HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 AND HUMAN T-CELL LYMPHOTROPIC VIRUS TYPE I AND II AMONG INTRAVENOUS DRUG USERS IN MALINDI SUB-COUNTY, KENYA

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Human Immunodeficiency Virus Type 1 and Human T-Cell Lymphotropic Virus Type I and II among Intravenous Drug Users in Malindi Sub-County, Kenya

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

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DEDICATION

This thesis is dedicated to my loving parents James and Jane Koech together with my brothers Erick and Jeff, and my sisters Betty and Maureen. May God bless you immensely for the support and encouragement. All my love and appreciation goes to you.

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ABBREVIATIONS AND ACRONYMS

ATL	Adult T cell leukemia/lymphoma
AIDS	Acquired Immunodeficiency Virus
CVR	Centre of Virus Research
DNA	Deoxyribonucleic acid
ELISA	Enzyme linked immunosorbent assays
HIV	Human Immunodeficiency Virus
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HTLV	Human T-cell Lymphotropic virus
HTLV-I	Human T-cell Lymphotropic virus type 1
HTLV-2	Human T-cell Lymphotropic virus type 2
HTLV-3	Human T-cell Lymphotropic virus type 3
HTLV-4	Human T-cell Lymphotropic virus type 4
HSV-2	Herpes Simplex Virus type 2
IDU	Intravenous drug use
IDUs	Intravenous drug users
KANCO	Kenya Aids NGOs Consortium

KEMRI	Kenya Medical Research Institute
LBCs	Liquid Based Cytology Samples
LTR	long terminal repeat
MTCT	Mother to child transmission
NGOs	Non-Governmental Organizations
ORF	Open reading frame
PCR	Polymerase chain reaction
PI	Principal Investigator
SERU	Scientific Ethics Review Unit
SPSS	Statistical Package for Social Sciences
SSC	Scientific Steering Committee
STIs	Sexually Transmitted Infections

ABSTRACT

Human T-cell Lymphotropic Virus type one and two (HTLV1/2) infections are highly prevalent among Human Immunodeficiency Virus (HIV) infected intravenous drug users (IDUs). The two viruses share similar routes of transmission and tropism for T-lymphocytes thus co-infection is common. This study aimed at determining prevalence of HIV and HTLV-1/2infections among IDUs in Omari and KANCO Drop-in centres in Malindi Sub-County. These findings were correlated with socio-demographic factors, injection and sexual practices of the study population. A cross-sectional study was conducted using structured questionnaires and laboratory testing of blood samples from 351 consenting adult IDUs. Purposive sampling was used to enroll IDUs from the two Drop-in Centres. Serology for HIV-1 and HTLV-1/2 was carried out using Vironostika HIVAg/Ab protocol and HTLV1/2 Enzyme-linked Immunosorbent Assay (ELISA) respectively. Logistic univariate regression was used to determine significant factors for HIV and HTLV infections at $p<0.05$. Of the 351 recruited IDUs (with a mean of 33.1and SD ± 6.5years), 9.7% (34/351) were positive for HIV, 5.8% (20/351) were HTLV1/2 positive while 0.9% (3/34) were HIV/HTLV-1/2 co-infected. HIV infection was significantly associated with homelessness (OR, 2.5; 95CI, 1.3-5.3; *p*=0.009), needle sharing (OR, 2.1; CI, 1.0-4.3; *p*=0.042) and previous history of gonorrhea and syphilis (OR, 3.7; CI, 1.9-7.5; *p*=0.000). HTLV-1/2 infection was significantly associated with Omari Centre (OR, 7.9, CI, 1.1-59.6; *p*=0.043), unprotected anal sex (OR, 3.1, CI, 1.1-8.5; *p*=0.029) and previous history of gonorrhea and syphilis infections (OR, 2.9; CI, 1.1-7.3; *p*=0.021). There were no significant factors for HIV/HTLV-1/2 co-infection. High risk injection and sexual behavior increase the risk of HIV and HTLV1/2 transmission. Routine testing of HTLV1/2 and harm reduction measures should be introduced in all outpatient IDU clinics so as to monitor prevalence estimates and mitigate further transmission.

CHAPTER ONE

INTRODUCTION

1.1 Background information

Globally, around 13 million people inject drugs (WHO, 2018). Intravenous Drug Users (IDUs) are particularly vulnerable to HIV and other blood-borne pathogens as a result of sharing contaminated syringes and other injecting equipment such as cookers, cotton and rinse water (Degenhardt and Hall, 2012). Intravenous Drug Use (1DU) results in other health complications, including drug overdose and sexually transmitted infections among users who may offer sex in exchange for drugs (German and Latkin, 2015). An estimated 250 million people between the ages of 15 and 64 years used drugs in 2014 with at least 29 million suffering drug use disorders (UNODC, 2016). The burden of drug use in Africa is compounded by the increasing availability of injection drugs such as heroin, cocaine and methamphetamine, especially in peri-urban and urban settings (Hobkirk *et al.,* 2016). There is still limited data on the true rate of IDU in sub-Saharan Africa however it is estimated that Kenya has between 18000-30000 IDUs (NASCOP, 2011). Available data indicate that the IDU population in Mombasa is between 7 to 15% although these numbers may be on the rise (Ngonga *et al.,* 2015). Omari and KANCO Drop-in centres have approximately 2000 IDUs (NASCOP, 2014)

An estimated 36.7 million people worldwide are infected with HIV while1.7 million IDUs are living with HIV. Intravenous drug use accounts for approximately 10% of HIV infections globally and 30% of those outside of Africa (WHO, 2018). Regional HIV prevalence rates are high in IDUs in all parts of the world with up to 15.5% in East and Southern Africa (WHO, 2018). Kenya has an average national HIV prevalence of 5.9% and the prevalence among IDUs is estimated to be 18.3% (NACC, 2016). While the risk of HIV is highest among the networks of drug users, evidence shows that IDUs contribute to the spread of HIV far beyond the circles of those who inject (Degenhardt and Hall, 2012). HIV prevalence in Mombasa County is 1.2 times higher than the

national prevalence at 7.5% while the prevalence in Kilifi County is less than the national prevalence at 4.5%. HIV positive cases in Kilifi County contributed to 2.1% of the total number of people living with HIV in Kenya, and are ranked the thirteenth highest nationally. IDUs in the county accounted for 44% of total HIV positive cases (NACC, 2016). In Malindi Sub-County, HIV prevalence among IDUs was estimated to be an alarming 53.1% (Ng'ong'a *et al*., 2015).

Data shows that at least 5-10 million people worldwide are infected with HTLV-1 (ECDC, 2015) and between 3-5 million people worldwide are infected with HTLV-2 (Gonzalez-Alcaide *et al*., 2016). HTLV-1 and HTLV-2 have a worldwide distribution; prevalence rates range from 5% to 27%, with higher rates occurring in certain populations where HTLV-1 is highly endemic. In the United States, HTLV-1/2 seroprevalence rates range from 7 to 49% among IDUs (Beilke, 2012). Determining prevalence of HTLV, a blood borne virus is important as these infections cause morbidity and mortality in IDUs (McIntyre *et al.,* 2001). History of injecting drugs increases the risk of acquiring HTLV-1/2 infection through unsafe injecting practices (Prasetyo and Sari, 2017). Despite numerous epidemiological studies and reports of sporadic cases, the situation concerning the level of HTLV-1 infection, is not documented in several African countries and regions of this large continent (Gessain and Cassar, 2012).

In Africa, the seroprevalence increases from the north to the south, varying from 0.6% in Morocco to greater than 5% in several sub-Saharan African countries such as Benin, Cameroon and Guinea-Bissau (Gonçalves *et al.*, 2010). HTLV-1 prevalence has been reported to range from 6.6% and 8.5% in Gabon, 1.05% in Guinea, 3.2% in Congo and 5.5% in Nigeria (Anyanwu *et al*., 2018). The first documented HTLV study in Kenya reported a HTLV-1 prevalence of 3.7% in 913 stored serum samples from suspected HIV-infected patients in Nairobi, Mombasa and Kisumu (Songok *et al.,* 1994). A recent study using cervical smears and carcinomas reported a HTLV-1 prevalence of 11.6% among HIV positive and negative women in Kenya (He *et al.,* 2016). HIV and HTLV share similar transmission routes such as mother to child transmission, sexual contact, transfusion, intravenous drug use and needle sharing (Pirayeshfard *et al.,* 2018**)**. Given

that these viruses share identical modes of horizontal and vertical transmission, co-infections with these viruses is common in endemic areas (Kozlowski *et al*., 2016).

Co-infection by HTLV-1 or HTLV-2 and HIV-1 occurs in a substantial number of persons with a history of IDU (Casoli *et al.,* 2007). The effects of HTLV co-infection on HIV have been widely studied. Available evidence suggests a protective role of HTLV-2 and adverse effect of HTLV-1 on HIV infection (Jogeda *et al*., 2016). HIV/HTLV-1 co-infection is associated with accelerated progression to Acquired Immunodeficiency Syndrome (AIDS) and worsens outcomes of HIV-related opportunistic infections. The viral loads are expected to be high contributing to increased incidence of drug resistance (Isache *et al.,* 2016). It is estimated that rates of HTLV-1 or HTLV-2 co-infections in HIV infected individuals are at least 100 to 500 times greater than in the general population (Isache *et al.,* 2016). Co-infection by HIV/HTLV-2 is more frequently reported in the USA and Europe, whereas HIV/HTLV-1 co-infection predominates in South America, the Caribbean and Africa (Gudo *et al.,* 2009). HIV/HTLV-1/2 co-infection prevalence of 6.7% was reported among IDUs in Italy (Turci *et al.,* 2006) whereas HTLV-2/HIV co-infection rate of 6.8% was reported in a cohort of HIV positive IDUs in USA (Casoli *et al.,* 2007). Mozambique reported a HIV/ HTLV-1 co-infection prevalence of 3.9% among HIV infected patients (Augusto *et al.,* 2017). In Kenya, a recent HIV/HTLV-1 co-infection prevalence of 19.5% was reported in liquid based cytology (LBC) samples from women attending Kenyatta National Hospital in Nairobi (He *et al*., 2016).

1.2 Statement of the problem

Emergence of HIV-1/HTLV-1/2 co-infection is a worldwide health problem in the last ten years due to increasing numbers of co-infected individuals. HTLV-1 was the first infectious agent to be discovered as the direct cause of human cancer and is the most carcinogenic of all oncoviruses. It contributes to 7.4% of reported cancer cases in Kenya by causing ATL through clonal expansion of T-Cells by the tax-1 gene (Macharia *et al.,* 2019). Increased incidence of neurologic disorders and liver disease in HIV/HTLV-2 co-infected patients has been reported (Toro *et al*., 2007). HIV infection among IDUs has

constantly been on the rise within the Kenyan coast where an estimated 17% of new HIV infections occur within this group (UNODC, 2015). Omari and KANCO Drop-in Centres are based in Malindi Sub-County which is a tourist destination along the Kenyan coast that has been reported to have a large drug injecting population (Nieburg and Carty, 2011). Due to sex tourism activities, IDUs engage in high risk practices such as men having sex with men, female sex work and needle sharing. These practices are a major public health concern as they aggravate the risk of infection and co-infection as well as the transfer of viral strains from the IDUs to the general population. IDUs often fail to seek medical intervention in cases of infections for fear of arrest and rebuttal from the local community. The situation is aggravated by the fact that neither a cure nor effective treatment is currently available for HTLV infection.

1.3 Justification

The principal routes of HIV and HTLV-1/2 transmission are similar making co-infection of HTLV among HIV patients common. The HIV/HTLV co-infection has been associated with reduced survival and increased risk of progression to AIDS. It is critical to investigate IDUs so as to create awareness and prevent further transmission as they act as a bridge of transmission to the local population. The two centres are based in Malindi Sub-County which receives tourists from all over the world, who interact sexually with the local population and if infected, they may transmit HIV and HTLV to them. This may lead to introduction of new strains into local population. The risk to health is not only exportation of the local strains of the viruses, but also importation of the foreign viral strains not known to circulate within the group. Since curative treatment of HTLV-1 associated diseases such Adult T-cell leukaemia/lymphoma (ATL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) is lacking and a vaccine is unavailable, mortality rates among HTLV infected IDUs could be higher. Studies that have documented the prevalence of HTLV-1/2 mono- or HTLV/HIV co-infections among IDUs are scanty. Furthermore, scanty data exists on the distribution of HTLV genotypes in Kenya. In Kenya, currently, no documented study has been done on HIV and HTLV among IDUs. This study therefore aimed to determine the prevalence of HIV and HTLV infections and among IDUs in Omari and KANCO drop in centres.

1.4 Research Questions

1. What is the prevalence of HIV-1 and HTLV-1/2mono and co-infections among IDUs in Omari and KANCO drop in centres?
2. What are the socio-demographic characteristics associated with HIV-1 infection among IDUs in Omari and KANCO drop in centres?
3. What are the socio-demographic characteristics associated with HTLV-1/2 infections among IDUs in Omari and KANCO drop in centres?

1.5 Objectives

1.5.1 Broad objective

To determine the prevalence and socio-demographic factors of HIV-1 and HTLV-1/2 infections among IDUs in Omari and KANCO Drop in Centres in Malindi Sub-County

1.5.2 Specific objectives

1. To determine the prevalence of HIV-1 and HTLV-1/2mono and co-infections among IDUs in Omari and KANCO drop in centres.
2. To determine the socio-demographic characteristics associated with HIV-1 infectionamong IDUs in Omari and KANCO drop in centres.
3. To determine the socio-demographic characteristics associated with HTLV-1/2 infection among IDUs in Omari and KANCO drop in centres.

CHAPTER TWO

LITERATURE REVIEW

2.1 Human T-Cell Lymphotropic Virus (HTLV) and associated diseases.

Human T-Cell Lymphotropic Virus (HTLV) is a member of the delta retrovirus genus of the *retroviridae* family (ICTV, 2017). The first retrovirus to be discovered in 1979 from a patient with cutaneous T-cell lymphoma was HTLV-1 which was later followed by the discovery of HTLV-2 in 1982 from a patient with hairy cell leukemia (Gallo, 2005). HTLVs are oncogenic retroviruses that both infect T cells with HTLV-1 infecting mainly $CD4^+$ T cells and HTLV-2 infecting $CD8^+$ T cells (Beilke, 2012). While their transmission routes are the same (transfusion of contaminated blood, mother to child, sexual contact), the clinical outcome of these viruses is quite different (Jogeda *et al.,* 2016). The transmission rate through blood and blood derivatives is approximately 12%, but the risk that individuals infected through blood might develop diseases associated with HTLV is low, perhaps due to the long latent period between infection and the clinical phase of the disease. Many infected carriers die beforehand due to underlying diseases (Viana *et al.,* 2014).

HTLV-1 is the causative agent of aggressive adult T-cell leukaemia/lymphoma (ATL) which is a blood cancer. It also causes the progressive chronic, disabling HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) which leads to a weakness in lower limbs (Futsch *et al.,* 2017). Other diseases have been associated with HTLV-1 infection including; polymyositis, sinusitis, broncho-alveolar pneumonia, keratoconjunctivitis sicca and bronchiectasis, indicating multi-systemic involvement (Nunes *et al.,* 2017). The cumulative risk of a HTLV-1 carrier developing ATL has been estimated at between 2.5% and 5% although a latency period of 50–70 years is typical (Fox *et al*., 2016). For HAM/TSP, an approximate 1% to 2% of HTLV-1 infected individuals will develop the infection (Futsch *et al.,* 2017). Both ATL and HAM/TSP have a low incidence among HTLV-1 carriers. ATL generally presents after a long

latency in patients infected during childhood. This is in contrast to HAM/TSP, which is associated with infection later in life (San-Martin *et al*., 2016).

The pathogenicity of HTLV-2 is low and has only occasionally been linked to sub-acute neurological syndromes (Gonzalez-Alcaide *et al*., 2016). HTLV-2 can produce a neurologic syndrome similar to HTLV-1-associated HAM/TSP, with spasticity in the lower limbs, leg weakness and bladder dysfunction (Zunt *et al.,* 2009). HTLV-2 though persistently associated with elevated lymphocyte and platelet counts together with an increase in overall cancer mortality, does not cause hematologic disorders and is only sporadically associated with myelopathy unlike HTLV-1 (Ciminale *et al.,* 2014). Unlike HTLV-1 infection, HTLV-2-associated myelopathy commonly also includes peripheral neuropathy and ataxia. Neurologic disease in patients with HTLV-2 infection is much less common than in patients infected with HTLV-1(Zunt *et al.,* 2009).

Human T-cell lymphotropic Virus type 3 (HTLV-3) was first described in two asymptomatic inhabitants from South Cameroon. Two other cases of HTLV- 3 infection in people living in Cameroon have been reported, suggesting that this virus is not extremely rare in the human population living in Central Africa (Mahieux and Gessain, 2011). Only one strain of Human T-cell Lymphotropic Virus type 4 (HTLV-4) has been identified in a person who also lived in Cameroon (Gonzalez-Alcaide *et al*., 2016). By 2014, no diseases had been reported in both HTLV-3 and HTLV-4 infected individuals (Larocque *et al.,* 2014).

2.2 Human T-Cell Lymphotropic Virus epidemiology

HTLV-1/2 infections show a worldwide distribution and its prevalence varies significantly according to geographic region, ethnic and/or racial group, and the risk factors of the population analyzed (Pinto *et al.,* 2012). Regions endemic for HTLV-1 include southern Japan, Caribbean islands, sub-Saharan Africa, localized areas of Iran (especially the area in the Northeast of the country), South America (regions of Brazil, Peru, Columbia, Chile, Argentina, and French Guyana) and Australo-Melanesia (Pirayeshfard *et al.,* 2018)**.** The burden of HTLV-2 infection in the world is about 6 to 12

fold lower than that of HTLV-1 (Murphy, 2015). The African continent has a population of over one billion and it represents the largest endemic area for HTLV-1 infection but with many data gaps on prevalence and genetic diversity (Fox *et al*., 2016).

HTLV-2 has a more restricted distribution than HTLV-1. It is more prevalent among some Native Americans, some Central African tribes and is relatively common among IDUs and their sex partners in Europe, North America and other regions of the world(Ma *etal*., 2013). A sero-survey across Africa established HTLV-2 prevalence rates of 14% from Bambuti pygmies in Congo and 2.3% from pygmies in Cameroon (Anyanwu *et al.*, 2018). Brazil has 2.5 million HTLV-I and HTLV-II seropositive individuals (Ma *et al*., 2013). In Europe where HTLV-2 infection is found almost exclusively among IDUs, about 20,000 to 40,000 persons are estimated to be infected. In Malawi, HTLV-2 prevalence of 1.7% and 1.3% was reported among mothers and their children who had childhood cancers (Fox *et al*., 2016). Only sporadic cases of ATL and/or TSP/HAM have been reported from East African countries (Murphy *et al.*, 2015).

2.3 Human T-Cell Lymphotropic Virus Transmission

There are three well-studied routes of human transmission for both HTLV-1 and HTLV-2; sexual contact, mother to child through breastfeeding and blood products containing HTLV infected lymphocytes (Anyanwu *et al.*, 2018). However for HTLV-1, the transmission in endemic areas primarily occurs from mother-to-child and/or through sexual intercourse. Concerning mother-to-child-transmission (MTCT) transmission, a review pointed out that in infants breastfed, the MTCT occurs at rates varying from 7.4% to 32% compared with a rate of less than 5% among bottle-fed children (Paiva *et al.*, 2018). Sexual transmission of HTLV-1 is more efficient from men to women, with a reported rate of 60.8% compared to 0.4% in the reciprocal direction (Nunes *et al.*, 2017). Higher concentrations of infected lymphocytes in semen than in vaginal secretions might be associated with more efficient viral transmission from men to women (Zunt *et al.*, 2009). HTLV-2 on the other hand is primarily transmitted sexually and through intravenous drug use. In contrast to HTLV-1, similar prevalence has been observed in males and females suggesting that sexual transmission of the virus might be equally

efficient between the sexes (Paiva and Casseb, 2014). Higher rates of HTLV-2 have been linked to IDU as compared to the other transmission routes (Zunt *et al.,* 2009).

2.4 Human Immunodeficiency Virus among intravenous drug users

IDUs have a higher risk of contracting and transmitting HIV, yet they also have the least access to prevention, care and treatment services because their behaviours are often stigmatized and even criminalized (NACC, 2016). In addition, IDUs are likely to delay HIV testing exacerbating the situation by transmitting HIV unknowingly (Ng'ong'a *et al*., 2015). In many settings, harm reduction programmes are not available or are extremely limited in accessibility and availability due to restrictive ineffective policies and laws (WHO 2018). Several studies indicate that IDUs are at a high risk for HIV transmission through unsafe practices such as sharing non-sterile injecting equipment and unprotected sex (Strathdee *et al.,* 2013; Shahesmaeili *et al.,* 2015). This can transfer HIV from IDU to non-IDU populations and extend or prolong the generalized epidemic (Brodish *et al*., 2012). Globally, one in seven IDUs is living with HIV (UNODC, 2016).

The efficiency of HIV transmission per injection is six times higher than for heterosexual sex thus HIV prevalence among IDUs can rapidly reach high levels of more than 50% and up to 90% (UNODC, 2010). Research in African countries has found HIV prevalence among IDUs far exceeding that in the general population, ranging from 9% to 50% (Brodish *et al.,* 2012). Compared with the general population, IDUs have an elevated risk of death, although mortality rates vary across settings. Drug overdose and AIDS-related illness are the primary causes of death (UNAIDS GAP Report, 2014).

2.5 Human T-Cell Lymphotropic Virus among intravenous drug users

The highest prevalence of HTLV has been observed among IDUs (Paiva and Casseb, 2014). HTLV-1 is more prevalent among IDUs in Brazil and New York whereas HTLV-2 is more prevalent among IDUs in other locations in North America and in Europe (Paiva and Casseb, 2014). The largest number of HTLV-2 infected persons is in the United States (400,000-500,000) reflecting the confluence of endemic Amerindian, hyper endemic IDUs and secondary sexual spread to the general population (Murphy *et al*.,

2016). This is because HTLV-2 is considered ancestral in the Americas and is transmitted to the general population and IDUs from the indigenous population (Paiva and Casseb, 2015). Needle sharing is hypothesized to be one of the major routes of HTLV-2 transmission in IDUs in the United States and Europe (Zunt *etal*., 2006).

In North American IDUs where HTLV-2 is endemic, seroprevalence rates vary between 8.8% to 17.6% (Jogeda *et al*., 2016). HTLV-1/2 prevalence of 19.1% was reported among IDUs in Argentina (Berini *et al*., 2007). In Europe, HTLV-2 mainly occurs among IDUs with prevalence of up to 15% and HTLV-1 among general population with prevalence of less than 1% (Jogeda *et al*., 2016). HTLV prevalence rates are high in these regions because of the high number of IDUs. A HTLV-1/2 prevalence of 16.7% and 22.9% was recorded among pregnant women and commercial sex workers respectively in South Western Nigeria (Forbi and Odetunde, 2007). Currently, there is no documented study on HTLV-1/2 among IDUs in Kenya and the rest of Africa.

2.6 HIV/HTLV co-infection

Retroviral co-infections with HIV and HTLV-1 or with HIV and HTLV-2 occur with variable frequencies throughout the world with the highest prevalence in large metropolitan areas in the Americas, Europe, and Africa (Beilke, 2012). These co-infections occur frequently in metropolitan areas where injection drug use is a common mode of viral transmission (Beilke, 2012). HIV and HTLV-1 co-infection has been extensively investigated in South America and Africa with prevalence ranging from 0.5 to 10.9% (Gudo *et al.,* 2009; Galetto *et al.,* 2014; Kozlowski *et al.,* 2016; Augusto *et al.,* 2017). Differences in regional endemicity, ethnic origin of the population, risk behaviors and study designs could account for such variability (Futsch *et al.,* 2017). Since HTLV-1 preferentially infects CD4+ T-cells and HTLV-2 has a tropism for CD8+ T-cells, the influence of co-infection on HIV-1 disease progression may be different. The effect of HIV-1/HTLV-1 co-infection on HIV-1 pathogenesis is controversial as soluble factors produced by HTLV-1 infected cells can either enhance or suppress HIV-1 infection (Casoli *et al.,* 2007). Some studies suggest a more severe clinical course with shortened

survival for AIDS patients co-infected with HTLV-1, whereas others demonstrated no detrimental effect of HTLV-1 upon progression of HIV infection (Nasir *et al.,* 2015).

Other studies have shown that there is increased HIV pathogenicity in cases of HIV-1/HTLV-1 co-infection (Gudo *et al.,* 2009; Beilke, 2012; Isache *et al.,* 2016). This is supported by data from *in vitro* studies, which have shown that HTLV-1 *tax* gene products enhance the release of infectious HIV-1 particles. This could be explained by the fact that both viruses preferentially infect CD4+ T cells (Gudo *et al*., 2009). Although the number of documented HIV-1/HTLV-1 co-infected cohorts remains low, it is believed that HTLV-1 worsens HIV-1 infection by accelerating progression to AIDS or increasing mortality. Usually, co-infected patients have significantly higher CD4+ T-cell counts than HIV-1 mono-infected patients and as a result their AIDS diagnosis may be impaired (Futsch *et al.,* 2017). HIV also appears to up-regulate HTLV-1 expression leading to a higher risk of HTLV-1 associated diseases, such as TSP/HAM and adult T-cell leukemia (Isache *et al*., 2016). HTLV-1 induces HIV viral replication and the transition from M- to T-tropic HIV phenotype, which is often a marker of HIV disease progression (Beilke *et al.,* 2007).

On the contrary, other researchers observed a delayed HIV disease progression in HTLV-1 co-infected patients when compared to HIV-1-mono-infected individuals (Beilke *et al.,* 2004; Brites *et al.,* 2005). However, it is generally accepted that HTLV-2 exerts a negative effect on HIV- 1 replication. In fact, several authors have associated HTLV-2 co-infection with a better outcome for HIV-1 positive individuals. It was observed that co-infected patients showed reduced HIV-1 replication presumably due to lower levels of T cell activation (Isache *et al*., 2016). United States of America reported HIV/HTLV-1/2 co-infection prevalence of 16% among IDUs in 2001 (Guimaraes *et al.,* 2001). In Africa, Mozambique reported a HIV/ HTLV-1/2 co-infection prevalence of 1.6% among HIV infected patients (Augusto *et al.,* 2017).

2.7 Risk factors for HIV and HTLV-1/2 infections

2.7.1 Risk factors associated with HIV infection

In Kenya, predictors of HIV in the general population include low income, marital separation, sex work, exposure to sexually transmitted infections (STIs) and gender. High risk sexual practices, exposure to STIs, sexual violence, sharing of needles and syringes as well as poly-substance use are associated with higher rates of HIV infection among IDUs (Budambula *et al.,* 2018). A wide range of socio-economic factors are associated with HIV infection and high-risk injecting behaviors among IDUs. Socio-demographic characteristics such as female gender, marital status, unemployment, low economic status, poor living condition and place of residence influence pattern of risk-behaviors among IDUs (Assari *et al.,* 2015). In addition correlates of sharing injection equipment among IDUs such as type and frequency of drug use, relationship to injection partners, composition of social networks, availability of clean injection equipment, homelessness, fear of police, and laws and policies governing syringe access may also contribute to high-risk injections of IDUs (Latkin *et al.,* 2008).

Drug addiction can elevate the probability of sharing injection equipment or having unprotected sex. Engaging in sex work under the influence of drugs or injecting drugs with clients can compromise one's ability to negotiate safe sex or avoid sharing injection equipment (Strathdee *et al.,* 2011). Drug use and accompanying withdrawal symptoms have also been associated with having unprotected sex in exchange for more money or being more likely to acquiesce to clients' demands to forgo condoms (Strathdee *et al.,* 2013). IDU impairs judgment regarding condom use and other safe sexual practices (Brodish *et al.*, 2012)**.** Women seem to be confronted with even more challenges to cope with drug addiction and social exclusion, and the lack of social support, making them more vulnerable to HIV risk behaviors and harmful injecting practices (Costa *et al.,* 2015).

2.7.2 Risk factors associated with HTLV infection

Injection with a syringe used by another injector (receptive syringe sharing), back loading of injection solution from one syringe to another and multiple sexual partners have been linked to higher rates of HTLV infections (Zunt *et al.,* 2009). Globally, HTLV

seroprevalence rates tend to increase with age, and they are higher in females than males (Nasir *et al.,* 2015). This is because male-to-female transmission is more common than female-to-male transmission, implying that HTLV infected CD8+ lymphocytes in semen may transmit infection more efficiently than infected female genital tract cells (Zunt *et al.,* 2006). High risk sexual behaviors such as unprotected sex, multiple sexual partners, sexual intercourse with IDUs, sexual partners from HTLV-endemic areas and a history of sexually transmitted diseases have been identified as risk factors for HTLV infection (Paiva and Casseb 2014). HTLV-2 infection is endemic among IDUs and is strongly associated with female gender, duration of intravenous drug use, black race and longer duration as an IDU (Zunt *et al.,* 2006). Generally Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infections are risk factors for HTLV infection among IDUs (Caterino de Araujo *et al.,* 2015).

2.7.3 Risk factors associated with HIV/HTLV co-infection

Socio-demographic factors such as; older age (Barcellos *et al.*, 2006), female gender (Augusto *et al.,* 2017), black race, intravenous drug use (Caterino de Araujo *et al.*, 2015) and low level of education (Etzel *et al.,* 2001) are significant risk factors for HIV/HTLV co-infection. Females are more vulnerable to HTLV infection well individuals of low income and black individuals. In addition, females could acquire HTLV infection during unprotected sex in exchange for drugs (Caterino de Araujo *et al.,* 2015). Other risk factors for co-infection include; tattooing, alcohol abuse and history of blood transfusion (Galetto *et al.,* 2014). Smoking, high number of marriages and high number of sexual partners increase the risk of acquiring HTLV among HIV infected patients (He *et al.,* 2016). Infections such as HCV infection and candidiasis in HIV patients also increase risk of acquiring HTLV (Castro Sansores *et al.,* 2015). The strong association between HTLV and HCV is due to the fact that these viruses share the same route of transmission (Caterino de Araujo *et al.,* 2015).

2.8 Human T-Cell Lymphotropic Virus genome

The complex HTLV genome codes for structural proteins; Gag, Pro, Pol (polymerase) and Env from unspliced or singly spliced mRNAs. The *gag* gene encodes three internal

structural proteins: matrix (p19), capsid (p24) and nucleocapsid (p15) (Coffin *et al.*, 1997). The *pol* gene encodes several enzymes including the reverse transcriptase which synthesizes viral DNA, intergrase which integrates viral DNA into the cell and RNAse which degrades RNA template and primer tRNA (Rafatpanah *et al.*, 2006). The *pro* gene encodes the viral protease that acts in late assembly of viral particles to proteolytically process proteins that are encoded by all these genes (Coffin *et al*., 1997). The *env* gene which is approximately 62 KD encodes surface protein (gp45) and transmembrane protein (gp20). The *rex* and *tax* are regulatory genes encoded by an open reading frame (ORF) IV and III respectively (Figure 2.1).

The *tax* which is the transactivator gene increases the rate of viral LTR-mediated transcription and also controls the transcription of numerous cellular genes that are involved in cell proliferation and differentiation, cell cycle control and DNA repair. The *rex* gene acts post transcriptionally by preferentially binding, stabilizing and selectively exporting viral mRNAs that contain introns from the nucleus to the cytoplasm (Kannian and Green, 2010). The genome is capped on either end by a long terminal repeat (LTR) which is the most divergent genomic region of HTLV therefore useful to characterize subtypes (Lindenmeyer *et al.*, 2001).

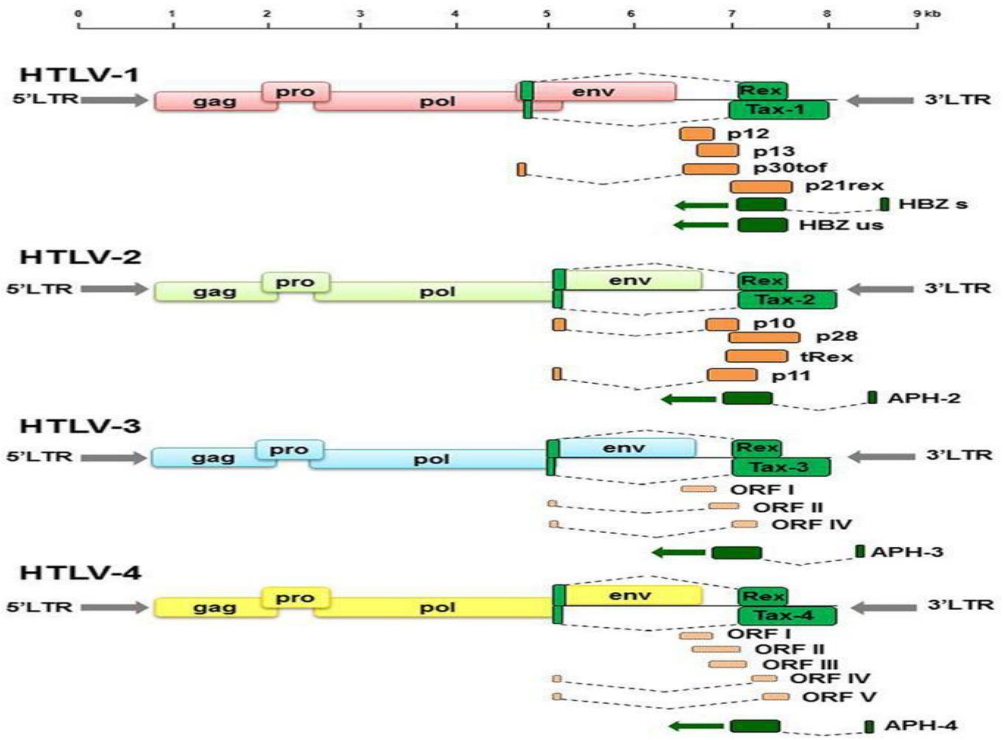


Figure 2.1: HTLV Genome (Romanelli *et al*., 2013).

The *tax* gene is encoded within the Px region of HTLV which is found between the *env* gene and 3'LTR. It is the highly conserved region among all the subtypes. There are four Tax proteins corresponding to the four HTLV types: Tax-1, Tax-2, Tax-3 and Tax-4. Tax-1 causes oncogenesis which is induced by HTLV-1 infection. It also has the capability of immortalizing and transforming human primary $CD4^+$ T cells (Romanelli *et al.*, 2013).

2.9 Human T-Cell Lymphotropic Virus genotypes

There are four genotypes of HTLV: namely; HTLV-I, HTLV-2, HTLV-3 and HTLV-4 based on the LTR of the HTLV genome. HTLV-1/2 are the most common pathogenic genotypes to humans (Beilke, 2012). All the four HTLV genotypes have been shown to originate from pygmy tribes in Africa as a result of zoonotic inter-species transmission from non- human primates to humans (Anyanwu *et al*., 2018). Japan and the African continent records the highest number of HTLV-1 infected persons (Gessain and Cassar,

2012). The most affected areas are East, Central and West Africa (Anyanwu *et al*., 2018). South America has also been considered as a very important focus of HTLV-1 carriers and associated diseases (Gessain and Cassar, 2012). HTLV-1 infection is found largely in migrants or the descendants of migrants from HTLV-1 endemic regions of the world. MTCT via breastfeeding continues to contribute significantly to HTLV-1 persistence (Cook and Taylor, 2014). It is more prevalent among blood donors, pregnant women and patients (ECDC, 2015). HTLV-2 is largely found in indigenous populations in the Americas as well as in IDUs (Ribeiro *et al.*, 2018). HTLV-3 and HTLV-4 have been reported in individuals (either pygmies or Bantus) living in villages or settlements of the rainforest South Cameroon as shown in Figure 2.3 (Mahieux and Gessain, 2011). This population has been shown to have frequent primate exposure risks, including hunting, butchering and keeping primate pets (Mahieux and Gessain, 2011). The presence of a circulating HTLV-1 genotype in Kenya has been documented from the study done among women attending Kenyatta National Hospital (He *et al.*, 2016). Figure 2.2 below shows global distribution of HTLVs.

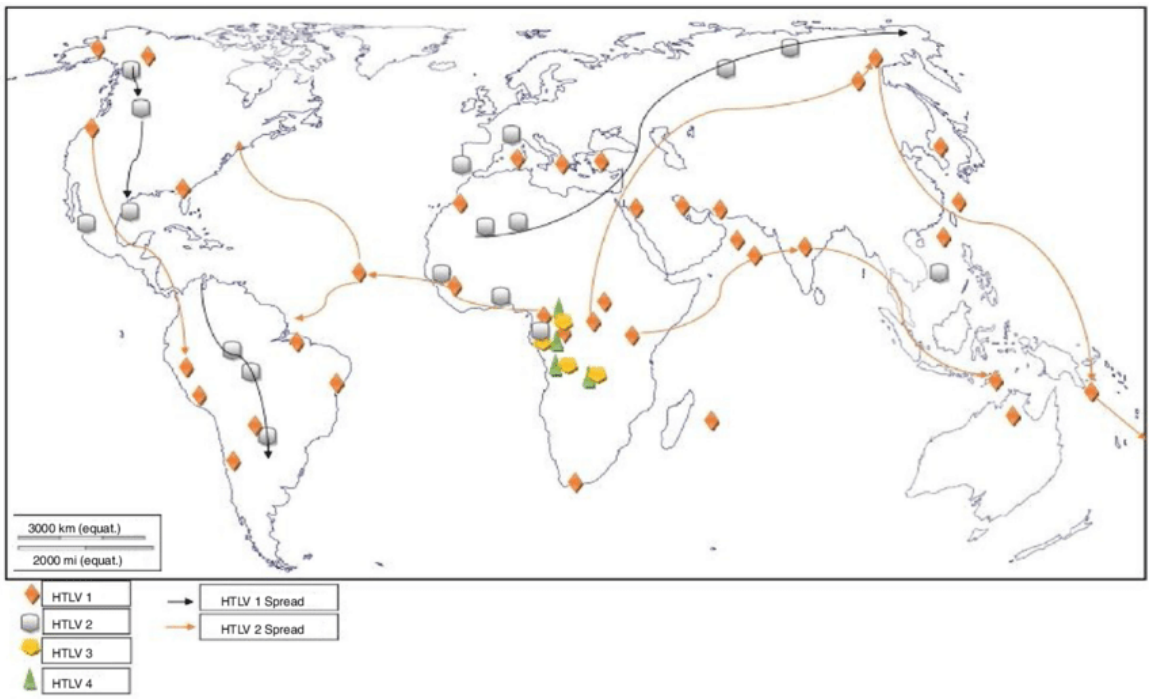


Figure 2.2: Map showing global distribution and spread of HTLVs (Anyanwu *et al*., 2018)

Figure 2.3: Geographical distribution HTLV-3 and HTLV-4 viruses in the African continent. HTLV-3 and HTLV-4 are designated in bold (Mahieux and Gessain, 2011)

2.10 Phylogeny of HTLV variants

T-Lymphotropic virus species are distinguished on the basis of sequence differences and each contains several subtypes (ICTV, 2017). HTLV-1/2 subtypes are clustered according to the geographic region (Tienen *et al*., 2012). There are seven subtypes of HTLV-I which are phylogenetically classified based on geographic distribution and nucleotide diversity of the long terminal repeat (LTR) and env gene sequences; subtype A which is cosmopolitan, subtype B found in central Africa, central Africa/pygmies

subtype C and Australian/Melanesian subtype D. The cosmopolitan subtype A is found in several geographic regions such as Japan, West and North Africa is the most widespread. Subtypes E, F, G are rare and a limited number of strains have been reported in central Africa (Paiva and Casseb, 2015). Subtype A can be divided into five subgroups based on geographical distribution: transcontinental (A), Japanese (B), West African/Caribbean (C), North African (D) and Black Peruvian (E) (Alcantara *et al.*, 2003).

Subtypes of HTLV-1/2 are genetically stable as they have co-existed with humans for thousands of years (Casoli *et al.*, 2007). Molecular epidemiology studies have distinguished four main HTLV-2 subtypes which are geographically dispersed. HTLV-2A and HTLV-2B are the most prevalent among IDUs from urban areas of the Americas and Europe and in the indigenous population of the Americas, with sporadic distribution in Asia and Africa (Magri *et al*., 2013). HTLV-2C variant was detected in the indigenous population of the Brazilian Amazon and in IDUs from urban populations in Brazil (Magri *et al*., 2013). Subtype HTLV-2D has been detected among Efe Bambuti pygmy tribe in the African Congo (Abad *et al*., 2011). HTLV-1 and HTLV-2 are similar, with approximately 60% of their structures based on the same sequence of nucleic acids and 70% on the same sequence of amino acids (Paiva and Casseb, 2015). HTLV-3 shares about 62% identity with HTLV-1 and HTLV-4 shares 62–71% nucleotide similarity with HTLV-1, HTLV-2 and HTLV-3 (Romanelli *et al*., 2013).

2.11 Laboratory detection of Human T-Cell Lymphotropic Virus

Novel triplex quantitative polymerase chain reaction (PCR) allows for simultaneous detection, amplification, quantification and genotyping of two or more target DNA sequences in one amplification reaction of proviral load of HTLV-1,-2 and -3 infections. Routine diagnosis of HTLV infection is based on conventional serological techniques such as enzyme-linked immunosorbent assay (ELISA) and Western blotting. To confirm and/or support serological assays, HTLV PCR such as real-time or quantitative Polymerase Chain Reaction (PCR) is used to confirm the diagnosis and at the same time quantify the HTLV proviral load (Moens *et al*., 2009). Genotyping of HTLV is based on

the LTR region because it is the most variable region of the HTLV genome. For sub typing, fragment of LTR is amplified by nested PCR using primers that target the *tax* region then sequenced (Hlela *et al.*, 2013).

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study area

The study was done in Omari and KANCO drop in centers (Figure 3.1) based in Malindi Sub-County between May 2016 and February 2017. These centers are run by Non-governmental Organizations (NGOs) that provide essential services for harm reduction to IDU population such as; provision of free needles and syringes, HIV counseling and testing, referring HIV positive clients for treatment in HAART centers, HBV screening and treatment, and STI treatment and detoxification programmes. The two centres were ideal for the study because; they had a high number of IDUs (approximately 2000), tourists interact with the local population and could transmit HIV or HTLV if infected to the local population which can lead to introduction of new strains and the drop in centers allowed easy access to the IDUs as they are a hard to reach group.

3.2 Study population

The study population were male and female IDUs, aged 18 years and above who had been recruited into Omari and KANCO drop in centers.

3.3 Study design

This was a descriptive cross-sectional study design involving consenting adult IDUs from Omari and KANCO drop in centers. Consecutive male or female IDUs attending the two drop in centers were recruited using purposive non probability sampling criteria whereby any IDU who walked in to the Drop- in Centre and fit the inclusion criteria was included in the study.

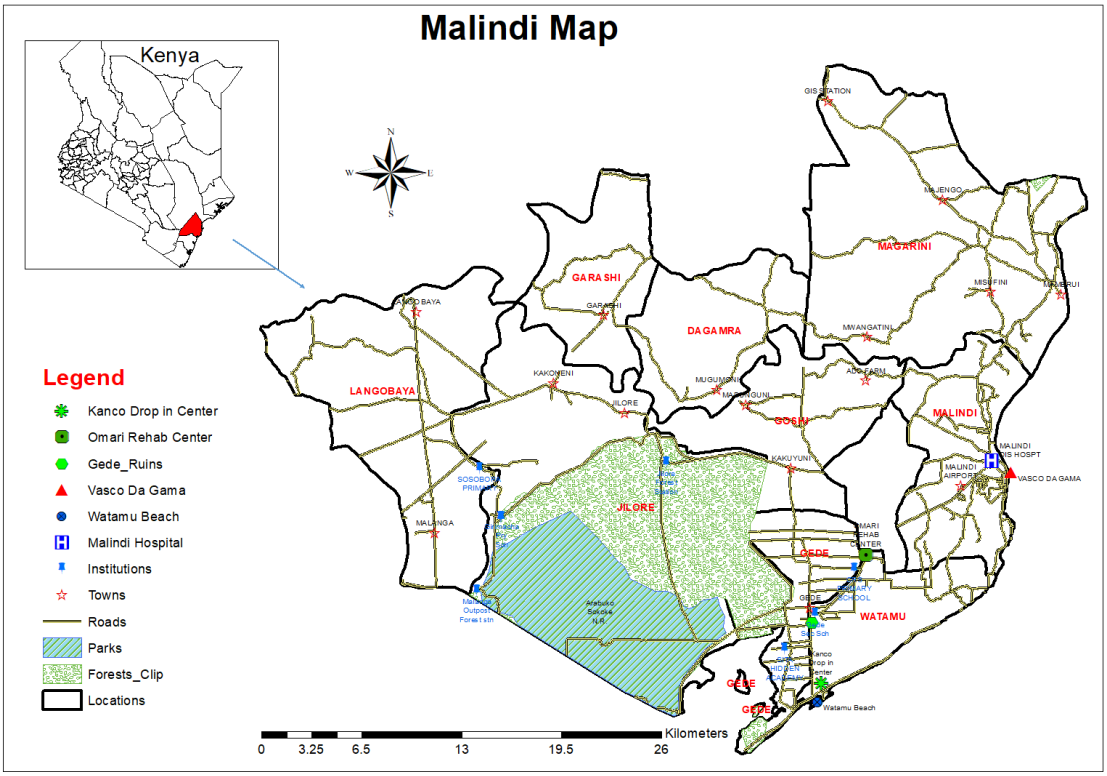


Figure 3.1: Map showing Omari and KANCO drug rehabilitation centers.

3.4 Inclusion criteria

The study included all IDUs attending Omari and KANCO drop in centers, who were 18 years and above who consented to the study.

3.5 Exclusion criteria

The study excluded all IDUs who did not consent to the study. Any uncooperative participant was also excluded.

3.6 Sample size determination

Fischer's exact test formula; (Fishers *et al*., 1998) was used to calculate the sample size using a HIV-HTLV-1 co-infection prevalence of 19.5% (He *et al*., 2016).

$$N = \frac{Z^2 P(1-P)}{D^2}$$

Where,

N= minimum sample size required

Z= Standard deviate for 95% confidence interval

P= Prevalence

D= inverse of 95%

Where D=0.05, P=0.195, 1-P=0.805, Z=1.96

$$\frac{1.96^2 \text{ X}0.195 \text{ X } 0.805 = 249}{0.05^2}$$

Hence a minimum of 249 IDUs were targeted in this study. An additional 102 samples were added thus a total of 351 IDUs were included in the study. This was done so as to increase the chances of obtaining a positive HTLV-1/2 result which has been demonstrated by preliminary studies on HTLV.

3.7 Blood collection

After consenting to participate in the study and filling the structured questionnaires which contained information on socio-demographic characteristics and behavioral risk factors, 5 ml of venous blood was collected for use in serological screening for HIV and HTLV. The collection of blood was done by a trained phlebotomist. A total of 351 blood samples were collected then transported in cold chain from site to Kenya Medical Research Institute in Nairobi. Further processing of samples for HIV and HTLV was carried out at the Center for Virus Research (CVR) in KEMRI at the HIV laboratory.

3.8 Laboratory Procedures

3.8.1 HIV testing

Diagnosis of HIV was done using rapid diagnostic testing algorithmn as per the Kenya National Guidelines (NASCOP, 2016). Determine^{TM} rapid test (Alere Diagnostics, USA) was used as the first rapid test for screening. Using a pipette, 50µl of plasma was added to the sample well. No buffer was added. The results were then read after 20 minutes by observing patient and control lines. A single line in the control line indicated a negative result while two lines both in the patient and control sections indicated a positive result. All cases reactive to the first test were screened again using the second rapid test UniGold^{TM} (Trinity Biotech, Ireland). In case of indeterminate results, HIV-1 Vironostika direct ELISA (Biomerieux Diagnostics, France) was used as a confirmatory test.

3.8.2 HTLV serology

HTLV-1/2 serology was done using IgG HTLV-1/2 ELISA (Cortez Diagnostics,USA). The procedure was as follows: The first 6 wells were labeled as negative control, positive control and blank. Using a pipette, 50µl of HRP-conjugate was added into each well except the blank followed by addition of 50µl of positive control, negative control and specimen into their respective wells. The contents were then mixed by gently tapping the plate and then the plate was covered and incubated at 60^{o}C for 37mins. Washing of each well was done 5 times with diluted wash buffer allowing the microwells to soak for 30-60 seconds. The plate was then turned down onto a blotting paper or paper towel and tapped to remove any remainders. A volume of 50µl of chromogen A and B was then added to all wells and incubated at 37°C for 30 minutes avoiding light. The enzymatic reaction between chromogen solution and Horseradish Peroxidase (HRP) conjugate produced an intense yellow colour in positive samples. The reaction was stopped by adding 50µl of stop solution and absorbance read at 450nm. The cut off value was calculated by averaging the absorbance values of the negative controls and adding 0.18. A test specimen was non-reactive if specimen absorbance was less than the cutoff value and reactive if specimen absorbance was greater than or equal to the cutoff value (HTLV-1/2 ELISA Protocol, Cortez Diagnostics).

3.9 Data management and analysis

All the filled questionnaires and laboratory data sheets were stored in a lockable cabinet in KEMRI and access to it was restricted to the principal investigator. Generated data was entered into Microsoft Excel, in personal computer whose password was only known to the PI, and later transferred to SPSS and STATA for analysis.All data was subsequently transferred to STATA version 15.1 (StataCorp, College Station, TX, USA) for analysis. The prevalence of HIV and HTLV mono and co-infections was calculated by dividing the number of positive cases by the total number of IDUs and then expressed as a percentage. Statistical Package for Social Sciences (SPSS) was used to calculated frequencies for categorical variables. Univariate logistic regression in STATA was used to test for associations between categorical variables in order to evaluate factors that were associated with HTLV/HIV mono and co-infections ($P \leq 0.05$).

4.0 Ethical consideration

Ethical approval for the study was granted by the KEMRI Scientific Steering committee (SSC) and Scientific Ethics Review Unit (SERU) at KEMRI (SSC No. 2914) on 5th February, 2015 (Appendix 1and 2). Approval to conduct the study in Malindi town was granted by the Department of Health Services in Kilifi County (Appendix 3). The participants were informed that, their participation in the study was voluntary and if they declined to participate or withdraw from the study, they would not be denied any service normally available for them. Equally the risks and benefit associated to the participation were adequately explained to them before asked to make decision to take part in the study or not. Consenting participants were recruited and counseled through a seamless collaboration with the local non-governmental Omari and KANCO drop in centers. English or Kiswahili informed consent forms (Appendix 4 and 5) was made available to the IDUs. The consent form was read to the participants by the counselor at recruitment, and upon accepting the participants either signed or used thumb print on the consent form. Upon consenting, the adult IDU participants were asked by a professional counselor to fill a structured questionnaire (Appendix 6). For illiterate IDUs, there were translators working at the centres who explained the informed consent to them in a local language that the participant understood. Information on demographic, risk and

behavioral factors was collected. The participants who were not able to answer questions, either due to the effect of recently injected drugs, or who were uncooperative for any reason, were excluded from the study. The participants were asked to donate 5ml of venous blood to be used for serological screening for HIV and HTLVs. Blood was obtained from participants by a well trained phlebotomist working at the Malindi Sub County hospital. All procedures were done following all biosafety and biosecurity requirements according to the KEMRI Office of Health and Safety guidelines. There was minimal risk of slight discomfort that the participants experienced when blood was drawn from them. It was also ensured that their names were not attached to the blood samples collected, instead an identification number was assigned to label the sample. This was to ensure confidentiality of the test results. Data was stored in password protected computers with passwords and participants were assured that their HIV and HTLV-1/2 infection status would be confidential and communicated back to the clinicians, only for clinical interventions. The participants benefited from this study by knowing their HIV and HTLV infection status which would enable their care clinicians to institute accurate care options. Participants were also given counseling on dangers of IDU.

CHAPTER FOUR

RESULTS

4.1 Prevalence of HIV, HTLV and HIV/HTLV-1/2 co-infection

A total of 351 IDUs were included in this study. The overall prevalence of HIV was 9.7% (34/351) while HTLV-1/2 prevalence was 5.8% (20/351). HIV/HTLV co-infection prevalence was 0.9% (3/34) (Figure 4.1). Male IDUs had higher rates of HIV (28/34), HTLV-1/2 (19/20) and HTLV/HIV infections (3/3) as compared to the female IDUs. IDUs in the 31-40 age group had the highest number of HIV (19/34) and HTLV/HIV (3/3) positive cases. This was in contrast to HTLV-1/2 which had 65% (13/20) of positive cases occurring in the 18-30 age group. Omari Drop-in Centre recorded the highest rates of HIV (26/34), HTLV-1/2 (19/20) and HTLV/HIV infections (2/3) as compared to KANCO (Table 4.1).

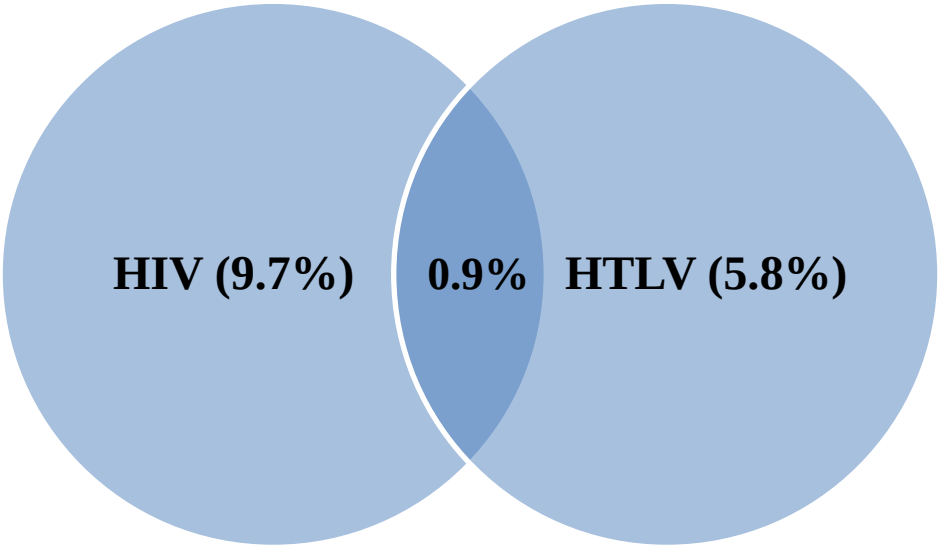


Figure 4.1: Prevalence of HIV, HTLV-1/2 and HIV/HTLV co-infection among IDUs in Omari and KANCO Drop-in centers**.**

Table 4.1: Prevalence of HIV, HTLV-1/2 and HIV/HTLV co-infection among IDUs in Omari and KANCO Drop-in centres across gender, age group and IDU centres

	INFECTION											
	HIV				HTLV-1/2				HIV/HTLV			
Variable	**Pos**	**P (%)**	**Neg**	**P (%)**	**Pos**	**P (%)**	**Neg**	**P (%)**	**Pos**	**P (%)**	**Neg**	**P (%)**
Gender												
Male	28	8.9	287	91.1	19	6	296	94	3	1	312	99
Female	6	16.8	30	83.2	1	2.8	35	97.2	0	0	36	100
Age group												
18-30	12	8.5	130	91.5	13	9.2	129	0.8	0	0	142	100
31-40	19	11.2	151	88.8	7	4.2	163	95.8	3	1.8	167	98.2
Above 41	3	7.7	36	92.3	0	0	39	100	0	0	39	100
Centres												
Omari	26	10.4	223	89.6	19	7.6	230	92.4	2	0.8	247	99.2
KANCO	8	7.8	94	92.2	1	1	101	99	1	1	101	99
Total	**34**		**317**		**20**		**331**		**3**		**348**	

P: Prevalence; Pos: Positive; Neg: Negative

4.2 Socio-demographic profiles of the IDUs

This study recruited 351 IDUs who were aged between 18 and 72 years with a mean age of 33.1 years, median age of 32 years and a range of 54. Variables analysed included Demographic (Gender, level of education, age, employment status, resident town and marital status), injection (needle sharing, blood flushing, duration and frequency of injection) and sexually related factors (sexual identity, number of sexual partners, condom use and previous history of sexually transmitted infections (STIs) as detailed in Table 4.2.

Table 4.2: Socio-demographic, injection and sexual factors of IDUs in Omari and KANCO Drop-in Centres in 2016/2017

Variable	N	%	Variable	N	%
Gender			**Frequncy of injecting**		
Male	315	89.8	Daily	337	96
Female	36	10.2	Infrequent	4	1.2
Educational Level			Not injected in the last 30 days	10	2.8
Primary	286	81.5	**Frequncy of daily injections**		
Secondary	47	13.4	1-3 times	307	87.5
Tertiary	1	0.3	4-6 times	44	12.5
NonFormal	17	4.8	**Needle sharing**		
Age			Yes	65	18.5
mean age	33.10		No	286	81.5
Standard Deviation	7		**Blood flushing**		
18-30	142	40.5	Yes	6	1.7
31-40	170	48.4	No	345	98.3
Above 41	39	11.1	**Sexual identity**		
Employment status			Homosexual	4	1.1
Employed	29	8.3	Heterosexual	331	94.3
Not employed	322	91.7	Bisexual	16	4.6
Centres			**Number of sexual partners**		
Omari	249	70.9	None	12	3.4
Kanco	102	29.1	1	61	17.4
Marital status			2to3	87	24.8
Single	243	69.2	>4	190	57.4
Married	64	18.2	**Condom use in vaginal sex**		
Divorced	34	9.7	Yes	107	30.5
Cohabiting	10	2.8	No	29	8.3
Homeless			Sometimes	215	61.3
Yes	62	17.7	**Condom use anal sex**		
No	289	82.3	Yes	6	1.7
Jail in past one year			No	36	10.3
Yes	122	34.8	Sometimes	125	35.6
No	229	65.2	Not applicable	184	52.7
Tattoo			**STIs**		
Yes	23	6.6	Gonorrhea and syphillis	66	18.8
No	328	93.4	Hepatitis B	17	4.8
Travelled out of the Country			UTIs	3	0.9
Yes	21	6.0	Herpes	6	1.7
No	330	94.0	None	259	73.8
Years of injecting					
0-2 yrs	56	16.0			
3-5 yrs	160	45.6			
6-9 yrs	54	15.4			
Above 10 yrs	81	23.0			

N - Total Number of IDUs; **%**:Percentage

4.3 Association of HIV Infection with socio-demographic, injection and sexual factors

4.3.1 Association of HIV with demographic factors

Education levels were not significant in HIV infection however IDUs who attained primary level of education had the highest number of HIV positive cases (27/34) as compared to secondary level (4/34) and non formal education (1/34). No positive case was reported in the tertiary level. Employment and HIV infection were not significantly associated (OR=0.7, p=0.616). However, unemployed IDUs had the highest number of HIV positive cases (32/34) as compared to employed IDUs who had only two positive cases (Table 4.3).

Single marital status (OR= 0.6. p=0.467), being married (OR= 0.3, p=0.138) and being divorced (OR=0.5, p=0.468) showed no significant association with HIV infection. Single IDUs had the highest number of HIV positive cases (26/34). There was a significant association between being homeless and HIV infection (OR=2.5, p=0.009). Homeless IDUs had the highest number of HIV cases (21/34) and were2.5 times more likely to contract HIV as compared to IDUs with a home (12/22). Association of all demographic factors with HIV infection using logistic regression is summarized in Table 4.3.

Table 4.3: Demographic, Injection and Sexual factors associated with HIV/HTLV infections among IDUs in Malindi in 2016/2017

	HIV infection				HTLV-1/2 infection			
Risk factors	**n**	**%**	**OR**	**p value**	**n**	**%**	**OR**	**p value**
Gender								
Male	28	82.4	0.5	0.162	19	95	2.2	0.450
Female	6	17.6	R		1	5	R	
Education Level								
Primary	27	79.4	0.5	0.304	18	90	1.1	0.948
Secondary	4	11.8	0.5	0.339	1	5	0.4	0.472
Tertiary	0	0	0	0.989	0	0	0	0.992
NonFormal	1	9.8	R		1	5	R	
Age								
18-30	12	35.3	1.1	0.084	13	65	0	0.987
31-40	19	55.9	1.1	0.548	7	35	0	0.987
Above 41	3	8.8	R		0	0	R	
Employment status								
Employed	2	5.9	0.7	0.616	1	5	0.5	0.601
Not employed	32	94.1	R		19	95	R	
Centre								
Omari	26	76.5	1.8	0.579	19	95	8.0	0.043
KANCO	8	23.5	R		1	5	R	
Marital status								
Single	26	76.5	0.6	0.467	14	70	0	0.993
Married	3	8.8	0.3	0.138	2	10	0	0.993
Divorced	4	11.8	0.5	0.468	4	20	0	0.992
Cohabiting	1	29	R		0	0	R	
Homeless								
Yes	22	64.7	2.5	**0.009**	0	0	0	0.993
No	12	35.3	R		20	100	R	
Jail in past one year								
Yes	17	50	1.7	0.098	5	25	0.6	0.304
No	17	50	R		15	75	R	
Tattoo								
Yes	1	2.9	0.4	0.408	1	5	0.8	0.78
No	33	97.1	R		19	95	R	
Travelled out of the Country								
Yes	3	8.8	1.2	0.753	2	10	1.4	0.659
No	31	91.2	R		18	90	R	

Risk factors	n	%	OR	p value	n	%	OR	p value
Years of injecting								
0-2 yrs	4	11.8	0.6	0.355	2	10	1.5	0.712
3-5 yrs	17	50	0.9	0.706	11	55	2.8	0.183
6-9 yrs	3	8.8	0.5	0.225	5	25	3.8	0.114
Above 10 yrs	10	29.4	R		2	10	R	
Frequncy of injecting								
Daily	31	91.2	0.3	0.051	20	100	0	0.991
Infrequent	0	0	0	0.996	0	0	0	1.000
Not injected in last 30 days	3	8.8	R		0	0	R	
Frequncy of daily injections								
1-3 times	29	85.3	0.8	0.663	19	95	2.6	0.342
4-6 times	5	14.7	R		1	5	R	
Needle sharing								
Yes	26	67.6	2.1	**0.042**	2	10	0.5	0.337
No	8	32.4	R		18	90	R	
Blood flushing								
Yes	0	0	0	0.999	1	5	3	0.280
No	34	100	R		19	95	R	
Sexual identity								
Homosexual	1	2.4	1.3	0.803	0	0	0	0.991
Heterosexual	30	88.2	0.4	0.23	18	90	0.4	0.264
Bisexual	3	8.8	R		2	10	R	
Number of sexual partners								
None	1	3	0	0.997	0	0	0	0.988
1	2	5.9	0.6	0.442	1	5	0.6	0.446
2to3	12	35.3	1.5	0.280	6	30	1.6	0.350
>4	19	55.8	R		13	65	R	
Condom use in vaginal sex								
Yes	14	41.2	1.5	0.265	4	20	0.5	0.218
No	1	3	0.4	0.359	16	80	0	1.000
Sometimes	19	55.8	R		0	0	R	
Condom use anal sex								
Yes	0	0	1.5	1.000	0	0	0	0.992
No	4	11.8	0.4	0.96	10	50	3.1	**0.029**
Sometimes	10	29.4	0	0.502	6	30	0.6	0.414
Not applicable	20	58.8	R		4	20	R	
STIs								
Gonorrhea and syphillis	20	58.8	3.7	**0.000**	16	80	3	**0.021**
Hepatitis B	1	3	0.9	0.924	1	5	1.4	0.747
UTIs	0	0	0	0.995	0	0	0	0.995
Herpes	0	0	0	0.994	0	0	0	0.994
None	13	38.2	R		3	15	R	

%-percentage; N-total numberof IDUs; n:number of positive cases

OR:Odds Ratio, R:Reference

4.3.2 Association of HIV infection with injection and sexually related factors

There was a significant association between needle sharing (OR=2.1, *p*=0.042) and HIV infection. Those who shared needles had a higher number of HIV positive cases (26/34) as compared to those who did not share needles (8/34). There was no significant difference between HIV infection and number of sexual partners however IDUs who had more than four partners in the past six months had the highest number of HIV positive cases (19/34) as compared to those with between two to three partners (12/34). Those with one partner (2/34) and no partner (1/34) had the least positive cases. IDUs with two to three partners were 1.5 times more at risk for HIV as compared to those with one partner who were 0.6 times more at risk (Table 4.3).

There was a significant association between HIV infection and previous history of gonorrhea and syphilis infection in the past six months (OR=3.7, *p*=0.000). HBV (OR=0.9, *p*=0.924), UTIs (OR=0, *p*=0.995) and herpes (OR=0, *p*=0.994) infections had no significant association with HIV infection. IDUs who reported previous history gonorrhea and syphilis had the highest number of HIV cases (20/34) and were also 3.7 times more at risk for HIV infection as compared to the other infections. No cases were reported in cases of UTIs and Herpes infections. Association of all injection and sexually related factors with HIV infection using logistic regression is summarized in Table 4.3.

4.4 Association of HTLV-1/2 Infection with socio-demographic, injection and sexual factors

4.4.1 Association of HTLV-1/2 with demographic factors

Most (95%) of the HIV positive cases were male. However, the association between male gender and HTLV-1/2 infection was not significant (OR=2.2, *p*=0.450). Male IDUs were twice more likely to contract risk HTLV-1/2 infection as compared to females (Table 4.3). The level of education was not significant to HTLV-1/2infection; primary level (OR=1.1, *p*=0.948), secondary level (OR=0.4, *p*=0.472) and tertiary level (OR=0, *p*=0.992). IDUs who had attained primary level of education had the highest number of HTLV positive cases (18/20) as compared to secondary level and non formal education.

No positive case was reported in the tertiary level. Employment showed no significant association with HTLV-1/2 infection (OR=0.5, *p*=0.601). Unemployed IDUs had the highest number of HTLV-1/2 positive cases (19/20) as compared to employed IDUs who had one positive case. There was a significant difference between HTLV-1/2 infection and IDUs from Omari Drop-in centre town (OR=7.9, *p*=0.043).IDUs from Omari had the highest number of HTLV positive cases (19/20) and were also eight times more at risk for HTLV-1/2 infections (Table 4.3).

4.4.2 Association of HTLV-1/2 infection with injection and sexually related factors

The IDUs who had more than four partners in the past six months had the highest number of HTLV positive cases (13/20) as compared to those with between two to three partners (6/20). IDUs with one partner had one positive case while there were no HTLV cases in IDUs who had no sexual partner. Those who did not use condoms during vaginal sex had the highest number of HTLV positive cases (16/20) as compared to those who used condoms (4/20). The association between HTLV-1/2 infection and IDUs who did not use condoms during anal sex was significant (OR=3.1, *p*=0.029). There was a significant association between HTLV-1/2 infection and previous history of gonorrhea and syphilis infection in the past six months (OR=3.0, *p*=0.021). HBV (OR=1.4, *p*=0.747), UTIs (OR=0, *p*=0.995) and herpes (OR=0, *p*=0.994) had no significant association with HTLV-1/2 infection. IDUs who reported previous history gonorrhea and syphilis had the highest number of HTLV-1/2 cases (16/20) and were also 3 times more at risk for HTLV-1/2 infection as compared to those with HBV infection as they were 1.4 times at risk. Those who had no previous history of STIs also had 3 positive cases (13/34). No cases were reported in cases of UTIs and herpes infections. Association of all injection and sexually related factors with HTLV-1/2 infection using logistic regression is summarized in Table 4.3.

4.5 Association of HIV/HTLV co-infection with socio demographic, injection and sexual factors.

After univariate analysis using logistic regression, there was no significant association between HIV/HTLV co-infection with all the demographic, injection and sexually related

factors at p value of less than 0.05. The three IDUS who were HIV/HTLV co-infected were all male, unemployed, single and homeless. In addition, two out of the three were from Omari injected daily, had been in jail for the past one year and had more than four sexual partners. Interestingly, two of the positive cases practiced safe sex, did not share needles and had no previous history of sexually transmitted infection.

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

This is the first documented study to be done in Kenya on HIV and HTLV co-infection among IDUs in Malindi, Kenya. In this study, HIV prevalence of 9.7% was reported among the IDUs. This prevalence was higher than the documented Kilifi County HIV prevalence of 4.5% in the general population (NACC, 2016). This finding of a higher prevalence was however expected since as opposed to the previous study which was within the general population as this study targeted a high risk population. This could be attributed to risk factors such as needle sharing, homelessness and previous history of gonorrhea and syphilis which were found to be significant in this group. However the prevalence was slightly lower as compared to a similar study done which recorded a cumulative prevalence of 11.1% among drug users from Nairobi, Mombasa and Kisumu cities (Oyaro *et al.,* 2018). The lower prevalence of HIV in the present study may be explained by the harm reduction measures set up by the KANCO and Omari Drop in centers over the last ten years such as; provision of free needles and syringes, provision of condoms, rehabilitation HIV testing and treatment and educational programmes to create awareness.

The HTLV-1/2 prevalence of 5.8% was reported among the IDUs in this study. Data on HTLV in the general population is scanty since there is only one other study reported in the general population in Kenya. The prevalence of 5.8% was lower when compared to a recent but not similar study done in women attending Kenyatta National Hospital which documented a HTLV-1prevalence of 11.6% (He *et al*., 2016). However the prevalence in this study is higher as compared to studies done among IDUs in other countries (Prasetyo *et al.*, 2013; Jogeda *et al.*, 2016). The higher prevalence could be attributed to risk factors such as low level of education, injecting daily, unprotected sex and sexually transmitted infections as they were observed in majority of the positive cases.

HIV/HTLV co-infection prevalence of 0.9% was recorded in the current study. This is lower as compared to the study done among HIV positive women in Nairobi, although not a similar study that documented a HIV/HTLV-1 co-infection prevalence of 19.5% (He *et al.,* 2016). However it was higher than the prevalence recorded from several studies done among HIV positive patients (Augusto *et al.,* 2017; Campos *et al.,* 2017) which reported co-infection prevalence of 1.55% and 4.2% respectively. HIV/HTLV-1 co-infection is of significance as it worsens HIV infection by accelerating progression to AIDS or increasing mortality. In addition, in comparison to HIV-1 mono-infected individuals, most co-infected individuals are more likely to suffer from myelopathy, thrombocytopenia, bronchitis, urinary tract infection or opportunistic infection, regardless of the age, ethnicity or CD4+ T-cells. Co-infection with HIV also has a worsening impact of HTLV-1 on the development of ATL or of TSP/HAM (Futsch *et al.,* 2017).

Age was not significant to HIV infection. IDUs in the age group 31-40 had higher rates of HIV infection as compared to those in the 18-30 age group. This finding was consistent with a similar study done among drug users at the Kenyan coast which suggested that increasing exposure to sexual activity and injection risk practices increases with age among IDUs (Budambula *et al.,* 2018). Homelessness was a significant risk factor for HIV among the IDUs. This is in agreement with previous studies by (Kennedy *et al.,* 2018; Santa Maria *et al.,* 2018). Homeless IDUs in this study had higher rates of HIV infection as compared to those in a home set up. Generally, homeless adults are 6–12 times more likely to become infected with HIV than housed ones, with prevalence rates as high as 13%. Homeless adults tend to have earlier sexual debut, are more likely to have multiple partners, trade sex for food, shelter, money or substances, use substances before sex and are less likely to use a condom or contraception than the stably housed ones. This places homeless adults at a greater risk of contracting HIV or HIV-related illnesses (Santa Maria *et al.,* 2018).

Although employment status was not significantly linked to HIV infection, it was noted that IDUs who were unemployed had the highest rates of infection as compared to those that were employed. This finding was comparable to the study by Budambula *et al.*

(2018) which found a significant association. There is a direct relationship between the HIV prevalence and unemployment as it may lead to engagement in high risk sexual behaviours such as sex for money, multiple sexual partners and unprotected sex that expose them and others to the virus (Sinkamba and Moseka, 2016).

Needle sharing was significantly associated with HIV infection. This finding was corroborated by several studies (Ngonga *et al.,* 2015; Tavitian-Exley *et al.,* 2018). In the injection substance using population, sharing of needles and syringes are associated with higher rates of HIV infection (Budambula *et al.,* 2018). The risk for getting or transmitting HIV is very high if an HIV-negative person uses injection equipment that someone living with HIV has used. This is because the needles may have blood in them, and blood can carry HIV. HIV can survive in a used needle for up to 42 days, depending on temperature and other factors (CDC, 2018).

Frequency of injecting drugs was not significant to HIV infection. This study noted that IDUs who injected daily had the highest rates of HIV infection as compared to those that did not frequently and those who had not injected in the last 30 days. This was an unexpected finding. In contrast, this finding was found significant in other studies (Broz *et al.,* 2018; Tavitian-Exley *et al.,* 2018). This finding could be explained by the fact that IDUs who inject daily are more prone to engage in high risk behaviour such as needle sharing and unprotected sex as compared to the other two groups.

Previous history of gonorrhea and syphilis was also significantly associated to HIV as infected IDUs had higher rates of HIV infection as compared to those with Herpes, UTIS or HBV and HCV infections. This finding was consistent with several studies (Budambula *et al.,* 2018; Novak *et al.,* 2018). Syphilis infection increases HIV viral load and decreases CD4 in HIV-infected persons, thereby increasing the chance of transmitting the virus (Landovitz *et al.,* 2018). Gonorrhea and syphilis are associated with a 2.5 fold increase of acquiring HIV. This is through decreased epithelial barrier integrity, chronic inflammation, and increased numbers of target cells for HIV in the genital tract (Reda *et al.,* 2018).

HTLV detected significant associations with IDUs from Omari Drop-in Centre. Interestingly, IDUs from Omari centre also had the highest rates of HIV infection and HTLV/HTLV co-infection as compared to those from KANCO. This finding could be explained by the fact that majority of the IDUs were from centre as compared to KANCO. A previous study reported a high prevalence of HIV (87.5%) and HCV (16.4%) among IDUs in Malindi Sub-County (Mwatelah *et al.,* 2015). A similar study reported a high HBV/HIV co-infection prevalence of 14.3% (Kerosi *et al.,* 2015) and HIV prevalence of 53.1% (Ng'ong'a *et al.,* 2015). There is widespread sexual tourism in Malindi sub-county where tourists especially from Italy, Germany and other European countries frequent (Ng'ong'a *et al.,* 2015). A plausible explanation could be since KANCO provides free needle and exchange program unlike Omari which assists in reducing risk of transmission and thus lower prevalence. There is a possibility of HTLV transmission from infected tourists to IDUs as a result of sex in exchange for money and drugs.

Age was not a significant factor to HTLV-1/2 infection. The present study showed that HTLV prevalence decreased with an increase in age suggesting that younger IDUs had higher rates of HTLV infection. This was consistent with a previous similar study (Berini *et al.,* 2007). In contrast, similar previous studies indicated that older age is significant for HTLV infection among IDUs (Zunt *et al.,* 2006; Blas *et al.,* 2013). This could be explained by the fact that younger IDUs are more likely to engage in high risk practices such as needle sharing, having multiple sexual partners and practicing unsafe sex, all of which increase the risk of acquiring HTLV (Zunt *et al.,* 2006).

HTLV was not significantly associated with level of education. This study observed that IDUs with the highest rates of HTLV infection were found in the primary level as compared to secondary and tertiary level. In contrast, other studies found a significant association with low level of education (Berini *et al.,* 2007; Hedayati-Moghaddam *et al.,* 2015). It seems that low education level reduces access to health information and may increase the prevalence of risk factors related to HTLV-1 infection such as risky sexual behaviors or contact with contaminated blood through tattooing or needle sharing

(Hedayati-Moghaddam *et al.,* 2015). Interestingly, sharing needles was not significantly associated with HTLV infection in this study. This is probably because IDUs with the highest prevalence of infection also reported the lowest rate of injection equipment sharing. This finding is in contrast with another study which found a significant association between needle sharing and HTLV (Rohwani-Rahbar *et al.,* 2004).

In the present study, HTLV infection was not significantly associated with having multiple sexual partners. However this study showed that IDUs with more than four sexual partners had the highest rates of infection as compared to those with less than three partners. This finding is supported by studies (Vahidnia *et al.,* 2015; He *et al.* 2016) which reported a significant association between having multiple sexual partners and HTLV infection. Higher number of sexual partners increases the risk of sexual transmission of HTLV-1 (Nunes *et al.,* 2017). Unprotected anal sex was a significant risk factor for HTLV infection in the present study. This finding was consistent with the study by Zunt *et al*. (2006). Unprotected anal intercourse has been associated with a higher risk of transmission than vaginal sex. Disruption of the normal rectal architecture as rectal secretion, fissures and hemorrhoids caused by anal sex increase the risk of acquiring HTLV (Zunt *et al.,* 2006).

Previous history of gonorrhea and syphilis was also significantly associated with HTLV as infected IDUs had higher rates of infection as compared to those with herpes, UTIS or HBV and HCV infections. This finding was consistent with several studies (Zunt *et al*., 2006; Paiva and Casseb, 2014; Nunes *et al.,* 2017). Ulcerative STIs such as gonorrhea and syphilis cause lesions that result in the breakdown of mucosal integrity and recruit activated target cells, including an enriched population of cells that carry CD4 cell receptors. This result in the recruitment of inflammatory cells and potentiates HTLV acquisition and transmission (Paiva and Casseb, 2014).

5.2 Study limitations

This study had a number of limitations. Since this study was conducted only in Omari and KANCO Drop-in Centres, the findings may not be representative of the other Kenyan

regions. The study was mainly carried out in a cohort of IDUs hence the results of this study remain only limited to HIV and HTLV infections within the IDU population in Omari and KANCO drop in centres and not in the general population.

5.3 Conclusion

This study concludes that:

1. The prevalence of HIV, HTLV-1/2 and HIV/HTLV co-infection was 9.7%, 5.8% and 0.9% respectively.
2. Homelessness, needle sharing as well as gonorrhea and syphilis infections are significant risk factors for HIV transmission among IDUs.
3. Omari Drop- in centre, unprotected anal sex and gonorrhea and syphilis infections are significant risk factors for HTLV transmission among IDUs.

5.4 Recommendations

This study recommends the following**:**

1. Regular screening of HTLV should be introduced in IDU clinics so as to assist in continuous monitoring of estimates.
2. Harm reduction measures such as provision of free needles and syringes, provision of condoms and STI testing coupled with educational programmes should be established in IDU drop-in centers so as to prevent and control HTLV/HIV transmission caused by high risk injection and sexual practices.
3. Further research should done on different IDU populations so as to determine prevalence estimates. This will assist in continuous monitoring and prevention of the infections.

REFERENCES

Abad, M., Dronda, F., Dominguez, E., Moreno, S. and Vallejo, A. (2011). HTLV-2b Among HIV Type 1-Coinfected. *Journal of AIDS Research and Human Retroviruses*, *27* (5), 579–583

Alere Diagnostics, Determine Rapid test protocol

Anyanwu, N. C. J., Ella, E. E., Ohwofasa, A. and Aminu, M. (2018). Re-emergence of Human T-Lymphotropic viruses in West Africa. *Brazilian journal of infectious diseases. 22,* 224-234

Augusto, A., Augusto, O., Taquimo, A., Nhachigule, C., Siyawadya, N., Tembe, N., Bhatt, N., Mbofana, F. and Gudo, E. S. (2017). First description of HTLV-1/2 seroprevalence in HIV-infected inmates in Mozambique. *Journal of Medical Virology*, *89* (8), 1498-1502

Alcantara, L. C. J., Shindo, N., Dooren, S. V., Salemi, M., Costa, M. C. R., Kashima, S., Vandamme, A. M. and Galvao-Castro, B. (2003). Brazilian HTLV Type 2a Strains from Intravenous Drug Users (IDUs) appear to have originated from two Sources : Brazilian Amerindians and European / North American IDUs. *Journal of AIDS Research and Human Retroviruses, 19,* 519–523

Assari, S., Ahmadi, K. and Rezazade, M. (2015). Socio-economic status determines risk of receptive syringe sharing behaviors among Iranian drug injectors; a national study. *Frontiers in Psychiatry*, *5,* 194

Barcellos, N. T., Fuchs, S. C., Mondini, L. G. and Murphy, E. L. (2006). Human T Lymphotropic Virus Type I/II Infection: Prevalence and Risk Factors in Individuals Testing for HIV in Counseling Centers From Southern Brazil. *Journal of Sexually Transmitted Diseases, 33* (5), 302–306

Beilke, M. A., Theall, K. P., O'Brien, M., Clayton, J. L., Benjamin, S. M., Winsor E. L. and Kissinger, P. J. (2004). Clinical outcomes and disease progression among patients coinfected with HIV and human T lymphotropic virus types 1 and 2. *Journal of Clinical Infectious Diseases, 39,* 256–263

Beilke, M. A., Dorge, V. L. T., Sirois, M., Bhuiyan, A., Murphy, E. L., Walls, J. M., Fagan, R., Winsor, E. L. and Kissinger, P. J. (2007). Relationship between Human T Lymphotropic Virus (HTLV) Type 1/2 Viral Burden and Clinical and Treatment Parameters among Patients with HIV Type 1 and HTLV-1/2 Co-infection. *Journal of Infectious Diseases*, *44* (9), 1229–1234

Beilke, M. A. (2012). Retroviral Coinfections : HIV and HTLV : Taking Stock of More Than a Quarter Century of Research. *Journal of AIDS Research and Human Retroviruses*, *28* (2), 139–147

Berini, C. A., Pando, M. A., Bautista, C. T., Eirin, M. E., Martinez-peralta, L., Weissenbacher, M. and Biglione, M. M. (2007). HTLV-1 / 2 Among High-Risk Groups in Argentina : Molecular Diagnosis and Prevalence of Different Sexual Transmitted Infections. *Journal of Medical Virology, 79,* 1914–1920

Biomerieux Diagnostics, France, Vironostika® HIV-1 Plus O Microelisa System

Blas, M., Alva, I. E., Garcı´a, P. L., Ca´rcamo, C., Montano, S. M., Mori, N., Mun˜ ante, R. and Zunt, J. R. (2013). High Prevalence of Human T-Lymphotropic Virus Infection in Indigenous Women from the Peruvian Amazon. *PloS One*, 8, e73978

Brites, C., Oliveira, A. S., Netto, E. M. (2005). Co-infection with HIV and human T lymphotropic virus type 1: what is the real impact on HIV disease? *Journal of Clinical Infectious Diseases*, *40* (2), 329–330

Brodish, P., Singh, K., Rinyuri, A., Njeru, C., Kingola, N., Mureithi, P., Sambisa, W. and Weir, S. (2012). Evidence of high-risk sexual behaviors among injection drug users in the Kenya Place Study. *Journal of Drug and Alcohol Dependence, 119,* 138–141

Broz, D., Zibbell, J., Foote, C., Roseberry, J. C., Patela, M. R., Conrad, C., Chapman, E., Peters, P. J., Needle, R., McAlister, C. and Duwve, J. M. (2018). Multiple injections per injection episode: High-risk injection practice among people who

injected pills during the 2015 HIV outbreak in Indiana. *International Journal of Drug Policy*, 52: 97–101

Budambula, V., Matoka, C., Ouma, J., Ahmed, A. A., M. F. and Were, T. (2018). Socio demographic and sexual practices associated with HIV infection in Kenyan injection and non-injection drug users. *Biomedcentral Public Health*, *18* (1), 193

Campos, K. R., Gonçalves, M. G., Costa, N. A. and Caterino-de-Araujo, A. (2017). Comparative performances of serologic and molecular assays for detecting human T lymphotropic virus type 1 and type 2 (HTLV-1 and HTLV-2) in patients infected with human immunodeficiency virus type 1 (HIV-1). *Brazilian Journal of Infectious diseases*, *21*, 297-305

Casoli C., Pilotti E., Bertazzoni U. (2007). Molecular and cellular interactions of HIV-1/HTLV co-infection and impact on AIDS progression. *Aids Review Journal, 9* (3), 140-149

Castro-Sansores, C. J., Santos-Rivero, A., Lara-Perera, D. M., Alonso-Salomon, G. and Gongora-Biach, R. A. (2006). Co-infection by the human T-cell lymphotropic virus type II in patients infected by the human immunodeficiency virus in Yucatan, Mexico. *Journal of Archives of Medical Research*, *37*, 365-369

Caterino de Araujo, A., Claudio T. S., Goncalves, M. G., Campos, K. R., Magri, M. C., Alencar, W. K. and the Group of Surveillance and Diagnosis of HTLV of Sao Paulo (GSuDiHTLV-SP). (2015). Short Communication :Current Prevalence and Risk Factors Associated with Human T Lymphotropic Virus Type 1and Human T Lymphotropic Virus Type 2 Infections Among HIV/AIDS Patients in Sao Paulo, Brazil. *Journal of AIDS Research and Human Retroviruses*, *31* (5), 543–549

Center of Disease Control (CDC) (2018). Report on Injection Drug Use and HIV Risk.

Ciminale, V., Rende, F., Bertazzoni, U.and Romanelli, M. G. (2014). HTLV-1 and HTLV-2: highly similar viruses with distinct oncogenic properties. *Frontiers in Microbiology, 5*, 398

Coffin, J.M., Hughes, S. H. and Varmus, H. E. (1997). *Retroviruses*. New York: Cold Spring Harbor Laboratory Press.

Cook, L. B. M. and Taylor, G. P. (2014). HTLV-1 and HTLV-2 Prevalence in the United States. *The Journal of Infectious Diseases, 209* (4), 486–487

Costa, E. C. V., Paiva, C. A., Ferreira, D. and Santos, S. (2015). Psychosocial and psychopathological predictors of HIV-risk injecting behavior among drug users in Portugal. *Análise Psicológica, 4*, 391-406

Cortez Diagnostics, HTLV-1/2 ELISA protocol

Degenhardt, L. and Hall, W. (2012). Extent of illicit drug use and dependence, and their contribution to the global burden of disease. *Lancet , 379* (9810), 55–70

Etzel, A., Shibata, G. Y.,Rozman M,Jorge, M.L.,Damas, C. D. and Segurado, A. A. (2001). HTLV-1 and HTLV-2 infections in HIV-infected individuals from Santos, Brazil: seroprevalence and risk factors. *Journal of Acquired Immune Deficiency Syndrome, 26*, 185-190

European Center of Disease Control (ECDC). (2015). Technical Report on Geographical distribution of areas with a high prevalence of HTLV-1 infection

Forbi, J. C. and Odetunde, A. B. (2007). Human T-cell lymphotropic virus in a population of pregnant women and commercial sex workers in South Western Nigeria. *African Health Sciences, 7*(3), 129-132

Fishers T.R., Lee K.Y., Berndt H., Benitez J.A. and M. Norton. (1998). Hydrology and Chemistry of the Choptank, River basin in theChesapeake Bay drainage. *Water Air and Soil Pollution, 105*(1-2), 387-397

Fox, J. M., Mutalima, N., Molyneux, E., Carpenter, L. M., Taylor, G. P., Bland, M. and Martin, F. (2016). Seroprevalence of HTLV-1 and HTLV-2 amongst mothers and children in Malawi within the context of a systematic review and meta-analysis of HTLV seroprevalence in Africa. *Journal of Tropical Medicine and International Health*, *21*(3), 312–324

Futsch, N., Mahieux, R. and Dutartre, H. (2017). HTLV-1, the Other Pathogenic Yet Neglected Human Retrovirus: From Transmission to Therapeutic Treatment. *Viruses*, *10* (1), 2-25

Gallo, R. C. (2005). The discovery of the first human retrovirus: HTLV-1 and HTLV-2. *Journal of Retrovirology*, *2*, 17

Galetto, L. R., Lunge, V. R., Beria, J. U., Tietzmann, D. C., Stein, A. T. and Simon, D. (2014). Short communication: Prevalence and risk factors for human T cell lymphotropic virus infection in southern brazilian HIV-positive patients. *Journal of AIDS Research and Human Retroviruses*, *30*, 907–911

German, D. and Latkin, C. A. (2015). HIV risk, health and social characteristics of sexual minority female injection drug users in Baltimore. *Journal of AIDS and Behaviour*, *19* (7), 1361–1365

Gessain, A. and Cassar, O. (2012). Epidemiological aspects and world distribution of HTLV-1 infection. *Frontiers in Microbiology*, *3*, 388

Gonçalves, D. U., Proietti, F. A., Ribas, J. G. R., Araújo, M. G., Pinheiro, S. R., Guedes, A. C. and Carneiro-Proietti, A. B. F. (2010). Epidemiology, treatment, and prevention of human T-cell leukemia virus type 1-associated diseases. *Clinical Microbiology Reviews*, *23* (3), 577–589

González-Alcaide, G., Ramos, J. M., Huamani, C., Mendoza, C. D. and Soriano, V. (2016). Human T-lymphotropic Virus 1 (HTLV-1) and Human T-lymphotropic virus 2 (HTLV-2): Geographical research trends and collaboration networks (1989-2012). *Revista do Instituto de Medicina Tropical de São Paulo***,** *58, 2-9*

Gudo, E. S., Bhatt, N. B., Bila, D. R., Abreu, C.M., Tanuri, A., Savino, W., Silva-Barbosa, S.D. and Jani, I. V. (2009). Co-infection by Human Immunodeficiency Virus type 1 (HIV-1) and Human T cell leukemia virus type 1 (HTLV-1): Does immune activation lead to a faster progression to AIDS? *Journal of Infectious Diseases*, *9*, 11-13

Guimaraes, M. L., Bastos, F. I., Telles, P. R., Galvao-Castro, B., Diaz, R. S. and Vera-Bongertz, M. G. M. (2001). Retrovirus infections in a sample of injecting drug users in Rio de Janeiro City , Brazil : prevalence of HIV-1 subtypes , and co-infection with HTLV-I / II. *Journal of Clinical Virology*, *21* (2), 143–151

He , X., Maranga, I. O., Oliver, A. W., Gichangi, P., Hampson, L. and Hampson, I. N. (2016). Analysis of the Prevalence of HTLV-1 Proviral DNA in Cervical Smears and Carcinomas from HIV Positive and Negative Kenyan Women. *Viruses, 245*, 1–12

Hedayati-Moghaddam, M. R., Tehranian, F. and Bayati, M. (2015). Human T-Lymphotropic Virus Type I (HTLV-1) Infection among Iranian Blood Donors: First Case-Control Study on the Risk Factors. *Viruses, 7* (11), 5736-5745

Hlela, C., Graham, N., Bhigjee, A. I., Taylor, G. P., and Nonhlanhla, P. (2013). Human Tcell lymphotropic virus type 1- associated infective dermatitis in KwaZulu. *BioMedCentral Dermatology*, *13*, 11

Hobkirk, A. L, Watt, M. H., Myers, B., Skinner, D. and Meade, C. S. (2016). A qualitative study of methamphetamine initiation in cape town, South Africa. *International Journal of Drug Policy, 30*, 99–106

International Committee on Taxonomy of Viruses. (2017). The 10th Report of the ICTV Virus Taxonomy: The Classification and Nomenclature of Viruses

Isache, C., Sands, M., Guzman, N. and Figueroa, D. (2016). HTLV-1 and HIV-1 co-infection: A case report and review of the literature. *Elsevier, 4*, 53-55

Jogeda, E. L., Avi , R., Pauskar, M., Kallas, E., Karki, T., Jarlais , D. D., Uusküla, A., Lutsar, I. and Huik, K. (2016). Human T-lymphotropic virus types 1 and 2 are rare among intravenous drug users in Eastern Europe. *Elsevier, 43*, 83–85

Kannian, P., and Green, P. L. (2010). Human T Lymphotropic Virus Type 1 (HTLV-1): Molecular Biology and Oncogenesis. *Viruses, 2* (9), 2037–2077

Kennedy, M. C., Kerr, T. H., Wood, E.,Shoveller, J. A., Montaner, J. S. G. and Milloy, M. S. (2018). Social and structural factors associated with greater time with a plasma HIV-1 RNA viral load above $\log_{10}$ (1500) copies/ml among illicit drug users. *Journal of AIDS, 32* (8), 1059–1067

Kerosi, D. O., Budambula, N. L. M., Odari, E., Lihana, R., Osman, S., Omire, A., Langat, H., Aman, R. and Lwembe, R. (2015). Human Immunodeficiency Virus -1 and Hepatitis B Virus Co-Infections among Injecting Drug Users in Malindi, Kenya. *Journal of Biology, Agriculture and Healthcare, 5*, 45-50

Kozlowski, A. R., De-Matos, M. A. D., Carneiro, M. A. D. S., Lopes, C. L. R., Teles, S. A., Vicente, C. P. and Martins, R. M. R. (2016). Seroprevalence of HTLV in a population of HIV1-infected patients in Midwestern Brazil. *Revista do Instituto de Medicina Tropical de São Paulo*, 58, 2–7

Landovitz, R. J., Gildner, J. L. and Leibowitz, A. A. (2018). Sexually Transmitted Infection Testing of HIV-Positive Medicare and Medicaid Enrollees Falls Short of Guidelines. *Journal of Sexually Transmitted Diseases, 45* (1), 8–13

Latkin, C. A., Buchanan, A. S., Metsch, L. R., Knight, K., Latka, M. H., Mizuno, Y., Knowlton, A. R. and the INSPIRE Team. (2008). Predictors of Sharing Injection Equipment by HIV Seropositive Injection Drug Users. *Journal of AIDS, 49*: 447–450

Larocque, E., André-Arpin, C., Borowiak, M., Lemay,G., Switzer, W. M., Dodon, M. D., Mesnard,J. M. and Barbeau, B. (2014). Human T-Cell Leukemia Virus Type 3

(HTLV-3) and HTLV-4 Antisense-Transcript-Encoded Proteins Interact and Transactivate Jun Family-Dependent Transcription via Their Atypical bZIP Motif. *Journal of Virology, 88* (16), 8956–8970

Lindenmeyer, M., Inacio, F., and Morgado, M. (2001). Retrovirus infections in a sample of injecting drug users in Rio de Janeiro City , Brazil : prevalence of HIV-1 subtypes , and co-infection with HTLV-I / II. *Journal of Clinical Virology, 21* (2), 143–151

Ma,Y., Zheng, S., Wang, N., Duan,Y., Sun,X., Jin, J., Zang,W., Li,M., Wang, Y. andZhao, G. (2013). Epidemiological Analysis of HTLV-1 and HTLV-2 Infection among Different Population in Central China. *PLoS One, 8*, e66795

Macharia, L.W., Mureithi, M. W. and Anzala, O. (2019). Cancer in Kenya: types and infection-attributable. Data from two National referral hospitals. *Research Gate, 77:* 102-110

Magri, M. C., Fernando, L., Brigido, D. M., Morimoto, H. K., and Caterino-de-araujo, A. (2013). Human T Cell Lymphotropic Virus Type 2a Strains Among HIV Type 1-Coinfected Patients from Brazil. *Journal of AIDS Research and Human Retroviruses, 29 (7),* 1010–1019

Mahieux, R. and Gessain, A. (2011). HTLV-3/STLV-3 and HTLV-4 viruses: discovery, epidemiology, serology and molecular aspects. *Viruses, 3*, 1074-1090

McIntyre, P. G., Hill, D. A., Appleyard, K., Taylor, A., Hutchinson, S. and Goldberg, D.J. (2001). Prevalence of Antibodies to Hepatitis C Virus, HIV and Human T-Cell Leukaemia/Lymphoma Viruses in Injecting Drug Users in Tayside, Scotland, 1993-7. *Epidemiology and Infection, 126* (1), 97-101

Moens, B., López, G., Adaui, V., Kerremans, L., Clark, D., Verdonck, K., and Dooren, S. Van. (2009). Development and Validation of a Multiplex Real-Time PCR Assay for Simultaneous Genotyping and Human T-Lymphotropic Virus Type 1, 2 and 3 Proviral Load. *Journal of Clinical Microbiology, 47,* 3682-3691

Murphy, E. L. (2016). Infection with human T-lymphotropic virus types-1 and -2 (HTLV-1 and -2): Implications for blood transfusion safety. *Transfusion Clinique et Biologique, 23,* 13–19

Murphy, E. L., Cassar, O. and Gessain, A. (2015). Estimating the number of HTLV-2 infected persons in the world. *Journal of Retrovirology*, 12, 05

Musyoki, H. (2012). An overview of programs for people who inject drugs. MARPs and Vulnerable Groups Program National AIDs/STI Control Programme

Mwatelah, R. S., Lwembe,R. M., Osman, S. A., Ogutu, B. R., Aman, R., Kitawi, R.C., Wangai,L. N., Oloo, F. A., Kokwaro, G. O., and Ochieng' W. (2015). Co-Infection Burden of Hepatitis C Virus and Human Immunodeficiency Virus among Injecting Heroin Users at the Kenyan Coast. *PLoS One, 10* (7), e0132287

National AIDS Control Council. (2016). Kenya AIDS response progress report

National AIDS and STI control programme. (2012). Geographic Mapping of Most at Risk Populations (MARPs) for HIV in Kenya

National AIDS and STI control programme. (2014). Key populations newsletter

National AIDS and STI control programme. (2016). The Kenya HIV Testing Services guidelines

Nasir, I. A., Ahmad, A. E., Emeribe, A. U., Shehu, M. S., Medugu, J. T. and Babayo, A. (2015). Molecular Detection and Clinical Implications of HTLV-1 Infections among Antiretroviral Therapy-Naïve HIV-1-Infected Individuals in Abuja , Nigeria. *Journal of Virology,Research and Treatment, 6,* 17–23

Neiburg P. and Carty A. (2011). HIV Prevention among Injection Drug Users in Kenya and Tanzania: New Opportunities for progress: Report of the CSIS Global health Policy Center, April 2011.

Ng'ong'a, G. O., Carol, H., Osman, S. and Lwembe, R. M. (2015). Predisposing Factors for HIV Infection among Injecting Drug Users in Malindi. *International Journal of Health Sciences & Research, 6,* 417–423

Novak, R. M., Ghanem, A., Hart, R., Ward, D., Armon, C., Buchacz, K. and HIV Outpatient Study Investigators. (2015). Risk factors and incidence of syphilis in HIV-infected persons, the HIV Outpatient Study, 1999-2015. *Clinical Infectious Diseases, 53,* 102-106

Nunes, D., Boa-Sorte, N., Grassi,M. F. R., Taylor,G. P., Teixeira, M. G., Barreto,M. L., Dourado, I. and Galvão-Castro, B. (2017). HTLV-1 is predominantly sexually transmitted in Salvador, the city with the highest HTLV-1 prevalence in Brazil. *PloS One, 12*, eo71303

Oyaro, M., Wylie, J.; Chien-Yu C., Ondondo, R. O. and Kramvis, Anna. (2018). Human immunodeficiency virus infection predictors and genetic diversity of hepatitis B virus and hepatitis C virus co-infections among drug users in three major Kenyan cities. *Southern African Journal of HIV Medicine, 19* (1), 1-9

Paiva, A. and Casseb, J. (2014). Sexual transmission of human T-cell lymphotropic virus type 1. *Revista da Sociedade Brasileira de Medicina Tropical, 47* (3), 265-274

Paiva, A. and Casseb, J. (2015). Origin and prevalence of human t-lymphotropic virus type 1 (htlv-1) and type 2 (htlv-2) among indigenous populations in the Americas *Revista da Sociedade Brasileira de Medicina Tropical, 57,* 1-14

Paiva, A. M., Assone, T., Haziot, M. E. J., Smid, J., Fonseca, L. A. M., Luiz, O. D. C., Oliveira, A. C. P. D. and Casseb, J. (2018). Risk factors associated with HTLV-1 vertical transmission in Brazil: longer breastfeeding, higher maternal proviral load and previous HTLV-1-infected offspring. *Scientific Reports, 8,* s41598-018-25939-y

Pinto, M. T., Rodrigues, E. S., Malta, T. M., Azevedo, R., Takayanagui, O. M., Valente, V.B.,Ubiali, E. M., Covas, D.T. and Kashima, S. (2012). HTLV-1/2

seroprevalence and coinfection rate in Brazilian first-time blood donors: an 11-year follow-up. *Revista do Instituto de Medicina Tropical de São Paulo***,** *54* (3), 123-129

Pirayeshfard, L., Sharifi, Z., Amini-Kafiabad, S. and Sadaghiani, N. H. (2018). Phylogenetic analysis of HTLV-1 in Iranian blood donors, HIV-1 positive patients and patients with beta thalassemia. *Journal of Medical Virology*, *90* (8), 1398-1405

Prasetyo, A. A., Dirgahayu, P., Sari , Y.,Hudiyono, H. and Kageyama S. (2013). Molecular epidemiology of HIV, HBV, HCV, and HTLV-1/2 in drug abuser inmates in central Javan prisons, Indonesia. *Journal of infection in developing countries*, *7*, 453-467

Prasetyo, A.A. and Sari' Y. (2017). Human T-lymphotropic virus-1/2 detected in drug abused men who have sex with men in Surakarta Indonesia. *AIP Conference Proceedings*, *1813*

Rafatpanah, H., Farid, R., Golanbar, G., and Jabbari Azad, F. (2006). HTLV-I Infection: virus structure, immune response to the virus and genetic association studies in HTLV-I-infected individuals. *Iranian Journal of Allergy, Asthma, and Immunology*, *5* (4), 153–166

Reda, S., Gonçalves, F. A., Mazepa, M. M. and Carvalho, N. S. (2018). Women infected with HIV and the impact of associated sexually transmitted infections. *International Journal of Gynaecolology and Obstetrisk*s, *142,* 143-147

Ribeiro, I. P., Kozlowski, A. G., Dias de Matos, M. A., da Costa, E. S. A. M., Dos Santos Carneiro, M. A., Vicente, A. C. Pand Martins, R. M. B. (2018). HTLV-1 and -2 in a first-time blood donor population in Northeastern Brazil: Prevalence, molecular characterization, and evidence of intrafamilial transmission. *Journal of Medical Virology, 56*, 89-97

Romanelli, M. G., Diani, E., Bergamo, E., Casoli, C., Ciminale, V., Bex, F., and Bertazzoni, U. (2013). Highlights on distinctive structural and functional properties of HTLV Tax proteins. *Frontiers in Microbiology*, *4*, 271

Rowhani-Rahbar , A., Tabatabaee-Yazdi, A. and Panahi, M. (2004). Prevalence of common blood-borne infections among imprisoned injection drug users in mashhad, north-east of iran. *Iranian Journal of Allergy, Asthma, and Immunology*, *7* (3), 190–194

San-Martin, D. L. S., Santos, D. N. D., Baptista, A. F. and Pain Study Group. (2016). Pain prevalence, characteristics and associated factors in human T-cell lymphotropic virus type 1 infected patients: a systematic review of the literature. *Brazilian Journal of Infectious Diseases, 20*, 592-598

Santa Maria, D., Hernandez, D. C., Arlinghaus, K. R., Gallardo, K. R., Maness, S. B., Kendzor, D. E., Reitzel, L. R. and Businelle, M. S. (2018). Current Age, Age at First Sex, Age at First Homelessness, and HIV Risk Perceptions Predict Sexual Risk Behaviors among Sexually Active Homeless Adults. *International Journal of Environment Research and Public Health*, *15* (2), 218

Shahesmaeili, A., Haghdoost, A. A. and Soori, H. (2015). Developing a Brief Scale to Measure HIV Transmission Risk among Injecting Drug Users. *International Journal of High Risk Behaviors and Addiction, 4,* e26159

Sinkamba, R. and Moseki-Lowani, T. (2016). Youth unemployment and HIV and AIDS: Insights from the 2013 Botswana AIDS Impact Survey. *Botswana Journal of African studies, 30,* 1-13

Songok, E. M., Tukei, P. M., Libondo, D., Gichogo, A. and Oogo, S. A. (1994). Low prevalence of HTLV-1 in HIV positive patients in Kenya. *Journal of AIDS, 7* (8), 1-10

Stata data analysis and statistical software version 15.1 (2017), Stata corperation, USA

Strathdee, S. A., Lozada, R., Martinez, G., Vera, A., Rusch, M., Nguyen, L., Pollini, R. A., Uribe-Salas, F., Beletsky, L. and Patterson, T. L. (2011). Social and structural factors associated with HIV infection among female sex workers who inject drugs in the Mexico-US border region. *PLoS One 6* (4), e19048

Strathdee, S. A., Abramovitz, D., Lozada, R., Martinez, G., Rangel, M. G., Vera, A., Staines, H., Magis-Rodriguez, C. and Patterson, T. L. (2013). Reductions in HIV/STI Incidence and Sharing of Injection Equipment among Female Sex Workers Who Inject Drugs: Results from a Randomized Controlled Trial. *PLoS ONE, 8,* e65812

Tavitian-Exley, I., Boily, M. C., Heimer, R., UuskU, A., Levina, O. and Maheu-Giroux, M. (2018). Polydrug Use and Heterogeneity in HIV Risk Among People Who Inject Drugs in Estonia and Russia: A Latent Class Analysis. J*ournal of AIDS and Behaviour, 2* (4), 1329–1340

Tienen, C. V., Silva, T. I. D., Alcantara, L. C. J., Onyango, C. O., Jarju, S., Goncalves, N., Vincent, T., Aaby, P., Whittle, H., Loeff, M. C. V. D. and Cotten, M. (2012). Molecular Epidemiology of Endemic Human T Lymphotropic Virus Type 1 in a Rural Community in Guinea-Bissau. *PLOS, 6,* 1-8

Toro, C., Blanco, F., Garcça-Gasco, P., Sheldon, J., Benito, J. M., Rallon, N. I. and Soriano, V. (2007). Human T Lymphotropic Virus Type 1-Associated Myelopathy/Tropical Spastic Paraparesis in an HIV-Positive Patient Coinfected with Human T Lymphotropic Virus Type 2 Following Initiation of Antiretroviral Therapy. *Journal of Clinical Infectious Diseases, 45* (9), 118–120

Trinity Biotechnologies, UniGold rapid test protocol

Turci, M., Pilotti, E., Ronzi, P., Magnani, G., Boschini, A., Parisi, S. G. and Bertazzoni, U. (2006). Coinfection With HIV-1 and Human T-Cell Lymphotropic Virus Type

II in Intravenous Drug Users Is Associated With Delayed Progression to AIDS. *Journal of AIDS, 41*, 100–106

Vahidnia, F., Stramer, S. L., Kessler, D. A., Krysztof, D. E., Dodd, R. Y., Notari, E., Glynn, S. and Custer, B. (2015). Risk factors and epidemiology of human T-lymphotropic virus types 1 and 2 in US blood donors. *Journal of Retrovirology, 12* (1), 84

Viana, G. M. D. C., Nascimento, M. D. D. S. B., Oliveira, R. A. S. D., Santos, A. C. D., Galvão, C. D. S. and Silva, M. A. C. N. D. (2014). Seroprevalence of HTLV-1/2 among blood donors in the state nof Maranhão, Brazil. *Brazilian Journal of Hematology and Hemotherapy, 36, 50-53*

World Health Organization. (2018). Report on People who inject drugs.

United Nations Programme on HIV/AIDS. (2014). GAP Report on people who inject drugs

United Nations Office on Drugs and Crime. (2010). World Drug Report, HIV/AIDS and Drugs

United Nations Office on Drugs and Crime. (2015). World Drug Report, HIV/AIDS and Drugs

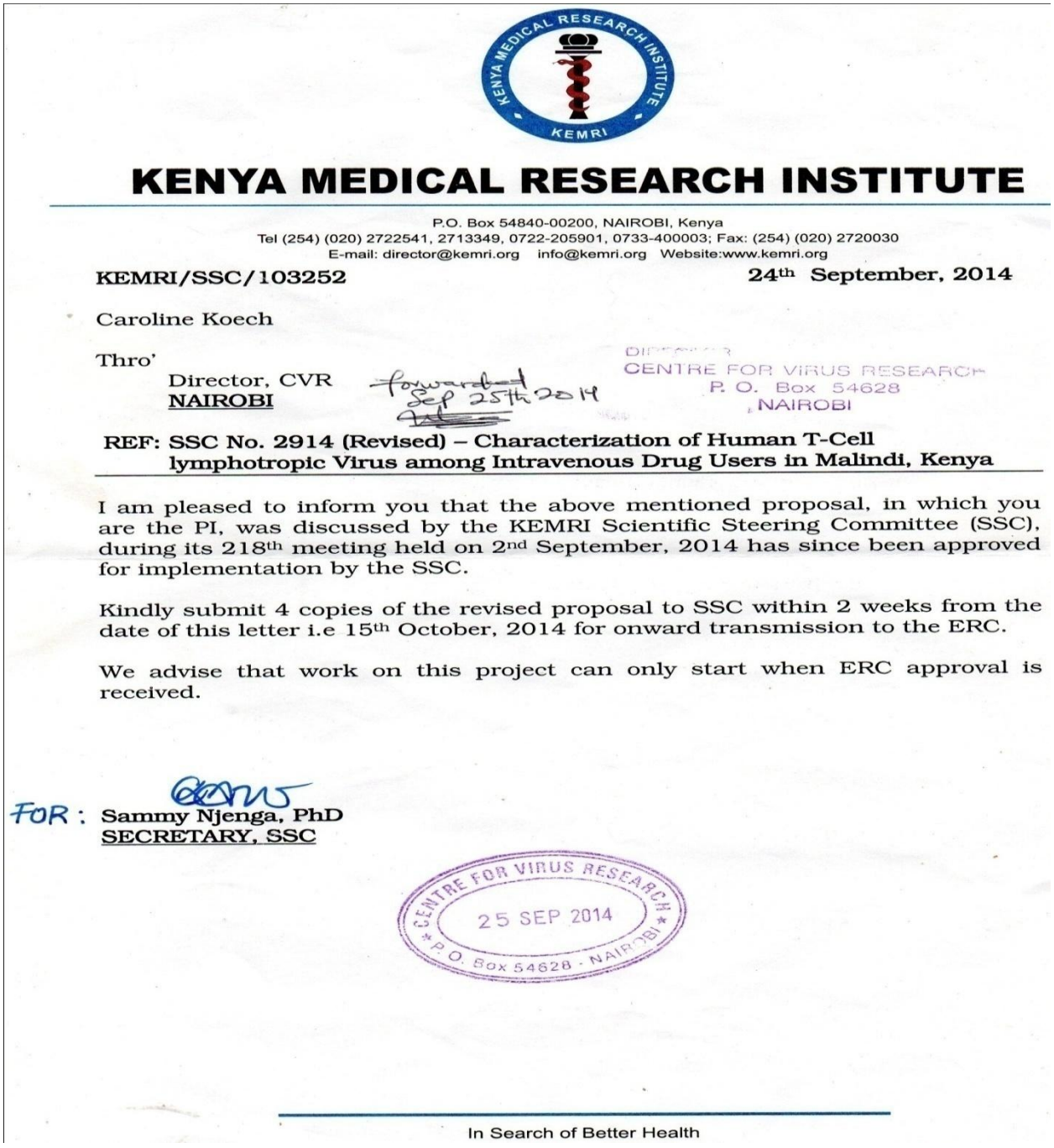
United Nations Office on Drugs and Crime. (2016). World Drug Report, HIV/AIDS and Drugs

Zunt, J. R., Rosa, A. M. L., Peinado, J., Lama, J. R., Suarez, L., Cabezas, M. P. C. and Sanchez, J. (2006). Risk factors for HTLV-ii infection in Peruvian Men who have sex with Men. *American Journal of Tropical Medicine and Hygieiene, 74* (5), 922–925

Zunt, J. R., Tapia, K. E. N., Thiede, H., Lee, R. and Hagan, H. (2009). HTLV-2 infection in injection drug users in King County, Washington. *Scandinavian Journal of Infectious Diseases, 38* (8), 654–663

APPENDICES

Appendix I: SSC Clearance



KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840-00200, NAIROBI, Kenya
Tel (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/SSC/103252 24th September, 2014

Caroline Koech

Thro'
Director, CVR
NAIROBI

Forwarded Sep 25th 2014

DIRECTOR
CENTRE FOR VIRUS RESEARCH
P. O. Box 54628
NAIROBI

REF: SSC No. 2914 (Revised) – Characterization of Human T-Cell lymphotropic Virus among Intravenous Drug Users in Malindi, Kenya

I am pleased to inform you that the above mentioned proposal, in which you are the PI, was discussed by the KEMRI Scientific Steering Committee (SSC), during its 218th meeting held on 2nd September, 2014 has since been approved for implementation by the SSC.

Kindly submit 4 copies of the revised proposal to SSC within 2 weeks from the date of this letter i.e 15th October, 2014 for onward transmission to the ERC.

We advise that work on this project can only start when ERC approval is received.

FOR: Sammy Njenga, PhD
SECRETARY, SSC

CENTRE FOR VIRUS RESEARCH * 25 SEP 2014 * P.O. Box 54628 - NAIROBI

In Search of Better Health

Appendix II: Ethical Clearance

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840-00200, NAIROBI, Kenya
Tel (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1 **February 5, 2015**

TO: **CAROLINE KOECH,**
PRINCIPAL INVESTIGATOR

THROUGH: **DR. GEORGE NAKITARE,**
THE DIRECTOR, CVR,
NAIROBI

DIRECTOR
CENTRE FOR VIRUS RESEARCH
P.O. BOX 54628
NAIROBI.

forwarded Feb 12th 2015

Dear Madam,

RE: SSC PROTOCOL NO. 2914 (*RESUBMITTED-INITIAL SUBMISSION*): CHARACTERIZATION OF THE HUMAN T- CELL LYMPHOTROPIC VIRUS AMONG INTRAVENOUS DRUG USERS IN MALINDI KENYA-(*VERSION 1.1 DATED 16TH DECEMBER, 2014*)

Reference is made to your letter dated 16th December, 2014. The Scientific and Ethics Review Unit (SERU) acknowledges receipt of the revised study protocol on December 18, 2015.

This is to inform you that the Committee reviewed the documents submitted and is satisfied that the issues raised at the 234th meeting of the KEMRI Ethics Review Committee (ERC) on 16th December, 2014 have been adequately addressed.

The study is granted approval for implementation effective this **5th February, 2015**. Please note that authorization to conduct this study will automatically expire on **4th February, 2016.** If you plan to continue with data collection or analysis beyond this date, please submit an application for continuing approval to SERU by **December 26, 2015**.

Any unanticipated problems resulting from the implementation of this protocol should be brought to the attention of SERU. You are also required to submit any proposed changes to this protocol to SERU prior to initiation and advise SERU when the study is completed or discontinued.

You may embark on the study.

Yours faithfully,

CAB

PROF. ELIZABETH BUKUSI,
ACTING SECRETARY,
KEMRI/ETHICS REVIEW COMMITTEE

CENTRE FOR VIRUS RESEARCH
11 FEB 2015
P.O. Box 54628 - NAIROBI

Appendix III: Kilifi County Clearance

THE COUNTY GOVERNMENT OF KILIFI
RESEARCH OFFICE, DEPARTMENT OF THE HEALTH

Telephone: 0721627306
0721843015
0721359983
Email: langat.eva@gmail.com
aceobonyo@gmail.com
kazunguwilfred@hotmail.com

P.O. BOX 519-10808
KILIFI, KENYA

Date 27 April 2015

When Replying/Telephoning quote
REF: DOH/KLF/RESCH/VOL.I/23

Koech Caroline Chepkorir

Dear Madam,
RE: AUTHORIZATION TO CARRY OUT A STUDY IN KILIFI COUNTY

The research committee of Health, Kilifi County has received your request to conduct a study on the **"Characterization of Human T-Cell Lymphotropic Virus Among Intravenous Drug Users In Malindi, Kenya"**

After going through your proposal, the committee is glad to grant you an institutional authorization to proceed with your research. This however should be conducted within the expiry date of your ethical approval.

Upon completion of you research, you are required to submit a written report to the Kilifi County Research Committee (KCRC) detailing the findings, conclusion and recommendations of your study.

We wish you the very best as you conduct your research.

Regards,

Evaline Langat
Research Coordinator
KILIFI COUNTY HEALTH RESEARCH COMMITTEE

Appendix IV: Consent to Participate in Research: English Version

Study Title: **HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 AND HUMAN T-CELL LYMPHOTROPIC VIRUS TYPE ONE AND TWO AMONG INTRAVENOUS DRUG USERS IN OMARI AND KANCO DROP-IN CENTRES IN MALINDI SUB-COUNTY, KENYA.**

My name is…….. And I am a student in KEMRI headquarters in Nairobi working on the above project.

Human Immunodeficiency Virus and Human T cell Lymphotropic viruses are viruses that are transmitted through sexual contact, intravenous drug use and from mother to child through breast feeding. HTLVs fall into four types: HTLV-1, HTLV-2, HTLV-3 and HTLV-4. HTLV type 1 and 2 cause lymphoma which is a blood cancer and the severely debilitating myelopathy or tropical spastic paraparesis. Currently there is no specific treatment to these diseases which makes it a serious threat to those infected as mortality rates are higher. An intravenous drug user (IDU) is at an increased risk of acquiring these viruses because of receptive needle sharing and back loading of blood from one IDU to another. Once infected, the virus persists in the body for life. It is therefore necessary and important to be screened for the presence of the virus in blood because in the initial stages, the disease is mostly asymptomatic so one becomes a carrier. Being a carrier is risky as one transmits the virus to others since he/she is unaware of being infected. In order to be sure you are informed about this project, I am going to read for you, or read with you this consent Form. This form tells you why this research study is being done, what will happen in the research study, and possible risks and benefits to you. If there is anything you do not understand, please ask questions.

Purpose of study:

The purpose of the study is to determine the prevalence and characterize HIV and HTLV among IDUs in Malindi, Kenya. This information will be useful to the government in their plans to stop drug abuse. The evidence generated from this study will be summarized and disseminated to stakeholders such as Ministry of Health and field of study.

Procedure:

To do this research study, we need your permission to collect some of your health information. This information may come from questions we ask and forms we ask you to fill out. We will only collect information needed for the study. All IDUs who will consent to the study to have their blood drawn and tested for HIV and HTLV will be recruited to participate in the study. If you agree to participate in this study, your arm will be sterilized by disinfectant. Five milliliters of blood will be taken from vein of your arm by phlebotomist for analysis in the laboratory to screen for the presence of HTLV and if found to be infected, further tests will be carried to determine the infecting subtype. We will use sterile and disposable instruments that are clean and safe. There will be no attachment of names to the blood samples, but an identification number assigned to you will be used to label the sample. This is to ensure complete confidentiality of the test results. This research will not disclose your HTLV status to anyone else without your permission. The sample will be taken to the laboratory, analyzed and final report concluded in less than one year. This work will be done in the KEMRI HIV laboratories.

Risks

Blood taking will expose you to no health risks except minimum discomfort associated with puncturing of your skin which will last only for few minutes. The vein puncturing activity will be done by a well-qualified phlebotomist.

Benefits

There are no costs to you for any activities in this study. You will not be paid for participating in this study. The direct benefit to you is that you will get to know your HIV and HTLV status and results will be sent to Omari and KANCO drop in centre where you can collect your results. In case the results are positive for HIV and HTLV, you will be offered referral in an appropriate clinic for care and management.

Participation and voluntarism

Your participation in this project is free and voluntary. You have a right to decline participation in the project at this time by failing to sign this form and if you decline to participate, you will not be denied any services that are normally available to you now and in the future. You may also stop at any time. If you choose to withdraw from this

study, your rights to be attended to this centre now and future will not be affected. You are encouraged to ask any questions on what occurs to you at this time in the course of your contact with investigators. You will also be given a copy of this agreement for your own information.

Confidentiality

The information you give in the questionnaire will be kept confidential and will only be shared by the project staff for analysis. We will make every effort to protect your identity and you will not be identified in any of report or publication of this study or its results.

Project contacts

If you have any questions about this project you may contact us through mobile number 0721447378(texts and calls) or email koech.caroline@yahoo.com Or the Kenya Medical Research Institute ethical committee on the below address.

The Secretary

KEMRI Ethics and Research committee

P.O. BOX 54840-00200 Nairobi

Tel. 020- 2722541 or 0722 205901 or 0733 400003.

Email address: **erc@kemri.org**

Subject permission: I GIVE MY CONSENT for my blood to be used for viral antibody testing and in case I am infected further analysis may be carried out to determine which subtype it is. **Consent for blood collection YES** ☐ **NO** ☐

Name of Participant …… Signature/Thumb mark ……

Date……

Consent Agreement Form

I participated in consent process and Acknowledge enrollment of this participant into the study. Name of Principal investigator/ Assistant…….

Signature……Date……

Appendix V: Consent to Participate in Research: Kiswahili Version

KIBALI CHA KUSHIRIKI KATIKA UTAFITI: TOLEO LA KINGEREZA

Mada ya Uchunguzi: UTAFUTAJI SIFA WA VIRUSI VYA BINANADAMU VYENYE SELI YA T VYA LYMFOTROFIA MIONGONI MWA WATUMIAJI WA DAWA ZA KULEVYA ZA KUDUNGA KWENYE MSHIPA KATIKA OMARI NA KANCO MJINI MALINDI, KENYA.

Mchunguzi mkuu:

Koech Caroline Chepkorir, Virolojia ya Kimatibabu MSC JKUAT

Anayesimamia, kuundwa kwa pendekezo, kuratibu kwa shughuli za maabara, usimamizi wa data na uandishi wa ripoti.

Jina langu ni……..na mimi ni mwanafunzi katika makao makuu ya KEMRI Jijini Nairobi na ninashughulikia mradi uliotajwa hapo juu.

Virusi vya binadamu vya Seli ya T vya LYFOTROPILA ni virusi ambavyo vinaenezwa kupitia katika kufanya mapenzi, matumizi ya dawa za kulevya za kujidunga kwenye mshipa na kutoka kwa mama hadi mtoto kupitia kwa unyonyeshaji. Virusi hivi vinaainishwa katika aina nne: HTLV-1, HTLV-2, HTLV-3, na HTLV-4. Aina ya 1 na 2 ya HTLV husababisha *lymphoma* ambayo ni saratani ya damu pamoja na *myelopathy* hatari na ya kudhoofisha au t*ropical spastic paraparesis*. Kwa sasa hakuna matibabu mahususi ya magonjwa haya na hivyo basi yanakuwa ni tishio kubwa kwa wale wanaoambukizwa kwani wale wanaopoteza maisha yao kutokana na magonjwa haya ni wengi. Mtumiaji wa dawa ya kulevya kwa kujidunga mshipa (IDU) yuko katika hatari iliyoongezeka ya kupata virusi hivi kutokana na matumizi ya pamoja ya sindano na ukusanyaji na uhamishaji wa damu kutoka kwa IDU mmoja hadi mwengine. Pindi tu virusi hivi vinapoambukizwa, vinabakia kwenye mwili daima maishani. Hivyo basi uchunguzi wa damu unahitajika na ni muhimu ili kuangalia uwepo wa virusi hivi kwa sababu katika awamu za mwanzomwanzo, ugonjwa huu mara nyingi huwa hauonyeshi dalili zozote na hivyo basi yule aliye nao huwa ni mbebaji tu. Kuwa mbebaji wa HTLV ni hatari kwani mtu hueneza virusi hivyo kwa wengine bila kujua kwamba ameambukizwa.

Ili kuwa na uhakika kuwa umefahamishwa kikamilifu kuhusu mradi huu, nitakusomea, au nitasoma pamoja nawe fomu hii ya kibali. Fomu hii inakuelezea ni kwa nini uchunguzi huu wa utafiti unafanywa, nini kitafanyika katika uchunguzi huu wa utafiti, na hatari pamoja na manufaa yanayowezekana kwako. Kama kuna kitu chochote ambacho huelewi, tafadhali uliza maswali.

Kusudio la uchunguzi:

Kusudio la uchunguzi ni kuweza kuamua uwepo na utafutaji sifa za molekula za virusi vya binadamu vya seli ya T vya lymfotrofia miongoni mwa watumiaji wa dawa za kulevya za kujidunga kwenye mshipa mjini Malindi, Kenya. Taarifa hii itakuwa yenye manufaa katika Serikali kwenye mipangilio yake ya kukomesha matumizi ya dawa za kulevya. Ushahidi utakaopatikana kutoka kwenye uchunguzi huu utaweza kuandikwa kwa muhtasari na kusambazwa kwa washika-dau kama vile wizara ya afya na uwanja wa uchunguzi.

Utaratibu

Ili kufanya uchunguzi huu wa utafiti, tunahitaji kibali chako cha kuweza kukusanya baadhi ya taarifa yako ya afya. Taarifa hii huenda ikatokana na maswali tutakayokuuliza na fomu tutakazokuomba uzijaze. Tutaweza kukusanya tu taarifa inayohitajika katika uchunguzi wala si nyingine yoyote. IDU wote ambao watakubali kushiriki katika uchunguzi huu na damu yao kutolewa na kupimwa ili kuwezakuchunguza HTLV wataweza kujiunga ili kushiriki katika uchunguzi. Kama utakubali kushiriki katika uchunguzi huu, mkono wako utaweza kutakaswa na dawa maalum. Mililita tano za damu zitaweza kuchukuliwa kupitia mshipa wa mkono wako na mwanaflebotomia ili kufanyiwa uchunguzi katika maabara na kuaangalia uwepo wa HTLV na kama damu hiyo itapatikana kuwa imeambukizwa vipimo zaidi vitaweza kufanywa ili kujua ni aina ndogo ipi ya virusi iliyoambukiza. Tutaweza kutumia vyombo vilivyotakaswa na vinavyotumika mara moja tu ambavyo ni safi na salama. Hakutakuwa na maambatisho yoyote ya majina katika sampuli za damu, ila nambari ya utambulisho tu ndiyo itakayoambatanishwa na wewe na kutumika kuweka lebo katika sampuli hiyo ya damu. Hii ni kuhakikisha kuwa usiri kamilifu wa matokeo ya vipimo hivyo unafikiwa. Utafiti huu hautafichua hali yako ya HTLV kwa yeyote mwengine bila ya kibali chako. Sampuli

hiyo itapelekwa katika maabara kuchunguzwa na ripoti ya mwisho kuhitimishwa kwa muda usiozidi mwaka mmoja. Kazi hii itafanyiwa katika maabara ya VVU ya KEMRI.

Hatari

Uchukuaji wa damu hautakufichua kwa hatari zozote za kiafya isipokuwa uchungu kidogo tu unaohusiana na kule kudungwa kwenye ngozi yako ambao utadumu kwa dakika chache tu. Hiyo shughuli ya kudunga kwenye mshipa wako itafanywa na mwanaflebotomia aliyefuzu-vizuri.

Manufaa

Hakuna gharama yoyote kwako katika shughuli zozote kwenye uchunguzi huu.Hautalipwa katika kushiriki kwenye uchunguzi huu. Manufaa ya moja kwa moja kwako ni kuwa utaweza kujua hali yako ya HTLV na matokeo yataweza kutumwa katika Kituo cha Urekebishaji tabia cha Omari ambapo unaweza kuchukua matokeo yako. Endapo matokeo haya yatakuwa si mazuri na kuonyesha kuwa umeaambukizwa HTLV, utaweza kupendekezewa ni wapi utaenda katika kiliniki inayofaa kwa utunzaji na usimamizi.

Kushiriki na kujitolea mhanga

Kushiriki kwako katika mradi huu ni bure na ni kwa kujitolea. Unayo haki ya kukataa kushiriki katika mradi huu wakati huu kwa kukataa kupiga saini katika fomu hii na endapo hutakubali kushiriki, hutanyimwa huduma zozote ambazo kawaida hupatikana na hutolewa kwako sasa na hata siku za usoni. Unaweza pia kupitia hapo wakati wowote. Kama utachagua kujiondoa kwenye uchunguzi huu, haki zako za kuhudumiwa katika kituo hiki sasa na hata katika siku za usoni hazitaathirika kwa vyovyote vile. Unahimizwa kuuliza maswali yoyote kuhusiana na ni nini kitafanyika kwako wakati huu wakati unapowasiliana na wachunguzi. Utaweza pia kupewa nakala ya mkataba huu kwa taarifa yako.

Usiri

Taarifa utakayotoa katika hojaji hii itawekwa kwa siri na itaweza kupewa tu wafanyikazi wa mradi huu kwa uchunguzi zaidi. Tutafanya kila jitihada kuulinda utambulisho wako na hautatambulishwa katika ripoti au chapisho lolote la uchunguzi huu au matokeo yake.

Anwani za mradi

Kama una swali lolote unaweza kuwasiliana nasi katika namba ya mkononi 0721 447 378 (arafa au hata kupiga simu) au baruapepe koech.caroline@yahoo.com Au Kamati ya Maadili ya Kimatibabu ya Taasisi ya Kenya kwa anwani ifuatayo.

Katibu

Kamati ya Utafiti na Maadili ya KEMRI

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KIBALI CHA MSHIRIKI

Kwa kuandika jina langu hapa chini, nathibitisha yafuatayo.

 Nimesoma (au nimesomewa) waraka huu wote wa kibali. Maswali yangu yote yamejibiwa kwa utoshelevu.

 Kusudio, taratibu, hatari na manufaa yanayowezekana katika uchunguzi huu yameweza kufafanuliwa kwangu.

 Nimejitolea mwenyewe kukubali kushiriki katika uchunguzi huu wa utafiti. Nakubali kufuata taratibu za uchunguzi kama nilivyoelekezwa. Nimeelezewa kwamba ninaweza kuusitisha wakati wowote.

Idhini ya mada: NATOA KIBALI CHANGU kwa damu yangu kuweza kutumiwa kwa upimaji wa antibodi wa virusi na endapo nimeambukizwa uchunguzi zaidi kufanywa ili kuamua ni aina ipi ndogo inahusika katika ambukizo hilo.

Kibali cha ukusanywaji wa damu **NDIYO** ☐ **LA** ☐

Jina la mshiriki ……

Saini/Alama ya kidole …….

Tarehe……

FOMU YA MKATABA WA KIBALI

Nilishiriki katika mchakato wa kibali na nathibitisha kujiunga kwa mshiriki huyu katika uchunguzi huu.Jina la Mchunguzi mkuu/Msaidizi…….

Saini ……Tarehe

Appendix VI: Questionnaire

STUDY TITLE: HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 AND HUMAN T-CELL LYMPHOTROPIC VIRUS TYPE ONE AND TWO AMONG INTRAVENOUS DRUG USERS IN OMARI AND KANCO DROP-IN CENTRES IN MALINDI SUB-COUNTY, KENYA.

Answer all questions by putting a tick where appropriate.

Unique Code……

1. Sex [ ] male [ ] female
2. Marital status [ ] Single [ ] Married
3. Race [ ] White [ ] Black [ ] Asian [ ] Mixed/Other
4. Age (Please state your age)……
5. Country of origin……. Residence City…….Location…….. ……..…
6. Level of Education [ ] None [ ] Primary [ ] Secondary [ ] Tertiary
7. Are you homeless [ ] Yes [ ] No
8. Are you employed [ ] Yes [ ] No
9. Have you ever been in jail for the past one year? [ ] Yes [ ] No
10. Do you have a tattoo? [ ] Yes [ ] No
11. Have you ever travelled out of the country and if yes did you share needles when you traveled? [ ] Yes? [ ] No? [ ]
12. How long have you been an intravenous drug user [ ] 0-2 yrs [ ] 3-5 yrs [ ] 6-9 yrs
13. [ ] 10+yrs
14. How frequently do you inject drugs? [ ] Not injected for last 30 days
15. [ ] Infrequent [ ] Daily
16. What is your frequency of weekly injections? [ ] Less than daily [ ] 1-3 times a day [ ] 4times a day
17. Do you share needles when injecting drugs? [ ] Yes [ ] No
18. Do you inject yourself with used needles? [ ] Yes [ ] No

19. Do you practice back loading of injection solution? [ ] Yes [ ] No

20. Sexual identity [ ] Heterosexual [ ] Homosexual/Bisexual

21. **Sexual history :Women**

a) Number of male partners for the past six months [ ] None [ ] 1 [ ] 1-3 [ ] 4+

b) Number of female partners for past six months [ ] None [ ] 1 [ ] 1-3 [ ] 4+

c) If vaginal sex, did you use a condom? [ ] Yes [ ] No [ ] sometimes

d) If anal sex did you use a condom? [ ] Yes [ ] No [ ] sometimes

27 **Sexual history :Men**

a) Number of male partners for the past six months [ ] None [ ] 1 [ ] 1-3 [ ] 4+

b) Number of female partners for past six months [ ] None [ ] 1 [ ] 1-3 [ ] 4+

c) If vaginal sex, did you use a condom? [ ] Yes [ ] No [ ] sometimes

d) If anal sex did you use a condom? [ ] Yes [ ] No [ ] sometimes

28 Have you ever been diagnosed for any of these sexually transmitted infection for the past six months and if yes did you seek treatment? [ ] HIV [ ] HEPATITIS B

[ ] HEPATITIS C [ ] Herpes virus [ ] Syphilis [ ] Gonorrhea

Treatment [ ] Yes [ ] No

29 Which among these infections have you been diagnosed with for the past six months

[ ] Malaria [ ] Leshmaniasis [ ] Helminthesis [ ] Flu [ ] Bilharzia

Appendix VII: Publication

MedCrave
Step into the World of Research
Journal of Human Virology & Retrovirology

Prevalence and Associated Risk Factors of HTLV/HIV Co-Infection among People who inject Drugs (PWIDs): A Review

Abstract

Human T-cell lymphotropic viruses type 1 and 2 (HTLV1/2) and Human Immunodeficiency Virus (HIV) co-infections show a worldwide distribution. The prevalence varies according to geographic region, racial group and population type. HTLVs and HIV share similar routes of transmission and tropism for T-lymphocytes thus co-infection is common. HTLV-HIV co- infections occur frequently among PWIDs (People Who Inject Drugs) and HIV positive patients. HTLV-1/HIV co-infection has been documented to accelerate progression to Acquired Immunodeficiency Syndrome (AIDS) while HTLV-2 has a protective effect as a result of reduced HIV replication. This review primarily analyzed the global trends of prevalence and associated risk factors of HTLV mono-infection and HTLV-HIV co-infection among PWIDs.

Secondary objectives included an analysis on the global trends in prevalence and risk factors of HTLV/HIV co-infections among HIV positive patients and an analysis on HTLV subtypes present among PWIDs and HTLV-HIV co-infected PWIDs and patients. Based on the three categories, PUBMED and Google Scholar were systematically searched for relevant articles published between January 1988 and May 2017. A total of 67 articles from different countries were reviewed and results were presented in tables. Iran reported the highest HTLV prevalence among PWIDs (52%) while USA (16%) and Kenya (19.3%) reported the highest prevalence among HTLV-HIV co-infected PWIDS and patients respectively. Introduction of subtypes to countries that were previously not endemic suggested transmissions through immigration and travel. Based on the studies, black race and older age were the common risk factors among HTLV-HIV co-infected PWIDs and patients as well as HTLV infected PWIDs. High risk injection and sexual risk factors varied from one study to another. We recommend introduction of regular HTLV screening alongside HIV screening in outpatient clinics that PWIDs attend so as to reduce risk of transmission and to create awareness.

Keywords: HTLV-1; HTLV-2; HIV; PWIDs; Risk factors; Subtypes

Review Article

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Abbreviations: HTLVs: Human T-Cell Lymphotropic Viruses; HTLV-1: Human T-Cell Lymphotropic Virus Type 1; HTLV-2: Human T-Cell Lymphotropic Virus Type 2; HIV: Human Immunodeficiency Virus; STLV-1: Simian T-Cell Lymphotropic Virus Type 1; PWIDs: People Who Inject Drugs; IDU: Intravenous Drug Use; AIDS: Acquired Immune Deficiency Syndrome; HBV: Hepatitis B Virus; HAV: Hepatitis A Virus; HCV: Hepatitis C Virus; ELISA: Enzyme Linked Immunosorbent Assay; PCR: Polymerase Chain Reaction; RIA: Radio Immuno Assay; PA: Particle Agglutination; WB: Western Blot; HAM/TSP: HTLV Associated Myelopathy/Tropical Spastic Paraparesis; ECDC: European Centre for Disease Prevention and Control; WHO: World Health Organization; UNODC: United Nations Office on Drugs and Crime; LTR: NACC: National AIDS Control Commission; Long Terminal Repeat; ICTV: International Committee on Taxonomy of Viruses

Introduction

HTLV-1 was the first retrovirus to be discovered in 1979 from a patient with cutaneous T-cell lymphoma which was later followed by the discovery of HTLV-2 in 1982 from a patient with hairy cell leukemia [1]. Data shows that at least five to ten million people worldwide are infected with HTLV-1 [2] and between three to five million people worldwide are infected with HTLV-2 [3]. Seroprevalence rates of HTLVs differ depending on the geographic area, socio-demographic composition and individual risk behaviors [1]. Globally, HTLV-1 Seroprevalence rates tend to increase with age and are higher in females than males as sexual transmission occurs more efficiently from men to women than women to men [4].

Regions endemic for HTLV-1 are found mainly in southeastern Japan, the Caribbean, parts of Africa, the Middle East and in the Pacific Islands of Melanesia [5]. The African continent has a population of over one billion and it represents the largest endemic area for HTLV infection but with many data gaps [6]. In Africa, the Seroprevalence increases from the north to the south, varying from 0.6% in Morocco to greater than 5% in several sub-Saharan African countries including Benin, Cameroon and Guinea-Bissau [1]. In Malawi, HTLV-2 prevalence of 1.7% and 1.3% was reported among mothers and their children who had childhood cancers [6]. HTLV-2 is more prevalent among some

Native Americans and some Central African tribes and is relatively common among PWIDs and their sex partners in Europe, North America and other regions of the world [7]. In Europe where HTLV-2 infection is found almost exclusively among PWIDs, about 20,000 to 40,000 persons are estimated to be infected [6]. In Kenya, HTLV prevalence in the general population has not been documented. The first study in Kenya was done on stored serum samples from suspected HIV-infected patients in Nairobi, Mombasa & Kisumu [8].

The samples were analyzed for HTLV-1 using Enzyme Linked Immunosorbent Assay (ELISA) and later confirmed by Western Blot. Out of 913 samples, 3.7% were found positive for HTLV-1 however only 0.44% was confirmed positive by western blot [8]. In Kenya a recent HTLV-1 prevalence of 19.3% was reported from liquid based cytology (LBC) samples among HIV positive women attending Kenyatta National Hospital in Nairobi [9].

The burden of HTLV-2 infection in the world is about 6 to 12 fold lower than that of HTLV-1 [9]. HTLV-1/2 transmission occurs through; unprotected sexual contact, from mother to child via breastfeeding, exchange of contaminated blood products and through intravenous drug use [7]. PWIDs are particularly vulnerable to HIV and other blood-borne pathogens as a result of sharing contaminated syringes and other injecting equipment such as cookers, cotton and rinse water [10]. Given that HTLV and HIV share identical modes of horizontal and vertical transmission, co-infections with these viruses is common in endemic areas [11]. Globally 36.7 million people are infected with HIV whereas in Eastern and Southern Africa, 19 million people are living with HIV. Kenya has an average national HIV prevalence of 5.9% and the prevalence among PWIDs is estimated to be 18.3% [12].

HTLV screening is not routinely performed in many countries and is not always recommended by physicians to outpatients thus Seroprevalence of co-infection may be underestimated [13]. Current evidence suggests a protective role of HTLV-2 and adverse effect of HTLV-1 on HIV infection [7]. This review examined prevalence estimates, risk factors and subtypes among HTLV/HIV co-infected PWIDs and patients together with HTLV-infected PWIDs. The findings will contribute to further understanding of HTLV distribution, risk factors and HTLV/HIV co-infection in PWIDs and HIV positive patients.

HTLV Genotypes and associated diseases

Human T-Cell Lymphotropic virus is a member of the delta retrovirus genus of the retroviridae family [14]. There are four genotypes of HTLV; HTLV-I, HTLV-2, HTLV-3 and HTLV-4. HTLV-1/2 is the most common pathogenic genotypes to humans. They are oncogenic retroviruses that both infect T cells with HTLV-1 infecting mainly CD4+ T cells and HTLV-2 infecting CD8+ T cells. HTLV-2 is especially prevalent among IDUs [15]. HTLV-1 is the causative agent of aggressive adult T-cell leukaemia/lymphoma (ATL) and the progressive chronic, disabling HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) as well as other inflammatory conditions such as infective dermatitis and uveitis. The cumulative risk of a HTLV-1 carrier developing ATL has been estimated at between 2.5% and 5% although a latency period of 50-70 years is typical [6]. Both ATL and HAM/TSP have a low incidence among HTLV-1 carriers. ATL generally presents after a long latency in patients infected during childhood. This is in contrast to HAM/TSP, which is associated with infection later in life [1]. There is no curative treatment for HTLV-1 or its associated pathologies. An effective vaccine is currently unavailable which puts a heavy social and financial burden on sufferers, their families and the healthcare systems [9]. The pathogenicity of HTLV-2 is low but has occasionally been linked to sub-acute neurological syndromes including HTLV-2-like paraparesis, neuropathies and bladder disturbances [1].

The genotype HTLV-3 was first described in two asymptomatic inhabitants from South Cameroon. Two other cases of HTLV-3 infection in people living in Cameroon have been reported, suggesting that this virus is not extremely rare in the human population living in Central Africa [16]. Only one strain of HTLV-4 has been identified in a person who also lived in Cameroon [3]. No disease has been reported in both HTLV-3 and HTLV-4 infected individuals. HTLV-1 and HTLV-2 have a similar genomic structure and share approximately 70% nucleotide sequence [1].

Epidemiology of HTLV subtypes

T-Lymphotropic virus species are distinguished on the basis of sequence differences and each contains several subtypes. HTLV-1/2 subtypes are clustered according to the geographic region. All HTLV-1 subtypes described have most probably originated from separate interspecies transmissions from simians to humans [14]. HTLV-1a is the only human restricted molecular subtype since the rest of the HTLV-1 subtypes could much more likely imply zoonotic transmission in African regions bordering non-human primate habitat. The other molecular HTLV-1 subtypes from humans in central Africa belong to composite clades that comprise HTLV-1 strains and Simian T-cell lymphotropic virus type 1 (STLV-1) strains derived from non-human primates [17].

Nonhuman primates in Africa could be the source of recurrent zoonotic transmissions of STLV-1 to local human population. STLV-1 found in non-human primates represents a measurable proportion of HTLV-1 infections [17]. There are seven subtypes of HTLV-I which are classified based on geographic distribution and nucleotide diversity of the long terminal repeat (LTR) and envgene sequences: Subtype a which is cosmopolitan, subtype b found in central Africa, central Africa/pygmies subtype c and Australian/Melanesian subtype d. The cosmopolitan subtype found in several geographic regions such as Japan, West and North Africa is the most widespread. Subtypes e, f, g are rare and limited numbers of strains have been reported in central Africa [18]. Subtype A can be divided into five subgroups based on geographical distribution: Transcontinental (A), Japanese (B), West African/Caribbean (C), North African (D) and Black Peruvian (E) [18].

Molecular epidemiology studies have distinguished four main HTLV-2 subtypes. HTLV-2a and HTLV-2b are the most prevalent among PWIDs from urban areas of the Americas and Europe; the subtypes are also prevalent in the indigenous population of the Americas, with sporadic distribution in Asia and Africa [19]. HTLV-2a has been reported in some American Indian tribes of North, Central and South America including; the Navajo and Pueblo in New Mexico as well as the Kayapo, Kraho and Kaxuyana in Brazil [20]. HTLV-2c variant was detected in the indigenous population of the Brazilian Amazon and in PWIDs from urban populations in Brazil [19]. Three different phylogroups within the 2a subtype (AI-AIII) and four different phylogroups within the 2b (BI-BIV) subtype have been described [20].

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HTLV among PWIDs

The highest prevalence of HTLV has been observed among PWIDs. HTLV-1/2 infection occurs more frequently among PWIDs [21]. Transmission has been associated with high-risk injection and sexual practices. Needle sharing is hypothesized to be one of the major routes of HTLV-2 transmission among PWIDs in the United States and Europe [4]. The largest number of HTLV-2 infected persons is in the United States (400,000-500,000) reflecting the confluence of endemic Amerindian, hyper endemic PWIDs and secondary sexual spread to the general population [22]. In North American PWIDs where HTLV-2 is endemic, Seroprevalence rates vary between 8.8% to 17.6% [7]. HTLV-1/2 prevalence of 19.1% was reported among PWIDs in Argentina [23]. In Europe, HTLV-2 mainly occurs among PWIDs with prevalence of up to 15% and HTLV-1 among general population with prevalence of less than 1% [7].

HIV among PWIDs

Intravenous drug use (IDU) is an important risk factor for infection with HIV. Studies indicate that PWIDs are at a high risk for HIV transmission through unsafe practices such as sharing non-sterile injecting equipment and unprotected sex. PWIDs often engage in more high-risk sexual behavior with multiple or concurrent partners. This can transfer HIV from PWID to non-PWID populations and extend or prolong the generalized epidemic [24]. One in seven PWIDs is living with HIV [25]. Globally, around 13 million people inject drugs and 1.7 million of them are living with HIV. PWIDs account for approximately 10% of HIV infections globally and 30% of HIV infections outside of Africa.

Regional HIV prevalence rates are high in people who inject drugs in all parts of the world with up to 15.5% in East and Southern Africa [26]. It has been estimated that 17% of new HIV infections at the Kenyan coast are linked to PWIDs. In Kenya, HIV prevalence among PWIDs in Malindi sub-county based was estimated to be 53.1% based on a study involving 211 PWIDs [27]. The efficiency of HIV transmission per injection is six times higher than for heterosexual route thus HIV prevalence among PWIDs can rapidly reach high levels of more than 50% and up to 90% [28]. HIV prevalence among African PWIDs far exceeds that in the general population, ranging from 9% to 50% [24].

HIV/HTLV Co-infection among PWIDs

HIV/HTLV co-infection is growing worldwide, mainly in South America and Africa [28]. The effects of HTLV-HIV co-infection on humans have been widely studied. HTLV-1 co-infection has been associated with a more rapid progression of HIV-1 disease, higher mortality and increased frequency of opportunistic infections but has also been associated with delaying HIV-1 disease progression [7]. It is generally accepted that HTLV-2 exerts a negative effect on HIV- 1 replication. Several authors have associated HTLV-2 co-infection with a better outcome for HIV-1 positive PWIDs as it was observed that co-infected patients showed reduced HIV-1 replication presumably due to lower levels of T cell activation [29].

Trends in the Global prevalence of HTLV/HIV Co-infection among PWIDs

Ten articles that reported HTLV/HIV co-infection among PWIDs from different countries were selected for analysis (Table 1). The country, HTLV virus tested, risk factors analyzed, authors and time were noted. Half of the studies analyzed HTLV-1/2/HIV co-infection whiles the remaining half analyzed HTLV-2/HIV co-infection. Out of the ten studies, 9 studies analyzed risk factors that were significant with HTLV/HIV co-infection among PWIDs. The trend in prevalence over time showed that HTLV-1/2/HIV co-infection decreased over years as the initial prevalence in 1990 was 14.6% while the last prevalence documented in 2006 was 6.7%. HTLV-2/HIV co-infection decreased steadily between 1995 and 2005 from 5.8% and 0.51%. The highest HTLV/HIV Co-infection prevalence was 16% from USA. Ireland had the second highest co-infection prevalence of 14.6%. The lowest prevalence was 0.51% from Portugal. Half of the studies were done in USA.

Table 1: Summary of HTLV/HIV Co-infection prevalence among PWIDs 1990-2006.

Country	Type of HTLV	P (%)	Risk Factors	Authors	Year
Ireland	HTLV-1/2	15	Black race p<0.01, older age p<0.01	Lee et al. [31]	1990
USA	HTLV-1/2	2.7	Black race p>0.001, older age p<0.001, females p< 0.001	Cantor et al. [32]	1991
USA	HTLV-2	5.8	Black race p<0.05,older age p<0.05,	Briggs et al. [33]	1995
			female gender p<0.05, HIV infection p<0.05		
USA	HTLV-2	3.3	None of the factors were significant	Giacomo et al. [34]	1995
USA	HTLV-2	2.3	None of the factors were significant	Hershow et al. [35]	1996
Brazil	HTLV-1/2	8.8	Black race p<0.001,old age p<0.001, longer duration of IVD use p<0.001, CD4:CD8 cell ratio p<0.001	Lentino et al. [21]	1997
Italy	HTLV-2	1.8	None of the factors were significant	Egal et al. [36]	1999
USA	HTLV-1/2	16	Risk factors not determined	Guimaraes et al. [37]	2001
Portugal	HTLV-2	0.5	None of the factors were significant	Silva et al. [38]	2005
Italy	HTLV-1/2	6.7	HCV serology p<0.0001, older age p<0.0001, CD4:CD8 cell ratio p<0.0001	Turci et al. [39]	2006

P(%)-Prevalence percentage, HCV-Hepatitis C virus, All the studies analyzed the blood samples using ELISA followed by confirmation with western blot except the study by Turci et al. [39], that used PCR (polymerase chain reaction). No published studies for the period 2007 to 2017 were retrieved.

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In USA, co-infection prevalence increased from 2.7% in 1991 to 16% in 2001. In Italy, prevalence of 1.8% and 6.7% were recorded in 1999 and 2006 respectively. The reduced HTLV/HIV co-infection prevalence over the years could be attributed to the establishment of harm reduction measures such as provision of free needles and syringes, education awareness, provision of condoms and HIV testing and counseling. All these measures play a major role in mitigating spread of the virus among the PWIDs. United States together with countries such as China, Russian Federation and Brazil are estimated to have the largest populations of PWIDs and together account for 45% of the total estimated worldwide population of PWIDs. Given that HIV infections are high among PWIDs in all areas of the world, HTLV rates could also be higher due to similar transmission patterns. These could all be possible explanations for the high prevalence observed in USA.

The origin of the HTLV-2 epidemic is not entirely defined but it is likely that the initial HTLV-2 epidemic in the United States occurred in PWIDs as early as the late 1960s [30]. This could explain why most of HTLV-2 studies focused on PWIDs. The low prevalence of 0.51% recorded in Portugal is attributed to the fact that this was the first time HTLV-2 cases were identified in Portugal [31]. This indicates that Portugal may not be an endemic area for HTLV-2. In addition it could imply that there are very few immigrants from endemic regions. Older age and Black race were reported in five studies as the main significant risk factors [21,32-35]. Others included female gender [33,34], longer duration of PWID [21], HCV infection 35 [39] and high CD4:CD8 T-cell ratio [21,35].

Trends in the Global prevalence of HTLV/HIV Co-infection among Hospital patients

Studies from different countries published between 2001 and 2017 were examined as summarized in (Table 2). Only fifteen studies that had analyzed HTLV-HIV co-infection among hospital based patients were selected. The country, HTLV virus tested, risk factors, authors and time were noted. Out of the twelve studies, eight analyzed HTLV-1/2/HIV Co-infection, five analyzed HTLV-1/HIV Co-infection and two analyzed HTLV-2/HIV Co-infection. Nine studies were from Brazil, three from Mozambique and one study each from Mexico, Nigeria and Kenya. Ten studies analyzed risk factors associated with HTLV/HIV co-infection among hospital based patients. The trend in prevalence over time showed that there was a decrease in HTLV-1/2/HIV co-infection from 5.0% in 2005 to 4.2% in 2017.

Table 2: Summary of HTLV/HIV Co-Infection prevalence among HTLV-HIV Co-infected Patients 2001-2017.

Country	Type of HTLV	P (%)	Risk Factors	Authors	Year
Brazil	HTLV-1	4.7	Risk Factors not determined	Ferreira et al. [41]	2001
Brazil	HTLV-1/2	5	Tattooing P=0.035, alcohol abuse P=0.008,	Galetto et al. [29]	2005
			history of blood transfusion P=0.039		
Brazil	HTLV-1/2	13.4	IDU P<0.01, HCV seropositivity P<0.01, non-white race P<0.01, Low level of education P<0.01	Etzel et al. [5]	2006
Brazil	HTLV-1/2	2.4	injecting cocaine(OR=5.2, P<0.001), older age (OR=1.7, P<0.001), HIV (OR=3, P<0.001)	Barcellos et al. [42]	2006
Brazil	HTLV-1/2	6.4	HCV (OR=22.6, P<0.05)	Morimoto et al. [43]	2006
Brazil	HTLV-1/2	3.11	female gender (OR=3.26, P<0.05), black/pardo race (OR=2.21, P<0.05), HCV (OR=24.4, P<0.05) IDU (OR=30.01 P<0.05)	Caterino de Araujo et al. [44]	2010
Nigeria	HTLV-1	4.9	Risk factors not determined	Nasir et al. [45]	2012
Brazil	HTLV-1/2	0.79	None of the factors were significant	Kozlowski et al. [11]	2014
Mexico	HTLV-2	12.5	Candidiasis p=0.0004, AIDS P=0.02	Castro Sansores et al. [46]	2015
Mozambique	HTLV-1	4.5	Risk factors not determined	Bhatt et al. [47]	2015
Brazil	HTLV-2	9.7	HCV P=0.006, Male gender P=0.03, IDU P=0.0005	Posada et al. [48]	2016
Kenya	HTLV-1	19.5	HIV P<0.01, Smoking p<0.01, high number of marriages p<0.01,high number of sexual partners p<0.05	He et al. [9]	2016
Mozambique	HTLV-1/2	1.55	Female gender	Augusto et al. [49]	2017
Mozambique	HTLV-1	3.9	Risk factors not determined	Ivan et al. [50]	2017
Brazil	HTLV-1/2	4.2	Risk factors not determined	Campos et al. [51]	2017

HTLV testing was done using enzyme linked immunosorbent assay (ELISA) followed by confirmation with western blot in all studies except the study by Galetto et al. [29], and He et al and Ivan et al which used PCR polymerase Chain Reaction and Campos et al which used INNO-LIA, Western Blot and PCR, IDU-intravenous drug use, HCV-Hepatitis C virus, HIV-Human Immunodeficiency Virus

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HTLV-1/HIV co-infection decreased from 4.7% in 2001 to 3.9% in 2017. The highest and lowest co-infection prevalence of 19.5% and 0.79% were recorded in Kenya and Brazil respectively. An increased HTLV/HIV co-infection among patients suggests involvement in high risk behaviors such as unprotected sex, multiple sex partners and high risk injection behaviors which aggravate the risk of infection. In addition, HIV infection increases the risk of HTLV transmission due to similar modes of transmission and tropism towards CD4 and CD8 T-Cells. Decreased co-infection prevalence could be due to establishment of harm reduction measures such as provision of free needles and syringes, education awareness, provision of condoms and HIV testing and counseling which play a major role in mitigating spread of the virus among the HIV-positive patients.

In Africa, Kenya had the highest prevalence of 19.5% followed by Nigeria and Mozambique with 4.9% and 4.5% respectively [9,36,37]. Africa is considered to be a large reservoir for HTLV-1 infection. The fact that the highest co-infection prevalence was documented in Kenya reinforces the finding that Kenya may be endemic for HTLV-1. This further confirms the association between HTLV-1 and HIV since HIV increases the risk of acquiring HTLV [9]. In Brazil, HTLV-1/2 Seroprevalence is relatively high in HIV- positive patients and according to the Brazilian regions that analyzed these rates; it is documented that they could reach 20% in some studies [29]. This explains why majority of the studies are conducted in Brazil for continuous monitoring of the prevalence rates.

The public health system in Brazil provides prevention programs as well as free and universal access to antiretroviral treatment for HIV/ AIDS [11]. This could account for the lowest prevalence documented in Brazil. Socio-demographic factors significantly associated with HTLV/HIV co-infection include older age, low level of education and non-white race. Significant risk factors for HTLV-HIV co-infection among Patients included; tattooing, alcohol abuse, history of blood transfusion, injecting cocaine, smoking, high number of marriages and high number of sexual partners. Infections such as HIV, HCV and candidiasis were also significantly associated with HTLV/HIV co-infection among hospital-based patients.

Trends in the Global prevalence of HTLV among PWIDs

A total of 29 studies that had analyzed HTLV infection among PWIDs were selected. The studies were summarized according to country, HTLV virus tested and risk factors analyzed as summarized in (Table 3). Majority (38%) of the studies were done in USA. There were two studies each from Elsavador, Argentina, Italy, Sweden and Spain. There was one study each from the following countries; Scotland, Mexico, Brazil, Indonesia, Iran and Estonia. Out of 29 studies, 4 studies analyzed HTLV-1 among PWIDs, 11 analyzed HTLV-2 among PWIDs and 14 analyzed HTLV-1/2 among PWIDs.

Twenty two studies analyzed risk factors associated with HTLV infection among PWIDs. Over time, there was a general increase in HTLV-1 prevalence from 6.6 % in 1988 to 52% in 2004 [38,39]. There was a general decrease in HTLV-2 prevalence from 10.7% in 1989 to 3.2% in 2011 [40,41]. There was also a decrease in HTLV-1/2 prevalence from 12.2% in 1990 to 0.3% in 2016 [7,32]. From USA, there were six studies each on HTLV-2 and HTLV-1/2. There was also a general increase in HTLV-2 prevalence unlike HTLV-1/2 where there was a decrease.

The highest documented prevalence of HTLV among PWIDs was 52% from Iran [39]. This could possibly be due to the increasing rate of addiction and injection drug use in Iran together with risky behaviors such as needle sharing, front loading, tattooing and multiple sexual partners [39]. The lowest prevalence recorded was 0.0% from Scotland. This could be explained by free needles and syringes which were made available to the PWIDs thus reduced needle sharing [42].

Estonia recorded a low prevalence of 0.3% [7]. This might be explained by three reasons. First, there are very few immigrants from HTLV-1/HTLV-2 endemic regions living in Estonia. Second, the PWIDs population in Estonia is relatively closed. Third, the studied PWIDs were relatively young (25-34) whereas HLTV causes lifelong infection and the prevalence is usually higher among older people [7]. The fact that HTLV-2 studies were only done in USA and Sweden supports the view that HTLV-2 is more frequent among (PWIDs) in United States and Europe [19]. This could also account for the majority of HTLV studies on PWIDs being done in USA.

Socio- demographic risk factors significantly associated with prevalent HTLV infection among PWIDs included increasing age, female gender, black race, Mexican American race and African-American race [21,32,33,43-45]. Injection related risk factors included needle sharing, longer duration of PWID, speed balling, tattoo, injecting opiates, frontloading and back loading [4,38,39,46,47]. Sexual risk factors included commercial sex and sexual promiscuity [38,46]. Prior history of HIV-1, HBV (Hepatitis B virus), HCV (Hepatitis C virus) and Syphilis infection was also significantly associated with HTLV seropositivity among PWIDs [4,23,44,45].

Analysis of HTLV Subtypes present among HTLV mono-infected PWIDs and HTLV-HIV co-infected PWIDs and Hospital based patients

Thirteen studies on HTLV subtypes were retrieved (Table 4). Only those studies on HTLV subtypes that focused on HTLV infected PWIDs, HTLV-HIV co-infected patients and HTLV-HIV co-infected PWIDs were selected for review. A total of eleven studies evaluated HTLV-2 subtypes: one was on HTLV-1 and two were on HTLV-1/2 subtypes. Only one study from USA that focused on HTLV infected PWIDs determined risk factors associated with HTLV-2a subtype. These included older age and black and white race [48]. HTLV-2 subtypes identified among HTLV/HIV co-infected PWIDs included HTLV-2a and HTLV-2b while HTLV-2a, 2b and 2c were identified among HTLV/HIV co-infected patients. HTLV 2a and 2b were identified among HTLV-2 infected PWIDs. HTLV-1 subtype a subgroup A (cosmopolitan) was identified among HTLV-HIV co-infected patients in Brazil. Prevalence of HTLV-2a and 2b subtypes among PWIDs in North America, South America and Europe reinforces the theory that HTLV-2a and 2b subtypes are endemic among PWIDs in the Americas and Europe [19].

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Table 3: Summary of HTLV prevalence among PWIDs 1988-2016.

Country	Type of HTLV	P (%)	Risk Factors	Authors	Year
Italy	HTLV-1	6.6	sexual promiscuity (OR=5.3, 95% CI 1.2-22.3), needle sharing (OR=31.9, 95% CI 1.03-64.9)	Titti et al. [52]	1988
USA	HTLV-2	10.7	Risk factors not determined	Ehrlich et al. [53]	1989
USA	HTLV-1/2	12.2	Black race p<0.05, Older age p<0.01	Lee et al. [31]	1990
Egypt	HTLV-1`	0.7	None significant	Constantine et al. [54]	1991
USA	HTLV-1/2	16.8	black race p<0.0001, increasing age, longer duration of IDU older age p<0.0001	Lentino et al. [21]	1991
USA	HTLV-2	11.5	increasing age P<0.001, female gender P<0.001, Black race P<0.001	Cantor et al. [32]	1991
USA	HTLV-2	8	Older age P<0.01	Khabbaz et al. [55]	1991
Italy	HTLV-1/2	4	HIV-1 seropositivity P<0.002, increasing age P<0.001 longer duration of IDU P<0.05	Zanetti et al. [56]	1992
Mexico	HTLV-1/2	21	None significant	Guerena-Burgueno et al. [57]	1992
USA	HTLV-1/2	1.7	Risk factors not determined	Palumbo et al. [58]	1992
Sweden	HTLV-2	3.2	HIV infection p<0.05, HAV infection p<0.05, age p<0.05 injecting opiates p<0.05 longer duration of IDU p<0.05,	Krook et al. [59]	1994
Italy	HTLV-2	1.6	Risk factors not determined	Giacomo et al. [34]	1995
Spain	HTLV-1/2	2.5	Risk factors not determined	Henrard et al. [60]	1995
USA	HTLV-2	15.1	older age p<0.001, female gender p<0.001, black race p<0.001	Briggs et al. [33]	1995
USA	HTLV-2	10.2	Back loading (OR=6.52, 95% C1 1.94-21.95),Female gender (OR=5.77, 95% C1 1.33-25.05) commercial sex (OR=3.36, 95% CI 1.32-8.57)	Vhalov et al. [61]	1995
USA	HTLV-1/2	19.3	Age p<0.05	Freeman et al. [62]	1995
Brazil	HTLV-1	35.2	needle sharing (OR=7.94, 95% C1 1.32-47.6), duration of IDU(OR=3.30, 95% C1 1.60-6.80) HIV-1 infection (OR=7.52, 95% C1 2.61-12.34), syphilis (OR=5.68, 95% C1 2.61-12.34)	Dourado et al. [63]	1999
El Salvador	HTLV-1/2	16.6	Risk factors not determined	Guimaraes et al. [37]	2001
Scotland	HTLV-1/2	0	Risk factors not determined	McIntyre et al. [64]	2001
Argentina	HTLV-1/2	16.8	None significant	Wessein bacher et al.[65]	2003
USA	HTLV-2	21	None significant	Trachtenberg et al. [66]	2004
Iran	HTLV-1	52	needle sharing 49%, frontloading 20%, Tattoo 57%	Rahbar-Rowhani et al. [67]	2004
USA	HTLV-2	7.4	Speed balling (OR=1.79, P<0.001), female gender (OR=3.17, P<0.001),African-American race (OR=8.80, P<0.001), longer duration of IDU (OR=3.7, P<0.001), HBV Infection (OR=2.58, P<0.001) HCV infection (OR=12.76, P<0.001)	Zunt et al. [4]	2004
Spain	HTLV-2	2.8	HIV-1 seropositivity (OR=5.7, 95% CI 2.2-14.8), injected in last 30 days,(OR=6.5, 95% CI 1.4-29.8)	Fluente et al. [68]	2006
Argentina	HTLV-1/2	19.1	Young age (OR=10.7 P=0.004), Low education level (OR=6.7 P=0.048)	Berini et al. [22]	2007
El Salvador	HTLV-1/2	4	None significant	Nunes et al. [69]	2007

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Sweden	HTLV-2	3.2	Risk factors not determined	Malm et al. [70]	2011
Indonesia	HTLV-1/2	3.7	None significant	prasetyo et al. [71]	2013
Estonia	HTLV-1/2	0.3	Risk factors not determined	Jogeda et al. [7]	2016

HTLV testing was done using enzyme linked immunosorbent assay (ELISA) followed by confirmation with western blot in all studies except the study by Jogeda et al. [7] which used PCR-polymerase chain reaction. The study by Guerena-Burqueno et al. [57] and Ehrlich et al. [53] used RIA-radioimmunoassay and PA-particle agglutination in addition to Elisa and WB, HAV-hepatitis A virus, HBV-hepatitis B virus, HIV-1-Human immunodeficiency virus type 1, IDU-intravenous drug use, OR-odds ratio

Table 4: HTLV subtypes among different populations 1995-2016.

Country	Population	Type of HTLV	Sub Types	Authors	Year
Italy	HTLV infected IDUs	HTLV-2	HTLV-2a, HTLV-2b	Salemi et al. [72]	1995
USA	HTLV infected IDUs	HTLV-2	HTLV-2a	Murphy et al.[73]	1998
Portugal	HTLV-HIV Co-infected IDUs	HTLV-2	HTLV-2b	Silva et al. [38]	1998
Europe	HTLV infected IDUs	HTLV-2	HTLV-2a,HTLV-2b	Salemi et al. [20]	1998
Brazil	HTLV infected IDUs	HTLV-2	HTLV-2a	Alcantara et al. [74]	2003
Ireland	HTLV-HIV Co-infected IDUs	HTLV-2	HTLV-2a	Egan et al. [36]	2004
Spain	HTLV infected IDUs	HTLV-2	HTLV-2b	Toro et al. [75]	2005
Brazil	HTLV-HIV Co-infected patients	HTLV-1/2	HTLV-1a subgroup a, HTLV-2c	laurentino et al. [76]	2005
Argentina	HTLV-HIV Co-infected IDUs	HTLV-2	HTLV-2a, HTLV-2b	Berini et al. [23]	2007
Brazil	HTLV-HIV Co-infected patients	HTLV-1/2	HTLV-1a subgroup A, HTLV-2c	Rego et al. [18]	2010
Spain	HTLV-HIV Co-infected IDUs	HTLV-2	HTLV-2b	Abad et al. [77]	2011
Brazil	HTLV-HIV Co-infected patients	HTLV-2	HTLV-2a, HTLV-2b, 2c	Magri et al. [19]	2013
Indonesia	HTLV-HIV Co-infected patients	HTLV-2	HTLV-2a	Prasetyo et al. [71]	2013
Brazil	HTLV-HIV Co-infected patients	HTLV-1	HTLV-1a subgroup A	Kozlowski et al. [11]	2016

IDUs-intravenous drug users OR-Odds Ratio CI-Confidence interval

Since HTLV subtypes are geographically dispersed, subtypes were analyzed according to the resident country. From Brazil, subtypes identified included HTLV-2a and 2b both from HTLV-infected and HTLV-HIV co-infected PWIDs. HTLV-1a cosmopolitan and HTLV-2c were also identified from HTLV-HIV co infected patients in Brazil. HTLV-2a is the most predominant subtype subtype in Brazil [23]. The finding of subtype 2a among PWIDs by clearly indicates that these PWIDs had little interaction with individuals or blood products from other geographic areas and also with PWIDs co-infected with HIV/HTLV-2 outside Brazil [49]. HTLV-2b in Brazilian States indicates spread of this subtype from the state of Rio Grande do Sul where this subtype is prevalent [19]. HTLV-1a subgroup A (transcontinental) is in agreement with studies reported in HIV1-infected patients in Brazil in whom this HTLV1 subgroup is predominant [11].

Recent studies suggest that the introduction of the transcontinental subgroup is probably the result of the Bantu population's migration over the last 3000 years from Central Africa to Southern Africa, then eventually to the State of Bahia [18]. Data from Brazil indicate that the HTLV-2c molecular variant was formerly present in native Indian tribes with posterior dissemination to the urban population of Brazil. Possibly this occurred through inter-ethnic contact by sexual intercourse and is maintained in Indians mostly by breast feeding [19]. From Argentina, HTLV-2a and 2b subtypes have been reported among HTLV-HIV co-infected PWIDs. HTLV-2b is the major strain circulating in an urban population of Argentina. Its presence may be due to the increasing internal migration of aborigines from the northeast region where subtype 2b is endemic to large urban centers [23].

HTLV-2a could have been introduced from endemic South American countries such as Brazil and because of contact with other populations such as PWIDs from Europe through migration and tourism [50]. HTLV-2a in Indonesia could have been introduced from USA where the subtype is common since the isolates resembled the USA subtype a [51]. HTLV-2a and 2b subtypes were identified from Portugal, Italy, Spain and Ireland (Europe) among HTLV-infected and HTLV-HIV co-infected PWIDs. HTLV-2b is the prevalent subtype in Western Europe (Italy, Spain and Portugal) where co-infection with HIV-1 is frequent. HTLV-2a is the main circulating variant in North America and Eastern Europe-Ireland [52-79]. HTLV-2a from Italy implies introduction from Brazil, North America or Eastern Europe where the subtype is predominant.

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Conclusion

This review has focused on prevalence, risk factors and subtypes among HTLV-HIV positive PWIDs, HIV positive patients and HTLV positive PWIDs. The prevalence varied between and within countries and population groups. Concerning HTLV-HIV co-infection among PWIDs, there has been a general decrease in prevalence over time. The highest documented prevalence was 16% from USA while the lowest was 0.51% from Portugal among HTLV-HIV co-infected PWIDS. Both HTLV-2/HIV and HTLV-1/HIV co-infection among HIV positive patients showed a decreasing trend over years. The highest HTLV-HIV co-infection prevalence among HIV infected patients was 19.3% from Kenya while the lowest was 0.79% from Brazil. There was a general decrease in HTLV-2 infection among PWIDs unlike HTLV-1 where an increase was observed.

Highest and lowest HTLV prevalence among PWIDs were 52% and 0.0% from Iran and Scotland respectively. Majority of the studies focused on HTLV-HIV co-infected and HTLV infected PWIDs were from USA. HTLV subtypes are geographically dispersed and an introduction of a new subtype to a particular geographical region indicates contact through immigration or tourists. Older age and black race were the main risk factors for HTLV-HIV co-infection among PWIDs, HIV positive patients and HTLV infected PWIDs. Other socio-demographic, injection and sexually related factors varied from one study to another.

Recommendations

The epidemic of HTLV-HIV co-infections among PWIDs and HIV positive patients constitutes a major public health problem and should be addressed to prevent further spread in the community. Harm reduction measures such as provision of free needles and syringes, HIV counseling and treatment coupled with educational programmes could be explored. Regular serological testing of HTLV-1/2 should be introduced among HIV-infected PWIDs especially in clinical settings where PWID is a major mode of HIV transmission. Frequent HTLV-HIV testing will assist in continuous monitoring of the prevalence rates. More research on HTLV infection is imperative for generating data on prevalence, elaborate public policies on educational and prophylactic measures, increase the awareness of the infection and reduce the viral transmission and infection-related disease.

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Conflict of Interest

None.

References

1. Gonçalves DU, Proietti FA, Ribas GR, Araújo MG, Pinheiro SR et al. (2010) Epidemiology, treatment, and prevention of human T-cell leukemia virus type 1-associated diseases. Clin Microbiol Rev 23 (3): 577-589.
2. ECDC (2015) Technical Report on Geographical distribution of areas with a high prevalence of HTLV-1 infection. Europe, p. 2-45.
3. González-Alcaide G, Ramos JM, Huamaní C, Mendoza CD, Soriano, V (2016) Human T-Lymphotropic Virus 1 (HTLV-1) and Human T-Lymphotropic Virus 2 (HTLV-2): Geographical Research Trends and Collaboration Networks (1989-2012). Rev Inst Med Trop Sao Paulo 58: 2-9.
4. Zunt JR, Tapia KEN, Thiede H, Lee R, Hagan H (2009) HTLV-2 infection in injection drug users in King County, Washington. Scand J Infect Dis 38(8): 654-663.
5. Etzel A, Shibata GY, Rozman M, Jorge MLSG, Damas CD, et al. (2001) HTLV-1and HTLV-2 Infections in HIV Infected from Santos, Brazil: seroprevalence and risk factors. J Acquir Immune Defic Syndr 26(2): 185-190.
6. Fox JM, Mutalima N, Molyneux E, Carpenter LM, Taylor GP, et al. (2016) Seroprevalence of HTLV-1 and HTLV-2 amongst mothers and children in Malawi within the context of a systematic review and meta-analysis of HTLV seroprevalence in Africa. Trop Med Int Health 21(3): 312-324.
7. Jõgeda EL, Avi R, Pauskar M, Kallas E, Karki T, et al. (2016) Human T-lymphotropic virus types 1 and 2 are rare among intravenous drug users in Eastern Europe. Infect Genet Evol 43: 83-85.
8. Songok EM, Tukei PM, Libondo D, Gichogo A, Oogo SA (1994) Low prevalence of HTLV-1 in HIV positive patients in Kenya. J Acquir Immune Defic Syndr 7(8): 876-877.
9. He X, Maranga IO, Oliver AW, Gichangi P, Hampson L, et al. (2016) Analysis of the Prevalence of HTLV-1 Proviral DNA in Cervical Smears and Carcinomas from HIV Positive and Negative Kenyan Women. Viruses 8(9): 245.
10. Degenhardt L, Hall W, (2012) Extent of illicit drug use and dependence, and their contribution to the global burden of disease. Lancet 379(9810): 55-70.
11. Kozlowski AR, De-Matos MAD, Carneiro MADS, Lopes CLR, TELES SA, et al. (2016) Seroprevalence of HTLV in a population of HIV I-infected patients in Midwestern Brazil. Rev Inst med Trop Sao Paulo 58: 1-80.
12. NACC (2016) Kenya AIDS response progress report. Kenya, p. 44-92.
13. Beilke MA (2012) Retroviral Coinfections: HIV and HTLV : Taking Stock of More Than a Quarter Century of Research. AIDS Research and Human Retroviruses 28(2): 139-147.
14. Pinto MT, Rodrigues ES, Malta TM, Azevedo R, Takayanagui OM, et al. (2012) HTLV-1/2 seroprevalence and co-infection rate in Brazilian First-time blood donors: an 11-year follow up. Rev Inst Med Trop Sao Paulo 54(3): 123-129.
15. Catalan-soares B, Carneiro-Proietti ABF, Proietti FA, (2005) Heterogeneous geographic distribution of human T-cell lymphotropic viruses I and II (HTLV-I/II): serological screening prevalence rates in blood donors from large urban areas in Brazil. Cad Saude Publica 21(3): 926-931.
16. Mahieux R, Gessain A (2011) HTLV-3/STLV-3 and HTLV-4 Viruses: Discovery, Epidemiology, Serology and Molecular Aspects. Viruses 3(7): 1074-1090.
17. Calvignac-Spencer, Adjogoua EV, Akoua-Koffi C, Hedemann C, Schubert G, et al. (2012) Origin of Human T Lymphotropic Virus Type 1 in Rural Côte d'Ivoire. Emerg Infect Dis 18(5): 830-833.
18. de Almeida Rego FF, Mota-Miranda A, de Souza Santos E, Galvão-Castro B, Alcantara LC, (2010) Seroprevalence and Molecular Epidemiology of HTLV-1. AIDS Res Hum Retroviruses 26(12): 1333-1339.

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19. Magri MC, Fernando L, Brigido DM, Morimoto HK, Caterino-de-araujo A (2013) Human T Cell Lymphotropic Virus Type 2a Strains Among HIV Type 1-Coinfected Patients from Brazil. AIDS Res Hum Retroviruses 29(7): 1010-1019.

20. Salemi M, Vandamme A, Gradozzi C, Laethem KV, Cattaneo E, et al. (1998) Evolutionary Rate and Genetic Heterogeneity of Human T-Cell Lymphotropic Virus Type II (HTLV-II) Using Isolates from European Injecting Drug Users. J Mol Evol 46(5): 602-611.

21. Lentino JR, Pachucki CT, Schaaff DM, Holzer TJ, Heynen C, et al. (1991) Seroprevalence of HTLV-1/2 and HIV-1 infections among Male PWIDs in Chicago. J Acquir Immune Defic Syndr 4: 901-909.

22. Murphy EL (2016) Infection with human T-lymphotropic virus types 1 and 2 (HTLV-1 and-2): Implications for blood transfusion safety. Transfus Clin Biol 23(1): 13-19.

23. Berini CA, Pando MA, Bautista CT, Eirin ME, Martinez-peralta L, et al. (2007) HTLV-1/2 Among High-Risk Groups in Argentina : Molecular Diagnosis and Prevalence of Different Sexual Transmitted Infections. J Med Virol 79(12): 1914-1920.

24. Brodish P, Singh K, Rinyuri A, Njeru C, Kingola N, et al. (2012) Evidence of high-risk sexual behaviors among injection drug users in the Kenya PLACE Study. Drug Alcohol Depend 119(1-2): 138-141.

25. UNODC (2016) World Drug Report, HIV/AIDS and Drugs. New York, USA, pp. 1-174.

26. WHO (2016) consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. USA, pp. 1-184.

27. Ng'ong'a GO, Carol H, Osman S, Lwembe RM (2015) Predisposing Factors for HIV Infection among Injecting Drug Users in Malindi Sub-County, Kenya. IJHSR 6(1): 417-434.

28. UNODC (2010) World Drug Report, HIV/AIDS and Drugs. New York, USA, pp. 1-313.

29. Isache C, Sands M, Guzman N, Figueroa D (2016) HTLV-1 and HIV-1 co-infection: A case report and review of the literature. Elsevier 4: 53-55.

30. Silva AF, Almeida C, Martins HC, Coutinho R, Leitão E, et al. (2005) Prevalence and Molecular Characterization of Human T Cell Leukemia Virus Type 2 in a Group of Intravenous Drug Users Coinfected with HIV Type 1 in Portugal. AIDS Res Hum Retroviruses 21(4): 249-255.

31. Lee, HH, Weiss SH, Brown LS, Mildvan D, Shorty V, et al. (2016) Patterns of HIV-1 and HTLV-I / II in Intravenous Drug Abusers from the Middle Atlantic and Central Regions of the USA. J Infect Dis 162(2): 347-352.

32. Cantor KP, Weiss SH, Goedert JJ, Battjes RJ, (1991) HTLV-I/II seroprevalence and HIV/HTLV coinfection among U.S. intravenous drug users. J Acquir Immune Defic Syndr 4(5): 460-467.

33. Briggs NC, Battjes RJ, Cantor KP, Blattner WA, Yellin FM, et al. (2016) Seroprevalence of Human T Cell Lymphotropic Virus Type II Infection, with or without Human Immunodeficiency Virus Type 1 Coinfection among US Intravenous Drug Users. J Infect Dis 172(1): 51-58.

34. Turci M, Pilotti E, Ronzi P, Magnani G, Boschini A, et al. (2006) Coinfection With HIV-1 and Human T-Cell Lymphotropic Virus Type II in Intravenous Drug Users Is Associated With Delayed Progression to AIDS. AIDS Res Hum Retroviruses 41(1): 100-106.

35. Nasir IA, Ahmad AE, Emeribe AU, Shehu MS, Medugu JT, et al. (2015) Molecular Detection and Clinical Implications of HTLV-1 Infections among Antiretroviral Therapy-Naïve HIV-1-Infected Individuals in Abuja, Nigeria. Virology (Auckl) 6: 17-23.

36. Bhatt NB, Gudo ES, Sema C, Bila D, Mattei PD, et al. (2009) Loss of correlation between HIV viral load and CD4 + T-cell counts in HIV / HTLV-1 co-infection in treatment naive Mozambican patients. Int J STD AIDS 20(12): 863-868.

37. Titti F, Rezza G, Verani P, Butto S, Sernicola L, et al. (1988) HIV, HTLV-1and HBV Infections in a Cohort of Italian Intravenous drug users: Analysis of risk factors. J Acquir Immune Defic Syndr 1(4): 405-411.

38. Rowhani-Rahbar A, Tabatabaee-Yazdi A, Panahi M, (2004) Prevalence of common blood-borne infections among imprisoned injection drug users in mashhad, north-east of iran. Arch Iran Med 7(3): 190-194.

39. Ehrlich GD, Glaser JB, Lavigne K, Quan D, Mildvan D, et al. (2011) Prevalence of human T-cell leukemia/lymphoma virus (HTLV) type II infection among high-risk individuals: type-specific identification of HTLVs by polymerase chain reaction. Blood 74 (5): 1658-1664.

40. Malm K, Hillgren K, Britton S, Andersson S (2011) HTLV-2 infection still prevalent among older injecting drug users in Stockholm, Sweden - indications of limited spread to the younger generation. Retrovirology (Auckl) 8(1): A67.

41. McIntyre PG, Hill DA, Appleyard K, Taylor A, Hutchinson S, et al. (2001) Prevalence of antibodies to hepatitis C virus, HIV and human T-cell leukaemia/lymphoma viruses in injecting drug users in Tayside, Scotland, 1993-7. Epidemiol Infect 126(1): 97-101.

42. Khabbaz RF, Hartel D, Lairmore M, Horsburgh CR, Schoenbaum EE, et al. (1991) Human T Lymphotropic Virus Type II (HTLV-II) Infection in a Cohort of New York Intravenous Drug Users : An Old Infection ? J Infect Dis 163(2): 252-256.

43. Zanetti AR, Zehender G, Tanzi E, Galli C, Rezza G (1992) HTLV-II among Italian intravenous drug users and hemophiliacs. European Journal of Epidemiology 8(5): 702-707.

44. Krook A, Albert J, Andersson S, Biberfeld G, Blomberg J, et al. (1997) Prevalence and Risk Factors for HTLV-II Infection in 913 Injecting Drug Users in Stockholm, 1994. J Acquir Immune Defic Syndr Hum Retrovirol 15(5): 381-386.

45. Vlahov D, Khabbaz RF, Cohn, S, Galai N, Taylor E, et al. (1995) Incidence and risk factors for human T- lymphotropic virus type II seroconversion among injecting drug users in Baltimore. J Acquir Immune Defic Syndr Hum Retrovirol 9(1): 89-96.

46. Dourado I, Andrade T, Carpenter CL, Galvao-castro B (1999) Risk Factors for Human T Cell Lymphotropic Virus Type I among Injecting Drug Users in Northeast Brazil: Possibly Greater Efficiency of Male to Female Transmission. Mem Inst Oswaldo Cruz 94(1): 13-18.

47. Murphy EL, Mahieux R, De TG, Tekaia F, Ameti D (1998) Molecular Epidemiology of HTLV-II among United States Blood Donors and Intravenous Drug Users : An Age ± Cohort Effect for HTLV-II RFLP Type a0. Virol J 242(2): 425-434.

48. Alcantara LCJ, Shindo N, Dooren SV, Salemi M, Costa MCR, et al. (2003) Brazilian HTLV Type 2a Strains from Intravenous Drug Users (IDUs) Appear to Have Originated from Two Sources : Brazilian Amerindians and European/North American IDUs. AIDS Res Hum Retroviruses 19(6): 519-523.

49. Berini CA, Eirin ME, Delfino CM, Weissenbacher M, Biglione MM (2012) Predominance of Human Lymphotropic T Cell Virus Type 2 Subtype b in Urban Populations of Argentina. AIDS Research and Human Retroviruses 28(9): 1102-1109.

50. Prasetyo AA, Sari, Y (2017) Human T-lymphotropic virus-1/2 detected in drug abused men who have sex with men in Surakarta Indonesia AIP Conference Proceedings: 1813(1).

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51. Abad M, Dronda F, Dominguez E, Moreno S, Vallejo A (2011) HTLV-2b Among HIV Type 1-Coinfected injecting drug users in Spain. AIDS Res Hum Retroviruses 27(5): 579-583.

52. Galetto LR, Lunge VR, Béria JU, Tietzmann DC, Stein AT, Simon D (2014) Short communication: Prevalence and risk factors for Human T cell lymphotropic virus infection in Southern Brazilian HIV-positive patients. AIDS Res Hum Retroviruses. 30(9): 907-911.

53. Lee, HH, Weiss SH, Brown LS, Mildvan D, Shorty V, et al. (2016) Patterns of HIV-1 and HTLV-I / II in Intravenous Drug Abusers from the Middle Atlantic and Central Regions of the USA. J Infect Dis 162 (2): 347-352.

54. Giacomo M, Franco EG, Claudio C, Carlo C, Antoni D, et al. (2016) Human T-Cell Leukemia Virus Type II Infection among High Risk Groups and Its Influence on HIV-1 Disease Progression. Eur J Epidemiol 11(5): 527-533.

55. Hershow RC, Galai N, Fukuda K, Graber J, Vlahov D, et al. (1996) An International Collaborative Study of the Effects of Coinfection with Human T-Lymphotropic Virus Type llon Human Immunodeficiency Virus Type 1 Disease Progression in Injection Drug Users. J Infect Dis 174: 309-317.

56. Egan JF, Leary BO, Lewis MJ, Mulcahy F, Sheehy N, et al. (2004) High Rate of Human T Lymphotropic Virus Type IIa Infection in HIV Type 1-Infected Intravenous Drug Abusers in Ireland. AIDS Res Hum Retroviruses 15(8): 699-705.

57. Guimaraes ML, Bastos FI, Telles PR, Galvao-Castro B, Diaz RS, et al. (2001) Retrovirus infections in a sample of injecting drug users in Rio de Janeiro City, Brazil : prevalence of HIV-1 subtypes , and co-infection with HTLV-I / II. J Clin Virol 21(2): 143-151.

58. Ferreira OC, Vaz RS, Carvalho MB, Guerra C, Fabron AL, et al. (1995) Human T-lymphotropic virus type I and type II infections and correlation with risk factors in blood donors from São Paulo, Brazil. Transfus Med 35(3): 258-263.

59. Barcellos NT, Fuchs SC, Mondini LG, Murphy EL (2006) Human T Lymphotropic Virus Type I/II Infection: Prevalence and Risk Factors in Individuals Testing for HIV in Counseling Centers From Southern Brazil. Sex Transm Dis 33(5): 302-306.

60. Morimoto HK, Caterino-de-araujo A, Morimoto AA, Reiche EMV, Ueda LT, et al. (2005) Seroprevalence and Risk Factors for Human T Cell Lymphotropic Virus Type 1 and 2 Infection in Human Immunodeficiency Virus-Infected Patients Attending AIDS Referral Center Health Units in Londrina and Other Communities in Paraná, Brazil. AIDS Res Hum Retroviruses 21(4): 256-262.

61. Caterino-de-Araujo A, Sacchi CT, Gonçalves MG, Campos KR, Magri MC, et al. (2015) Short Communication :Current Prevalence and Risk Factors Associated with Human T Lymphotropic Virus Type 1and Human T Lymphotropic Virus Type 2 Infections Among HIV/AIDS Patients in Sao Paulo, Brazil. AIDS Res Hum Retroviruses 31(5): 543-549.

62. Castro-Sansores CJ, Santos-Rivero A, Lara-Perera DM, Alonso-Salomon G, et al. (2006) Co-infection by the human T-cell lymphotropic virus type II in patients infected by the human immunodeficiency virus in Yucatan, Mexico. Arch Med Res 37(3): 365-369.

63. Posada-Vergara MP, Montanheiro P, Fukumori LMI, Bonasser F, Duarte AJDS, et al. (2006) Clinical and epidemiological aspects of HTLV-II infection in São Paulo, Brazil: Presence of tropical spastic paraparesis/HTLV-associated myelopathy (TSP/HAM) simile diagnosis in HIV-1-co-infected subjects. Rev. Inst. Med. trop. Sao Paulo 48(4): 207-210.

64. Augusto Â, Augusto O2, Taquimo A3, Nhachigule C3, Siyawadya N, et al. (2017) First description of HTLV-1/2 seroprevalence in HIV-infected inmates in Mozambique. J Med Virol 89(8): 1498-1502.

65. Ivan M, Nilesh B, Nália M, Egidio N, Beatriz, G, et al. (2017) First Report of Prevalence of HTLV-1 Among HIV-1/2Infected Children in Mozambique. AIDS Res Hum Retroviruses 74(2): 54-56.

66. Campos KR, Gonçalves MG, Costa NA, Caterino-de-Araujo A (2017) Comparative performances of serologic and molecular assays for detecting human T lymphotropic virus type 1 and type 2 (HTLV-1 and HTLV-2) in patients infected with human immunodeficiency virus type 1 (HIV-1). Braz J Infect Dis 21(3): 297-305.

67. Constantine NT, Sheba MF, Corwin A, Danahy RS, Callahan JD, et al. (1991) A serosurvey for HTLV-I among high-risk populations and normal adults in Egypt. Epidemiol Inifect 107(2): 429-433.

68. Guerena-Burgueno F, Benenson AS, Sepulveda-Amor J, Ascher MS, Vugia DJ, et al. (1992) Prevalence of human T cell lymphotropic virus types 1 and 2 (HTLV-1/2) in selected Tijuana subpopulations. Am J Trop Med Hyg 47(2): 127-132.

69. Palumbo PE, Weiss S, Mccreedy BJ, Alexander SS, Denny TN, et al. (1990) Evaluation of Human T Cell Lymphotropic Virus Infection in a Cohort of Injecting Drug Users. J Infect Dis 166(4): 1990-1993.

70. Henrard DR, Soriano V, Robertson E, Gutierrez M, Stephens J, et al. (1995) Prevalence of Human T-Cell Lymphotropic Virus Type 1 (HTLV-1) and HTLV-2 Infection among Spanish Drug Users Measured by HTLV-1 Assay and HTLV-1 and -2 Assay. J Clin Microbiol 33(7): 1735-1738.

71. Freeman RC, Rodriguez GM, French GF (1995) Seroprevalence and Risk Factors Associated with HTLV-I / II Infection in Injection Drug Users in Northern New Jersey. J Addict Dis 14(3): 51-66.

72. Weissenbacher M, Rossi D, Radulich G, Sosa-esta S, Vila M, et al. (2003) High Seroprevalence of Bloodborne Viruses among Street-Recruited Injection Drug Users from Buenos Aires, Argentina. Clin Infect Dis 37(5): 348-352.

73. Trachtenberg AI, Gaudino JA, Hanson CV (1991) Human T-Cell Lymphotrophic Virus in California Injection Drug Users. J Psychoactive Drugs 23(2): 225-232.

74. Fuente LDL, Toro C, Soriano V, Brugal MT, Vallejo F, et al. (2006) HTLV infection among young injection and non-injection heroin users in Spain : Prevalence and correlates. J Clin Virol 35(3): 244-249.

75. Nunes CLX, Andrade T, Galvão-Castro B, Bastos FI, Reingold A (2007) Assessing Risk Behaviors and Prevalence of Sexually Transmitted and Blood-Borne Infections among Female Crack Cocaine Users in Salvador -Bahia, Brazil. Braz J Infect Dis 11(6): 561-566.

76. Prasetyo AA, Dirgahayu P, Sari Y, Hudiyono H, Kageyama S (2013) Molecular epidemiology of HIV, HBV , HCV , and HTLV-1 / 2 in drug abuser inmates in central Javan prisons , Indonesia. J Infect Dev Ctries 7(6): 453-467.

77. Salemi M, Cattaneo E, Casoli C, Bertazzoni U (1995) Identification of IIa and IIb molecular subtypes of human T-cell lymphotropic virus type II among Italian injecting drug users. J Acquir Immune Defic Syndr Hum Retrovirol 8(5): 516-520.

78. Toro C, Rodes B, Bassani S, Jimenez V, Tuset C, et al. (2005) Molecular epidemiology of HTLV-2 infection among intravenous drug users in Spain. J Clin Virol 33(1): 65-70.

79. Laurentino RV, Lopes IGL, Azevedo VN, Machado LFA, Moreira et al. (2005) Molecular characterization of human T-cell lymphotropic virus coinfecting human immunodeficiency virus 1 infected patients in the Amazon region of Brazil. Mem Inst Oswaldo Cruz 100(4): 371-376.

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