



Musculoskeletal symptoms and non-prescribed treatments are common in an urban African population of people living with HIV

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Abstract

There are no data from West Africa reporting musculoskeletal (MSK) disease in people living with HIV (PLWH). Our primary outcome was to measure the prevalence of MSK symptoms in PLWH in urban West Africa. Our secondary outcomes were to describe the disability, impact on work and treatment use associated with the presence of MSK pain. We conducted an e-questionnaire-based point prevalence study of musculoskeletal symptoms, associated disability and treatment in 292 PLWH attending routine follow-up in Lagos, Nigeria. Seventy-three (25%) patients reported MSK pain; 28 (38%) reported chronic symptoms (> 3 months). HIV suppression rates were high in this population ($n=240$, 82%) and comparable between individuals with and without chronic pain. MSK pain was associated with female gender and higher body mass index (BMI). Mechanical pain was the most common pain syndrome identified ($n=34$, 47%). Lumbar spine and knee were the most common sites. Chronic pain was associated with increased disability compared with the presence of any MSK pain. High rates of treatment-seeking behaviour were seen in those individuals reporting MSK pain ($n=62$, 85%). The majority of these individuals sought traditional treatments ($n=48$, 66%). Chronic MSK pain and non-prescribed treatments are common in PLWH established on ART in urban West Africa. Studies are required to measure the long-term impact of these symptoms and medicines on retention in HIV care and ART adherence, besides other long-term health outcomes.

Keywords HIV · Musculoskeletal disease · Africa · Pain

Introduction

More than 36 million people live with HIV worldwide: 70% of this population live in sub-Saharan Africa (SSA) [1]. Life expectancy of people living with HIV (PLWH) is increasing as early highly active anti-retroviral therapy (HAART) coverage advances [2]. In this ageing population non-communicable diseases (NCDs) have emerged as the leading causes

of morbidity and mortality [3]. Globally musculoskeletal (MSK) disease is the second leading cause of years lived with disability [4].

Arthralgia is a common symptom reported in questionnaire-based studies of MSK disease in PLWH in Europe and America, but these data pre-date modern ART treatment programmes [5]. There are also data that associate HIV infection with increased incidence of diverse rheumatic conditions such as reactive arthritis, psoriatic arthritis and osteoporosis [6]. However, high-quality studies describing the prevalence of MSK disease in PLWH are absent and most data originate from single-centre retrospective studies in settings of low HIV prevalence [7]. Contemporary data from a single clinic in East Africa suggest that MSK symptoms are common in PLWH, however ART uptake was very low in this cohort [8]. Besides the virus itself and other risk factors in this setting, key ART agents, such as tenofovir and protease inhibitor class drugs, are associated with increased risk of symptomatic osteoporosis [9].

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The primary aim of our study was to describe the prevalence of MSK symptoms in HIV-infected individuals in urban West Africa. The study also aimed to describe disability associated with MSK pain, HIV risk factors associated with MSK pain and treatment-seeking behaviours in individuals with MSK symptoms. Although Central and West Africa account for nearly 20% of the global population of PLWH, there are no published data regarding MSK disease from this region at all [1]. Our study is the first to describe the impact of MSK symptoms on the lives of PLWH in SSA and what treatments are used in this setting.

Methods

Study population

This cross-sectional study was conducted at the HIV outpatient clinic of the Nigerian Institute of Medical Research (NIMR) in Lagos, Nigeria from April to August 2017. Eligibility criteria were: documented HIV-1 infection; age 18 years and above; not currently receiving treatment for tuberculosis (TB); willingness to provide informed consent. The centre is one of the 25 sentinel centres that commenced HIV treatment in Nigeria in 2002. The centre has enrolled over 24,000 PLWH in southern Nigeria. Enrolled individuals have diverse and representative tribal and socio-economic backgrounds for the region; approximately 91.1% have at least secondary school education [10]. PLWH managed at NIMR attend routine bi-annual outpatient clinic follow-up. Approximately 300 adults present for outpatient clinic follow-up per week. Since June 2016 NIMR have initiated ART for all patients diagnosed with HIV infection consistent with World Health Organisation (WHO) guidelines [11]. In Nigeria approximately one-third of PLWH have suppressed HIV infection on ART [12].

Routine follow-up encompasses healthcare worker (HCW) delivered health questionnaire, drug history, clinical observations (height, weight, body mass index (kg/m^2), BP), and blood tests (viral load (VL) testing, CD4+ T cell count, renal biochemistry). Abnormal renal function was defined by $\text{GFR} < 60 \text{ ml}/\text{min}/1.73 \text{ m}^2$. Occupation and skill level were defined by the International Standard Classification of Occupation [13].

Systematic random sampling was used to select the study population: on each clinic day the first ten attending patients were numbered and one patient selected by balloting. This individual became the first potential study patient of the day and every fifth patient on the clinic list became the subsequent potential study participants. A tablet-based structured e-questionnaire was delivered by local medical officers at the time of clinic attendance who would not be directly involved in the care of individual participants, but who work in the

facility and are experienced at delivering similar tools in this setting. Five individuals approached to participate were not included in the study owing to lack of valid consent or missing data.

HIV outcomes

HIV clinical and treatment history, and laboratory data are collected routinely in the NIMR database. These data were linked to the questionnaire data by hospital number. We recorded the immune status [most recent CD4+ T cell count (cells/mm^3)] and HIV control [HIV-1 VL (copies/ml)] of each patient which were all within the 12 months preceding study inclusion. Second line ART is defined by the use of any protease inhibitors (PIs) in this setting [11]. Suppressed VL was defined as $< 200 \text{ copies}/\text{ml}$.

MSK assessment

Collected data included presence of joint, soft tissue or bone pain (defined as MSK pain), joint stiffness, and joint swelling. Duration of symptoms and diurnal patterns (morning, rest of day, evening, constant) were collected. Symptoms in the week preceding the study defined point prevalence. Two groups were defined by the presence (group 1) or absence (group 2) of MSK pain. Chronic symptoms were defined as duration exceeding 3 months. Pain location was assessed using a modified mannequin adapted from the Standardised Nordic Questionnaire [14]. Pain severity was assessed using the four grades of the Graded Chronic Pain Scale in conjunction with a visual analogue scale (VAS) [15]. The 12-item WHO Disability Assessment Schedule 2.0 (12-item WHO-DAS2) was used to assess disability [16]. Structured questions were prepared with local rheumatology physicians for setting-specific treatment interventions. ‘Mixing’ describes purchase of small bags of mixed non-prescribed unlabelled medicines from street hawkers. Self-reported history of significant trauma, rheumatoid arthritis (RA) and psoriasis were collected. Significant trauma was defined as seeking medical or surgical consultation. Local rheumatology physicians suggest that we limit self-reported diagnoses to RA and psoriasis as they are the most common diagnoses seen in the two government rheumatology clinics in Lagos [17].

We pre-defined three MSK pain syndromes. We considered pain to be inflammatory pain if the following three criteria were satisfied: pain during the night or early morning, pain in > 1 joint, morning stiffness ≥ 60 min. Mechanical pain was defined by the presence of the following three criteria: association of pain with use of joint, improvement at rest, morning stiffness < 60 min. Arthralgia was defined as joint pain in the absence of stiffness or swelling and no association with use of joint.

Those individuals identified with symptoms thought to warrant specialist review by the data collector were discussed with OE and referred to the local government rheumatology clinic if indicated.

Data collection and statistical analysis

The Open Data Kit software (<http://www.opendatakit.org/>) was used to build the e-questionnaire, to collect and collate data online and then export these data as CSV files for analysis [18]. In collaboration with Nigerian rheumatology colleagues, pretesting of the questionnaire was conducted by six local medical officers at NIMR in 12 consented clinic patients.

The calculated sample size was 246 aimed to detect a MSK pain prevalence of 20% based on *Z* value 1.96 and *d* value 0.05. Assumed prevalence (*P*) was based at the time of study design on the only available COPCORD (Community Oriented Program for the Control of Rheumatic Diseases) studies in Africa [19].

Statistical analysis was performed using STATA 14.0 (StataCorp LP, TX, USA). Data were analysed using Chi square test for categorical variables (presented as frequencies and percentages) and using Mann–Whitney test for continuous variables (presented as the median and interquartile range, IQR). A *p* value of <0.05 was considered significant.

Results

Study population

292 individuals were recruited to the study during routine follow-up. The age of the study population ranged between 18 and 64 years (median 41 years). 65% were female. The median BMI of the study population was 25 (IQR 22–28). 79% of the study population (*n* = 230) were employed in skill level 1 or 2 occupations; 13% were unemployed (*n* = 39) and 2% retired (*n* = 6).

HIV outcomes

Ninety-nine percent of group 1 (pain present group) were prescribed ART at the time of the study and 81% had an undetectable HIV VL. There was no significant difference between individuals with or without pain or chronic pain in terms of ART adherence, duration of ART, unsuppressed HIV, median CD4+ T cell count and prior treatment for TB (Table 1). Tenofovir- and protease inhibitor-containing ART regimens were also equally distributed between the two groups.

MSK symptoms

Out of 292 individuals recruited for the study, the point prevalence of MSK pain was 25% (*n* = 73). The presence of MSK pain was associated with female gender (*n* = 56, 77%; *p* = 0.02) but not age (*p* = 0.61). The group with MSK pain (group 1) had a significantly higher median BMI compared with the group without MSK pain (group 2, pain absent group; *p* = 0.01). Abnormal renal function and concomitant diabetes were not associated with MSK pain.

According to pre-determined criteria, four individuals had inflammatory pain, 34 (47%) mechanical pain and 14 (19%) arthralgia. Location of MSK pain is summarised in Table 2. 38% of group 1 reported chronic MSK pain. History of significant trauma in the preceding 12 months was comparable between the two groups (10% and 9% respectively; *p* = 0.91).

Three individuals reported a pre-existing diagnosis of rheumatoid arthritis and no individuals reported pre-existing psoriasis diagnosis: none of these patients met the study criteria for inflammatory pain.

Ninety-six percent (*n* = 70) of MSK pain reported was grade 1 or 2 using VAS. Three patients (4%) reported grade 3 pain: two of these individuals had arthralgia, one inflammatory pain. The median total disability score for individuals reporting any duration MSK pain was 2% (IQR 0–6). The median total disability score was significantly higher for individuals reporting chronic MSK pain [8% (IQR 0–11.5); *p* < 0.001]. Three individuals with chronic pain (3/28, 11%) experienced moderate or severe disability: one individual had mechanical pain and two had arthralgia. Six individuals with chronic pain (6/28, 21%) reported stopping work due to MSK pain.

Management of MSK pain

Eighty-five percent (62/73) of group 1 individuals sought treatment for their MSK pain. Sixty-six percent (41/62) of treatment-seeking individuals sought non-prescribed traditional treatments alone; 15% (9/62) sought both traditional and conventional medicines. Two individuals consulted a specialist rheumatologist; one individual with inflammatory pain was referred to rheumatology services during the study. In terms of non-prescribed conventional medicines: 21% (61/292) of all individuals reported using medicines prescribed for other people and 23% (67/292) reported ‘mixing’ unlabelled medicines.

Discussion

In this study in urban West Africa, one quarter of HIV-infected individuals attending routine clinical follow-up reported MSK pain and nearly 40% of this pain was chronic.

Table 1 Patient characteristics of groups with (group 1) and without (group 2) musculoskeletal pain (group 1)

	Group 1 (MSK pain)	Group 2 (no MSK pain)	<i>p</i> value
Total, <i>n</i> (%)	73 (25)	219 (75)	
Chronic pain	28 (38)		
Age, years	41 (38–48)	42 (37–49)	0.61
Female, <i>n</i> (%)	56 (77)	134 (61)	0.02
BMI	27.5 (22–30)	24.8 (21–28)	0.01
Employed, <i>n</i> (%)	62 (85)	185 (84)	0.86
Prescribed ART, <i>n</i> (%)	72 (99)	211 (96)	0.33
Tenofovir-containing regimen, <i>n</i> (%)	39 (53)	118 (54)	
Duration ART (months)	77 (52–122)	91 (54–118)	0.45
CD4+ T cell count (cells/mm ³)	525 (363–711)	488 (349–667)	0.35
Detectable HIV VL, <i>n</i> (%)	14 (19)	39 (18)	0.79
Previously treated for TB, <i>n</i> (%)	5 (7)	23 (11)	0.49
History of significant trauma	7 (10)	20 (9)	0.91
Use of mixing, <i>n</i> (%)	13 (18)	53 (24)	0.26
Use of non-prescribed medicines, <i>n</i> (%)	49 (67)	152 (69)	0.72
Use of medicines prescribed for other individuals, <i>n</i> (%)	13 (18)	49 (22)	0.41
Sought treatment for MSK pain, <i>n</i> (%)	62 (85)		
Herbalist	29		
Traditional healer	16		
Blood-letter	15		
Doctor	12		
Pharmacy retailer	8		
Surgeon	7		
Spiritual healer	3		
Rheumatologist	2		

Values are given as the median (interquartile range) unless otherwise stated. Statistically significant *p* values shown in bold

MSK musculoskeletal; chronic pain defined as duration > 3 months, VL viral load

Table 2 Overall point prevalence and location of musculoskeletal pain organised by total number of anatomical sites and by pre-defined pain syndrome groups

	Total	Mechanical	Inflammatory	Arthralgia	Non-specific
Overall point prevalence, <i>n</i> (%)	73	34 (47)	4 (5)	14 (19)	21 (29)
Location, <i>n</i> (%) where <i>n</i> > 10)					
Spine					
Neck	3	1	0	2	0
Thoracic	4	1	1	1	1
Lumbar	23 (32)	12 (35)	1	1	9
Upper limbs					
Shoulders	8	4	0	4	0
Elbows	5	2	1	1	1
Wrists	4	3	0	1	0
Fingers	2	1	0	0	1
Lower limbs					
Hips	6	5	0	1	0
Knees	22 (30)	9	2	3	8
Ankles/feet	13 (18)	8	0	3	2

Overall this suggests that nearly 10% of all PLWH in this population suffer chronic MSK pain. Although reported pain severity was mostly mild, disability was significantly increased in those individuals reporting chronic MSK pain and 21% were forced to stop work owing to their MSK pain. A major strength of the study is the fact that it represents the first data ever from West Africa to describe the burden of MSK symptoms in HIV-infected individuals. Further these are the first data from the entire continent of Africa since the HIV test and treat era looking at MSK symptom prevalence. A further strength of the study was the high rates of ART uptake and viral suppression in the study population. This makes the data sentinel for the future of HIV care in Africa as ART rollout continues and may help inform future relevant studies. The findings are similar to an East African single-centre study which found 27% prevalence of rheumatic manifestations in a cohort of HIV-infected individuals with much lower rates of HIV treatment, 21% compared with 81% in our study [8]. The study is also the first to address the disquieting scarcity of data regarding MSK disease and associated treatments across Africa. More than two-thirds of the population use non-prescribed treatments which is alarmingly high and under-reported in the available literature.

This study suggests that rates of MSK symptoms remain high despite effective HIV treatment. Importantly presence of MSK pain did not appear to impact ART adherence or retention in care. Across SSA, where HIV is most prevalent, travel distance from rural settings to urban treatment centres is a major barrier to ART adherence [20]. Individuals may collect ART on behalf of family members if they are too unwell to attend pharmacy. However, this is also associated with lower ART adherence and poor clinic attendance itself predicts poor outcomes [20]. This study was not powered to measure the impact of MSK disease on long-term ART adherence and outcomes. Long-term longitudinal studies are required to assess whether MSK symptoms and disease significantly contribute to poor clinic attendance and HIV outcomes across SSA. The study also identified high rates of medicine-seeking behaviour in individuals with MSK pain, consistent with other regional studies in non-HIV infected individuals [21]. In this setting, the potentially deleterious drug interactions with ART of both traditional and conventional medicines, such as corticosteroid, also require further study.

As a single centre study, these data are not representative of all PLWH in low and middle income countries (LMICs) where rates of HIV diagnosis, ART uptake and HIV suppression may be lower. However, since 2016 WHO have advocated ART initiation for all individuals diagnosed with HIV rather than treatment strategies guided by immune status (test and treat) [22]. Consistent with this policy, these data are representative of an

urban African population of PLWH with high rates of ART adherence and viral suppression which is the planned future for the continent. As ART coverage advances across SSA so does life expectancy but also incidence of NCDs. It is essential at this time to consider the implications of NCDs in these countries where specialist knowledge is significantly lacking in order to plan future health care policy and provision [23]. Further study is urgently required to better characterise the burden of all NCDs and impact on long-term HIV care outcomes [18]. The questionnaire did not aim to directly capture all possible infectious and non-infectious co-morbidities that might be associated with MSK symptoms in this setting, such as malignancy, and the prevalence of these factors may be significantly different between our two patient groups, with and without pain.

As a questionnaire-based study there is a risk of responder bias. However, the questionnaires were delivered by medical officers not directly connected to the care of the individual study participants which should reduce the effect of this problem. It is likely that this study also underestimates the burden and severity of MSK disease in PLWH in West Africa. The most disabled individuals may have been excluded from our study by being unable to attend clinic owing to limited mobility. As it was not possible to include clinical assessment by a specialist rheumatologist, this study was also not designed to capture specific diagnoses such as fibromyalgia, the prevalence of specific diagnoses also necessitates rigorous study.

High-quality epidemiology of MSK and autoimmune disease is urgently needed for both HIV-infected and HIV-uninfected populations across sub-Saharan Africa. The tools used to capture MSK data lag behind other fields [18]. This study successfully used an interactive open access e-questionnaire software which can operate on any Android smartphone and could enhance the study of rheumatology epidemiology in LMICs. This study points to a significant burden of rheumatic morbidity in PLWH in West Africa which needs high-quality longitudinal study in comparison with an HIV-uninfected cohort to delineate the natural history of rheumatic disease in this population, potential interaction with HIV and its treatment, and its impact on socioeconomic productivity in SSA.

In conclusion, this study suggests that MSK symptoms and associated disability are common in PLWH in urban west Africa despite high rates of successful ART in the test and treat era. Non-prescribed conventional and traditional treatments are commonly used by PLWH experiencing MSK pain. Further study is required to understand the implications of this morbidity and informal therapy on HIV outcomes in Africa.

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this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

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Compliance with ethical standards

Conflict of interest Doug Fink declares that he has no conflict of interest. David Oladele declares that he has no conflict of interest. Oseme Etomi declares that she has no conflict of interest. Agatha Wapmuk declares that she has no conflict of interest. Tomi Musari-Martins declares that she has no conflict of interest. Endurance Agahowa declares that she has no conflict of interest. Sabdat Ekama declares that she has no conflict of interest. Adaobi Okechukwu declares that she has no conflict of interest. Christian Mallen declares that he has no conflict of interest. Oliver Ezechi declares that he has no conflict of interest. Babtunde Salako declares that he has no conflict of interest.

Informed consent Informed consent was obtained from all individual participants included in the study.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Scientific Review Committees of both NIMR and UCL (10153/001; 13/01/2017). This article does not contain any studies with animals performed by any of the authors.

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