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Prevalence of hypertension and its association to HIV related factors among HIV patients on antiretroviral medications in Bagamoyo district, Tanzania

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PREVALENCE OF HYPERTENSION AND ITS ASSOCIATION TO HIV RELATED FACTORS AMONG HIV PATIENTS ON ANTIRETROVIRAL MEDICATIONS IN BAGAMOYO DISTRICT, TANZANIA

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A Dissertation Submitted in Partial Fulfilment of the Requirements for the Degree in Master of Science in Public Health Research at Nelson Mandela African Institution of Science and Technology

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ABSTRACT

Effective use of antiretroviral therapy (ART), has greatly upgraded the quality of life and survival of individuals suffering from HIV/AIDS. However, the incidence rate of hypertension is reported growing up. The overall aim was to find out the prevalence of hypertension and its association with HIV related factors in HIV patients on ART, in Bagamoyo district Tanzania. The design was a cross-sectional study of HIV patients on ART visiting care and treatment clinics. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or being on medications for hypertension. Logistic regression was applied during the analysis. The study investigated 328 HIV patients on ART, 64.6% were female, and 92.68% on non-protease inhibitors medication and 14% had a prior history of TB in the past 5 years. The overall prevalence of hypertension was 29.3% and it was significantly and positively associated with increasing age (years): 40-59, 3.40 (1.80-6.41) 0.001, ≥ 60, 9.25 (3.96-21.60) 0.001, obesity 3.63 (1.60-8.26) 0.002, non-protease inhibitors 4.31 (1.16-16.03) 0.029 and tenofovir 4.27 (1.15-15.96) 0.031. Both of the duration since HIV diagnosed, recent CD4+cell count and history of TB in the past 5 years were not statistically significant associated with increased odds of having hypertension. In conclusion the prevalence of hypertension in HIV patients on ART was 29.3% and it was significantly and positively associated with increasing age, obesity, and non-protease inhibitors. Regular monitoring of blood pressure, anthropometrics, and ART drug toxicity are crucial among HIV patients.

Keywords: ART, CTC, HIV, HIV related factors, Hypertension, Non-protease inhibitors

DECLARATION

I, Getera Isack Nyangi declare that this work has been prepared entirely by myself and that it has not been submitted, in whole or in part, in any previous application for degree. Besides where explained otherwise by citation or acknowledgments, the document submitted is completely my own.

Getera Isack Nyangi

23/3/2020

Date

The above declaration is confirmed

Dr. Ally Olotu

Supervisor

23/3/2020

Date

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CERTIFICATION

I, hereby approve that the dissertation entitled "Prevalence of Hypertension and its association to HIV related factors in HIV patients on ART in Bagamoyo district, Tanzania" submitted by Getera Isack Nyangi to Nelson Mandela African Institution of Science and Technology, Tanzania in partial fulfillment of the requirements for the award of Master of Science in Public Health Research is a valid composition and has been prepared under my guidance.

Dr. Ally Olotu

Supervisor

23/3/2020

Date

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LIST OF ABBREVIATIONS

AIDS	-	Acquired Immunodeficiency Syndrome
ART	-	Antiretroviral Therapy
ARV	-	Antiretroviral
BMI	-	Body Mass Index
cART	-	Combination Antiretroviral Therapy
CD4	-	Cluster of Differentiation
CTC	-	Care and Treatment Clinic
HIV	-	Human Immunodeficiency Virus
MOHCDGEC	-	Ministry of Health Community Development Gender Elderly and Children
MSc-PHR	-	Master of Science Public Health Research
PI	-	Protease Inhibitor
PLHIV	-	People Living with HIV
RAAS	-	Renin-Angiotensin-Aldosterone System
TB	-	Tuberculosis
THIS	-	Tanzania HIV Impact Survey
UNAIDS	-	United Nations on HIV/AIDS
WHO	-	World Health Organization

CHAPTER ONE

INTRODUCTION

1.1 Background of the problem

Effective use of antiretroviral therapy (ART), has greatly upgraded the quality of life and survival of individuals suffering from HIV/AIDS (Chastain, Henderson & Stover, 2015). However, the incidence rate and mortality from cardiovascular risk factors including hypertension are reported to growing up (Xu, Chen & Wang, 2017). For example, in a recent meta-analysis study prevalence of hypertension was 34.7% among HIV patients on ART compared to 12.7% in ART naïve individuals (Xu *et al*., 2017). In Tanzania, the prevalence of hypertension among HIV patients using antiretroviral therapy has been reported to be 28.3% (Peck *et al*., 2014). This was higher than the prevalence of 5.3% and 16.3% in HIV ART-naïve and HIV negative individuals respectively (Peck *et al*., 2014).

Hypertension (the greatest risk factor of mortality) is a growing health challenge in individuals living with HIV/AIDs (Nduka, Stranges, Sarki, Kimani & Uthman, 2016; Gakidou *et al*., 2017). However, the contributions of HIV related factors to hypertension have not been extensively investigated in Tanzania. Besides the traditional risk factors, hypertension in HIV patients can be attributed to, inflammations, ART toxicity, and immune response (Madhur *et al*., 2016). For instance, tenofovir an ART belongs to non-protease inhibitors class has been reported to contribute to hypertension due to its ability to cause renal failure and therefore secondary hypertension (Ojeh *et al*., 2018). Also, higher CD+ cell count (following immune reconstitution after initiation of ART) has been reported to associate with elevated blood pressure in adults HIV infected individuals (Peck *et al*., 2014). However, a separate study has indicated a lack of association between CD4+cell count and hypertension (Medina-Torne *et al*., 2012).

Traditional risks include risks such as increasing age, sex, and increasing body mass index (Riaz *et al*., 2016). However, it's unknown if traditional risk factors may interact with HIV related factors to increase the risk of hypertension. Therefore, the cross-sectional study was undertaken to investigate the prevalence of hypertension and its association with HIV related factors in HIV patients on ART while adjusting for other covariates in Bagamoyo district, eastern Tanzania.

1.2 Statement of the problem

Hypertension is the relevant public health problem including in the individuals suffering from HIV/AIDS (Medina-Torne *et al.,* 2012). Effective use of antiretroviral therapy (ART), has greatly upgraded the quality of life and survival of individuals living with HIV/AIDS (Chastain *et al*., 2015). However, the incidence rates from cardiovascular risk factors including hypertension are reported to be growing up among individuals living with HIV/AIDS (Nsagha *et al*., 2015).

Besides the traditional risk factors, hypertension in HIV patients can be linked to, inflammations and immune response (Madhur *et al*., 2016). However, it's unclear whether traditional risk factors may interact with additional factors in HIV patients to increase the risk of hypertension. Therefore, there is a need to explore more on the prevalence of hypertension and the way it can be influenced by HIV related factors.

1.3 Rationale of the study

The hypertension is a unique challenge to the health system including to the treating physician. Although there are previous studies that have been undertaken to explore hypertension and associated factors in HIV patients, however, the true cause of hypertension in HIV patients remains unclear. Furthermore, a small number of studies have been undertaken in Tanzania to find out the prevalence of hypertension and associated factors. Therefore data from this study will support the improvement of quality health care among HIV/AIDS patients, particularly in the screening, prevention, management and control of hypertension. Furthermore, it will inform decision-makers and key stakeholders for the better allocation of resources concerning hypertension in HIV/AIDS patients.

1.4 Objectives

1.4.1 General objective

The broad objective of the study was to determine the prevalence of hypertension and its association with selected HIV related factors in HIV infected adults on ART in the Bagamoyo district council.

1.4.2 Specific objectives

(i) To achieve the above broad objective, the study has the list of specific objectives mention below:

(ii) To determine the prevalence of hypertension in HIV infected adults on ART attended the selected care and Treatment Clinics (CTCs) of the Bagamoyo district council.

(iii) To assess selected HIV related factors contributing to hypertension in HIV infected adults on ART attended the selected care and Treatment Clinics (CTCs) of the Bagamoyo district council.

1.5 Research questions

(i) Is the prevalence of hypertension among HIV patients higher among females than in the male?

(ii) Is there an association between HIV related factors and hypertension among HIV patients who are on ART?

1.6 Research hypothesis

(i) Prevalence of hypertension among HIV patients is higher among females than in the male.

(ii) There is an association between HIV related factors and hypertension among HIV patients who are on ART.

1.7 Significance of the study

The study has provided data that can inform the integrated approaches of HIV and hypertension as well as other issues that might affect the health and wellbeing of HIV infected persons at care and treatment clinics (CTCs). The findings of the study are going to inform the formulation of strategies and interventions for efficient prevention and management of hypertension among individuals suffering from.

Also, the study contributes to the knowledge of the magnitude of hypertension and its association with HIV related factors in Bagamoyo district, eastern Tanzania and outlines a need for future studies to explore more on the causes of hypertension in the context of HIV/AIDS.

1.8 Delineanation of the study

Hypertension in HIV/AIDS context is a very relevant public health problem. Risk factors for hypertension among HIV patients can be either traditional or non-traditional risks. Traditional risks are established risks include age, obesity, and smoking. However, it's unknown if traditional risk factors may interact with HIV related factors to increase the risk of hypertension.

There is previous studies which have investigated the prevalence of hypertension and associated factors. The scope of this dissertation is to provide the information regarding the prevalence of hypertension and its association to HIV related factors in Bagamoyo districts, a cross-sectional study without a control group.

CHAPTER TWO

LITERATURE REVIEW

2.1 General information about hypertension and HIV

Hypertension is the leading cause of premature deaths and disability worldwide (Forouzanfar *et al*., 2015). In the years 2010, it was estimated that about 1.3 billion adults were hypertensive worldwide (Bloch, 2016). In Tanzania, the magnitude of hypertension in the community has been approximated to range between 16% and 22% (Kavishe *et al*., 2015). Hypertension has also been reported as a leading cause of deaths related to stroke and heart failure among hospitalized patients in Tanzania (Peck *et al*., 2013).

About HIV/AIDS, in the year 2018, it was reported that 37.9 million people were living with HIV/AIDS and 20.9 million among them were on ART, globally (UNAIDS, 2019). According to the Unaids, in the year 2017, 1.5 million people were living with HIV/AIDS and 65 000 had new HIV infections in Tanzania (UNAIDS, 2018).

2.2 Background information about hypertension in HIV patients

Effective use of antiretroviral therapy (ART), has greatly upgraded the quality of life and survival of individuals suffering from HIV/AIDS (Chastain *et al*., 2015). However, the incidence, prevalence rate and mortality from cardiovascular risk factors including hypertension are reported to be growing up (Furrer *et al*., 2017; Nduka *et al*., 2016). For instance, in a meta-analysis of HIV patients, the prevalence of hypertension was 34.7% in the HIV infected individuals on ART in comparison to 12.7% in those who were not in the use of ART (Xu *et al.*, 2017). In Tanzania, the hypertension prevalence rate of 28.3% has been reported in HIV patients on ART and this was higher compared to the prevalence of 5.3% in HIV ART-naïve and 16.3% in those without HIV infection (Peck *et al*., 2014).

Besides the traditional risk factors, hypertension in HIV patients can be linked to, inflammations and immune reactions (Madhur *et al*., 2016). Traditional risks include risks such as increasing age, sex and increasing body mass index (Riaz *et al*., 2016). However, it's unclear whether traditional risk factors may interact with additional factors in HIV patients to increase the risk of hypertension. Therefore, it's important to investigate if selected HIV-related factors influence the risk of hypertension in individuals living with HIV/AIDS.

2.3 Pathophysiology of hypertension in HIV patients

The mechanism of hypertension in HIV/AIDS patients is complex (Calisman, 2017). The key steps in the mechanism of hypertension in HIV patients have been summarized in Fig.1.

Factors that may contribute to the pathogenesis of hypertension in HIV patients include aging, obesity, dyslipidemia, insulin resistance, ART toxicity, viral chronic inflammation, and immune activation (Calisman, 2017).

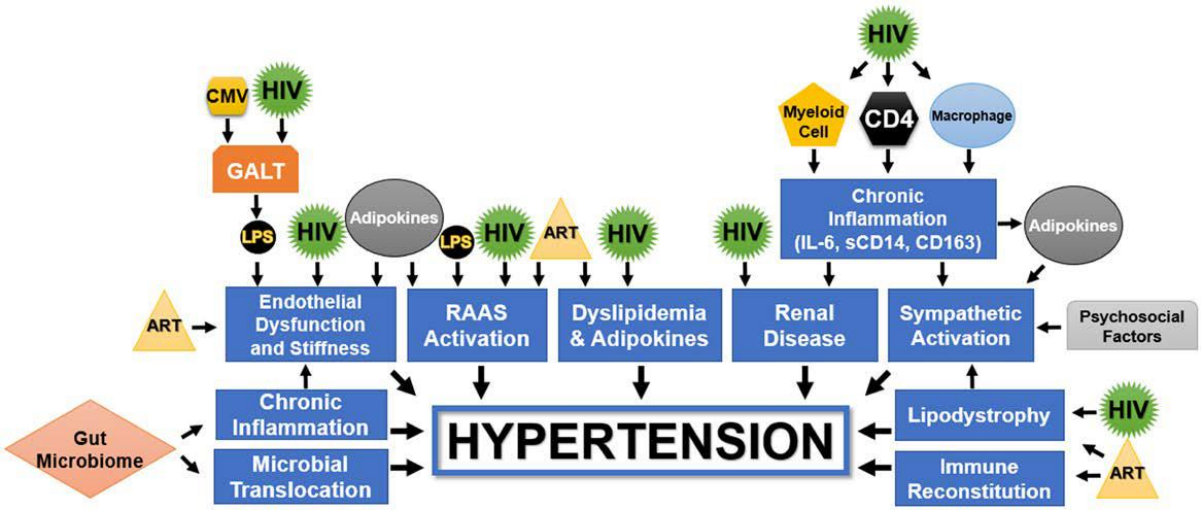

Figure 1: Diagram of the mechanism of hypertension in HIV positive patients
(Fahme, Bloomfield & Peck 2016)

Key:

ART = antiretroviral therapy; CD163 = cluster of differentiation 163 protein, CD4 = cluster of differentiation 4, CMV = *cytomegalovirus*, GALT = gut-associated lymphoid tissue, IL-6 = interleukin-6, LPS = lipopolysaccharide, RAAS = renin-angiotensin-aldosterone system and sCD14 = soluble cluster of differentiation 14 protein.

2.4 Hypertension and antiretroviral therapy in HIV patients

Use of antiretroviral therapy has been attributed to the pathophysiology of hypertension perhaps through drug toxicity, lipodystrophy, inflammation and immune response (Villa *et al*., 2018; Madhur *et al*., 2016). For instance, tenofovir a non-protease inhibitor can cause hypertension due to its ability to cause renal failure, leading to secondary hypertension (Ojeh*et al*., 2018).

Protease inhibitors such as atazanavir and lopinavir can contribute to hypertension through dyslipidemia, lipodystrophy, and atherosclerosis (Zhou, Pandak, Lyall, Natarajan & Hylemon, 2005). An observational study indicated that both lipoatrophy and lipohypertrophy significantly associated with elevation of blood pressure in HIV patients (Crane, 2010).

Despite that, there is a variation of results from past studies that have analyzed the association between ART exposure and hypertension in HIV patients. For example, one cross-sectional study indicated a lack of an association between the tenofovir-based regime and hypertension (Medina-torne *et al*., 2012), contrary to a prospective cohort that found a significant and positive association between tenofovir-based regime and hypertension (Crane, Rompaey & Kitahata, 2006). Regarding ART classes, a cross-sectional study from Uganda conducted in 2017, found that non-protease inhibitors users had a double risk of hypertension compared to the individual who was not using non-protease inhibitors (Munderi, 2017).

Protease inhibitors were reported to be associated with hypertension in HIV patients (Fahme, Bloomfield & Peck, 2016). The mechanism by which PIs may contribute to hypertension in HIV patients includes lipodystrophy, dyslipidemia, and atherosclerosis (Dressman *et al*., 2003). Furthermore, Protease inhibitors have been implicated to cause hypertension through the renin-angiotensin-aldosterone system (RAAS) activation (Boccara *et al*., 2010). The possible mechanism is that PIs may activate the adipokine-mediated route which may cause the operation of the adipose RAAS (Boccara *et al*., 2010). The activation of RAAS in turn can cause salt/ water retention and a rise in blood pressure.

Despite that, there are inconsistencies in the results of the association between PIs and hypertension from previous studies. For instance, a cohort study conducted in the USA reported that prior exposure to lopinavir/ritonavir had an association with elevated blood pressure (Crane, Rompaey & Kitahata, 2006). However, in a cross-sectional study by Medina-Torne *et al*. (2012), lopinavir/ritonavir was not significantly associated with elevated blood pressure (Medina-Torne *et al*., 2012).

2.5 Hypertension and the immune system in HIV patients

Hypertension has been also reported to associate with the immune system in HIV patients (Peck *et al*., 2014). Though the precise mechanism is not well understood, the proposed mechanism may involve persisting immune response, including an elevated level of CD4+ T cell and CD+8 T cell (Brites-alves *et al*., 2018; Calisman, 2017). For example, following

initiation of ART, there is an initial drop of the CD4+T cell followed by a rapid recovery of the immune system, a process known as immune reconstitution inflammatory syndrome (IRIS). According to previous studies, lower nadir CD4+ cell counts (the lowest CD4 count of an individual ever recorded) have been linked to a higher incidence of hypertension among HIV patients who are on ART (Peck *et al*., 2014; Manner *et al*., 2013).

Also, the immune mechanism has been involved in the mechanism of hypertension in HIV patients through microbial translocation. HIV can infect CD4+T the gut-associated lymphoid tissues weakening and destroying the integrity of the natural immune system in the gut mucosa (Blodget *et al*., 2012; Chun *et al*., 2008). This facilitates the pathogens to enter into systemic blood circulation causing an elevation of lipopolysaccharides a marker of microbial translocation (Kelesidis *et al*., 2012; Jiang *et al*., 2009). A high level of lipopolysaccharides may cause hypertension through several mechanisms. According to previous studies conducted in mice, lipopolysaccharides has been shown to stimulate the production of Prostaglandin E2, angiotension11, RAAS activation, and trigger of the sympathetic nervous system which can end up to hypertension (Lund, Brooks, Faraci & Heistad, 2019).

Association between CD4+T cell count and hypertension in HIV patients has been investigated in HIV patients (Peck *et al*., 2014; Medina-torne *et al*., 2012). However, there is a variation in the results from previous studies regarding the association between CD4+T cell count and hypertension. For example, an observational study conducted in America reported a lack of an association between hypertension and recent CD4+cell count (Medina-Torne *et al*., 2012). While, an observational study from north-western Tanzania has indicated a positive association between Hypertension and higher current CD4+ cell count (Peck *et al*., 2014). Generally, there is inconsistency in results from previous studies regarding the association between CD4+cell count and Hypertension.

2.6 Hypertension and tuberculosis in HIV patients

There has been some evidence that TB may increase cardiovascular risk including hypertension risk through inflammatory and autoimmune processes (Calisman, 2017; Borchsenius, Rudolf & Wejse, 2017). It has been postulated that immune activation and cytokine production during inflammatory reactions tend to speed up the atherosclerosis process which can cause hypertension (Rajendran *et al*., 2013). Furthermore, TB has been associated with hypertension, because it can lead to the diabetes mellitus (Ogbera *et al*., 2015), and diabetes mellitus itself is the potential predictor of the overall cardiovascular risk

including hypertension (Petrie *et al*., 2018). Additionally, hypertension may occur secondarily from renal failure after TB causing extensive destruction of kidney parenchyma tissues (Shen *et al*., 2015).

Even though TB is the most prevalent and severe co-infection in HIV patients (Calisman, 2017; Fatou *et al*., 2017), there has been relatively little research into how TB infection influences hypertension in HIV patients in sub-Sahara Africa. In Tanzania, Njelekela *et al.* (2016), reported that no significant association between current TB/HIV co-infection and hypertension in adults HIV naïve patients (Njelekela *et al.*, 2016). Although the same study by Njelekela *et al*. (2016), reported that a prior history of TB tends to decreases the risk of hypertension in adults HIV naïve patients (Njelekela *et al.*, 2016).

From the literature, much of what has been pinpointed regarding the influences of TB on hypertension comes from studies that were conducted in the general population in developed countries. A little has been done to investigate the association between TB and hypertension among individuals living with HIV/AIDS in Sub-Saharan Africa including Tanzania.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study design and location

The design of the study was cross-sectional involving HIV patients who were on ART conducted between March and May 2019, in Bagamoyo district, eastern Tanzania. The district is located in the coastal region which has an HIV prevalence rate of 6.4% (Ministry of Health, 2016). Data were collected from 2 public clinics (Bagamoyo district hospital and Kerege health center) which were purposively selected based on their relatively large size and presence of established patient's record database (computer-based record system). The two clinics provide care and treatments based on the national HIV/AIDS guidelines of Tanzania (Ministry of Health, 2017).

3.2 Inclusion and exclusion criteria

The inclusion criteria were being HIV positive, aged above 18, on ART, who gave consent for participation. Women who reported to be pregnant and those on contraceptive pills were excluded.

3.3 Sample size estimates

To calculate the sample size the formula below was used:

$$N=P\ (1-P)\ (Z/E)$$

Whereby margin of error (E) = 5%, P=Prevalence

N=estimated required sample size, Z= 95% confidence interval = 1.96, attrition of 10% for missing data. Pravelence (P) 26.2% from a study by Kagaruki *et al*. 2014

0.262(1-0.262) (1.96/0.05)2, margin of error (E) = 5%, P=Prevalence

Sample size = 328

3.4 Blood pressure measurement and definition

Blood pressure was measured as per required standards in the right arm, utilizing a mercury sphygmomanometer of appropriate size, with individual participants in sitting in a relaxed position and upright position (Joint National Committee, 2004). Two readings were taken 10 minutes apart and an average of two results was turned to account in the final analysis. Hypertension was defined as systolic blood pressure (SBP) of $\geq$ 140 mmHg, diastolic blood pressure (DBP) of $\geq$ 90 mmHg (Joint National Committee, 2004) or taking ant-hypertensive medications regardless of the blood pressure value measured on the day of data collection.

3.5 Anthropometric measurement

Bodyweight (precision of 0.1 kg) was weighed using the patients weighing machine (seca scale) with individual participants at minimal clothes and wearing no shoes. Body height was assessed using a stadiometer (precision of 0.1 cm) participant wearing no shoes. Body mass index (BMI) was computed utilizing the formula: weight in kilogram (kg) divided by the square of height in meters (Kg/m^2). BMI was classified and defined using the WHO protocol as follows; underweight < 18.5 kg/m^2, normal body weight 18.5—24.9 kg/m^2, overweight 25—29.9 kg/m^2, and obese $\geq$ 30 kg/m^2 (World Health Organization, 2004).

3.6 Sociodemographic, HIV related factors collection and definition

The structured questionnaire administered by trained health care workers was used to collect the sociodemographic, family history of hypertension, current history of TB and history of TB in the past 5 years.

In addition to the individual interview, the following information was extracted directly from patient record card or computerized patients' database system: duration since HIV diagnosed, recent CD4+cell count, the current class of ART, and individual cART.

Duration since HIV diagnosis was defined as the time in years at which HIV diagnosis was confirmed as it was documented in patient record cards. Recent CD4+cell count was defined as the CD4+T cell count measured in the past 6 months. Current TB was defined as currently being on anti-TB medication after sputum analysis or chest radiography. History of TB in the past 5 years was defined as being on anti-TB medication for at least 6 months within the last 5 years.

3.7 Exposure, outcome and confounding Variables

The primary outcome variable of interest was hypertension defined as blood pressure ≥ 140/90 mmHg, or being on medications for hypertension. Exposure variables of interest in the study were: duration since HIV diagnosis, recent CD4+cell count, the current class of ART, individual cART, current TB/HIV co-infection, and history of TB in the past 5 years. The potential confounders included during the analysis were: age, sex, obesity, and family history of hypertension.

3.8 Data management and analysis

Data was gathered by a means of a structured questionnaire and then entered into an Excel sheet. Before data was entered in the Excel sheet, a completed questionnaire was reviewed for completeness and clarity. Before data analysis, another review was done for errors, missing data, and inconsistencies. The analysis was done using STATA version 13. We included 328 participants in the final analysis and 33 participants had missing data regarding the recent CD4+cell count. In 33 participants with missed data on CD4+cell count, they had CD4+cell count either not taken at all or taken in a period of more than 6 months. A descriptive analysis (percentage) was used to summarize the data.

Logistic regression was executed to check for an association between HIV related factors and hypertension. In the multivariate analysis, we included factors from univariate analysis with p-value ≤ 0.005 include age, body mass index, and family history of hypertension. Sex and current class of ART were included as a forced variable during multivariate analysis. However, ART as the class was not adjusted together with the individual combination of ART during multivariate analysis because of co-linearity. In multivariate analysis variables were added by a forward selection technique with the variables of greater theoretical significance entered first.

3.9 Ethical approval

The protocol of the study was reviewed and certified by the research ethics committee of the Ifakara Health Institute, Bagamoyo district executive director office as well as the authority of the respective health facility. Written informed consent was attained from each of the participants ahead of data gathering.

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1 Results

4.1.1 Sociodemographic factors and clinical profile of the participants

A total of 328 study participants were included in the analysis. Out of 328 participants, 212 (64.6%) were females and 116 (35.4%) male (Table 1). In the descriptive analysis of the age in years, 132 (40.24%), 151 (46.06%) and 45 (13.72%) were individuals aged 18-39 years, 40-59 years, and ≥ 60 years, respectively (Fig. 2). Out of 328 participants, 213 (64.9%) were peasants and 115 (35.06%) non-peasants (Table 1).

In further analysis out of 328 participants, 89 (25%) were either obese or overweight, and 161 (49%) of the participants diagnosed with HIV within the last 5 years (Table 1). Current alcohol drinker and cigarette smokers were observed in 42 (12.8%) and 17 (5.18%) respectively (Table 1).

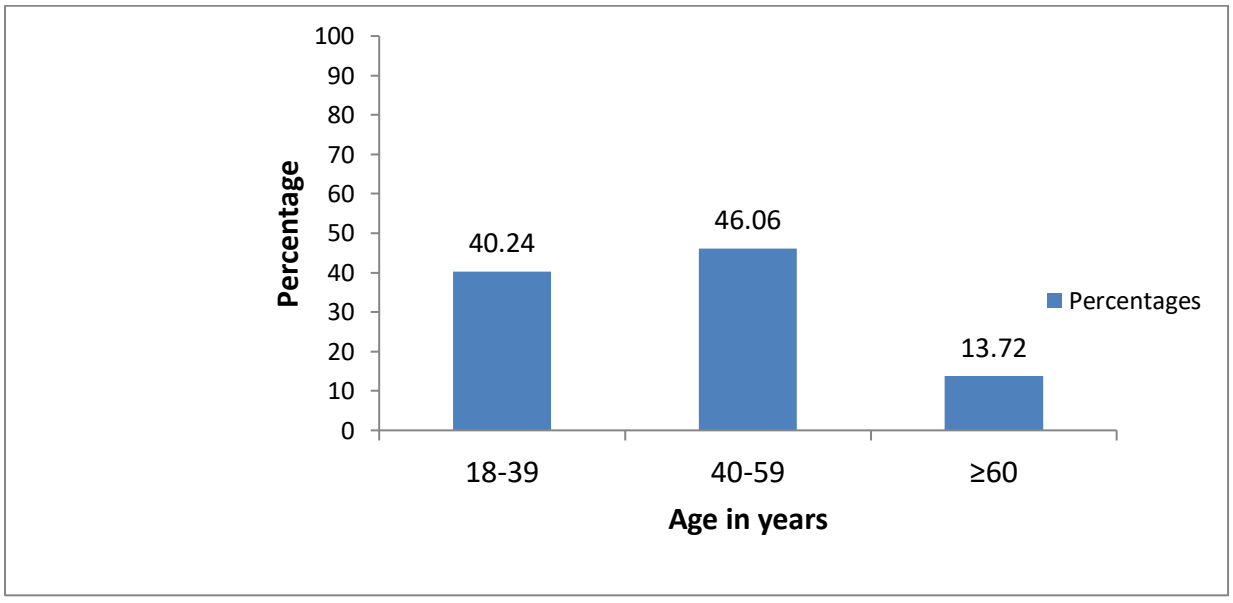

Figure 2: Age of the participants

Table 1: Socio demographic and clinical profile of the participants

Factors of interest	n (%)
Age (Years)	
18-39	132 (40.24)
40-59	151 (46.06)
≥ 60	45 (13.72)
Sex	
Female	212 (64.63)
Male	116 (35.37)
Occupation	
Peasants	213 (64.94)
Others	115 (35.06)
Alcohol drinker	42 (12.80)
Current cigarette smokers	17 (5.18)
BMI (kg/m^2)	
Underweight (<18.5)	46 (14.02)
Normal weight(18.5—24.9)	193 (58.84)
Overweight (25—29.9)	51 (15.55)
Obese (≥ 30)	38 (11.59)
Family history of hypertension	41 (12.50)
Overall	**328**

The HIV related factors characteristics of the participants were as follows; Out of 328 participants, 161 (49.09%), 110 (33.54%) and 57 (17.38%) had duration since HIV diagnosis of < 5 years, 5-9 years and ≥ 10 years respectively (Table 2). There were 304 (92.68%) patients on non-protease inhibitors and 24 (7.32%) on protease inhibitors as the class of ART (Table 2). The majority of patients 285 (86.89%) were on tenofovir based cART and the rest had been either on zidovudine or atazanavir (Table 2). Regarding the TB status, out of 328 participants, 2 (0.61%) patients had a current HIV/TB co-infected and 46 (14%) of patients had a history of TB in the past 5 years (Table 2).

Data on the recently CD4+ cell was available in 25 (8.47%), 75 (25.42%), 75 (25.42%) and 120 (40.68%) of the patients with CD4+ cell count of < 100, 100-349, 350-499 and ≥ 500 respectively (Table 2). However, there were missed data for CD4+cell count in 33 participants, which is equivalent to 10 percent of all the participants. Furthermore, out of 328,

2 (0.61%) patients had current HIV/TB co-infected and 46 (14%) of patients had a history of TB in the past 5 years (Table 2).

Table 2: HIV related factors characteristics of the participants

Factors of interest	n (%)
Duration since HIV diagnosed (years)	
< 5	161 (49.09)
5—9	110 (33.54)
≥ 10	57 (17.38)
Recently CD4 +cell count(cell/µl)	
<100	25 (8.47)
100- 349	75 (25.42)
350—449	75 (25.42)
≥ 500	120 (40.68)
Current class of ART	
Protease inhibitors	24 (7.32)
Non-protease inhibitors	304 (92.68)
Individual cART	
Zidovudine	19 (5.79)
Tenofovir	285 (86.89)
Atazanavir	24 (7.32)
History of TB	
Current TB/HIV co-infection	2 (0.61)
History of TB in past 5 years	46 (14.02)
Overall	**328**

4.1.2 The prevalence of hypertension

In the current study, the overall prevalence of hypertension in HIV patients on ART was 29.3 % (Table 3). According to gender, the prevalence was 33 (28.5%) in males and 63 (29.7%) in females (Table 3). The prevalence of hypertension was higher in the individuals aged ≥ 60 years 24 (53.3%), compared to 50 (33.1%) in the individuals aged 40-59 years, and 22 (16.7%) in the individuals aged 18-39 years (Table 3). Regarding the BMI, the prevalence of hypertension was 55.3%, 39.2%, 27.5% and 4.4% in obese, overweight, normal weight and underweight respectively (Table 3).

Table 3: Socio demographic characteristics associated with hypertension

Factors of interest	Hypertensive n (%)	Non hypertensive n (%)	TOTAL
Age (Years)			
18-39	22 (16.7)	111 (83.3)	132
40-59	50 (33.1)	101 (66.9)	151
≥ 60	24(53.3)	21 (46.7)	45
Sex			
Female	63 (29.7)	149 (70.3)	212
Male	33(28.5)	83 (71.5)	116
Occupation			
Peasants	63 (29.6)	150 (70.4)	213
Others	33 (28.7)	82 (71.3)	115
Alcohol drinker	13 (30.9)	29 (69.1)	42
Smoking cigarette	7 (41.2)	10 (58.8)	17
BMI (kg/m^2)			
Underweight (<18.5)	2 (4.4)	44 (95.6)	46
Normal weight (18.5—24.9)	53 (27.5)	140 (72.5)	193
Overweight (25—29.9)	20 (39.2)	31 (61.8)	51
Obese (≥ 30)	21 (55.3)	17 (44.7)	38
Family history of hypertension	20 (48.8)	21 (51.2)	41
Overall	**96 (29.3)**	**232 (70.7)**	**328**

BMI: Body mass index.

Furthermore, during the descriptive analysis of HIV related factors, the prevalence of hypertension was 28%, 30.7%, 29.3% and 30.0% in the participants with the CD4+ cell counts of < 100, 100-349, 350-499 and ≥ 500 respectively (Table 4). Also, the prevalence of hypertension was 12.5% and 30.6% in the participants who were on protease inhibitors and non-protease inhibitors respectively (Table 4). The participants with current TB-HIV co-infection had a prevalence of 50% and participants with a history of TB in the past 5 years had a prevalence of 32.6% (Table 4).

Table 4: HIV related factors associated with hypertension

Factors of interest	Hypertensive n (%)	Non- hypertensive n (%)	TOTAL
Duration since HIV diagnosed (years)			
< 5	48 (29.8)	113 (70.2)	161
5—9	33 (30.0)	77 (70.0)	110
≥ 10	15 (26.3)	42 (73.7)	57
Recent CD4 +cell count(cell/µl)			
<100	7 (28)	18 (72)	25
100- 349	23 (30.7)	52 (69.3)	75
350—449	22 (29.3)	53 (70.7)	75
≥ 500	36 (30.0)	84 (70.0)	120
Current class of ART			
Protease inhibitors	3 (12.5)	21 (87.5)	24
Non- protease inhibitors	93 (30.6)	211 (69.4)	304
Individual cART			
Zivodune	8 (42.1)	11 (57.9)	19
Tenofovir	85 (29.4)	204 (70.6)	289
Atazanavir	3 (12.5)	21 (87.50)	24
History of TB			
Current TB/HIV co-infections	1 (50.0)	1 (50.0)	2
History of TB in past 5 years	15 (32.6)	31 (67.4)	46
Overall	**96 (29.3)**	**232(70.7)**	**328**

cART = combination antiretroviral therapy, CD4 = cluster of differentiation 4, HIV = human immunodeficiency virus, and TB = tuberculosis.

4.1.3 Univariate analysis

In the univariate logistic regression analysis, the sociodemographic factors that significantly associated with increased odds of having hypertension were: increasing age, higher BMI, and family history of hypertension. The odds for hypertension were highest among individuals aged ≥ 60 years 5.71 (2.72-12.01) < 0.001 and the age group 40-59 years had an odds ratio of 2.48 (1.40-4.37) < 0.005 (Table 5).

Regarding body mass index, Obese hold highest odds ratio of 3.3 (1.60-6.66) < 0.001, followed by overweight 1.70 (0.89-3.25) 0.105 (Table 5). Also, family history of hypertension was significantly associated with increasing odds of having hypertension having an odds ratio of 2.64 (1.36-5.15) 0.004 (Table 5). Both of sex (female) 1.06 (0.65-1.78) 0.809, occupation (non-peasant) 0.96 (0.58-1.58) 0.867, current alcohol drinker 1.10

(0.54-2.21) 0.80 and current cigarette smokers 1.75 (0.64-4.73) 0.273 were not significantly associated with hypertension (Table 5).

Table 5: Univariate analysis of sociodemographic associated with hypertension (N=328)

Factor of interest	n	Odds ratios (95% CI)	P value
Age (years)			
18-39	132	1	
40-59	151	2.48 (1.40-4.37)	0.002
≥ 60	45	5.71 (2.72-12.01)	0.001
Sex			
Male	116	1	
Female	212	1.06 (0.65-1.78)	0.809
Occupation status			
Peasant	213	1	
Non peasant	115	0.96 (0.58-1.58)	0.867
Alcohol drinker			
No	286	1	
Yes	42	1.10 (0.54-2.21)	0.797
Smoking cigarette			
No	311	1	
Yes	17	1.75 (0.64-4.73	0.273
BMI (kg/m^2)			
Normal weight(18.5—24.9)	193	1	
Underweight (<18.5)	46	0.12 (0.28-0.51)	0.004
Overweight (25—29.9)	51	1.70 (0.89-3.25)	0.105
Obese (≥ 30)	38	3.3 (1.6-6.66)	0.001
Family history of hypertension			
No	287	1	
Yes	41	2.64 (1.36-5.15)	0.004

BMI: Body mass index

About HIV related factors, univariate analysis revealed that the only factor significantly associated with increased odds of hypertension was zidovudine 5.09 (0.86-10.24) 0.04 (Table 6). Both of duration since HIV diagnosis, CD4+cell count, tenofovir, current TB/ HIV co-infection, and history of TB in the past 5 years were not significantly associated with increased odds of having hypertension (Table 6).

Table 6: Univariate analysis of HIV related factors

Factor of interest		n	Odds ratios (95% CI)	P value
Duration since HIV diagnosed (years)				
< 5		161	1	
5—9		110	1.01 (0.59-1.71)	0.974
≥ 10		57	0.84 (0.42-1.66)	0.617
Recent CD4 + cell count(cell/µl)				
<100		25	1	
100-349		75	1.13 (0.42-3.09)	0.801
350—499		75	1.07 (0.39-2.91)	0.899
≥ 500		120	1.10 (0.42-2.87)	0.842
Current class of ART				
Protease inhibitors		24	1	
Non-protease inhibitors		304	3.09 (0.89-10.6)	0.074
Individual cART				
Zidovudine		19	5.09 (1.12-23.14)	0.493
Tenofovir		289	2.98 (0.86-10.24)	0.001
Atazanavir		20	Omitted	
History of TB				
Current TB/HIV co-infections				
	No	326	1	
	Yes	2	2.42 (0.15-39.28)	0.531
History of TB in past 5 years				
	No	282	1	0.595
	Yes	46	1.2 (0.62-2.34)	0.592

cART = combination antiretroviral therapy, CD4 = cluster of differentiation 4, HIV= human immunodeficiency virus and TB = tuberculosis.

4.1.4 Multivariate analysis

In multivariate analysis, the sociodemographic characteristics that associated with increased odds of hypertension were age group of 40-59 years, 3.40 (1.80-6.41) 0.001, ≥ 60 years, 9.25 (3.96-21.60) 0.001, current smokers 2.12 (0.65-6.90) 0.214 (Table 7), obesity 3.63 (1.60-8.26) 0.002, and family history of hypertension 2.73 (1.27-5.84) < 0.009 (Table 7).

Table 7: Multivariate analysis sociodemographic associated with hypertension (N=328)

Factor of interest	n	Odds ratios (95% CI)	P value
Age (years)			
18-39	132	1	
40-59	151	3.40 (1.80-6.41)	0.000
≥ 60	45	9.25 (3.96-21.60)	0.000
Sex			
Male	116	1	
Female	212	0.78 (0.43-1.40)	0.402
Occupation status			
Peasant	213	1	
Non-peasant	115	1.24 (0.69-2.24)	0.472
Current social behaviour			
Alcohol drinker			
No	286	1	
Yes	42	1.09 (0.54-2.21	0.797
Smoking cigarette			
No	311	1	
Yes	17	1.29 (0.57-2.92)	0.214
BMI (kg/m^2)			
Normal weight (18.5—24.9)	193	1	
Underweight (<18.5)	46	0.70 (0.02-0.32)	0.001
Overweight (25—29.9)	51	1.61 (0.77-3.36)	0.201
Obese (≥ 30)	38	3.63 (1.60-8.26)	0.002
Family history of hypertension			
No	287	1	
Yes	41	2.73 (1.27-5.84)	0.009

In further multivariate analysis, HIV related factors that were independently associate with increased odds of hypertension were, non-protease inhibitors 4.31 (1.16-16.03) 0.029, and tenofovir 4.27 (1.15-15.96) 0.031 (Table 8). However, the duration since HIV diagnosis, recent CD4+count, zidovudine, current TB/HIV co-infection and history of TB in the past 5 years were not found to have statistical significance with hypertension in multivariate analysis (Table 8).

Table 8: Multivariate analysis HIV related factors associated with hypertension (N=328)

Factor of interest		n	Odds ratios (95% CI)	P value
Duration since HIV diagnosed (years)				
< 5		161	1	
5—9		110	0.82 (0.44-1.51)	0.521
≥ 10		57	0.61 (0.27-1.35)	0.222
Recent CD4 + cell count(cell/µl) [c]				
<100		25	1	
100-349		75	0.90 (0.30-2.70)	0.845
350—499		75	1.04 (0.34-3.16)	0.940
≥ 500		120	1.25 (0.43-3.60)	0.677
Current class of ART				
Protease inhibitors		24	1	
Non -protease inhibitors		304	4.31 (1.16-16.03)	0.029
Individual cART				
Zidovudine		19	4.66 (0.91-23.99)	0.065
Tenofovir		285	4.27 (1.15-15.96)	0.031
Atazanavir		24	Omitted	
Current TB/HIV co-infections				
	No	326	1	
	Yes	2	3.13 (0.12-80.41)	0.491
History of TB in past 5 years				
	No	282	1	
	Yes	46	1.15 (0.55-2.43)	0.711

cART= combination antiretroviral therapy, CD4= cluster of differentiation 4, HIV= human immunodeficiency virus and TB = tuberculosis.

4.2 Discussion of the results

The study found the prevalence of hypertension among HIV patients on ART to be 29.3%%. The odds of having hypertension were significantly and positively associated with increasing age, obesity, and family history of hypertension, non-protease inhibitors, and tenofovir. Both of duration since HIV diagnosis, recently CD4+cell count, zidovudine and history of the TB infection in the last past 5 years were found not significantly associated with increased odds of hypertension. The high prevalence (29.3%) in the study, is similar to the observed prevalence in previous studies in HIV patients on ART (Xu *et al*., 2017; Peck *et al*., 2014). The result together with those from previous studies strengthens the evidence that the prevalence of hypertension is greater among individuals living with HIV/AIDS on ART.

The observed significant and positive association between socio-demographic(increasing age, and obesity) is concordant with preceding studies (Furrer *et al*., 2017; Fatou *et al*., 2017). The findings support the evidence that traditional risk factors are potential predictors of hypertension even in HIV patients.

About HIV related factors, duration since HIV diagnosis was found not associated with increasing odds of having hypertension, similar to what has been reported in a previous prospective observation cohort (Krauskopf *et al*., 2013). However, the result differs from what was reported by Medina-Torne *et al*. (2012). According to the analyzed data by Medina-Torne *et al*. (2012) there was a positive and significant association between the duration of HIV infection and hypertension (Medina-torne *et al*., 2012). The difference might be explained by the way duration of HIV was defined in the two settings. In the study by Medina-Torne *et al*. (2012), the duration of HIV was defined as the mid-point between the first HIV positive test and the last negative test to the time of data collection (Medina-torne *et al*., 2012). While the definition used in the current study was the time difference from the first seropositive and the time of study initiation.

The study also investigated whether there is an association between ART and hypertension. There are prior studies that have explored the association between ART and hypertension in HIV patients (Munderi, 2017; Medina-Torne *et al*., 2012). The current study found that non-protease inhibitors as the class of ART were significant and positively associated with

hypertension, similar to what has been communicated in an observational study conducted in Uganda (Munderi, 2017).

In further analysis of the individual ART combination therapy, tenofovir was significantly and positively associated with increased odds of having hypertension, similar to what has been reported in a previous study (Villa *et al*., 2018). Tenofovir has been implicated to cause hypertension due to its kidney toxicity (Ru *et al*., 2018). However, the current study didn't measure the serum level of tenofovir to check for the tenofovir toxicity, therefore the study cannot conclude whether observed hypertension was directly linked to tenofovir toxicity.

Furthermore, zidovudine based ART was found associated with increased odds of having hypertension in the multivariate analysis though the association was not statistically significant, contrary to the findings in research conducted in North America which indicated a lack of significant association (Medina-Torne *et al*., 2012). The contrasting results possibly are due to the dissimilarity in ethnicity, socio-demographic profiles and study design between two studies.

The study also investigated the influences of the immune response on hypertension in HIV patients who were on ART. There was no significant association between recent CD4+cell count and hypertension, similar to results reported from previous studies (Furrer *et al.*, 2017; Dimala *et al*., 2016; Medina-torne *et al*., 2012). However, the result from the current study differs from what has been reported in a previous study in north-western Tanzania which reported a positive association between hypertension and a high CD4+cellcount (Peck *et al.*, 2014). The difference might be explained by the inclusion criteria and definition for CD4+cell count used in the two studies. According to Peck *et al.* (2014), the inclusion criteria were being an HIV patient on ART for at least 2 years, contrary to the current study which had no time limit when ART was initiated. Also, in the study by Peck *et al.* (2014) the blood sample for CD4+cell count, was taken on the same day as the measurement of first BP (Peck *et al.*, 2014). But, in the current study, CD4+cell count was obtained from patient's records with a focus to the CD+ cell count which was taken and measured in a period of not more than the past 6 months counting from the day of recruitment.

The study also investigated whether there is an association between TB and hypertension in adult HIV patients on ART. The interaction between TB infection and hypertension in HIV patients has been reported in the literature (Calisman, 2017). The possible mechanism by

which TB can cause hypertension is through the inflammatory process which can cause atherosclerosis (a risk factor for hypertension) (Calisman, 2017). The current study found that current TB/HIV co-infection increases the odds of having hypertension 3.13 (0.12-80.41) 0.491, though the association was not statistically significance. The result differs from the study by Njelekela *et al*. (2016) which indicates a lack of association between current TB/HIV co-infection and hypertension (Njelekela *et al*., 2016). However, the result from the current study should be interpreted with caution because of a small proportional (0.61%) of patients with current TB/HIV co-infection which was included in the final analysis. The association between current TB and hypertension cannot be justified based on only 2 patients with current TB infection which is a very small number to conclude. Therefore, the interpretation in the current study concerning the association between current TB/HIV co-infection and hypertension in HIV patients on ART should be made with caution.

Finally, the study established that history of TB in the past 5 years was associated with increased odds of having hypertension though the association was not statistically significance, contrary to a study by Njelekela *et al*. (2016). In a cross-sectional study by Njelekela *et al*. (2016) conducted in Dar es Salaam, Tanzania reported a protective effect of a prior history of TB against hypertension (Njelekela *et al*., 2016). However, there are differences to explain between the two studies. The current study had limit the history of the previous TB to a period of within the past 5 years whereas in the investigation by Njelekela *et al*. (2016), it had no time limit regarding the prior history of TB. Also, the current study recruited HIV patients who were on ART whereas Njelekela *et al*. (2016) recruited HIV-ART naïve patients. Furthermore, the current study included potential confounders of hypertension in the multivariate analysis whereas, Njelekela *et al*. (2016) did not.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

In conclusion, the current study established that the prevalence of hypertension in adults HIV patients on ART was high (29.3%) and was similar between female and male. The hypertension was significantly and positively associated with medications belong to the non-protease inhibitors namely zidovudine and tenofovir based combinations therapy even after adjusting for other covariates. Both of the duration since HIV diagnosed, recent CD4+cell count and history of TB in the past 5 years were not associated with increased odds of having hypertension.

5.2 Recommendations

Derived from the outcome of the study, the following are the recommendations;

(i) Routine screening and monitoring of blood pressure in HIV patients is required when attending HIV outpatient clinics.

(ii) There should be the inclusion of lifestyle modification awareness programs into existing outpatient HIV clinics in Tanzania.

(iii) Future prospective studies are recommended to investigate the incidence of hypertension and its association with HIV related factors.

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APPENDIX

Appendix 1: Questionnaire

1. **Sex (circle only one)**

   1. Male 2. Female

2. **Age of participant……** (Completed years).

3. **What is your occupation?** (Circle only one)

   1. Peasant 2.Employed 3.Business 4.Unemployed 5.Others

4. **Do you currently drink alcohol?** (circle only one)

   1. Yes 2.No

4.1 If Yes above, how many bottles on average do you drink per week?

   1. (1-2) 2. (3--7) 3. (>7)

5. **Do you currently use any of the following tobacco products?**
   1. Smokes cigars 2. Tobacco pipes 3.None

6. **Is there a family history of hypertension?(circle only one)**
   1. Yes 2.No

B Blood pressure and anthropometric measurements

7. **Blood pressure measurement**

Blood pressure reading1		Systolic… Diastolic…
Blood pressure reading2		Systolic… Diastolic…
Average blood pressure		Systolic… Diastolic…

8. **Body mass index**

   Bodyweight in kg (shoes removed)…….

   Height in meter.....

   Body mass index (Weight (kg)/m^2)……

History of hypertension and diabetes mellitus (QN 9 and 10)

9. **Are you currently taking ant-hypertensive medication**?
   1. Yes 2. No

10. **Are you currently taking medications for diabetes?**
    1. Yes 2. No

HIV Related factors

11. **How long since your were diagnosed with HIV**
    1. <5, 2.5 -- 9 3. ≥ 10

12. **What is the CD4 COUNT? (**taking within the last 6 months)
Obtain the answer from patient card/CTC2.

    1. < 100 2. 100---349 3. 350 ---4994. 4. ≥ 500

13. **For how long since you started taking ARV medications?** (months)
    Obtain the answer from patient card/CTC2.

    1. < 6 2.6 --12 3. > 12

14. **What ARV drug regime is currently taken by a participant?**
    Obtain the answer from patient card/CTC2.
    1. Protease inhibitor 2. Non- protease inhibitors

15. **Which specific ARV regime a taken by a participant?**
    (Obtain the answer from patient card/CTC2)**.**

1. Zidovudine based cART 2.Tenofovir based cART 3.Lopinavir 4.Atazanavir

16. **Are you current known to have tuberculosis or taking TB medication?** (If yes check CTC2 card for verification and then go to question 17.0) if the answer is No go to question 18.0).

    1. Yes but not on ant-TB medication 2. Yes, on ant-TB medication 3.No

17. **If yes in QN 16 above which types/form of tuberculosis is**? (Check patient registry, TB treatment card or clinic database to confirm for the form of TB.)
    1. Pulmonary TB 2. Extra pulmonary TB

18. **If no in QN 16 above have you ever suffered from TB in the past 5years**?

1. Yes, and ant-TB drugs were taken 2.No 3. Can't remember