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An Evaluation of Common Neuropathies and the Rate of Physiotherapy Referral among Adults on Highly Active Antiretroviral Therapy (HAART) at Maina Soko Military Hospital, Lusaka, Zambia

Margaret M. Mweshi[1, *], Richwell Hakacha[2], Martha Banda-Chalwe[1], Peter D. C. Phiri[1], Elliot Kafumukache[3], Stephanie Nixon[4]

[1]Department of Physiotherapy, School of Medicine, University of Zambia, Lusaka, Zambia

[2]Department of Physiotherapy, Maina Soko Military Hospital, Lusaka, Zambia

[3]Department of Anatomy, School of Medicine, University of Zambia, Lusaka, Zambia

[4]Department of Physiotherapy, University of Toronto, Toronto, Canada

Email address:

srmmweshi@gmail.com (M. M. Mweshi)

[*]Corresponding author

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Abstract: *Background:* The advent of highly active antiretroviral therapy (HAART) has changed the prognosis of patients with Human Immunodeficiency Virus (HIV) from invariable death to a manageable chronic condition, with a near-normal life expectancy. However, sensory peripheral neuropathy remains the common complication despite the effective combination of HAART. Little has been reported on the extent of the problem of common neuropathies in adults on HAART in Zambia. *Purpose:* To determine the prevalence of common neuropathies in adults on HAART and rate of physiotherapy referral among the patients that were seen at the Maina Soko Military Hospital (MSMH). *Methods and Results:* Data was collected retrospectively from clinical files of patients that were treated on HAART between the years 2011-2013 using a checklist. The statistical package for social sciences (SPSS) version 20 was used for descriptive analysis. A total of 214 clinical files of adults on HAART were identified during the period under review and only 24 cases had some form neuropathies giving a period prevalence of 11.2%. The majority 46% (n=11) age range being 31 to 45 years with more 58% (n=14) females than males 42% (n=10). Almost half 54% (n=13) of the patients were on tenofovir, lamivudine and efavirenz. The most common type of neuropathy 59% (n=14) was polyneuropathy with autonomic neuropathies as co-morbidities and most of these patients 75% (n=18) had not been referred to physiotherapy. *Conclusions:* Neuropathies are becoming a common problem in patients on HAART given the rising prevalence. Rate of physiotherapy referral among the cases is very low. It is highly recommended that another study on prevalence of neuropathies in adults on HAART be done over a longer period of time to include other hospitals in Zambia. Physiotherapists in Zambia are also challenged to provide evidence on the impact of the interventions given to patients with neuropathies on HAART.

Keywords: HAART, HIV/AIDS, Prevalence, Neuropathies, Physiotherapy, Zambia

1. Background

An estimated 34 million people in the world lived with Human Immunodeficiency Virus (HIV) infection/ Acquired Immune Deficiency Syndrome (AIDS) in 2010 [1]. Prevalence of HIV/AIDS varies substantially with geography,

concentrated in the poorest of nations, but also among the most deprived living in the richest nations. However, it is also reported that the African continent is also disproportionately affected by the HIV pandemic. For instance, countries like Zambia, Swaziland, Botswana and Lesotho have infection rates as high as 20-30%, [2] while HIV prevalence in Western and Eastern Africa is low to moderate ranging from 0.5% in Senegal to 6% in Kenya [3]. Although the sub-Saharan region represents only 12% of the world's population, nearly 70% of the world's cases of HIV and 72% of the world's HIV death related cases are found there [2, 4, 5].

Since first reported in 1981, HIV/AIDS has claimed the lives of nearly 27 million people worldwide [1]. The advent of highly active antiretroviral therapy (HAART) combined with other medical advances and psychosocial support mechanism available to patients have changed the prognosis of HIV from invariable death to a manageable lifelong with a near-normal life expectancy [6-8]. This reduction in mortality has transformed HIV into a long-term chronic illness for many patients, characterized by an ageing HIV-infected population who are increasingly affected by age-related non-communicable diseases (NCDs). Such advances of increased life spans suggests that many people living with HIV face new or worsening experiences of disability [5, 8, 9]. However, HIV-associated neurologic manifestations remain a subject of active research interest in the HAART era, as a growing body of literature now demonstrates that HIV infection can exert diverse influences on the central and peripheral nervous systems and can produce both acute and chronic changes in affected patients [10, 11]. Furthermore, the link between HIV and disability is thought to be due to the direct action of HIV, its secondary conditions and/or side effects of medications used for treatment, which may lead to impairments in a wide range of areas such as cognition, vision, hearing, mental health and musculoskeletal functioning [5, 12, 13]. However, sensory peripheral neuropathy remains the common complication despite effective combination of HAART [14, 15]. Although the side effects of HAART have a wide range of symptoms, [5] peripheral nervous system infection by HIV is very common and can affect all stages of infection [15]. HIV can be neuroinvasive, neurotropic, and neurovirulent and many peripheral neuropathic syndromes have been reported in the context of HIV infection, including HIV-associated distal sensory neuropathy, neurotoxic nucleoside neuropathy, and inflammatory demyelinating neuropathy [16]. Even though several potential pathogenic mechanisms have been proposed, the underlying pathology remains elusive [17]. Conceptually, antiretroviral central nervous system (CNS) neurotoxicity may be mediated by either direct or indirect mechanisms. Direct toxicity to peripheral nerves is a frequent side effect associated with the older nucleoside reverse transcriptase inhibitors (NRTIs), particularly the dideoxy-nucleosides.

Ultimately, the HIV can affect directly the dorsal root ganglions neurons, the infiltration of activated macrophage which secrets the neurotoxins cytokines and other toxic metabolites. The neurotoxic action of the antiretroviral drugs can explain some parts of the distal sensory polyneuropathy (DSP) [16]. The distal sensory polyneuropathy is the most frequent forms and factors associated with them are the virus itself, opportunistic infections and antiretroviral therapy [17]. The unavailability of electromyography makes diagnosis more difficult, often based on clinical criteria in Africa compared with the USA which has developed a purely clinical diagnostic tool to diagnose [16]. However, therapeutic exercises have been known to help patients with ARVs.

Nonetheless, health professionals are concerned to know more about the use of exercise as a complementary therapeutic modality for individuals infected with HIV because there are gaps in knowledge regarding the optimal mode, duration, frequency, and intensity of exercises prescribed to HIV/AIDS patients by physiotherapists [18]. Exercise can delay the progression of the disease and improve quality of life (QOL) in adults living with HIV infection [19]. Furthermore, they are generally regarded as safe because they do not compromise the immune function, and are beneficial in boosting functional capacity, strength, physical fitness, mood, and sense of wellbeing, and in ameliorating wasting and lipodystrophy. Exercise studies in HIV patients have assessed the impact of exercises on immune function, psychological factors, cardiorespiratory fitness, strength, body composition, and QOL as well as HAART-induced metabolic complications in HIV/AIDS patients and the results indicate that they are safe and actually elicit favourable and beneficial changes in an HIV-infected population [18].

Despite the impact of neurologic complications on the HIV/AIDS population, the prevalence of common neuropathies and rate of physiotherapy referral data available has been limited in Zambia. Considering such limited information, we set out to establish the prevalence of common neuropathies in adults on HAART and also evaluate the rate of physiotherapy referral at MSMH between 2011 and 2013.

2. Methodology

We collected data in a cross-sectional design retrospectively from clinical files of patients that were treated on HAART from 2011 to 2013 at the MSMH using a checklist. The MSMH is a Military Hospital which is a referral hospital for all Defense Force Health Centers in Zambia. The hospital is known to have an efficient Family Support Unit that deals with HAART equipped with modern data processing and storage facilities known as Smart Care System. Study clearance and approval was sought from the University of Zambia Biomedical Research Ethics Committee (UNZABREC). We used the statistical package for social sciences (SPSS) version 20 for descriptive analysis of the data.

3. Results

3.1. Demographic Characteristics of Cases Identified with Neuropathies

A total of 214 clinical files of adults on HAART were identified during the period under review and only 24 cases had some form neuropathies giving a period prevalence of 11.2%. The majority 46% (n=11) age range being 31 to 45 years with more 58% (n=14) females than males 42% (n=10). Figure 1 shows the age ranges of patients with neuropathies.

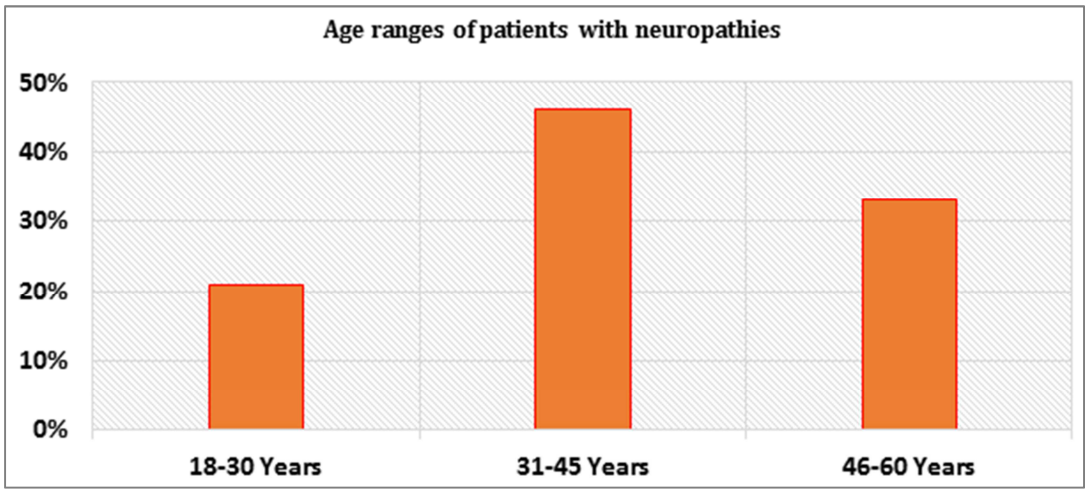

Figure 1. *Age ranges of patients on HAART with neuropathies.*

3.2. Indicated Types of Neuropathies among the Cases and Common HAART Drugs

Figure 2 shows the common neuropathies of the participants. The most common type of neuropathy 59% (n=14) was polyneuropathy with autonomic neuropathies as co-morbidities, sensory peripheral neuropathies 29% (n=7), mono-neuropathies 8% (n=2) and poly radiculopathy 4% (n=1). The majority of these patients 75% (n= 18) had not been referred to physiotherapy.

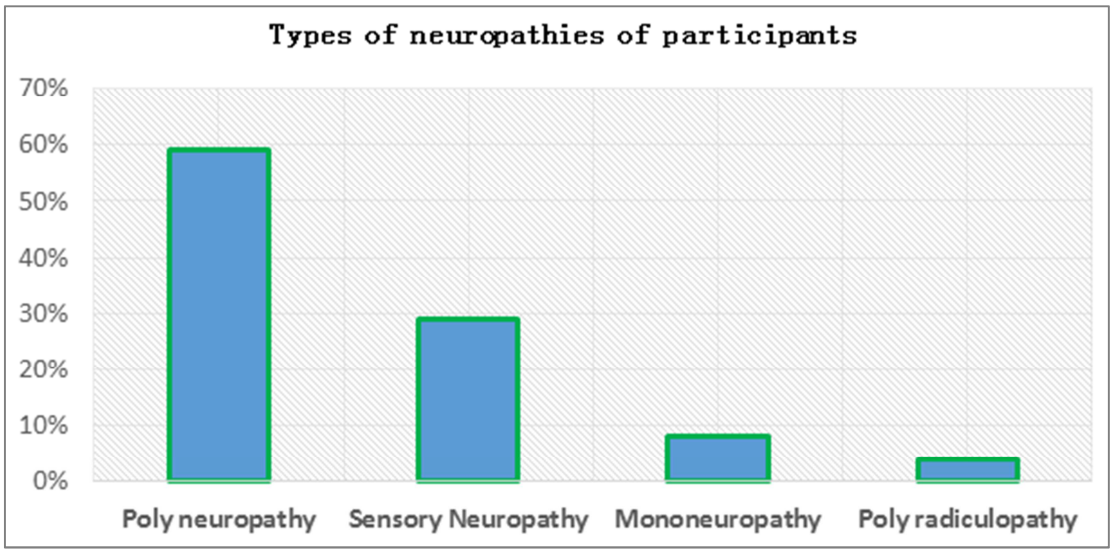

Figure 2. *Types of neuropathies.*

Almost half 54% (n=13) of the patients were on tenofovir, lamivudine and efavirenz followed by 25% (n=6) on tenofovir, efavirenz and nevirapine, then 8% (n=2) on tenofovir, atazanavir and lopinavir, 4% (n=1) on tenofovir, nevirapine and lamivudine, 4% (n=1) on atazanavir, lapinavir and lamivudine and 5% (n=2). Figure 3 shows the drugs used in the antiretroviral therapy.

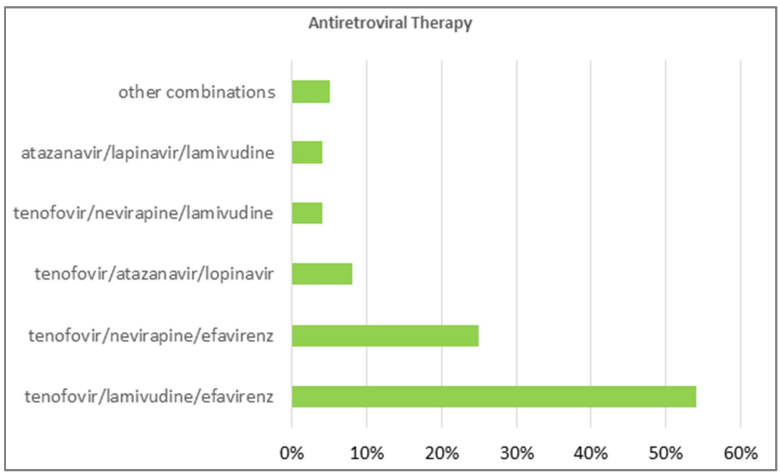

Figure 3. *Antiretroviral therapy.*

4. Discussion

Period prevalence an epidemiological mathematical determinant for disease surveillance was used to determine the 11.2% (0.112 per 100, 000) prevalence of neuropathies among patients on HAART in this study. The results of this current study showed that the prevalence rate found was lower than that reported in Burkina Faso that has reported a rate as high as 38% [20]. However, other studies have reported low prevalence rates like the results of a study done in Thailand showing a prevalence of 3.8% [21] and Uganda is even lower with 1.73% [22].

The current study showed that there were more females than males presenting with neuropathies though the difference was not significant. Our results are in line with the results of a study done in Kenya [23]. Studies done in some rich resource countries have shown that women tolerate NRTI-containing regimens less well than men [24]. This could probably explain why there were more women than men. In contrast, results of a study done in Indonesia and Malaysia did not show any significant gender difference [25]. However, considering the results of our study, it was difficult to conclude that the presence of neuropathies among HIV/AIDS patients on HAART is gender sensitive because this would be misleading given a small sample size that we investigated. Further, the results of this study showed that the majority of patients with neuropathies were aged between 31 to 45 years old. Such results are consistent with the results of a study done in Nigeria which reflected that the mean age of patients with neuropathies was 38 years old.

Although some studies have shown that the commonest neuropathies in patients on HAART is sensory peripheral neuropathies [26-28], our results showed that only 29% of the patients had problems with neuritis. However, polyneuropathy with some autonomic neuropathies as co-morbidities was the commonest among the patients that were reviewed. Our results are similar to the results of a study done in Uganda [29] that showed that peripheral polyneuropathy was the commonest and partially similar to the results of a study done by Menezes and colleagues [30] in Brazil which showed that the commonly encountered side effect were gastrointestinal alongside central nervous system side effects. There is a strong association that exists between GBS and HIV/AIDS [31] and as such, most of these patients could have also had some form of GBS though we did not isolate the pathology from the general picture of patients with some form of neuropathies.

In Zambia, approximately 82,700 people had HIV in 2009 with the overall adult prevalence of the disease being 14%, and 1.6% of the adult population become newly infected with HIV each year [32]. Acquired immune deficiency syndrome caused by human immunodeficiency virus is an important health concern worldwide, and AIDS-related morbidity and mortality have seen a sharp decline due to the introduction of HAART. Highly Active Antiretroviral Therapy comprises of a combination of at least three drugs from at least two different classes: for example, a combination of two (2) Nucleoside Reverse Transcriptase Inhibitors (NRTIs) plus one (1) Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) or two (2) NRTIs plus Protease Inhibitors (PI). However, use of antiretroviral drugs has been associated with a number of toxicities, including those affecting the nervous system and also the kidneys [33]. The results of our study showed that almost half of the patients were on tenofovir, lamivudine and efavirenz. The World Health Organization strongly recommended that the first-line of ART consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI); tenofovir (TDF) and lamivudine (3TC) or emtricitabine (FTC) as the two NRTI plus efavirenz (EFV) or nevirapine (NVP) as the NNRTI to be administered as a fixed-dose combination to initiate ART [34-37]. The results of the study shows that the majority of the patients were on the regime recommended by WHO.

The current study revealed that most of the patients with neuropathies were not referred for physiotherapy. This is in line with the results of the study done by Saisha and others [38] which revealed that physiotherapy is under-utilized at the UTH in the care of neuropathies found in patients with

Gullian-Barre Syndrome. One would perhaps speculate that medical practitioners might not have seen or overlooked the need for physiotherapy. Some authors have argued that there was no evidence of the impact of physiotherapy in the management of patients with some form of neuropathies [39, 40]. Nonetheless, health professionals are concerned to know more about the use of exercise as a complementary therapeutic modality for individuals infected with HIV because there are gaps in our knowledge regarding the optimal mode, duration, frequency, and intensity of exercises prescribed to HIV/AIDS patients by physiotherapists [18]. Exercise can delay the progression of the disease and improve quality of life (QOL) in adults living with HIV infection [19]. Furthermore, they are generally regarded as safe because they does not compromise the immune function, and is beneficial in boosting functional capacity, strength, physical fitness, mood, and sense of wellbeing, and in ameliorating wasting and lipodystrophy. Exercise studies in HIV patients have assessed the impact of exercises on immune function, psychological factors, cardiorespiratory fitness, strength, body composition, and QOL as well as HAART-induced metabolic complications in HIV/AIDS patients and the results indicate that they are safe and actually elicit favourable and beneficial changes in an HIV-infected population [18].

Other authors who have also investigated the effects of physical rehabilitation therapies and interventions on people with polyneuropathies cautioned in their conclusion that lack of evidence should not be interpreted as proof of the ineffectiveness of physical rehabilitation. Physical rehabilitation in people with critical illness polyneuropathy seems to be a complex intervention and not easy to study. In the absence of any high quality evidence, clinicians should base their decisions on clinical experience, individual circumstances and patient preferences as appropriate [41]. It is therefore, inevitable for physiotherapy specialists to explore any negative impact physiotherapy may cause on patients with some form of neuropathies especially those on HAART. It is highly recommended that another study on prevalence of common neuropathies be done over a longer period and other hospitals in Zambia must be included. Physiotherapists in Zambia are challenged to provide evidence of the impact of the interventions given to patients with neuropathies among patients on antiretroviral therapy.

5. Conclusion

Neuropathies are becoming a common problem in patients with HIV/AIDS on HAART among members of the defense force being treated at MSMH in Zambia. Polyneuropathies were the commonest symptoms among the patients under review while the common drug combination used was tenofovir, lamivudine and efavirenz which maybe could be attributed to the rise in the occurrence of neuropathies. From the outcomes of this study, it is evident that in management of neuropathies, physiotherapy interventions are under-utilized at the hospital.

List of Abbreviations and Their Meanings

AIDS: Acquired Immune deficiency Syndrome (viral infection)

ARVs: Antiretroviral drugs (drugs for suppressing the HIV infection)

CNS: Central Nervous System (composition of the brain and spinal cord)

DSP: Distal Sensory Polyneuropathy (damage to sensory nerves)

EFV: Efavirenz (antiretroviral drug)

FTC: Emtricitabine (antiretroviral drug)

HAART: Highly Active Antiretroviral Therapy (treatment for suppressing the HIV infection)

HIV: Human Immunodeficiency Virus (virus attacking the immune system)

MSMH: Maina Soko Military Hospital (main Referral Military Hospital in Zambia)

NRTI: Nucleoside Reverse Transcriptase Inhibitor (antiretroviral drug)

NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor (antiretroviral drug)

NVP: Nevirapine (antiretroviral drug)

QOL: Quality of Life (measure for assessing the quality of life)

TDF: Tenofovir (antiretroviral drug)

SPSS: Statistical Package for Social Scientists (Package for analyzing data)

UTH: University Teaching Hospital (Main Referral Hospital in Zambia)

UNZABREC: University of Zambia Biomedical Research Ethics Committee (Responsible for research ethical approval involving human participants)

WHO: World Health Organization (specialized agency responsible for international public health)

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