Prevalence of fibromyalgia in ambulatory HIV positive patients with musculoskeletal pain at Comprehensive Care Clinic, Kenyatta National Hospital,

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Abstract

Background: Fibromyalgia is a rheumatic condition that is characterized by chronic widespread musculoskeletal pain with painful pressure points. There are other symptoms that are associated with this condition and they include fatigue, sleep disturbance and depression. The cause of this condition is unknown however chronic viral infections eg HIV have been associated with fibromyalgia.
Objective: This study aimed to determine the prevalence of fibromyalgia in HIV positive patients.
Design: This was a cross-sectional descriptive study.
Setting: The study was carried out at the Comprehensive Care Centre, Kenyatta National Hospital**.**
Methods: The patients attending the clinic between the month of February 2013 and April 2013 were assessed for chronic musculoskeletal pain and subsequently fibromyalgia using the American College of Rheumatology criteria**.** Those found to have fibromyalgia were given the FIQR and those without were given the SIQR for comparison purposes. Clinical details eg WHO clinical stage, CD4 counts and HAART regimen for those on HAART were also documented.
Results: A total of 380 patients were evaluated. The prevalence of fibromyalgia in HIV positive patients at the Comprehensive Care Centre, Kenyatta National Hospital was 68 (17.9%). The mean age of these patients was 42.2 years with a median of 40.5 years.There was a female preponderance of 60 (88.2%). Fibromyalgia was independently associated with female gender, OR=2.75, unemployment status, OR=5.68 and retired status, OR=3.01. A majority of the patients were in WHO clinical stage 3 and the mean CD4 count was 276.2. There was however no association between fibromyalgia and WHO clinical stage, CD4 count and use of HAART or the specific HAART regimens. The mean FIQR was 50.1 which was significantly higher than the mean SIQR score of 12.4 in those without fibromyalgia.
Conclusion: Fibromyalgia is a prevalent rheumatologic condition among HIV positive patients with chronic musculoskeletal pain. It is also associated with a high FIQR score.

Introduction

Fibromyalgia syndrome is an increasingly recognized disorder characterized by chronic, widespread musculoskeletal pain, stiffness, fatigue and sleep disturbance. Physical examination elicits increased tenderness at muscle and tendon insertion sites, known as tender points [1].

The prevalence is related to both age and sex. It is a common condition occurring in the population and mostly seen in women. Older individuals tend to get it more compared to younger people. A study done in Wichita, Kansas[2] found the prevalence of fibromyalgia in the general population to be 2%. They found that the prevalence increases with age from 40 years onwards and it was more common in females.

Locally there is paucity of data on its prevalence; however a study done in 2011 by Dokwe *et al*[3], in Kenyatta National Hospital estimated it to be at about 11% in patients with chronic musculoskeletal pain attending the medical outpatient and rheumatology clinics. The overall prevalence was found to be 1%.

Fibromyalgia has been classified as a neurosensory disorder where central sensitization and abnormal central nociceptive processing have been found in these patients. The overall effect is that the patients have a lower threshold of stimulation of neurons that receive pain[4].

The cause of this condition is unknown. However, certain infectious agents for example chronic viral infections have been linked with fibromyalgia. This connection has been documented with regard to agents like Hepatitis C[5], Lyme disease[6], and HIV[7]. It is suggested that these infectious agents act as triggers for fibromyalgia [8].

In a study done by Simms *et al*[7] in a hospital in Boston City, out of 140 HIV positive patients investigated for rheumatologic conditions, 15 of them had probable or definite fibromyalgia; a prevalence of 41% in those with musculoskeletal pain, and overall prevalence of 11%. Fibromyalgia was associated with a longer duration of the HIV infection. There were more females compared to male and the mean age of the patients was 37 years . Patients who were on zidovudine based therapy did not have an increased frequency of fibromyalgia. This was also noted in another study done by Buskila *et al*[9] where they did not find an association between fibromyalgia and use of AZT.

The diagnosis of fibromyalgia is based on the 1990 American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia; and includes:

(i) The presence of widespread pain lasting 3 months or more

(ii) The presence of more than 11 out of 18 possible tender points[10]

Other symptoms associated with fibromyalgia can be assessed using the FIQR whose three domains asses for symptoms, functionality and overall impact of the condition. The SIQR can be used to compare patients who don't have fibromyalgia as it has similar questions as that of the FIQR[11].

Serge Perrot[12] and his colleagues used several investigative tools to assess the burden of this disease. These included the Fibromyalgia Impact Questionnaire (FIQ), EuroQol, the Medical Outcome Study (MOS) Sleep Scale, the Brief Pain Inventory- Short Form (BPI- sf) and the Hospital Anxiety and Depression Scale (HADS). It was demonstrated that fibromyalgia patients incurred costs mainly on physician office visits and prescription medication. There was gross poor health related quality of life in these patients due to the attendant pain, poor functionality, sleep disturbance, anxiety and depression.

Materials and Methods

Subjects: Participants in this study were a consecutive sample population of HIV positive patients with chronic musculoskeletal pain at Kenyatta National Hospital (KNH) Comprehensive Care Clinic(CCC). A total of 2644 patients were assessed between the months of February 2013 and April 2013. Three hundred and ninety eight had chronic musculoskeletal pain among which 5 were excluded due to being below 18 years of age, 2 were in CCC for Post Exposure Prophylaxis hence HIV negative, 4 had neurocognitive impairment and 7 did not give consent. This left us with 380 patients for enrolement into the study.

We obtained wtitten consent from those who we recruited. Approval to conduct the study was undertaken from KNH/UoN-Ethics and Research Committee.

Data collection: Patients attending CCC during the study period were assessed for chronic musculoskeletal pain. This involved interviewing them on the presence of current pain involving any of the parts of the musculoskeletal system which included bones, joints, muscles and tendons. Those who had chronic muscloskeletal pain and fulfilled the rest of the inclusion criteria were enrolled in the study (380 patients). Determination of the HIV status was based on documentation from the file. An interviewer-administered study proforma was used to obtain demographic and clinical data. Clinical data entailed documentation of the current WHO clinical stage, recent CD4 count (within 3 months) and HAART status and regimen were derived from the file.

The ACR criteria was used to establish cases of chronic widespread pain and fibromyalgia. A targeted physical examination was done to establish the number of tender points. A total of 18 specified points were examined for tenderness by digital palpation whereby a force of 4 Kilograms (that which causes blanching of examiner's finger) was applied.

Patients who satisfied the ACR criteria of chronic widespread pain and eleven or more tender points were diagnosed to have fibromyalgia. Thereafter the FIQR was used to assess the frequency and severity of the fibromyalgia related symptoms. Those who did not fit the criteria for fibromyalgia were given the SIQR to assess their overall functionality and symptoms. For those who did not have a recent CD4 count (done within the previous 3 months), blood was drawn at the end of questionnaire administration for this purpose.

CD4 count assessment: Blood was drawn from the antecubital fossa via aseptic means; 3 milliliters was adequate for CD4 count. The blood was put in an EDTA bottle then taken to the laboratory within CCC where it was processed. Since this was done immediately, it did not require any special storage or transport. Determination of CD4 count was done using an automated BD FACSCalibur® machine. Results were available the following day and were also availed in the patients' file.

Statistical analyses: Data was entered and managed in Microsoft Access database. Data cleaning was done and the Access database was exported to SPSS version 17.0 for statistical analysis.

Prevalence was calculated as the number of patients with fibromyalgia divided by the total number of patients with chronic musculoskeletal pain and expressed as a percentage with 95% confidence interval.

Continuous data (age and CD4 count) was summarized into means and standard deviation while categorical data (gender, marital status, occupation, WHO stage and HAART status) was presented as proportions. CD4 counts were also analysed into categories. Comparison between those who have fibromyalgia and those without fibromyalgia was done with Student's T test for continuous data and Chi square test for categorical data. Fibromyalgia-related symptoms were analyzed and presented as mean scores for each patient and then compared with the mean scores of those without fibromyalgia using Student's t test.

Fibromyalgia was correlated with WHO clinical stage and the use of HAART using Chi square test and odds ratios (ORs) calculated to show the estimated risk ratios. Median CD4 count between patients with fibromyalgia

and those without the condition was compared using Mann Whitney U test. For all the variables associated with fibromyalgia, logistic regression analysis was done to control confounding factors and determine independent predictors of fibromyalgia in HIV patients. All the statistical tests were performed at 5% level of significance (95% confidence interval).

RESULTS

A total of 2644 HIV positive patients attending CCC were assessed for musculoskeletal pain between the months of February 2013 and April 2013. This was done by interviewing the patients on the presence of pain in the bones, joints and muscles. Out of these, 1902 did not have any musculoskeletal pain while 344 had pain that had been present for less than three months. Three hundred and ninety eight patients had chronic musculoskeletal pain though 18 were excluded because they did not meet the rest of the inclusion criteria (4 had neurocognitive impairment, 5 were below the age of 18 years, 7 declined to give consent while 2 were HIV negative and they had come to CCC for post exposure prophylaxis). We enrolled 380 patients in the study. Out of the 380, 68 patients had fibromyalgia giving a prevalence of 17.9% (95% CI, 14.2 - 22.1). The mean age of the patients was 41.1 years (SD = 9.9) with a range from 18 to 75 years. Most of the patients (70%) were aged between 30-49 years. Majority of the patients in the study, 282 (74.2%), were female giving a male-to-female ratio of 1: 2.9. Fifty-five percent of the patients were married and 23.4% were single (Table 1).

Thirty one patients (45.6%) were aged between 40-49 years. The mean age of these patients was 42.2 years. Sixty patients (88.2%) were of the females. There was a statistically significant association between fibromyalgia and female gender (p = 0.004). The odds of fibromyalgia was three-fold greater (OR = 3.0, 95% CI 1.4-6.6) among the female. Married patients, 37 accounted for 54.4% of all fibromyalgia cases. None of the marital status was statistically significantly associated with fibromyalgia (all p values > 0.05). There was a statistically significant association between patient occupation and fibromyalgia. The odds of fibromyalgia were significantly higher among unemployed, OR = 5.4 (95%CI 1.1-25) and retired patients, OR= 3.4 (95% CI 2.0-6.0) (Table 2).

Table 1: Demographic characteristics of the patients (n=380)

Demographic characteristics	Frequency n (%)	95%CI
Mean age in years (SD)	41.1 (9.9)	
Sex		
Female	282(74.2)	(69.8-78.6)
Male	98(25.8)	(21.4-30.2)
Marital status, n (%)		
Single	89(23.4)	(19.1-27.7)
Married	212(55.8)	(50.8-60.8)
Separated/ divorced	21(5.5)	(3.2-7.8)
Widowed	58(15.5)	(11.6-18.9)
Daily activities, n (%)		
Manual	188(49.5)	(44.4-54.5)
Not manual	192(50.5)	(45.5-55.6)
Occupation, n (%)		
Employed	277(72.9)	(68.4-77.4)
Unemployed	96(25.2)	(20.9-29.7)
Retired	7(1.8)	(0.5-3.2)

Table 2: Demographic characteristics of HIV positive patients with and without fibromyalgia

Demographic characteristic	Fibromyalgia (n=68)	No Fibromyalgia (n=312)	OR (95% CI)	P value
Mean age (SD)	42.2 (9.2)	40.9 (10)	-	0.34
Sex				
Male	8 (11.8)	90 (28.8)	1.0	
Female	60(88.2)	222(71.2)	3.0(1.4-6.6)	0.004
Marital status, n (%)				
Single	13(19.2)	76(24.4)	0.8(0.4-1.6)	0.55
Married	37(54.4)	175(56.1)	1.0	
Separated/Divorced	5(7.4)	16(5.1)	1.5(0.5-4.3)	0.47
Widowed	13(19.1)	45(14.4)	1.4(0.7-2.8)	0.39
Occupation, n (%)				
Employed	34(50.0)	243(78.9)	1.0	
Unemployed	31(45.6)	65(20.8)	5.4(1.1-25)	<0.001
Retired	3(4.4)	4(1.3)	3.4(2.0-6.0)	0.02
Daily activities, n (%)				
Manual	36(52.9)	152(48.7)	1.0	
Not manual	32(47.1)	160(51.3)	0.8(0.5-1.4)	0.53

Thirty seven patients (54.4%) with fibromyalgia were in stage III of HIV. The mean CD4 counts for those with fibromyalgia and those were 276.2 cells/ml. Fifty six patients (82.4%) of those with fibromyalgia were on HAART. Thirty nine (69.6%) of the patients on HAART therapy with fibromyalgia were on a regimen consisting of tenofovir, while 12 (21.4%) patients were on zidovudine-based therapy (Table 3).

Table 3: Clinical characteristic of HIV positive with and without fibromyalgia

Clinical characteristic	Fibromyalgia (n=68)	No Fibromyalgia (n=312)	OR(95% CI)	P value
HIV clinical staging				
I	7(10.3)	37(11.9)	1.0	
II	12(17.7)	70(22.4)	0.9(0.3-2.5)	0.85
III	37(54.4)	166(53.2)	1.2(0.5-2.8)	0.72
IV	12(17.7)	39(12.5)	1.6(0.6-4.6)	0.36
CD 4 count				
Mean counts(SD)	276(144)	325(203.1)	-	0.06
HAART				
Yes	56(82.4)	248(79.5)	1.0	0.59
No	12(17.6)	64(20.5)	1.2(0.6-2.4)	
HAART regimen				
Tenofovir	39(69.6)	158(63.7)	1.0	
Zidovidune	12(21.4)	78(31.5)	0.6(0.3-1.3)	0.19
Other	5(9.0)	12(4.8)	1.7(0.6-5.1)	0.35

Table 4: Frequency and severity of fibromyalgia related symptoms; FIQR &SIQR Scores

Symptom (n=68)	Frequency (%)	Severity (score out of 10) 0 n(%)	1-3 n(%)	4-6 n(%)	7-10 n(%)
Pain	68(100)	0(0)	11(16.2)	25(36.7)	32(47.1)
Lack of energy	64(94.1)	4(5.9)	17(25)	28(41.2)	19(27.9)
Stiff	51(75)	17(25)	32(47.1)	16(23.5)	3(4.4)
Sleep disturbance	64(94.1)	4(5.9)	4(5.9)	18(26.5)	42(61.7)
Depression	63(92.7)	5(7.3)	13(19.1)	32(47.1)	18(26.5)
Memory	56(82.4)	12(17.6)	28(41.2)	21(30.9)	7(10.3)
Anxiety	58(85.3)	10(14.7)	22(32.4)	23(33.8)	13(19.1)
Tenderness	68(100)	0(0)	22(32.3)	28(41.2)	18(26.5)
Imbalance	57(83.8)	11(16.2)	25(36.7)	21(30.9)	11(16.2)
Sensitivity to noise,light	61(89.7)	7(10.3)	21(30.9)	25(36.7)	15(22.1)

	Fibromyalgia (FIQR)	No Fibromyalgia (SIQR)	P value
Mean scores (SD)			
Total	50.1(17.5)	12.4(8.5)	<0.001
Activity subtotal	16.9(8.3)	4.1(3.3)	<0.001
Impact subtotal	10.4(3.8)	2.6(2.2)	<0.001
Symptom subtotal	22.8(8.6)	5.7(3.8)	<0.001

The average FIQR score for the 68 patients with fibromyalgia was 50.1(SD 17). All the 68 patients with fibromyalgia presented with pain and tenderness. The other frequently reported symptoms occurring in at least 90% of all fibromyalgia cases were lack of energy (94.1%), sleep disturbance (94.1%) and depression (92.7%). Comparison of symptom severity showed that sleep disorder and pain were the most severe fibromyalgia related symptoms. The average FIQR score was higher among patients with fibromyalgia with a mean score of 50.1 (SD = 17.5) compared to the patients without fibromyalgia who had a mean SIQR score of 12.4 (SD = 8.5) (Table 4).

Discussion

The study was carried out at the CCC KNH which offers care to HIV positive patients. We sampled 380 patients with chronic musculoskeletal pain. A majority were females (74.2%) and this may be due to the fact that musculoskeletal symptoms are commonly seen in women[13]. Another explanation could be that according to the KDHS survey (2008-9), women were found to have a higher prevalence (8%) of HIV compared to men (4.3%)[14]. Most of the study population was in advanced stages of HIV (Stage 3 and 4) with CD4 counts below 350cells/ml. We found that a majority of the patients were on Tenofovir which is a first line therapy option according to the Kenyan guidelines[16].

The prevalence of fibromyalgia amongst HIV positive patients with chronic musculoskeletal pain was found to be 17.9%. Simms *et al*[7] in Boston found a higher prevalence of 40%, and this could have been due to population based differences whereby the patients in Simm's study were predominantly Caucasian males.

Simms' study was also conducted among patients who had IVDU[7]. We found that female gender was independently associated with fibromyalgia, OR 5.68. This mirrors findings of other studies on fibromyalgia that show a female preponderance. Females commonly experience rheumatologic conditions and the exact reasons for this remain unclear. However, it is postulated that sex hormones especially estrogen, could play a role in pain perception [13]. The younger age group in our study could be a reflection of the overall study population.. The odds of fibromyalgia were significantly higher among those who were unemployed (OR 5.4) and those retired (OR 3.4). This is relevant because negative life events like being unemployed have been noted to be psychological stressors that could increase one's risk of having fibromyalgia.. Alternatively, the chronicity and severity of fibromyalgia symptoms may make patients unable/unwilling to work or opt for early retirement.

The study did not show any associations with any of the clinical characteristics that we observed in our patients. These included CD4 count, WHO clinical stage or use of HAART. This may have been due to the small number of subjects with fibromyalgia and the fact that this study was not powered to look for these differences. This lack of association has also been seen in other similar studies done in the HIV positive population[19, 20].

The mean FIQR score was 50.1 which meant that overall, our patients were experiencing moderate disease. On analyzing the responses to the third domain of the

FIQR, we found that pain was the predominant symptom. It is thought to be because these patients have a lower threshold of stimulation of neurons that receive pain. The other commonly occurring symptoms included sleep disturbance and lack of energy which occurred in up to 94% of the population. The patients reported that they woke up feeling 'unrefreshed' and the lack of energy meant they were tired most of the days and hence unable to carry out the goals they had set out to do.

Patients with FM have been found to have disturbed sleep patterns. Intrusion of alpha waves into slow delta wave stage 4 sleep has been observed. They thus tend to sleep less at night followed by a day full of painful episodes[17]. In a different study, it was shown that FM symptoms can be induced in normal subjects by intentionally disturbing stage 4 of Non REM sleep[18]. Depression and anxiety were also found to exist amongst 92% of the study population with FM. Patients with fibromyalgia had a higher mean FIQR score of 50.1 compared to those without who had a mean of 12.4 on the SIQR. This showed that those with fibromyalgia had more difficulties in terms of being able to carry out certain activities, overall impact and symptom score.

This study was limited in that self reporting of the severity of symptoms associated with fibromyalgia could have been subjective. Secondly, recall bias may have been introduced when patients had to report the symptoms associated with fibromyalgia in accordance with FIQR.

We recommend that clinicians should be made aware of the presence of fibromyalgia in the HIV positive patients with chronic musculoskeletal pain. Patients found to have the condition should also be assessed for the associated symptoms and hence be offered the available modes of therapy.

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