

**PREVALENCE, ASSOCIATED FACTORS AND SUSCEPTIBILITY  
PATTERN OF COMMON ISOLATES ASSOCIATED WITH  
ASYMPTOMATIC BACTERIURIA IN HIV-INFECTED CHILDREN  
AGED 5-18 YEARS AT MUHIMBILI NATIONAL HOSPITAL, DAR  
ES SALAAM.**

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**MMED Pediatric and Child health Dissertation  
Muhimbili University of Health and Allied Science  
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**Muhimbili University of Health and Allied Sciences**  
**Department of Pediatric and child health**



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**By**

**Luka Mkeni Lui**

**A dissertation submitted in (partial) fulfillment of the requirement for the  
Masters of Medicine in Pediatric and child health of the  
Muhimbili University of Health and Allied Sciences  
January 2020**

**CERTIFICATION**

The undersigned certify that they have read and hereby recommend for examination of the dissertation titled “**prevalence and risk factors associated with asymptomatic bacteriuria in HIV infected children at Muhimbili national hospital, Dar es salaam**” in Partial fulfillment of the requirement for Masters of medicine in Pediatric and Child Health Science in Applied Epidemiology of the Muhimbili University of Health and Allied Sciences.

.....

**Dr. Helga Naburi**  
**(Supervisor)**

**Date.....**

.....

**Dr. Francis Furia**  
**(Co-supervisor)**

**Date.....**

**DECLARATION AND COPYRIGHT**

I, Lui, Luka Mkeni, hereby declare that this dissertation is my original work and it that has not been presented and will not be presented to any other university for similar or any other 3 degree award.

Signature..... Date.....

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## **LIST OF ABBREVIATIONS**

- ABU - Asymptomatic Bacteriuria
- CKD -Chronic Kidney Disease
- CTC - Care and Treatment Clinic
- HIV - Human Immunodeficiency Virus
- HAART - Highly Active Anti-Retroviral Therapy
- HIVAN - HIV-associated nephropathy
- HIVICK - HIV immune complex kidney disease
- IRB - Institution Research Board
- MSU - Mid-stream Urine
- MNH - Muhimbili National Hospital
- MUHAS - Muhimbili University of Health and Allied Science
- STIs - Sexual Transmitted Infections
- UTI - Urinary Tract Infections
- WHO - World Health Organization

## **DEFINITION OF TERMS**

Urinary Tract Infection =an infection of the kidney, ureter, bladder or urethra

Pyelonephritis= inflammatory process of the kidney or upper urinary tract

Bacteriuria=colonization of one or more organisms in the urine without symptoms or infection

Chronic kidney disease=long standing disease of the kidney leading to renal failure.

## **ABSTRACT**

### **BACKGROUND**

Asymptomatic bacteriuria (ABU) refers to a condition in which there is positive urine culture without any manifestation of infection. People living with Human Immunodeficiency Virus (HIV) are more prone to opportunistic infection including urinary tract infection (UTI) due to progressive immune dysfunction by the virus.

**OBJECTIVE:** To determine prevalence, associated factors and antimicrobial susceptibility of common isolates associated with asymptomatic bacteriuria among children living with HIV attending Care and Treatment Center at Muhimbili National Hospital.

**METHODOLOGY:** A hospital based cross sectional study was conducted at MNH, among 300 participants who were consecutively recruited. A standardized structured questionnaire developed for purpose of this study was used to collect information and urine cultures were done. Antimicrobial susceptibility was done using disc diffusion method in every positive urine culture. Data were analyzed using SPSS version 20 and a *P-value* of 0.05 or less was considered to be statistically significant.

**RESULTS:** Out of the 300 children living with HIV recruited and screened for ABU, 159(53%) were male. The results revealed the prevalence of ABU to be 7.7%. Female gender and children with viral load less than 1000 copies/ml had statistically significant higher odds of being positive for ABU compared to counterparts.

**CONCLUSION AND RECOMMENDATION:** Asymptomatic bacteriuria was observed among HIV-infected children especially female children and children with VL<1000 copies/ml. Thus screening for ABU should be routine in the work up of children living with HIV at care and treatment clinic.

## **MUHUTASARI**

### **UTANGULIZI**

Uambukizi wa bakteria katika mfumo wa mkojo usiokuwa na dalili ni ile hali ya kuwa na maambukizi ya bakteria katika mfumo wa mkojo pasipo muathirika kuonyesha dalili zozote. Maambukizi haya huanzia sehemu chini ya kutolea mkojo itwaayo urethra kuelekea sehemu ya juu ikihusisha kibovu cha mkojo na hatimaye kwenye figo na ndipo madhara makubwa huonekana kama mgonjwa hakupapata matibabu stahiki.

Watu waishio na virusi vya UKIMWI wako kwenye hatari kubwa zaidi kulinganisha na watu ambao hawana virusi hivyo. Sababu inayopelekea watu wenye VVU kuwa hatarini zaid ni pamoja na uwezo hafifu wa miili yao kukabiliana na magonjwa mbali mbali yakiwemo magonjwa nyemelezi.

### **DHUMUNI LA UTAFITI**

Utafiti huu ulikuwa na lengo la kujua ukubwa wa tatizo hli kwenye jamii, sababu zinazoweza kupelekea maambukizi, aina ya bakteria na utambuzi wa dawa zinazoweza kuwadhhibiti ipasyo. Utafiti huu umehusisha watoto waishio na virusi vya UKIMWI kati ya umri wa miaka mitano na kumi na nane wanaotibiwa katika hospitali ya taifa ya Muhimbili.

### **MBINU**

Kati ya washiriki mia tatu (300) waishio na virusi vya UKIMWI waliweza kufanyiwa utafiti. Kati ya washiriki hao mia moja hamsini tisa walikuwa wanaume, sawa na asilimia hamsini na tatu (53%). Dodoso yenye maswali ya utafiti ilitumika ipasavyo kukusanya maelezo ya kina ya mgonjwa ikifuatiwa na mgonjwa kuchukuliwa mkojo wa kuotesha. Utaalamu wa kimaabara ulitumika kugundua aina ya bakteria pamoja na dawa zilizoweza kuwadhhibiti bakteria hao.

## **MATOKEO YA UTAFITI**

Matokeo ya utafiti yalionyesha ukubwa wa tatizo hili ni asilimia 7.7% .Watoto wa jinsia ya kike na wenye wenye idadi VVU kati ya kopi 1000 kurudi chini walionekana kuwa na maambukizi ya bakteria kwenye mfumo wa mkojo ukilinganisha na makundi mengine.Dawa ina ya meropenemu na ciprofloxacin zilionyesha uwezo mkubwa wa kuwaua bakteria hao.

## **HITIMISHO**

Maambukizi ya bakteria kwenye mfumo wa mkojo kwa watoto waishio na VVU yaliweza kuonekana katika utafiti huu na yalikuwa mengi zaidi kwa watoto wa jinsia ya kike na wenye idadi ya virusi kati kopi 1000 kurudi chini. Kwa mantiki hii,uchunguzi wa maambukizi ya bakteria katika mfumo wa mkojo ni muhimu kwa watoto waishio na VVU.

## **1. INTRODUCTION**

### **1.1 Background**

Asymptomatic bacteriuria refers to a condition in which there is positive urine culture without any manifestation of infection (1). The incidence is <1% in preschool and school aged girls and rare in boys. The condition is benign and if left untreated, can result in a symptomatic UTI. In healthy children, ABU is colonization of the bladder with non virulent organisms. These organisms can resolve without spread to other organs and is beneficially because presence of these organisms prevents infection from more virulent organisms by competition for nutrients or receptor site, therefore treatment is not recommended.

### **1.2 Pathophysiology**

Most of urinary infections are ascending infections resulting from fecal flora colonizing the perineum and eventually extend to bladder through the urethra. These organisms colonize and multiply within the urinary bladder and it can induce inflammation (cystitis) or without inflammation (ABU). If ABU is left untreated may turn to symptomatic UTI in children with chronic illnesses like severe malnutrition, sickle cell disease and altered immune status(2). Infection may extend to the kidneys and cause pyelonephritis and renal abscess. UTI may even result in complications such as Septicemia and death. Renal scarring is noted in 10% to 30% of children after UTI (1, 3).

### **1.3 Laboratory investigation**

Laboratory diagnosis of ABU is confirmed through culture of midstream clean catch urine. For female two consecutive specimens with isolation of at least 100,000 colony forming unit (CFU) per ml of the same bacterial species and for male, a single specimen with isolation of at least 100,000 colony forming unit (CFU) per ml of single bacterial species

### **1.4 Treatment**

No treatment is required in asymptomatic bacteriuria in health children. In some chronic conditions after the culture and sensitivity result are available, empiric antibiotic should be considered based on local antimicrobial sensitivity patterns. This is crucial in order to prevent symptomatic UTI, its complications and long term sequelae.

## **1.5 UTI and HIV**

People living with Human Immunodeficiency Virus (HIV) are more prone to opportunistic infection including urinary tract infection (UTI) due to progressive immune dysfunction by the virus. HIV infection is well documented risk for development of UTI. The hallmark of Human Immunodeficiency Virus (HIV) disease is the profound immunosuppression that results from continued depletion of CD4 cells. This immune deficient state predisposes to a wide variety of infections, such that even non virulent organisms become pathogenic. In addition; some HIV infected children are malnourished (4). It is possible therefore that the prevalence as well as the clinical significance of ABU in children infected with HIV may be different from that of healthy children. Studies in adult population have also documented a higher prevalence of symptomatic urinary tract infection in HIV infected adolescent/young adults compared to healthy general population. There is however paucity of information on ABU in HIV infected children (4)

In severe infection lead to a clinical syndrome called HIV/AIDS, a state which make the body unable to fight against infections caused by various organisms including, bacterial, fungal, and viral and protozoa infections (5).UTI is common infection among HIV infected patients (6).The incidence of urinary tract infections in HIV population is clearly related to infection and immune function, determined by lymphocytes CD4+ cells count (7).

For the case of children living with HIV, UTI has been highly associated. A lot of factors that contributes to UTI among HIV children as compared to health ones have been extensively studied. Other studies were done to explore the association HIV disease stage, CD4 count, Duration of Illness, Viral load, history of hospitalization and prophylactic use of antibiotics

## **1.6 Problem statement**

Asymptomatic bacteriuria (ABU) is not uncommon in HIV- infected children and if left untreated may turn to symptomatic UTI and its complications. There is limited data on prevalence, risk factors, etiological causes and its antimicrobial susceptibility. The magnitude of this problem among HIV infected children in Sub Saharan Africa including Tanzania is not known. Apart from currently there is increased in antimicrobial resistance to commonly daily used antibiotics.

### **1.7 Rationale**

The range, extent and factors associated with ABU in HIV-infected children are under reported in Sub-Saharan Africa including Tanzania. This study enable us to identify common bacterial isolates causing ABU among HIV-infected children aged 5 to 18 years attending CTC at MNH. The sensitivity patterns will also shed some light on the best antimicrobial combinations for empirical treatment of UTI in HIV-infected children in our setting. This will help to reduce hospitalization if children are treated early with the most appropriate antibiotics. The findings will also contribute to the development of MNH pediatric guidelines on antibiotic choices for management of UTI among HIV-infected children which can potentially lead to the reduction of frequent changes and irrational/improper use of antibiotics.

### **1.8 Conceptual framework**

Once the diagnosis of ABU is made where the local epidemiology pattern and susceptibility is unknown, it will lead to symptomatic UTI, incorrect prescription of medication and subsequently progression to UTI complications. In order to prevent this, we need to intervene by nutritional improvement, ART adherence will reduce viral load and reduce advanced HIV disease staging, urinalysis; urine culture and sensitivity and start antibiotics based on known local susceptibility pattern



**INDEPENDENT VARIABLE**

**Factors**

- **Acute malnutrition**
- **Viral load**
- **CD4 count**
- **Disease stage**
- **Age**
- **Sex**
- **Recent antibiotic use**



**ABU**



**ANTIMICROBIAL  
TREATMENT**



**UTI**

### **1.9 Research questions**

1. What is the prevalence of asymptomatic bacteriuria in HIV- infected children followed at MNH?
2. What are the factors associated with asymptomatic bacteriuria among HIV- infected children followed at MNH
3. What is the sensitivity pattern of isolated bacteria causing asymptomatic bacteriuria in HIV- infected children at MNH?

### **1.10 Research objective**

### **1.11 Broad objective**

To determine prevalence, associated factors, susceptibility pattern and common isolates associated with asymptomatic bacteriuria among children living with HIV aged 5-18years attending CTC clinic at MNH.

### **1.12 Specific objectives**

1. To determine the prevalence of asymptomatic bacteriuria in HIV-infected children aged 5-18years at Muhimbili National hospital
2. To determine the factors associated with asymptomatic bacteriuria in HIV- infected children aged 5-18years at Muhimbili National Hospital
3. To determine sensitivity pattern and common isolates causing asymptomatic bacteriuria in HIV-infected children aged 5-18years at Muhimbili National Hospital

## **2.0 LITERATURE REVIEW**

### **2.1 Prevalence of asymptomatic bacteriuria**

Urinary Tract Infection (UTI) occurs in 1-3% of girls 1% of boys. In girls the first UTI usually occurs by the age of five years with peaks during infancy and toilet training. In boys mostly UTI occurs mostly during the first year of life. (6)

Iduoriyekemweni did a study in 2012 in Nigeria to determine the prevalence of asymptomatic bacteriuria among 155 HIV-infected children in Nigeria. The prevalence of asymptomatic bacteriuria was found to be 10.3%. Study also found a significant higher proportion of bacteriuria in female 7.7% as compared to male 2.6%. Findings had however revealed no correlation between UTI with neither CD4 count nor HIV disease stage (4).

In Lagos Nigeria, a study by Adeseye et al to determine the Prevalence and risk factors for bacteriuria, findings had shown a significant higher proportion of UTI, 24.7% among children living with HIV as compared to 8.2% among un-infected ones (8).

With regards to gender Adeseye et al had reported a significant higher proportion of female HIV children who had UTI (17.7%) as compared to their male counterpart (7%) (8). the reasons commonly adduced for female susceptibility to asymptomatic bacteriuria are the relatively shorter length of the urethra, the proximity of the urethra to the anal opening and the absence of a prostatic like fluid in the female which is thought to be bacteriostatic (9,10).

In other countries several studies have reported varying prevalence rates of UTI in children ranging from 3.3 in USA to 37.5% in Pakistan. The review study was done in Poland to all collected medical information on patients who were routinely followed for 21 years up to 2015. The prevalence of urine culture positive UTI cases was found to be 23.3%. Moreover likelihood of UTI was higher among female gender and those with lower CD4 counts (11).

### **2.2 Associated factors for asymptomatic bacteriuria**

People living with Human Immunodeficiency Virus (HIV) are likely to be more predisposed to urinary tract infections due to the suppression of their immunity and women in this category tend to get UTI more often due to the nature of their anatomy (12). The incidence of UTI is

higher in HIV-infected than HIV seronegative individuals (13). It is also higher amongst HIV-infected individuals with low CD4 counts (14). It has been seen in many studies that asymptomatic bacteriuria has a positive correlation with HIV among different populations. Young patients however seem to be at an increased risk (15).

Ibadin *et al.* revealed HIV/AIDS to be a predisposing factor for increased incidence of urinary tract infection in the young. The implication of urinary tract infection associated with HIV is the increased cost of care for HIV/AIDS patients (16)

Study done by Iyang-Etoh shows statistically significant difference in proportion of UTI based on gender. The prevalence of asymptomatic bacteriuria among children was found to be 40%, almost five times that of a matched control (16).

Bunu and colleagues conducted a study in India in 2013 to look for asymptomatic bacteriuria in HIV positive individuals in a tertiary hospital that recruited 300 HIV positive individuals aged 1 to 70 years. The prevalence of asymptomatic bacteriuria was found to be 4%. Bacteriuria in HIV infected patients was significantly higher in females than in males. However, there was no difference in prevalence of UTI based on age differences (18). Several studies found the inverse correlation between lymphocytes CD4+ count and UTI among HIV-infected patients (6, 18).

HIV positive children are at high risk of febrile urinary tract infections and have the highest incidence during the first year of life in both sexes. After infancy, urinary tract infections confined to the bladder are generally accompanied by localized symptoms and are easily treated (19).

### **2.3 common isolates and sensitivity pattern**

In a Nigerian study, a microbial sensitivity pattern of isolated microorganisms was done and revealed a higher sensitivity to quinolones like ciprofloxacin, Refloxacin and Ofloxacin. The study also revealed an appreciable sensitivity pattern of Augmentin to isolates (16).

With regards to antimicrobials susceptibility pattern, a study in Tanzania by Furia reported high resistance to co-trimoxazole, ampicillin and clavulanic acid-potentiated amoxicillin by all

isolated pathogens (20). Irrational prescription of these drugs due to their frequent use at the health facility might be the factor for the higher resistance observed.

Asymptomatic bacteriuria, emerging antimicrobial resistance and delay of standard treatment need to be well addressed. There is a higher prevalence of urinary tract infections (UTIs) in HIV-infected patients ranging from lower tract involvement to pyelonephritis. UTIs in these patients seem to be caused by malnutrition than from immunosuppression due to HIV infection (21)

### **3.0 METHODOLOGY**

#### **3.1 Study design**

This was a hospital based cross sectional study to determine the magnitude of ABU among HIV-infected children attending CTC clinic at MNH.

#### **3.2 Study area**

This study was carried out at the care and treatment clinic (CTC) in Muhimbili National Hospital (MNH), in Dar-es-salaam, Tanzania. It is a national tertiary level referral hospital with a bed capacity of 1400 patients; it serves 1000 to 1200 outpatients per day in a different specialty and super- specialty and it has 1000 to 1200 admissions per week. It serves as a teaching hospital for Muhimbili University of Health and Allied Sciences. (MUHAS). HIV Care and Treatment clinic is located at the main outpatient department building of MNH.

The CTC is supported by Management and Development for Health (MDH) with support from the US president's Emergency's Plan for AIDS Relief (PEPFAR). The program funds only the supplies for HIV test, Ant Retrovirus Treatments (ART's) as well as testing for Viral Load and CD 4 cell count. Patients get these tests and antiretroviral treatment free of charge. The clinic operates daily from Monday to Friday; with the patient care provided by specialists, residents and general practitioners from infectious disease unit in the Department of Pediatrics and Child health at MNH. On average 10 to 20, HIV positive children attend the clinic per day and approximately 600 children per month. New registrations per month are approximately 10 to 15 new HIV-infected children who are newly diagnosed in the wards and referred to the clinic for registration, counseling, and initiation of antiretroviral therapy. There is a Youth Club, which hold meetings on a Friday of each month. It involves pre-adolescents and adolescent who understand the disease and their status in full. They provide psychosocial support, sexual and reproductive education, routine health checkup and monthly refills. The club caters for an average 60 patients each month, currently, there are 255 children enrolled from age 12 to 18years.

### 3.3 Study population

All children aged 5years to18years attending CT clinic at MNH from June to December 2019.

### 3.4 Sample selection and technique

All eligible participants whose parents/guardians granted written informed consent were recruited and older children who were eligible assent was obtained consecutively into the study until the required sample size was attained. Recruitment of participants was carried out exclusively on working days.

### 3.5 Inclusion criteria

All HIV-infected children aged 5years to 18years attending CTC clinic at MNH.

#### 3.6.1 Exclusion criteria

- Children with complaints suggestive to symptomatic UTI e.g. fever, flunk abdominal pain, dysuria, vomiting consent.
- Recent use of antibiotics (other than cotrimoxazole and isoniazid) defined as period less than 7 days prior to the study.

#### 3.7.2 Sample size calculation

Sample size was calculated from the following formula

$$n = \frac{z^2 p(100-p)}{\epsilon^2}$$

Where

z= level of confidence (1.96 for 95% confidence level)

p = expected proportion= 24.7% this is the estimated prevalence of ABU among HIV-infected children in Nigeria according to study done by Adeseye and Chinyere (2018) (8)

$\epsilon$  = margin of error = 5%

$$n = (1.96 \times 1.96 \times 24.7 \times 75.3) / 25$$

$$282$$

$$10/100 \times 282 = 28$$

$$28 + 282 = 310$$

After adjusting of non response rate of 10% the sample size become 310.

### **3.8 Data collection technique**

Demographic and clinical information was obtained from the face to face interview with the study participant. Information extracted from CTC cards number 1 and 2, eg CD4 count, viral load and information was then documented in standardized structured questionnaire.

Nutritional status was assessed using BMI calculated as weight in kilograms divided by height in meters squared. Weight was measured by using a SECA weighing scale made in China and recorded in kilograms to the nearest 0.01grams with a child in standing in standing position wearing light cloths and with no shoes. Height of participant was measured while standing using a stadiometer made from Korea with the child standing at right angle in front of height board and a researcher sliding head piece to bring it in contact with the child's head.

Height was recorded in meters to the nearest 10millimeters. WHO standard were used to interpret the BMI (kg/m<sup>2</sup>) result and classify the malnutrition status. Z score between mean and 1SD was classified as: normal nutrition status, between -1SD and -2SD as: mild wasting, between -2SD and -3SD as moderate wasting and below -3SD as; severe wasting.

Specimen collection for urine culture and sensitivity pattern was obtained in aseptic technique from a toilet trained children. Midstream urine was obtained at the clinic. The introitus was cleaned after demonstration to the patient before obtaining the specimen. In uncircumcised boys, the prepuce was retracted before obtaining the specimen. In females samples were collected after cleaning the urethral orifice. A sterile container was used to collect 5milliliters of urine and each sample was transported immediately to the central pathology laboratory (CPL) research and clinical laboratory and clinical laboratory of MNH within 2hours of collection. Were necessary urine specimen was temporarily stored in a refrigerator at a temperature of 4 degrees Celsius before transported to the laboratory.

Urine sample were inoculated in plates, and pure growth plates colony count were performed before performing gram staining and bacterial identification of suspected organisms. Finally susceptibility test was performed using routinely antimicrobial agents. In doubtful bacteriuria isolate was identified and susceptibility test was carried out.



- Colony count of  $\geq 100,000$  CFU considered as significant bacteriuria.
  - CFU  $\geq 10,000$  but less than 100, 000 CUF ml was considered as doubtful bacteriuria.
  - Colony count  $< 10,000$  CUF/ millimeter was considered as insignificant bacteriuria
- Other test that was performed was viral load and CD4 analysis only to those participants whose results were not available in the past six months.

### **3.9 Data processing and analysis**

Data were then entered into the statistical package for social science (SPSS) version 20. For continuous variable mean, median, standard deviation and interquartile range were used. Student T test was used to compare means (SD) of data which were normally distributed and Mann-Whitney U test was used to compare medians (IQR) for skewed data. Categorical variable were summarized using frequencies and proportions. The differences in proportions were tested using Chi square test or Fisher's exact test. The respective 95% confidence intervals were determined and a p-value equal or less than 0.05 was considered statistically significant.

### **3.10 Ethical clearance**

Ethical clearance was sought from MUHAS IRB and permission to conduct this study was obtained from Directorate of Research, Training and Consultancy at MNH. Patients, Parents and Caregivers were informed about the study, regarding the importance of the study and for those who agreed to participate were requested to sign a written informed consent before enrollment. Children above 10 years were required to sign assents forms and their caregivers were required to sign consent form if they were accepting to participate in this study.

Strict confidentiality was maintained by use of a study identification number assigned to each participant. For those who urine culture was positive, result and other relevant information pertaining disease treatment was shared to the attending clinicians

## 4.0 RESULTS

### 4.1 Clinical characteristics of participants

A total of four hundred and twenty (420) HIV infected children attended CTC follow up clinic during the study period. Three hundred (300) participants met the inclusion criteria and were randomly selected in the study as shown in the figure below.

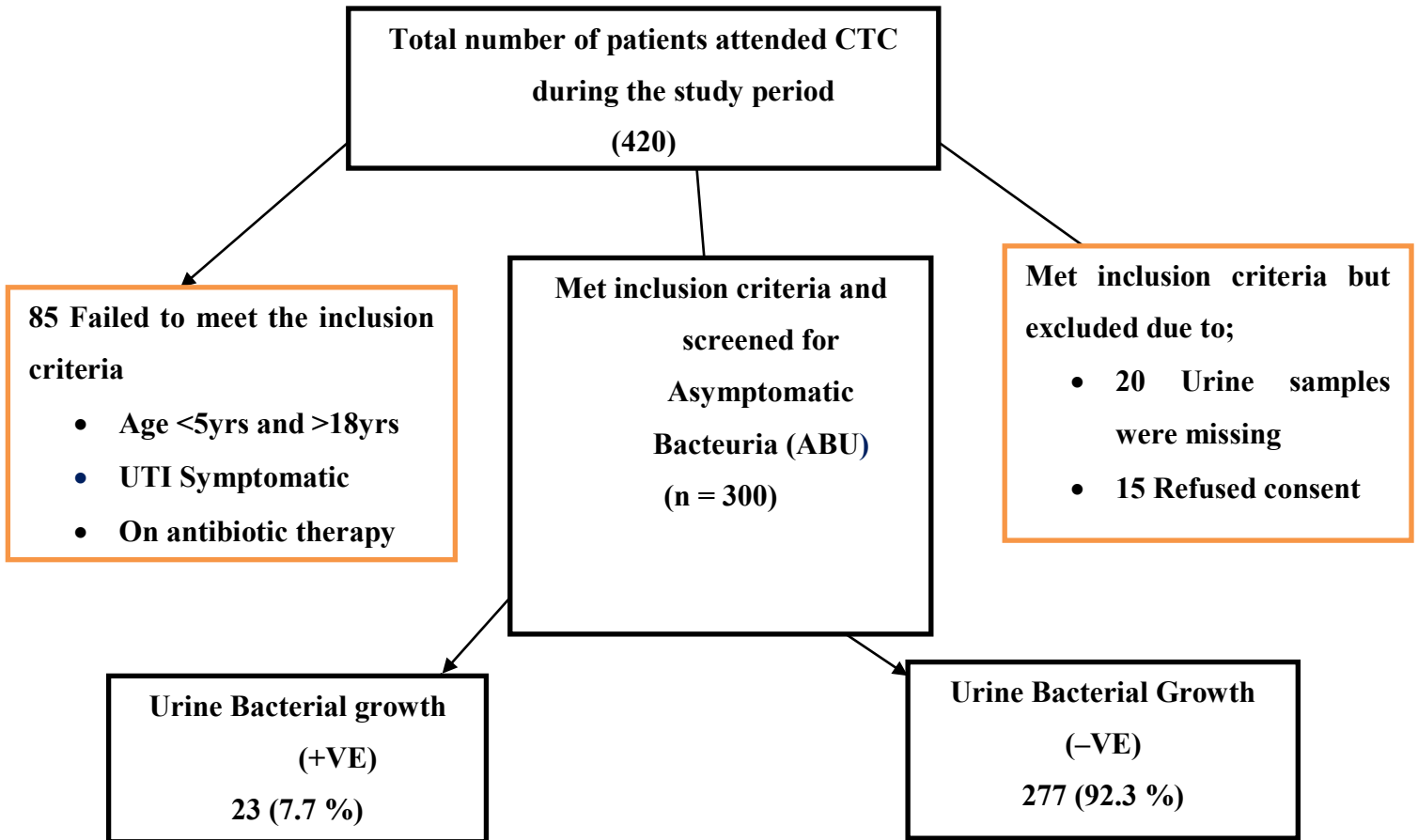


Figure 1: Flow Chart Showing Recruitment and sampling of participants

## 4.2 Characteristics of study population

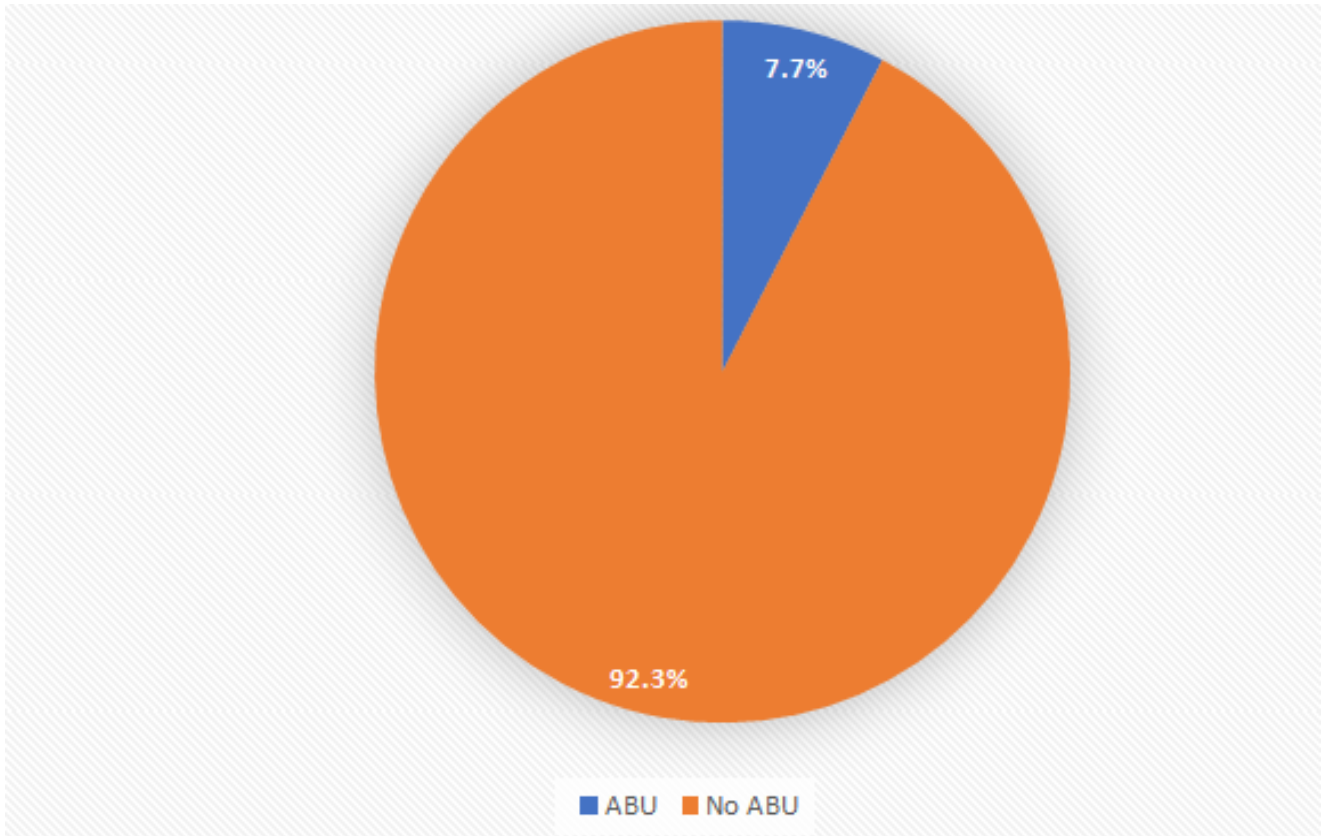
From 300 participants who were screened for Asymptomatic Bacteremia (ABU), 158 (52.7%) were males. Out of these 215 (71.7%) were taking cotrimoxazole prophylaxis and over two thirds of children 205 (68.3%) were in WHO disease clinical stage 3. (Table1)

**Table 1: clinical Characteristics of children with screened for ABU attending CTC clinic at MNH.**

<b>Variables</b>	<b>Category</b>	<b>N (%)</b>
Age	5-10	56 (18.7)
	10-15	106 (35.3)
	>15	138 (46)
Sex	Female	142 (47.3)
	Male	158 (52.7)
Viral load (copies/ml)	≤1000	219(73)
	>1000	81(27)
WHO disease stage	I	32 (10.7)
	II	22 (7.3)
	III	205 (68.3)
	IV	41 (13.7)
Cotrimoxazole use	Yes	215 (71.7)
	No	85 (28.3)
BMI	Underweight	158 (52.7)
	Normal	120 (40)
	Overweight	22 (7.3)
<b>TOTAL</b>		<b>300 (100)</b>

### 4.3 Prevalence of asymptomatic bacteraia

Out of the 300 HIV positive children attending CTC at MNH and who were screened for asymptomatic bacteraia 23 (7.7%) were positive as shown in the figure one below.



**Figure 2: Prevalence of Asymptomatic Bacteraia (ABU) among HIV infected Children attending CTC at MN**

### 4.4 Factors associated with asymptomatic bacteriuria among HIV positive children attending, MNH

Univariate analysis was performed to find the association between the studied factors and the outcome. From these findings female gender and children with viral load less than 1000 copies had higher odds of being positive for ABU compared to counterparts and this association was statistically significant. (Table 2.)

**Table 2: Distribution characteristics for Association between HIV positive and development of ABU.**

Variable	ABU (+) N (%)23	ABU (-) N (%)277	P -Value
AGE (years)			
5-10	13(9.4)	125(90.6)	P=0.43
10-15	3 (5.4)	53 (94.6)	P=0.76
Above 15	7 (6.6)	99 (93.4)	
SEX			
Female	22(15.5)	120(84.5)	*P=0.05
Male	1 ( 0.63)	157 (99.37)	
WHO CLINICAL STAGE			
III- IV	19 (7.7)	227 (92.3)	P=1.00
I-II	4 (7.4)	50 (92.6)	
CD4 COUNT/mm <sup>3</sup>			
>500	9 (10)	81(90)	P=0.32
≤500	14(6.7)	196 (93.3)	
VIRAL LOAD(copies/ml)			
≤1000	21 ( 9.6)	198( 90.4)	*P =0.005
>1000	2 ( 2.5)	79( 97.5)	
NUTRITIONAL STATUS			
Normal	12 (10)	108 (90)	P =0.43
Underweight	10 (6.3)	148 (93.7)	P= 0.74
Overweight/Obese	1 (4.6)	21 (95.4)	

\*P= fisher exact test

**Table 3: Univariate and multivariate logistic regression analysis of factors associated with ABU among HIV children at MNH.**

variables	CRUDE O R	95%CI	P VALUE	Adjusted OR	95% CI
Age(years)					
5-10	0.81	0.22-2.44	0.72	-	-
10-15	0.74	0.27-1.92			
>15	Ref				
Sex					
Male	Ref			Ref	
Female	28.78	3.83-216.29		25.86	3.43-19.5
CLINICAL STAGE	Ref				-
I-II	1.01	0.37-3.99	0.83		
III-IV					
CD4 COUNT//mm <sup>3</sup>					
≤ 500	Ref			-	-
>500	0.32	0.04-0.84	0.37		
V. load(copies/m)					
>1000	Ref			Ref	
≤1000	4.19	0.96-18.29		2.89	0.64-13.07
NUTRITIONAL STSTATUS	Ref				
Normal	0.67				
Under weight	0.56	0.28-1.59	0.45		
Over weight					

In the Univariate analysis sex and viral load shows that there was significant difference in development of ABU and in multivariate analysis only sex show association of HIV positive and development of ABU.

#### 4.5 Organisms isolated from urine culture of study participant with asymptomatic bacteruria.

Common organism isolates from urine culture samples of HIV infected children with asymptomatic bacteruria include the following; *Escherichia coli* 8(34.7%), *Pseudomonasaeruginosa* 6(26.1 %), *Klebsiella species*5 (21.7%), *proteus species*3 (13.4%) and *staphylococcusaureus*1 (4.3%)(Table 4.)

**Table 4: Distribution of organism isolated from HIV infected children with asymptomatic bacteruria at MNH.**

Organisms	Frequency N=23	%
<i>Escherichia coli</i>	8	34.78
<i>Pseudomonas aeruginosa</i>	6	26.09
<i>Klebsiella spp</i>	5	21.74
<i>Proteus spp</i>	3	13.04
<i>Staphylococcus aureus</i>	1	4.35

#### 4.5 Antibiotic sensitivity pattern

Most organisms were sensitive to, imepenem and ciprofloxacin and least sensitive to gentamicin and nitrofurantoin. *E. coli* was sensitive to imepenem and ciprofloxacin by 87.5% and 62.5% respectively.

**Table 5: Antibiotics sensitivity pattern to common bacteria's isolated from urine of HIV infected children at MNH.**

N %	CIPRO	MERO	GENTA	NITRO	TOTAL
<i>E. coli</i>	5(62.5)	7(87.5)	1(12.5)	2(25.0)	8
<i>K.pneumoniae</i>	3(60.0)	4(80.0)	2(40.0)	1(20.0)	5
<i>Proteus spp</i>	1(33.3)	2(66.7)	1(33)	1(33.3)	3
<i>P.aureginosa</i>	3(50.0)	5(83.3)	1(16.0)	2(33.3)	6
<i>S. aureus</i>	0	1(100)	0	0	1
Total					23

## **5.0 DISCUSSION**

### **5.1 Prevalence of asymptomatic bacteriuria among HIV infected children**

Asymptomatic bacteriuria (ABU) contributes to morbidity and mortality in Immune compromised patients including those living with HIV/AIDS. The aim of this study was to determine the prevalence of asymptomatic bacteriuria (ABU), associated risk factors, causative agent and their antimicrobial susceptibility pattern among HIV-infected children attended CTC clinic at Muhimbili National Hospital.

The overall prevalence of ABU in this study was 7.7%, which is lower compared to 24.7% reported by Adeseye et al and 10.3% reported by Iduoriyekemweni et al, in Nigeria(4,8). The lower prevalence in this study could be explained by fact that large number of participants was already on ART with good drug adherence and also majorities were using cotrimoxazole. Cotrimoxazole has intrinsic activity against broad spectrum of bacterial and has been shown to have benefit in prevention of UTI as well (22).

### **5.2 Associated factors for asymptomatic bacteriuria in HIV infected children**

Females had higher odds (twenty five more times) of ABU as compared to males. The findings in this study were consistent with literature and also findings on other similar studies conducted in Nigeria (4). The findings from this study and studies done in Nigeria is a reflection of what is already known that female children are more disposed due to short length of the female urethra and the close proximity of its orifice to the anus resulting in easy contamination by organisms from the rectum compared with males who have long urethra which reduce contamination. Furthermore females lack prostatic like fluid which is present in males and is thought to be bacteriostatic.

Most of participant with ABU in this study were between 5-10years of age though the association was not statistically significant. Iduoriyekemwen also observed a high prevalence of asymptomatic bacteriuria in HIV infected children in school age group. The findings from these studies could be explained by the fact that in school these children use shared public toilets with limited facilities to ensure proper hygiene. Nearly half of the study participant with ABU was malnourished but this was not significantly different from children without ABU. UTI has been found to be more prevalent in malnourished than well –nourished children regardless of HIV status (6). However since children with HIV are prone to have



asymptomatic bacteriuria (15). It is plausible to speculate that HIV infected children with malnutrition will have higher rates of ABU. There are possibilities that this was not observed in the current study because of small numbers of children who had both HIV and malnutrition, and those who had malnutrition did not present with severe form of malnutrition. This is because the effect of malnutrition on the immune system already depressed by HIV infection further includes reduced cell mediated immunity, diminished IgA response, reduced level of complements and decreased efficacy of phagocytes (21).

Children with CD4 less than 500cells/mm<sup>3</sup> and those children with WHO stage three and four of the disease had higher odds of being positive ABU, but the difference observed and was not statistically significant. However Olowe et al in Nigeria showed a significant association among young adult with CD4 cells counts and presence of ABU (15). Another study conducted at Calabar Nigeria by Iyang et al among HIV infected patients aged 5 to 69 that individuals with low CD4 cells counts and viral load <200cp/ml had significantly high chance to develop ABU (6,16). Furthermore Adeseye et al demonstrated that the stage of the disease and CD4 cell count are both risk factors for asymptomatic bacteriuria among children living with HIV. Finding from these studies are shows that immunosuppression is a risk factor for asymptomatic bacteriuria resulting possibly from progressive immune dysfunction induced by the virus.

### **5.3 Sensitivity pattern of isolated bacteria**

*Escherichia coli* were the most common from urine of HIV infected children at MNH, followed by *Pseudomonas aureginosa*. This finding is accordance with other findings reported by Iduoriyekemweni *et al* in a study conducted at Lagos Nigeria where *Escherichia coli*, *Klebsiella spp*, and *Staphylococcus aureus* were the common isolates cultured from the urine (4). Other isolate observed in this study were *Klebsiella spp* and *Proteus spp*. Other studies conducted at a different location in Nigeria by Olowe *et al* also showed the common isolate to be *Klebsiella pneumoniae*(35.3%) followed by *E.coli*(31.4%) and *Proteus spp*(15). *Staphylococcus aureus* was the only gram positive organism isolated in this study, this is not a common uropathogenic organisms thus there are possibilities that it was a contaminant during sample collection since this bacteria is a normal flora on the skin. However it could also be a

true isolate from the urine as it can cause UTI in immunocompromised patients. This type of bacteria have been reported in various studies such as Iyang *et al a* in study involving HIV infected individual on ART conducted in Nigeria were *Staphylococcus aureus* had the highest frequency followed by *Escherichia coli* (16).

Sensitivity pattern of common isolate was conducted in this study and the result shows that most of the Uropathogens were highly sensitive to the imepenem and less sensitive to the commonly used antibiotics for treatment of UTI in children. For example, *E coli* the common bacterial isolate in this study was highly sensitive to imepenem and least sensitive to gentamicin and nitrofurantoin. Similarly *Klebsiella spp* was also highly sensitive imepenem (80%) and least sensitive to nitrofurantoin. *Pseudomonas aureginosa*, an unusual uropathogen was sensitive to imepenem and less sensitive to gentamicin.

Other remaining isolates *Proteus spp and S.aureus* which were moderately and highly sensitive to imepenem respectively. Other studies conducted in Nigeria showed that the same common bacterial isolates were resistant to cotrimoxazole, ampicillin, amoxycillin, erythromycin and piperacilin (15).

However it is an expected finding since these medications are known to be more effective against gram positive organisms. Furthermore was notably an increase in resistance to gentamicin and nitrofurantoin which are the common used antibiotics for treatment of UTI in outpatient clinic. From this study imepenem and ciprofloxacin showed good actively against both gram positive and negative bacteria isolated from the urine. This is probably because these medications are not commonly used, thus has not developed resistance against them.

## **6.0 CONCLUSION AND RECOMMENDATION**

### **6.1 Conclusion**

Asymptomatic bacteriuria (ABU) is a fairly prevalent problem among HIV-infected children and more pronounced in female children.

### **6.2 Recommendations**

1. HIV-infected children, especially females and those with viral load <1000 copies attending CTC clinics should be routinely evaluated for ABU.
2. Selection of antibiotics for treatment of ABU/UTI should be based on local sensitivity pattern where possible.
3. Further long term studies are needed to determine the relation between asymptomatic bacteriuria and development of symptomatic UTI.

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**Appendix i: QUESTIONNAIRE**

**PART A: SOCIODEMOGRAPHIC DATA**

- 1. NAME .....
- 2. AGE.....
- 3. SEX :  
                    (a) MALE       (b) FEMALE

- 4. CONTACT DETAILS.....

**ANTHROPOMETRIC MEASUREMENTS (NUTRITION STATUS)**

- 5. HEIGHT (M).....
- 6. WEIGHT (KG).....
- 7. BMI (kg/m<sup>2</sup>).....

**HIV RELATED INFORMATION**

- 8. CTC file number.....
- 9. Current CD 4 COUNT (last 6 months).....  
                    (a) >500/mm<sup>3</sup>  
                    (b) ≤ 500/ mm<sup>3</sup>
- 10. Current VIRAL LOAD copies/ml (last 6 months).....  
                    a) ≤ 1000 copies /ml  
                    b) >1000 copies/ml
- 11. WHO clinical stage.....
- 12. For how long on ART? .....
- 13. Are you on any other medications other than ART?  
                    (a) YES       (b) NO

If YES which medications? List them and their duration



(a) >500/mm<sup>3</sup>      (b) 350-499/mm<sup>3</sup>      (c) 200-349/mm<sup>3</sup>      (d) <200/mm<sup>3</sup>

10. Idadi ya virus

11. Daraja la ugonjwa.....

12. Je unatumia dawa za ART

(a) ndio      (b) hapana

13. Umekuwa ukitungia ARV kwa kipindi cha muda gani?.....

14. Unatumia ARV kundi la aina gani?. Jina la dawa ya ARV.....

15. Unatumia dawa nyingine tofauti na ART?

(a) ndio      (b) hapana

Kama jibu ni ndio, taja majina ya dawa hizo na muda ambao umekuwa ukitungia

.....  
.....  
.....  
.....

16. Umelazwa hospitali siku za hivi karibuni?

(a) Ndiyo      (b) Hapana

18. Je una dalili zifuatazo

(a) maumivu ya tumbo

(b) homa

(c) maumivu wakati wa kukojoa

19. Majibu baada ya kuotesha mkojo;-

Aina ya bacteria walioota \_\_\_\_\_, \_\_\_\_\_

Dawa zilizoweza kuwadhibiti ni \_\_\_\_\_, \_\_\_\_\_



## **Appendix ii: Consent form**

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES (MUHAS)

An informed consent form for study on prevalence and risk factors associated with ABU in HIV-infected children

### INTRODUCTION

My name is Dr Luka Mkeni LUI a resident at Muhimbili University of Health and Allied Sciences, Dar es Salaam. I'm doing a research on prevalence and risk factors associated with ABU in HIV-infected children at MNH.

I am going to give you information and invite you to be part of this research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. If you have questions, please ask me or the doctor/nurse.

Purpose of the research

The purpose of this research is to determine the prevalence and risk factors associated with ABU in HIV-infected children attending CT clinic at MNH so as to know the best antibiotics to use during management of in HIV-infected children before urine culture result. This will help in reducing using irrational use of antibiotics and other complications which may result ABU.

What does participation involves?

This research will involve a questionnaire which will assess the child if she/he qualify to be enrolled in to the study. You sign this consent form and answer the questions in the questionnaire as well as you can. It will take approximately 3 minutes.

We are inviting all children together with parents/caregivers who admitted to MNH to participate.

Your participation in this research is entirely voluntary. Whether you choose to participate or not, all the services you receive at this hospital will continue and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

**Confidentiality**

Information about you that will be collected during the research will be kept confidential and no-one but the researchers will be able to see it. We will not be sharing the identity of those participating in the research. We will disclose blood culture result to you and the attending pediatrician so that he/she can prescribe antibiotics to which microorganism is sensitive to.

**Risks**

By participating in this research you will not be subject to any risk

**Benefits**

Your child will be given antibiotics based on result of blood culture result Your participation is likely to help us find the answer to the research question.

**Certificate of Consent**

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Name of Participant \_\_\_\_\_

Signature of Participant \_\_\_\_\_

Date \_\_\_\_\_

Day/month/year

**Study Title:** *Prevalence and risk factors associated with asymptomatic bacteriuria in HIV-infected children at Muhimbili National Hospital, Dar-Es-Salaam: A cross-sectional study*

ID no.....

LUKA MKENI LUI  
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lukamkeni@gmail.com  
18<sup>TH</sup> January, 2021.

DIRECTOR OF POSTGRADUATE STUDIES,  
P.O. Box 65001  
MUHAS

**U.F.S:** Dean School of Medicine,  
MUHAS

**U.F.S:** Head of Department, Pediatrics and Child Health,  
MUHAS

**U.F.S:** Main Supervisor,  
Dr Helga Naburi.

Dear Sir/Madam,

**RE: SUBMISSION OF LOOSE-BOUND FREE ERROR DISSERTATION**

With reference to the above heading,

I am Dr LUKA MKENI LUI with Reg. No **HD/MUH/T.186/2017** MMed Pediatrics and Child Health. I hereby would like to submit my dissertation report titled. **PREVALENCE AND FACTORS ASSOCIATED WITH ASYMPTOMATIC BACTERIURIA IN HIV-INFECTED CHILDREN AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM**

Yours Sincerely,

---

**LUKA MKENI LUI**

