UNIVERSITY OF GHANA MEDICAL SCHOOL

DEPARTMENT OF PHYSIOLOGY

BLOOD PRESSURE VARIABILITY INDICES AND SELF-REPORTED QUALITY OF SLEEP AMONG ADOLESCENTS LIVING WITH HIV

BY

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THIS DISSERTATION IS SUBMITTED TO UNIVERSITY OF GHANA, LEGON

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF MPHIL PHYSIOLOGY DEGREE

OCTOBER 2023

DECLARATION

I Agyiri Kofi, the Principal Investigator of this study titled "**BLOOD PRESSURE VARIABILITY INDICES AND SELF-REPORTED QUALITY OF SLEEP AMONG ADOLESCENTS LIVING WITH HIV"** and on behalf of my supervisors, I pledge to uphold all ethical norms, including the principles of beneficence and non-maleficence.

The aforementioned ethical guidelines was followed throughout the study to ensure that all rights are reserved. Transcripts and field notes was kept in cabinets under lock and key.

Throughout the investigation, we shall scrupulously follow all ethical standards and rules. The information gathered was used strictly for this study.

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AKNOWLEDGEMENT

Firstly, my gratitude goes to Almighty God, for giving me the strength to commence and complete this work.

I thank my project supervisors; Dr. Kwame Yeboah and Dr. Nyonuku Akosua Baddoo for their tireless efforts and also for their immense contributions, commitment, dedication and constant guidance. Without them this project wouldn't have been successful.

I am also very grateful to all the lecturers and staff of the Physiology Department, who over the years have taken time and efforts to instill in me the knowledge required to be at par with the demands and challenges of this field. I also appreciate the study participants and their parents for availing themselves for this study to be conducted.

I wish to express my gratitude to my Parents Mr. and Mrs. Ewusi Mensah for their prayers and support and also a big thank you to Dr. Raphael Adu-Gyamfi, for his assistance in providing me with devices for my data collection. I appreciate my Pastor, Rev Dr. Solomon Ocquaye and his wife for their advice and prayers during throughout the period of this research. I am grateful to all my friends who supported me at one point or the other.

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Abstract

Background:

Children and adolescents living with HIV (ALHIV) are highly prone to develop cardiovascular diseases (CVDs) in the future. Blood pressure is a predictor for future development of cardiovascular diseases. Ambulatory Blood pressure indices predicts changes in blood pressure better than Office blood pressure. However, most healthcare facilities in Ghana use Office BP and Ambulatory blood pressure has not been used a lot. Most research evaluating the relation between HIV and blood pressure (BP) measurements have mainly focused on the conventional sphygmomanometric method, which carries a significant risk of human error and inaccuracy and does not accurately reflect the blood pressure characteristics of HIV positive patients BP variability Ambulatory blood pressure monitoring (ABPM), is a key instrument for evaluating blood pressure variability (BPV) which is a predictor of hypertensive end-organ damage. This study is a novel study and there is scanty literature on evaluating Blood pressure variability among ALHIV. This study may provide data and literature on blood pressure variability indices and self-reported sleep to help in the management of cardiovascular risk among ALHIV.

Cardiovascular disorders among children and adolescents may also be contributed by poor sleep quality. Blood pressure changes over a 24-hour period might occur in HIV positive patients who have sleep disturbances. Lack of sleep may cause sympathetic activity to rise, which could raise blood pressure.

General aim of study:

The study aims to investigate the relationship between 24-hour ambulatory blood pressure variability indices and self-reported sleep quality among adolescents living with HIV.

Methods:

A cross-sectional study design was employed for this study. A cluster-randomized sampling technique was used to recruit health facilities and 122 adolescents living with HIV (ALHIV). A 24-hour ABPM was performed using a validated portable ABPM 50 device with the BP readings set at 15 minutes intervals, from 7 am to 10 pm for daytime, and 20 minutes intervals during the night, from 10 pm to 6 am. The Pittsburg Sleep Quality Index (PSQI) Questionnaire was used to assess the quality of sleep. Anthropometric measurement of participants was also conducted. Body weight (in kilograms) and height (in meters) were taken for the calculation of Body mass index (BMI). Variables such as Self-reported sleep quality, BMI, and ART regimen was held as independent variables while Beat-to-beat BPV variables and circadian variability variables were held as dependent variables

Results:

Ages of participants were from 6 years to 19 years; with a mean age of 13.6 ± 3.2 years. The males were (N=56(45.9%)) and the females were (N=66 (54.1%)). Most of the females (N=32(48.5%)) were aged 14 years and above. Females (N=21(31.8%)) had a healthier BMI compared to males (N=18(32.1%)). There was no significant relationship between gender and BMI of participants, p-value= 0.25. Relationship between gender and antiretroviral therapy (ART) regimen was not significant, p-value=0.304. For sleep quality comparison among genders, most females reported poor sleep quality, (N=18(27.3%)). Most females had good sleep quality (N=48(72.7%)). Hypertension was reported among (N=13 (10.6)) of which (N=2 (1.64%) reported Hypertension

stage 1 (>=pct90 and <pct95 mmHg), Hypertension stage II was (N=1 (0.82%)), Isolated Diastolic Hypertension (IDH) was (N=6 (4.82)), Isolated Systolic Hypertension (ISH) (>(pct99+5 mmHg/<pct90mmHg) was (N=3 (2.5%). The outcome showed no significant association between sleep quality and SD blood pressure Variability since all recorded p-values > 0.05. The p-value for the association between self-reported sleep and circadian variability (Nocturnal dip, p-value=0.984, BP surge, p-value = 0.695). Findings from this study showed a significant association between cardiovascular outcomes and blood pressure variability. Cardiovascular outcomes of ALHIV was determined by ambulatory systolic blood pressure and office systolic blood pressure levels. For Ambulatory BP levels, study showed Blood pressure variability; Awake SD BPV increases with increasing ambulatory and office blood pressure, at an R-Squared value = 0.038 and p-value =0.03.

Conclusion:

Blood pressure variability may have a relationship with cardiovascular outcomes among ALHIV**.** Findings from this study shows that, as blood pressure variability increases, there is a tendency for blood pressure to also rise. Self-reported sleep quality did not have any significant association with short term blood pressure variability and circadian variability. ART and BMI showed some association with blood pressure variability. The study showed that most ALHIV have elevated blood pressure.

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List of Abbreviation

ABPM Ambulatory Blood Pressure Monitor

ALHIV Adolescent Living with HIV

ARV Absolute Real Variability

BMI Body Mass Index

BP Blood Pressure

BPV Blood Pressure Variability

CI Confidence Interval

CV Cardiovascular

CVD Cardiovascular Disease

DBP Diastolic Blood Pressure

EFV Efavirenz

HIV Human Immunodeficiency Virus

LVMI Left Ventricular Hypertrophy and Left Ventricular Mass index

MH Masked Hypertension

OBP Office Blood Pressure

PLHIV People Living with HIV

SBP Systolic Blood Pressure

SD Standard Deviation

TLD tenofovir/lamivudine/dolutegravir

WCHT White Coat Hypertension

CHAPTER ONE

1.0 BACKGROUND

Acquired Immunodeficiency Syndrome (AIDS) is caused by the Human Immunodeficiency Virus (HIV) and has been s public health concern for a long time (Chen, 2020). According to WHO, 33 million individuals had died from HIV-related illnesses by the end of 2020, whereas an estimated 38 million people were predicted to be HIV-positive in 2019 (World Health Organisation, 2020). According to other epidemiology research, 2.2 million of the estimated 35.3 million HIV-positive people living today were teenagers aged 10 to 19 years old (Idele et al., 2014). In Ghana, as at 2019, 342,307 were living with HIV with 24,263 being adolescent (Ghana AIDS Commission 2019). In a study comparing teenagers with and without HIV infection, it was found that those with HIV infection have a greater risk of cardiovascular disease (de CB Giuliano, de Freitas, de Souza, & Caramelli, 2008). Studies reported prevalence of hypertension in children and Adolescents living with HIV (ALHIV) to be 27% in the US and 18% in South Africa (Kamkuemah, Gausi, & Oni, 2020). Most adolescents contract HIV directly, through mother-child transmission and therefore stands the risk of developing cardiovascular disorders very early in life (Augustemak de Lima et al., 2018).

Most adults compared to adolescents, contract HIV and associated cardiovascular disorders, later in life. People living with HIV (PLHIV) are highly prone to develop cardiovascular diseases (CVD) because of associated chronic inflammation, which may result from atherosclerosis, and exacerbation of cardiovascular risk factors which possibly from intima-media thickening of the carotid artery (Augustemak de Lima, et al., 2018). Most research evaluating the relation between HIV and blood pressure (BP) measurements have only been using the conventional

sphygmomanometric method, which carries a significant risk of human error and inaccuracy and does not accurately reflect the blood pressure characteristics of HIV positive patients (Giuseppe, et al., 2010). Blood pressure is distinguished by consistent dynamic fluctuations that happen from beat to beat and over the course of a 24-hour period. These fluctuations are a result of neural reflexes, specifically the central sympathetic drive and the reflex modulation of the arterial and cardiopulmonary reflexes that are involved in maintaining homeostasis. The variation in blood pressure over the course of a 24-hour period is also an illustration of the homeostatic reaction to humoral mechanisms, which include responses to catecholamines, insulin, angiotensin II, nitric oxide, and rheological mechanisms to changing environmental conditions, behavioral, and emotional stimuli (Giofranco et al., 2013). These mechanisms with the accompanying blood pressure fluctuation and the resultant BP "homeostasis" are intended to ensure constantly adequate organ perfusion, being able to adjust BP levels to match the demands of different organs. The size and patterns characterizing this blood pressure variation are known as Blood Pressure Variability (BPV). Studies have revealed that, for practically any ambulatory blood pressure monitoring (ABPM), people with low BPV reported decreased prevalence and severity of organ damage compared to those with high BPV. BPV is a significant driver of hypertensive end-organ damage. (Chen, 2008). BPV indices are evaluated in detail by employing 24-hour Ambulatory Blood Pressure Monitoring (ABPM).

ABPM provides pertinent and unique information on the Circadian BP pattern (De Socio et al., 2010). Circadian rhythm is endogenous, meaning it comes from within the body and is responsive to its surroundings (Edgar et al., 2012). The brain needs sleep as a natural mechanism in order to continue operating properly and to keep the body healthy. 40 to 70 percent of HIV positive patients report having sleep problems (Mengistu et al., 2021). Blood pressure changes over a 24-hour

period might occur in HIV positive patients who have sleep disturbances. Lack of sleep may cause sympathetic activity to rise, which could raise blood pressure (Gangwisch et al., 2006).

1.1 Problem Statement

Studies have shown a great burden of high blood pressure among Adolescents Living with HIV (ALHIV) (Ferrand et al., 2010). A study conducted in a cohort of children and adolescents living with HIV showed that 20% of this cohort were having high blood pressure (Chatterton-Kirchmeier, et al., 2015). This finding is alarming among ALHIV because high blood pressure predicts cardiovascular diseases, which contributes to high mortality rate among HIV positive patients (Dominick et al., 2020). Therefore, there is a need to routinely monitor the blood pressure of HIV adolescents, for effective management of the disease. However, there are several challenges involving blood pressure monitoring among HIV adolescents. These challenges include lack of blood pressure monitoring tools, faulty BP monitoring tools, non-adherence to Ghanaian clinical practice guidelines, and the deceiving measure of office blood pressure, which is defined as the blood pressure monitored during a patient's visit to a physician's "office". For every BP measured, there is a possible misrepresentation of patients BP that may consequently lead to wrong diagnosis.

According to a study by Rabin et al, individuals with chronic diseases such as HIV, are poorly managed due to a lack of evaluation and monitoring equipment (Connor, Hopkins, Tollman, Thorogood, & Modi, 2006; Rabkin et al., 2012). According to Maher et al, monitoring and evaluation systems in most African health settings for HIV and related comorbidities are not encouraging. This finding explains why, in some clinics in Ghana, routine blood pressure monitoring for PLHIV is not done. Most studies on the relationship between HIV infection and blood pressure are based on sphygmomanometric technique or office blood pressure monitoring. Office blood pressure monitoring does not give a true representation of the patient's actual blood

pressure but 24-hr ABPM gives the actual representation of the patient's blood pressure (Giusepp et al., 2010). However, most healthcare facilities use OBP and ABPM is not used a lot. This may lead to mismanagement of ALHIV who may later develop complications of high BP which includes, stroke, kidney failure, and heart failure among others. There is also a study gap and scanty literature concerning the study. In Ghana, no study has been done in the ALHIV population, investigating sleep quality and their 24 hour ambulatory blood pressure.

1.2 Research Aim

The study aims to investigate the relationship between 24-hour ambulatory blood pressure variability indices and self-reported sleep quality among ALHIV.

1.3 Research Objectives

1. To determine short-term blood pressure variability by assessing beat-to-beat variability and circadian variability.
2. To determine the association between self-reported sleep quality and short-term blood pressure variability in ALHIV.
3. To determine the association between blood pressure variability indices and risk factors such as Antiretroviral Therapy (ART) and Body Mass Index (BMI).
4. To determine the association between Cardiovascular outcome and Blood pressure variability

1.4 Justification of Study

The importance of blood pressure monitoring as a tool to investigate cardiovascular risk in the adult population living with HIV has been long documented unlike BP monitoring in children and ALHIV until recently. Cardiovascular disorders such as hypertension is a more expected disorder in the adult population living with HIV, however, it becomes a bigger issue when it is found in children and adolescents living with HIV. ALHIV tends to live with cardiovascular complications from their early childhood through adolescence to adulthood. This study therefore may provide data and literature on blood pressure variability indices and self- reported sleep to help in the management of cardiovascular risk among ALHIV and to contribute to future studies.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1ALHIV and Cardiovascular Complications

Studies have revealed that the HIV epidemic is a global burden among young people and adolescents. In 2019, UNICEF data revealed 1.6 million people between age 10 and 19 years live with HIV and 190,000 are newly infected (UNICEF., 2019). HIV is the second leading cause of death among young people globally, and adolescents are the only group for which mortality is not declining (Kteily-Hawa et al., 2022). Some of these infected children in early adolescence present with pronounced immunosuppression with longstanding lung and cardiac complications (Ferrand et al., 2012). Cardiovascular complications among ALHIV is a well-defined burden in both high resourced and low resourced settings. Studies have shown a high burden of cardiovascular complications among ALHIV where in one instance, a study done among hospitalized ALHIV in Zimbabwe showed that 12% of these hospitalized patients battled with one cardiovascular complication or the other (Ferrand et al., 2010). Another study conducted among ALHIV in which more than half were asymptomatic, had severe echocardiographic abnormalities and the findings also showed the need to employ monitoring procedures such as ambulatory blood pressure monitoring and other screening methods, in other to diagnose cardiovascular complications at their onset(Miller et al., 2013).

2.2 HIV-Related CVD Risk Factors

Compared to non HIV individuals, PLHIV have an increased risk of cardiovascular disease (Abebe et al., 2014).HIV-specific risk factors as well as traditional CVD risk factors are the main factors influencing this risk (Dominick, et al., 2020). The source of literature about the relationship between HIV and clinical cardiovascular disease, risk factors, and risk assessment comes mainly from Europe and North America. Africa has been the most HIV infected continent with 25.6 million infection out of a projected 37.9 million HIV-positive people globally (Dominick, et al., 2020). However, very little is known about the prevalence of cardiovascular disease and the weight of risk factors that contribute to it in Africa. There is mounting evidence that an individual's socioeconomic class (SES) and place of residence can have an impact on their health through behavioral decisions such as smoking, substance misuse, diet, and physical inactivity (Pollitt et al., 2007).

2.3 Substance Abuse and CVD complication among PLHIV

Compared to healthy controls and non-smoking PLHIV, CVD risk is around two times higher in PLHIV (Lifson & Lando, 2012). In a cross-sectional study, CD4+ and CD8+ T cells activation (levels of antigen-specific IL-2, interferon) were significantly lower in HIV-positive smoking people compared with HIV-positive non-smokers(Xiao, Wu, & Chou, 2011) . It also showed that smoking was associated with higher immune activation and increased gut microbial translocation which is associated with hypertension (Vemuri et al., 2022) . These findings show that using drugs increases the risk of CVD in PLHIV by causing immunological dysregulation, which results in chronic inflammation and endothelial dysfunction (Deeks, Lewin, & Havlir, 2013). Studies has shown substance abuse involving cocaine, marijuana and tobacco results in sudden Blood pressure elevation (Büttner, 2011).

2.4 Physical Inactivity and CVD complication among PLHIV

Several studies has demonstrated a significant association between physical inactivity and advanced CVD in PLHIV (Frantz & Murenzi, 2013; Vancampfort et al., 2017). According to study conducted in Nigeria, physical inability as a risk factor for hypertension was reported among 70% of PLHIV (Odukoya, et al, 2020) . Increasing oxidative stress is linked to increased physical inactivity, and IL-6 and tumor necrosis factor (TNF) production are two proinflammatory cytokines that are produced as a result (Bronas & Dengel, 2010). Such proinflammatory cytokines can worsen HIV-related CVD by promoting platelets, adhesion molecules, and coagulation factors, which can result in endothelial dysfunction (Hussain et al., 2016).

2.5 Dietary lifestyle and CVD complications among PLHIV

Poor dietary habit is one of the most significant risk factors contributing to CVDs and mortality among PLHIV (Khatri et al., 2020). Poor dietary habit such as high salt in take has been reported to contribute to hypertension among PLHIV even in the face of viral suppression from ART (Masenga et al., 2020) .Numerous studies have examined the relationship between food and the risk of developing cardiovascular disease, and numerous dietary interventions have been developed to lessen these negative consequences (O'Neil et al., 2015; Ruiz-Canela et al., 2015). Sadly, there aren't many studies on the eating patterns of PLHIV, which shows a vacuum in our knowledge. The limited studies that have been done so far show that PLHIV frequently make poor food decisions that are connected to socioeconomic status (Darmon & Drewnowski, 2008; Gaikwa, et al, 2011).

2.6 Antiretroviral Therapy and CVD complication in PLHIV

Antiretroviral therapy has negative cardio-metabolic side effects, including increases in blood pressure, in about two-thirds of HIV-infected people. Antiretroviral medications alter the vascular endothelial cells' ability to produce biological substances that are known to control blood pressure, like nitric oxide (Nduka, et al, 2016). Although the widespread distribution of ART is essential to fighting the HIV pandemic and has saved many lives, it can eventually lead to the development of CVD (Triant, 2013). When ART was started, there was a lower probability of mortality and AIDS-defining events in PLHIV than when treatment was postponed (CD4+ count fell to 350 cells/mm3)(Dominick, et al., 2020). Longer medication exposure periods due to earlier ART initiation and longer lifespans will probably raise the risk of CVD for PLHIV (IeDEA et al., 2020). Although, effective ART can reduce inflammation and partially restore immunological function, treated HIV+ persons nevertheless have heightened CVD risk and higher levels of inflammatory biomarkers (Hemkens & Bucher, 2014; Ipp & Zemlin, 2013). According to a systematic review, individual studies that included samples of HIV+ patients who were above 80% or 0% on ART, PLHIV were likely to have non-dipping SBP pattern compared to than people without HIV (Kent et al., 2016). Additionally, a trial included in the review indicated that, HIV-negative controls compared to the prevalence of a non-dipping SBP pattern in HIV+ persons was 80% and 82% before and after 6 months of ART, respectively (Megan Borkum et al., 2014).

2.7 Persistent Immune Activation and CVD risk among PLHIV

Despite excellent ART and ongoing viral suppression, HIV infection is accompanied by persistent immunological activation, inflammation, and immune dysfunction (Lawn et al., 2007). A prolonged state of immune activation and inflammation that results in an increase in the generation of pro-inflammatory cytokines is supported by the virus' persistence (Aishwarya & Shamsiya, 2015). Additionally, ongoing inflammation in PLWH worsens tissue damage, especially in the gastrointestinal tract, and promotes inflammation by allowing microorganisms to move into the bloodstream (microbial translocation) (Zevin et al., 2016). HIV infection causes a persistent inflammatory state that raises the risk of CVD in this population (Ipp & Zemlin, 2013). Similar to this, it has been noted that people with a non-dipping SBP pattern have greater levels of inflammatory biomarkers (Erdogan et al., 2013).

2.8 Prevalence of Mother-to-child transmission of HIV

The scientific and research community in the west has contributed massively in stopping the vertical spread of HIV from mother-to-child, but in Africa, mother-to-child transmission still happens (Belachew et al., 2020). In a study aimed at assessing the prevalence of vertical spread of HIV infection and its associated factors, HIV-exposed infants in East Africa, was discovered to be 7.68%. This finding disrupts WHO goals of setting strategies of achieving zero incidences of new HIV infection among HIV-exposed infants (Zeng et al., 2016).

According to a study, Ethiopia had the highest prevalence of Mother-to-Child Transmission for HIV (32.1%), whereas Rwanda had the lowest prevalence (1.58%)(Hassen & Tsegaye, 2014; Mugwaneza et al., 2018). The results demonstrated a substantial relationship between vertical HIV transmission and the place of delivery. Babies born at home had a 2 to 1 odds ratio (AOR: 2.00, 95% CI 1.01, 3.00) of contracting HIV infection compared to babies born in medical facilities. Studies examining the impact of the mother's time on ART with vertical HIV infection found that moms taking ART for less than 4 weeks were 1.92 times more likely to pass HIV to their exposed newborn than mothers taking ART for more than 4 weeks(Mama et al, 2017; Teclebirhan, et al, 2009).

2.9 The concept of blood pressure variability

A study done among children and adolescents living with HIV showed that 20% of this cohort were having high blood pressure (Chatterton-Kirchmeier, et al., 2015). Blood pressure variability is a well-established concept borne out of numerous studies by researchers over the years (Mancia, G., 2012).BP over time has been documented since the 18th century and has shown to be a very vital diagnostic parameter in health (Parati G. , 2005). BPV is a physiological parameter that is characterized by continuous dynamic variations occurring on a beat-to-beat basis and within the 24-hour time range, representing a homeostatic response of neural reflexes comprising central sympathetic drive and its associated reflex modulation by arterial and cardiopulmonary reflexes. Blood pressure variability within the 24-hour time range is also a representation of homeostatic response to humoral mechanisms comprising responses to catecholamines, insulin, angiotensin II, nitric oxide; and rheological mechanisms (i.e. blood viscosity) to changing environmental condition, behavioral and emotional stimuli. (Giofranco, Juan, Carolina, & Grzegorz, 2013). It shows a spontaneous variation over more prolonged periods because of obvious differences among days, months, and seasons (Mancia, G., 2012). BPV characterizes a tendency for systolic BP to increase over the years and for diastolic BP to display an age-related biphasic change (Wolf-Maier, et al., 2003). BPV is a key determinant of hypertensive end-organ damage and current studies have shown that, for nearly any 24-hr mean arterial blood pressure level, hypertensive individuals with low 24-hr BPV reported lower prevalence and severity of organ damage compared to those with high BPV (A. F. Chen, 2008).

2.10 Classification of Blood Pressure Variability

Research data reveals four main classifications of BPV, which includes ultra-short term BPV, short-term BPV, mid-term BPV and long-term BPV (Chadachan, Ye, Tay, Subramaniam, & Setia, 2018). These classifications are based on different BPV time ranges . Ultra-short term is BPV within beat to beat range, short-term BPV is within 24 hour, minute-minute, hour-to-hour, and day-to-night range, mid-term BPV is within day-to-day range and long-term BPV is within visits-to-visits over weeks, months and years range(Schutte, Kollias, & Stergiou, 2022). These different time ranges forming a basis for BPV classification is a reflection of the complex strands of dynamic changes taking place in the human system in response to intrinsic and extrinsic factors that contribute to BP homeostasis, ensuring good organ perfusion (Parati, Torlasco, Pengo, Bilo, & Ochoa, 2020).

2.11 Ultra-short Term Blood Pressure Variability

Ultra-short term or very short term BPV refers to beat-to-beat blood pressure changes which occurs as a result of regulatory cardiovascular systems including baroreceptor reflexes, renin-angiotensin systems endothelial response to nitric oxide and vascular myogenic response (Höcht, 2013). Ultra-short term BPV is also as a result of sympathetic activity, emotional responses and sleep(Parati, et al., 2013). It was assessed in the past through an invasive technique known as the Oxford intra-arterial method but currently, a non-invasive technique known as the Penaz method, where finger sensors are used in photoplesthysmography, to determine ultra-short BPV (Parati, Ochoa, Lombardi, & Bilo, 2015).

2.12 Long term Blood Pressure Variability

Long term BPV captures blood pressure fluctuations occurring within day-to-day, visits-to-visits and season-to-season time ranges(Chenniappan, 2015). Findings regarding factors contributing to long term BPV are scattered and unclear(Höcht, 2013). Some studies isolate long term BPV, from mid-term BPV (day-to-day BP variation), while other studies merge mid-term BPV with long-term BPV, by maintaining day-to-day BP variation as a part of long term BPV, therefore making the differences between mid-term BPV and long term BPV unclear. Day-to-day BP variation as a component of long term BPV has been reported to be influenced by individual behavior within the day, in that, BP readings from ambulatory monitoring showing different trend of BP variations in working days (weekdays) and weekends(Mancia, 2012). Other studies report follow-up visits of patients receiving anti-hypertensive treatment may result in anti-hypertensive related factors such as inconsistent control of BP, poor adherence to prescribed BP drugs, dose omission and improper dosing contributes to long term BPV (Parati, et al., 2020). Reports from large population studies has shown an association between increasing long term BPV and increasing age, gender, sleep disorders, cardiovascular disorders, higher mean systolic BP readings and associated pulse pressures(Muntner et al., 2011)

2.13 Short term Blood Pressure Variability

Short term BPV refers to the fluctuation of BP within the 24 hour time range which occurs as a result of autonomic function and arterial elasticity (Parati, et al., 2013). Short term BPV is characterized by circadian BP variation, which includes nocturnal BP dipping and morning BP rise (Chenniappan, 2015). There are two main instruments used to monitor short-term BPV and these include ABPM, measuring BP every 15-30 minutes for 24 hours and Home Blood Pressure Monitors (HBPM) during periods of sleep(Shimamoto et al., 2014). Short term BPV is represented and assessed by various indices known as Blood pressure variability indices (Chadachan, et al., 2018; Höcht, 2013). BPV indices are very instrumental in assessing and quantifying overall blood pressure variability, by taking into account the various standard deviations, sequence of day and nighttime BP readings, irregularity in BP levels and early morning BP rise(Parati, et al., 2013; Parati, et al., 2020).Current research has identified four main metrics or indices that characterize blood pressure variability and these indices include, Standard deviation (SD), Coefficient of variation(CoV), Average real variability (ARV) and Variability independent of mean (VIM) (Kim et al., 2019). The earliest and mostly used indices in quantifying and assessing BP variability is the standard deviation(Schutte, et al., 2022). Research has identified SD of average BP as an index influencing both significant and insignificant association between BPV and cardiovascular events(CE) even in the presence of notable risk factors(Mena et al., 2005). The European Society of Hypertension (ESH) and European Society of Cardiology's (Marfella et al.) task force for the management of arterial hypertension has reported that organ damage and related cardiovascular events are determined by BPV assessed by SD(Mancia & Grassi, 2008). Current research has shown some limitation of SD in quatifying BP variation in that, SD reflects the variation around the mean but does not reveal the order in which BP measurements were determined (Pierdomenico

et al., 2009). Due to these limitations most researchers prefer BPV indices such as 24 hour weighted SD, CoV, and ARV. These indices do not have equal prognostic outcomes since they assess different aspects of the BPV complex (Kim, et al., 2019). These indices include the Coefficient of variation, standard deviation, average real variability (ARV), and Variability independent of the mean (VIM).

2.14 Circadian Rhythm and Blood Pressure Profile during 24-Hour ABPM among ALHIV

Circadian Rhythm is a natural internal process that regulates the sleep-wake cycle and repeats roughly every 24 hours. Circadian rhythms originate from within the organism, thus it is endogenous and is sensitive to the environment (Edgar, et al., 2012). The 24-hour cycles that do not originate from within an organism cannot be said to be a circadian rhythm but are termed as diurnal rhythms (Vitaterna,Takahashi,& Turek, 2001). Intraarterial blood pressure measurements and noninvasive 24-hour ambulatory blood pressure monitoring (ABPM) have been used to study the definite and consistent circadian rhythm that blood pressure (BP) exhibits (Burnier et al., 2020). During the transition from sleep to waking, there is a sharp morning spike in blood pressure that can reach 15 to 25 mmHg (Sarkar, Mukherjee, Chai-Coetzer, & McEvoy, 2018). Then, although it fluctuates, the blood pressure remains very consistent, reaching its maximum points in the morning and the evening(Burnier, et al., 2020). As you get ready for bed, your blood pressure gradually drops until it reaches its lowest points while you sleep at night. In addition to this circadian rhythm, BP changes happen in reaction to a number of outside variables that significantly contribute to the overall 24-h BP variability, with the baroreflex having a strong antioscillatory effect(Suwanprathes et al., 2010). In 24-Hour ABPM, it is very important to determine circadian blood pressure profile. Circadian Blood Pressure profiles outlined by ABPM, comprises daytime BP profiles and nighttime BP profiles. Nighttime BP profiles can be divided into three patterns: Dippers (individuals whose BP falls at night), Non-dippers (Individuals who's BP does not fall at night) and finally reverse dippers or risers (individuals whose BP rises at night). Each pattern connotes a peculiar cardiovascular event or characteristic. Risers or reverse dippers are common among the older populace, nighttime dippers predict lower cardiovascular risk, and nighttime rise

is associated with higher cardiovascular risk. In 2010, Giuseppe Vitoro and his colleagues reported the negative influence of HIV infection on day-night blood pressure variability. They compared circadian BP profiles in treatment-naïve HIV-infected patients and healthy controlled subjects. They discovered HIV infection affected circadian rhythm. They also concluded that findings on day-night BP changes might play a role in the HIV-related increase in CV risk.

2.14 Ambulatory Blood Pressure Monitoring

According to existing data, the diagnosis of hypertension based on Office Blood Pressure (OBP) measurement in children and adolescents is defined by BP ≥95th percentile for age, sex, and height; or ≥130/80 mm Hg for adolescents ≥13 years old. (NICE, 2011). However, this OBP is insufficient in diagnosing hypertension accurately. A more accurate tool for diagnosing Hypertension is, therefore, the Ambulatory Blood Pressure Monitoring tool. ABPM is capable of determining blood pressure levels, blood pressure load, and blood pressure variability(Hodgkinson et al., 2011). The use of ambulatory Blood Pressure Monitoring (ABPM) has been accepted worldwide, as a diagnostic tool to predict cardiovascular complications (O'Brien, Asmar, & Beilin, 2003). According to history, the European Society of Hypertension held one of its maiden meetings to deliberate on the use of ABPM in the year 1978, and after this meeting, several consensus conferences have been held on ABPM (O'Brien, Asmar, & Beilin, 2003). It has been a subject of keen interest by the scientific community, with over 10,000 publications in PubMed in the year 2012 (O'Brien, Asmar, & Beilin, 2003). Ambulatory blood pressure monitoring comprises short-term blood pressure monitoring which is referred to as 24-hour blood pressure monitoring and long-term blood pressure monitoring (Mancia, G., 2012). 24-hour ambulatory blood pressure is known as one of the most accurate noninvasive diagnostic techniques for diagnosing hypertension (Mancia & Verdecchia, 2015). This diagnostic technique can be used to characterize circadian BP profiles and nighttime BP. In normal individuals, BP decreases during sleep by 10% to 20% and increases on waking (Giuseppe, et al., 2010). For a given hypertensive group who had undergone ambulatory blood pressure monitoring, there can be differences in outcome in their blood pressure when comparing ambulatory blood pressure to normal clinical blood pressure (office blood pressure) measured by physicians (Korljan Babić et al., 2009). One of these outcomes is where the OBP is elevated but the ambulatory blood

pressure is normal. This outcome is known as “White-Coat” Hypertension (WCHT) (Takayoshi, et al., 2005). There is another outcome whereby individuals have elevated ambulatory blood pressure but normal OBP, this is known as “masked” hypertension (WHT) (Pickering, Davidson, & Gerin, 2002). These varying outcomes in hypertension are because of ABPM.

2.15 Nocturnal BP among PLHIV

Dipping is a physiological phenomena where a person has a 10-15% nocturnal reduction ("dipping") in blood pressure while they are resting at night (Sachdeva & Weder, 2006). Studies done in sub-Saharan Africa have shown evidence that non-dipping blood pressure is more common in PLWH (MS Borkum et al., 2017). According to earlier research, PLHIV may have an irregular diurnal blood pressure pattern more frequently than HIV-negative people (Kent, et al., 2016). People who have less nocturnal BP fall may find it beneficial to take antihypertensive medicine at night rather than in the morning (Mahabala, Kamath, Bhaskaran, Pai, & Pai, 2013). Taking antihypertensive medicine at night as opposed to during the day was linked to a considerably bigger nocturnal Systolic BP and Diastolic BP dip and a decrease in CVD events among a randomized controlled study of 2,156 members of the general population (Hermida, Ayala, Mojón, & Fernández, 2010). According to this research, for every 5% increase in nocturnal Systolic BP and Diastolic BP dipping, hazard ratios for CVD were 0.87 (95% CI: 0.81, 0.94) and 0.86 (95% CI: 0.80, 0.92), respectively, after adjusting for mean BP on ABPM (Hermida, et al., 2010). However, this study used a 2 days ABPM period rather than the customary 24-hour period and only included subjects who were of the same ethnicity in a single Spanish facility (Schillaci, Battista, Settimi, Schillaci, & Pucci, 2015). Additionally, African Americans with renal illness found that taking antihypertensive medication at night did not lower nighttime BP compared to

taking medication in the morning (Rahman et al., 2013). Addressing sleep issues and psychosocial stress present in this community, which may adversely affect BP dipping, is another promising, but understudied, strategy to promote nocturnal BP drops in HIV+ patients(Seay et al., 2013; Sherr et al., 2011). There are limited data on how interventions addressing psychological factors might alter nocturnal BP reductions, despite the fact that these interventions are crucial for improving the quality of life and care for HIV+ patients (Kent, et al., 2016). In the general population, sleep apnoea treatment has been found to lower overnight blood pressure, and this helps HIV+ people with non-dipping SBP (Baguet et al., 2015). There are few other studies examining the impact of treating insomnia and other types of sleep disruptions on the reduction of nocturnal blood pressure(Yilmaz et al., 2007).

2.16 Early morning BP surge among PLHIV

A typical physiological occurrence of circadian or diurnal BPV is a morning BP rise (Sogunuru et al., 2019). It has been described as the difference between the lowest nighttime BP and the morning BP (taken two hours after awakening) (Kario et al., 2003; Sogunuru, et al., 2019). High morning surge may harm target organs such the heart, including left ventricular hypertrophy and left ventricular mass index (LVMI), the arteries, including arterial stiffness and carotid atherosclerosis(Marfella, et al., 2007). In reaction to the sympathetic nervous system's natural activation on morning awakening, blood pressure increases dramatically in the early morning (Peixoto & White, 2007). Other significant hemodynamic and neuro-hormonal changes, including an increase in heart rate, vascular tone and blood viscosity, as well as a decrease in vagal activity, are also connected to this early morning surge (Peixoto & White, 2007).

2.17 Self-reported Sleep and Blood Pressure Variability in HIV adolescents

Sleep as a behavioral characteristic can induce variation in blood pressure over 24 hours. The neurological, cardiovascular, respiratory, endocrine, and immunological systems all demonstrate reciprocal interplay during sleep. An increased risk of cognitive problems, poor academic performance, behavioral disorders, accidents, as well as chronic conditions including obesity and hypertension is linked to poor sleep quality (Carskadon, 2011). The physiology of sleep has particular characteristics during adolescence, a stage defined by noticeable physiological transformations like puberty and sociocultural changes like the development of personality(Gazini et al., 2012). Although there is disagreement on the definition of sleep needs, it is widely agreed that most adolescents require at least nine hours of sleep each day(Owens, Belon, & Moss, 2010). A lag in phases, which is characterized by a delay in the sleep-wake cycle and is shown by delayed sleeping and waking times, is the primary physiological mechanism behind this trait (Carskadon, 2011). However, a sizable part of teenagers suffer from sleep disorders, which are primarily due to insufficient sleep, a need for social connection, insufficient school schedules, subpar living situations, and chronic ailments(De-La-Llata-Romero et al., 2011). In normal individuals, blood pressure decreases between the ranges 10% and 20% during sleep (Giuseppe, et al., 2010). Sleep involves calmness and a state of unconsciousness of our external environment which reflects a significant decrease in BP during the night(Silvani, 2008). Sleep deprivation because of sleep disturbance of any form therefore do not reflect a decrease in BP at night (Chadachan, et al., 2018). Currently, two large epidemiological research reported an association between sleep duration and the prevalence of hypertension. Loss of sleep may induce an increase in sympathetic activity that may result in an increase in blood pressure (Gangwisch et al., 2006). Another study that was done among hypertensive HIV positive patients showed the prevalence of nocturnal dip

in blood pressure as a result of different lifestyles coupled with different sleep periods (Bernardino et al., 2011). Individuals with nocturnal dip stand a great risk of organ damage (Giuseppe, et al., 2010).

Although sleep difficulties are a common issue globally, they are more severe in people who are HIV positive than in the general population and can have an impact on these patients' quality of life(Reid & Dwyer, 2005). Studies has reported that, the intensity of HIV symptoms and low ART adherence may result in poor sleep quality(Babson, Heinz, & Bonn-Miller, 2013). In a study done among Iranian PLHIV population, 47.5% patients who qualified for antiretroviral therapy, reported sleep problems and in other HIV positive groups, sleep problems have been documented in 63% to 100% of people(Wibbeler, Reichelt, Husstedt, & Evers, 2012). Traditionally, efavirenz (EFV) has been the medicine most frequently linked to sleep disturbances when it comes to the interaction between antiretrovirals (ARV) and sleep disorders. Vibrant dreams and nightmares have been linked to EFV, which some research suggest may potentially affect sleep physiology (Moyle, Fletcher, Brown, Mandalia, & Gazzard, 2006). Further studies reveal insomnia prevalence is 56% among PLHIV, and Odd Ratio (OR) of 1.17 (95% CI 1.04 -1.34), confirming an association between the severity of HIV symptom and insomnia (Gamaldo et al., 2013). Additionally, 73% of PLHIV reports some sleep difficulty, resulting from upper airway obstruction (Obstructive sleep syndrome)(Patil et al., 2014). Sleep disorder and poor sleep quality among PLHIV reflects variation in prevalence among different studies(Kunisaki et al., 2015). Sleep disorder and poor sleep quality may result in increased CVD risk (Marin et al., 2012). Another study reports that, a significant risk factor for obesity and CVD is inadequate sleep (Lucassen, Rother, & Cizza, 2012).

2.18 Association between BPV and selected risk factors

Studies have reported an association of BP variability with age, absolute BP levels and adiposity (Li et al., 2010).Age, male sex, absolute BP levels, obesity, and low socioeconomic position are all characteristics that are generally similar to established predictors of high cardiovascular risk(Schillaci & Parati, 2010). Prior research had demonstrated that BP variability rises with age and BP levels (Yano et al., 2020). Age, male sex, average BP, adiposity, and low socioeconomic status assessed at the baseline evaluation all predicted a higher 24-h BP variability in the following years in a longitudinal analysis of an ethnically mixed cohort of 641 young subjects prospectively followed for up to 15 years with repeated (up to 12) ambulatory BP-monitoring sessions (Schillaci & Parati, 2010).

Another study that utilized ARV to measure BPV found that greater mean 24-hour SBP, larger waist circumference, and older age were also linked to increased 24-hour SBP variability. Increased mean 24-h DBP, larger waist circumference, and female gender were linked to higher 24-h DBP variability (Tanner et al., 2015). A U-shaped curve association between BPV and cardiovascular risk seems to exist, and it is considerably more pronounced in individuals with hypertension than in those with normal blood pressure (Kario, 2015). As a result, both low BPV and high BPV seem to be pathogenic. Numerous epidemiological studies have shown a considerable correlation between the diurnal variation in blood pressure and the timing of the beginning of cardiovascular events(Amici et al., 2009). Additionally, it has been demonstrated that aberrant circadian BPV with a non-dipping pattern raises the possibility of experiencing a stroke event (Sogunuru, et al., 2019). Reduced BP decreases could partially account for the elevated CVD risk that exists in HIV+ people (Shimbo et al.,, 2015). A meta-analysis of three studies found that HIV+ people had a higher risk of CVD outcomes than HIV negative people (Islam et al., 2012).

After justifying outcomes of CVD risk variables, such as hypertension based on clinic blood pressure measurements and antihypertensive medication, there are still problems of high CVD risk associated with HIV+ status (Hemkens & Bucher, 2014). After controlling for therapy and blood pressure, reports from the general population have shown a non-dipping systolic blood pressure pattern which was linked to a higher risk of CVD and death (Boggia, 2007). For instance, after adjusting for 24-hour mean SBP, a research conducted in a cohort of patients with systolic hypertension that was not treated found that for each 10% absolute increase in the nighttime-to-daytime SBP, the ratio was linked with a hazard ratio for CVD events of 1.41 (95% CI: 1.03, 1.94)(Kent, et al., 2016). According to another study, systolic blood pressure (SBP) of non-dipping population was linked to a 2.50 (97% CI: 1.28, 4.88) hazard ratio for CVD mortality (Boggia, 2007; Kent, et al., 2016). In the general population, a non-dipping SBP pattern has also been linked to a higher risk of congestive heart failure and non-cardiovascular death (Ingelsson et al.,, 2006).

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Setting

The study was conducted in antiretroviral therapy facilities in the Greater Accra Region. Facilities with a minimum of 40 adolescent clients on treatment as of December 2021 was eligible for inclusion. However, facilities that did not consent to participate was not included. Because HIV infection is a sensitive issue colored with stigmatization in Ghana, the identity of participant clinics and visitation was not revealed.

3.1 Study Population

HIV positive patients between the ages of 6 - 19 years attending various HIV clinics in Accra qualified to be part of the study.

3.2 Study Design

A prospective cross-sectional study design was used for this study.

3.3 Sampling Technique

A cluster-randomized sampling technique was used for this study. Recruitment was done on two levels: health facilities and adolescents living with HIV.

a. Health facility recruitment

There was random allocation of health facilities by clusters. Potential participating clusters (i.e. health facilities) through their respective administrators were invited to participate. In each consenting facility, a primary contact person was identified for the research team.

b. Participant (ALHIV) recruitment

Using a random sequence provided by the study team, a random sample of 20 children and adolescents living with HIV per facility was selected for the purpose of this study.

3.3.1 Sample size calculation

The sample size was calculated by power analysis of individual proportions. From the literature search, no study has reported on the utility of various indices of ABPM in diagnosing hypertension or other CVDs in ALHIV. Therefore, the minimum sample size of 122 was calculated based on the prevalence of hypertension using ABPM in non-HIV adolescents from Tanzania(Nsanya et al., 2021), which was reported as 2.6%; and the prevalence of hypertension using OBP in ALHIV from South Africa (Kamkuemah, et al., 2020) which was reported as 14%. With the certainty that the true require sample size may fall within this prevalence, the minimum sample size was computed with IBM SPSS version as below:

```
POWER PROPORTIONS INDEPENDENT
  /PARAMETERS TEST=NONDIRECTIONAL SIGNIFICANCE=0.05 POWER=.9 NRATIO =1 PROP
ORTIONS=.026 .14
    METHOD=CHISQ ESTIMATE=NORMAL POOLED=TRUE.
```

Power Analysis - Independent Proportions

Power Analysis Table

				Test Assumptions	
	N1	N2	Actual Power[b]	Power	Risk Difference
Test for Proportion Difference[a]	122	122	.900	.9	-.114

Power Analysis Table

	Test Assumptions		
	Risk Ratio	Odds Ratio	Sig.
Test for Proportion Difference[a]	.186	.164	.05

a. Two-sided test using large-sample approximation.

b. The estimation of power is based on the Pearson Chi-Square test and the pooled standard deviation.

3.3.2 Inclusion Criteria

Ghanaian adolescents between ages 6 and 19 years with HIV infection, living in Accra and attending ART clinic who has given a formal assent and consent with their caregivers and guardians to participate in this study.

3.3.3 Exclusion Criteria

1. Adolescents with HIV infection whose caregivers or guardians do not give a formal consent.

2. Adolescents with far advanced (stage 3 and stage 4) HIV infection who are very weak and are unable to participate in the study.

3.4 Data Collection

3.4.1 Ambulatory monitoring assessment

All BP readings were reviewed to eliminate out-of-range readings and errors that may have resulted from equipment problems or motion of artifacts using predetermined acceptable ranges of Systolic and Diastolic blood pressures (Hickson et al., 2011). There were 7 available ABPM machines, and therefore, data was collected from 7 patients each day till the fourth week. A 24-hour ABPM was performed using ABPM 50 with the BP readings set at 15 minutes intervals during the daytime, 10 am to 8 pm, and 20 minutes intervals during the night, 10 pm to 6 am because according to literature, the frequency of measurements within the 24 hours should not be more than every 15 minutes during the day since normal daily activity could be massively affected and if less than 30 minutes, there could be an inadequate number of measurements (O'brein, E., 2008). Frequent measurements at night may also interrupt sleep and reduce the prognostic value of ABPM (Verdecchia et al., 2007). Registries were performed on working days, non-dominant arms and subjects was instructed to maintain their usual

activities and keep their arm extended and immobile at the time of cuff inflation. Time was allotted for fitting the monitor and preparing the patient for the monitoring period to ensure good results because research has shown that educating patients on the process of monitoring leads to successful ABPM (O'brein, E., 2008). Short-term reading-reading blood pressure variability was measured by using the standard deviation of daytime (SDd) and standard deviation of nighttime (Sdn). BPV is expressed as Blood pressure variability = (The SD of daytime systolic blood pressure +The SD of daytime diastolic blood pressure +The SD of nighttime systolic blood pressure + SD of nighttime diastolic blood pressure)/4. Other Blood pressure variability indices such as average real variability (ARV), mean absolute differences between successive Blood pressure measurements, and Coefficient of variation (CV) will also be determined by dividing the various SDs with the mean

3.4.2 Questionnaire administration and anthropometric measurement

A structured questionnaire was used to collect socio-demographic and lifestyle data (age, gender, personal medical history, smoking, and alcohol intake). Sleep quality was assessed using the Pittsburgh sleep quality index (PSQI). The PSQI is a nineteen-item, validated questionnaire that measures sleep quality over the past month. The first four questions ask participants to report the time they went to bed (not necessarily the time they fell asleep), the number of minutes it took to fall asleep when they awoke, and hours of sleep per night. The next ten questions ask how often the participant had trouble sleeping because of reasons such as having to get up to use the restroom, feeling too hot or too cold, having pain, or waking up in the middle of the night, with questions answered on a four-point scale ranging from ‘never’ to ‘three times or more a week’. Participants would also rate their use of medication on the same four-point scale , how often they have had trouble staying awake during social activity, and if enthusiasm to complete tasks has reduced.

Lastly, participants would provide a subjective rating of their sleep quality on a four-point scale from 'very good' to 'very bad'.The PSQI questions were combined into seven different scores ranging from 0 (no difficulty) to 3 (severe difficulty) on topics of sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, sleep medication, and daytime dysfunction per the PSQI scoring guidelines. The seven component scores were summed for a final PSQI score that ranged from 0 to 21, with sleep quality declining with each increase in the score. PSQI scores >5 was indicative of poor sleep quality.

Anthropometric measurement of participants was also conducted. Body weight (in kilograms) and height (in meters) were taken for the calculation of Body mass index (BMI). Height was measured using a stadiometer , where participant was required to stand upright having only the head and buttocks touching the meter rule. Weight of participants were measured with a medical weighing scale.

3.4.3 Data Processing and Analyses

Data was analyzed using Excel 2016 and SPSS version 25. Excel was used to code and clean the data before exporting to SPSS. Continuous variables among data was expressed as means ± SD, while frequencies and percentages was used for categorical variables. Data was summarized using tables and graphs such as pie charts, and scatter plots. Association between ART, BMI and sleep quality with circadian and Beat-to-beat BP variability were presented in merged bar graph with logistic regression tables. Circadian variability indices such as early morning surge and nocturnal dip was calculated in excel. Variables such as Self-reported sleep quality, BMI, and ART regimen was held as independent variables while Beat-to-beat BPV variables and circadian variability variables were held as dependent variables. Nocturnal dip was calculated based on Systolic Blood pressure using the formula : $100 \times (\text{daytime} - \text{nighttime SBP})/(\text{daytime SBP})$ and was further

grouped in four categories: Dipper (≥10% but < 20%); non-dipper (≥0% but < 10%); extreme dipper (≥20%); and reverse dipper (<0%) (Williams et al., 2018). Early morning BP surge was calculated using this formula: BP surge= Morning SBP on rising – SBP on supine >30 minutes before rising (Kario, 2010). Blood pressure calculation and classification of BP levels was based on European Society of Hypertension guidelines (ESH) guidelines for management of Hypertension in children and adolescents.

Multivariate logistic regression was used to analyze the association between sleep quality and blood pressure variability (Average real variability, ARV and Standard deviation, SD} and circadian variation (day-time vs night-time BP, nocturnal dip, morning rise). Linear regression was used to analyze the association between cardiovascular outcomes and blood pressure variability, presenting outcomes in merged linear regression scatter plot diagrams with regression tables.

3.4.4 Data Management

Data collected from patients was stored in a folder on the researchers' laptop, locked with a password that only the researcher can have access to. Hardcopies of research documents were burnt for the sake of patients confidentiality and information from electronic questionnaires were deleted and removed from the server where information from participants was stored for the sake of confidentiality of the participant. Documents was kept till the study is completed.

3.4.5 Dissemination of Results

The findings of this study were for academic purposes and was submitted to the University of Ghana School Of Graduate Studies. The findings will also be published in scientific journals and was presented at scientific seminars and workshops. A copy of the research will also be presented to the Ghana AIDS Commission and the clinics and hospitals where the participants go for healthcare.

3.4.6 Ethical Consideration

Ethical approval was sought from the College of Health Sciences Ethics and Protocol Review Committee before the commencement of the study. Written informed consent was obtained from the participants and their parent(s)/guardian(s) after a thorough discussion of the rationale, risks, and benefits of the study, as well as addressing all their concerns. Confidentiality of the data provided by the study participants was safeguarded by using codes instead of names to identify participants, storage of hard copies of data in a secured locker, and softcopies using a password-protected file. Only the lead investigators can have access to participants' data. All the data collected from the study participants was used for this study only. Participants will not be coerced or enticed by any means to consent to the study, and they was made to understand that they were at liberty to withdraw from the study at their own will without any repercussions.

CHAPTER FOUR

4.0 RESULTS

Table 1. Demographic characteristics of ALHIV Population

Characteristics	GENDER		χ 2	P-value
	Male N(%)= 56(45.9)	Female N(%)= 66(54.1)		
Age group(years)				
6-9	4(7.1%)	4(6.1%)	.790	.674
10-13	21(37.5%)	30(45.5%)		
>=14	31(55.4%)	32(48.5%)		
BMI				
Healthy	18(32.1%)	21(31.8%)	4.065	.254
Underweight	27(48.2%)	29(43.9%)		
Overweight	6(10.7%)	3(4.5%)		
Obese	5(8.9%)	13(19.7%)		
ART REGIMEN				
EFV based	30(53.6%)	30(45.5%)	3.631	.304
Lamivudine based	3(5.4%)	4(6.1%)		
TLD based	21(37.5%)	32(48.5%)		
NVP based	2(3.6%)	0(0%)		
SLEEP QUALITY(GSPQI)				
Poor sleep quality	12(21.4%)	18(27.3%)	.558	.455
Good sleep quality	44(78.6%)	48(72.7%)		
BP DIAGNOSIS				
Masked Hypertension	11(19.6%)	9(13.8%)	1.23	.746
Normal BP	45(80.4%)	56(86.2%)		
OFFICE BP				
Normal BP	43(76.8%)	53(80.3%)	.733	.382
Elevated BP	3(5.4%)	5(7.6%)		
Hypertension	10(17.8%)	8(12.1%)		

AMBULATORY BP				
Normal BP	50(89.3%)	64(97%)	2.91	0.08
Elevated BP	6(10.7%)	2(3%)		
NOCTURNAL BP				
Dippers	27(48.2%)	29(43.9%)		
Non Dippers	18(32.1%)	21(31.8%)	4.07	0.25
Extreme Dippers	6(10.7%)	3(4.5%)		
Reverse Dippers	5(8.9%)	13(19.7%)		

4.1 Demographic Characteristics of ALHIV Population.

.Ages of participants were from 6 years to 19 years; with a mean age of 13.6 ± 3.2 years. The males were (N=56(45.9%)) and the females were (N=66 (54.1%)). Most of the females (N=32(48.5%)) were aged 14 years and above. Females (N=21(31.8%)) had a healthier BMI compared to males (N=18(32.1%)). There was no significant relationship between gender and BMI of participants, p-value= 0.25. There were more Males on EFV compared to females, (N=30(53.6%)).There were more females, (N=4(6.1%)) on lamivudine compared to males (N=3(5.4%)). There were more females, (N=32(48.5%)) on TLD regimen compared to males 21(37.5%). Only males were on Nevirapine, (N=2(3.6%)). Relationship between Gender and ART was not significant, p-value=0.304. For sleep quality comparison among genders, most females reported poor sleep quality, (N=18(27.3%)). Most females had good sleep quality (N=48(72.7%)). Relationship between Gender and sleep quality was not significant, p-value=0.455. For BP diagnosis, more males (N=11(19.6%)) had masked hypertension compared to females. More females, (N=56(86.2%)) reported normal BP compared to males (N=45(80.4%)). Relationship between gender and BP diagnosis was not statistically significant, p-value=0.76. For office BP, more females, (N=53(80.3%)) reported normal BP compared to males (N=43(76.8%)). More females (N=5(7.6%)) reported elevated office BP compared to males 3(5.4%). More males had their BP in the hypertension range, (N=10(17.8%)) compared to females (N=8(12.1%)). Relationship between gender and Office BP was not statistically significant, p-value=0.382. For Ambulatory BP, more females, 64(97%) reported Normal BP compared to males,

50(89.3%). P-value=0.08, which shows a statistically insignificant association between Gender and

ambulatory BP. For Nocturnal dip, most females, (N=29(43.9%)) were Dippers, most females 21(31.8%) were non-dippers, most males were extreme dipper (N=6(10.7%)), and most females were reverse dippers (N=13(19.7%)). Relationship between Gender and Nocturnal BP were insignificant, p-value= 0.25.

4.2 Prevalence of High blood pressure among ALHIV

From Fig1a, Based on ESH guidelines, majority of ALHIV recorded a normal BP (<90 BPpct/(<90 BPpct mmHg) of (N=70 (57.4%)) , followed by normotensive BP (N=33(27%)) and High normal (>=90pct mmHg/ <95pct mmHg). Hypertension was reported among (N=13 (10.6)) of which (N=2 (1.64%) reported Hypertension stage 1 (>=pct90 and <pct95 mmHg), Hypertension stage II was (N=1 (0.82%)), Isolated Diastolic Hypertension (IDH) was (N=6 (4.82)), Isolated Systolic Hypertension (ISH) (>(pct99+5 mmHg/<pct90mmHg) was (N=3 (2.5%).

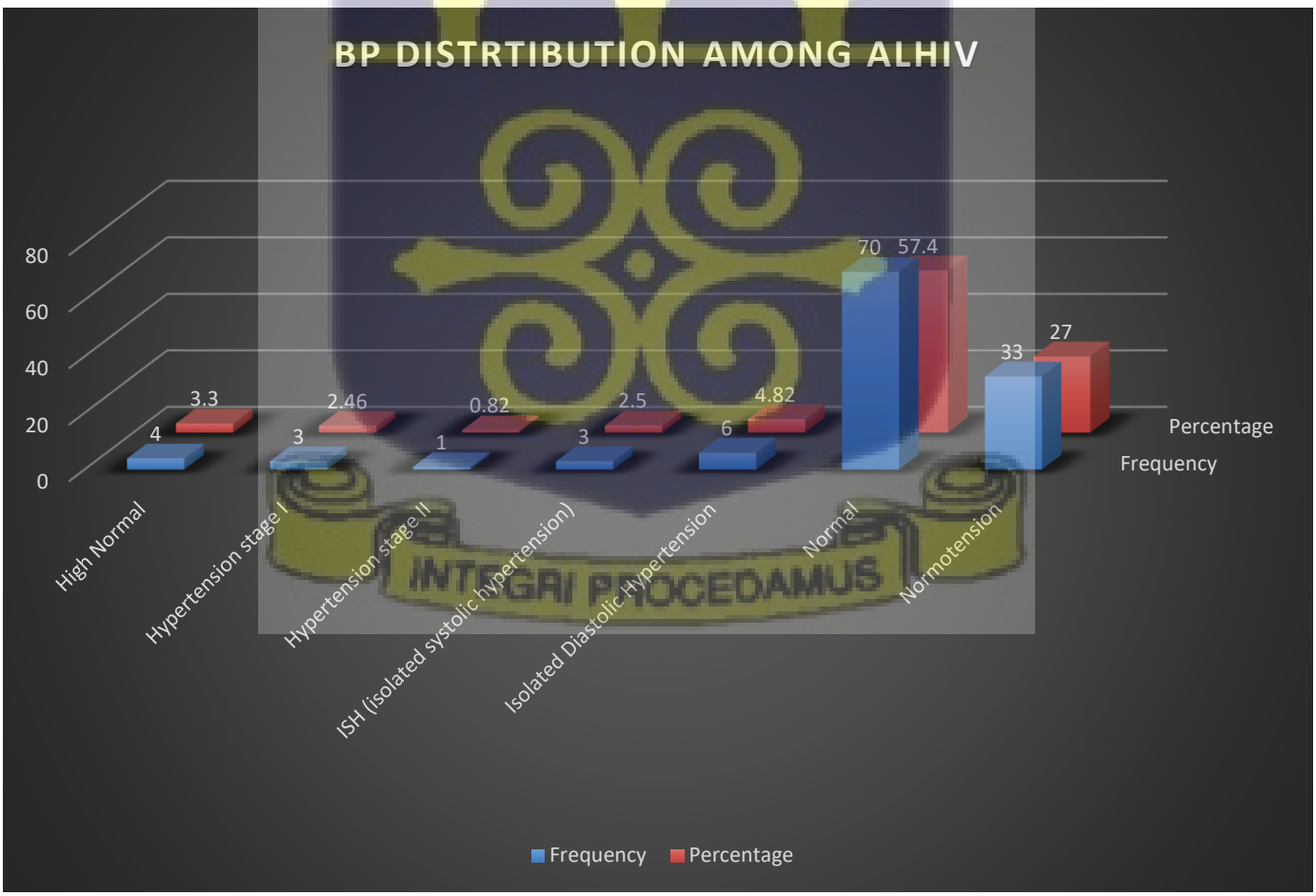
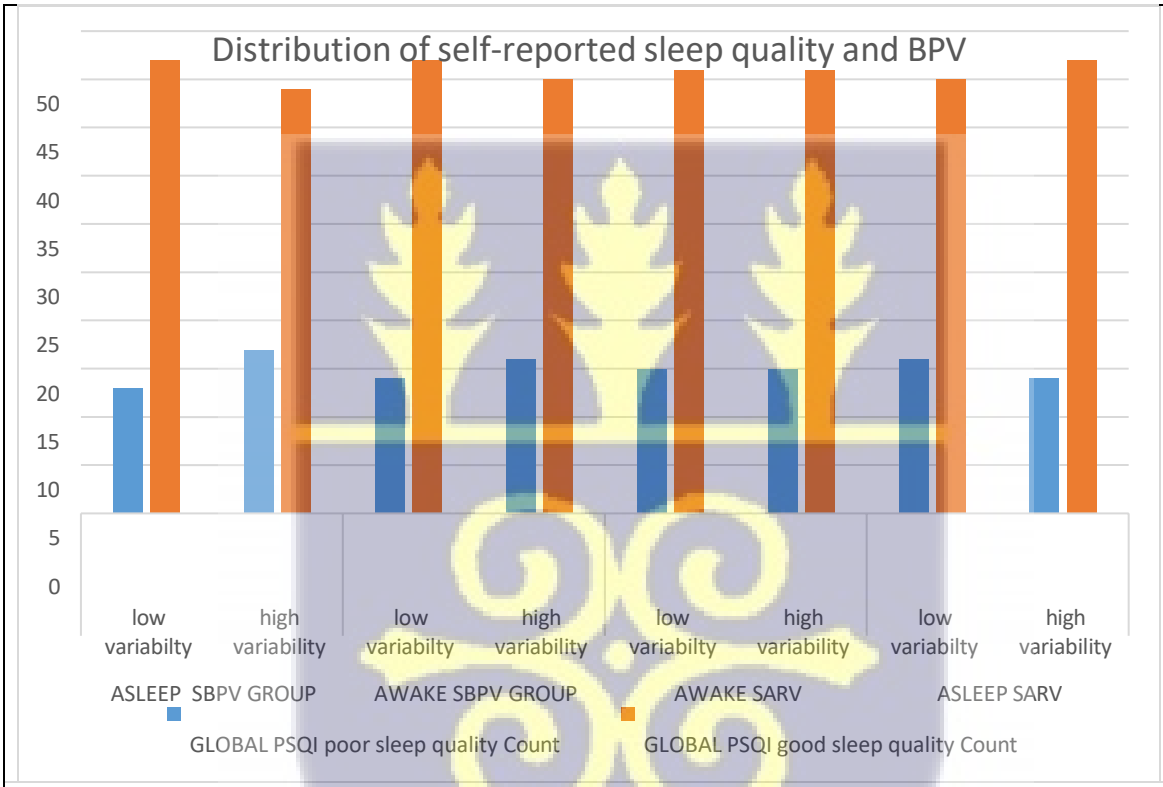


Fig 1a: Distribution of Blood Pressure Level among ALHIV

4.3 Association between Self-reported sleep quality and beat-to-beat variability among ALHIV

The outcome showed no significant association between sleep quality and SD blood pressure

Variability since all recorded p-values > 0.05.



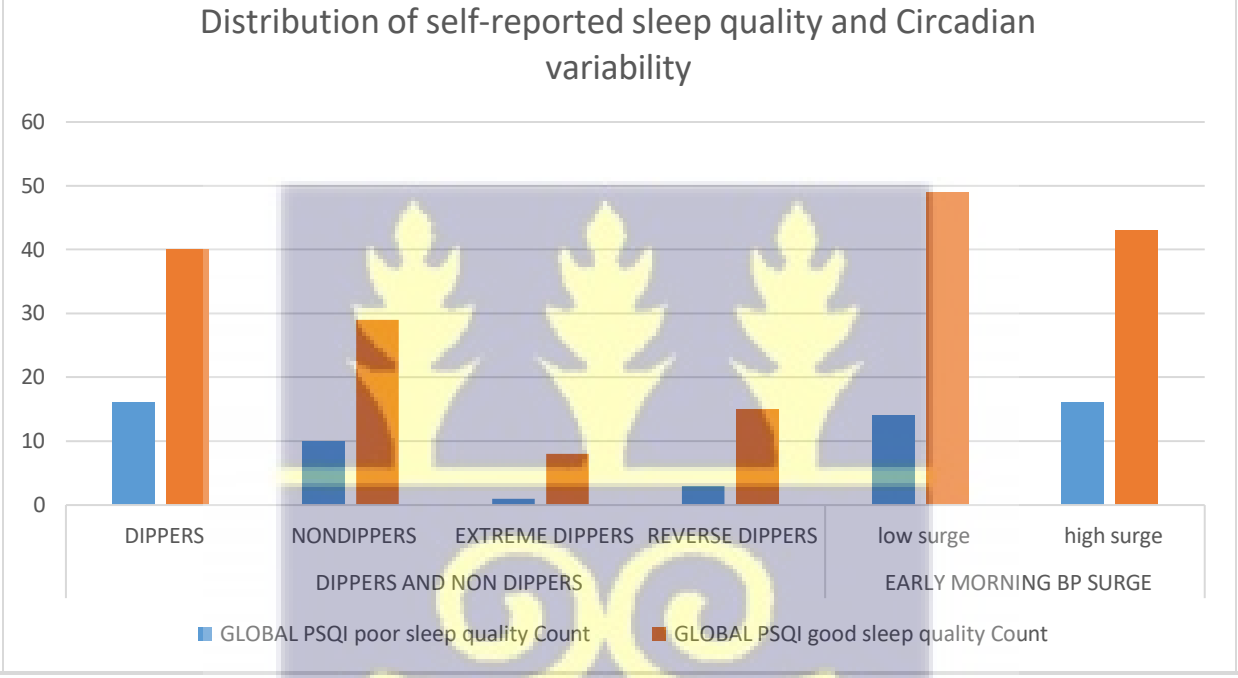
A Binary logistic regression between sleep quality and Blood pressure variability (beat-to-beat blood pressure and circadian variability)

variable	β	SE	Wald	OR(95% CI)	P-value
24 SD BPV	-0.004	0.31	0.16	1.00(0.94-1.06)	0.899
Asleep ARV	0.023	0.039	0.357	1.02(0.95-1.10)	0.550
Awake ARV	0.008	0.062	0.018	1.01(0.89-1.14)	0.894
Awake SD BPV	0.014	0.034	0.183	1.01(0.95-1.10)	.670
Asleep SD BPV	-0.024	0.038	0.410	0.98(0.91-1.05)	0.522

Fig 1b: logistic regression table showing the distribution of the association of self-reported sleep quality and beat-to-beat BP variability

4.4 Self-reported sleep quality and circadian variability among ALHIV.

The p-value for the association between self-reported sleep and circadian variability (Nocturnal dip, p-value=0.984, BP surge, p-value = 0.695)



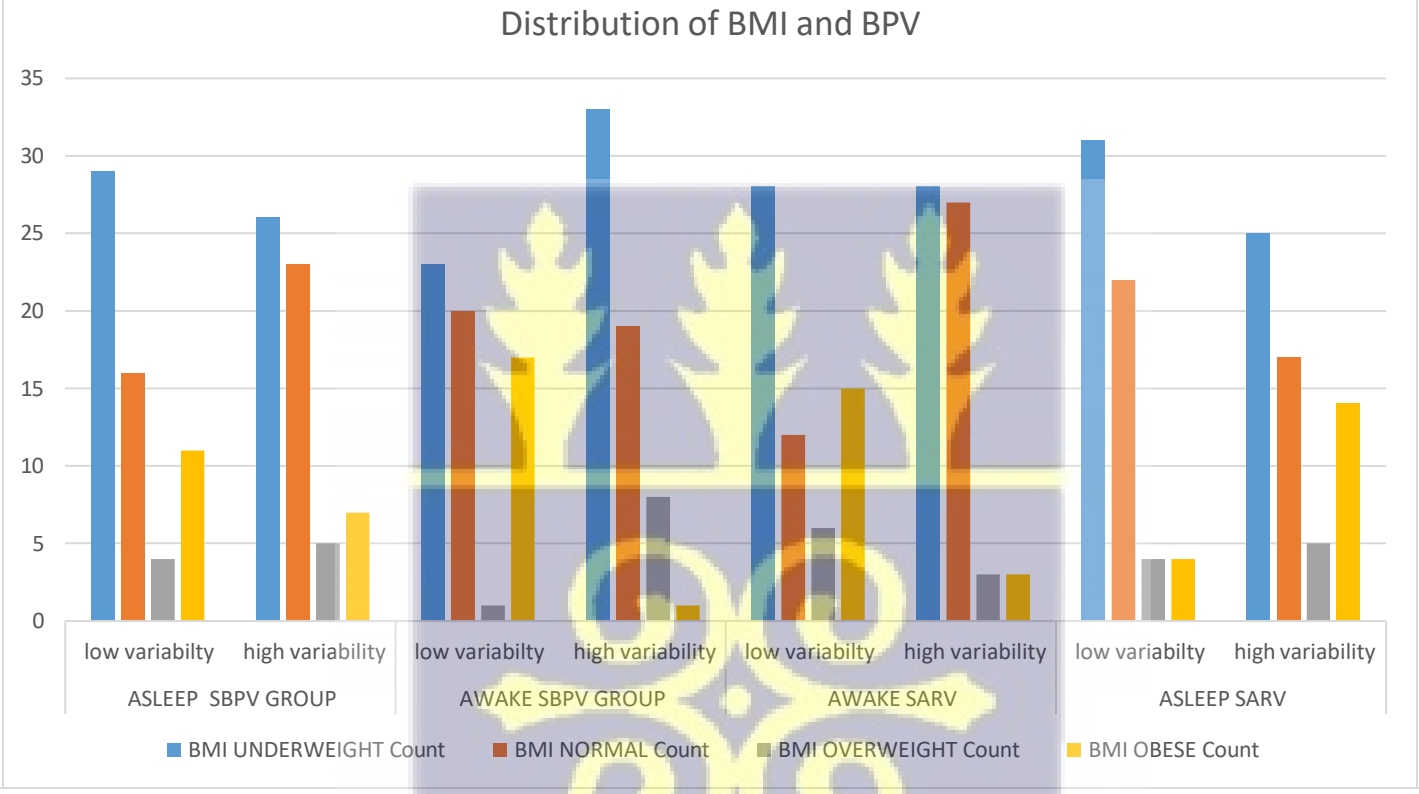
A Binary logistic regression between sleep quality and Circadian BP variability)

variable	β	SE	Wald	OR(95% CI)	P-value
Nocturnal dip	-0.012	0.33	0.131	0.988(0.92-1.05)	0.984
BP surge	0.005	0.012	0.154	1.01(0.98-1.05)	0.695

Fig 2a: A logistic regression table showing the distribution of the association of self-reported sleep quality and beat-to-beat BP variability

4.5 Association between BMI and Beat-to-beat BP variability among ALHIV

There was no significant association between BMI and beat-to-beat BP variability indices since all p-values recorded were greater than 0.05.

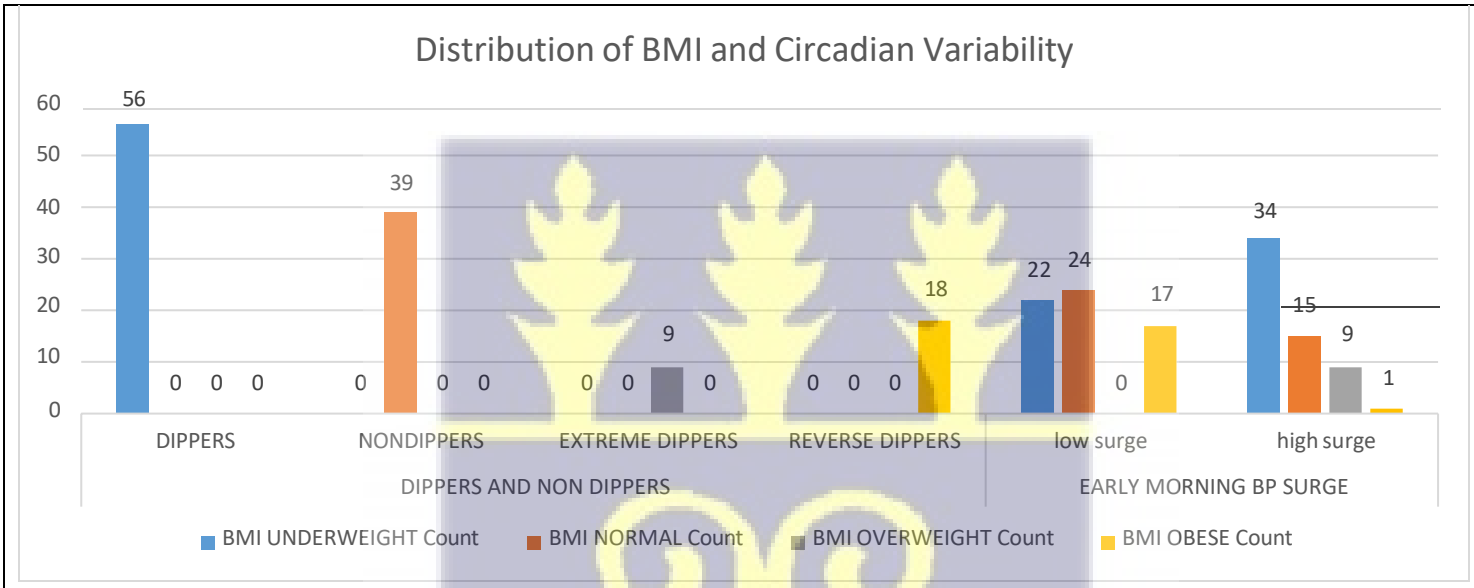


BPV indices	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p-value	Lower Bound	Upper Bound
AWAKE SD BPV	.009	.012	.068	.783	.435	-.014	.032
ASLEEP SD BPV	.002	.014	.011	.121	.904	-.025	.029
ASLEEP SARV	.022	.014	.156	1.547	.125	-.006	.049
AWAKE SARV	-.012	.022	-.054	-.544	.588	-.055	.032

Fig 2b: A linear regression table showing the association between BMI and beat- BP variability among ALHIV

4.6 Association between BMI and Circadian variability indices of ALHIV

From the results below, most dippers were underweight, N= 56 and most participants with high morning surge BP were also underweight, N=34. There was a significant association between BMI and Nocturnal dip, p-value=0.00

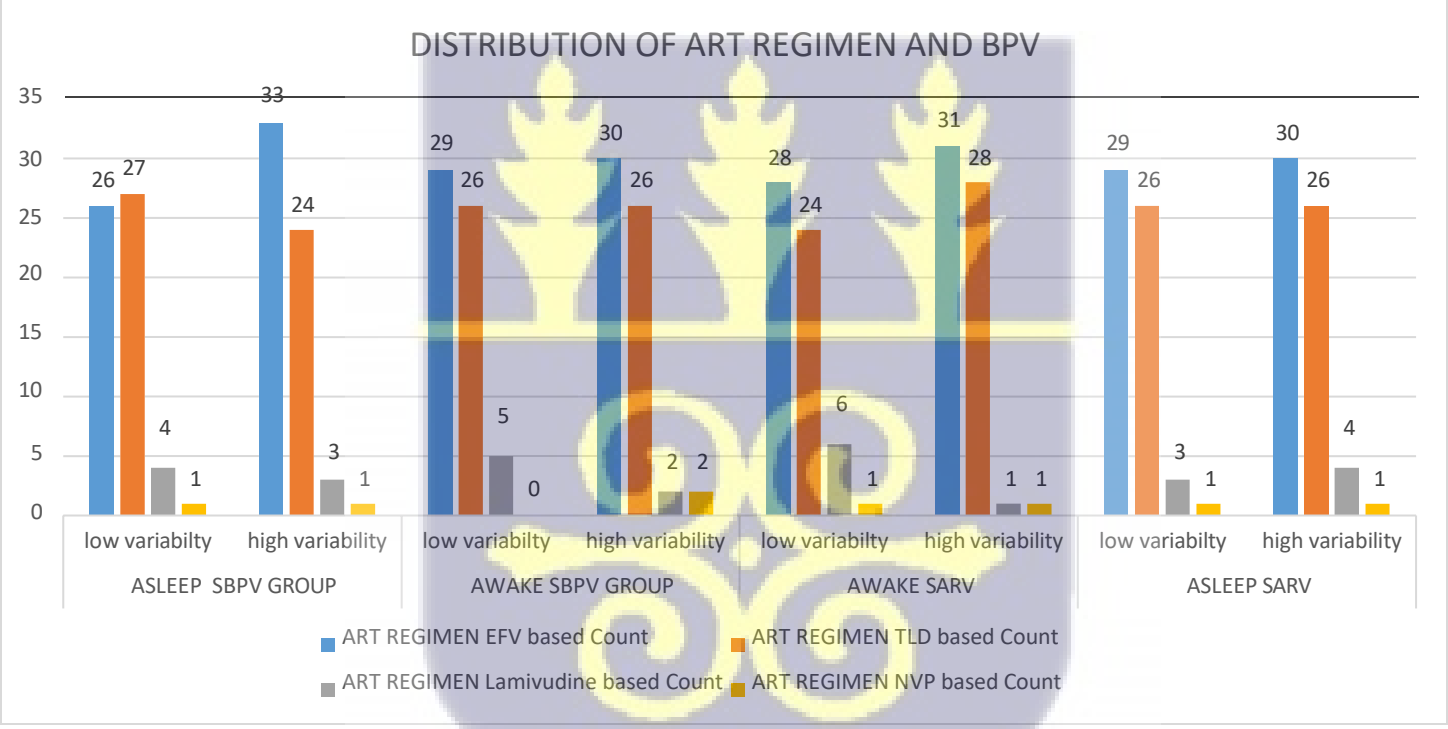


CIRCADIAN BPV	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p-value	Lower Bound	Upper Bound
NOCTURNAL DIP	-.074	.010	-.599	-7.305	.000	-.094	-.054
BP SURGE	-.001	.004	-.011	-.128	.898	-.008	.007

Fig 3a:A linear regression table showing association between BMI and Circadian variability.

4.7 Association between ART and Blood pressure variability indices

Majority of the participants, N=33, were on EFV based ART regimen under high Asleep BPV. There was a significant association between ART and BPV indices; Asleep ARV and Awake ARV, p-value=0.006 and p-value=0.013 respectively.

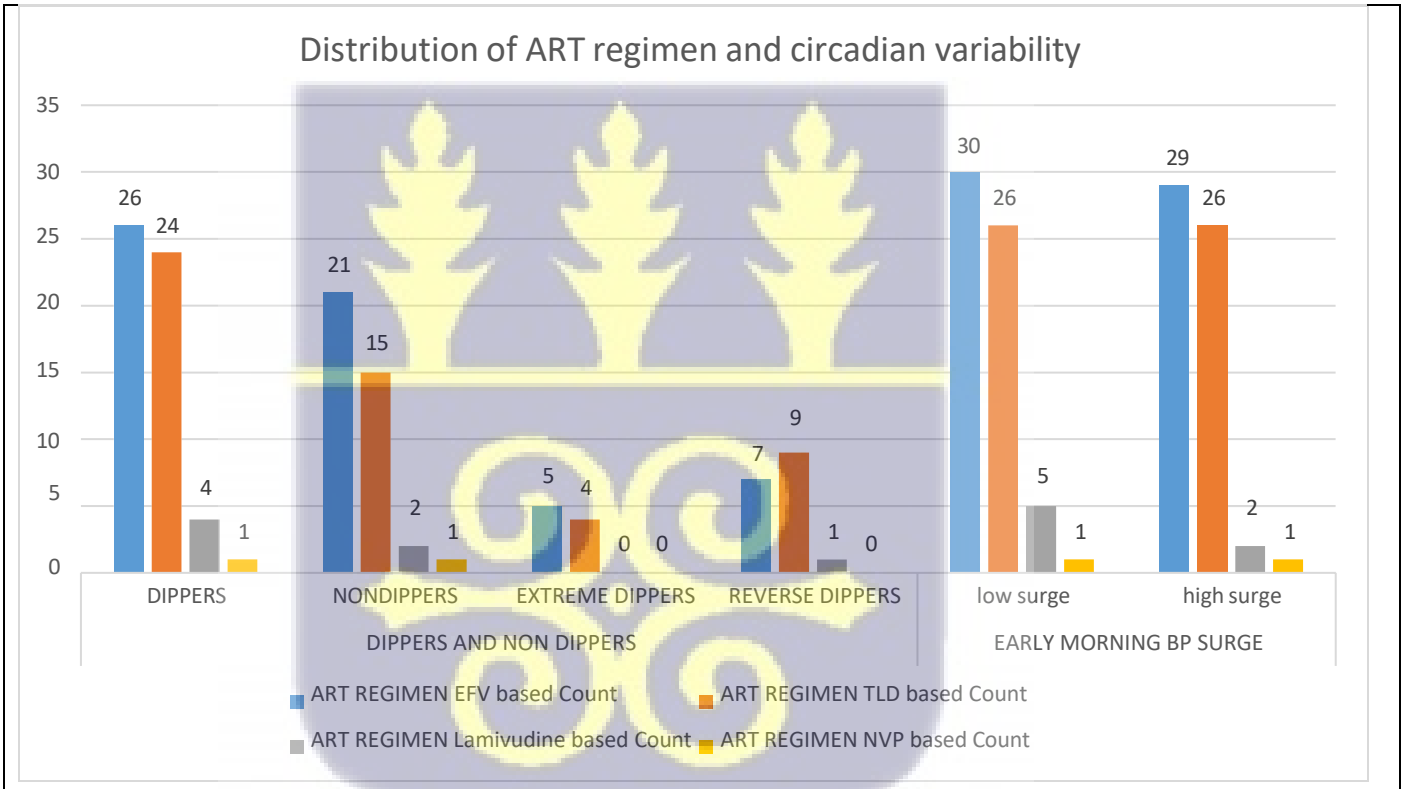


BPV indices	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p-value	Lower Bound	Upper Bound
AWAKE BPV	-.005	.011	-.039	-.427	.670	-.026	.017
ASLEEP BPV	-.013	.013	-.096	-.977	.331	-.039	.013
ASLEEP ARV	-.041	.015	-.338	-2.797	.006	-.070	-.012
AWAKE ARV	-.059	.023	-.306	-2.518	.013	-.105	-.013

Fig 3b:A linear regression table showing association between ART and BPV indices

4.8 Association between ART and Circadian BP variability indices

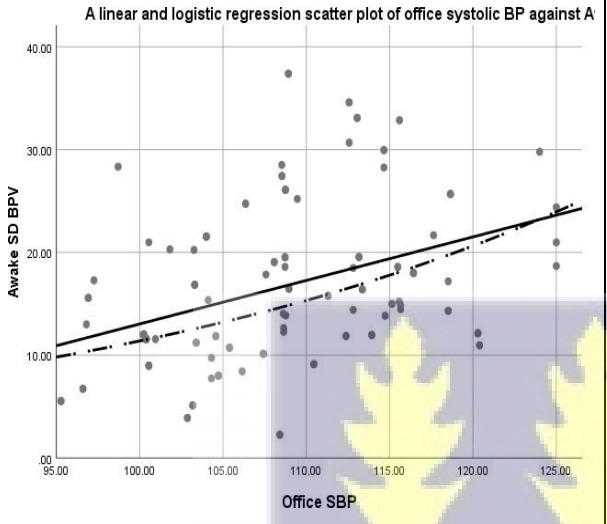
Majority of participants were on EFV based ART regimen for both nocturnal Dip (N=26) and BP surge (N=30). ART did not show a significant association with any of the circadian BP variability variables; Nocturnal dip, p-value=0.482 and BP surge, p-value= 0.878.



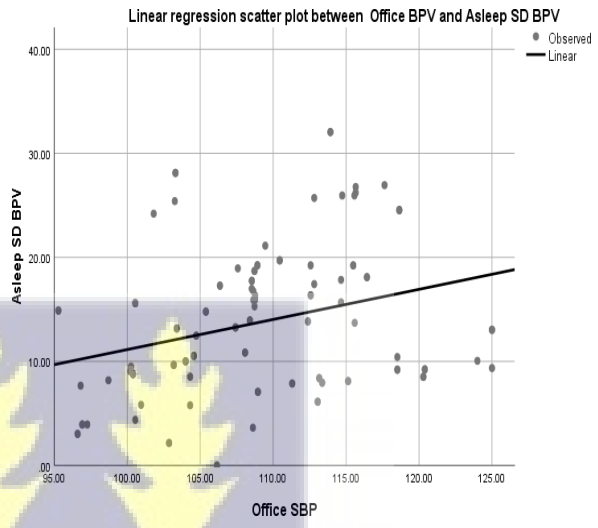
Circadian BP variability	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
NOCTURNAL DIP	-.008	.011	-.072	-.705	.482	-.030	.014
BP SURGE	-.001	.004	-.016	-.154	.878	-.009	.008

Fig 4a: Association between ART and Circadian BP variability indices

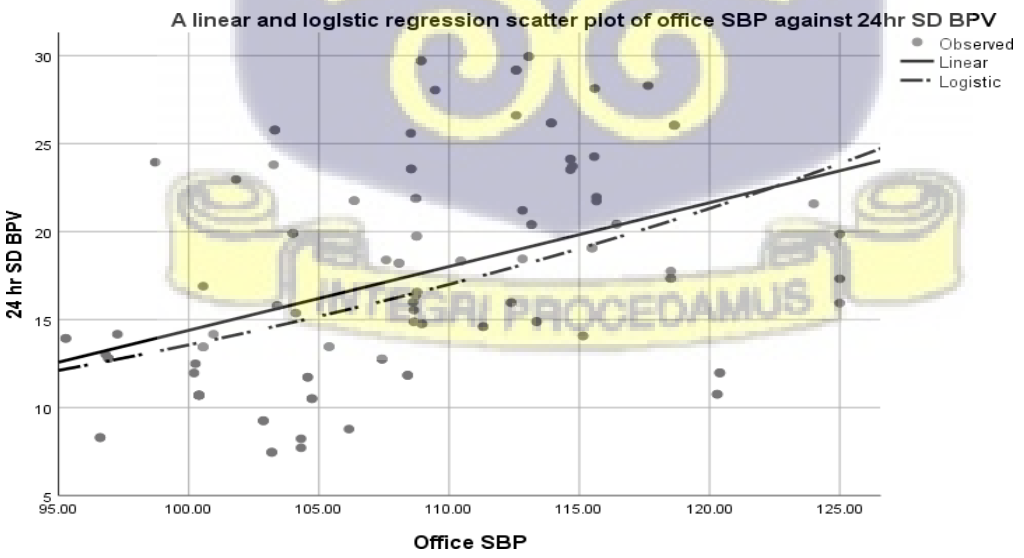
Fig 4b: A Linear and logistic regression plot of Office BP against SD (Blood pressure variability)



Equation	R square	F-value	Df2	P-value
Linear	0.141	19.68	120	0.00
Logistic	0.151	21.40	120	0.00



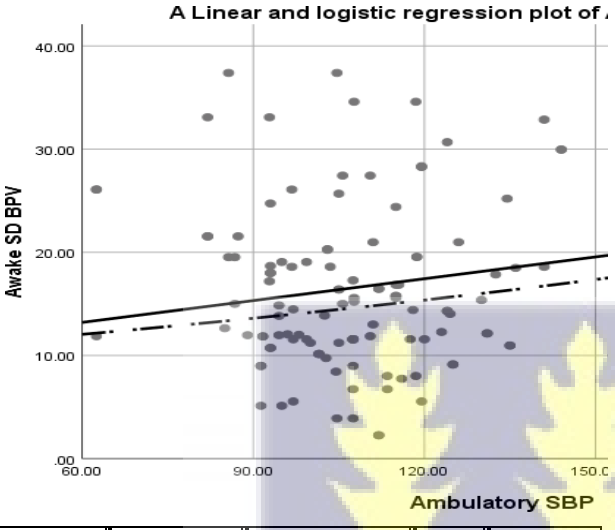
Equation	R square	F-value	Df2	p-value
linear	0.09	11.8	119	0.001



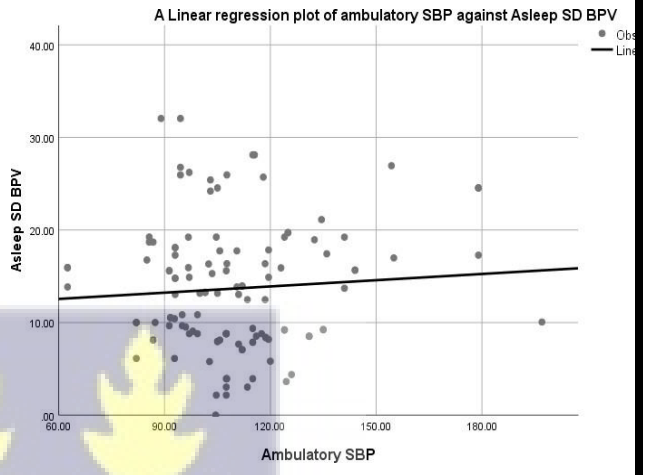
equation	R square	f-value	Df2	P-value
linear	0.180	26.27	120	0.00
logistic	0.199	29.79	120	0.00

4.9 A Linear and logistic regression plot of Office BP against SD (Blood pressure variability)
The scatter plot for linear regression chart above (*fig4b*), shows an association between Office blood pressure and SD BPV; Awake SD BPV, Asleep SD BPV and 24Hr SD BPV with p-values; 0.00, 0.001, 0.00 respectively with R squared 0.14 ,0.09 and 0.18.

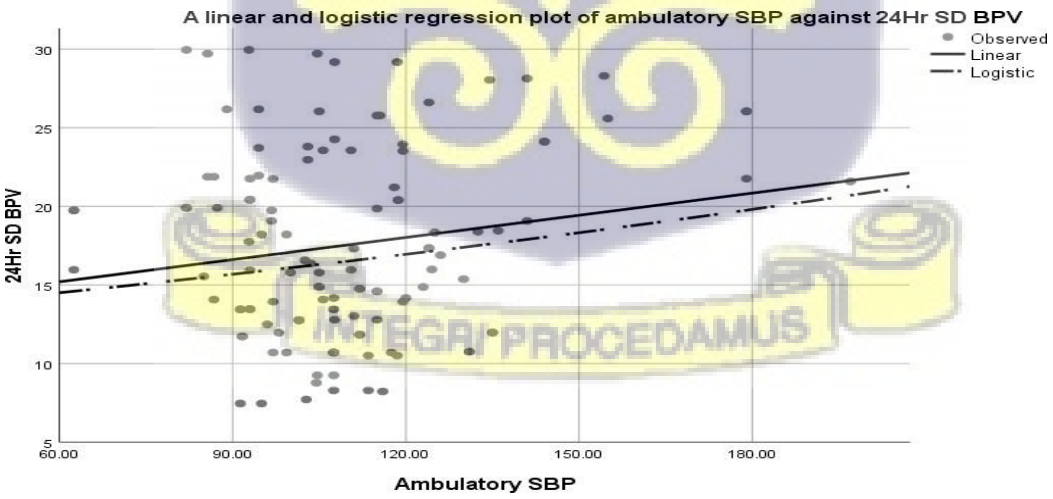
Fig 5a: A Linear and logistic regression plot of Ambulatory BP against SD (Blood pressure variability)



Equation	R square	F-value	Df2	P-value
Linear	0.038	4.688	120	0.03
Logistic	0.027	3.347	120	0.07



Equation	R square	F-value	Df 2	p-value
linear	0.005	0.623	119	0.43



equation	R square	f-value	Df2	P-value
linear	0.29	3.584	120	0.06
logistic	0.25	3.105	120	0.08

4.10 A Linear and logistic regression plot of Ambulatory BP against SD (Blood pressure variability)

The scatter plot for linear regression chart above (*Fig5a*), shows an association between systolic Ambulatory blood pressure and SD BPV; Awake SD BPV, Asleep SD BPV and 24Hr SD BPV. There was a significant association between systolic ambulatory BP and awake SD BPV, P-value = 0.03 and R square= 0.038, meaning 3.8% of the distribution depicts a linear relationship between systolic Ambulatory BP and awake SD BPV.

CHAPTER FIVE

5.0 DISCUSSION, RECOMMENDATION AND CONCLUSION

5.1 Demographic Characteristics of the ALHIV.

The ages of participants ranged from 6 to 19 years; with a mean age of 13.6 ± 3.2 years. The males were 56(45.9%) and females were 66 (54.1%). Most of the female were age 14 and above, 32(48.5%). These findings paints a similar picture from UNICEF's report that reveal HIV as a global burden affecting significant number of adolescents globally with a larger proportion emanating from Africa (UNICEF., 2019). A study that was done in Tanzania among HIV adolescents also showed HIV as a burden. The study from Tanzania also showed a consistent findings with our findings as more females 131(50.4%) got infected compared to males (N=129(49.6%)) (Irira et al., 2020). There were more females, 32(48.5%) on TLD regimen compared to males 21(37.5%). Only males were on Nevirapine, 2(3.6%). Relationship between Gender and ART was not significant, p-value=0.304. For sleep quality comparison among genders, most females reported poor sleep quality, 18(27.3%). Most females had good sleep quality 48(72.7%). Relationship between Gender and sleep quality and sleep quality was not significant, p-value=0.455. Findings from this study agrees with other studies on self-reported sleep quality among HIV adolescents, where there was no statistically significant difference between gender and age associated with sleep quality (Brand et al., 2016).

5.2 Prevalence of High blood pressure among ALHIV

Based on ESH guidelines, majority of ALHIV recorded a normal BP (<90 BPpct/(<90 BPpct mmHg) of (N=70 (57.4%)) , followed by normotensive BP (N=33(27%)) and High normal (>=90pct mmHg/ <95pct mmHg). Hypertension was reported among (N=13 (10.6)) of which (N=2 (1.64%) reported Hypertension stage 1 (>=pct90 and <pct95 mmHg), Hypertension stage II was (N=1 (0.82%)), Isolated Diastolic Hypertension (IDH) was (N=6 (4.82)), Isolated Systolic Hypertension (ISH) (>(pct99+5 mmHg/<pct90mmHg) was (N=3 (2.5%). Similar studies in different ALHIV population in different countries have reported varying findings. A study by Chatterton- Kirchmeier et al, which was done in HIV adolescent population revealed elevated BP prevalence of 18% out of a sample size of 226 (Chatterton-Kirchmeier, et al., 2015). Compared to the findings of this study, lower elevated BP prevalence was revealed in Chatterton-Kirchmeier's study, probably due to lifestyle differences. Lifestyle differences could be a factor for the different outcome because the African Ghanaian adolescent may have a different BP outcome compared to an adolescent in Europe. A study that was performed in Zimbabwe among ALHIV revealed high burden of cardiovascular complication being attributed to low resourced medical settings (Ferrand, et al., 2012). Prevalence of elevated BP in this study could also be attributed to inadequate medical resources in our various medical centers. Another study conducted among ALHIV in which more than half were asymptomatic, had severe echocardiographic abnormalities. This finding shows the need to employ monitoring procedures such as ambulatory blood pressure monitoring and other screening methods, in other to diagnose cardiovascular complications at their onset (Miller, et al., 2013).

5.3 Association between ART and BPV among children and ALHIV.

There was a significant association between ART and BPV indices; Asleep ARV and Awake ARV, p-value=0.006 and p-value=0.013 respectively. From these findings, the various significant values for the association between ART regimen and the various beat-to-beat BP measures; 24hr SD (BPV), Asleep SD (BPV), Awake SD (BPV), and circadian parameters; nocturnal dip and early morning surge was not statistically significant. These findings agree with a study done in Africa, which sought to investigate the ambulatory blood pressure profiles in subset of HIV positive. patient's pre and post Antiretroviral Therapy (Megan Borkum, et al., 2014). The study also could not find a statistically significant association between ART regimen and beat-to-beat blood pressure parameters even though the design for the study was longitudinal and ours is cross-sectional. Among all the BPV indices, only Asleep BPV and Awake BPV was statistically significant Studies have reported that, the intensity of HIV symptoms and low ART adherence may result in poor sleep quality(Babson, et al., 2013). In a study done among Iranian PLHIV population, 47.5% patients who qualified for antiretroviral therapy, reported sleep problems and in other HIV positive groups, sleep problems have been documented in 63% to 100% of people (Wibbeler, et al., 2012). Traditionally, efavirenz (EFV) has been the medicine most frequently linked to sleep disturbances when it comes to the interaction between antiretroviral (ARV) and sleep disorders. Vibrant dreams and nightmares have been linked to EFV, which some research suggest may potentially affect sleep physiology (Moyle, et al., 2006). Further studies reveal insomnia prevalence is 56% among PLHIV, and Odd Ratio (OR) of 1.17 (95% CI 1.04 -1.34), confirming an association between the severity of HIV symptom and insomnia (Gamaldo, et al., 2013).

5.4 Self-reported sleep quality and beat-to-beat variability among ALHIV

Findings from this study showed no significant association between sleep quality and beat-to-beat BPV, P> 0.05, which is at variance with findings from other studies. A number of teenagers suffer from sleep disorders, which was primarily due to insufficient sleep, a need for social connection, insufficient school schedules, subpar living situations, and chronic ailments (De-La-Llata-Romero, et al., 2011). In normal individuals, blood pressure decreases between the ranges 10% and 20% during sleep (Giuseppe, et al., 2010). Sleep involves calmness and a state of unconsciousness of our external environment which reflects a significant decrease in BP during the night (Silvani, 2008). Sleep deprivation because of sleep disturbance of any form therefore do not reflect a decrease in BP at night (Chadachan, et al., 2018).The possible reasons why the findings do not agree with the studies in comparison could be the differences in the demographic characteristics of the study population. Our study was done among Africans while the other studies were performed among American and European adolescents.

5.5 Association Between BMI and BP variability among ALHIV

The study revealed no significant association between BMI and BP variability indices, P-value for all BPV indices was greater than 0.05, except nocturnal dip, p-value= 0.00. The insignificant association of various BPV indices with BMI from this study has a differing outcome compared with a 2010 study, which was done among a similar population. This study reported a significant association between BP variability and BMI, p-value< 0.05 (Li, et al., 2010). Our findings showing a significant association between nocturnal dip and BMI concurs with a study that was done in 2016 among a pediatric and young adolescent population (Macumber, Weiss, Halbach, Hanevold, & Flynn, 2016).

5.6 Association between Cardiovascular outcomes and BP variability among ALHIV

Findings from this study showed a significant association between cardiovascular outcomes and blood pressure variability. Cardiovascular outcomes of ALHIV was determined by ambulatory systolic blood pressure and office systolic blood pressure levels. For Ambulatory BP levels, study showed Blood pressure variability; Awake SD BPV increases with in increasing ambulatory and office blood pressure, at an R-Squared value = 0.038 and p-value =0.03. For Office BP levels, study showed Blood pressure variability; Awake SD BPV, Asleep SD BPV and 24Hr SD BPV increases with increasing Office BP having p-values; 0.00, 0.001, 0.00 respectively with R squared 0.14 ,0.09 and 0.18. Recent studies done in the HIV adolescents population concur with our studies in that, they discovered an association between BPV and cardiovascular outcomes such as high blood pressure (Zawadzki, Small, & Gerin, 2017). Another study done among HIV adolescents with Obstructive Sleep Apnea revealed a significant association between BP variability and increasing Blood pressure (Stabouli et al., 2015). A study also revealed Blood pressure variability is a vital determinant of hypertensive end-organ damage and for nearly any 24-hr mean arterial blood pressure level, hypertensive individuals with low 24-hr BPV reported lower prevalence and severity of organ damage compared to those with high BPV (Chen, 2008).

CONCLUSION AND RECOMMENDATION

6.1Conclusion

Blood pressure variability may have a relationship with cardiovascular outcomes among ALHIV**.** Findings from this study shows that, as blood pressure variability increases, there is a tendency for blood pressure to also rise. Self-reported sleep quality did not have any significant association with short term blood pressure variability and circadian variability. ART and BMI showed some association with blood pressure variability. The study showed that most ALHIV have elevated blood pressure.

6.2 Recommendation

Based on the outcome of this study, the following are recommended:

1. Parents should be educated on the possible cardiovascular outcomes of their wards on ART and the need to ensure their wards are punctual in visiting the ART units.
2. Scientists and researchers in Ghana should do further research into Blood pressure variability among ALHIV.

6.2.1 Limitation of study

Sleep quality was analyzed with the PSQI but could have used Actigraphy, a device that gives a more comprehensive detail sleep outcome. The study was a cross-sectional study and cannot establish a more detailed cause-and-effect relationship between blood pressure variability and cardiovascular outcome over a period.

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Appendix 1:Assent form for participants

Participant ID Number: _____Participant Name: _____

This Assent Form is for adolescents who are invited to participate in this research titled "Ambulatory blood pressure variability and self-reported quality of sleep among HIV adolescents".

HIV infection and treatment can cause cardiovascular disorders by increasing the pressure in the blood vessels. Blood pressure (BP) changes by minute-to-minute and hour-to-hour, and such changes are called BP variability. Also, the mental burden of HIV infection and possible adverse effects of the medication may interfere with normal sleep. The burden of high BP variability and poor quality of sleep in Ghanaian adolescents living with HIV (ALHIV) is yet to be determined. In addition, the prevalence of impaired glucose and fat metabolism among Ghanaian ALHIV on treatment is not known. This research is being conducted to find out the association between BP variability and quality of sleep among Ghanaian ALHIV patients.

Your participation in this research is voluntary. It is your choice whether to partake or not. Whether you choose to partake or not, all the services you receive at your HTC/ART clinic will continue, and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

You are likely to spend the best part of the morning in the Research Room at the Department of Physiology, UGMS. For you to qualify to be part of this study, you should be 6-19 years of age. If you want to take part in the study, you would be asked to report to the Department of Physiology at 7:00 in the morning after you have fasted for 8-12 hours the night before. You will be asked to give information about yourself, your health, and your sleep status. You may feel uneasy giving out such information. Furthermore, your blood pressure, height, weight, and amount of fat in your

body was measured. Additionally, some unique medical equipment that measures blood pressure and stiffness of the blood vessel was applied to your arms and legs. These procedures are painless and might give a slight tingling impression for a few seconds when the cuffs inflate. Afterward, an amount of blood equivalent to 3 teaspoonfuls was drawn to measure substances in the bloodstream that may be abnormal. This amount of blood is not very different from what they take when you go to the Hospital. You are guaranteed that this amount will not affect your health. Before you leave, a small machine that will measure your blood pressure for the next 24 hours would be applied to your arm. You would return the next day with the machine. All the tests we will do for you about this study was free of charge.

Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. The information will only be available to those taking part of this study. You are further guaranteed that if a report of this research is prepared for the scientific and medical community you will not be identified by name.You may experience a minor bruise and/or brief discomfort at the site of the blood draw and this risk is no more than you will usually be subjected to for having a blood draw routinely at our hospital. We will reduce the discomfort by asking skilled staff to take the blood. All your test results was explained to you. As you partake in this research, you will be made to know if you have high blood pressure and are referred to a physician for further management. The research will enable us to recognize the significance of measuring blood pressure for 24 hours in Ghanaian ALHIV. The study will a help put in place strategies to screen for these conditions and allow early treatment.

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: Mr. Kofi Agyiri, University of

Ghana Medical School, Physiology department, P.O. Box 4236, Accra /0242400156 or Dr. Kwame Yeboah also of the same department, to answer any questions you may have.

ASSENT

I have fully explained to _____the nature and purpose of the above-described research, its procedures, risks and benefits. I have allowed the subject to ask questions and have answered and to the best of my ability, all questions relating to the study.

_____	_____	_____
Signature	Full Name of Investigator	Date

I _____, have read (or have had read to me in a language that I fully understand) the proposed study and that I have understood what is going to be done. Also, any concerns I have, have fully been addressed. My signature or thumbprint below indicates that I have understood what is going to be done and that I agree to take part in the study.

_____ Date: _____

(Signature/thumbprint of Subject)

_____ Date: _____

(Signature: Witness)

Voluntary informed consent for participants

Appendix 1.1: Consent forms for Parents/Guardians

Participant ID Number: _____Participant Name: _____

This Informed Consent Form is for parents/guardians of adolescents who are invited to participate in this research titled "Ambulatory blood pressure variability and self-reported quality of sleep among HIV adolescents".

Background

HIV infection and treatment can cause cardiovascular disorders by increasing the pressure in the blood vessels. Blood pressure (BP) changes by minute-to-minute and hour-to-hour, and such changes are called BP variability. Also, the mental burden of HIV infection and possible adverse effects of the medication may interfere with normal sleep. The burden of high BP variability and poor quality of sleep in Ghanaian adolescents living with HIV (ALHIV) is yet to be determined. In addition, the prevalence of impaired glucose and fat metabolism among Ghanaian ALHIV on treatment is not known. This research is being conducted to find out the association between BP variability and quality of sleep among Ghanaian ALHIV patients.

Your participation in this research is voluntary. It is your choice whether to partake or not. Whether you choose to partake or not, all the services you receive at your HTC/ART clinic will continue, and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

You are likely to spend the best part of the morning in the Research Room at the Department of Physiology, UGMS. For you to qualify to be part of this study, you should be 6-19 years of age. If you want to take part in the study, you would be asked to report to the Department of Physiology at 7:00 in the morning after you have fasted for 8-12 hours the night before. You will be asked to

give information about yourself, your health, and your sleep status. You may feel uneasy giving out such information. Furthermore, your blood pressure, height, weight, and amount of fat in your body was measured. Additionally, some unique medical equipment that measures blood pressure and stiffness of the blood vessel was applied to your arms and legs. These procedures are painless and might give a slight tingling impression for a few seconds when the cuffs inflate. Afterward, an amount of blood equivalent to 3 teaspoonful was drawn to measure substances in the bloodstream that may be abnormal. This amount of blood is not very different from what they take when you go to the Hospital. You are guaranteed that this amount will not affect your health. Before you leave, a small machine that will measure your blood pressure for the next 24 hours would be applied to your arm. You would return the next day with the machine. All the tests we will do for you about this study was free of charge.

Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. The information will only be available to those taking part of this study. You are further guaranteed that if a report of this research is prepared for the scientific and medical community you will not be identified by name.

You may experience a minor bruise and/or brief discomfort at the site of the blood draw and this risk is no more than you will usually be subjected to for having a blood draw routinely at our hospital. We will reduce the discomfort by asking skilled staff to take the blood. All your test results was explained to you. As you partake in this research, you will be made to know if you have high blood pressure and are referred to a physician for further management. The research will enable us to recognize the significance of measuring blood pressure for 24 hours in Ghanaian ALHIV. The study will a help put in place strategies to screen for these conditions and allow early

treatment.

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: Mr. Kofi Agyiri, University of Ghana Medical School, Physiology department, P.O. Box 4236, Accra /0242400156 or Dr. Kwame Yeboah also of the same department, to give answers to any question pertaining to this study.

CONSENT

I have fully explained to _____the nature and purpose of the above-described research, its procedures, risks and benefits. I have allowed the parent/guardian to ask questions and have answered and to the best of my ability, all questions relating to the study.

_____	_____	_____
Signature	Full Name of Investigator	Date

I _____, have read (or have had read to me in a language that I fully understand) the proposed study and that I have understood what is going to be done. Also, any concerns I have, have fully been addressed. My signature or thumbprint below indicates that I have understood what is going to be done and that I agree to take part in the study.

_____ Date: _____

(Signature/thumbprint of Subject)

_____ Date: _____

(Signature: Witness)

Appendix 2: Sleep Quality Questionnaires

QUESTIONNAIRE ON DEMOGRAPHIC & QUALITY OF SLEEP STATUS OF PARTICIPANTS

Questionnaire number……

SECTION 1: SOCIO-DEMOGRAPHICS

1. Age ..... years

2. Gender…… [ ] Male [ ] Female

3. Religion. [ ] Christian [ ] Muslim [ ] African Traditionalist [ ] Other

4. Do you smoke? [ ] Yes [ ] No

5. Do you take alcohol? [ ] Yes [ ] No.

If not then skip to SECTION 2.

6. How often do you normally take alcohol? [ ] Daily [ ] Weekly [ ] Monthly [ ] 2-3 times weekly [ ] more than 3 times weekly [ ] on occasions [ ]

7. Why do you take alcoholic drinks? [ ] Fun [ ] to Feel good [ ] Make friends happy [ ] Prove adulthood [ ] No reason [ ] Other.....

SECTION 2: ANTHROPOMETRY MEASUREMENTS

PARAMETER	READING
Weight	
Height	
Visceral fat	
Total body fat	
Total skeletal muscle	
BMR	
Muscle Mass	

BMI.....

SECTION 3: SLEEP QUALITY ASSESSMENT

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions. During the past month,

1. When have you usually gone to bed? _____

2. How long (in minutes) has it taken you to fall asleep each night? _____

3. When have you usually get up in the morning? _____

4. How many hours of actual sleep do you get at night? (This may be different than the number of hours you spend in bed) _____

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month (Hodgkinson, et al.)	Less than once a week (Hodgkinson, et al.)	Once or twice a week (Hodgkinson, et al.)	Three or more times week (Hodgkinson, et al.)
Cannot get to sleep within 30 minutes				
Wake up in the middle of the night or early morning				
. Have to get up to use the bathroom				
Cannot breathe comfortably				
Cough or snore loudly				
Feel too cold				
Feel too hot				
Have bad dreams				
Have pain				
Other reason(s), please describe, including how often you have had trouble sleeping because of this reason(s):				

During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in the social activity?				
During the past month, how much of a problem has it been for you to keep up the enthusiasm to get things done?				

9. During the past month, how would you rate your sleep quality overall? Very good ( ) Fairly good ( ) fairly bad ( ) very bad ( )

10. Has anyone complained to you that you snore at night? Yes ( ) No ( )

Appendix 3: Ethical clearance

UNIVERSITY OF GHANA

COLLEGE OF HEALTH SCIENCES

ETHICAL AND PROTOCOL REVIEW COMMITTEE

EPRC/SEP/2022

September 22, 2022

Mr. Kofi Agyiri
Department of Physiology
University of Ghana Medical School
Korle Bu

ETHICAL CLEARANCE

Protocol Identification Number: ***CHS-Et/M.1 – P4.8/2021-2022***

FWA: 000185779 **IORG: 0005170** **IRB: 00006220**

The College of Health Sciences Ethical and Protocol Review Committee (EPRC) on September 22, 2021 reviewed and approved your research protocol.

Title of Protocol: **"Blood pressure variability indices and self-reported quality of sleep among adolescents living with HIV"**

Principal Investigator: **Mr Kofi Agyiri**

This approval requires that you submit six-monthly review report(s) of the study to the Committee and a final full review report to the EPRC at the completion of the study. The Committee may observe, or cause to be observed, procedures and records of the study before, during and after implementation.

Please note that any significant modification(s) to this project/study must be submitted to the Committee for review and approval before its implementation.

You are required to report all serious adverse events related to this study to the EPRC within seven (7) days verbally and fourteen (14) days in writing.

As part of the review process, it is the Committee's duty to review the ethical aspects of any manuscript that may be produced from this study. You will therefore be required to furnish the Committee with any manuscript for publication.

This ethical clearance is valid till September 22, 2023.

Please always quote the protocol identification number in all future correspondence in relation to this protocol.

Signed: .....

Professor Andrew Anthony Adjei
Chair, Ethical and Protocol Review Committee

cc: Provost, CHS
Dean, UGMS
Head, Physiology

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