PREVALENCE AND PATTERN OF CATHETER ASSOCIATED
URINARY TRACT INFECTION AT LAGOS UNIVERSITY TEACHING
HOSPITAL, IDI ARABA

BY

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MBBS (ABSU)

AF/009/09/002/979

A DISSERTATION SUBMITTED TO THE NATIONAL POSTGRADUATE
MEDICAL COLLEGE OF NIGERIA IN PARTIAL FULFILMENT OF THE
REQUIREMENTS FOR THE AWARD OF THE FELLOWSHIP OF THE
COLLEGE IN INTERNAL MEDICINE

(NEPHROLOGY SUBSPECIALTY)

MAY, 2018
DECLARATION

I hereby declare that this work is original unless otherwise acknowledged. The work has not been presented to any other college for a fellowship nor has it been submitted elsewhere for publication.

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DEDICATION

This work is dedicated to all patients living with kidney disease.
ACKNOWLEDGEMENT

All praise and adoration be to the Almighty God who makes all things beautiful in His time.

I most sincerely appreciate my supervisors Dr. B.T. Bello and Dr. R.O. Oladele for their tutelage and effort at ensuring the completion of this work.

I am indebted to the head of renal unit Dr. M.O. Mabayoje. I also wish to express my profound appreciation to all the consultant nephrologists in the department of medicine, Dr. C.O. Amira, Dr. R.W. Braimoh and Dr. O. Adewunmi.

I also wish to express my appreciation to all the consultants in the department of medicine for the wonderful role they played in my training.

I am grateful to my wife and children for their love and understanding during my period of study.

I appreciate my colleagues Dr Okolo, Dr Orolu, Dr Long-John, Dr Olowoyo, Dr Johnson, Dr Ogbonna and Dr Ikebudu for their assistance in this study.
<table>
<thead>
<tr>
<th>Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title page</td>
<td>i</td>
</tr>
<tr>
<td>Declaration Page</td>
<td>ii</td>
</tr>
<tr>
<td>Certification by Supervisors</td>
<td>iii</td>
</tr>
<tr>
<td>Attestation by Head of Department</td>
<td>iv</td>
</tr>
<tr>
<td>Dedication</td>
<td>v</td>
</tr>
<tr>
<td>Acknowledgement</td>
<td>vi</td>
</tr>
<tr>
<td>Tables and Legends</td>
<td>x</td>
</tr>
<tr>
<td>Abbreviations and Acronyms</td>
<td>xi</td>
</tr>
<tr>
<td>Abstract</td>
<td>xiii</td>
</tr>
<tr>
<td>Chapter 1</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>1.1 Background</td>
<td>1</td>
</tr>
<tr>
<td>1.2 Consequences of Indwelling Urinary Catheter Use</td>
<td>2</td>
</tr>
<tr>
<td>1.3 Guidelines of Indwelling Urinary Catheter Use</td>
<td>2</td>
</tr>
<tr>
<td>1.4 Indications for Indwelling Urinary Catheters</td>
<td>2</td>
</tr>
<tr>
<td>1.5 Justification</td>
<td>3</td>
</tr>
<tr>
<td>1.6 Aim and Objectives</td>
<td>4</td>
</tr>
<tr>
<td>Chapter 2</td>
<td>5 - 23</td>
</tr>
<tr>
<td>Literature review</td>
<td>5</td>
</tr>
<tr>
<td>2.1 Introduction and Definitions</td>
<td>5</td>
</tr>
<tr>
<td>2.2 Epidemiology of Catheter-Associated Urinary Tract Infection</td>
<td>6</td>
</tr>
<tr>
<td>2.3 Indications for Urethral Catheterization</td>
<td>8</td>
</tr>
<tr>
<td>2.4 Aetio-pathogenesis of Catheter-Associated Urinary Tract Infection</td>
<td>9</td>
</tr>
<tr>
<td>2.5 Factors Predisposing to Catheter-Associated Urinary Tract Infection</td>
<td>11</td>
</tr>
<tr>
<td>2.6 Guidelines for Urethral Catheter Insertion</td>
<td>14</td>
</tr>
</tbody>
</table>
Chapter 2

2.7 Clinical Manifestations of Catheter Associated Urinary Tract Infection 15
2.8 Diagnosis 17
2.9 Short and Long-term Effects of Catheter-Associated Urinary Tract Infection 17
2.10 Treatment Modalities of Catheter-Associated Urinary Tract Infection 18
2.11 Prevention of Catheter Associated Urinary Tract Infection 19

Chapter 3 24 - 33

Study design and methods 24
3.1 Study Site 24
3.2 Study Design 24
3.3 Study Population 24
3.4 Exclusion Criteria 24
3.5 Inclusion Criteria 25
3.6 Sampling Method 25
3.7 Sample Size Determination 28
3.8 Study Duration 26
3.9 Ethical Approval/Consent/Title Registration 26
3.10 Patient Recruitment Procedure 27
3.11 Study Questionnaire 28
3.12 Definition of Terms 31
3.13 Primary Endpoint 29
3.14 Secondary Endpoint 30
3.15 Specimen Processing 30
3.16 Antimicrobial Susceptibility Testing 31
3.17 Materials and Equipment 32
3.18 Data Analysis 33

Chapter 4 34 - 56

Results 34
4.1 Baseline Characteristics of the Study Population 34
4.2 Indications for and Duration of Indwelling Urinary Catheter Use 37
4.3 Frequency of Catheter-Associated Urinary Tract Infection 40
4.4 Microbiological Profile of Isolates 41
4.5 Antibiotic Susceptibility Pattern of the Bacterial Isolates 44
4.6 Factors Associated with the Development of Bacteriuria 46

Chapter 5 57 - 64
Discussion 57
5.1 Introduction and Description of the Study and its Participants 57
5.2 Indications for Indwelling Urethral Catheter Placement 57
5.3 Incidence of Catheter Associated Bacteriuria 58
5.4 Spectrum of Organisms causing Catheter-Associated Bacteriuria 59
5.5 Incidence of Catheter Associated Candiduria 60
5.6 Antibiotic Susceptibility Pattern of the Organisms causing CA-Bacteriuria 61
5.7 Factors associated with the development of Catheter-Associated Bacteriuria 62
5.8 Strengths and Weaknesses of the Study 64

Chapter 6 65 - 66
Limitations, Conclusions and Recommendations 65
6.1 Limitations 65
6.2 Conclusions 65
6.3 Recommendations 66
References 67
Tables and Legends

Table 1  Baseline clinical characteristics of the study population  36
Table 2  Indications for continuous bladder drainage via an indwelling urethral catheter stratified according to gender  38
Table 3  The indications for continuous bladder drainage via an indwelling urethral catheterization stratified according to age range  39
Table 4  Distribution of microbial isolates  42
Table 5  Distribution of various isolates in relation to age  43
Table 6  Distribution of the antibiotic sensitivity pattern of the bacterial isolates  45
Table 7  Univariate analysis of factors associated with bacteriuria  55
Table 8  Logistic regression analysis of factors associated with bacteriuria  56
Figure 1  Age-range distribution of the study population  35
Figure 2  Frequency of bacteriuria over the duration of the study  48
Figure 3  Frequency of CA-ASB among study participants across the various age ranges  49
Figure 4  Frequency of Bacteriuria among Male and Female Study Participants  50
Figure 5  Frequency of Bacteriuria among Patients with and without Diabetes  51
Figure 6  Frequency of Bacteriuria among Patients with and without Hypertension  52
Figure 7  Frequency of Bacteriuria among Patients with and without Renal Insufficiency  53
Figure 8  Frequency of Bacteriuria among Patients with and without Urinary Tract Obstruction  54
### Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMC</td>
<td>Amoxicillin/Clavulanate, Amoxicillin and Clavulanate</td>
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<td>AK</td>
<td>Amikacin</td>
</tr>
<tr>
<td>BPH</td>
<td>Benign Prostatic Hyperplasia</td>
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<td>CA-ASB</td>
<td>Catheter Associated Asymptomatic Bacteriuria</td>
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<td>CA-UTI</td>
<td>Catheter Associated Urinary Tract Infection</td>
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<tr>
<td>CAZ</td>
<td>Ceftazidime, Ceftazidime,</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>CKD</td>
<td>Chronic Kidney Disease</td>
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<tr>
<td>CKD-EPI</td>
<td>Chronic Kidney Disease Epidemiology Collaboration</td>
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<tr>
<td>CIP</td>
<td>Ciprofloxacin</td>
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<tr>
<td>CLSI</td>
<td>Clinical and Laboratory Standards Institute</td>
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<tr>
<td>CN</td>
<td>Gentamycin</td>
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<tr>
<td>CRO</td>
<td>Ceftriaxone</td>
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<tr>
<td>FEP</td>
<td>Cefepime</td>
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<tr>
<td>GFR</td>
<td>Glomerular Filtration Rate</td>
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<tr>
<td>HAI</td>
<td>Hospital Acquired Infection</td>
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<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
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<tr>
<td>IDMS</td>
<td>Isotope Dilution Mass Spectrometry</td>
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<tr>
<td>IDSA</td>
<td>Infectious Diseases Society of America</td>
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<tr>
<td>IUC</td>
<td>Indwelling Urinary Catheter</td>
</tr>
<tr>
<td>LEV</td>
<td>Levofloxacin</td>
</tr>
</tbody>
</table>
LTCF  Long Term Care Facilities
LUTH  Lagos University Teaching Hospital
MEM   Meropenem
NAUTH Nnamdi Azikiwe University Teaching Hospital
RCT   Randomized Controlled Trial
TZP   Piperacillin/Taxobactam
UTI   Urinary Tract Infection
Abstract

Background to Study
Almost all healthcare-associated urinary tract infections (UTI) are caused by instrumentation of the urinary tract with about 80% of these being associated with the presence of an indwelling urinary catheter (IUC). This study aimed to determine the prevalence and pattern of catheter-associated urinary tract infection at the Lagos University Teaching Hospital.

Study Design and Methods
The study was a prospective observational study of 200 participants aged 18 and 65 years who had an IUC inserted as part of their care at the hospital between July 2015 and May 2016. 5ml samples of urine were obtained for culture at the time of urethral catheterization and on days 3, 7, 10, 14 and 28 post catheterization. The primary endpoint of the study was the development of CA-UTI.

Data was analysed using SPSS version 22. Continuous data are presented as means and standard deviation while categorical data are presented as percentages. Comparison between means was done using the Student’s t-test, while comparison between percentages was done using chi-square test. Logistic regression analysis was subsequently used to determine the factors that were independently associated with the development of bacteriuria. The level of statistical significance was set at a p-value ≤0.05.

Result
The overall frequency of CA-UTI was 43%. The most common microbial isolate was E. coli which accounted for 29(33.7%) of all isolates cases. The other isolates in decreasing order of frequency were; C. albicans 25(29.1%), P. aeruginosa 14(16.3%), K. pneumonia 10(11.6%), enterococcus
2(2.3%) and A. iwoffii 2(2.3%). In 4(4.7%) of the participants, more than one organism was isolated (E.coli and C. albicans).

Bacteriuria was associated with duration of catheterization (p-value = 0.001); age (p-value < 0.0001); presence of diabetes (p-value < 0.001); presence of hypertension (p-value = 0.005); presence of renal insufficiency (p-value = 0.001) and presence of urinary tract obstruction (p-value = 0.003) on univariate analysis. However, logistic regression analysis identified duration of catheterization (odds ratio (OR) = 12.0; 95% confidence interval (CI) = 5.6 - 25.5; p-value <0.001), presence of diabetes (OR = 5.6; 95% CI = 1.5 - 20.9; p-value = 0.01), presence of urinary tract obstruction (OR = 3.9; 95% CI = 1.3 - 11.3; p-value = 0.013) and age (OR = 1.1; 95% CI = 1.0 - 1.1; p-value = 0.001) as the factors independently associated with bacteriuria.

Conclusion

Bacteriuria was a frequent complication among patients with IUC in this study. The predominant causative organism was E. coli. Duration of catheterization, presence of diabetes, presence of urinary tract obstruction and older age were the factors associated with development of bacteriuria.
CHAPTER 1

INTRODUCTION

1.1 Background
The urinary tract is the commonest site of hospital-acquired infections (HAI).\(^1\) Urinary tract infections (UTIs) account for as much as 40% of all HAI in some reports.\(^2\) Practically all healthcare-associated UTIs are caused by instrumentation of the urinary tract and it is estimated that 80% of hospital acquired UTIs are associated with the presence of an indwelling urinary catheter (IUC),\(^3\) leading to enormous morbidity in both men and women even though it is largely preventable. This is because urinary catheters in some cases are placed unnecessarily, remain in place without the physician being aware, and in many cases, are not removed as soon as possible when no longer required.\(^4\)

1.2 Consequences of Indwelling Urinary Catheter Use
The use of IUC is associated with several consequences; including pain and discomfort, bacteriuria, urethritis, erosion of the urethra, creation of false passage as well as development of urethral strictures.\(^5,6\) In addition, IUC use may cause haematuria, catheter-associated urinary tract infection (CA-UTI), bacteremia, frequent febrile episodes, catheter obstruction, renal and bladder stone formation associated with urease-producing uropathogens, local genitourinary infections, fistula formation, incontinence, and bladder cancer.\(^7\)
1.3 Guidelines of Indwelling Urinary Catheter Use

The 2009 Centers for Disease Control and Prevention (CDC) guidelines for prevention of CA-UTI recommends catheter use only for appropriate indications. Catheter use and duration should be minimized in all patients, especially those at higher risk for CA-UTI (e.g., women, elderly persons, and patients with impaired immunity). Catheters should be kept in place only for as long as needed. Indwelling catheters placed in patients undergoing surgery should be removed as soon as possible postoperatively. The use of urinary catheters as treatment for urinary incontinence in patients and nursing home residents should be avoided. Clinicians are also advised to avoid using systemic antimicrobials routinely to prevent CA-UTI in patients requiring either short- or long-term catheterization.

The 2009 guidelines of the Infectious Diseases Society of America (IDSA) for prevention of CA-UTI however state that an indwelling catheter may be used at the patient’s request in exceptional cases and when other approaches to incontinence management have been ineffective. The guidelines also states that if an indwelling catheter had been in place for more than 2 weeks at the onset of CA-UTI and remains indicated, the catheter should be replaced to promote continued resolution of symptoms and to reduce the risk of subsequent catheter-associated infection.

1.4 Indications for Indwelling Urinary Catheters

The following are recommended indications for use of an indwelling urinary catheter:

1. Acute urinary retention or bladder outlet obstruction.

2. Need for accurate measurement of urinary output in critically ill patients.
3. In the perioperative period for selected surgical procedures. These include urologic surgeries or other surgeries on contiguous structures of the urinary tract.

4. Anticipated prolonged duration of surgery. In this case the catheter should be removed in post-anaesthesia care unit.

5. Surgeries involving large volume infusions or use of diuretics.

6. Cases where there is need for intraoperative monitoring of urinary output.

7. To assist in healing of open sacral or perineal wounds in incontinent patients.

8. Some cases of prolonged immobilization such as in potentially unstable thoracic or lumbar spine injuries, or multiple traumatic injuries such as pelvic fractures.

9. To improve comfort for end-of-life care.

1.5 Justification

Catheter-associated bacteriuria is the most common healthcare-associated infection worldwide and is a result of the widespread use of urinary catheterization in hospitals and long-term care facilities (LTCF). Prompt initiation of effective antimicrobial therapy is associated with improved renal and patient outcomes by reducing the risk of ascending infection; reducing morbidity and mortality as well as reducing the overall cost of care. However, the spectrum of bacteria causing CA-UTI as well as their antimicrobial sensitivity pattern is largely unknown in our environment.

This fact, combined with delays in obtaining urine culture results due to non-availability of facilities for culture and/or inability of patients to pay for investigations due to financial constraints frequently leads to delays in instituting effective therapy with its resultant risk of complications such as ascending infections, renal impairment and mortality.
This study will provide information about the spectrum of bacteria causing CA-UTI at the Lagos University Teaching Hospital (LUTH) as well as their antibiotic sensitivity pattern. The study findings will provide a guide to physicians in their choice of initial antibiotic therapy while awaiting results of urine culture and thereby reduce delays in initiation of effective antimicrobial therapy.

1.6 Aim and Objectives

Broad Objective
This is to determine the prevalence and pattern of catheter-associated urinary tract infection at the Lagos University Teaching Hospital.

Specific Objectives

1. To identify the indications for indwelling urinary catheter use in patients admitted to the wards and compare these with internationally accepted indications.

2. Determine the frequency of occurrence of CA-UTI in patients with indwelling urinary catheters.

3. Determine the spectrum of organisms that cause CA-UTI and their antibiotic susceptibility pattern.

4. Identify the factors associated with the development of CA-UTI in patients with indwelling urinary catheters.
CHAPTER 2

LITERATURE REVIEW

2.1 Introduction and Definitions

An IUC is a drainage tube that is inserted into the urinary bladder and left in place. It is usually connected to a closed collection system and ensures continuous drainage of the urinary bladder. Between 15% and 25% of patients in general hospitals have a urinary catheter inserted at some time during their stay,\textsuperscript{11,12} and the rate of catheter use appears to be increasing.\textsuperscript{13} Most hospitalized patients are catheterized for only 2 to 4 days,\textsuperscript{7} but many are catheterized for longer durations. Between 5% and 10% of nursing home residents are also managed with urethral catheterization, in some cases for years.\textsuperscript{14-16} Because urethral catheters are commonly used in healthcare facilities, the control of infections due to these devices should be an essential goal of healthcare infection prevention programs.

Although indwelling catheters are the most commonly used means of draining the urinary bladder, alternative methods are available and include; intermittent catheterization, and external catheters. Intermittent catheterization involves brief insertion of a catheter into the bladder through the urethra to drain urine at intervals. An external catheter is a urine containment device that fits over the genitalia and is attached to a urine drainage bag. The most commonly used external catheter is a soft flexible sheath that fits over the penis otherwise known as a condom catheter.

Bacteriuria commonly complicates the use of urinary catheters as a means of draining the urinary tract. Most cases of catheter-associated bacteriuria are attributable to use of an IUC. Indwelling urinary catheters are generally considered to be of short term if they are left in-situ for a period less 30 days while they are considered to be long term when in-situ for 30 days or more.\textsuperscript{9} Urinary
catheter acquired infection may manifest as catheter-associated asymptomatic bacteriuria (CA-ASB) or CA-UTI. CA-ASB is diagnosed when one or more organisms are present at quantitative counts ≥10⁵ cfu/ml from an appropriately collected urine specimen in a patient with no symptoms attributable to urinary tract infection while the term CA-UTI is used when presence of bacteriuria in a catheterized individual is accompanied by symptoms compatible with the presence of urinary tract infection.

2.2 Epidemiology of Catheter-Associated Urinary Tract Infection

Catheter-associated bacteriuria (CA-bacteriuria) is the most common healthcare-associated infection worldwide. It accounts for up to 40% of hospital-acquired infections and most of the 900,000 patients with nosocomial bacteriuria in US hospitals each year. CA-bacteriuria is also among the most common infections in LTCF, although symptomatic CA-bacteriuria is less common than respiratory, skin and soft-tissue infections. Dougnon and co-workers reported the prevalence of CA-UTI at a hospital in Zinvie, Benin to be 23.3% 48 hours after catheterization. In this prospective observational study, urine samples were taken 10 minutes after passage of urethral catheter and a repeat sample taken 48 hours post-catheterization. Aseptic procedures were ensured in the course of this study. These measures were geared towards ensuring elimination of prior infection and introduction of iatrogenic infection. This study demonstrated a relatively high prevalence considering the short duration of study.

Data from Nigeria suggests that CA-UTI is quite common. In Abeokuta, South-west Nigeria, Abaeze and Abasiama reported a prevalence of 41.1% while Taiwo and Aderounmu reported a prevalence of 74.6% at the Ladoke Akintola University Teaching Hospital, Osogbo also in South-west Nigeria. The relatively higher incidence of CA-UTI as reported by Taiwo and
Aderounmu can be explained by the differences in the characteristics of the patients studied. The population studied by Taiwo and Aderounmu consisted of mainly patients attending a urology clinic, most of whom had benign prostatic hyperplasia (BPH) and had been on prolonged urethral catheterization.

Onipede et al in a prospective study at Obafemi Awolowo University Teaching Hospitals Complex reported a CA-UTI prevalence of 60.9%. The frequency of CA-UTI was found to be higher among males (78%) compared to females (70.6%). This is at variance with studies that have demonstrated a higher frequency in women. However, in this study, the duration of catheterization as well as other factors associated with the development of CA-UTI were not stratified according to gender; as these may account for a difference in the frequency of CA-UTI one cannot conclusively say that males were at a higher risk.

Onyegbule and co-workers, at Nnamdi Azikiwe University Teaching Hospital (NAUTH), reported the overall incidence of CA-UTI after 72 hours of urethral catheterization to be 9.0%. In this study, a total of 156 women undergoing caesarean section had a urethral catheter inserted immediately before surgery. Of these, one group comprising 79 women had their urethral catheters removed 24 hours after caesarean section and in them, the incidence rate of CA-UTI was 11.4% while in the other group comprising 77 participants who had their urethral catheters removed immediately after surgery, the incidence rate of CAUTI was 6.5%. Olarinde et al studied urinary catheter related infections in Federal Medical Centre Abeokuta Nigeria and reported a prevalence of 41%. In this study, the duration of catheterization was not stated thereby making the interpretation of the magnitude of the prevalence difficult.
2.3 **Indications for Urethral Catheterization**

Current guidelines recommend the following indications for use of indwelling urinary catheters\(^{10}\)

1. Acute urinary retention or bladder outlet obstruction.
2. Need for accurate measurement of urinary output in critically ill patients.
3. In the perioperative period for selected surgical procedures. These include urologic surgery or other surgery on contiguous structures of the urinary tract.
4. Anticipated prolonged duration of surgery. In this case the catheter should be removed in post-anaesthesia care unit.
5. Surgeries involving large volume infusions or use of diuretics.
6. Cases where there is need for intraoperative monitoring of urinary output.
7. To assist in healing of open sacral or perineal wounds in incontinent patients.
8. Some cases of prolonged immobilization such as in potentially unstable thoracic or lumbar spine injuries, or multiple traumatic injuries such as pelvic fractures.
9. To improve comfort for end-of-life care.

Despite these recommendations however, many patients who do not meet these indications continue to be catheterized. In the study by Taiwo and Aderounmu\(^{24}\) which evaluated 122 patients with indwelling urinary catheters at the Ladoke Akintola University Teaching Hospital, the commonest indication for catheterization was bladder outflow obstruction due to benign prostatic hyperplasia (BPH) in 76 (62.3%) patients. Other indications were postoperative 14 (11.5%), carcinoma of the pancreas 8 (6.6%), urethral stricture 8 (6.6%), cerebrovascular disease 4 (3.3%), testicular tumour 2 (1.6%), intestinal obstruction 2 (1.6%), and others 8 (8.2%).
2.4 Aetio-pathogenesis of Catheter-Associated Urinary Tract Infection

The presence of a urinary catheter is the most important risk factor for bacteriuria. This is because the presence of the catheter facilitates bacteria entry into the urinary tract and once in the urinary tract the bacteria form a biofilm along both the external and internal surfaces of the catheter that protects them from the host defences. The process of catheter insertion predisposes to bacteriuria by introducing an inoculum of bacteria into the bladder. The presence of the catheter also facilitates ascension of uropathogens from the meatus to the bladder via the catheter-mucosa interface. Intraluminal ascension of pathogens to the bladder may also occur if the collecting tube or drainage bag becomes contaminated. In addition to this, the catheter tends to compromise complete bladder emptying, and provides a frequently manipulated foreign body on which pathogens are deposited via the hands of the patient and/or healthcare personnel.

Enteric pathogens (e.g. *Escherichia coli*) are the organisms most commonly responsible for CA-UTI but *Pseudomonas* species, *Enterococcus* species, *Staphylococcus aureus*, coagulase negative staphylococci, *Enterobacter* species, and yeast also are known to cause infection. Proteus and *Pseudomonas* species are organisms most commonly associated with biofilm growth on catheters. Approximately two-thirds of the uropathogens that cause CA-bacteriuria in patients with IUCs are extra-luminally acquired by ascension along the catheter-urethral mucosa interface, while about one-third are intra-luminally acquired through reflux of organisms gaining access to the catheter lumen from failure of closed drainage or contamination of collection bag urine. Only about 5% of episodes of CA-bacteriuria follow introduction of periurethral organisms into the bladder at the time of catheter insertion.

Evidence in support of extra-luminal ascension as the dominant pathway for bacteria to gain entry into the bladder comes from a study that showed only three of 29 episodes of bacteriuria with
gram-negative bacilli or enterococci occurred in patients with negative meatal cultures for these organisms.\textsuperscript{32} In addition, patients remain at increased risk of bacteriuria for at least 24 hours after removal of the catheter,\textsuperscript{33} a fact that suggests that colonization of the urethra persists even after the catheter is removed. The causative pathogen can be found in the urethra in up to 67\% of women and 29\% of men just prior to the development of CA-bacteriuria, which suggests also, that entry of uropathogens via the urethral route occurs more often in women that it does in men.\textsuperscript{34,35}

The biofilm is a complex organic material consisting of micro-organisms growing in colonies within an extracellular mucopolysaccharide substance which they produce. Normal constituents of urine such as Tamm-Horsfall protein, and magnesium and calcium ions are incorporated into this material. Formation of biofilm begins immediately after catheter insertion, when organisms adhere to a film of host proteins which forms along the catheter surfaces. With time more and more extracellular material are deposited and the bacterial colonies replicate within it. The biofilm promotes colonization of the urine by; providing a surface for bacterial adhesion, protecting the bacteria from host defenses and causing constant mucosal irritation.\textsuperscript{36} It leads to a situation where organisms are constantly inoculated into the bladder even after they have been eradicated from the urine.

A single bacterial species is usually seen during the initial episode of bacteriuria that follows insertion of an indwelling catheter. After development of a mature biofilm, colonization is generally polymicrobial. For individuals with long-term indwelling catheters, three to five different organisms are usually isolated.\textsuperscript{20,37} The microbiology of the biofilm on an indwelling catheter changes with continuing turnover of organisms in the biofilm while the catheter remains in-situ.\textsuperscript{38} This is because organisms growing in the biofilm are in an environment where they are relatively protected from antimicrobials and host defenses.
2.5 Factors Predisposing to Catheter-Associated Urinary Tract Infection

Several factors predisposing to the development of CA-UTI have been identified. These include:

*Duration of Catheterization:*

The duration of catheterization is the single most important risk factor for the development of CA-bacteriuria.\(^\text{39}\) Thus, rates vary in published studies according to how long the patients had been catheterized for and how often urine cultures were performed.\(^\text{22,23}\) Once a urethral catheter is placed, the daily incidence of bacteriuria ranges between 3% and 10%. Between 10% and 30% of patients who undergo short-term catheterization develop bacteriuria and are asymptomatic while between 90% and 100% of patients who undergo long-term catheterization develop bacteriuria. By one month, nearly all patients with an indwelling catheter will be bacteriuric.

The study by Onyegbule *et al* demonstrates this importance of duration of catheterization in determining the likelihood of development of CA-UTI. In this study, the 79 women who had their urethral catheter removed 24 hours after caesarean section had a CA-UTI incidence rate of 11.4% which was significantly higher than the 6.5% reported in the second group whose urethral catheters were removed immediately after caesarean section.\(^\text{26}\) Lee and colleagues\(^\text{40,41}\) also demonstrated that longer duration of catheterization was associated with a higher risk of CA-UTI in hospitalized pediatric patients. In another study, the relative risk of catheterization for more than 6 days was found to be 5.1 – 6.8.\(^\text{42}\) In a multivariate analysis reviewed by Salgado *et al*; duration of catheterization was one of five factors found to be later associated with CA-UTI.\(^\text{43}\) Longer duration of catheterization as a risk factor for CA-UTI was also corroborated by Platt and co-workers.\(^\text{44}\)

*Gender*

There is a large body of evidence that suggests CA-UTI is commoner in females. In a retrospective study aimed at defining the relationships between age, sex and HAI rates among 85,461 patients
hospitalized between January 1, 2009, and December 31, 2011; all groups except younger female surgical patients had higher CA-UTI rates than male patients. The outcome of this study showed that the relationship between sex and the rate of HAIs varied depending on the underlying acute indication for hospital admission.\textsuperscript{45}

In another retrospective study by Lee and co-workers\textsuperscript{41}, the occurrence of CA-UTI was found to be higher in females with an odd ratio (OR) of 1.97 using univariate analysis and an OR of 2.17 following multivariate analysis. According to Maki and Tambyah\textsuperscript{42}, the relative risk of CA-UTI using multivariate analysis was 2.5-3.7. In another prospective observational study undertaken between June 1979 and April 1981 at New England Deaconess Hospital, Boston, Massachusetts, in which 134 out of 1,458 adult inpatients developed UTI following bladder catheterization; the aid of multiple logistic regression analysis identified female sex as one of the nine factors significantly associated with acquisition of CA-UTI.\textsuperscript{44}

The shorter urethra in females, which shortens the distance that bacteria must travel to reach the bladder is purported to be one of the underlying mechanisms responsible for the higher incidence of CA-UTI in women.

*Age*

CA-UTI is commoner in the elderly compared to younger age groups. Rosser and co-workers demonstrated that age (more than 60 years) was one of the independent risk factors associated with the development of hospital-acquired UTI among patients with IUC.\textsuperscript{46} There was a higher incidence of CA-UTI among patients 60 years and older. According to Chenoweth and Saint, age greater than 50 is one of the non-modifiable patient related risk factors for developing CA-UTI.\textsuperscript{47}
**Diabetes:**

The presence of diabetes has been reported to be associated with an increased risk of developing CA-UTI. In the retrospective study by Lee *et al* aimed at identifying the risk factors for CA-UTI, patients with diabetes were 4.55 times more likely to develop CA-UTI than were those without diabetes.\(^{41}\) Platt *et al* also reported the presence of diabetes as a risk factor for development of CA-UTI. Platt and co-workers suggested two possibilities for why diabetic patients are at increased risk of acquiring infection: these were increased prevalence of perineal colonization by potential pathogens and an increased capacity of the urine of some patients with diabetes to support microbial growth.\(^{44}\)

A probable cause of this increased frequency of infections is defective immunity. It has been observed that among individuals with diabetes, impaired granulocyte function, and the effects of glucosuria on the growth of uropathogens contribute to a higher UTI prevalence. Additionally, some microorganisms become more virulent in the presence of hyperglycaemia. Another mechanism which can lead to the increased frequency of infections in diabetic patients is an increased adherence of microorganisms to diabetic compared to non-diabetic cells.\(^{48}\) This has been described for *Candida albicans*.

**Systemic Antibiotics Use:**

Systemic antibiotic use though not routinely recommended has been found in some studies to reduce the frequency of occurrence of CA-UTI. In the study by Lee *et al*, there appeared to be a 65% reduction in the risk of CA-UTI when the patients received systemic antibiotics,\(^{41}\) although this did not reach statistical significance.
Presence of Renal Impairment:

Following a prospective study by Maki and Tambyah, one of the identified risk factors for the development of CA-UTI was serum creatinine >2.0 mg/dL. Using multivariate statistical modelling the relative risk of renal azotaemia (serum creatinine >2.0 mg/dL) was found to be 2.1-2.6.

Catheter Insertion outside the Operating Theater.

According to in a prospective observational study involving daily urine cultures, one of the risk factors for CA-UTI noted was catheter insertion outside the operating theater. Using multivariate statistical modelling the relative risk for CA-UTI was found to be 2.0-5.3.

Other Active Sites of Infection:

In a prospective observational study by Temiz and co-workers, the presence of a HAI at another site was an independent risk factor for the development of CA-UTI and its presence was found to modify the effects of other risk factors for development of CA-UTI.

2.6 Guidelines for Urethral Catheter Insertion

The guidelines for urethral catheter insertion require the following conditions to be met in all situations where urinary catheters are being inserted;

1. Urethral catheters should be inserted only for appropriate indications and left in place only as long as needed.
2. Ensure hand hygiene immediately before and after insertion or any manipulation of the catheter device or site.
3. Only properly trained persons who know the correct technique of aseptic catheter insertion and maintenance should be allowed to insert catheters.
Below is a summary of the steps to be followed when inserting a urinary catheter:

i. Select an appropriate catheter type and size.

ii. Wash hands and wear gloves.

iii. Thoroughly wash the external genitalia with soap and water and in females also identify the urethra.

iv. Open the catheter kit using sterile procedure.

v. Drape and cleanse urethral meatus and surrounding areas. In uncircumcised males, retract foreskin and clean prepuce area. In females open the labia and clean the area.

vi. The catheter is gently inserted.

vii. Obtain urine flow through the catheter.

viii. Gently inflate the balloon.

ix. Secure the catheter in place.

x. Position drainage bag lower than the bladder.

xi. Drainage tubing is secured to avoid falling below drainage bag.

4. Ensure the catheter is properly secured after insertion to prevent movement and urethral traction.

### 2.7 Clinical Manifestations of Catheter Associated Urinary Tract Infection

Catheterized patients with CA-UTI often do not manifest the classic symptoms of dysuria, frequent urination, and urgent urination, although patients may experience these symptoms after the catheter is removed. In certain patients with indwelling catheters, such as those with neurogenic bladders, the absence of sensation in the pelvis, make ascertainment of classical symptoms of UTI
difficult. It has in fact been shown that majority of patients with CA-bacteriuria have no symptoms referable to the urinary tract.\(^{50}\)

When 1,497 newly catheterized patients were observed prospectively with daily urine cultures, urine leukocytes counts, and symptom assessment, 224 patients developed 235 episodes of CA-bacteriuria (defined as a colony count >10\(^3\) cfu/mL). Of the 194 patients with CA-bacteriuria who could respond to symptoms assessment in the study, only 15 (8\%) reported subjective symptoms referable to the urinary tract, including pain, urgent urination, or dysuria, although bacteriuria and pyuria were present in most patients for many days. In addition, there were no significant differences between catheterized patients with and without CA-bacteriuria in terms of signs or symptoms commonly associated with UTI (fever, dysuria, urgent urination, or flank pain) or with respect to leukocytosis.\(^{51}\)

Thus, for a hospitalized patient with an IUC, symptoms referable to the urinary catheter, fever, or peripheral leukocytosis have little predictive value for the diagnosis of CA-UTI. The lack of an association between fever and CA-bacteriuria was also demonstrated in studies of LTCF residents. A prospective study by Kunin et al,\(^{52}\) involving elderly nursing home patients found that, although 74\% of catheterized patients developed CA-bacteriuria, <2\% had a temperature >38°C. Likewise, Warren et al found the incidence of febrile episodes of possible urinary origin to be 1.1 cases per 100 patient-days of catheterization, despite a high prevalence of CA-bacteriuria, and most fever episodes resolved spontaneously.\(^{53}\)

Foul-smelling and/or cloudy urine is often interpreted as warranting antimicrobial treatment in catheterized patients with bacteriuria.\(^{54}\) The foul smell of urine around patients with urine incontinence is thought to be attributable mainly to the production of ammonia from urea by bacterial ureases.\(^{55}\) However, not all individuals with UTI have an unpleasant odour to their urine,
and not all urine with an unpleasant odour is indicative of bacteriuria.\textsuperscript{56} Malodorous or cloudy urine alone should not be used to determine the presence of CA-bacteriuria and, in particular, to distinguish CA-ASB from CA-UTI, and alternate interventions, such as improved continence management or hydration, rather than antimicrobial therapy, should be instituted.\textsuperscript{56} Unfortunately, most signs and symptoms in bacteriuric catheterized patients are nonspecific and place a burden on the clinician who wishes to use antimicrobials appropriately.

2.8 Diagnosis.

CA-UTI in patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization is defined by the presence of symptoms or signs compatible with UTI with no other identified source along with $\geq 10^3$ cfu/mL of one or more bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral, suprapubic or condom catheter has been removed within the previous 48 hours. CA-ASB in patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization is defined by the presence of $\geq 10^5$ cfu/mL of one or more bacterial species in a single catheter urine specimen in a patient without symptoms compatible with UTI.

2.9 Short and Long-term Effects of Catheter-Associated Urinary Tract Infection

Patients with short-term indwelling urethral catheters are at risk of developing bacteriuria, urethritis, and erosion of the urethra, creation of false passage as well as development of urethral strictures. As long as the indwelling urethral catheter is in-situ the daily incidence of CA-UTI increases. This can lead to bacteremia and sepsis. Long-term catheterization may be associated
with catheter obstruction, urinary tract stones, chronic renal inflammation, chronic pyelonephritis, renal impairment and over years may lead to the occurrence of bladder cancer.

CA-UTI may lead to sepsis and subsequently acute kidney injury. This can lead to loss of renal function, prolonged hospital stay and an increase in cost of health care.

### 2.10 Treatment Modalities of Catheter-Associated Urinary Tract Infection

A urine specimen for culture should be obtained prior to commencing antimicrobial therapy for presumed CA-UTI because of the wide spectrum of potential infecting organisms and the increased likelihood of antimicrobial resistance. If an indwelling urethral catheter has been in place for more than 14 days at the onset of CA-UTI and is still indicated, the catheter should be replaced to hasten resolution of symptoms. This will also reduce the risk of subsequent CA-bacteriuria and CA-UTI.

The urine sample for culture should be obtained from the freshly passed catheter prior to the initiation of antimicrobial therapy. In cases where catheter use is discontinued, a culture of a voided midstream urine specimen should also be obtained prior to the initiation of antimicrobial therapy to help guide treatment.

The recommended duration of antimicrobial treatment for patients with CA-UTI who have prompt resolution of symptoms is seven days, while in those with a delayed response regardless of whether the patients remain catheterized or not, it is recommended that they receive antimicrobial therapy for a period of 10 to 14 days.⁹
2.11 Prevention of Catheter Associated Urinary Tract Infection

Strict adherence to a sterile and continually closed drainage system have traditionally been the cornerstones of infection prevention during catheterization for continuous bladder drainage. Trautner and Darouiche demonstrated that use of a closed drainage system, or catheter drainage into a connected bag, rather than into an open container reduced the incidence of significant bacteriuria to approximately 50% at 14 days of continuous catheterization as against the documented 95% bacteriuria rates in patients with open catheter drainage after 96 hours. An effective approach to preventing CA-UTI is to avoid prolonged catheterization, or even to avoid catheterization at all. The rates of bacteriuria and UTI have been found to be lower with intermittent catheterization, condom catheters, and suprapubic catheterization than with chronic indwelling urethral catheters although randomized comparisons of these are lacking. Clean, non-sterile, intermittent catheterization can lead to bladder colonization rates as low as 20% to 40% over more than a year of follow-up.

Considering the fact that the strongest predictor of catheter-associated bacteriuria is the duration of catheterization, a series of interventions have been applied to shorten this period. Some assessment and process intervention methods have been found to be effective in identifying catheterized patients, leading to their further review and discontinuation of their catheters when no longer needed. Some of these measures include.

1. Assessing the Need for a Urinary Catheter on a Daily Basis

Strategies to integrate assessment of the need for continued usage of IUC into daily rounds have been found to be effective in reducing the rates of CA-UTI. During rounds, each patient should be assessed for the presence of a urinary catheter. The purpose for its use is reviewed and if there is
no indication for its continued use, nurses are instructed to contact physicians to obtain a mandate to discontinue the catheter.

2. **Physician Reminder Systems**

To reduce the prevalence and period of catheter use, it is important to assess and communicate the presence of a urinary catheter to the physicians on a daily basis. Physicians are often unaware that a patient has an IUC. Reilly *et al* demonstrated that in patients admitted in intensive care unit (ICU), a simple, continuous quality improvement program centered on nursing staff reminding physicians to remove unnecessary catheters significantly reduced the duration of urinary catheterization as well as the frequency of CA-UTI. Similar outcomes were attained when a specially trained nurse joined in daily multidisciplinary rounds on 10 medical/surgical units. Patients with catheters were assessed, and if they fail to meet appropriate criteria, the patient’s nurse was requested to obtain an order to remove the catheters.

Cornia and co-workers studied an automated reminder system that generates reminders to physicians through a computerized medical record. They found that the average length of catheterization was decreased, although there was insufficient data to determine if there was a corresponding decrease in UTIs. Another related study used a simple written reminder in a pre-test/post-test design with a non-equivalent control group. The intervention notification, which was attached to patients’ charts, was designed to remind the healthcare providers that the patient had a urinary catheter. The primary outcome measure in this study was the number of catheter days and the rate of re-catheterization. After adjusting for age, sex, and length of stay, the duration patients were catheterized decreased significantly in the intervention group. However, there was no significant difference in the rate of re-catheterization.
3. **Automatic Stop Orders**

This is a technological intervention aimed at reducing the duration of catheterization. In this process, a computerized physician order entry system allows the physician to select an option for minimizing the duration of catheter use. This CA-UTI preventive tool which has been used at Yale New Haven Hospital sends electronic report to the patient’s physician, prompting him/her to choose among discontinuing the device, maintaining the catheter for a predetermined time period, or maintaining it on a long-term.\(^{65}\) Another related study at the VA Puget Sound Health Care System used a computer order for each IUC. The computer entry required an indication for placement and routine care instructions, and noted a default stop date of 72 hours after placement. These two studies demonstrated decreased catheter duration as a result of the interventions.\(^{63}\)

4. **Nurse-driven Protocols**

Nurse-driven protocols have been applied with success in some institutions. These protocols allow a nurse to discontinue catheter use independent of a physician order when the patient no longer meets established criteria for catheter use. Such protocols usually are part of a procedure that excludes patients who meet criteria for continued urinary catheter usage.\(^{61,66}\)

5. **Catheter Use in Surgical Patients**

Perioperative urinary catheterization is intended to reduce bladder dysfunction related to surgical effects of anesthesia, analgesia and immobility. Wald and colleagues examined catheter usage in 35,904 Medicare patients undergoing major surgery, it was identified that 50% of these patients had urinary catheters for longer than two days, and were twice as likely to develop urinary tract infections as those with catheterization of two days or less. The conclusion from this study was that IUCs are routinely left in place longer than two days postoperatively. This may in return lead to excess CA-UTIs and other adverse outcomes such as increased length of hospital stay or
readmission. The recommendation from this study was that association of longer duration of catheterization with adverse outcomes makes postoperative catheter duration a reasonable target of infection control and surgical quality-improvement initiatives.67

6. Use of Bladder Scanners

Bladder scanners have been used to assess urinary retention, and this investigative tool may lead to the reduction of the need for catheterization. A systematic review concluded that protocols which implemented bladder scans were found to reduce the number of intermittent catheterizations and potentially decrease UTIs.68 Bladder scanners have also proved effective in reducing unnecessary irrigation by confirming whether a decrease in urine output is due to a blockage or reduced urine in the bladder, thereby minimizing breaks in the closed drainage system.68 A number of performance improvement schemes related to reduction of CA-UTIs include routine use of bladder scanners.

7. Antibiotic-Coated and Antiseptic-Coated Urinary Catheters

A limited number of studies have investigated the efficacy of antibiotic-coated urinary catheters for the prevention of bacteriuria in patients with short-term urinary catheterization. Although there have been some promising results, there are too few studies to adequately evaluate this technology.69 Silver ions are known to have broad-spectrum activity against gram-positive, gram-negative, aerobic, and anaerobic microorganisms. A number of studies have evaluated the efficacy of antiseptic urinary catheters in preventing bacteriuria and CA-UTI. One such study performed at the Nebraska Medical Center found a significant reduction in CA-UTI rates with the use of antibiotic coated catheter.70 In another study, a randomized controlled trial (RCT) involving the use of silver-coated catheters, the risk of infection declined by 21% among those randomized to
silver-coated catheters, and by 32% among patients in whom silver-coated catheters were used on the wards.\textsuperscript{71}
CHAPTER 3

STUDY DESIGN AND METHODS

3.1 Study Site

The study was conducted at LUTH, Idi Araba, Lagos state, a tertiary hospital which serves as a referral center for other hospitals in Lagos and neighbouring states such as Ogun state and countries e.g. (Republic of Benin). Lagos state had a population of 9,113,605 as at 2006 census.\(^7\)

3.2 Study Design

This was a prospective observational study of 200 patients who had a urethral catheter inserted for the purpose of continuous bladder drainage during the course of treatment at the Lagos University Teaching Hospital (LUTH).

3.3 Study Population

The study was carried out among patients admitted into the accident and emergency department, medical, surgical and gynaecology wards of LUTH who had continuous bladder drainage via a urethral catheter during the course of their treatment at LUTH. The decision as to the need for catheterization as well as the instruction to insert the catheters was taken by the managing physicians. No patient was catheterized solely for the purpose of this study and the catheters were not unduly left in place for the purpose of this study.

3.4 Exclusion Criteria

Exclusion criteria for the study were:

1. Age less than 18 or greater than 65 years.
2. Symptoms of UTI prior to urethral catheter being passed. For patients who were unconscious at the time of catheterization, cloudy urine on macroscopic examination of urine was taken as equivalent to symptoms of UTI.

3. Positive leukocyte esterase or nitrite test on urinalysis.

4. Urethral catheterization before presenting to the hospital.

5. Urethral catheterization for longer than 24 hours before being evaluated for possible recruitment into the study.

3.5 Inclusion Criteria

The eligibility criteria for the study were:

1. Age between 18 and 65 years.

2. Had continuous bladder drainage via a urethral catheter during the course of their treatment.

3. Informed consent.

3.6 Sampling Method

Study participants were recruited from consecutive patients who had catheter inserted for continuous bladder drainage at the accident and emergency department, medical, surgical and gynaecological wards of the hospital.

3.7 Sample Size Determination

The minimum sample size was determined using Fisher’s statistical formula.

Sample size \((N) = \frac{Z^2 \cdot P \cdot Q}{D^2}\)
Where $Z = 1.96$, that is normal standard deviation at 95% confidence interval

$P = \text{Prevalence rate}$

$Q = 1 - P$

$D = 0.07$, Precision

Assuming a CA-UTI prevalence of 41% from a study by Olarinde et al.\textsuperscript{27}

\[ N = \frac{1.96^2 \times 0.41 \times 0.59}{(0.07)^2} = 189 \]

### 3.8 Study Duration

The study was carried out over a ten month period between July 2015 and May 2016.

### 3.9 Ethical Approval/Consent/Title Registration

Ethical approval was obtained from the Health Research Ethics Committee of the Lagos University Teaching Hospital prior to commencement of patient recruitment (Appendix 1). Each participant also provided written informed consent at the time of recruitment into the study. For patients who were unconscious, consent was obtained from their next-of-kin (Appendix 2). The study proposal was also approved by the National Postgraduate Medical College of Nigeria (Appendix 3).
3.10 Patient Recruitment Procedure

Prior to commencement of the study, a meeting was held with resident doctors and house officers in the departments from which patients were to be recruited. The purpose of the meeting was to inform them about the study and to seek their cooperation in the area of informing the researcher when patients were catheterized in their various units. In addition, the researcher’s contact phone numbers were made available to all residents and house officers and notices concerning the study and contact details of the researcher were posted on all wards where patient recruitment was conducted.

Prospective patients were reviewed as quickly as possible following catheterization to determine their eligibility for inclusion into the study.

The following steps were followed in patient recruitment:

1. Conscious patients were asked about the presence of symptoms of UTI prior to the urinary catheter being passed. Those that had dysuria, frequency of micturition or suprapubic pain prior to presentation were excluded
2. A 5-10 ml sample of catheter specimen was obtained from the patient in a sterile universal bottle. The urine samples were obtained through puncturing the catheter tubing using a needle and syringe.
3. The sample was examined macroscopically for cloudiness.
4. Urinalysis was carried out immediately using a 10-point Uriscreen urinalysis dipsticks. Patients whose urine sample tested positive to leukocyte esterase or nitrite were excluded.
5. The study questionnaire was used to retrieve relevant clinical information from each eligible patients.
6. Five milliliters of blood was also collected from the ante-cubital fossa to evaluate white blood count, haemoglobin concentration, serum creatinine and fasting blood sugar.

7. Urine samples obtained from eligible patients were transported to the medical microbiology laboratory in leak proof/zip lock bags where the samples underwent microscopy and culture.

8. Following recruitment into the study, each patient was reviewed daily. During each review, the patients were asked specifically about the presence of symptoms of UTI. Also each patient’s charts was inspected for the presence of fever spikes and physical examinations were carried out to determine the likely cause of the fever when present.

9. Further urine samples were obtained for repeat culture on days 3, 7, 10, 14 and 28 post catheterization.

10. In patients whose urethral catheters were removed prior to meeting the study endpoint, a midstream voided urine specimen was obtained 48 hours after catheter removal for culture.

11. Patients who met the primary end point at any point during the study had no further urine samples obtained for culture.

3.11 **Study Questionnaire**

A structured researcher-administered questionnaire was used to retrieve information from the study participants. Information regarding the subjects’ demographic characteristics, personal and family history of chronic diseases, current drug therapy and indication for catheterization were obtained.
3.12 Definition of Terms

For the purpose of this study, the following definitions were applied.

3.12.1 Diabetes Mellitus: Diabetes mellitus was defined as fasting plasma glucose >7.0 mmol/L (126 mg/dL), a previous diagnosis of diabetes made by a doctor or requirement of antidiabetic medications to control blood sugar.

3.12.2 Hypertension: Hypertension was defined as a systolic blood pressure ≥140 mmHg and or diastolic blood pressure of ≥90 mmHg, a previous diagnosis of hypertension made by a doctor or requirement of antihypertensive medications to control blood pressure.

3.12.3 Renal Insufficiency: This was defined as an eGFR less than 60 ml/min/1.73 m².

3.12.4 Obstructive Uropathy: Obstructive uropathy was defined as present when a patient had any of the following on ultrasound imaging of the urinary tract:

   i. Significant post-void urine volume

   ii. Hydronephrosis and/or

   iii. Hydroureters.

3.13 Primary Endpoint

The primary endpoint of the study was the development of CA-UTI. For the purpose of this study, this was defined as the presence of symptoms or signs compatible with UTI with no other identified source along with ≥10³ cfu/mL of one or more bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral catheter had been removed within the previous 48 hours.
3.14 Secondary Endpoint

The secondary endpoint of the study was the development of CA-ASB. For the purpose of this study, this was defined as the presence of $\geq 10^5$ cfu/mL of one or more bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral catheter had been removed within the previous 48 hours; in a patient without symptoms compatible with UTI.

3.15 Specimen Processing

3.15.1 Urine specimen processing

All urine samples were examined microscopically (gram stain and wet preparation) before they were subjected to culture and subsequently sensitivity in cases of growth. The samples were streaked on appropriate media (blood agar and MacConkey agar) and incubated at 37°C for 24 to 48 hours. Significant bacteriuria was determined using growth on blood agar. Isolates obtained after incubation were sub-cultured using isolation media. To eliminate the risk of the cultured organism being a contaminants, the following precautions were taken:

i. The urine samples were obtained by puncturing the catheter tubing using a sterile needle and syringe.

ii. The presence of significant pyuria was mandatory before any microbial growth was considered to be due to infection of the urine.

3.15.2 Blood Sample Processing

Full blood count was assessed using the Coulter auto-analyser while the serum creatinine was determined using the Kinetic Jaffé Picrate method with a Roche kit that had been standardized.
against Isotope Dilution Mass Spectrometry (IDMS). Blood glucose testing was done using glucose oxidase method.

3.16 Antimicrobial Susceptibility Testing

All bacterial isolates were tested for their susceptibility to the following antibiotics: Amoxicillin/Clavulanate 20/10 µg, Piperacillin/Taxobactam 100/10 µg, Levofloxacin 5 µg, Gentamycin 10 µg, Amikacin Ceftriaxone 30 µg, ceftazidime 30µg, Cefepime 30 µg, Ciprofloxacin 5 µg, Meropenem 30 µg. Antibiotic susceptibility testing were determined using Kirby-Bauer disc diffusion method, using Mueller Hinton plates. The discs employed for antibiotic susceptibility testing were similar to those routinely used at the microbiology laboratory of the hospital for day-to-day antibiotic susceptibility testing.

Bacterial suspension was prepared with peptone water to give concentration equivalent of 0.5 Mc Farland standards. The suspension was inoculated on Mueller Hinton agar plate by swabbing to give a growth lawn, and antibiotic discs were placed on them, and incubated at 37°C for 24 hours. The zone of inhibition diameter was measured using calibrated ruler and interpreted as sensitive (S), intermediate (I), or resistant (R) in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. Quality control organisms such as ATCC strains of E. coli (25922) and P. aeruginosa (27853) were used.

The spectrum of antimicrobials used for sensitivity testing in this study was predicated to reflect the commonly used antimicrobials at LUTH, however the choice was made to represent the different classes.
3.17 Materials and Equipment

The following were used during the course of this study.

1. Sterile 5 ml and 10 ml syringes and needles
2. Chlorhexidine and cotton wool
3. Forceps for clamping urethral catheters
4. Surgical gloves
5. Sterile universal specimen bottles
6. Blood specimen bottles (EDTA, fluoride, lithium heparin)
7. Leak proof/zip lock bags
8. Thermometer
9. Sphygmomanometer (Littman)
10. Stethoscope (Accoson)
11. Refrigerator
3.18 Data Analysis

The study data was entered into excel spreadsheet and analyzed using the statistical package for social sciences (SPSS), IBM version 22. Continuous data are presented as means and standard deviation while categorical data are presented as percentages. Comparison between means was done using the Student’s t-test, while comparison between percentages was done using chi-square test.

The frequency of occurrence CA-ASB is presented as a percentage. The incidence rate of CA-ASB were determined by dividing the total number of positive cultures obtained during the study by the overall number of days that study participants were catheterized and expressed as number of infections per thousand catheter days. Indications for IUC use and the microbial organisms isolated on culture are expressed as percentages. Susceptibility of the bacterial isolates to the various antibiotics against which they were tested are also expressed as percentages.

Seven factors, including age, gender, duration of catheterization, glomerular filtration rate (GFR) as well as the presence of diabetes, hypertension and obstructive uropathy were examined using univariate analysis for association with development of bacteriuria. Logistic regression analysis was subsequently used to determine the factors that were independently associated with the development of bacteriuria. For the purpose of the logistic regression model, age, duration of catheterization and GFR were modelled as dichotomous variables. Patients with duration of catheterization less than seven days were compared with those catheterized for seven or more days; patients with GFR less than 60 ml/min/1.73 m² (renal insufficiency) were compared with those with GFR of at least 60 ml/min/1.73 m² (no renal insufficiency); and patients age 50 years or more were compared with patients aged less than 50 years.

The level of statistical significance was set at a p-value less than 0.05.
CHAPTER 4
RESULTS

4.1 Baseline Characteristics of the Study Population

A total of 200 participants were recruited for this study. Seventy eight (39%) were males while 122 (61%) were females. The mean age of the study population was 47.4 ± 12.2 years with a range of 20 to 65 years. Figure 1 shows the age range distribution of the study population. The mean GFR of the study population was 71.3 ± 40.9 ml/min/1.73 m$^2$ with a range of 3.9 to 144.2 ml/min/1.73 m$^2$.

The admitting diagnoses of the study participants were cerebrovascular disease 46(23%), acute kidney injury and acute exacerbation of chronic kidney disease 22(11%), bladder-outlet obstruction due to an enlarged prostate 22(11%), diabetes mellitus and its complications 19(9.5%), surgical emergencies 16(8%), paraparesis 12(6%), acute confusional state 12(6%), gynaecological malignancies 5(2.5%), and heart failure 5(2.5%). Others were venous thromboembolism 4(2%), hepatic encephalopathy 4(2%), cerebral malaria 3(1.5%), encephalitis 2(1%), and Stevens-Johnson syndrome 1(0.5%).

The baseline characteristics of the study population, stratified according to gender, are shown in Table 1. Compared to male study participants, female participants had significantly lower mean age, mean GFR, and mean haemoglobin concentration as well as a higher frequency of diabetes and a lower frequency of urinary tract obstruction.
Figure 1. Age-range distribution of the study population
Table 1: Baseline clinical characteristics of the study population

<table>
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<th>Parameter</th>
<th>All Patients</th>
<th>Males</th>
<th>Females</th>
<th>P-Value</th>
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<td>Mean age (years)</td>
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<td>45.47±12.68</td>
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<td>Mean GFR (ml/min/1.73 m²)</td>
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<td>81.16±45.12</td>
<td>63.64±36.07</td>
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<tr>
<td>Mean SBP (mmHg)</td>
<td>131.29±17.34</td>
<td>131.90±16.66</td>
<td>130.90±17.82</td>
<td>0.693</td>
</tr>
<tr>
<td>Mean DBP (mmHg)</td>
<td>82.21±9.83</td>
<td>82.87±9.32</td>
<td>81.79±10.17</td>
<td>0.448</td>
</tr>
<tr>
<td>FBS (mg/dL)</td>
<td>82.46±17.60</td>
<td>81.80±15.73</td>
<td>82.89±18.76</td>
<td>0.671</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>12.10±1.47</td>
<td>12.53±1.44</td>
<td>11.83±1.43</td>
<td>0.001*</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9.5%</td>
<td>2.5%</td>
<td>7%</td>
<td>0.001*</td>
</tr>
<tr>
<td>Steroid use</td>
<td>2%</td>
<td>2%</td>
<td>0%</td>
<td>0.103</td>
</tr>
<tr>
<td>HIV infection</td>
<td>2%</td>
<td>0%</td>
<td>2%</td>
<td>0.103</td>
</tr>
<tr>
<td>Urinary tract obstruction</td>
<td>11%</td>
<td>7.5%</td>
<td>3.5%</td>
<td>0.004*</td>
</tr>
</tbody>
</table>

GFR = glomerular filtration rate; HIV = human immunodeficiency virus; DBP = diastolic blood pressure, SBP = systolic blood pressure; FBS = fasting blood sugar; Hb. = Haemoglobin concentration; WBC = white cell count
4.2   Indications for and Duration of Indwelling Urinary Catheter Use

The indications for continuous bladder drainage via an indwelling urethral catheter in the study population, stratified according to gender, are shown in Table 2. The two most common indications were the monitoring of urinary output and the need to keep patients dry because of altered consciousness, together accounting for 62% of all indications for catheterization [76(38%) and 48(24%) of cases respectively]. In 16(8%) of cases, the reasons for urethral catheterization were not clearly outlined by the managing unit.

The indications for continuous bladder drainage via an indwelling urethral catheterization in the study population, stratified according to age range are shown in Table 3. Monitoring urine output in ill patient was the commonest indication for urethral catheterization among patients in the age range 18 – 29 years and 30 – 39 years representing 60% and 51.35% respectively, this also applied to age range 40 – 49 years accounting for 33.96%. Relief of urinary retention was the commonest indication among patients 60 years and older where it accounted for 34.62% of cases. Keeping patients dry was the commonest indication among patients of the 50 – 59 age range.
Table 2. Indications for continuous bladder drainage via an indwelling urethral catheter stratified according to gender

<table>
<thead>
<tr>
<th>Indication for Urethral Catheterization</th>
<th>All Patients n(%)</th>
<th>Female n(%)</th>
<th>Male n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improve comfort</td>
<td>8(4.0)</td>
<td>8(6.6)</td>
<td>--</td>
</tr>
<tr>
<td>Monitoring urine output in ill patient</td>
<td>76(38.0)</td>
<td>50(41.0)</td>
<td>26(33.3)</td>
</tr>
<tr>
<td>Need for intraoperative monitoring</td>
<td>11(5.5)</td>
<td>5(4.1)</td>
<td>6(7.7)</td>
</tr>
<tr>
<td>Relief of urinary retention</td>
<td>31(15.5)</td>
<td>9(7.4)</td>
<td>22(28.2)</td>
</tr>
<tr>
<td>Prolonged immobilization</td>
<td>10(5.0)</td>
<td>10(8.2)</td>
<td>--</td>
</tr>
<tr>
<td>To keep unconscious patients dry</td>
<td>48(24.0)</td>
<td>34(27.9)</td>
<td>14(18.0)</td>
</tr>
<tr>
<td>No clear indication</td>
<td>16(8.0)</td>
<td>6(4.9)</td>
<td>10(12.8)</td>
</tr>
</tbody>
</table>
Table 3. The indications for continuous bladder drainage via an indwelling urethral catheterization stratified according to age range

<table>
<thead>
<tr>
<th>Indication for Catheterization</th>
<th>All Patients</th>
<th>18-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>≥60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improve comfort</td>
<td>8(4.0</td>
<td>-(-)</td>
<td>-(-)</td>
<td>5(9.4)</td>
<td>3(7.9)</td>
<td>-</td>
</tr>
<tr>
<td>Monitoring urine output in ill patient</td>
<td>76(38)</td>
<td>12(60)</td>
<td>19(51.4)</td>
<td>18(34)</td>
<td>10(26.3)</td>
<td>17(32.7)</td>
</tr>
<tr>
<td>Need for intraoperative monitoring</td>
<td>11(5.5)</td>
<td>--</td>
<td>5(13.5)</td>
<td>6(11.3)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Urine retention</td>
<td>31(15.5)</td>
<td>--</td>
<td>5(13.5)</td>
<td>5(9.4)</td>
<td>3(7.9)</td>
<td>18(34.6)</td>
</tr>
<tr>
<td>Prolonged immobilization</td>
<td>10(5.0)</td>
<td>--</td>
<td>--</td>
<td>3(5.7)</td>
<td>4(10.5)</td>
<td>3(5.8)</td>
</tr>
<tr>
<td>Keep unconscious patients dry</td>
<td>48(24.0)</td>
<td>5(25.0)</td>
<td>3(8.1)</td>
<td>11(20.8)</td>
<td>15(39.5)</td>
<td>14(26.9)</td>
</tr>
<tr>
<td>No clear indication</td>
<td>16(8.0)</td>
<td>3(15.0)</td>
<td>5(13.5)</td>
<td>5(9.4)</td>
<td>3(7.9)</td>
<td>--</td>
</tr>
</tbody>
</table>
4.3 Frequency of Catheter-Associated Urinary Tract Infection

During the study period, the 200 participants were catheterized for a total of 1,702 days. The mean duration of urethral catheterization was 8.51 ± 2.9 days with a range of 2 days to 28 days. A total of 722 urine samples were obtained from 200 participants during the study period. There were no microbial isolates from the baseline urine samples of all 200 study participants. From the subsequent serial urine samples obtained for culture, a positive microbial growth was obtained in 86 of the samples with all bacterial colony counts exceeding $10^5$ cfu/ml, giving a frequency of bacteriuria of 43%.

Of the 86 patients with bacteriuria, 22 were unconscious and thus could not volunteer information regarding presence of symptoms of UTI. Among the remaining 64 patients that could respond to questions, none volunteered symptoms suggestive of UTI even when they were specifically asked concerning the presence of these symptoms. Therefore, none of the participants met the study criteria for diagnosis of CA-UTI.

However, all 86 participants with positive urine cultures met the criteria for the diagnosis of CA-ASB. Hence, the incidence rate of CA-ASB in this study was approximately 51 infections per 1000 catheter days.
4.4 Microbiological Profile of Isolates

Of the 86 urine specimens with significant microbial growths, 55(64%) were due to gram-negative bacteria, 2(2.3%) due to gram-positive bacteria while 25(29%) were due to fungi. In 4(4.7%) of the cases, both fungi and bacteria were isolated. Table 4 shows the distribution of the microbial isolates. The most common microbial isolate was *E. coli* which accounted for 29(33.7%) of all isolates.

4.4.1 Distribution of isolates in relation to gender of participants

Amongst females study participants, *E. coli* was the commonest microbial isolate 20(35.1%) followed by *C. albicans* 19(33.3%). Similarly, among male study participants, *E. coli* was the commonest microbial isolate representing 9(31%) of cases, however, this was followed by *P. aeruginosa* 8(27.6%).

4.4.2 Distribution of isolates in relation to age of participants

The distribution of microbial isolates according to the age range of study participants is shown in table 5. *E. coli* was the commonest isolate among patients in the age range 18 – 29 years and 40 – 49 years (50% and 41.2% respectively). Among patients 30 – 39 years, *K. pneumonia* (62.5%) was the commonest isolate. *C. albicans* (38.1%) was the commonest isolate among patients aged 50 – 59 years while among patients 60 year or older, both *E. coli* and *C. albicans* each accounted for 29.4% of isolates.
Table 4. Distribution of microbial isolates.

<table>
<thead>
<tr>
<th>Microbial Isolate</th>
<th>All Isolates n(%) N = 86</th>
<th>Isolates from Females n(%) N = 57</th>
<th>Isolates from Males n(%) N = 29</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>29(33.7)</td>
<td>20(35.1)</td>
<td>9(31)</td>
</tr>
<tr>
<td>C. albicans</td>
<td>25(29.1)</td>
<td>19(33.3)</td>
<td>6(20.7)</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>14(16.3)</td>
<td>6(10.5)</td>
<td>8(27.6)</td>
</tr>
<tr>
<td>K. pneumonia</td>
<td>10(11.6)</td>
<td>7(12.3)</td>
<td>3(10.3)</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>2(2.3)</td>
<td>0(0)</td>
<td>2(6.9)</td>
</tr>
<tr>
<td>A. iwoffii</td>
<td>2(2.3)</td>
<td>2(3.5)</td>
<td>0(0)</td>
</tr>
<tr>
<td>E. coli, + C albicans</td>
<td>4(4.7)</td>
<td>3(5.3)</td>
<td>1(3.4)</td>
</tr>
</tbody>
</table>
**Table 5. Distribution of various isolates in relation to age**

<table>
<thead>
<tr>
<th>Microbial Isolate</th>
<th>18 – 29yrs n(%)</th>
<th>30 – 39yrs n(%)</th>
<th>40 – 49yrs n(%)</th>
<th>50 – 59yrs n(%)</th>
<th>≥60yrs n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em></td>
<td>3(50)</td>
<td>2(25)</td>
<td>7(41.2)</td>
<td>7(33.3)</td>
<td>10(29.4)</td>
</tr>
<tr>
<td><em>C. albicans</em></td>
<td>2(33.3)</td>
<td>--</td>
<td>5(29.4)</td>
<td>8(38.1)</td>
<td>10(29.4)</td>
</tr>
<tr>
<td><em>P. aeruginosa</em></td>
<td>1(16.7)</td>
<td>1(12.5)</td>
<td>2(11.8)</td>
<td>2(9.5)</td>
<td>8(23.5)</td>
</tr>
<tr>
<td><em>K. pneumonia</em></td>
<td>--</td>
<td>5(62.5)</td>
<td>1(5.9)</td>
<td>2(9.5)</td>
<td>2(5.9)</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>--</td>
<td>--</td>
<td>1(5.9)</td>
<td>--</td>
<td>1(2.9)</td>
</tr>
<tr>
<td><em>A. iwoffii</em></td>
<td>--</td>
<td>--</td>
<td>1(5.9)</td>
<td>--</td>
<td>1(2.9)</td>
</tr>
<tr>
<td><em>E. coli, + C. albicans</em></td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>2(9.5)</td>
<td>2(5.9)</td>
</tr>
</tbody>
</table>
4.5 Antibiotic Susceptibility Pattern of the Bacterial Isolates

In this study, six microbial organisms comprising; *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Enterococcus*, *Acinobacter iwofii* and *Candida albicans* were isolated from the participants who developed CA-ASB. The antibiotic susceptibility pattern of the various bacterial isolates is shown in Table 6.

Among *E. coli* isolates, 79% were susceptible to meropenem, 76% to amikacin, 72% to levofloxacin, 66% each to ciprofloxacin and cefepime. Only 10% of *E. coli* isolates were sensitive to amoxicillin/clavulanic acid. Among *pseudomonas* isolates, 86% were susceptible to meropenem, 71% each to amikacin and ceftazidime, and 64% each to piperacillin/taxobactam and cefepime. None of the pseudomonas isolates was susceptible to Amoxicillin/clavulanic acid. Among *Klebsiella* isolates, 90% were susceptible to meropenem, 50% to levofloxacin, 40% each to ciprofloxacin and piperacillin/tazobactam. All *Enterococcus* (100%) isolates were susceptible to amoxicillin/clavulanate and meropenem, while both acinobacter isolates were resistant to all the antibiotics they were tested against.
Table 6. Distribution of the antibiotic sensitivity pattern of the bacterial isolates

<table>
<thead>
<tr>
<th></th>
<th>E. coli n = 29</th>
<th>Pseudomonas n = 14</th>
<th>Klebsiella n = 10</th>
<th>Enterococcus n = 2</th>
<th>Acinobacter n = 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMC</td>
<td>3(10%)</td>
<td>--</td>
<td>--</td>
<td>2 (100%)</td>
<td>--</td>
</tr>
<tr>
<td>CRO</td>
<td>15(52%)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CAZ</td>
<td>16(55%)</td>
<td>10(71%)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>FEP</td>
<td>19(66%)</td>
<td>9(64%)</td>
<td>1(10%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>AK</td>
<td>22(76%)</td>
<td>10(71%)</td>
<td>3(30%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CN</td>
<td>14(48%)</td>
<td>7(50%)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>LEV</td>
<td>21(72%)</td>
<td>4(29%)</td>
<td>5(50%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CIP</td>
<td>19(66%)</td>
<td>4(29%)</td>
<td>4(40%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>MEM</td>
<td>23(79%)</td>
<td>12(86%)</td>
<td>9(90%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>TZP</td>
<td>21(72%)</td>
<td>9(64%)</td>
<td>4(40%)</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

AMC- Amoxicillin/Clavulanate, CRO- Ceftriaxone, CAZ- Ceftazidine, FEP- Cefepime, AK- Amikacin, CN- Gentamycin, LEV- Levofloxacin, CIP- Ciprofloxacin, MEM- Meropenem, TZP- Piperacillin/Taxobactam
4.6 Factors Associated with the Development of Bacteriuria

In this study, duration of catheterization, gender, age, presence of renal insufficiency and urinary tract obstruction, underlying diabetes and hypertension were considered for association with the development of bacteriuria.

4.6.1 Duration of Catheterization.

Figure 2 shows the frequency of bacteriuria over the duration of the study. The frequency of positive urine cultures increased progressively in cultures obtained on days 0, 3, 7, 10, 14. There were however no additional positive urine cultures between days 14 and 28.

4.6.2 Age of Study Participants

The frequency of CA-ASB across the various age ranges of the study participants are as shown in figure 3. The lowest frequency of CA-ASB was found in those participants in the age range 30 - 39 years and the highest in those aged 60 years and above.

4.6.3 Gender, Diabetes, Hypertension, Renal Insufficiency and Urinary Tract Obstruction.

Figures 4 – 8 show the frequencies of bacteriuria amongst: male and female participants; participants with and without diabetes; with and without hypertension; with and without renal insufficiency and with and without urinary tract obstruction.

4.6.4 Univariate Analysis of Factors Associated with Bacteriuria.

The univariate analyses of the factors associated with the development of bacteriuria are shown in table 8. Duration of catheterization (p-value = 0.001); age (p-value < 0.0001); presence of diabetes (p-value < 0.001); presence of hypertension (p-value = 0.005); presence of renal insufficiency (p-value = 0.001) and presence of urinary tract obstruction (p-value = 0.003) were the factors found to be significantly associated with the development of bacteriuria.
4.6.5 Logistic Regression Analysis of Factors Associated with Bacteriuria.

The multivariate logistic regression analysis of the factors associated with bacteriuria is shown in Table 8. After correcting for confounding using logistic regression analysis, the factors that remained significantly associated with the development of bacteriuria among study participants were: duration of catheterization (odds ratio (OR) = 12.0; 95% CI = 5.6 - 25.5; p-value <0.001), presence of diabetes (OR = 5.6; 95% CI = 1.5 - 20.9; p-value = 0.01), presence of urinary tract obstruction (OR = 3.9; 95% CI = 1.3 - 11.3; p-value = 0.013) and age (OR = 1.1; 95% CI = 1.0 - 1.1; p-value = 0.001).
**Figure 2.** Frequency of bacteriuria over the duration of the study.
Figure 3. Frequency of CA-ASB among study participants across the various age ranges.
**Figure 4.** Frequency of Bacteriuria among Male and Female Study Participants.
Figure 5. Frequency of Bacteriuria among Patients with and without Diabetes.
Figure 6. Frequency of Bacteriuria among Participants with and without Hypertension.
Figure 7. Frequency of Bacteriuria among Patients with and without Renal Insufficiency.
Figure 8. Frequency of Bacteriuria among Patients with and without Urinary Tract Obstruction.
Table 7. Univariate analysis of factors associated with bacteriuria.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number of Participants</th>
<th>Percentage with Bacteriuria n(%)</th>
<th>Chi square</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of catheterization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td>2(1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 7</td>
<td>17(8.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 10</td>
<td>54(27)</td>
<td>52.36</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Day 14</td>
<td>86(43)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 28</td>
<td>86(43)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>122</td>
<td>58(47.5)</td>
<td>2.63</td>
<td>0.105</td>
</tr>
<tr>
<td>Male</td>
<td>78</td>
<td>28(35.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age Range</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 – 29 years</td>
<td>20</td>
<td>6(30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 – 39 years</td>
<td>37</td>
<td>8(21.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 – 49 years</td>
<td>53</td>
<td>16(30.2)</td>
<td>25.69</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>50 – 59 years</td>
<td>39</td>
<td>23(58.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥60 years</td>
<td>51</td>
<td>33(64.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>19</td>
<td>16(84.2)</td>
<td>14.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Absent</td>
<td>181</td>
<td>70(38.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>76</td>
<td>42(55.3)</td>
<td>7.52</td>
<td>0.005</td>
</tr>
<tr>
<td>Absent</td>
<td>124</td>
<td>44(35.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Renal insufficiency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>94</td>
<td>55(58.5%)</td>
<td>17.41</td>
<td>.001</td>
</tr>
<tr>
<td>Absent</td>
<td>106</td>
<td>31(29.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urinary Tract Obstruction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>22</td>
<td>16(72.7%)</td>
<td>8.91</td>
<td>.003</td>
</tr>
<tr>
<td>Absent</td>
<td>178</td>
<td>70(39.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 8. Logistic regression analysis of factors associated with bacteriuria.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds ratio</th>
<th>95% C.I.</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of Catheterization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(≥7 days vs &lt;7 days)</td>
<td>12.72</td>
<td>5.71 – 28.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(≥50 years vs &lt;50 years)</td>
<td>4.27</td>
<td>1.80 – 10.08</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Female vs Male)</td>
<td>2.07</td>
<td>0.92 – 4.65</td>
<td>0.078</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Yes vs No)</td>
<td>0.65</td>
<td>0.24 – 1.77</td>
<td>0.406</td>
</tr>
<tr>
<td><strong>Renal impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Yes vs No)</td>
<td>1.92</td>
<td>0.74 – 4.94</td>
<td>0.176</td>
</tr>
<tr>
<td><strong>Obstructive Uropathy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Yes vs No)</td>
<td>4.27</td>
<td>1.15 – 15.82</td>
<td>0.029</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Yes vs No)</td>
<td>4.99</td>
<td>1.07 – 23.15</td>
<td>0.040</td>
</tr>
</tbody>
</table>

C.I = Confidence Interval.
CHAPTER 5
DISCUSSION

5.1 Introduction and Description of the Study and its Participants

The study population consisted of patients who were admitted into the medical, surgical, gynaecology as well as the accident and emergency wards of the hospital. The spectrum of clinical diagnoses of the participants in this study covered a wide range and is spread across different departments and specialties. They therefore can be said to be a representative population of patients that are commonly seen in a tertiary hospital setting. Also, its prospective design.

The relative female preponderance among participants in this study is most likely a result of the inclusion of patients admitted to the gynaecology ward of the hospital.

5.2 Indications for Indwelling Urethral Catheter Placement

In this study, the indications for indwelling urinary catheter placement were grouped into six including monitoring of urine output in critically ill patients, intraoperative monitoring of urinary output, prolonged immobilization, relief of urine retention, to keep dry and manageable because of loss of consciousness as well as to improve comfort. In addition to these, there was a group of study participants in whom the indication for urethral catheter placement was unclear.

In three of these groups (monitoring of urine output in critically ill patients, intraoperative monitoring of urinary output, relief of urine retention), consisting of 59% of study participant, the indications clearly complied with internationally accepted guidelines. In two groups (to improve comfort and prolonged immobilization) consisting 9% of the study population, the indications could be considered to comply with internationally accepted guidelines. In the remaining 32% of
study participants (24% catheterized to keep them dry and manageable because of loss of consciousness and 8% whose indication for catheterization were not obvious) the indications clearly did not comply with internationally accepted guidelines.

Similar high percentages of inappropriately catheterized patients have been reported in the literature. Bhatia and co-workers reported that 28.8% of their study participants were inappropriately catheterized,\textsuperscript{75} while Apisarnthanarak \textit{et al} reported that, no clear indication for urethral catheterization was found in 28%, while there was inappropriate urine output monitoring in 26% of participants.\textsuperscript{76} In the study by Gokula and co-workers only 46% of patients were appropriately catheterized,\textsuperscript{77} while in the study by Saint \textit{et al} it was observed that catheter use was inappropriate in 31% of the patients.\textsuperscript{4}

\subsection*{5.3 Incidence of Catheter Associated Bacteriuria}

In this study 43\% of participants had developed bacteriuria at 28 days of follow-up with an incidence rate equivalent to 51 infections for every 1000 days that an IUC was left in place. The fact that none of the patients who developed bacteriuria had symptoms compatible with the presence of UTI meant that no patient met the study criteria for CA-UTI; however, all met the study criteria for CA-ASB. Catheterized patients who develop bacteriuria have been known not to experience classical symptoms that are seen in non-catheterized patients who have UTI.\textsuperscript{50} In the study by Tambyah et al, only 8\% of 194 patients who had CA-bacteriuria and could respond to questions volunteered symptoms referable to the urinary tract.

Differing rates of catheter-associated bacteriuria have been reported from various centers in Nigeria. Taiwo and Aderounmu,\textsuperscript{24} reported an incidence of 88.5\%; Onipede et al\textsuperscript{25} reported an
incidence of 60.9%; Olarinde et al\textsuperscript{27} reported an incidence of 41% while Onyegbule et al\textsuperscript{26} reported an incidence of 6.5% – 11.4%. Although these studies were all conducted in tertiary hospitals in Nigeria, they reported widely varying incidences of catheter-associated bacteriuria mainly because of differences in patient populations studied and study methodology.

Taiwo and Aderounmu who reported the highest incidence of 88.5% studied mainly urology patients and although the duration of catheterization was not stated, it is likely that these patients had been on prolonged catheterization. On the other hand, Onyegbule et al reported the lowest incidence of 6.5% among women who were catheterized for less than 24 hours. This pattern of increasing incidence with duration of catheterization was also found in this study. For patients catheterized for 1 – 3 days, the incidence of bacteriuria was 12.5%, increasing to 18.9% among those catheterized for 4 - 7 days and 69% among those catheterized for greater than one week.

5.4 Spectrum of Organisms causing Catheter-Associated Bacteriuria

A broad spectrum of organisms has been reported to cause catheter-associated bacteriuria. Of these, Enterobacteriaceae are the most commonly isolated.\textsuperscript{7,29,30} In this study, the Enterobacteriaceae were also the most commonly isolated organisms, accounting for about 50% of isolates. The predominance of Enterobacteriaceae in causing catheter-associated bacteriuria has been explained by two mechanisms; CA-UTI is thought to occur as a result of contamination of the urethral catheter by gut bacteria and ascension of the organism into the bladder and Enterobacteriaceae form the largest group of organisms in the gut.

In this study, \textit{E. coli} was the single most common microbial isolate accounting for 33.7% of isolates. This finding is similar to those reported by Kazi \textit{et al},\textsuperscript{78} from Pune, India, which reported \textit{E. coli} to be responsible for 30.5% of cases of catheter-associated bacteriuria, and Olairinde \textit{et al}\textsuperscript{27}
in Abeokuta, Nigeria who found *E. coli* to be responsible for 35.36% of cases. In the study by Taiwo and Aderounmu et al however, Pseudomonas was the most commonly isolated bacteria with *E. coli* being the third most commonly isolated, accounting for 20.6% of isolates.

The spectrum of organisms responsible for catheter-associated bacteriuria in this study was also similar to that reported in the studies by Kazi *et al* and Olarinde *et al*. A broader spectrum of microbial organisms comprising *A. iwoffii, Citrobacter freundii, E. coli, Enterobacter agglomerans, K. oxytoca, K. pneumonia, Proteus vulgaris, Providencial spp, P. aeruginosa, Serratia marcescens, S. aureus* and *Yersinia enterocolitica* was however reported in a similar study at Ile-Ife.\(^{25}\)

### 5.5 Incidence of Catheter Associated Candiduria

Candiduria is infrequently encountered in healthy individuals. The prevalence of candiduria is higher among hospitalized patients with indwelling devices and accounts for around 10 to 15% of hospital-acquired UTIs.\(^7^9\) In this study, *C. albicans* accounted for 29.1% of microbial isolates. This is similar to the findings from the study by Platt and co-workers who reported that 26.5% of all isolates from UTIs related to indwelling catheters were caused by fungi.\(^4^4\) Rishpana and Kappan also reported that candida accounted for 26% of hospital acquired UTIs.\(^8^0\) However, in the study by Taiwo and Aderounmu,\(^2^4\) *C. albicans* accounted for only 3.2% of the organisms isolated while Onyegbule *et al* did not report any *C. albicans* isolates. There was a relatively high proportion of female participants and a significant number of patients with diabetes among study participants and this may explain the relatively high prevalence of candiduria.
5.6 Antibiotic Susceptibility Pattern of the Organisms causing CA-Bacteriuria

The bacterial isolates in the study were tested for susceptibility to the following antibiotics: amoxicillin/clavulanate, ceftriaxone, ceftazidime, cepefime, meropenem, amikacin, gentamycin, piperacillin/tazobactam, ciprofloxacin and levofloxacin. The susceptibility pattern of the isolates to the antibiotics varied significantly from most E. coli isolates that were susceptible to majority of the antibiotics they were tested against to acinobacter isolates that were resistant to all antibiotics they were tested against.

Among E. coli isolates, only 10% were susceptible to amoxicillin/clavulanate, 48%–66% were susceptible to gentamycin, the third generation cephalosporins, ciprofloxacin and cefepime, while more than 70% were susceptible to amikacin, levofloxacin, piperacillin/tazobactam and meropenem. None of the Pseudomonas isolates were susceptible to either ceftriaxone or amoxicillin/clavulanate, less than 30% were susceptible to the quinolones, 50%–64% were susceptible to gentamycin, cefepime and piperacillin/tazobactam, more than 70% were susceptible to ceftazidime, and amikacin while more than 85% were susceptible to meropenem.

Among Klebsiella isolates, none was susceptible to amoxicillin/clavulanate, ceftriaxone, ceftazidime or gentamycin. 10%–30% were susceptible to cefepime and amikacin, 40%–50% were susceptible to the quinolones however, 90% were susceptible to meropenem. The two enterococcus isolates were susceptible to both amoxicillin/clavulanate and meropenem while being resistant to all other antibiotics and neither of the two acinobacter isolates was susceptible to any of the antibiotics they were tested against.

The sensitivity pattern observed in this study is in some respects similar to those reported by Kazi et al, which showed a 100% resistance with amoxicillin among E. coli, Pseudomonas and
Klebsiella isolates,\textsuperscript{78} and Olarinde et al,\textsuperscript{27} which showed high resistance to beta-lactam antibiotics (penicillin and cephalosporin) among, and about 50% susceptibility to quinolones K. pneumonia. The implication of this susceptibility pattern are two-fold; firstly, it is clear that susceptibility testing is required for determining appropriate antibiotic therapy in patients with CA-bacteriuria, equally clear from this study is that, while waiting for results of susceptibility testing, the antibiotics that guarantee the widest possible coverage in patients with CA-bacteriuria are amikacin and meropenem. In deciding which of the antibiotic to prescribe, physicians should take consideration other factors such as cost, adverse effect profile as well as presence of co-morbidities such as renal impairment.

5.7 Factors associated with the development of Catheter-Associated Bacteriuria

Variables that, in previous studies, have been identified as risk factors for the development of bacteriuria following use of IUC include; catheterization for more than six days, female gender, insertion of catheter outside the operating room, presence of diabetes mellitus, presence of renal impairment and concomitant placement of ureteral stent. In this study, four factors independently associated with development of bacteriuria following the use of IUC were identified. These were; duration of catheterization greater than seven days, age 50 years or older, presence of diabetes and presence of urinary tract obstruction.

In this study, patients who were catheterized for longer than seven days had an almost 13-fold increased odds of developing bacteriuria compared with those catheterized for seven days or less; patients with urinary tract obstruction had a five-fold increased odds of developing bacteriuria, while patients who were aged 50 years or older or had diabetes mellitus had a four-fold increased odds of developing bacteriuria compared to those aged less than 50 years and those without
diabetes mellitus respectively. These findings are in keeping with findings from previous studies of CA-bacteriuria.

Duration of catheterization is thought to be the most important risk factor for the development of catheter-associated bacteriuria. Evidence suggests that once a urethral catheter is placed, the daily incidence of bacteriuria ranges between 3% and 10%. Onyegbule et al.,26 Hagerty et al.,81 Lee et al.,41 Salgado et al,43 and Platt et al,44 have all reported an association between the duration of catheterization and an increased risk of CA-bacteriuria. Similarly, the association between increasing age and the risk of catheter-associated bacteriuria has been documented.20 Hagerty et al reported in their study that the odds of developing CA-bacteriuria increased by 6% for every one year increase in age.81

The association between presence of diabetes and development of CA-bacteriuria has also been previously reported. Hagerty et al.,81 reported that patients with a blood sugar > 200 mg/dl had a 13-fold increased odds of catheter associated bacteriuria while Lee et al reported that individuals with diabetes were 4.5 times more likely to have CA-bacteriuria than those without diabetes.81 The reported rates of CA-bacteriuria among patients with urinary tract obstruction are quite high24,25. However, these high rates are generally thought to be due to the prolonged duration of catheterization. Although urinary stasis associated with obstruction of the urinary tract is known to predispose to bacterial proliferation in the urine, studies reporting urinary tract obstruction as an independent predictor of CA-bacteriuria are few. This study clearly demonstrates that obstruction of the urinary tract on its own is associated with development of CA-bacteriuria, independent of the effect of duration of catheterization. In a prospective observational study, Maki and Tambyah42 noted that relative risk among patients with obstructive uropathy was 2.0 – 4.0.
5.8 Strengths and Weaknesses of the Study

One major strength of this study was the prospective nature of the study design. However, susceptibility testing against more antibiotics as well as testing the candida isolates for sensitivity to antifungal would have improved the strength of the study.
CHAPTER 6

LIMITATIONS, CONCLUSIONS AND RECOMMENDATIONS

6.1 Limitations

1. Because of the culture techniques employed in the study, there could have been infections caused by fastidious organisms that were not detected.

2. As only patients with Foley’s catheters were included in the study, the results may not apply to those with other types of catheters e.g. silicone catheters.

3. Sensitivity testing, though carried out against several antibiotics from different classes, did not include all available antibiotics in Lagos.

6.2 Conclusions

1. The commonest indication for the use of IUC is the monitoring of urinary output in ill patients, however, a significant proportion of patients continue to be catheterized for indications other than those recommended by internationally accepted guidelines.

2. Indwelling urethral catheter use is associated with catheter-associated bacteriuria with an incidence rate of approximately 51 episodes per 1000 catheter days.

3. Enterobacteriaceae are the commonest cause of catheter-associated bacteriuria with \textit{E.coli} being the single organism. Amoxicillin/clavulanic acid had the lowest sensitivity for \textit{E. coli} the while the highest sensitivity was recorded for meropenem.

4. Duration of catheterization greater that seven days, age greater 50 years, presence of diabetes, and presence of urinary tract obstruction were the factors associated with development of catheter-associated bacteriuria among patients with IUC.
6.3 Recommendations

1. There is need for healthcare professionals to be conversant with the guidelines on acceptable indications for IUC use.

2. Urinary catheters should only be inserted when clearly indicated and once inserted, physicians should regularly evaluate each patient to determine if the catheter continues to be required. Such catheters should be removed promptly once the need for them no longer exists.

3. Patients who are catheterised for longer than seven days, those that are aged 50 years or older, those that have diabetes, and those with urinary tract obstruction would benefit from more frequent urine cultures to determine the presence of bacteriuria and therapy guided by susceptibility testing instituted.
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Appendix I Ethical approval from LUTH Health Research and Ethics Committee
LAGOS UNIVERSITY TEACHING HOSPITAL
HEALTH RESEARCH AND ETHICS COMMITTEE
PRIVATE MAIL BAG 12085, LAGOS, NIGERIA
e-mail address: luthethics@yahoo.com

Chief Medical Director:
PROF. ABIN. OSIMOGU
MBBS (Lagos), MPH (Columbia), FACP, FWACP

Chairman, Medical Advisory Committee
DR. M. O. OGUIUWE
BDS, FWACS.

Chancellor:
ASSOC. PROF. N. U. OKUBADEJO
MBBS, CM, FRCP.

Administrative Secretary:
MRS, D. S. IMAN
B.SC. BUS. ADMIN, MIHDR.

LAGOS UNIVERSITY TEACHING HOSPITAL
6TH FLOOR, LUTH ADMINISTRATIVE BLOCK
OFFICE ADDRESS: ROOM 807, 1ST FLOOR, LUTH ADMINISTRATIVE BLOCK
TELEPHONE: 023 2-3459759, 0802785, 0802295, 0802139, 0802158

25TH JUNE, 2014

NOTICE OF EXPEDITED REVIEW AND APPROVAL

PROJECT TITLE: "PREVALENCE AND PATTERN OF CATHETER-ASSOCIATED URINARY TRACT INFECTION AT LAGOS
UNIVERSITY TEACHING HOSPITAL".

HEALTH RESEARCH COMMITTEE ASSIGNED NO.: ADM/DCST/HREC/APP/1796

NAME OF PRINCIPAL INVESTIGATOR: DR. SYLVERIOUS IGBOJIA IGBOJIA

ADDRESS OF PRINCIPAL INVESTIGATOR: DEPT. OF MEDICINE, LUTH.

DATE OF RECEIPT OF VALID APPLICATION: 14-04-14

This is to inform you that the research described in the submitted protocol, the consent forms, and all other
related materials where relevant have been reviewed and given full approval by the Lagos University Teaching
Hospital Health Research Ethics Committee (LUTH-HREC).

This approval dates from 25-06-2014 to 25-06-2015. If there is delay in starting the research, please inform the
HREC so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related
to this research may be conducted outside of this dates. All informed consent forms used in this study must carry
the HREC assigned number and duration of HREC approval of the study. In multyear research, endeavor to submit
your annual report to the HREC early in order to obtain renewal of your approval and avoid disruption of your
research.

The National code for Health Research Ethics requires you to comply with all institutional guidelines, rules and
regulations and with the tenets of the code including ensuring that all adverse events are reported promptly to the
HREC. No changes are permitted in the research without prior approval by the HREC except in circumstances
outlined in the code. The HREC reserves the right to conduct compliance visits to your research site without
prior notification.

HEALTH RESEARCH ETHICS COMMITTEE

DR. N. U. OKUBADEJO
CHAIRMAN, LUTH HEALTH RESEARCH ETHICS COMMITTEE
Appendix 2

Patient information leaflet

Dear potential study participant,

You are being invited to participate in this study titled “Prevalence and Pattern of Catheter Associated Urinary Tract Infection at the Lagos University Teaching Hospital” because the doctors treating you have placed a catheter in your bladder.

Name and Sponsor of Research

Dr. Sylvernus Igbudu, a Senior Registrar in the Department of Medicine of Lagos University Teaching Hospital, Idi Araba. This research is to be sponsored by the researcher. Source of funding shall be his personal income.

Procedure of the research

I shall recruit 208 subjects requiring the passage of urinary catheter. These shall be patients on admission on the medical and surgical wards. Each subject will be asked questions about their health and medical examination conducted. Urine samples will be taken to carry to carry out some tests including urinalysis and urine microscopy, culture and sensitivity. Blood sample will also be taken for fasting blood sugar and full blood count.

What is the purpose of the study?

This study is being carried out in an attempt to answer the following questions.

1. What are the reasons why at the Lagos University Teaching Hospital place catheters in the bladder of patients?
2. How frequently does the urine of patients who have had a catheter placed in their bladder become infected with germs?

3. What are the factors that predict that the urine of a patient with a catheter in their bladder will become infected with germs?

**What will be the benefits of the study?**

The possible benefits that may result from findings in this study include

1. By identifying the factors that predict that a patient’s urine will become infected when catheters are placed in their bladders, doctors may be able to take steps to prevent these infections from occurring or identify and treat the infections early.

2. It will also help to bring to the doctor’s attention situations in which placing a catheter in a patient’s bladder may not be necessary and therefore reduce the frequency with which catheters are placed in patients’ bladders.

**If I decide to participate in the study will I be exposed to any risks?**

The placement of catheters has some consequences but you will not be exposed to any further risk as a result of the research which is only a prospective observational study. These consequences are as a result of bladder catheterization since the study will not increase the duration of catheterization you will not be at any further risk. I expect that your doctor must have explained that to you but I can still give you further clarification.

**What will happen to the information collected?**

All information collected during the study will be kept confidential. All individuals taking part in the study will be assigned a number which shall not be directly linked to their names. From the
point of collection of information onwards, it is by this number that the information and samples collected will be identified.

The results of this study may be presented at scientific conferences and may also be published in medical journals. There will be no direct reference to you during any of these situations.

**What if I decide not to participate in the study?**

Your decision to participate in this study should be entirely voluntary and of your own volition. This decision should only be made after you have clearly understood what the study entails. Also if you initially decide to participate in the study, you are free to opt out of the study at any time should you wish to do so.

If you choose not to participate in this study, please be rest assured that your decision will in no way adversely affect the type of quality of care you will receive in this hospital.

**If I decide to participate in the study what will be expected of me?**

Should you choose to participate in the study; the following will be required of you:

1. A sample of your urine will be collected within 24 hours of the catheter being passed and will be taken to the laboratory to be checked for the presence of germs. This process will be repeated on days 3, 7, 10, 14, and 28 after the catheter is passed but this shall be only if there is need for the catheter to remain in place. The duration of catheterization will not be influenced by the study. A sample of urine will be taken 48 hours after if the catheter is removed earlier than this.

2. You will be expected to sign a consent form if you are found to be eligible for the study. This shall be done before you are recruited into the study.
Are these tests routinely done on all patients or are they for the purpose of the research and who will pay for them?

The tests are different from the ones that are routinely carried out on patients and they are being carried out solely for the purpose of the research. However, if during the study it is found your urine is infected with germs, your doctors will be informed immediately.

You will not be asked to pay for the tests being carried out for the purpose of the research as the researcher has made arrangements to pay for these tests.

If I require further clarification concerning the study, is there anyone I can reach?

You can contact

1. Dr. Sylvernus Igbudu
   Department of Medicine, LUTH
   sylvaigbudu@yahoo.com
   08066155033, 08022143800

2. LUTH Health Research and Ethics Committee
   Room 107 Administrative Building, LUTH
CONSENT FORM

I hereby consent to participate in the study titled “PREVALENCE AND PATTERN OF CATHETER ASSOCIATED URINARY TRACT INFECTION AT LAGOS UNIVERSITY TEACHING HOSPITAL”.

I confirm that Dr. ……………………………………………………………………………………………………………………………
informed me about the nature of the study as well as its possible benefits and risks in a language that I clearly understand. He/She has also assured me that my decision to participate in the study will in no way interfere with my care.

Name of patient: ……………………………………………………………………………………………………………………………

Patient’s signature/ Right thumb print ……………………………. Date ……………………………

Witness name ……………………………………………………………………………………………………………………………

Witness signature/ Right thumb print ……………………………. Date ……………………………

As a physician responsible for recruiting for the above mentioned study, I confirm that I have explained the nature and purpose of this study to the above named patient in a language that he/she understands.

Clinician’s name ……………………………………………………………………………………………………………………………

Clinician’s signature…………………………………………. Date …………………………

xcvi
Study Questionnaire

Bio data:

1. Study number
2. Name (Initials)
3. Age
4. Gender
5. Hospital number
6. Contact phone number
7. Admitting diagnosis
8. Date of catheterization
9. What material is the urethral catheter made from?

Medical history

10. Diarrhea (a) Yes (No)
11. Diabetes
12. Renal insufficiency
13. Steroid use
14. HIV infection
15. Past history of urologic surgery
16. Other underlying disease states (please specify)

Decisions regarding catheterization

17. Decision to catheterize taken by: (a) Nurse (b) House Officer (c) Registrar (d) Senior Registrar (e) Consultant
18. Catheter passed by: (a) Nurse (b) House Officer (c) Registrar (d) Senior Registrar (e) Consultant

19. Is the patient on antibiotics (a) Yes (b) No

20. If yes, list all antibiotics and duration of use

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

21. Has the catheter been changed since it was passed? (a) Yes (b) No

22. If yes, how many times .................

23. For how long was each catheter left in-situ?

1\textsuperscript{st} catheter .................................................................

2\textsuperscript{nd} catheter .................................................................

3\textsuperscript{rd} catheter .................................................................

4\textsuperscript{th} catheter .................................................................

24. Which of the following documented indications for catheterization is present in the patient.

i. Urinary retention

ii. Monitoring urine output in critically ill patients

iii. To keep the patient dry and manageable when obtunded or comatose

iv. As part of urologic studies e.g. checking urinary residual volumes

v. Need for intraoperative monitoring of urinary output

vi. Open sacral or perineal wounds in incontinent patients

vii. Patients preference after failure of each other specific continence interventions
viii. To improve comfort for end of life care
ix. Other indications

Ancillary investigations

Urinalysis

Urine microscopy, culture and sensitivity

Full blood count

Fasting blood sugar
Appendix 3 Study proposal approval by the National Postgraduate Medical College of Nigeria

NATIONAL POSTGRADUATE MEDICAL COLLEGE OF NIGERIA

COLLEGE REGISTRAR
Dr. O.A. Atoyibi,
FMCS, FWACS, FICS.
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Date: 30TH JUNE, 2015

Our Ref: AF/069/09/002/979

DR. IGBUDU S.O
DEPARTMENT OF MEDICINE
LUTH
LAGOS.

Dear Dr,

RE: REGISTRATION OF TITLE OF DISSERTATION: ASSESSMENT OF PROPOSAL FOR
THE PART II EXAMINATIONS IN THE FACULTY OF INTERNAL MEDICINE.
We wish to refer to your letter on the above subject matter and inform you that your proposal
Titled: “PREVALENCE AND PATTERN OF CATHETER ASSOCIATED URINARY TRACT
INFECTION AT LAGOS UNIVERSITY TEACHING HOSPITAL” has been assessed.

The attached are the comments and recommendations of the assessor(s) for guidance, in the
conduct of your project.

You may now proceed with the study.

We wish you the best of luck.

Yours faithfully

Mrs. E. A. Akpabio
Examination Officer
E-mail: adanmaakpabio@yahoo.com
For: College Registrar