Human Immunodeficiency Virus and Malaria Co-Infection among Adults in the North-Central Zone of Nigeria, in the era of Improved access to Prevention and Control: A Study Protocol

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Abstract

Background: Despite a notable reduction in the incidence and prevalence of HIV and malaria, both diseases remain the leading cause of morbidity and mortality, especially in sub-Saharan Africa. The aim of the research study is to provide epidemiological data of malaria among HIV positive individuals, establish the socio-economic determinants associated with HIV-malaria co-infection, and develop a co-infection intervention model. This research study will enable health policymakers to develop new health policies in the management and care of HIV-malaria co-infected patients.

Methods and Analysis: The study design will be a retrospective, descriptive cross-sectional study. Case files of HIV positive individuals receiving care and treatment will be randomly selected at six selected peri-urban secondary hospitals. Interviews will be conducted among HIV positive patients, health managers, and doctors at selected hospitals. A mixed method (quantitative and qualitative) will be adopted in the research study. Proportional allocation will be used to select an estimated 1,652 case files of registered patients to be reviewed across the study location.

Statistical Package for Social Sciences version 25.0 will be used for data analysis. The categorical variable will be illustrated as a percentage and compared using Chi-square and Fisher's exact test. Backward multivariate analysis will be used to evaluate HIV-malaria co-infection and associated health outcomes. The continuous variables will be summarised as mean, ± SD or median, interquartile range, and compared using student t-test or Wilcoxon test. Values of $P < 0.05$ will be considered significant. Qualitative data will be analysed using NVivo 12 software.

Strengths and Limitations of This Study

Strengths

- ➢ The proposed large sample size of case files to be reviewed will enhance the validity and precision of the research study.

Limitations

- ➢ Data that will be generated might not be adequate to make a generalized conclusion for the whole country.
- ➢ Since the study involves the use of secondary data (generated from patient case files), missing data is anticipated.
- ➢ Strike actions by health care workers were also expected.
- ➢ Another limitation is that the research study will not be conducted as a prospective cohort study.

Ethics and Dissemination

Considering the research study involves the use of secondary data, the ethical approval issued to conduct the study covers the informed consent of the participants' information. Copies of written informed consent, participant

consent, and confidentiality forms will be provided to the participants both in English and in the native language, notably Hausa, TIV, and Yoruba. Verbal informed and signed informed consent to take part in the study will be obtained from the participants. This study was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC)-Reference Number: (BE654/17). Ethical approval was also obtained from the Kwara State Ministry of Health (MOH/KS/EU/777/225), Benue State Ministry of Health (MOH/STA/204/56), and the Nasarawa State Ministry of Health: NHREC 18/06/2017.

Findings from this study will be published in peer-reviewed local and international journals. Findings will also be made available to health policymakers at the state ministry of health and hospital facilities selected for the study. The principal investigators and the health providers will sensitize patients on the study outcome.

Keywords: HIV, malaria, co-infection, adults, control, prevention, and Nigeria.

1. Introduction

There are no substantial policies to control the Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome (HIV/AIDS) and malaria in Nigeria, a region greatly impacted by HIV and malaria co-infection. Despite access to adequate health care services being improved, malaria in HIV positive patients still presents a great threat to effective treatment, prevention, and control (Focà, Odolini, Brianese, & Carosi, 2012). HIV-malaria co-infection interaction has continued to be a potential risk, even in malaria-free regions due to importation, common among international HIV positive individuals traveling to endemic malaria areas (Focà et al., 2012). Despite the global reduction in the incidence and prevalence of both infections, HIV/AIDS, a viral infection transmitted sexually and malaria, a mosquito-borne parasitic infection is responsible for millions of deaths annually in sub-Saharan Africa (SSA), South America (SA) and South East Asia (SEA) (Naing, Sandhu, & Wai, 2016).

In the SSA, malaria is one of the major causes of death among HIV seropositive individuals (Holmes, Losina, Walensky, Yazdanpanah, & Freedberg, 2003). Pregnant adults and children under-five are at higher risk of malaria-related morbidity and mortality (Kwenti, Kwenti, Latz, Njunda, & Nkuo-Akenji, 2017), while HIV is common among young adult women (UNAIDS, 2014). There is a higher risk of malaria among People Living with HIV/AIDS (PLWHA), which can result in a sustained viral load with an increased likelihood of transmitting HIV responsible for the disease (Cuadros & García-Ramos, 2012). There is also a potential threat of HIV/AIDS transmission among vulnerable individuals such as female sex workers, homosexuals, young women, children, prisoners, and injecting drug users (Blair C, 2015). It was observed that the transmission of HIV and malaria does not affect the proliferation of each other as observed among HIV-malaria co-infected mothers using Highly Active Antiretroviral Therapy (HAART) (Sadoh & Eki-Udoko, 2018). Sadoh, in his study, suggested that the use of HAART could reduce the immune suppression pose by HIV, depending on the duration of HAART (Sadoh & Eki-Udoko, 2018). Ottichilo et al., (2017) observed that PLWHA who are on Antiretroviral Therapy (ART) with continued use of Co-trimoxazole (CTX) offers a semi immunity to malaria and provide a rapid reduction in malaria parasitaemia and future episodes (Ottichilo et al., 2017). Similarly, a notable reduction in the transmission of HIV has been attributed to the use of HAART (Agboghoroma, Sagay, & Ikechebelu, 2013). The rate of transmission is relatively higher among infants during the pre-HAART era (Sadoh, Omoigberale, Esene et al., 2008). Findings from previous studies documented a lower prevalence between 2.1% and 2.46% (Sadoh et al., 2008); furthermore, a high prevalence of 7% was recorded in the HAART era (Esene & Omoigberale, 2012).

A High level of HIV-malaria co-infection has been documented during the post-ART era. Akinbo et al., in his research study, reported HIV-malaria co-infection prevalence of 9.8% and 7.8%, respectively (Akinbo Omoregie et al., 2013; Akinbo, Anate et al., 2016). Similarly, the relatively higher prevalence was reported among participants on ART. Jegede et al. (2017), in his research study conducted among patients attending ART clinic in Kano Northwestern Nigeria, reported a 27.7% percent of HIV-malaria co-infection (Jegede et al., 2017). The highest prevalence documented during the post HAART era was 74.3%, reported in Benin-city Nigeria, by Omoti et al., (2013) (Omoti, Ojide, Lofor, E. Eze, & J. C. Eze, 2013), and of recent, Izuka et al., (2017) reported a 68.6% of placental malaria among HIV seropositive women (Izuka et al., 2017).

HIV and malaria co-infection does not only affect the health of infected individuals but also affects the economy. In SSA, HIV-malaria co-infection is responsible for a significant proportion of 12-billion-dollar loss due to a decrease in productivity and more than 300,000 HIV/AIDS-related mortality in 2003 (World Health Organization, 2005). Approximately 28.5 million individuals in the SSA region are HIV seropositive, a region with over 350 million new malaria cases annually (Wumba et al., 2015). In the year 2005, an estimated 65,000 deaths and additional three million clinical malaria cases, amounting to about 1.3% increase in prevalence and 4.9% increase in malaria-related mortality were attributed to HIV-malaria co-infection interaction (Korenromp et al., 2005).

Abu-Raddad et al. (2006) observed that 980,000 new malaria cases and 8,500 new HIV infections were attributed to co-infection between the 1980s and 2006 in Kenya (Abu-Raddad, Patnaik, & Kublin, 2006). In Nigeria, the indirect impact of malaria such as cost of transportation to health facilities, cost of health care, and loss of working hours due to absenteeism from work accounts for more than 132 billion Naira a loss annually and impacts heavily on the economy (Federal Republic of Nigeria, 2005). Progression from HIV to AIDS usually happens between 7–10 years. However, co-infection interaction stimulates a rapid progression to AIDS (WHO, 2016). There is a high level of interaction between HIV infection and malaria in geographical areas where transmission of both diseases is favored (WHO, 2016). In malaria-endemic regions, there is a high risk of malaria infection notable among individuals with impaired immune systems caused by HIV/AIDS.

Similarly, in regions where malaria transmission is endemic, there is an increased risk of severe malaria and death among HIV infected individuals (WHO, 2016). Individuals in such regions are considered to have developed a host-related immunity to malaria; however, infection and immunosuppression with HIV/AIDS render such individuals susceptible to clinical malaria as a result of diminished host acquired immunity to malaria (WHO, 2016). It has also been advocated that co-infection interaction between HIV and malaria hurts public health prevention and management practices and will further lead to decreased control efforts (WHO, 2016). HIV-malaria co-infection interaction is said to be associated with higher in-hospital mortality (Berg et al., 2014).

The majority of the studies conducted in Nigeria, including the North Central Zone (NCZ), reported a co-infection between HIV and malaria with high prevalence. HIV was indicated as an important risk factor for malaria with a notable impact on CD4 + T - cell counts (Izuka et al., 2017; Iroezindu et al., 2012; Dada, 2015; Jegede et al., 2017; Ojurongbe et al., 2014). Gossele et al. (2007) reported a relatively lower albumin concentration (Gossele, Onwuliri, & Onwuliri, 2007), while congenital malaria was reported among new-borns of co-infected mothers (Eki-Udoko, Sadoh, Ibadin, & Omoigberale, 2017). Notable impacts of malaria on biochemical indicators were observed among HIV positive patients with a rapid reduction of serum iron. The burden of co-morbidity was reported to be three times higher among symptomatic HIV positive individuals and recommended repeated malaria screening as a policy to control co-infection in the endemic area due to malaria-related mortality (Onyenekwe et al., 2007). Studies continue to document a high level of co-infection in recent studies (Jegede et al., 2017; Izuka et al., 2017).

In SSA, including Nigeria, HIV/AIDS, and malaria co-infection are the main causes of death. However, there is no appropriate reporting and documentation to understand and explain the extent and the level of interaction between these co-infections. A comprehensive understanding of this interaction will go a long way in making informed decisions and appropriate interventions regarding the synergy between these co-infections. Studies have documented that HIV seropositive individuals are more susceptible to malaria and hence, might be at greater risk of experiencing severe disease burden in terms of morbidity and mortality than HIV seronegative individuals. Among patients using antimalarial and antiretroviral medicine simultaneously, a couple of notable adverse reactions to the medication have been documented. Being on cotrimoxazole and sulfadoxine-pyrimethamine at the same time is not advocated during pregnancy, due to the likelihood of sulfonamide associated toxicity (Kwenti, 2018). Studies conducted in Nigeria have reported a high prevalence of malaria among PLWHA; however, a limited clinical association between HIV and malaria has been documented in Nigeria (Olorukooba et al., 2016). Therefore, understanding the basis of the interactions between HIV and malaria is significant in developing an intervention plan, and the management and care of co-infected patients. Furthermore, this study will also provide epidemiological data of malaria among HIV positive individuals and its socio-economic determinants, to determine the trend in seasonal variation and develop an intervention model in the NCZ, Nigeria. This study hopes to serve as a benchmark for future studies on HIV-malaria co-infection.

2. Scope of the Study

The scope of the study is to develop an HIV-malaria co-infection intervention model. The study will also review hospital records (case files) of medically diagnosed HIV positive adults receiving care at six secondary hospitals at three states randomly selected in the NCZ, Nigeria. The study will review and extract data from case files of PLWHA retrospectively over five years (2013 to 2017) using a purpose-made data collection tool, while in-depth interviews will be conducted among the head of the HIV clinics.

Since all the patients are HIV positive, the case files of the patient will be reviewed for malaria diagnosis and the date and season when the diagnosis was conducted (early raining/late raining and early dry/late dry), the measurement will be related with the closest CD4+ T-cell count. The most widely recommended socio-economic variables that will be used as health determinants for both diseases in this study are; education/educational level, residence, level of income, occupational status, and occupation. HIV and malaria overlap significantly in the SSA, coupled with the global reduction in malaria incidence (WHO, 2015). It is fundamental to continually initiate and

update data on the burden of malaria among PLWHA to prevent new cases of the disease and guide clinical practice in sub-Saharan Africa, especially in Nigeria (WHO, 2015). The majority of the published articles pay little or no attention to the impact of malaria on HIV, rather on the public health effect of HIV on malaria (Kwenti, 2018). This research study aims to provide additional epidemiological data of malaria among HIV seropositive individuals over five years to establish the trend in prevalence while also putting the seasonal variation into consideration. The study will also determine the prevalence of malaria among HIV positive patients and develop a predictive model. Of recent, Zheng et al., (2017), reported that malaria in HIV among children and adults pose a great risk to the health of the general public (Zheng et al., 2017). It was further advocated that; adequate control strategy is required to improve the life expectancy and quality of life of HIV-malaria co-infected individuals (Zheng et al., 2017).

Furthermore, the retrospective, descriptive cross-sectional design proposed for this study will give room for measurements of the outcome, which makes it easier to induce a causal preference from the case files. Control efforts for notable infectious diseases like malaria may have a positive impact when the gaps between urban and rural regions initiated by the socio-economic variables determined were minimized (Owusu, Cremers, Brown, Mens, & Grobusch, 2018). There appear to be gaps in the available literature regarding the management of HIV-malaria co-infection interaction in the SSA, including Nigeria (Focà et al., 2012). There is also no joint control strategy nor public health policy to effectively manage the impact of co-infection interaction coupled with a need for proper integration of control and prevention efforts (Focà et al., 2012). Data generated from the study will be an essential component in the assessment of the effectiveness of both malaria and HIV control and elimination interventions and encourage synergized efforts against HIV-malaria co-infection interaction. Findings from this study will also yield information in updating policy and guidelines on HIV-malaria co-infection prevention and control strategies. Publications from the study will contribute to the knowledge of the scientific community, including the public health policymakers. This study will, therefore, determine the socio-economic determinants of HIV-malaria co-infection and seasonal co-infection rate with associated health outcomes in a typical peri-urban setting in Nigeria. Findings from this study will be used to develop a replicable co-infection prevention and control strategy and develop an HIV-malaria coinfection intervention model for Nigeria. This will help policymakers to develop programs to reduce the public health impact of HIV-malaria co-infection.

2.1 Key Terms

CD4+ T - cell Count: A test that measures the number of CD4 T lymphocytes (CD4+ T - cells) in a cubic millimeter of blood. A normal count ranges between 500 – 1500 cells per cubic millimeter of blood.

Co-Infection: A simultaneous infection of a single host by more than one pathogenic agent.

Health Outcome: Health outcome is an organize assessment used in the modification of the health status of patients, to enhance the quality care, health of the general public, and reduce the cost of healthcare services.

Malaria: A life-threatening preventable and communicable disease caused by *Plasmodium spp*. Transmitted to humans bitten by infected female *Anopheles* mosquitoes.

Malaria episode: A reported malaria case clinically diagnosed to be positive and treated.

Prevalence: The number of cases of a disease or condition that are present in a population at a given time.

Socio-economic factors

Socio-economic factors are an important determinant of quality of life and health outcomes.

Socio-economic status

Socio-economic status is an important health indicator with many components, and on which other health determinants depend.

3. Research Aim and Objectives

The research aim is to provide epidemiological data of malaria among HIV positive individuals and determine the prevalence of HIV-malaria co-infection. The study will also determine the social and economic determinants of HIV-malaria co-infection that will result in a usable and replicable HIV-malaria co-infection intervention model for the NCZ, Nigeria.

The specific objectives of the study are to:

1) Develop and publish a study protocol and a literature review.
2) Determine the prevalence of malaria among HIV positive patients in NCZ Nigeria.

3) Determine the socio-economic determinants of HIV-malaria co-infection among adults in the North Central Zone, Nigeria.

4) Time analysis of HIV-malaria co-infection and associated health outcomes from January 2013 to December 2017 among Nigerian adults.

5) Explore the available HIV-malaria co-infection interaction management practice and procedure at semi-urban secondary health care centers in the northcentral zone, Nigeria.

6) Develop a usable and replicable HIV-malaria co-infection intervention model for Nigeria.

4. Research Question

1) What is the prevalence of HIV-malaria co-infection in the North Central Zone, Nigeria?

2) Is there any relationship between the socio-economic determinants and HIV-malaria co-infection among adults in the north-central zone?

3) Are there any determinant factors highly important in the effective management of HIV- malaria co-infection interaction at the secondary level of care?

4) Is there any association between the health outcome and HIV-malaria co-infection among Nigerian adults?

5) Is there any available HIV-malaria co-infection management practice and procedure at the secondary health care level?

5. The Research Paradigm

A research paradigm is "the set of common beliefs and agreements on how problems should be understood and addressed" (Kuhn, 1962). Paradigm is research components which include; ontology and epistemology. Both ontology and epistemology provide a comprehensive approach to the perspective in which we view knowledge and see our self as an individual corresponding to the knowledge and the approach with which it was achieved. The quality, reproducibility, as well as the theoretical postulate of a research study, will increase the creativity of the researcher. Therefore, this study will employ an epistemology/positivism approach. A hypothesis made about the type of knowledge can simply be referred to as epistemology (Richards, 2003). Epistemology is a way of looking at and making sense of the world, which involves having a perception of what knowledge is all about. According to Cohen et al., (2007), epistemology is making a knowledge-based assumption and how it could be conveyed to others (Cohen, Manion, & Morrison, 2007).

5.1 Positivism and Objectivism

As an epistemological position, positivism depends on the fairness of the researcher is looking for the truth without interference. Findings from such a study should not be impacted by the view of the researcher to conduct an objective and value-free inquiry (Snape & Spencer, 2003). Similarly, in positivism and objectivism paradigm, the validity of the research study is always the same and unbiased if conducted in the right manner, which includes; careful observation and not by assumption (Ormston, Spencer, Barnard, & Snape, 2014).

5.2 Co-Infection Intervention Model

A model is the description of an approach comprises of an idea, to help an individual to comprehend the content displayed by the model (Tatomir et al., 2018). Similarly, a model is a set of communication or pronouncement about a framework that is being studied, which must be more than an ordinary graphic representation. An adequate interpretation of the use of such a model depends on what is being modeled, as well as models acquired from it (Seidewitz, 2003). The application of a successful HIV intervention in combination with the malaria programme will encourage sustainable HIV-malaria co-infection prevention and reduce the public health impact of both infectious diseases (Seidewitz, 2003). This HIV-malaria co-infection model, when developed, is of public health importance and paramount in the reduction of HIV-malaria co-infection transmission and rapid progression to AIDS coupled with multiple episodes of severe malaria cases in the absence of effective HIV and malaria vaccine. "From the literature review, there is no intervention or preventive model available to manage the public health impact" (Abu-Raddad et al., 2006). Similarly, it is also beneficial to relate malaria health care services with that of HIV infection (Abu-Raddad et al., 2006). The model will address the factors contributing to increased HIV-malaria co-infection, as shown in the conceptual framework (Figure 1).
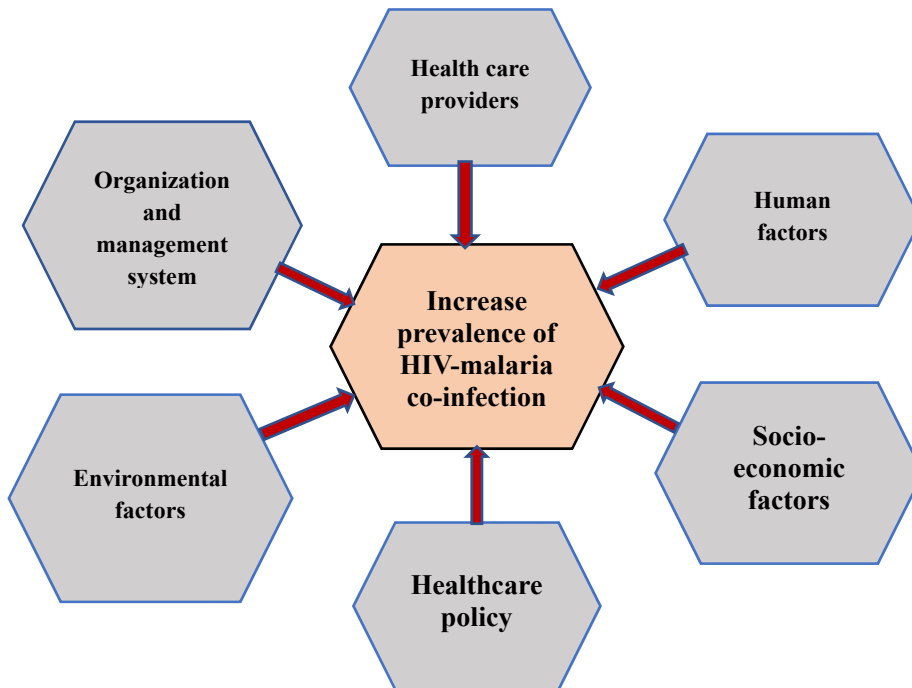
Figure 1. Conceptual framework: The category of factors contributing to increased HIV/malaria co-infection

6. Research Settings

The federal republic of Nigeria covers an approximately 923, 768 km2 (356,669 sq. mi) (CIA, 2017), lies between latitudes 40 and 140N, and longitudes 20 and 150E, bordering Chad and Cameroon in the east, Niger in the north and Benin in the west. Nigeria is made up of 36 states and the Federal Capital Territory (FCT) situated in Abuja, which is further divided into 774 local government areas and six geo-political zones. The NCZ comprises six states (Kwara, Kogi, Plateau, Nasarawa, Niger, Benue state) and the FCT, Abuja (Figure 2).
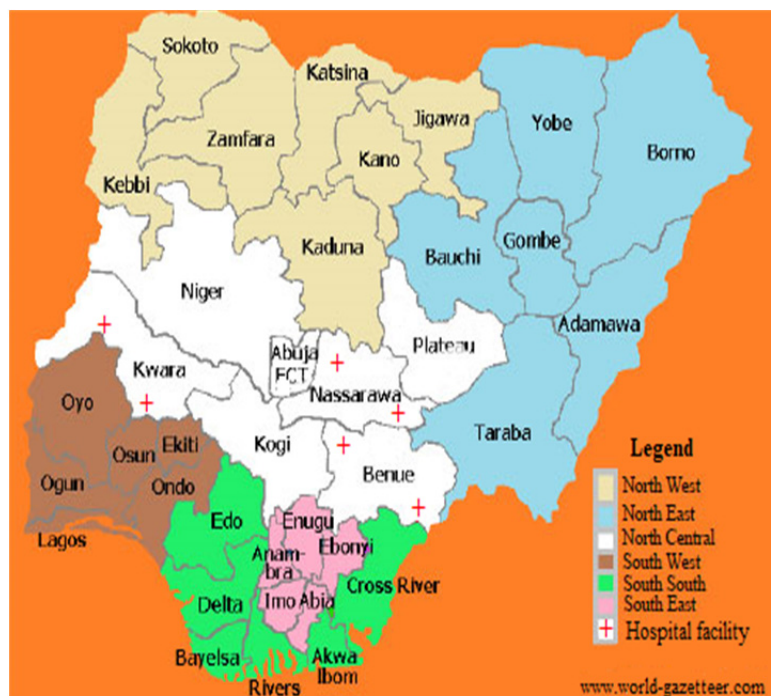

Figure 2. Showing the map of Nigeria, the North Central Zone and the hospital facilities where the study will be conducted

7. Study State

The study will be conducted in three states; Kwara, Benue and Nasarawa state, all in the NCZ Nigeria.

7.1 Kwara State

On the 27th of May 1967, Kwara state was inaugurated as part of the twelve states of the federation by then the federal military government. Kwara state is situated in the western part of Nigeria, and Ilorin, the state capital, is 454.6 kilometers from Abuja, the federal capital territory. The prominent ethnic group in the state is Yoruba. Kwara state is made up of a total population of 2,365,353 (Federal Republic of Nigeria, 2007).

7.2 Kwara State Study Sites

The study will be conducted in two sites in Kwara states, one each from two randomly selected senatorial districts. The study sites are;

❖ **Specialist hospital, Omu-Aran:** The hospital facility is situated in **Omu-Aran,** Kwara state. The hospital is about 80.9 kilometers from Ilorin, the Kwara state capital. The hospital facility is a 50-bed compliment and provides HIV services on Mondays and Wednesdays.

❖ **Specialist hospital Offa:** Offa specialist hospital is in Offa, Offa local government area of Kwara state. The hospital facility provides quality health care services for Offa town and the environs and as a referral center for several primary health care facilities. The hospital facility provides HIV services at the HIV clinic two days of the week, Tuesdays, and Wednesdays.

7.3 Benue State

Benue State was created on the 3rd of February 1976 with Makurdi as the state capital. The state is situated in the NCZ Nigeria with an estimated population of 4,253,641, according to the 2006 population census, with the landmass of 34,059 Km (Federal Republic of Nigeria, 2007). Makurdi, the state capital, was established in the 1920s and became the headquarters of the then Benue province. The Tiv are the dominant ethnic group.

7.4 Benue State Study Sites

Two study sites were selected for the research study in Benue state; the study sites include; Gboko general hospital and Katsina-Ala general hospital

❖ **Gboko general hospital:** The general hospital is located at Gboko, Gboko local government area of Benue state in Benue North-West geopolitical zone (Zone B). The general hospital is a 46-bed facility situated 86.0 km from Makurdi, the State capital, and provides referral services for primary health care facilities.

❖ **Katsina-Ala General Hospital:** The hospital is in Katsina-Ala, Katsina-Ala local government of the state 130.8 Km from Makurdi Benue state capital, representing (Zone A) the Benue North-East. The secondary hospital facility selected for the study is a 40-Bed capacity with an HIV clinic where HIV services are provided.

7.5 Nasarawa State

Nasarawa state was inaugurated by the then military government on the 1st of October 1996 with Lafia, the state capital. The state is made up of 13 local government areas further divided into three senatorial districts (Nasarawa west, Nasarawa North and Nasarawa south) with an estimated population of 1,869, 377, according to the 2006 population census. Lafia, the state capital, is 192.3 Km from Abuja, the federal capital territory (Federal Republic of Nigeria, 2007). The major source of gross domestic product is from agricultural products and mineral resources

7.6 Nasarawa State Study Site

Two study sites were selected in Nasarawa state, which includes; Nasarawa-Eggon general hospital and Obi general hospital.

❖ **General hospital Nasarawa-Eggon:** The hospital facility is located at Eggon in Nasarawa-Eggon local government area in Nasarawa North senatorial district. The hospital facility is 34.7 km from Lafia, the state capital, and was established by the state government and serves as a referral hospital for several primary health care facilities.

❖ **Obi general hospital:** General hospital Obi is situated in Obi, Obi local government area of Nasarawa state in Nasarawa South senatorial district. Obi general hospital is 39.4 Km from Lafia, the state capital. The 34- bed hospital facility and take a referral from comprehensive and primary health care in the local government and beyond.

7.7 Inclusion Criteria

a)   Health care providers and managers currently employed in the HIV/AIDs clinic (unit) at the selected peri-urban secondary hospitals with more than six months of working experience were included in the study.

b)   Case files of HIV/AIDs positive patients, male and female adult's pregnant HIV positive patients, 18 years and above. Who had not missed their schedule visit for more than three times was included in the study and were reviewed retrospectively?

7.8 Exclusion Criteria

Health care providers who were not working at the HIV/AIDs clinic (unit) at the selected secondary hospitals and those with less than six-months' working experience were excluded. Case file of HIV positive patients who did not give consent to participate, and those that were less than 18 years were not selected for review.

Primary and tertiary health care centers and secondary health care facilities in urban areas that provide HIV services were excluded from the study. Case file of HIV positive patients who had missed clinic appointments for more than three times was also excluded from the research study.

8. Methods

8.1 Quantitative Sampling

The hospital checklist forms will be administered to all the staff's doctors, nurses at the HIV clinic. A multi-stage sampling technique will be used in selecting the case files of the subjects for study.

Stage I: Purposive sampling will be used to select three out of the six states in the North-Central Zone based on the HIV prevalence. Two states where the HIV prevalence is higher than the national HIV seroprevalence would be selected in preference to others, while one state where the HIV prevalence is lower than the national HIV seroprevalence rate will also be selected for comparison.

Stage II: Random sampling technique by balloting will be used to select two senatorial districts from each selected state.

Stage III: Purposive sampling will then be used to select one semi-urban secondary health facility, each from the two senatorial districts where the study will be carried out.

Stage IV: Proportionate sampling would be used to determine the number of case files to be reviewed in each selected hospital facility.

Stage V: Sampling interval will be calculated to ensure that an equal number of case files of HIV patients will be reviewed with the data collection tool at a regular interval.

8.2 Qualitative Sampling

Purposive sampling technique will be used to select the head of the HIV clinic for the interview, six in-depth interviews (one at each selected secondary hospital) will be conducted at all the selected secondary hospitals. Health managers or the head of the HIV clinics with more than one year of working experience in the selected facility will be selected for the in-depth interview.

9. Patient and Public Involvement

Before the development of the research tool/questions, stakeholder's engagement meeting will be conducted among the individuals that will be impacted by the project. To ensure that issues, interests, and concerns of the participants are taken into consideration. It also enables the Principal Investigator (PI) to develop questions that reflect the priorities, experience, and preferences of all the stakeholders that will be affected by the project, using the stakeholder's consultation questionnaire. This will help the principal investigator in asking good questions and help to establish stronger credibility with stakeholders and right holders.

Patients and participants that will be selected for the research study will be randomly selected at all study locations. However, neither the patients nor the participants will, in any way, be involved in the recruitment of the participants, as well as the conduct of the research study.

After the research study, the outcome will be disseminated to all the stakeholder's involved (the state ministry of health, the hospital management board, and the hospital facilities), while the PI and the health care providers will sensitize patients on the study outcome as stipulated in the stakeholder's engagement forum.

10. Measures Taken to Ensure a Scientifically Valid Study

10.1 Pre-Test

A pre-test of the research tools (review tool, the hospital checklist form, and interviewers guide) will be conducted to improve the quality of the data collection instrument, process, and methodology. Ten percent of the data collection instruments will be pre-tested for validity before the research study at a secondary health care facility in general hospital Ogbomoso Oyo State Nigeria. After pre-testing, data collected will be interpreted and analyzed. Pretesting the research tools will aid in establishing reliability and validity.

10.2 Quality Control

Ten percent of the completed purpose-made data collection tools, and ten percent of the checklist form completed at each of the hospitals will be validated with the patient's case files that will be completed. Data collected will be verified with medical attendants, laboratory records for confirmed malaria cases resulting in admissions, discharges, HIV and malaria diagnoses, and testing and death records. Ten percent of completed forms will also be verified on-site before leaving the hospital facility.

All laboratories used for malaria microscopy are public health institutions and are governed by standards of care, and quality control processes as prescribed for public laboratory services in the federal ministry of health, Nigeria. At each test site, the PI had acquainted himself with the Rapid Diagnostic Test (RDT) in use, including the information on due process and interpretation of results. At least five RDTs were witnessed per site to ensure validity. This was done by the principal investigator (PI).

11. Data Collection

A pretested and modified data collection tool adapted from Adu-Gyasi et al., (Adu-Gyasi D et al., 2013), will be used as a research instrument for retrospective chart review of case files. An estimated one thousand six hundred and fifty-two (1,652) case files of HIV positive patients will be randomly selected and reviewed. Data to be collected from the case files include; date and age at which the patient registered in the hospital facility, gender, socio-demographic, and socio-economic profile. Other information that will be collected is; confirmed diagnosis of malaria, evidence of treatment success, health outcomes, and information on CD4 + T - cell count measurement, among others. Notable health outcomes that would be considered in this study is; hospitalization, referral, deaths, renal disease, meningitis, anaemia, among others. Another research tool that will be utilized during the research study is the hospital checklist form. Sixty-four (64) hospital checklist forms will be administered to health providers across the six-study locations and one (1) participant interview session with the head of the HIV clinic for qualitative data collection.

11.1 Data Availability Statement

Since this is a research protocol, data were not generated nor analyzed during the study. All data relevant to the study are uploaded as supplementary information.

Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

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