

**FACTORS ASSOCIATED WITH LATE PRESENTATION OF SYMPTOMATIC
CANCERS AMONG HIV INFECTED PERSONS IN JOS, PLATEAU STATE**

BY

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ATTESTATION

I declare that the work in the thesis titled “Factors associated with delay in presentation of symptomatic cancers among HIV infected persons in Jos, Plateau State” was performed by me in the Department of Community, Ahmadu Bello University Zaria under the supervision of Prof. Kabiru Sabitu and Dr Aisha Abubakar.

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CERTIFICATION

I certify that the work of this dissertation entitled: factors associated with late presentation of symptomatic cancers among HIV infected persons in Jos, Plateau State by Mercy Wakili Isichei meets the regulation governing the award of the degree of Masters in Public Health Field Epidemiology, of Ahmadu Bello University Zaria carried and is approved for its literary contribution to knowledge and literary presentations.

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DEDICATION

*In memory of my dear mother mama **Annah Wakili** whose love and support will forever remain in my heart.*

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SUMMARY

Cancer is a disease defined to be a tissue growth that continues even after cessation of the stimulus that first evoked it. The cancer symbol is synonymous with the animal "Crab" which has many fingers depicting the multidirectional spread of the disease. Late presentation is the most important factor responsible for high morbidity and mortality due to cancer in Nigeria. Site based studies show the proportion of late stage presentation range between 60-92% in the last 10years. It is predicted that by 2020, new cases of cancer in the world will increase to over 15 million while deaths attributable to cancers about 12 million. Much of the burden of cancer morbidity and mortality will occur in the developing world because of cancer associated infectious diseases of which HIV infection carries a large proportion and late diagnosis of cancer. Nigeria has the second highest HIV burden worldwide, Plateau State ranked 6th in the country sentinel survey of the year 2010.

A mixed method study consisting of quantitative and qualitative component, was carried out and data collected. Variables on type of cancer, Patient and health service factors associated with late presentation of cancers among the respondents were carried out. Quantitative data was analyzed using Epi-info version 3.5.3 and Microsoft Excel while thematic analysis was done for qualitative data.

There were 503 respondents, males 252(50.1%) and females 251(49.9%). The mean age was 48.7 ± 13.5 years. Majority 432(85.9%) of the respondents were married and only 71(14.1%) were single. Approximately 362(74%) of the respondents were self-employed and 141(26%) were government workers. Among the respondents, 401(93%) of them had some education while 37(7.4%) of respondents have not had any formal education. Logistic regression of socio-demographic factors and late presentation of cancer indicated that there was a significant association between Age range 36-45 years OR 2.7, (P=0.0005), Male sex OR 2.5, (P=0.002), Farming occupation OR 1.7, (P=0.0005) and Primary education OR 2.0, (P=0.0005) status of respondents. Religious affiliation was not a significant factor. Kaposi sarcoma 173(31.63%) was the commonest occurring cancer among the respondents. Majority of respondents 349(69%) presented more than six months after onset of symptom. There Initial reaction to health issues was mainly the

use of Alternative remedies 234(46.5) CI 42.1-51.0. The most frequent symptoms among respondents was pain 462(45.70%) followed by swelling 237(23.44%) and skin changes 210(20.77). Waiting time to obtain histological diagnosis from time of presentation to health facility was mainly 3-6months 274(54.47%). Laboratory related issues 199(39.56%) and Long booking time 163(32.40%) were the most common reasons for delay in initiating treatment.

Delay occurred at three phases in the study, First was the interval between the patient first noticing a symptom and first consulting a doctor, Second, between first consultation and obtaining histological diagnosis and Third between diagnosis and referral or initiating treatment. In addition to outlining the various points during which factors have influenced time to presentation and referral, considering delay in these phases has enabled identification of areas where interventions can be designed to reduce delay.

Key words: Late Presentation, Cancer, HIV/AIDS, Factors

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LIST OF ACRONYMNS

AIDS	Acquired immune deficiency Syndrome
ASCO	American Society of Clinical Oncologist
AJCC	American Joint Committee on Cancer
CDC	Centre for Disease Control
CD4	Cluster of Differentiation
CTS	Computerized tomography Scan
DNA	Deoxyribonucleic Acid
EBV	Epstein Barr Virus
EPV	Epstein Barr Virus
HAART	Highly Active Antiretroviral therapy
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HTLV-III	Human T-Lymphocyte Virus III
KSHV	Kaposi Sarcoma-Associated Herpes Virus
KS	Kaposi Sarcoma
LAV	Lymphadenopathy Associated Virus
NHL	Non-Hodgkin's Lymphoma
MRI	Magnetic Resonance Imaging
PCNSL	Primary Central Nervous System Lymphoma
PEL	Primary Effusion Lymphoma
PETS	Positron Emission Tomography Scan
PLWHA	People Living With HIV and AIDS
RNA	Ribonucleic Acid
TNM	T= Tumor size, N= Nodal status, M= Metastasis
VIA	Visual Inspection with Acetic acid
YYYYY	

CHAPTER ONE - INTRODUCTION

1.1 Background

Cancer is becoming one of the leading causes of increased morbidity and mortality worldwide. It is predicted that by 2020, new cases of cancer in the world will increase to over 15 million while deaths attributable to cancers about 12 million.¹ Much of the burden of cancer morbidity and mortality will occur in the developing countries because of the tilt to industrialization, change in diet from high roughages to refined foods with a sedentary life style, increased tobacco use as well as the compounding burden of cancers associated with infectious diseases of which HIV infection carries a large proportion.² Nigeria has the second highest number of people living with HIV/AIDS in the world, with 1000 new cases of infection daily and 217,148 related deaths, one third attributed to cancers.³

Cancers associated with HIV infection are classified into AIDS defining and Non AIDS defining. The exact mechanism by which these cancers occur is not well understood but they are associated with low immunity measured in the blood as the "Cluster of Differentiation" 4 and 8 cells (CD4 and CD8 cell counts). AIDS defining cancers are Kaposi sarcoma, Non Hodgkin's lymphoma and cervical cancer.⁴ Non HIV associated cancers refers to any other cancer outside the three in an HIV infected person. Although there is scarcity of information on the prevalence of various cancers among HIV infected persons in Nigeria, studies evaluating incidence of cancers among HIV infected individuals show a 1.7 to 3 fold increased incidence of non AIDS defining malignancies among HIV infected individuals than general population irrespective of being on Highly Active Antiretroviral therapy (HAART).⁵

Cancer development is complex, it has gone through series of research and modifications to arrive at an acceptable classification as well as staging. Cancer can be classified according to:

1. Site or organ of origin for example the prostate, cervix, breast and bone.
2. Tissue of origin which refers to the molecular cell from which it arise e.g. carcinoma from epithelial cells, Sarcoma from soft tissue and Leukemia from blood cells.
3. Tumour grade refers to how much the cells has changed from its original normal cell to an abnormal cell this is also called degree of differentiation and summarizes as:-
 - i. Well differentiated that is not different from cell of origin.
 - ii. Moderately differentiated in which there is a mixture of normal and abnormal cells.
 - iii. Poorly differentiated in which case it no longer resembles the parent cell.
 - iv. Anaplastic where cells are immature and undifferentiated.

Staging of cancer: There are numerous staging systems but that developed by the American Joint Committee on Cancer (AJCC) accepted worldwide is the TNM staging where: T= Tumour size, N= Nodal status, M= Metastasis. Based on this staging system a person's stage of cancer at presentation can be grouped as 'Early disease' that is 'curable' or 'Late disease' that is 'incurable'. Stage 0 indicates cancer being in situ or limited within the cells while stage I indicates cancer being limited to the tissue of origin. Stage II indicates limited local spread; Stage III indicates extensive local and regional spread while stage IV is advanced cancer with distant spread and metastasis.⁶

HIV associated malignancies have a historical perspective which dates back to 1981 when the first 8(eight) cases of Kaposi sarcoma (KS) were reported among men who had

sex with men (Homosexuals) in San Francisco and New York. Again in 1982 first 4 (four) cases of Non Hodgkin's lymphoma (NHL) were reported. In the same year Primary Central Nervous System Lymphoma (PCNSL) were discovered and reported in HIV infected persons. In 1984 Lymphadenopathy associated virus (LAV) and HTLV-III were isolated in HIV infected blood samples. These two malignancies found to be frequent among HIV infected persons were then defined by Centre for Disease Control (CDC) as "AIDS defining conditions". In 1993 cervical cancer was added as an AIDS defining condition.⁷ Presently cancer accounts for about 30% of death in HIV infected persons.⁷

Kaposi Sarcoma being one of the first cancers to be associated with HIV in the 1980s was sort for as a marker in all suspected case of HIV infection and clinically described to appears like visible purplish-black patches, lesions or nodules on the skin, mucous membranes including internal organs also referred to as the visceral type of KS. KS arises from cells that develop into blood vessels and lymphatics and commonly starts on the skin, then visceral and the eye. It can affect persons in all stages of HIV infection, all ages and has no sex predisposition. It is however more severe in persons with CD4 below 250cells/ μ l. KS is also linked to Human Herpes virus (HHV-8) which is also implicated in the development of primary effusion lymphoma, and multicentre Castleman disease.

KS severity is graded using a staging system called the TIS [Tumour = T, Immune System = I and Systemic illness = S] staging system.

This staging system is clinically translated in patient management into:

T0: tumour confined to skin, and or lymph nodes and or oral disease; I0: CD4 >200; S0: No history of thrush or opportunistic infection and (Quality of life) Kronofsky score >70; denotes good prognosis.

While a T1: tumour associated with oedema or ulceration, Gastrointestinal KS, Oral KS and other non nodal KS; I1: CD4<200; S1: presence of oral thrush, opportunistic infection, Kronofsky score of <70 and other AIDS related illnesses.

In the T1 group, the prognosis is poor. Definitive diagnosis of KS is by tissue biopsy while treatment is using Highly Active Antiretroviral Therapy (HAART) especially Protease inhibitors, Emticitabine in combination with anticancer agents such as Interferon, Paclitaxale and even surgical excision where indicated.⁷

Non Hodgkin's Lymphoma (NHL), another malignancy commonly associated with HIV is 70-90% high grade B-cell lymphoma. Common types of NHL associated with HIV are Primary Central Nervous System Lymphoma (PCNCL15%) and Primary Effusion Lymphoma (PEL) also called body cavity lymphoma. It occurs commonly in HIV stage 4 diseases with extra nodal manifestation. It can affect multiple organs of the body such as gastrointestinal system, lungs bones etc. The lower the CD4 count, the higher the risk of developing NHL. Epstein Barr Virus (EPV) and HHPV-8 are oncogenic viruses implicated in the development of NHL in both HIV and non HIV associated lymphomas. Diagnosis is made by obtaining core tissue or excision biopsy not fine needle aspiration cytology because it does not allow visualization of the key features that will help in making a diagnosis. NHL treatments with routine chemotherapeutic combination agents are not effective instead second line chemotherapeutic agents in combination with

HAART are used. The diseases manifest with multiple organ involvement and therefore require multi-disciplinary treatment approach.⁷

Primary Effusion Lymphoma is a rare disease, associated with HHV-8 infection. It causes serious effusion in the peritoneal, pericardial, pleural and joint cavities. It does not cause mass lesion, effusion can be mistaken for others disease conditions. It has very poor prognosis.

Primary Central Nervous System Lymphoma (PCNSL) is associated with EBV infection and occurs at very low CD4 of 50-100 cells μl^{-1} ; it affects mainly the brain, with very poor prognosis even with the advent of HAART.⁷

Cervical cancer is a vaccine preventable disease, it is the second commonest cancer in Women in Nigeria and was associated with HIV in 1983 but became an AIDS defining illness in 1993. Human papilloma virus (HPV) 16 and 18 infection the causative agent is vaccine preventable. Major risk factors for contacting HPV infection is HIV, low socio-economic status, first intercourse at early age, sexual promiscuity, and increasing number of pregnancies. Studies show both increasing HIV plasma RNA levels and decreasing CD4 counts are associated with increased risk of abnormal cervical cytology. Highly active antiretroviral therapy (HAART) is used as part of treatment measure.⁷

The goal for a favourable outcome for a cancer patient is early detection, these are at pre cancer stage, stage I and II. Cancer control can then be achieved when the patient presents early or is detected during routine screening for cancer. In developed countries, cancer treatment facilities are equipped for screening, quick and efficient diagnosis, treatment and follow up. The reverse is the case in our setting, patients are known to

present late for medical treatment most of the time with advanced diseases.⁸ Studies have shown it is a common finding in our setting for patients to come to the hospital when they can no longer be managed at home or when alternative medications/management has failed.⁹

There are factors that are responsible for the late presentation and can be classified into broad categories: the Individual's and his society, socioeconomic status and the traditional practices; the medical institutions and the governmental response to cancer treatment.

The individual

There is an individualized response to change in state of health among Nigerians generally. Some are very sensitive to a change in their health status while some are not.⁹ For those that are sensitive, the action taken are also varied, they may see the doctor, visit a chemist/pharmacy shop, visit a traditional healer, spiritualist, prayer house or self medicate.¹⁰ These choices may become a source of delay for early presentation of cancer. If the doctor has low index of suspicion for cancer, he may not gear his diagnosis toward screening for probable presence of cancer warranting repeated visits and delays. The chemist/pharmacy administers symptomatic treatment masking the real problem.

The traditional healer and spiritualist tries to convince the patient against seeking medical solution to his or her problem, giving a spiritual explanation that could range from punishment for disobedience to witches and wizards after his/her life. Such patients often get sent to the hospital when it is too late.¹⁰ The trend in prayer houses is diverse, while some compliment medical treatment by spiritual and psychological therapy an important

form of palliative care; some worsen the problem by discouraging patients from seeking medical help. Self medication is common in our setting, using any available medication they hear of from friends, family members etc. Sometimes drugs are shared believing the ailment is same but most often it's not. They try different medications until pain becomes unbearable then they seek medical help; pain is a common symptom in advanced stage of cancer.

The African societal setting is a closely knitted together; extended family system is the norm. This closeness affects the decision making processes sometimes the affected person does not have a say in actions taken. The husband who is the head/bread winner of the family has a larger say in decision making concerning health in the family. Sometimes older members of the family are contacted; meetings may need to be convened before consent to treatment is obtained. There are some religious believes that do not support certain medical interventions such as Apostolic Faith believe in healing by faith, some may allow with restriction like blood transfusion in Jehovah witness faithfuls. Some have restrictions on women like the pudah, such women can go to hospital at certain period of the day or accompanied by their husbands who may not be available until it becomes an emergency situation often times with complications of the cancer.¹⁰

Cancer in the African society is a stigma, a disease that has no cure. Persons suspected to have cancer tend to hide the disease. Cancers in hidden and sensitive areas like the perineum in both sexes commonly present late unless picked up during evaluation for other diseases.¹¹ Africans tend to be very secretive about diseases affecting the urogenital and the reproductive system. Cancers in obvious sites that may require surgical removal and leaving behind a defect is not a favourable option. This due to the stigma associated

with losing any part of the body and it may also mean incurable diseases.¹² Although amputation at early stage is very beneficial, often times the consent is delayed thereby changing the stage of the disease. These cases then become a reference point for others who develop cancer and may be a factor in not going to the hospital. Surgical removal of cancerous tissue is a very important step in local and regional control, reducing the tumour burden and improving prognosis especially at early stage. This very vital step often is the bond of contention therefore other alternative sources of treatment that do not require surgery become more favourable to the patient.

Socio-economic factors

Cancer treatment is very expensive and is a serious burden even for the financially buoyant persons. Statistics show that cost of treating a cancer patient is beyond the reach of the average Nigerian, follow up not included; this maybe doubled in advanced cancer which will require multiple expensive drugs, longer hospital stay and multiple organ complications from metastasis. Majority of Nigerians fall below the poverty line. Method of hospital care in Nigeria is “Out of pocket” with federal worker benefitting from National Health Insurance Scheme (NHIS) which most state governments are yet to implement some states have implemented free medical care for pregnant women and children under five years but drugs are not available most of the time. Majority of the Nigerian population are farmers and traders who survive on daily sales. Cash flow is determined by market trend. The incessant communal, insecurity and the general economic meltdown has negatively affected the market trend leading a drastic fall in cash flow. In the case of the salary earner, the minimum wage of eighteen thousand naira per

month is yet to be implemented by some state governments , strikes have resulted in punitive measures of “no work, no pay”.

The patient with cancer may require several visits to the hospital before referral to multiple centres before a diagnosis is made. To confirm cancer, a “tissue diagnosis” is required, followed by staging and extent of disease using modalities like Ultrasound, X-rays, CT scan MRI, PET scan in addition to others biochemical and non biochemical tests as maybe required. These diagnostic modalities are very expensive and beyond the reach of the common man who studies show is more at risk of contracting HIV infection and subsequent development of cancer.¹² Some patients may seek medical care early but financial constraint may delay diagnosis and presentation to the specialist for appropriate management.

The health institutions

For those who can afford it, other factors may be responsible for delay in presentation, the health facilities are themselves a factor in the delay process. The hospital structure is divided into primary health centres (PHCs) which serve mostly the rural areas; secondary facilities such as the general and specialist hospital situated in semi urban areas and serve as referral centre for the PHCs; the tertiary centres situated in the cities, training and referral centres for the health facilities. These facilities were built and equipped by the government many years ago based on common diseases that were prevalent in the society. With change in the epidemiology of diseases, there has been no commensurate upgrading of the facilities.

Cancer was a rare finding in our setting but now on the increase due to infectious diseases such as HIV which is endemic in our country. The diagnostic tools for cancers are absent in most of the facilities below tertiary level, even at the tertiary level it is inadequate, obsolete or not available. Facilities are often broken down leading to long waiting time and delays. A person suspected to have cancer is referred from primary to secondary then to tertiary facility where they meet a long booking and waiting time to see a consultant who may not be a specialist in that field but can start the process of diagnosis, depending on the diagnostic ability of the facility. When eventually a tissue diagnosis is obtained, another round of staging and preparation for treatment begins. Depending on the site of cancer, the time interval from first presentation to diagnosis may range from few months to years. For a slow growing tumour, there may be hope but a fast growing tumour will end up at a late stage.

The drugs for cancer treatment are very expensive and not readily available. They are not stock up routinely in the government hospitals and the private pharmacies out sources them on request. Radiotherapy is another vital component of cancer treatment. At present there are less than ten facilities that offer radiotherapy treatment for 170 million Nigerians; these are also often broken down due to over use, erratic electricity/power effect on equipment and poor maintenance. The waiting time to get a slot may range from three to six months, lots of time for tumour spread and recurrence if it has been excised.

There is dearth of available trained personnel that are sensitized to suspect cancer when patient present with symptoms that are not responding to routine treatment for the suspected ailment. Knowledge of cancer among health workers in our setting is low; this may be a factor in the delays encountered in between referrals.¹³

The government

In developed countries, cancer treatment facilities are equipped for screening, quick and efficient diagnosis, treatment and follow up by the government. Patients including government officials are referred from developing countries to institutions in developed countries for cancer treatment. The facilities in these countries are as a result of commitment by their governments. Our government health policy does not encourage cancer care. The Nigerian HIV treatment program although support screening of some AIDS defining cancers has not equipped the program to carry out these procedures.¹⁴ Cervical cancer screening using Pap smear or VIA can detect cancers at early stages.

These tests though available in some government hospitals are sited in other departments not related to the HIV clinic, are expensive and not discounted for these financially overburdened individuals making the procedure not easily accessible to these vulnerable groups.

There are other screening procedures aimed at reducing the risk as well as early detection and treatment for other cancers as well.

The key to good outcome in cancer treatment is early detection and control. A lot of effort and funding has gone to educating people on HIV which has resulted in greater uptake of HIV programmes, the reverse is the case however with cancer. Patients still present late with very high mortality rates. Antiretroviral drugs has improved and increased survival rates therefore more people are living longer with HIV at suppressed level but the risk of developing cancer remains the greatest threat to life. Poverty, lack of education, socio cultural beliefs, myths, stigma and the general attitude of the health

practitioner to cancer has been implicated in the delay in diagnosis of cancer in our environment.^(15, 16) The same was the case with HIV in Nigeria seventeen years ago but with increased education, enlightenment, institution preventative strategies and support from developed countries there is significant decline in HIV related deaths and decreasing prevalence to 3.4% in 2013.^{16,17}

Again this study seeks to find out the factors associated with delay in presentation, of cancer in HIV infected persons. The findings may be useful in developing preventive programmes that will reduce the morbidity and mortality associated with cancer in our HIV infected persons.

1.2 Problem Statement

Late presentation is the most important factor responsible for high morbidity and mortality due to cancer in Nigeria. Site based studies show that a large proportion of cancers diagnosed in Nigeria present late. The proportion of late stage cancers range between 60-92% in the last 10years. Cancer is becoming a leading cause of death worldwide, with 18% of these cancer due to infection. HIV is one of the key infections implicated in infection induced cancer. The burden of cancers will therefore be highest in developing countries such as ours because of the high prevalence of infection further compounded by lack of exercise, smoking and change in diet from high roughages to refined foods.

Nigeria has the second highest world HIV burden but the prevalence of the disease vary in the 36 states and the Federal Capital territory. The prevalence range from 3.6% to 10.3% in some Local government areas, while the Plateau State prevalence was 7.7%

and thus among the high prevalence states.¹⁸ A person infected with HIV has 1.7 to 3 times risk of developing non HIV associated cancer which is responsible for causing a third of deaths in HIV infected persons. The HIV infected persons in Nigeria are therefore at high risk of developing cancer and dying from it. There is however scarcity of information on the sex and age distribution of late presentation of cancer among HIV infected persons in Nigeria despite the high proportion of persons living with HIV.

Cancer in this group of persons is more difficult to treat and it requires highly specialized cancer management which is expensive in terms of care and drugs. Despite all efforts, outcome in cases that are diagnosed late is very poor. Report on the pattern of cancer presentation in Nigeria showed that about 80-85% of common malignancies in Nigeria presented late in 2009 alone with a mortality of over 90% associated with the late stage disease in the patients. Early detection achieved through routine clinical examination and other screening modalities are methods that has been found to increase early detection of cancer. Treatment at the early stage is cheaper, prognosis better and low morbidity and mortality.

The individual knowledge of cancer, societal norms/influences, state of our health institutions and the government health policies may play a role in late presentation of cancer. Health education, equipping health facilities, training health personnel and improving general health status through cancer control policies and programmes are efforts geared towards cancer prevention and early diagnosis. These efforts have not been implemented at national and state levels; consequently there is no significant effect on late presentation of cancer among HIV infected persons in Nigeria.

We characterized the different types of cancer among HIV infected persons in Plateau state, analyzed the time taken from first symptom to presentation at a health facility, diagnosis and commencement of treatment with a view to identifying factors responsible for late presentation. Information obtained could be used in formulating strategies for cancer screening, early diagnosis and treatment in HIV infected persons in the state.

1.3 Rationale/Justification for Study

The rationale of this study is based on the fact that there is increased risk of developing malignancies in HIV-infected individuals compared to the general population with or without combination antiretroviral therapy. It is a significant factor that places the many HIV infected persons on the Plateau at risk of developing cancer. There is poor outcome of cancer treatment resulting in high mortality reported in HIV-Infected persons affected by malignancies. The high mortality occurs as a consequence of late cancer presentation in combination with immunosuppression.¹⁸ The study will determine late presentation of cancer among HIV infected persons in Plateau state and will fill information gap on the reasons for late presentation.

This is the first study on late presentation of cancer on the Plateau among HIV infected persons and has served as a reference for similar studies. It has served as a scaffold for evidence based interventions geared toward reducing morbidity and mortality due to late presentation of cancers. The interventions can be replicated in the care of other HIV infected persons in Nigeria and other parts of the World. Routine screening of AIDS defining and non AIDS defining cancers, in HIV clinics will ensure early diagnosis and treatment which will ultimately lead to a better outcome in the HIV infected persons.

To achieve the above, data was collected on the types of cancers found among HIV infected persons, the patient mediated and service mediated factors that encourage delay in cancer presentation among HIV infected persons. The study has given information on the possible factors responsible for late presentation of cancers among HIV infected patients in Plateau state.

1.4 Research Questions

1. What are the type of cancers that HIV infected persons developed?
2. What type of care did the HIV infected cancer patients receive prior to presenting to health centers?
3. What was the duration of care?
4. What are the factors responsible for the delay in presentation at health centre?

1.5 General and Specific Objectives

1.5.1 General objectives

To determine the factors associated with late presentation of cancers among HIV infected persons in Plateau State

1.5.2 Specific objectives

1. To determine the type of cancers among HIV infected patients in Plateau state.
2. To identify socio- demographic factors associated with late presentation of cancers in the HIV infected persons on Plateau State.
3. To identify patient-mediated factors associated with initial diagnosis of late-stage cancers in HIV infected persons in Plateau State.

4. To identify the service related factors contributing to late presentation of cancer from time of first presentation to health facility, to time of diagnosis of cancer in HIV infected patients.

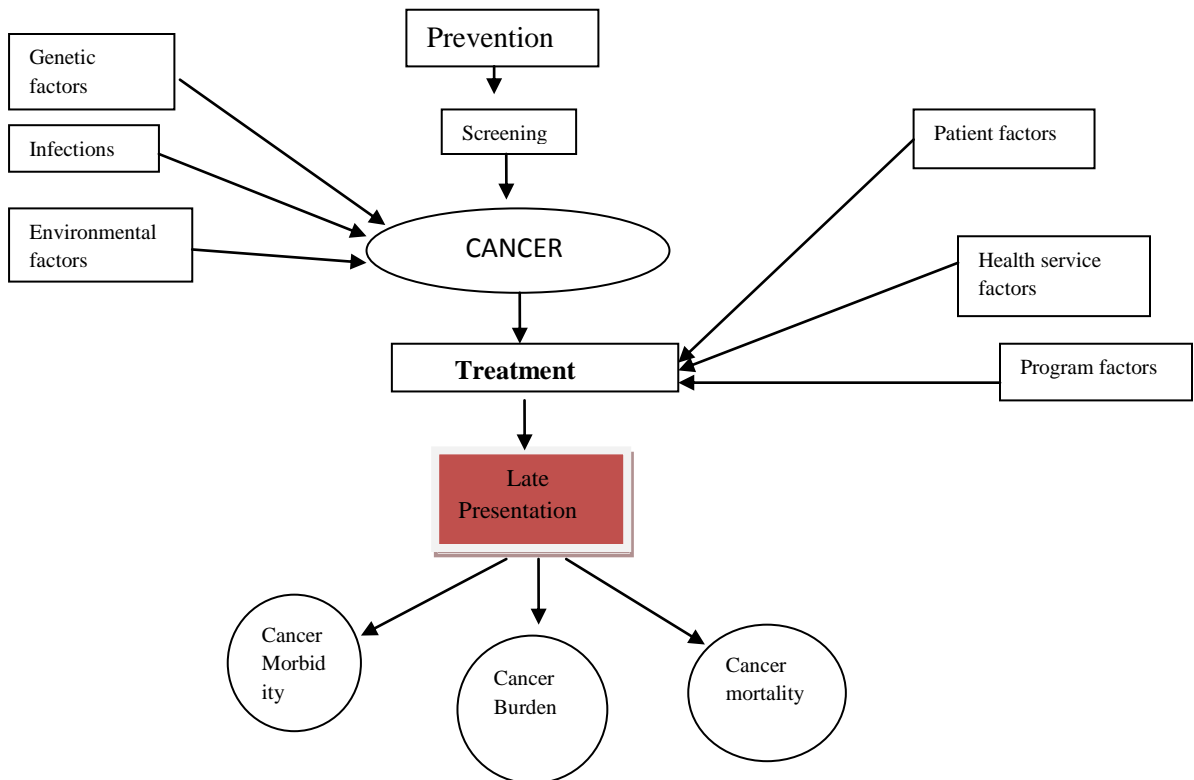
CHAPTER TWO - LITERATURE REVIEW

Review of literature on Malignancy in HIV infected persons show that studies have been conducted in different parts of the World and within Nigeria on the subject. Cancer in the HIV infected came to the lime light in 1981 when Kaposi's Sarcoma (KS) which used to be a rare form of relatively benign cancer that tended to occur in older people was notice in some individuals.. By March 1981 at least eight cases of a more aggressive form of KS had occurred amongst young gay men in New York. An increase, in the number of cases of a rare lung infection *Pneumocystis carinii* pneumonia in both California and New York, (PCP) was also reported at about the same time. Following these reports and other rare life-threatening opportunistic infections, the Centre for Disease Control (CDC) formed a Task Force on Kaposi's Sarcoma and Opportunistic Infections (KSOI). They reported the disease occurred as a result of decrease in the immune system but the cause was not known. In May 1983, doctors at the Institute Pasteur in France reported that they had isolated a new virus, which they suggested might be the cause of Acquired Immune Deficiency Syndrome (AIDS) and was supported by findings from by CDC.

By this time, scientists had accumulated enough evidence to form an overview of AIDS in Africa. It was associated with lesions that were predominant in the infected individuals. Slim disease in Kinshasa Zaire (late 1970s,,)Slim disease in Uganda and Tanzania (early 1980s), Esophagel candidiasis in Rwanda (from 1983), Aggressive Kaposi's sarcoma in Kinshasa Zaire (early 1980s), Aggressive Kaposi's sarcoma in Zambia and Uganda (from 1982 and 1983), Cryptococcal meningitis in Kinshasa Zaire (late 1970s to early 1980s)."These studies suggested that while isolated cases of AIDS may have occurred in Africa earlier, it was probably rare until the late 1970's and early

1980's, a pattern similar to that in the United States and Haiti." As in Western countries, AIDS in Africa was found to primarily affect young and middle-aged people, especially those who were unmarried. The sex and age distributions were seen to reflect other sexually transmitted diseases, and the major transmission routes had been identified. The discovery of two cancers, Cervical cancer and Non Hodgkin's Lymphoma frequently seen in the HIV infected formed the bases for labeling them HIV associated cancers while other cancers remained Non HIV associated cancers. These cancers were incorporated into the protocol for AIDS defining conditions.

Conceptual frame work: Cancer Burden



2.1 HIV Infection and Type of Cancers That Affect Them

Human Immuno Deficiency Virus (HIV) infection predisposes an individual to a state of low immunity which renders the individual susceptible to development of cancer. Studies have found HIV infection to be associated with two types of cancers, broadly classified “HIV associated cancers” and “Non HIV associated cancers”¹⁹: HIV associated cancers are cancers that develop in a patient due to the depressed state of the immune system, some of the cancers are triggered by viruses in the individual. It has been estimated that about 15 percent of all human cancers worldwide may have been triggered by viruses.²⁰ Viruses are classified into double stranded Deoxyribonucleic acid (DNA) and single stranded Ribonucleic acid (RNA) based on the type of proteins they are made of and the two types of viruses have been found to be capable of causing cancers in humans.

There are four DNA and two RNA viruses implicated in cancer formation namely Epstein-Barr virus, human papilloma virus, hepatitis B virus, and human herpes virus-8 and T lymphotropic virus type 1 and hepatitis C viruses respectively. Although HIV is not directly a causative agent, co infection with these viruses is the trigger for cancer formation. The most important of these cancer-related viruses in HIV infection among Humans are the Herpesvirus 8 (HHV-8) cause Kaposi sarcoma, Epstein Barr virus (EBV) causative agent for non-Hodgkin and Hodgkin lymphoma, Human papillomavirus (HPV) which causes cervical cancer, anal, penile, vaginal, vulvar, head and neck cancer. Others are Hepatitis B virus (HBV) and hepatitis C virus (HCV) both causes of liver cancer.²¹

Major cancers associated with being infected with HIV that have been identified and studied are Kaposi sarcoma (KS), Non Hodgkin’s lymphomas (NHL) and cervical

cancer. Non HIV associated cancers are those cancers that arise in the presence of a normal immune system and can still arise in an HIV infected persons whose immune system is not depleted by reason of treatment with Anti Retroviral Drugs (ARVs). Study reported from Italy described a 3-fold increased risk of non-virus-related non-AIDS-defining cancers (NADCs) among HIV-infected persons compared to the general population, the use of ARVs was found to be beneficial in reducing the risk of developing HIV associated cancer in these group of persons by reducing the amount of circulating HIV virus in the blood leading to increase in the immune cells and raised immune system function. The ARVs currently used in Nigeria are classified as Highly Active Antiretroviral Therapy (HAART).

Despite the proven efficacy of HAART, the risk remains high because the immune system function remains impaired in the individuals once infected by HIV. There is also the possibility of developing resistance to the drugs used in HAART.²² An infected individual is therefore several thousand times more likely to be diagnosed with Kaposi sarcoma, at least 70 times more likely to be diagnosed with non-Hodgkin lymphoma, and, for women at least 5 times more likely to be diagnosed with cervical cancer than a non HIV positive individual.²³ Studies on the incidence of cervical cancer among the HIV infected women has remained high even among those on HAART because of the impaired immune competence which has a likely hood of increased incidence of cancers.^{24,25}

Although there is paucity of knowledge on the true and accurate epidemiology of cancers among HIV infected persons in Nigeria, reports from the few functional cancer registries suggest an increasing trend of cancer in Nigeria.²⁶ The increase in cancer in Nigeria has

been reported to be among other reasons due to the high prevalence of HIV infection. There is also a direct increase in Morbidity and Mortality due to delay in seeking treatment for cancer in the general population as well as among the HIV infected patients.²⁷

2.2 Late Presentation of Cancer

The definition of Late Presentation and Delay in presentation of cancer is still undergoing revision. Late presentation often used synonymously with delay in presentation refers to "Individual seeking medical help when the cancer has penetrated outside the primary organ of development" to surrounding or other organs also referred to as having "spread or metastasized".

Late presentation occurs as a result of delay in taking the appropriate steps at the early stage when symptoms were first noticed. Delay can therefore occur at various stages of the disease, these are: When the individual starts having symptoms but not seeking medical attention, when medical attention is sort but there is delay in definitive(histological) diagnosis or when there is a diagnosis but delay in getting treatment initiated.

Alok et al classified factors associated with delay in presentation of cancer into three levels.

Level I - Socio-economic and demographic factors

Level II - Non Medical factors

Level III - Medical factors

Level I is sub divided into primary, secondary and tertiary delay. Primary delay refers to onset of sign/symptoms, secondary delay from first contact to medical provider and tertiary delay from place of cancer diagnosis to place of initiation of treatment. Level II refers to Patient factors and psychosocial factors while Level III refers to factors related to misdiagnosis, symptomatic treatment, inadequate treatment, referrals and others.²⁸ Review of studies on Late/Delay in cancer presentation shows that combination of factors are responsible.

2.3 Socio-demographic Factors Associated with Late Presentation of Cancer

The African setting is a closely knitted and extended family system that is to some extent largely controlled by norms in the society. The right of an individual to take certain decisions even on health issues may be influenced by these norms. The Age, sex, marital status, educational level, socioeconomic stand, religious and even place of abode (being in the rural or urban) set up may influence an individual's decision making especially regarding health issues. The extremes of age, very young and very old depend on family or care givers in taking decisions even regarding health issues and this can be a reason for delay. Married women especially in some religions require permission from husbands to visit a doctor.

Educational level of individuals may play a significant role in the way they react to health issues. Sometimes even the highly educated may choose to believe stories or myths about a disease such as cancer than scientific evidence. Myths about cancer have been implicated as major reasons for delay in presentation of cancer and was used as the theme for the 2013 World cancer day to increase cancer awareness all over the world.²⁹

Common myths recognized are:

1. Cancer is just a health issue: this myth has erroneously made people think cancer is something that can be treated at any stage. It is commonly painless and if it is growing in a hidden part of the body or perineum where there are no cosmetic issues, individual may allow tumour to grow for years without medical attention. Pain then becomes the major reason for presenting to a health care institution then tumour would be at the advanced stage. HIV infected person will likely concentrate more on their infection, survival, “what are people saying about me?” Stigma then becomes a more important issue rather than a painless swellings on the body.
2. Cancer is a disease of the wealthy, elderly and developed countries: the media announcements on wealthy persons such as political icons, popular entertainment industry icons and others who died of cancer especially in the developed countries might have made the common man to think cancer is associated with affluence. Cancer is a disease that is scientifically proven to be associated with aging, increased incidence of cancer among the elderly has made many to believe it’s only those with advanced age that are affected with cancer. HIV infected person in developing countries like ours who are mainly young seem to believe they are exempted from cancer.
3. Cancer is a death sentence: While some understand cancer can affect them, they give up once they suspect that they have cancer because of the high mortality rate associated with the disease. If such person is diagnosed with cancer they may not seek medical advice because they believe they are destined to die. While some who are not brave enough to find out their diagnosis tends to delay receiving

definitive diagnosis by hiding because they don't want to hear that sentence. For a HIV infected persons it can come as a double blow and shock, which can lead to depression and a tendency to negligence. `

4. It's my fate: these groups of people give up without a fight because they believe they are destined to have cancer with or without precaution. These group of people might have been influenced by some cultural, religious or psychological believe that they are victims of circumstance that is without remedy. That was the face of cancer in the early 19th century when little was known about the disease but now with improved dedicated cancer research and the discovery of newer drugs as a result of greater insight into tumour genesis, the management of cancer has been revolutionized. Genetic predispositions tend to give credence to the faith belief.

Cancer treatment is now targeted and evidence based and this has lead to a better outcome, reduction in morbidity and mortality with up to 50% decrease in cancer related death in the United States of America. While it is story of success for developed countries in the fight to "Conquer Cancer", it is the reverse for developing countries where five year survival rate is less than 20%.³⁰ Myths are part of the societal norms that may play a significant role in late presentation of cancer in our setting. Fear of the unknown is considered to be the most important factor for delay in breast cancer patients, followed by traditional and religious beliefs.³¹

2.4 Patient-Mediated Factors Associated with Delay in Cancer Presentation

Patient responses to health problems invariably determine the outcome of their health problems. Some may have very keen interest in every form of change in their body system and would find every means available to them to unravel the mystery. Such individuals may not delay in accessing treatment or may waste precious time trying to figure it out them self. On the contrary some do not pay attention to such changes and may seek help only when it becomes unbearable. HIV infection is associated with a lot of stigma and discrimination this is a likely factor that has shaped the lives of people living with HIV affecting their willingness to seek medical care.³¹

In United States of America and developed countries, People Living With HIV and AIDS (PLWHA) reveal that fears of stigma and social consequences of revealing their HIV status, and concerns about medications, as influencing care seeking.³² Similar trends in factors found to have enacted and internalized stigmas in HIV infected persons in Africa were found to be a significant factor for delays in seeking care by individuals after testing HIV positive in India.³³ Reports from studies done in Ethiopia assessing reasons for delay in seeking treatment among HIV infected persons show low awareness, non-disclosure, perceived ART side effects and HIV stigma were the major barriers for late presentation to HIV/AIDS care.³⁴

Increased efforts at enlightenment, community involvement, modification in HIV treatment programmes to help reduce stigma and the advent of a structured anti retroviral treatment programmes and adherence to drugs is one of the major reasons that more people are living longer with the disease worldwide and in Nigeria although they are at increased risk of cancer a phenomenon found to be similar to the experience in other

parts of the world.³⁵ The increased risk of cancer is however more pronounced in infected persons who have low CD4 cell count commonly found in persons who did not start treatment early or who are not compliant with their drugs as such develop resistance to HAART.³⁶ Studies done to find Independent predictors of mortality after cancer diagnosis among HIV-infected persons showed that poor immune status, failure to suppress HIV-RNA on HAART, late cancer stage, and lack of cancer treatment to be very significant.

Persons presenting late with cancer have been reported to be a very significant factor for poor prognosis in our setting and the delay could range from few months to years.³⁷ Delay for more than 3 months before seeking medical attention was observed in 81% of breast cancer patients in Lagos. The significant factors reported to be associated with the delay were being a single parenthood, primary level of education, negative history of benign breast disease, pre-menopause, Ignorance of the nature of illness, belief in spiritual healing, fear of loosing their breast largely because of ignorance and belief in herbal treatment.³⁸ In a study in Lagos University Teaching Hospital, however, they found fear of the unknown to be the most significant factor for delay in presentation.⁴⁰ Fear could be due to ignorance of the disease and not knowing what is happening to one self.

2.5 Health Service Factors Contributing to Late Presentation of Cancers

The effectiveness or non effectiveness of a health service system ultimately directs the outcome of services rendered to end users. The more organized the system, the more effective it is likely to be in prevention and control of diseases for which it render service.

The opposite is also the case, poor output where there is disorganization in health service system and poor disease control.

The health system structure in Nigeria is stratified into Primary, secondary and Tertiary. The primary is located in the rural areas and is managed by community based health workers. The secondary facilities are located in semi urban and urban areas, managed by doctors who are mainly medical officers that may not be interested in sub specialization. Few consultants who are specialized may be working in the specialist hospitals situated in the cities. The tertiary facilities serve as referral centres and located in the cities, some are affiliated to medical schools such as the teaching hospitals.

Medical facilities that can adequately diagnose and manage cancer cases are limited, most of which are tertiary health facilities mainly located in the urban areas. These facilities require referral from the primary or secondary facility doctors before being attended to. Referrals are often delayed from the primary facilities who are also handicapped due to non accessibility to diagnostic tools. Patients have to be sent to other hospitals or private facilities for investigation which maybe delayed due to logistics and long waiting time. Fully functional confirmatory facilities with complete pathology laboratories are not available in all tertiary hospitals. To be referred by a doctor from either primary or secondary facility requires the doctors to have high index of suspicion of cancer in a person and to act quickly. Studies to assess the knowledge, attitude and practice of health personnel to cancer show gross paucity of knowledge on the subject. This has resulted in unnecessary delays in diagnosis and appropriate referral of patients.⁴⁰

Cancer screening is a method of preventing and controlling cancer in a population and it is an important aspect of a country public health programme should include in the health policy, although the Nigerian HIV treatment guide line includes AIDS defining malignancies as a criteria for staging in stages three and four. In the section one of the guideline, it how ever did not include cancer treatment in the treatment options and not included in the diagnostic workup, not in the follow up and monitoring/evaluation or the palliative care section.⁴¹ Cancer screening is absent in the guide line. The exclusion of routine cancer treatment in the HIV programme could be a major factor in the diagnostic delays. The care giver and the patients are not constantly being reminded of the possibility of cancer in this vulnerable group resulting in no active search for it neither do the patients get educated on it to watch out.

There are a lot of jingles in the media and posters on HIV, signs and symptoms but very few publicity and enlightenment on cancers. Although it is silent yet it is a major cause of morbidity and mortality in HIV patients. Signs and symptoms of cancer in the HIV patient may then be regarded as not important by both the care giver and infected person. Intensified cancer screening programs for all ages has lead to increased level of cancer awareness in developed countries this has improved cancer outcome to that of a chronic disease rather than a killer. The absence of such screening programs in our HIV curriculum may be a contributory factor to the low or lack of urgency regarding cancer.

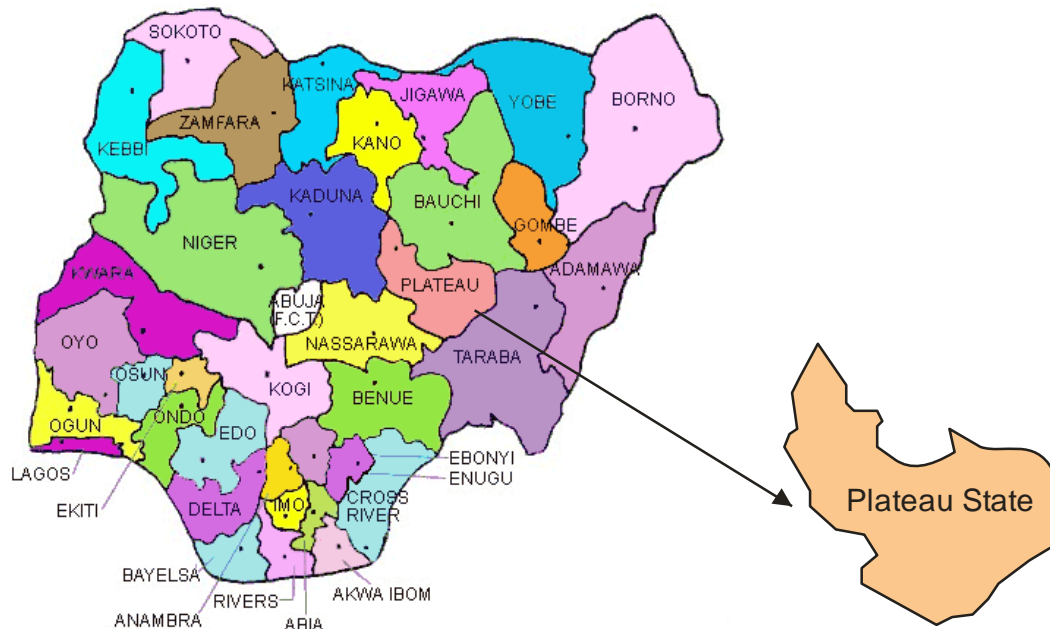
The cost of cancer treatment is a great challenge in our setting; often the effort is not commensurate with the outcome. Government support for health in this sector is absent or very little.⁴² The search for cure has led many to alternative medicine. The patronage of prayer house, traditional healer and herbalists contribute significantly to delay in

diagnosis.⁴³ Affected individuals end up in the hospital often after spending so much money and valuable time doing alternative treatment. Some modern herbal medications may be beneficial in boosting the immune system, its role as a cure for cancer is yet to be ascertained. Delay in diagnosis of cancer in HIV patients can be improved upon or even eliminated if the factors associated with the delay in our setting is identified and corrected.

CHAPTER THREE - MATERIALS AND METHODS

3.1 Description of Study Area

The study was conducted in Plateau State, one of the 36 states in Nigeria. It lies in the North central geo-political zone of the country and is the 12th largest state in Nigeria. It has a population of 3,178,712, divided into 17 Local Governments Areas. It shares boundary with Bauchi State in the North, Kaduna to the West, Nasarawa toward South and Taraba in the West as shown in Figure 1 below.



The Federal Republic of Nigeria is a Country located in the West Africa. This part of Africa is also referred to as the Sub Saharan Africa. It lies between Latitudes $4^{\circ} 1'$ and $13^{\circ} 9'$ North and Longitude $2^{\circ} 2'$ and $14^{\circ} 30'$ East of the Equator. It occupies a land mass of about 923, 76sq.km. It shares boundary with Niger Republic in the North, Atlantic Ocean in the South, Republic of Chad and Cameroon in the East while in the West lies Republic of Benin. It is made up of 36 States with a Federal Capital situated in Abuja and 774

Local Governments. The system of government in Nigeria is three- tiered: the Federal, States and the Local governments. GLOBALCAN estimated Nigeria's population from the 2012 national census to be 166.4 million people. There is high diversity in culture and 400 different ethnic groups.

Plateau State is located in Nigeria's middle belt covering an area land mass of 26,899 square kilometers. It is located between latitude 8°24'N and longitude 8°32' and 10°38' east. The altitude ranges from around 1,200 meters (about 4000 feet) to a peak of 1,829 meters above sea level in the Shere Hills range near Jos. Years of tin mining have also left the area strewn with deep gorges and lakes.

Plateau State has an estimated population of about three million people. The HIV prevalence in Plateau state has fluctuated around 7.7% at 2010, ranking 6th in the country.⁴⁴ The state has frequent religious and ethnic crisis for over ten years now. This has resulted in sudden migration in search of shelter, food and safety. Many engage in risky behaviors to make ends meet, while alcohol, local brews and guskolo (spirit) consumption compounded by redeployment of large number of security forces to maintain peace. These are habits that have been found to be associated with increased risk for HIV infection, a probable reason for the sudden increase in HIV prevalence on the plateau.

The health institutions in Plateau are tertiary, secondary, primary and private. There are also many chemist shops and diagnostic laboratories that serve as easier alternative to hospitals for patients and so many security forces because they do not require referrals to be accessed, no long waiting time and it appears to be cheaper. Other competing

institutions are the traditional medicine and herbal treatment that promise cure and quick solution; while others are the prayer houses and religious people who believe in prayer/alms and sacrifices for healing. The above poses a great challenge for the HIV infected person on the plateau.

Jos University Teaching Hospital (JUTH) is the referral centre for cancer cases. It has an Oncology unit, a functional Histopathology Department, Palliative care, Computerized Tomography (CT) scan, Magnetic Resonance Imaging (MRI) machine, and other Laboratory diagnostic facilities. It offers cancer Diagnosis and Treatment. The hospital however does not have a Radiotherapy unit therefore patients requiring radiation treatment are referred to other hospitals that offer such facilities.

3.2 Study Design

A Mixed method study design, consisting of quantitative and qualitative component.

3.3 Study Period

The study preparation period was from August 2013 to September 2013, the actual study and analysis was done from September 2013 to March 2014 (Appendix 6).

3.4 Study Population

The study population was HIV infected individuals accessing medical care at treatment facilities in Plateau State. The respondents were sampled HIV infected persons of any sex from the age of 18years above who have been diagnosed with cancer or those who have clinical features suggestive of cancer without histological diagnosis who were referred to JUTH.

3.4.1 Inclusion criteria

Inclusion criteria:

- a. HIV positive adults 18years and above with already histological diagnoses of cancer, newly diagnosed symptomatic cancer patients who are HIV positive.
- b. HIV positive individuals with s highly suggestive clinical features of cancer without histological diagnosis.

3.4.2 Exclusion criteria

Exclusion criteria:

HIV positive children <18years with symptomatic cancer, symptomatic cancer patients who are not HIV positive and HIV positive individuals with asymptomatic cancers were be excluded.

3.4.3 Definition of Late Presentation of cancer:

Late presentations defined and adopted for this study was:

- Patient delay “interval between the onset of symptoms and the first visit to a physician to be 3 months or more”.
- Provider delay “interval between first presentation to physician and diagnosis delay 3 months or more. Gallo 1938.
- Cancer stage 2 locally advanced, advanced stages 3 and 4.

3.4.4 Sample size determination

Prevalence: The prevalence of cancer in Nigeria is not available but site based cancer prevalence have been reported. There is paucity of information on prevalence of cancers

among HIV infected persons in Nigeria. Therefore in this study a prevalence of 50% was used.

- i. Prevalence of cancer in the HIV infected in Nigeria is yet to be determined therefore a prevalence of 50% is used.
- ii. Significance level of 0.05(for 2-tail test of significance), $Z_{\alpha/2} = 1.96$
- iii. Precision (d) of $\pm 5\%$

Manual Sample size estimation:

$$n = z^2 p q/d^2$$

$$Z = 1.96$$

$$p = 50\% (0.50)$$

$$q = 1 - 0.50$$

$$n = \frac{(1.96)^2 \times 0.50 \times 0.50}{(0.05)^2}$$

$$= \frac{0.9604}{0.0025}$$

$$n = 384.16$$

None response rate of 10% of calculated sample size: $10/100 \times 384.16 = 38.416$

Total sample size: $384.16 + 38.416 = 422.576$

Total estimated sample size rounded up to be = 500

The sample was rounded up to 500 because previous studies showed that there is a reluctance in releasing information by HIV infected person due to fear of stigma. The higher number is to accommodate for likelihood of invalid result greater than the 10% non response rate.

3.5 Sampling Technique

Selection of HIV treatment centers with 1000 patients was done, these clinic have doctors managing them. Only five treatment centers met the criteria.

Then followed by selection of clinics offering cancer care (diagnosis, treatment and monitoring), only one hospital the University of Jos teaching hospital met the criteria.

At the Oncology clinic:

Patients were stratified into cancer patients who are HIV positive and HIV Negative. All patients presenting to the clinic for cancer related issues were seen, those with symptomatic cancer and a HIV positive result referred from a HIV treatment centre to the clinic were recruited into the study. Symptomatic cancer patients not referred from HIV clinics who were found to be HIV positive at routine cancer management work up were also recruited into the study. New symptomatic cancer patients who did not know their HIV status were counseled and tested as part of routine cancer management in the cancer unit, positive patients were also recruited into the study.

3.6 Study instrument

Structured questionnaire was developed and used for this study. The questionnaires contained close- ended questions to facilitate data collection and entry and few open-ended questions to allow respondents expressed views on vital issues that may add quality to the study. Trucut tissue biopsy and histopathological diagnoses was done for undiagnosed cancers.

3.7 Data Collection Technique

Data was collected using mixed method consisting of qualitative and quantitative methods. The qualitative method was done through Focus Group Discussion and Key informant interview using interview guides on various cancer related issues in HIV infection. Two Focus group discussions were conducted, each sessions with a group of 10(Ten) HIV positive men and 10(Ten) HIV positive women. The sessions were conducted by an interviewer and a note taker, each session lasted between 1hour 25minutes to 1hour 55 minutes. The same interviewer facilitated to ensure quality control.

Qualitative method was done using structured, pretested interviewer administered questionnaire. The questionnaire was numbered serially using a unique identification number ranging from 001 to 503, respondents name was not included. Confidentiality of information, voluntary participation and respect for human rights of respondents were ensured. Participants knew their individual numbers and were only allowed access to their own results.

Six interviewers were engaged based on the number of respondents and duration of the study. Two doctors in the oncology unit took biopsies for respondents who did not have histological diagnosis. Interviewers were both males and females. The females were very important, they interviewed females with gynecologic malignancies.

Biopsy for undiagnosed cases

After administering the questionnaire, the interviewer took respondents who required biopsy to the doctor who reviewed and counsel the respondents. For suspected cancers in

sites where biopsy could be taken same day, it was done. For those who required preparation such as bowel preps, clotting profile or image guidance to obtain biopsy, they were scheduled and biopsies were taken. Biopsy was performed using minimally invasive procedure under local anesthesia to reduce pain. Based on prior arrangement with the histopathology department, results were obtained within one month.

Linked anonymous method was used to link participants to their results. They were called and result disclosed to them with the oncologist who also took over management. For those whose biopsy results were negative for malignancy they were referred to the appropriate subspeciality unit and followed up till we were sure they have been accepted for treatment. All doctors and field workers that participated in the study were trained in the various assignments they carried out.

3.8 Quality Assurance Procedures

To ensure the data collected and information obtained is of high quality, all personnel involved in the study were carefully selected and found to have the required knowledge and skill required. Training of data collectors and pilot study was done to ensure all personnel understood the use of data collection instruments. Same interviewer for qualitative data collection.

3.8.1 Pre Test

Two week before the start of data collection, the questionnaire were pretested in a pilot study exercise to ensure acceptability, validity, reliability and clarity of study tool. Pilot study was done at the Jos University Teaching Hospital, same site of the study with field workers. A two day training on methodology and correction of tools was done prior to the

start of pilot study. Ten respondents were enrolled after an obtained an informed consent. Questionnaire was administered and two biopsies were taken. All respondents 10(100%) answered the questionnaire, only 1(10%) did not turn up for biopsy within the pilot study period but came for biopsy 4(four) weeks later within our data collection period.

Findings from the pilot study used to improve respondents participation and conduct of main study were:

1. The questionnaire had some ambiguous questions that had to be reviewed.
2. Respondents that require biopsy spent long waiting time to get biopsied so a new schedule was drawn and biopsy days were allocated. This allowed the doctors to dedicate those days to taking biopsies only and this reduced the waiting time.
3. Some of the cancers were attended to at subspeciality clinics for example the gynaecologic clinic before being referred to the oncology unit. To avoid double counting we used case notes and intra unit referrals to confirm respondent being interviewed.
4. The female respondents who had gynaecologic cancers were more comfortable with female interviewers. The females interviewed all females that had gynaecologic cancers.

3.8.2 Training of field workers

Training of the field worker were conducted before commencement of data collection. At the training field workers were introduced to the study design, data collection method, obtaining consent and referral for biopsy if required. The worker were mainly medical

health workers who were familiar with research protocols, patient interaction, they spoke English, pigin english and local hausa dielect.

3.9 Data Management

3.9.1 Data collection and retrieval

The interviewers collected the information from respondent using the questionnaire and they submitted same to the investigator on daily basis. Questionnaires were checked for errors and omissions and corrected immediately. The biopsy collection process was monitored to ensure all informed consent and specimen collection procedure were done according to the study protocol. Problems encountered during daily reviews were immediately addressed.

3.9.2 Measurement of variables

Data collected for this study were the following variables (appendix 2,3,and 4), Dependent variables Age, Sex, Marital status, Occupation, Level of education, Religion and HIV status. Independent Variables were: Reaction to health issues, type of cancer, symptoms first noticed, duration of symptoms before first presentation to a health facility, reason for not visiting a health facility immediately, duration from first facility visit to obtaining histological diagnosis, duration from diagnosis to initiation of treatment.

3.9.3 Statistical analysis

Manual editing and review of filled questionnaire were done before electronic data entry. Data was entered into Microsoft Excel 2007 and Epi - info software (version 3.5.3) after which data cleaning and random check was done to exclude incomplete, inconsistent and inaccurate data. Electronic data back up was undertaken using a flash drive and email.

Analysis of data was done using Microsoft excel 2007 and Epi-info software version 3.5.3 for univariate analysis using frequencies and proportions, bivariate analysis of the association between cancer and late presentation, socio demographic and other factors using prevalence, Odds ratios, and Chi square (χ^2) test of statistical significance, multivariate analysis and Logistic regression to identify independent predictors of late presentation of cancer. Data summary was done using tables and charts for key indicators.

3.9.4 Criteria used in assessing delay

Patient delay of three months from the "Time patient first noticed a symptom to first presentation at a health facility" and Provider delay "Interval between first presentation to physician to time of obtaining a diagnosis; and from diagnosis to start of treatment as 3 months". While delay is considered "undue delay" if the interval is more than 6(six) months as adopted for this study. This was based on study done by Gallo in 1938 which has been used by researchers. Although, late presentation can be assessed based on stage of disease at presentation, it was not used for this study because of lack of available diagnostic equipment that can accurately stage the cancer at the study site.

3.10 Ethical Consideration

- i. Ethical clearance was obtained from the Jos University Teaching Hospital Institutional Review Board (IRB) prior to the commencement of the study (Appendix 5).
- ii. Written and signed informed consent in English and Hausa (Appendices 1a and 1b) was obtained from each respondent before a questionnaire was administered or biopsy taken.

- iii. Participants were educated on their rights to decline answering if they chose not to continue. They were also free to refuse biopsy being taken and there were no penalty. Results were only disclosed to a respondent alone and referral effected in agreement with the respondent in keeping with stated confidentiality policy of the study.
- iv. Confidentiality was strictly observed, participation was voluntary and respect for human participants was ensured. Identification numbers were used not names, case notes used were linked to participants number using unique identification. Hard copy of data collected was kept with the Principal Investigator in a filing cabinet under lock and key while Soft copy was only accessed using pass word known to principal investigator.

3.11 Limitations (and efforts made to reduce the effect of limitations)

- 1. There is no standard definition of late presentation of cancer therefore” Patient and Provider delay of three months from the time patient first noticed a symptom to first presentation at a health facility” was adopted for this study.
- 2. Stage of the disease was not used in this study because there was lack of equipments to accurately stage the disease.
- 3. There was possibility of recall bias and some patients were not sure of the type of cancers they had. Case notes were then used to extract and correct information.

3.12 Scope of the Study

- i. The study determined that HIV infected persons with symptomatic cancers presented late for medical intervention
- ii. It identified the patient related factors associated with the delay in presentation
- iii. It identified the service related factors responsible the the delay

iv. It identified the type of cancers found among the respondents

3.13 Dissemination Plan

Copies of the study findings and report will be submitted to the Ahmadu Bello University Zaria, The Plateau State Ministry of Health, Jos University Teaching Hospital, Nigeria Field Epidemiology and Laboratory Training Programme (N-FELTP), Federal Ministry of Health department of Cancer Control, National Agency for AIDS Control (NACA), Centre for Disease Control (CDC), Nigeria Centre for Disease Control (NCDC) and other stake holders.

It will be presented at workshops, seminars and meetings. Articles and manuscripts will be published in scientific journals so as to add to body of knowledge.

CHAPTER FOUR – RESULTS

This chapter presents the findings of the study according to the two methods of data collected.

There were 505 respondents enrolled, two (2) questionnaires were incorrectly filled. The non-response rate was 0% while exclusion was 1.39%.

Table 1: Type of cancers among the respondents (n=547), Plateau State late presentation of cancer in HIV infected study 2014

Types	Frequency	Percent (%)
Kaposi sarcoma	173	31.63
Breast cancer	89	16.27
Prostate cancer	74	13.52
Cancer of the bladder	49	8.95
Colonic cancer	38	6.94
Cervical cancer	24	4.38
Endometrial cancer	17	3.10
Soft tissue sarcoma	14	2.55
Testicular cancer	12	2.18
Squamous-cell carcinoma	12	2.18
Ovarian cancer	10	1.82
Liver cancer	10	1.82
Pancreatic cancer	9	1.63
Gastric cancer	8	1.44
Renal cancer	6	1.09
Oesophageal cancer	4	0.72
Penile cancer	4	0.72
Lung cancer	2	0.36
Thyroid cancer	2	0.36
Melanoma	2	0.36

Analysis of the type of cancers found among HIV respondents indicated that Kaposi sarcoma 173(31.63%) was the commonest occurring cancer among the respondents, however 44(8.04%) respondents had multiple cancers.

Table 2: Socio-demographic Characteristics of Patients

Variables	Frequency (n=503)	Percent (%)
Age Group (years)		
≤ 25	6	1.2
26-36	159	31.6
37- 47	114	22.7
48- 58	95	18.9
59- 69	111	22.1
>75	18	3.6
Sex		
Male	252	50.1
Female	251	49.9
Marital Status		
Single	68	13.5
Married	432	85.9
Widowed	3	0.6
Occupation		
Business	123	24.5
Civil servant	157	31.2
Farmer	144	28.6
Housewife	45	8.9
Student	34	6.8
Religion		
Christianity	387	76.9
Islam	116	23.1
Educational Status		
None	37	7.4
Primary	195	38.8
Secondary	169	33.6
Tertiary	102	20.3

This table shows the socio-demographic characteristics of the study population, characteristics considered included age, sex, level of education, occupation, religion, marital status.

Age distribution

Table 2a: Age distribution of respondents (n = 503), Plateau State late presentation of cancers in HIV infected study participants 2014.

Age Group (years)	Frequency	Percent (%)
<25	6	1.2
26-35	47	9.3
36-45	112	22.3
46-55	114	22.7
56-65	95	18.9
66-75	111	22.0
> 75	18	3.6

The age distribution of the participants showed that nearly half (45%) of the respondents were within the age ranges of 36 -55 years. Median age is range 36 - 40years.

Sex Distribution

Table 2b: Sex distribution of respondents (n = 503), Plateau State late presentation of cancers in HIV infected study participants 2014

Gender	Frequency	Percent (%)
Male	252	50.1
Female	251	49.9

The sex distribution of the subjects analyzed showed that males (50.1%) were slightly higher than the female (49.9%) subjects.

Marital status

Table 2c: Marital status of respondents (n = 503), Plateau State late presentation of cancer in HIV infected study participants 2014

Marital Status	Frequency	Percent (%)
Single	71	14.1
Married	432	85.9

Majority 432(85.9%) of the respondents were married and only 71(14.1%) were single.

Occupational Distribution

Table 2d: Distribution of occupation of the respondents (n = 503), Plateau State late presentation of cancers in HIV infected participants of study 2014

Occupation	Frequency	Percent (%)
Applicant	3	0.6
Traders	123	24.5
Civil servant	104	20.7
Farmer	144	28.6
Housewife	45	8.9
Retiree	50	9.9
Student	34	6.8

Majority of the respondents 144(28.6%) were farmers. Approximately 362(74%) of the respondents were self-employed.

Religious affiliations of the subjects

Table 2e: Distribution of religious affiliation of respondents (n = 503), Plateau State late presentation of cancers in HIV infected participants of study 2014

Religion	Frequency	Percent (%)
Christianity	387	76.9
Islam	116	23.1

The religious affiliation of majority of the participants 387(76.9%) were Christianity based.

Educational Status

Table 2f: Distribution of educational status of respondents (n=503), Plateau State late presentation of cancers in HIV infected participants of study 2014

Educational Status	Frequency	Percent (%)
None	37	7.4
Primary	195	38.8
Secondary	169	33.6
Tertiary	102	20.3

Among the respondents, 401(93%) of them had some education or another (primary school, secondary and tertiary education) and only 37(7.4%) of respondents have not had any form of education.

Socio-Demographic factors associated with late presentation

Table 3: Socio demographic factors associated with late presentation of cancers among respondents (n = 503), Plateau State late presentation of cancer in HIV infected participants of study 2014

Variables	Cancer Presentation		Chi-square (χ^2)	df	p-value
	Early n (%)	Late n (%)			
Age Group (years)					
≤ 25	4 (2.6)	2 (0.6)	128.2	6	0.0005
26-35	35 (23.2)	12 (3.4)			
36-45	59 (39.1)	53 (15.1)			
46-55	34 (22.5)	80 (22.7)			
56-65	11 (7.3)	84 (23.9)			
66-75	4 (2.6)	107 (30.4)			
> 75	4 (2.6)	14 (4.0)			
Sex					
Male	60 (39.7)	192 (54.5)	9.3	1	0.002
Female	91 (60.3)	160 (45.5)			
Marital Status					
Single	43 (28.5)	25 (7.1)	37.8	2	0.0005
Married	107 (70.9)	325 (92.3)			
Widowed	1 (0.7)	2 (0.6)			
Occupation					
Applicant	2 (1.3)	1 (0.3)	62.6	6	0.0005
Business	49 (32.5)	74 (21.0)			
Civil servant	45 (29.8)	59 (16.8)			
Farmer	21 (13.9)	123 (34.9)			
Housewife	9 (6.0)	36 (10.2)			
Retiree	4 (2.6)	46 (13.1)			
Student	21 (13.9)	13 (3.7)			
Religion					
Christianity	123 (81.5)	264 (75.0)	2.5	1	0.115
Islam	28 (18.5)	88 (25.5)			
Educational Status					
None	13 (8.6)	24 (6.8)	40.8	3	0.0005
Primary	31 (20.5)	164 (46.6)			
Secondary	55 (36.4)	114 (32.4)			
Tertiary	52 (34.4)	50 (14.2)			

Results indicated that there was a significant association between Age range 36-45 (P= 0.001).

Male sex (P= 0.002), being Married (P= 0.001), Farming occupation (P= 0.001), Primary education (P= 0.001) status of respondents and late presentation. Religious affiliation, Christianity (P= 0.115) was not a significant factor.

Table 4: Logistic regression of socio demographic factors Plateau State late presentation of cancer in HIV infected participants of study 2014

Variables	Adjusted Odds ratio	p value
Age 36 = 35 years	2.7 (1.01 - 7.55)	0.001
Male sex	2.5(1.09 - 5.86)	0.002
Farmer	1.7(1.56 - 8.67)	0.001
Primary level education	2.0(3.08 - 31.23)	0.001

Result show that Age, male sex, farming and primary level education are significant factors.

Health facility visit on account of cancer related symptoms

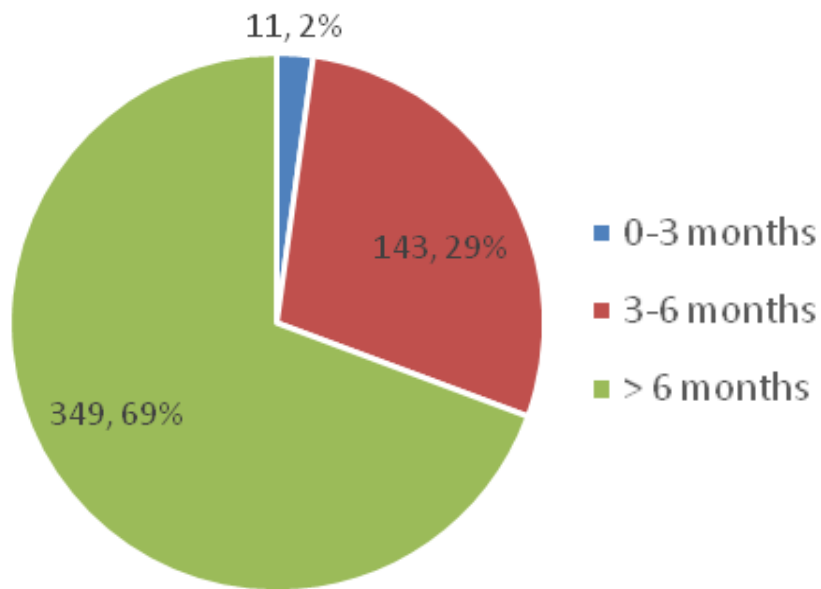


Figure 1: Pie chart showing length of time from onset of symptom to first presentation of respondents (n=503) to health facility, Plateau State late presentation of cancer in HIV infected participants study of 2014.

Majority of respondents 349(69%) presented more than six months after onset of symptom.

Patient mediated treatment actions

Table 5: Showing treatment measure by respondents (n=503) prior to first presentation at a health facility, Plateau state late presentation of cancers in HIV infected participants study of 2014

Reason for delay	Frequency	Percent (%)	95% Confidence Limits
Alternative remedies	234	46.5	42.1-51.0
Considered not serious problem	43	8.5	6.3-11.4
Fear of unknown	45	8.9	6.7-11.9
Lack of funds	87	17.3	14.2-21.0
Self-medication	24	4.8	3.1-7.1
Traditional belief	18	3.6	2.2-5.7
Visit chemist	52	10.3	7.9-13.4

Initial reaction of respondents to health issue were mainly the use of alternative remedies 234(46.5) CI 42.1-51.0.

Mode of initial reaction to health issues

Table 6: Showing mode of initial reaction of respondents (n=503) to health problem, Plateau State late presentation of cancers in HIV infected participants study of 2014

Reaction	Frequency	Percent (%)	95% Confidence Limits
Alternatives remedies	163	32.4	28.4-36.7
Ignore it	34	6.8	4.8-9.4
Self-medication	99	19.7	16.4-23.5
Visit hospital	132	26.2	22.5-30.4
Visit medicine store	75	14.9	12.0-18.4

Initial reaction of respondents to health issues show that use of Alternative remedies 163(32.4%) comes first before other measures.

Symptoms noticed

Table 7: Types of Symptoms first noticed by respondents (n=1011), Plateau State late presentation of cancer in HIV infected participants study of 2014

Symptoms	Frequency	Percent (%)
Abdominal distention	20	1.98
Vaginal Bleeding	30	2.97
Blood in urine	8	0.79
Skin changes	210	20.77
Blood in stool	25	2.47
Pain	462	45.70
Redness	4	0.40
Stiffness	1	0.10
Swelling	237	23.44
Ulcer	14	1.38

The most frequent symptoms among respondents was pain 462(45.70%) followed by swelling 237(23.44%) and skin changes 210(20.77).

Health services

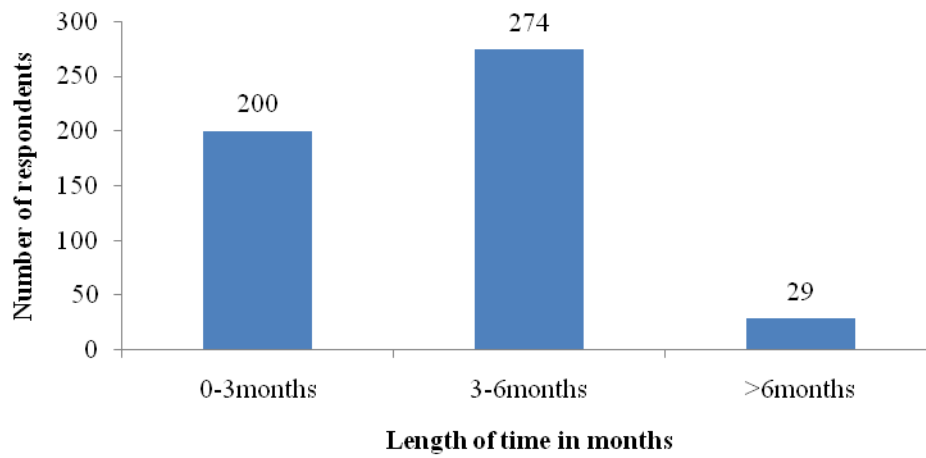


Figure 2: Time from first presentation of respondents (n=503) to a health facility to receiving definitive diagnosis, Plateau State late presentation of cancers in HIV infected participants study of 2014

Waiting time to obtain histological diagnosis from time of presentation to health facility was mainly 3-6 months 274(54.47%).

Service Factors

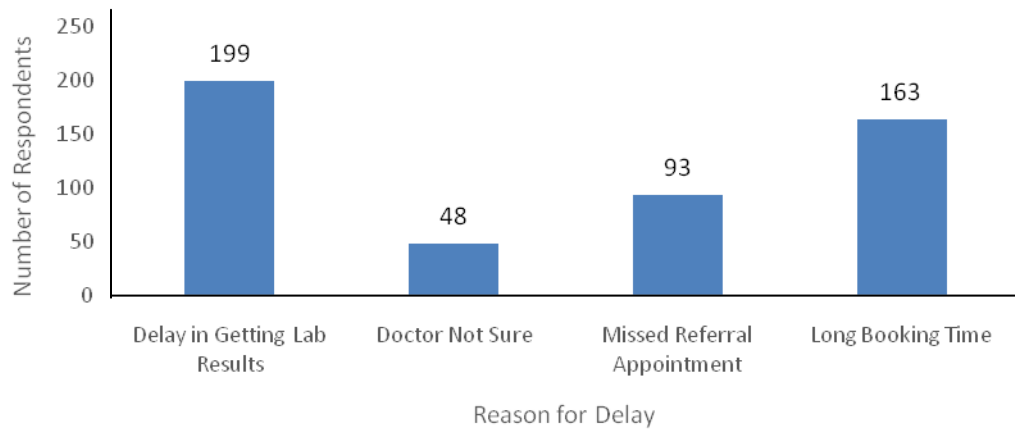


Figure 3: Reason for delay in initiating treatment among respondents (n=503) at health facilities, Plateau State late presentation of cancers in HIV infected participants study of 2014

Laboratory related issues 199(39.56%) and Long booking time 163(32.40%) were the most common reasons for delay in initiating treatment.

Qualitative findings

The hospital staff interviewed said:

The hospital has one oncology unit that receives referrals from other units within the hospital, the HIV clinic and other hospitals within Plateau state. Most patients were referred with a histological diagnosis, those who do not had to undergo procedure for obtaining a tissue diagnosis. The unit administer chemotherapy, immunotherapy and surgery if required. Patients are referred to hospitals outside Jos for radiotherapy. Unit has 10 staff and oversee on the average 50patients per week. Challenges in managing patients include clinic interruptions due to industrial actions/dispute, delay in getting histological diagnosis and difficulties starting treatment due to lack of drugs or resources to obtain them by the participants/patients.

The participants at the Focused Group Discussion (FGD) were all HIV positive, number of years diagnosed positive range from 10months to 13 years. The youngest was 25 years and oldest was 47 years. All were enrolled into a HIV management program. 16 were already on Anti-retroviral drugs according to national guidelines.

Usual clinic follow up after enrolment included questioning about new problems, follow up blood samples for laboratory investigations and getting drug refills. They also attended clinic health talks on HIV prevention, control and adherence to drugs.

They attended HIV/AIDS and cancer support group meetings and discussed issues affecting the HIV infected person, issues on cancer were however not discussed except in cancer support group meeting. Cancer did not feature during health talks either for the

HIV/AIDS support group meetings. They were eager to know more about cancer prevention and control.

About what is cancer, one of them said:

It is like HIV, no cure.

Another said:

The disease is only cured by traditional medicine. Sometimes it is an attack from enemies.

Another:

It is a disease you get when you eat too much meat

Someone said:

It can be cured by prayer and fasting

CHAPTER FIVE - DISCUSSION

The findings on late presentation of cancers among HIV infected individuals in Plateau State and the factors associated with it were discussed in this chapter. There was willingness to participate in the study and opened the much needed door to finding a solution to the unfavourable outcome of the disease cancer. The physical and emotional turmoil that often characterized the disease aroused the interest of individuals, medical personnel, families and friends of participants. The study determined the types of cancers that respondents presented with, established that there were late presentation cancers among the study population. It identified the socio demographic, patient medicated and service related factors contributing to late presentation of cancers, also offered insight into the reasons for the delay in the HIV infected persons.

Delay occurred at three phases in the study, First was the interval between "first noticing a symptom and first consulting a doctor". Second is between "first consultation and obtaining histological diagnosis" and Third, between "diagnosis and referral or initiating treatment". The various points during which factors influenced time to presentation presented in the discussion centered on Phase one, the Patient mediated factors which are socio-demographic, clinical symptom and general reaction of the individual to the cancers affecting them. Phase two and three, together were the service related factors. In addition to outlining the various points during which factors have influenced time to presentation and referral, considering delay in these phases has enabled identification of areas where interventions can be designed to reduce delay.

The types of cancer found in the study population varied from HIV associated to non HIV associated cancers. The commonest malignancy found was Kaposi Sarcoma 173(31.63%), an HIV associated cancer. Study done of cancers in HIV infection reported that KS is the commonest cancer in HIV infection especially in the presence of a low CD4 cell count.⁴⁴ Kaposi Sarcoma has been reported to have declined with antiretroviral drug due to increase in the individual's CD4 cell count as the viral load decrease allowing the immune system to increase.⁴⁴ The timing of initiation of ARVs and duration of use provided the ARVs are used judiciously and adhered to were factors that determine rise in the level of the immune system. The growth of the Kaposi Sarcomas is discouraged by the increasing CD4 cell count.

In this study the CD4 cell count of the patients were not determined how ever all respondents have been on ARVs for a period of not less than one year. None adherence of ARVs, other co infections, late initiation of ARVs and type of ARVs used could have attributed to the high incidence of KS in the study population. Bohlius reported in South Africa that HIV infection associated with late initiation of ARVs and a low CD4 cell count is a risk factor for developing Kaposi Sarcoma.⁴⁵

Other malignancies found among the respondents included Cancer of the Breast, Prostate, Gynecologic, Gastrointestinal, Sarcomas and the least Melanoma. This is in keeping with the five common cancers found in Nigeria reported by Fatima, Ibadan 2009. The findings reflected the increased risk of Non HIV associated cancer in the HIV infected persons also reported by Patel *et al.*⁴⁶ The HIV treatment programme in Nigeria has been in existence for about 15 years now, infected persons are living longer with the disease on

the ARVs there is therefore increased risk and pattern of cancers that were seen in the study population.

Patient delays are also influenced by a range of demographic and psychosocial factors. Taken together, factors that were associated with late presentation of cancers among the study group were the age range 36-45 years, male sex, being married, being a farmer and having primary education.

Majority of respondents were within the active age group 36-45 years ($P=0.001$) and this age group falls into the category of persons 19-45 years reported to be at high risk for HIV infection.⁴⁷ Ramirez in 1999 reported older age to be a significant risk factor for delay because they depend on others for help.⁴⁸ In a study on delay in presentation among colorectal cancer patients, Mitchell reported age was unrelated to delay.⁴⁹ In this study however we found that delay was related to active age group who have developed cancer most probably due to their HIV status but being at this age are expected to be more sensitive to changes affecting their health and to act quickly. However the delay in this group maybe related to stigma and discrimination among the HIV infected persons often found to be associated with reluctance in seeking help.

There were more males ($P=0.002$) than females contrary to the study reported by Clifford in Nigeria on help seeking behaviour related to stigma and discrimination among HIV infected persons that more women seek help earlier compared to men.⁴⁸ In a study comparing men and women delay in bladder cancer, Mammsen reported delay was longer in men than women.⁵⁰ While sex was not been found to be a significant factor for delay in GIT tumours reported by Macdonalds *et al* 2006.⁵¹ In Nigeria however,

Adebomowo *et al* found sex to be significant factor for delay in presentation of the different types of cancers.⁵² The male preponderance In the study, still followed the trend that the men sort help late compared to the women.

The sex of an individual and marriage are interwoven n the African context, being married (P=0.001) found to be related to late presentation of cancers in this study demands certain responsibilities and expectation for both sexes. The weight of responsibilities could be overwhelming sometimes making the individuals to pay less attention to his or her health. Sometimes one's health becomes the opportunity cost, a cheaper more affordable alternative such as medicine store to obtain pain relief may suffice until pain can no longer be suppressed or tumour seems to have become very large, then a more formal medical help is sort. Sometimes a spouse may require permission from the partner or family members to visit a doctor.⁵³ Alvesson *et al*, in a study at Loa, reported that Care-seeking is influenced by family and community-based relationships, which are found to be an integral part of people's everyday life.⁸ In his study on delay presentation of gastrointestinal and urologic cancers, Macdonald *et al*, 2006 did not find any relationship between marital status and late presentation.⁵¹ The findings of Macdonald compared to ours is not surprising because in developed countries spouses excise their individual rights while ours largely depended on the man's decisions. A delay in taking decision or not being available to take a decision could be a factor for the delay in this study.

Farming ($p=0.001$), in this study were small scale farmers who employed the use of manual labour and are regarded to be of low socio economic status were found to associated with increased delay in cancer presentation. The delay in this group could be

due to the seasonal farming periods during which farmer wants to put in all the labour and time he or she can to obtain maximal yield. Health issues during farming seasons maybe managed symptomatically until the farming season is minimally over. Fitzpatrick *et al* reported low socio economic status was associated with increased delay in men with prostate cancer.⁵⁴ This is similar to our findings in the study. However Mitchell *et al* did not find any relationship between socio economic status and delay in colorectal cancer in the United kingdom.⁴⁹ The difference may be due difference in health policy where medical treatment is largely based on Health Insurance policy in most developing countries, in Nigeria it is largely "Out of Pocket". The study participants harvested and sold produce before they could pay medical bills which was grossly inadequate to compared to the very high cost of cancer treatment in the country.

The low educational status ($P = 0.001$) found to be a significant factor associated with delay in this study may have influenced the ability of the participants to interpret symptoms correctly. This finding is similar to the report by Ramirez *et al* that lower educational attainment was associated with greater delay for patients with breast cancer.⁴⁸ Educational status is related to delay irrespective of study area. The participants were at a disadvantaged position to understand the probable implication of their symptoms and to seek medical care early.

Religious inclination ($P= 0.115$) was found not to be related to delay in the study group. Mitchell *et al* reported "Religious intervention in place of treatment" rather than religious inclination were found to related to delay.⁴⁹ Similar findings were also reported in Eastern Nigeria by Anyawu *et al*, they found belief in prayer was thought to cure breast cancer (miracle cure).^{55,56} Religious inclination although not a direct factor for delay, was still

found to be the foundation for accepting religious treatment which is abandoned for medical treatment when it failed.

Across the common cancers, then demographic risk factors for patient delay seem inconsistent. This may be a consequence of the fact that the cancers have not been equally researched in terms of risk factors for delay.

Clinical symptoms, The type of symptoms with which patients present has a marked impact on presenting behaviour. In this study, up to 92% of respondents had symptoms for more than 3 months before seeking medical attention and the most frequent symptoms were pains and swellings. Although the study participants had multiple symptoms, pain was found to be a common reason to seek medical help. For a majority of cancer groups studied, patients were more likely to present when symptoms became, more incapacitating and affected daily activities according to *Sanden et al, 2000*.⁵⁷ These symptoms were described as warning signs by *Quaife et al* who reported the need to educate the community to recognize these signs and to act quickly.⁵⁸ The onset of vague or non-specific or more common as well as multiple symptoms was likely to increase delay *Goff et al, 2000; Fitch et al, 2002*.^{59,60}

Reasons for delay in presentation by participants may have been influenced by a lack of interpretation by patients of the serious nature of their symptoms. Across the common cancers, symptom type is predictive of delay in presentation. If a symptom is atypical, or vague in nature, the risk of delayed presentation can be increased. However, if the symptom was more serious associated with bleeding or pain, then the risk of delayed presentation was reduced. Patients may fail to recognize or appreciate atypical or vague

symptoms, which may have mediated in delayed presentation. Where symptoms were understood and thought to be serious, there was a reduced time to presentation. Another dilemma encountered was that common cancer symptoms are often attributable to benign disease. For example when there is lump in breast cancer, patients delay less, compared with the less recognized non-lump symptoms, which result in greater delay.

Other Reason for delay in presentation included the use of alternative remedies, fear of the unknown, lack of funds, self medication, traditional belief and visiting chemist stores for symptomatic treatment.

Belief in alternative remedies (CI 28.4-36.7) being cure for various ailments including cancer. *Andreson et al* stated that use of alternative remedies among some cancer patients and found there were benefits provided it is used as an adjuvant to standard therapy and it did not constitute delay in their setting.^{61,62} In this study however it was used as a first line of treatment by the patient and therefore leads to delay in presentation. Complementary and alternative medicine (CAM) recognized in medical practice is the term for medical products and practices that are not part of standard medical care. While "Complementary medicine" refers to treatments that are used with standard treatment, "Alternative medicine" refers to treatments that are used instead of standard treatment.⁶³ The choice of alternative medicine rather than complementary medicine by the participants in this study resulted in delayed presentation.

An adjuvant to alternative medicine was patronizing patent medicine stores and self medication found to be a risk factor for delay in the study participants. Qualitative response from respondents showed that it was a cheaper and faster means of getting relief

and with less financial burden. Survey reports showed that people hold negative beliefs and attitudes about the benefits of seeking medical help for cancer, they are embarrassed and reluctant to bother the general practitioner about cancer treatments according to Grunfeld *et al.*⁶⁴

Not paying attention to symptoms and considering them Not serious (CI =6.3-11.4) was a risk factor for delay in this study, some respondents felt symptoms were not something serious so did not seek any medical advise until symptoms became intractable and could no longer be ignored. Symptom awareness, and interpretation of symptoms, non-recognition of the seriousness of symptoms, lack of knowledge about the disease, was reported to be the predominant risk factor for delay across all cancer sites by *de Nooijer et al.*⁶⁵ Delay was often related to patients adopting a ‘wait and see’ approach, denying or redefining their symptoms in relation to benign disease or self-diagnosing and self-medicating before presentation to a practitioner according to Macdonald *et al.*⁵⁰ In this study a wait and see approach might have been adopted by participants leading to the delay in presentation.

Traditional and religious beliefs in healing were also a significant reasons for delay in the study group. Some of these beliefs gathered from qualitative interview revealed that some respondents believed that *cancer is incurable so there was no need seeking medical treatment*. While others believed *cancer occurred as a result of witch craft activities which can only be treated by non-medical means*. These non-medical methods include use of charms, sacrifices, abstinence from certain foods, incisions on swellings into which substances (content could not be verified) were rubbed into incision sites. Although religion was not a significant socio demographic factor in this study, a religious

practice as an alternative method of treatment for cancer was found to be a significant factor for delay. Prayers for the sick could last from few minutes to hours, days, weeks or months. Some of the study subjects volunteered information on *not being allowed to take medically prescribed treatment because that would mean lack of faith.*

Studies in some Nigerian institutions evaluating factors for delays in cancer presentation reported fear as a very strong factors followed by religious, financial constraint, preference for alternative remedies and unbelief about the disease according to Smith *et al.*⁶⁶ Lack of knowledge about their ailment may be a reason for thinking they could take care of themselves rather than see a doctor. Fear of the unknown was significant reason for refusing mastectomy reported by Ajekigbe *et al.*²⁰ Fear in this case might be largely due to not knowing the basics of cancer and its management.

When we considered the Initial reaction of respondents to health issues in the this study which has contributed to decisions made by the respondents , we found use of Alternative remedies, Ignore it, Self medicate, Visit hospital or Visit medicine stores to be contributory factors for delay. These factors buttress the findings discussed above as being supporting reasons for delay in the study participants.

Service related factors were found set of the second and third phases of delay in this study. Time taken from presentation to a medical facility and obtaining a definitive diagnosis was >3 months in 303(60.23%) of respondents in the study. Reasons for delay were time taken to obtain laboratory results are prolonged due to unavailability of diagnostic equipment at the peripheral hospital levels, lack of specialized manpower, long turnaround time and misdiagnosis/practitioner not sure of diagnosis. Delayed

referral across the cancer sites related to initial diagnosis and activity of the practitioner is a risk factor for increased delay. Misdiagnosis, occurring either through treating patients symptomatically or by relating symptoms to a health problem other than cancer, resulted in increased time to referral. Failure to fully or adequately examine patients, use of inappropriate or inadequate tests and receiving or failing to follow-up inconclusive, negative or false negative test results contributed to the Goff *et al*, 2000.⁵⁹ There are some evidence to suggest that appropriate referral and use of referral guidelines is associated with reduced delay for upper gastrointestinal cancers according to Macdonald *et al* and colorectal cancer Mitchell *et al*.^{48,49} When participants in this study presented to their doctors with potential cancer symptoms, timely investigation and onwards referral were clearly important. The study suggest that patients with particular demographic profiles, those from primary health centres before being referred or sites where there was no oncologist , participants with cancers at sites difficult to diagnoses and those with lower educational attainment experienced practitioner delay. This study also suggests the need for effective use of referral guidelines for general practitioners, as well as better use of, and access to, diagnostic services.

CHAPTER SIX - CONCLUSION AND RECOMMENDATION

6.1 Conclusion

Delay occurred at three phases in the study, first was the interval between the patient first notice of a symptom and first consulting a doctor second, between first consultation and obtaining histological diagnosis and third, between diagnosis and referral or initiating treatment. In addition to outlining the various points during which factors have influenced time to presentation and referral, considering delay in these phases has enabled identification of areas where interventions can be designed to reduce delay.

These factors are intricately inter related therefore it has to be addressed together. There was low levels of symptom awareness which partly explain why the type of symptom and recognition of the seriousness of symptoms are consistent risk factors for delayed patient presentation. The study also suggest that cancer symptom awareness is poorer among those who are less educated, as well as those with lower socio-economic status. Also proven is the fact that people hold negative beliefs and attitudes about the benefits of seeking medical help for cancer, which include fear, stigma, traditional beliefs and religious influences.

Reported barriers to early help seeking were vague and mild symptoms, belief that the symptom will go away, intermittent symptoms, lack of awareness of cancer risk and previous benign diagnosis. Competing demands and priorities, fears about cancer treatments and anxieties about cancer have enabled the identification of eventual triggers to help seeking such as worsening symptoms, new additional symptoms, the presence of a symptom that is recognized as serious or is affecting daily life and the influence of family and friends

A more in-depth knowledge of cancer is required for both the sufferer and the care giver. The services in various institutions that offer health care need upgrading to be able to carry out the basic necessary investigations to reduce the long waiting time. Early presentation of cancer will greatly reduce the morbidity and mortality associated with late presentation of cancer.

6.2 Recommendation

1. The patients:

HIV positive patients with symptoms suggestive of cancer spend valuable time in symptomatic treatment thereby losing valuable time leading to delay. Increase awareness of cancer in HIV positive patient through including cancer prevention and screening in daily health talk by health personnel can be introduced as part of regular clinic procedures and it will help increase cancer awareness and to know where to go for help.

2. The service:

- HIV treatment facilities are not equipped with cancer diagnostic equipments leading to delay in diagnosis. Hospital management to acquire basic cancer diagnostic sets for quick assessment and maintained linkages to other hospitals with diagnostic facilities to ensure early diagnosis.
- Health personnel attending to HIV infected patients are not sensitized to search out for cancer in these patients. Conduct continuous medical education on cancer management in HIV positive patients for health worker at primary, secondary and tertiary health care levels through regular clinical meetings and tumor boards. This can be done through the Nigerian medical association regular Continuous medical education programs being extended to those serving in rural areas. This will enhance recognition and prompt diagnoses of cancer cases.

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APPENDICES

Appendix 1a - Consent Form

Factors associated with late presentation of symptomatic cancer among HIV infected persons in Plateau state consent form.

You are being asked to take part in a research study of why patients with can symptoms suggestive of cancer present late to hospitals for treatment. We are asking you to take part because you are in the clinic today for a reason and have agreed to give us tell us why you are here today. Please read this form carefully and ask any questions you may have before agreeing to take part in the study.

What the study is about: The purpose of this study is to learn about the things that make people with not to come to hospital for treatment the moment they notice something abnormal in their body. What we will ask you to do: If you agree to be in this study, we will conduct an interview with you. The interview will include questions about your job, family, when you discovered the disease, when and why you started seeking medical help, and what has been done now. The interview will take about 30 minutes to complete.

Risks and benefits:

There is the risk that you may find some of the questions about your job conditions to be sensitive. I do not anticipate any risks to you participating in this study other than those encountered in day-to-day life. The result will help us know how to give patients better information on early diagnosis which leads to early treatment.

Your answers will be confidential. The records of this study will be kept private, any part of the report we make public we will not include any information that will make it possible to identify you. Research records will be kept in a locked file; only the researchers will have access to the records. If we tape-record the interview, we will destroy the tape after it has been transcribed, which we anticipate will be within two months of its taping.

Taking part is voluntary: Taking part in this study is completely voluntary. If you decide not to take part it will not affect your current or future relationship with this clinic. If you decide to take part, you are free to withdraw at any time.

If you have questions: The researcher conducting this study is Mercy Isichei, please ask any questions you have now or you may contact me at mercyisichei@yahoo.com, 08028105121. If you have any questions or concerns regarding your rights as a subject in this study, you may contact the Institutional Review Board (IRB) at Jos North local government.

Statement of Consent: I have read the above information, and have received answers to any questions I asked. I consent to take part in the study.

Your Signature _____ Date _____

Your Name (printed) _____

Signature of person obtaining consent _____ Date _____

Printed name of person obtaining consent _____

Thank you for your time and for participating in this study.

Appendix 1b

Consent Form in Hausa

Shedan Amincewa da Binchike

Abubuwan da ke sa mutanen da ke bayana da alamomin cutar daji a sakanin masu Cutar da ke karya garkuwan jiki (SIDA), su makara a wajen neman jinya a Jihar Pilato, shedan amincewa da binchike

Ana bukatar ka/ki kasanche a binchike a kan dalilai da ke sa mutanen da ke da cutar SIDA da kuma suna da alamomin cutar daji, ke makara wajen neman jinya a asibitochi. Muna wanan tambayoyin ne domin ka/kin zo asibiti yau da wani dalili, kuma ka/kin aminche ka/ki gaya mana abinda ya sa ka/kin zo yau. Karanta wanan takarda da kyau ka/ki yi tambiya a kan wannan binchike kamin aminchewa ka/ki zama a sakanin wadanda za a yi wannan binchike da su.

Dalilin wanan binchike: Dalilin wannan binchike shine, domin a sani dalilen da ke sa mutanen da ke da alamomin cututuka masu bayana kamar daji, ke yin jikirin zuwa asibiti domin jinya, yayin da suke ganin alamomi da ba dai dai ba a jikunan su.

Abubuwan da za mu sa ku, ku yi: Idan ka/kin aminche ka/ki kasanche a chikin wannan binchike, za mu yi wasu tambayoyi a kan aikin da ka na/ki ke yi, iyali, lokachin da ka/kin sani cewa ka/ki na da wanan cutan. Lokachin da ka/kin fara zuwa jinya a asibiti, da abubuwan da an rigaya an yi, wadannan tambayoyi za su doiki akalla mintuna talatin.

Hatsari da amfaninin wannan binchike: mai yiuwa wadansu tambayoyi da za a yi ma ka/ki a kan aiki, iyali ko yanayin lafiyan ka/ki za su zama abubuwan da ba za ka/ki so ka/ki fada ma wani ba, amma tambayoyin nan za su shafi alamuran yau da kullum ne

kawai. Amfanin su kuma, shi ne zai sa mu fada ma masu jinya abubuwan da za su taimake su wajen gane alamun chututuka da sauri, da kuma bukatan yin jinya da sauri.

Tambayoyin da za a yi maka/ki za su zama a asirche, baza a bayana wa kowa ba, dukan wuraren da za'a bayana ba zai kunshi in da zai sa a gane wai kai/ke bane. Takardun binchiken za su zama a kulle, mai binchike ne kadai za ta sami daman ganin su. In da an yi amfanin da na'uran doukar murya a wajen yin tambayyoyi, za a kone su bayan an rubuta su, a chikin watani biu bayan doukan muryan.

Kasanchewa a chikin wannan binchike da izinin ka/ki ne. Idan ba ka/ki ke so ka/ki kasanche a chikin wannan binchike ba, ba zai shafi dangantakan ka/ki da wannan abibitin ba. Za ka/ki iya ka/ki janye daga wannan binchike a dukan lokachin da ka/kin ga dama.

Idan akwai wani tambaya? Mai binchike ita che Dr. Mercy Ishichei, ka/ki na da daman yin dukan tambayoyin da ka/ki na da su yanzu, ko kuma a kira lambar waya 08028105121 ko kuma, ta yanar gizo a mercyishichei@yahoo.com. Idan kuma ka/ki na son sanin in da an sami izinin gudanar da wannan binchike, a tuntubi Institutional Review Board (IRB) na Hukuman Kiwon Lafiya na Jihar Pilato

Sa Hanu.....Kwanan
wata.....

Suna.....

Sa Hanu Mai neman izini.....Kwanan wata.....

Sunan Mai neman izini.....

Ina godiya dayawa

Appendix 2

FACTORS ASSOCIATED WITH LATE PRESENTATION OF SYMPTOMATIC CANCERS AMONG HIV INFECTED PERSONS IN JOS, PLATEAU STATE

Key Informant Interview Guide

For use with Doctors, Nurses and Laboratory Staff of Jos University Teaching Hospital and the Oncology Unit

Introduction: Thank you for agreeing to participate in this study.

This is an interview that will provide a better understanding of cancer in the HIV infected and the factors that are driving late presentation of cancers even when symptoms are obvious or when the affected individual presents at a health facility.

This interview will add value to the quantitative study that has been conducted in Jos University Teaching Hospital.

The interview will take between 45 - 60 minutes.

Time started:

Background

- Can you tell about the oncology programmes in your hospital?
- Is there a special program targeting the HIV infected persons?
- Do you have data on number of HIV infected persons that develop cancer?
- Cancer Knowledge, Attitudes, and Practice in Hospital
- What do you know about cancer?
- What do you understand by cancer screening?
- Do you know about any screening procedure? please describe, have you done any cancer screening on yourself?
- Is there any cancer screening centre in your hospital your hospital, is it easy to access it?
- What about cancer diagnosis in your hospital
- How long does it take to get a diagnostic test done?
- Do you have the needed equipment for cancer diagnosis?
- Are there trained personnel who manage and treat cancer patients?
- What happens when a person is diagnosed? is there a referral system in place?

- What are the challenges with cancer diagnosis in your hospital?

Resources

- How do you maintain your screening programmes, is there sustainability program in place?
- How is the diagnostic equipments maintained?
- Is funding for cancer prevention and control adequate?
- Is there a government cancer control program that affected persons can leverage on to reduce the burden associated with cancer treatment?
- Is there any information you would like to tell us that will help with this study?

System strengthening

- What in your opinion is the government doing and that can be done to improve cancer prevention and control in our country?
- What is your opinion on the health system cancer management, what can be done to improve it?
- Time closed:

Thank participant for their time and invite questions or comments they may wish to make.

Appendix 3

FOCUS GROUP DISCUSSION GUIDE

Introduction: Thank you for agreeing to participate in this focus group discussion.

This is an interview that will provide a better understanding of cancer in the HIV infected and the factors that are driving late presentation of cancers even when symptoms are obvious or when the affected individual presents at a health facility.

This interview will add value to the quantitative study that has been conducted in Jos University Teaching Hospital.

The discussion will take between 45 - 60 minutes.

Time started:

Background

- Can you tell me when you were diagnosed with HIV?
- Are you already in a treatment program?
- Are you in any treatment program?
- Cancer Knowledge, Attitudes and Practice
- What is cancer?
- How can a person know they have cancer?
- Are there signs and symptoms of cancer?
- What in your opinion is the cause of cancer?
- Have you ever been diagnosed with cancer?
- Can cancer be prevented?
- Have heard of cancer screening?

- Have been screened for any cancer before?
- Did you have to pay for the screening?
- Was it easy to access the screening program
- Do you think cancer is treatable?
- How is it treated?
- Do you know anyone who was treated with cancer? what is the outcome?

HIV clinic services

- Do you attend a HIV clinic follow ups regularly?
- Do you get examined for signs of cancer?
- Do you get cancer messages at health talks? Do you understand the messages?
- Do you get screened for cancer during clinic visits?
- What is your opinion on inter departmental and intra clinic referral system? how easy is it to get absorbed into another hospital

System strengthening

- What is your opinion on cancer prevention and control for the HIV infected persons, what can be done to prevent it?
- What is your opinion on hospital based cancer control programmes and what can be done to improve it?
- Time closed:

Thank participant for their time and invite questions or comments they may wish to make.

Appendix 4
Questionnaire

FACTORS ASSOCIATED WITH LATE PRESENTATION OF SYMPTOMATIC CANCERS AMONG HIV POSITIVE
PATIENTS IN PLATEAU STATE

Dr ISICHEI M.W.

Socio- Demographic

Name (Optional):.....

Age (Yrs)	<input type="checkbox"/> 1-5	<input type="checkbox"/> 26-30	<input type="checkbox"/> 51-55
	<input type="checkbox"/> 6-10	<input type="checkbox"/> 31-35	<input type="checkbox"/> 56-60
	<input type="checkbox"/> 11-15	<input type="checkbox"/> 36-40	<input type="checkbox"/> 61-65
	<input type="checkbox"/> 16-20	<input type="checkbox"/> 41-45	<input type="checkbox"/> 66-70
	<input type="checkbox"/> 21-25	<input type="checkbox"/> 46-50	<input type="checkbox"/> 70 and above

Gender	<input type="checkbox"/> Male
	<input type="checkbox"/> Female

Religion	<input type="checkbox"/> Christian	<input type="checkbox"/> Others (Specify)
	<input type="checkbox"/> Muslim	

Educational Status	<input type="checkbox"/> Primary	<input type="checkbox"/> Tertiary
	<input type="checkbox"/> Secondary	<input type="checkbox"/> Illiterate

Employment status	<input type="checkbox"/> Employed	<input type="checkbox"/> Unemployed
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Place of abode	
----------------	--

Distance from nearest Health facility	<input type="checkbox"/> Less than 10KM	<input type="checkbox"/> 10 -20KM	<input type="checkbox"/> >20KM
---------------------------------------	---	-----------------------------------	--------------------------------

Number of dependant family members	<input type="checkbox"/> 0-3	<input type="checkbox"/> 4-6	<input type="checkbox"/> > 6
------------------------------------	------------------------------	------------------------------	------------------------------

Date of HIV diagnosis:	
Duration on therapy	
Drug regimen	

**FACTORS ASSOCIATED WITH LATE PRESENTATION OF SYMPTOMATIC CANCERS AMONG HIV POSITIVE PATIENTS
IN PLATEAU STATE**

11 What is your normal reaction to health problem?

a) Ignore it b) Self medicate c) Alternative remedies

d) Patent medicine store e) Visit hospital

Clinical signs

12 i When did you notice the symptoms suggestive of cancer?

a) Pre- ART b) Post-ART c) Unsure

ii If a), How long after HIV diagnosis did you notice the symptoms?

a) <6 months b) 6-12months c) >12 months

iii If b), How long after initiation of ART did you notice the symptoms

a) <6 months b) 6-12months c) >12 months

13 Which symptoms did you notice?

a) Swelling b) Itching c) Redness

d) Sores e) Others (Specify)

14 i What did you do when you notice the symptoms?

a) Ignore it b) Self medicate c) Use alternative remedies

d) Visit patent medicine store Visit healing homes

f) Visit hospital

ii If f), How long from the onset of the symptom did you to visit the hospital?

a) Days b) weeks c) months

d) years

iii If d), What made you delay that long?

a) Too sick b) Lack of funds d) Traditional belief

e) Use alternative remedies

Service related factors

15 How much did it cost you to get the hospital?

a) <1000NGN b) 1000-5000NGN c) >5000NGN

16 Can you describe the attitude of the hospital staff to you when you got to there?

a) Cordial b) Unfriendly c) Indifferent

17 Were you told the diagnosis of your condition at the hospital?

a) Yes b) No

18 What was the diagnosis of your condition?

19 What was the time interval between your visit and diagnosis?

a) <3 months b) 3-6 months c) >6months

FACTORS ASSOCIATED WITH LATE PRESENTATION OF SYMPTOMATIC CANCERS AMONG HIV POSITIVE PATIENTS

IN PLATEAU STATE

20 i In your opinion, what caused the delay in diagnosis?

a) Doctor was not sure of the diagnosis	b) Long waiting time to see the doctor
c) Delay in getting the lab result	d) I did not keep up with my follow up visit

ii If d), What was the cause?

a) Too sick	b) Lack of funds	c) Long distance to clinic
d) Felt it was not unnecessary	e) Others (Specify)	

21 How many times did you visit the hospital before you were given a diagnosis?

a) <3 times	b) 3-6times	c) >6 times
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22 What was the time interval for each visit?

a) Monthly	b) Bimonthly	e) Others (Specify)
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THANK YOU FOR YOUR TIME

Appendix 5

Ethical Clearance

JOS UNIVERSITY TEACHING HOSPITAL JOS, NIGERIA

Phone: 073-450226 - 9
E-mail: juth@infoweb.abs.net



Cables & Telegram: JUTH
P.M.B. 2076
Jos.

Ref: JUTH/DCS/ADM/127/XXII/ 5748

Date: 13th August, 2013.

Dr. Isichie M. W,
Department of Surgery,
Jos University Teaching Hospital,
Jos- Nigeria.

RE: ETHICAL CLEARANCE/APPROVAL

I am directed to refer to your application dated 5th August, 2013 on the research proposal titled:

'Factors Associated with Late Presentation of Symptomatic Cancers in Plateau State, Nigeria' and your appearance before the Ethical Committee on 7th August, 2013

Following recommendation from the Institutional Health Research Ethical Committee, I am to inform you that Management has given approval for you to proceed on your research topic as indicated.

You are however required to obtain a separate approval for use of patients and facilities from the department(s) you intend to use for your research.

The Principal Investigator is required to send a progress report to the Ethical Committee at the expiration of three (3) months after ethical clearance to enable the Committee carry out its oversight function.

Submission of final research work should be made to the Institutional Health Research Ethical Committee through the **Secretary in Room 2, Administration Department**, please.

On behalf of the Management of this Hospital, I wish you a successful research outing.


Hajia R. Danfillo
For: Chairman, MAC



Appendix 6

Activity and Evaluation Work-Plan (Gantt Chart)

Objective	Activities	Implementation August 2013- March 2014												Means of Verification (MOV)	Responsible		
		J	J	A	S	O	N	D	J	F	M	A	M			J	
To determine the factors associated with late presentation of cancers among HIV infected persons in	Advocacy to Stakeholder	X														Jos University Teaching Hospital	Resident / Supervisors
	Protocol Development	X	X													Finalised protocol available	Resident / Supervisors
	Ethical Clearance		X	X												Ethical clearance letter	Resident / Supervisors
	Development/ Printing of Tools questionnaires and guides		X	X												Evaluation tools available	Resident / Supervisors
	Training of assisting data collector(s)			X	X											Reports of training Workshop and pretest	Resident
	Data collection and Field work				X	X	X	X	X							Questionnaire administration and testing	Resident
	Analysis										X	X				Data Analysis report	Resident
	Report Writing										X	X				Finalised report available	Resident
	Dissemination / Defense		X													Thesis Report of dissemination Developed advocacy report of meeting, printed report	Resident / Supervisors Stakeholders
	Logistics , Meeting Transportation Communication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Report and Excel retirement	Resident / Supervisors