7 days prior to the survey. This period of prevalence of pain, while not as high as other reports for people living with HIV in Southern Africa[27,43-45] (possibly due to prior use of untested tools, measurement among advanced populations, and use of long periods of time), is still higher than the 17% found in a sample of 839 HIV-negative adults attending an urban clinic for sexually transmitted diseases in Malawi,[48] the 33% reported in a community sample in a resource-poor area of Cape Town, South Africa, whose HIV status was unknown,[29] and the 24% reported in a Norwegian general population.[51]

This sample frequently experienced pain in the head, chest and abdomen, sites which have been consistently documented in HIV-infected patients.[2,25,43,65]

The study findings also indicate a low level of prescription of opioids. Of the 39 patients who reported severe pain on the day of the survey, only 13 (33%) were prescribed a strong opioid analgesic in line with the WHO pain ladder.[69] The reluctance by care providers to prescribe morphine for severe pain has been cited as a barrier to effective pain management in Africa, and the need to emphasise morphine supply and management skills remains important.[22] On the whole, patients expressed a degree of dissatisfaction with their pain treatment, and 57% expressed the need for a stronger type of pain medication. Those who were on pain medication reported an average pain relief of 68%, reinforcing the existence of pain undertreatment in this sample, as previously reported in similar populations.[12,13,35,36,39]

Pain in the immediate past has a substantial negative impact on a person's QOL; 47% of the sample were in pain during the 7 days before completing the BPI and had a notably poorer QOL on a range of dimensions compared with those who were not in pain, and impairment increased with increasing pain intensity. The physical and role function domains, as well as physical and self-care limitations, seemed most useful in differentiating the pain and pain-free groups. The QOL scores reported by patients with pain were comparable to summary scores reported by HIV-infected adults at the time of highly active antiretroviral therapy (HAART) initiation.[59] Mean summary scores reported by the "pain-free group" were comparable to those reported in HIV-infected adults on HAART after 12 months of follow-up, and comparable to those previously reported among HIV-infected asymptomatic populations.[49,58] The 3 pain groups reported almost similar scores in general health, suggesting an interesting cultural perspective that in Africa, despite pain, people's perceptions about their health are quite similar. However, the groups were significantly different on role and physical function domains, demonstrating that even a little pain reduces work ability enormously. Either pain in the immediate past creates a substantial erosion of QOL across a wide range of indicators or else this decrement enhances the pain and discomfort they feel.[56] Our findings thus provide supporting evidence in the primary care setting that demonstrate how damaging treatment delays can be to the physical and psychological well-being of pain sufferers.[62,64]

The authors found WHO clinical stage 4 to be associated with an increased relative risk of experiencing severe pain and higher CD4+T-cell count was associated with reduced relative risk of experiencing severe pain. Our findings suggest a relationship between pain intensity and several indices of disease progression and thus an association between pain and disease progression as suggested in literature.[5,43,57] The authors found no association between the use of ART and pain. There has however, been conflicting evidence on the relationship between the use of ART and pain. Jelsma et al[30] found ART to be associated with reduced pain/discomfort, and Harding et al[21] found ART to be associated with a higher symptom burden, including pain, while Breitbart et al[5] found the absence of ART to be associated with the presence of pain. As these studies were conducted in economically developed countries, there is a need to explore this issue further among African populations.

Consistent with our hypothesis, after controlling for relevant sociodemographic, psychological, and clinical factors, there was no association between gender and pain intensity. The present findings are in agreement with several literature in HIV-positive populations.[8,17,36] However, the current findings are at odds with the positive finding for sex-based differences in pain in HIV positive sample.[3,5] This divergence may be due to variations in cultural settings of the sample compositions, and previous studies did not control for psychological symptom distress in the final models; yet evidence suggests a strong relationship between psychological distress and pain among HIV positive persons.[50,60] The association between pain intensity and psychological symptom distress was also evident in the current findings and psychological symptoms were indeed the most prevalent.[26] Further work is needed to identify explanatory gender, disease, and cultural factors.[29]

Studies on the effects of pain in African patients have yielded conflicting results.[18,21,38] Our findings show that HIV/AIDS patients of African ancestry respond in a similar fashion to the interference caused by their pain, as pain evidently affected several domains of patient well-being, including activity, enjoyment, mood, walking, relations, and work, and the interference increased with increasing pain intensity,[62] demonstrating a positive relationship between ratings of pain severity and ratings of pain's interference.[6,54] The latter observation has been found to be robust across 4 different countries and cultures[54] and our findings further demonstrate this robustness.

A number of study limitations are worth noting. The cross-sectional nature of the study precludes the ability to establish causal relationships among the associated symptoms and the cause of pain among this study population. In order to participate, patients were required to be well enough to engage in self-reported data collection, which may bias our data against those with significant disease progression and those nearing the end of life who may have a higher prevalence and burden of symptoms. There might be a response bias according to whether they self completed or researcher completed. This study did not explore the pain aetiologies, and future studies should consider exploring the aetiologies of pain in HIV/AIDS patients.

A number of conclusions can be drawn for the findings. First, pain is highly prevalent among well-functioning ambulatory HIV/AIDS patients, very common at diagnosis and throughout the disease trajectory. Pain has a debilitating effect on QOL. There was a significant level of unmet need for pain relief, which further highlights the need for strengthening quality pain management in similar settings. The successful performance of this survey suggests that pain assessment is feasible in outpatient settings and should be promoted. The relationship between pain intensity and pain interference in function seems robust and was further confirmed in this study. Moreover, the lack of association between pain presence or intensity and use of ART underscores the need for ongoing pain assessment.

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