PREVALENCE OF UROPATHOGENIC CANDIDA CAUSING URINARY TRACT INFECTION

BY

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DECLARATION

I hereby declare that this project has been written by me and is a record of my own research work. It has never been submitted in a prior application for a higher degree from this university or another. All citations and sources of information are clearly acknowledged by means of reference.

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OYEWOLE, ESTHER BOLUWATIFE

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Date

CERTIFICATION

This is to attest that this project material entitled "Prevalence of Uropathogenic *Candida* in Urinary Tract Disease" was prepared and submitted by **OYEWOLE ESTHER BOLUWATIFE** as a requirement for the degree of **BACHELOR OF SCIENCE IN MICROBIOLOGY.** This original research was done under my direction and is approved.

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Date

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(Ag. Head of Department)

DEDICATION

To the one whose life I live. Abba

ACKNOWLEDGEMENTS

My genuine gratitude is to God who in his infinite mercies gave me wisdom, knowledge, understanding and strength for the successful completion of my project and for the gift of men.

I want to use this medium to appreciate the HOD of biological science, Dr (Mrs.) Ayolabi C.I, my supervisor, Mr Tosin Ogunbiyi and his wonderful family for their sacrifices in terms of strength, time, resources, patience and knowledge. God bless you abundantly. I am immensely grateful.

To my wonderful parents, thanking for yielding to God and helping me grow. For all the support and prayers, God bless you. The ones who look up to me, big sis is proud of you. Thank you for helping me in every way. For your prayers, God heard and He answered.

I'm grateful for the gift of a support system and best friend. Thank you for taking every step with me. It is less tough cause we do it together.

For everyone God brought my way to help me, Pastor Olumide Tanimowo, Dr Abiala, Odu Temilayo, Dada Oreoluwa, Apanpa David, Michael Divine, thank you so much, I am grateful.

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ABBREVATIONS

- SDA- Sabouraud dextrose agar
- UTI- Urinary tract infection
- GT- Germ tube test
- UPC- Uropathogenic Candida
- C. albicans- Candida albicans
- C. tropicalis Candida tropicalis
- C krusie Candida krusie
- C. glabrata- Candida glabrata

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ABSTRACT

Background of the study: Urinary tract infection, one of the most common infectious diseases, is frequently found in developing countries. Urinary tract infections are included among some of the prevalent microbial illnesses in older people and women (UTI). Despite the fact that this type of infection can result in less serious, life-threatening conditions, the patient nonetheless feels a significant deal of distress. True urinary tract infection (UTI) is uncommon in adult males under the age of 50. (approximately 5-8 per year per 10,000), UTI developing in adult women is 30 times more probable than in males. Examples of microbial pathogens implicated in cases of UTI are Uropathogenic *Escherichia coli, Trichomonas vaginalis*, and *Candida* spp. Research so far has shown that the percentage of *Candida albicans* that affects the urinary tract is more prevalent than any other *candida spp* in existence. Previous researches had investigated the occurrence of *Candida* spp. in UTI in humans but not in toilets. Hence, this research aims to investigate the prevalence of uropathogenic *candida* in male and female toilet hostels in a tertiary institution in Ogun state.

Methodology: With the consent of the students, 92 swab samples were acquired from the toilet bowl from the rooms in the hostel. Sabauroud dextrose agar, Germ tube test, Growth at 45°C, CHROMAgar[™] were techniques used for *Candida* identification.

Result: 51 samples grew on Sabauroud dextrose agar. Analysis of the samples showed *Candida* prevalence to be 55.4% on Saboraud dextrose agar. Further analysis showed *Candida albicans* prevalence to be 74.5% in females and 25.5% in males.

Conclusion: This study revealed the prevalence of pathogenic *Candida* spp. in the study population. Exposure of students to such pathogens increases the risk and onset of *Candida*-associated UTI. To guarantee proper cleanliness among this student body, action must be taken.

Keywords: *Candida*, **Prevalence**, **Uropathogenic** *Candida*, *Urinary* **tract infection**, **Biochemical test**.

CHAPTER ONE

INTRODUCTION

1.1 Background of Study

UTI, the second-ranking infectious disease, are thought to be a serious global health issue. Every year, UTIs cost governments around the world tens of millions of dollars (Issakhanian and Behzadi, 2019). Urinary tract infections are one of the infectious disorders that are most frequently found in developing countries (UTI). A urinary system infection is known as a urinary tract infection (UTI). A disorder known as urethritis, pyelonephritis, or cystitis are all examples of this type of infection that can affect the urethra, kidneys, or bladder (Sims, Lemos et al., 2005). Urinary tract infections are included among the most common bacterial illnesses in older people and women (UTI). The patient experiences a great lot of distress even though UTIs can lead to less severe, life-threatening complications. (Sheerin and Glover, 2019). In hospital and community infections, *Escherichia coli* predominates (75–90% of isolates), while Proteus mirabilis, *Staphylococcus saprophyticus* (which is frequently isolated from younger females), Enterococcus faecalis, Klebsiella pneumoniae, and Pseudomonas aeruginosa play a less significant role (Sheerin, 2019; Kasper, Fauci et al., 2018). The fimbrial adhesions expressed by uropathogenic bacteria allow them to bind to the glycolipids and glycoproteins on the epithelial surface. Thus, bacteria can survive the transit of urine in the urinary tract and continue to grow there. Among the various substances the bacteria produce are hemolysin, toxins, and colonynecrotizing agents. The risk of infection is enhanced as a result of these compounds' breakdown of epithelial integrity and facilitation of bacterial invasion (Behzadi, 2019). In order to multiply inside host epithelial cells, uropathogens can also internalize into those cells providing a reservoir for reoccurrence (Sheerin., 2019).

True urinary tract infection (UTI) is uncommon in adult males under the age of 50. (approximately 5-8 per year per 10,000), UTI developing in adult women is 30 times more probable than in males. The incidence of UTI in men approaches that of women only in men older than 60 years (Guclu, Halis *et al.*, 2021). Urinary tract infection in female is frequent due to the short distance and the width of the urethra that makes it liable to trauma during sexual intercourse as well as pathogens moving through the urethra to the bladder during pregnancy.

The moist environment of the female genitals also favors microbial growth as fungi and bacteria thrive in moist environment (Nicolle, 2005). More than a quarter of women have a second infection. Although both host and agent characteristics have been postulated, it is unclear why seemingly healthy women with no known anatomical defects experience numerous recurrences. Most experts, however, agree with Kunin's assertion that the risk of a second infection is higher than the first, and that the first "sets the stage" for subsequent infections. (Foxman *et al.*, 1990).

Some of the pathogens that cause urinary tract infection and its reoccurrence are: *Escherichia coli*, *Proteus mirabilis*, *Enterobacter spp*, *Staphylococcus aureus*, *Candida*, *Klebsiella pneumonia*, and several *Enterobacter* species are the organisms most frequently responsible for UTIs (Davenport *et al.*, 2017).

Urinary tract infections (UTIs) are rare in adult males younger than 50 years but increase in incidence thereafter. Many experts consider UTIs in males, by definition, to be complicated (i.e., more likely to be associated with anatomic abnormalities, requiring surgical intervention to prevent sequelae)

Candida species are yeasts that live in the human commensal microbial population. They are found on the skin and mucosal membranes of the oral cavity, gastrointestinal, and genitourinary tracts (Romob and Kumamoto, 2020; Pérez, 2021). There are many species of *Candida*. The main choice that needs to be taken when *Candida* organisms are found in urine is whether this indicates an infection of the upper or lower urinary tract, colonization of the bladder, or contamination of the urine sample. The doctor should neither disregard the discovery out of hand nor start antifungal therapy on an empirical basis. Contamination can be differentiated from colonization or infection by obtaining another urine sample to verify funguria (Sobel, 2006).

The most common fungus in humans, *Candida* albicans, can cause everything from minor mucosal infections to fatal systemic infections (Calderone and Clancy, 2011; Ganguly and Mitchell, 2011; Pfaller and Diekema, 2012). The mucous membranes of the respiratory, gastrointestinal, and female genital tracts normally contain *C. albicans* as part of their natural flora. Numerous species live in hosts, including humans, as innocuous endosymbionts or commensals, but when mucosal defenses are breached or the immune system is weakened, they can invade and spread disease. *C.albicans*, a diploid dimorphic fungus, is the most common

cause of fungal nosocomial UTIs and systemic candidiasis globally. One of the most well-known harmful characteristics of the dimorphic fungus *C. albicans* is its shape flexibility, as demonstrated by its ability to flip between yeast and filamentous forms (Mahmoudabadi *et al.*, 2014). Additionally, as urinary tract candidiasis has increased, antifungal-resistant *Candida* species have also emerged. Most mucosal surfaces, particularly those of the gastrointestinal tract, as well as the skin, are home to *Candida*. *Candida* produces a yeasty stench on agar plates when it is produced in a lab. *Candida* appears as huge, spherical, white or cream (the Latin word albicans means "whitish") colonies. Because C. albicans ferments glucose, maltose, and sucrose into acids instead of lactose, it can be distinguished from other *Candida* species (Meyers, 1978). There are numerous treatment options available for people who have symptomatic *Candida* urinary tract infections. The preferred antifungal is fluconazole, which, in its oral formulation, produces high urine concentrations. (Anurag *et al.*, 2014).

1.2 Statement of the Problem

Studies on Urinary Tract Infections (UTIs) associated with *Candida* spp have revealed that *Candida albicans* is still the most important cause of *Candida* urinary tract infections and are also responsible for multifactorial nosocomial infections. Recent studies have also shown that as a result of prolonged hospitalization, immuno-compromised patients, uncontrolled use of antibiotics, prophylaxis by antifungal agents, catheterization, urinary tract surgeries and long period stays in intensive care units, the frequency of funguria and specially uropathogenic yeasts are getting increased (Behzadi, Yazdanbod, 2010).

Studies so far have shown that *Candida albicans* has been the most prevalent causes of urinary tract infection and its reoccurrence. The purpose of this research is to explore the prevalence of *Candida* spp that have not been studied, to asses and validate the claims made about the *Candida* spp, and to also quantify the proportion of specific population affected by uropathogenic *Candida* spp.

1.3 Aim and Objectives of the Study

This study aims to investigate the occurrence of uropathogenic *Candida* spp. in male and female student hostels in a tertiary institution in Ogun State.

Based on this, the following are the study's specific objectives;

- 1. To examine the occurrence of uropathogenic *Candida* in male and female students hostel using classical mycology techniques.
- 2. To examine the prevalence of each *candida* species.
- 3. To sensitize people and create more awareness on how to manage and prevent urinary tract infection.

1.4 Significance of the Study

Millions of people get urinary tract infections (UTI), a major health issue, every year. They account for about 8.3 million hospital visits annually and are the second most frequent type of infection in the body (Fatima and Mussaed, 2018). *Candida spp* is a leading cause of fungi urinary tract disease in the world. *Candida* albicans is a common commensal fungus in general population (Umeh and Emelugo, 2011; Giovanni *et al.*, 2015; Yang *et al.*, 2015). Molecular identification has been used to identify emerging *C. albicans* in cases of candidiasis (Li *et al.*, 2008; Bettini *et al.*, 2013; Criseo *et al.*, 2015). Toilet swab of male and female hostels were used for this study. This study will provide information on the prevalence of uropathogenic *Candida* spp in urinary tract infections using biochemical test.

1.5 Definition of Terms

Prevalence: the percentage of a population that has a condition found to impact them (often a condition or risk factor (like smoking or wearing a seatbelt) at a certain moment.

Uropathogens: A microorganism capable of causing disease of the urinary tract.

Candiduria: Candiduria is a common nosocomial infection afflicting the urinary tract. It can also be referred to as the presence of the *Candida* specie in the urinary tract.

Opportunistic infection: opportunistic infections are such that affect those with compromised immune systems more frequently or more severely than those with healthy immune systems. They are caused by bacteria, fungi, viruses, or parasites that normally that usually do not cause disease, but become pathogenic as result of impaired defense system.

Nosocomial Infections: Nosocomial infections also referred to as health-care associated infections or hospital acquired infections (HAI), they are infections acquired in hospitals, health-care facilities. For an infection to be considered nosocomial, the infection must not be present at

the time of admission, but rather develop at least 48 hours after admission. Nosocomial infections can lead to serious problems like sepsis and can even lead to death.

Urinary Tract Infection (UTIs): A UTI is an infection that develops as a result of the invasion of microbes in the urinary tracts which includes the kidneys, ureters, bladder, and urethra.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction to Urinary Tract Infections (UTIs)

UTIs are infections caused by pathogenic bacteria, protozoa, and fungi that defy the host defense barrier and invade the urinary system (urethra, bladder, ureter, and kidney) (Sims, Lemos *et al.*, 2005). The most prevalent infection in humans has been determined to be urinary tract infection. It affects people of all ages and genders, as well as those in the community and in hospital. Compared to men, women have a higher risk of getting a UTI. A bladder-specific infection can be uncomfortable and unpleasant. But if a UTI spreads to the kidneys, it can have serious implications. About 50% of all females experience urinary tract infections, including relapses. Female genital anatomy makes urinary tract infections more common in women than in men. Pregnant and sexually active females are also more likely to have it. Because of the narrowness and vulnerability of the urethra to trauma during sexual contact and the possibility of germs migrating from the urethra trough to the bladder during pregnancy, females are more likely than males to get urinary tract infections. The moist environment (Nicolle, 2005).

Over 25% of women have a secondary infection. It is unclear why seemingly healthy women with no known anatomical anomalies endure repeated recurrences, in spite of the fact that both host and agent characteristics have been hypothesized. However, the majority of specialists concur with Kunin's claim that the risk of a subsequent infection is larger than that of the initial infection and that the initial infection "sets the stage" for later infections. (Foxman *et al.*, 1990). When present in children and accompanied with anomalies such vesicoureteral and reflux nephropathy, UTI can cause pyelonephritis and severe morbidity if left untreated. Long-term effects of UTI include parenchymal scarring, hypertension, reduced renal function, and renal scarring (Chang, 2006; Wang, 2018). Because of this, UTI significantly increases the risk of mortality and morbidity in children. But when acknowledged, renal sequelae are rare.

Candida sp. are the most prevalent cause of fungal UTI. *Candida* UTI can develop in the lower urinary tract or, in rare circumstances, might progress to the kidney. *Candida species* cause reoccurring UTI by either hematogenous routes (via the bloodstream, from a distant source of infection is delivered to the urethra and bladder) or direct infection to the bladder (Sobel *et al.*, 2003). Frequent occurrence and colonization by *Candida* species native to the host's gastrointestinal tract are the prevalent causes of *Candida* infections.

2.2 Pathogens of Candida

The *Candida* species, which can cause mucosal and cutaneous infections as well as systemic infections, are the prevalent human fungal pathogens (Papon et al., 2013). Candida albicans accounts for 65.3% of cases of candidiasis, followed by Candida glabrata (11.3%), Candida tropicalis (7.2%), and C. Candida krusei (2.4%) and parapsilosis (6.0%) (Pfaller et al., 2010). In a group of species known as wholegenome duplicators, the species *glabrata* is far more closely related to Saccharomyces cerevisiae than to Candida albicans (Fitzpatrik et al., 2006). The Candida glabrata contains every gene required for meiosis and reproduction (Wong et al., 2003), and documented mating type switching (Brockert et al., 2003; Butler et al., 2004; Edskes and Wickner, 2013). Traditionally nonpathogenic commensal fungal microbe of human mucosal tissues, Candida glabrata was once thought of be such. However, due to mucosal and systemic infections caused by C. difficile, the usage of immunosuppressive medicines is increasing. Glabrata have significantly increased, especially in the HIV-infected population. Natural resistance of C.glabrata to azole antimycotic drugs, which are very effective in treating infections brought on by other Candida species, is a significant barrier. In contrast to other Candida species, Candida glabrata, originally known as Torulopsis glabrata, has a haploid genome and a nondimorphic blastoconidial structure. Right now, C. Glabrata, which can affect the mouth, esophagus, vagina, or urinary system, is the second- or third-most frequent nosocomial cause of systemic candidal infections (Fidel et al., 1999).

C. krusei infections are relatively uncommon, however the organism is extremely concerning due to its relative resistance to azoles and other antifungal medications (Drago *et al.*,2004). Although it is less frequently reported than other *Candida* species, *Candida krusei*, also known

by the synonymous names *Pichia kudriavzevii* and *Issatchenkia orientalis*, causes candidemia with the lowest 90-day survival rate (Pfaller, Neofytos, *et al.*, 2012). Fluconazole is a typical empirical treatment for candidemia outside of North America and Europe, however *C. krusei* is inherently resistant to this antifungal (Jamiu, Albertyn, *et al.*, 2021). Fluconazole has the ability to stop the development of other microorganisms while promoting the survival of fluconazole-resistant species. As a result, fluconazole prophylaxis may also increase the likelihood of *C. krusei* infections (Wingard, Merz, *et al.*, 1991). The potential danger posed by this pathogen is highlighted by reports of decreased susceptibility to other antifungals such flucytosine, amphotericin B, and caspofungin (Cuenca-Estrella *et al.*, 2001, Hakki, *et al.*, 2006; Majoros, *et al.*, 2006).

2.3 Causes of Urinary Tract Infection

Incomplete use of medication by the patient during first occurrence: When medications prescribed during the first occurrence are not used completely, the pathogens regenerate themselves in the body and reinfect the urinary tract.

Wearing the same set of underwear after the first treatment: It is advised to change the underwear after first treatment so as to avoid reinfection by pathogens that are present in the underwear.

Poor hygiene: Wearing wet pant creates a moist environment for microorganisms to grow. Wearing one sanitary pad for long is a habit that leads to an increase in the number of microorganisms present. Menstrual blood discharge is a bodily waste that contains a variety of harmful microorganisms..

Using dirty water to clean up after using the toilet: Dirty water contains microorganisms. The use of such water using the toilet allows for the introduction of microorganisms present in the water to infect the body.

Use of catheter: UTIs are often more common in those who can't urinate on their own and urinate through a tube (catheter). Persons who are hospitalized, people with neurological issues

that make it difficult to control their urination, and people who are paralyzed may all fall into this category (Kauffman *et al.*, 2000).

Use of spermicide: Consistent use of spermicides kills lactobacilli which is a beneficial microorganism in the vaginal, making it easier for microorganisms to move in.

Suppressed immune system due to the presence of disease: Disease such as diabetes, hypertension, etc. suppresses the immune system. This allows for the growth of microorganisms in the body as the defense system is too weak to fight them. (McNulty *et al.*, 2003).

Unchecked and excessive use of antibiotics that causes antibiotic resistance: When certain antibiotics are prescribed repeatedly, the microorganisms they target can grow resistant to them. Ingesting wrong dose of antibiotics at a subclinical dosage could kill the beneficial microflora present thereby allowing the growth of pathogenic growth (Nwadioha *et al.*, 2013).

2.4 Other Causes of UTIs

Most infections arise from one type of bacteria, *E. coli* which normally lies in the colon. E. *coli*, *P. aeruginosa, Nocardia, Streptococcus faecalis, Klebsiella pneumoniae, Proteus mirabilis, Mycobacterium tuberculosis, Candida, Actinomycetes, Staphylococcus aureus* etc. are the organisms most frequently linked to catheter-associated UTIs. Mycoplasma and Chlamydia may also be connected to STIs that are transferred sexually. Infections of the urinary tract in men can also be brought on by: prostatitis, epididymitis, orchitis. In adult male, pyelonephritis, cystitis, and urethritis.

2.5 Symptoms of UTIs

Urinary tract infections do not always cause signs and symptoms, but when they do, they may include:

- A strong, continuous urge to urinate,
- A burning sensation while urinating, or painful urination,
- Urinating frequently and in tiny amounts,
- Urine that appears cloudy,

- Urine that appears red, bright pink or cola-colored a sign of blood in the urine,
- Strong-smelling urine,
- Pelvic pain, in women especially in the center of the pelvis and around the vicinity of the pubic bone,
- Colored discharge (darkish brown, brown or green),
- Itching.

UTIs may be overlooked or mistaken for other conditions in older adults.

2.6 Risk Factors associated With UTIs

Female Anatomy: Because a woman's urethra is shorter than a man's, bacteria travel a lesser distance to reach the bladder. If microorganisms ejected after using the toilet are not wiped properly, from front to back, microorganisms will be wiped to the vaginal and then enter the urinary system.

Sexual activity: Sexually active women have a higher rate of UTIs than women who aren't. Most sexually active women with recurrent UTI have several sexual partners who have unidentified infections in their bodies. The bacteria then infect the sexual partner of men with UTI.

Specific Birth Control Types: Women who use spermicidal products and diaphragms for birth control may be more vulnerable. Diaphragms and spermicides affect the urinary tract; they kill the beneficial microorganisms.

Menopause: A decrease in circulating estrogen after menopause causes alterations in the urinary tract, making one more susceptible to infection.

Wearing of Tight Materials: This creates a moist environment for the pathogens to grow. Bacteria and fungi enjoy growing in moist environment.

Improper Cleaning of Pubic Area (Wiping the anus from back to front): the anus is to be wiped from the front to the back for proper cleaning and preventing the spread of pathogens to the front.

Immuno-compromised system: Diabetes and other diseases that compromise the immune system's ability to fight germs can increase the chance of UTIs.

Catheter use: UTIs are more common amongst those who cannot urinate on their own and urinate through a tube (catheter). Persons who are hospitalized, people with neurological issues that make it difficult to control their urination, and people who are paralyzed may all fall into this category.

A recent urinary procedure: Urinary surgery or medically assisted examination of the urinary tract can both raise the risk of a urinary tract infection.

2.7 Epidemiology of Candida UTI

Candida is found in only 1% of samples of clean-voided pee from healthy persons, but it causes 5%–10% of urine culture results that are positive in hospitals and other tertiary care institutions, primarily in patients with indwelling bladder catheters (Rivett *et al.*, 1986; Kauffman., 2005). Infection rates in burn units are three times higher than those in medical and surgical critical care units (ICUs) (Bougnoux, 2008). Most newborn babies with candiduria, especially those who were born prematurely, is caused by hematogenous (antegrade) urinary tract infection and candidemia (Sobel., 2011). The majority of people with diabetes mellitus, those who are confined to beds, or those taking antibiotics will develop community-acquired candiduria. (Colodner, 2008).

When *Candida* species are found in the urinary tract, it is referred to as candiduria. According to studies, The organism that is most frequently discovered in urine samples (between 50% and 70%) is *Candida albicans*. Candida species like *C. glabraia* and *C. krusei* are known to increase antifungal medication resistance, which is a clinical problem despite the fact that Candida albicans is the most typical cause of candidiasis. (Perlroth *et al.*, 2007).

A prevalent fungal illness that affects 150 million people worldwide each year is UTI. (Kåhrström, 2015). It is common in 50-60% of adult women. The prevalence increases with age (Stamm, 2001). Reoccurring UTI before menopause for women increases due to the use of spermicides which kills *Lactobacilli*, a beneficial organism in the vaginal. Infection rates rise

after menopause due to various anatomical changes and a natural decrease in Lactobacilli in the vagina. The effect of UTI is from a mild self-limiting to acute sepsis and then leading to death.

According to (Alimehr *et al.*, 2015), a study of antifungal susceptibility pattern of *Candida* species in Milad hospital, Tehran, Iran was done. 50 patients who were hospitalized to Milad ICUs between April and September 2013 provided *Candida* isolates. Morphological and polymerase chain reaction assays were used to identify the isolates. Using the E-test approach, resistance to antifungal medications containing caspofungin, posoconazole, voriconazole, and amphotericin B was identified. 47.8% of the 67 Candida isolates were Candida glabrata, followed by C. albicans, 28.3%, 7.5% C. tropicalis, 7% C. guilliermondii, 3% C. krusei, and C. dubliniensis, which accounted for the remaining 2%. The least susceptible species was C. glabrata, which had isolates that were 6.3% and 9.4% resistant to posoconazole and voriconazole, respectively, and 9.4% resistant to amphotericin B. There was no evidence of caspofungin resistance in C. glabrata isolates. One of the C. krusei isolates was resistant to amphotericin B, but none of the C. krusei strains tested negative for resistance to voriconazole, caspofungin, or posoconazole. Clinicians who care for ICU patients have expressed concern about the rise in the incidence of antifungal-resistant non-C. albicans species in recent years.

In Nasarawa State University, Keffi, a total of 56 (38.89%) *Candida* species were isolated from 144 samples in the study of candiduria among students. Males made up 10 (15.63%) of the isolated *Candida* species, whereas female students had a predominance of 46 (57.50%). The study's most frequent *Candida* species, *Candida tropicalis* 24, was discovered primarily in samples taken from female students (30%). In contrast, *C. utilis* 5 (7.8%) and *C. albicans* 5 (7.8%) were only found in the male pupils. The sociodemographic study also shows that students between the ages of 16 and 20 (27.5%), 26 to 30 (20%), under 31 (22.2%), and married people (25%) were most likely to contract candiduria from *C. tropicalis*. However, *C. albicans* was primarily isolated in unmarried people (14%) and students between the ages of 21 and 25 (12.5%) (Tsaku *et al.*, 2019).

In an experiment carried out to identify *Candida* on Chromagar by a university in Niger state, the species with the highest frequency (64.7%) was *C. albicans* (Yang *et al.*, 2003; Marinho *et al.*, 2010). Various cases have been recorded where there is a higher prevalence of *C. albicans* than non-albicans *Candida*. As an alternative, a higher prevalence of nonalbicans *Candida* (63.3%)

versus 36.7%) has also been noted (Mohandas *et al.*, 2011; Deorukhkar, *et al.*, 2014). Over the past ten years, there have been a lot more reports of systemic disorders. Both albicans and nonalbicans *Candida* species, as well as mucosal yeast infections (Hobson, 2003). *C. tropicalis* was the study's dominant species among nonalbicans species, which is consistent with the results of related research projects carried out in Nepal (Tamang *et al.*, 2006) and other places (Basu *et al.*, 2003). C. tropicalis (11.7%) was the most typical species isolated in this investigation, accounting for 35.3% of the non-albicans *Candida* species. One of the most prevalent diseases, *Candida* species has been discovered to account for up to 15% of nosocomial bloodstream infections and to have a death rate between 5-71% (Falagas *et al.*, 2006).

The prevalence of fungi has a higher frequency among the very young and a gradual increase with age in both men and women. Up until the age of 60 and beyond, women have a much higher incidence than men. The pattern of symptomatic infection is slightly different, with women between the ages of 15 and 29 having the highest prevalence(approaching 20%). One hypothesis is that the initial, index infection leads to a resetting of the host response, so that—like an oversensitive smoke detector—symptoms are generated when faced with the same fungi that would, before the index infection, have caused only a transient and asymptomatic colonization of the urinary tract (Kåhrström, 2015). Over time, the response drifts back to its pre-index UTI level. This hypothesis is in line with the finding that a woman's likelihood of remaining symptom-free increases with time. According to anecdotal data, women who refrain from sexual activity for a while can treat recurring UTI, become pregnant, or switch sex partners. Another theory proposes that though the host defense mechanism exfoliates microorganism-bound bladder cells, the bladder is more vulnerable to attack by additional infections until it can fully repair (Kåhrström, 2015).

2.8 Pathogenesis of *Candida* UTI

C. albicans is the most prevalent fungus in humans, causing everything including superficial mucosal infections to life-threatening systemic infections (Pfaller and Diekema, 2007; Calderone and Clancy, 2011; Ganguly and Mitchell, 2011). This opportunistic pathogen is a part of the

commensal human microflora that colonizes various parts of the human body asymptomatically, with the host immune system regulating its proliferation (Williams *et al.*, 2013). *C. albicans*, on the other hand, can transform into a pathogen in the presence of immune suppression or any change to the host, causing a variety of infections (Finkel and Mitchell, 2011; Mathe and Van Dijck, 2013).

C. albicans, in fact, is one of the most often discovered agents in nosocomial infections, capable of entering practically every site of the human host, from deep tissues and organs to superficial areas (Perlroth *et al.*, 2007). More importantly, C. albicans is the third most often isolated bloodstream infection in hospitalized patients and has a 50% mortality risk because to its exceptional adhesion to catheters and other indwelling medical implants (Wisplinghoff *et al.*, 2004; Tournu and Van Dijck, 2012; Mathe and Van Dijck, 2013). The primary factor in *C. albicans'* ability to change morphologically between yeast and hyphal forms, which is essential to its pathogenicity and biofilm development, is its capacity to go from being a commensal to a pathogen. (Kruppa and Jabra-Rizk, 2004; Chauvel *et al.*, 2012). In fact, biofilm formation on host or abiotic surfaces is linked to the bulk of disorders produced by this infection (Nett and Andes, 2006; Mathe and Van Dijck, 2013).

Embedded in an extracellular polysaccharide matrix, surface-associated microbial populations form 3D communities known as biofilms, which are thought to provide a protective framework for the cells that make up the biofilms (O'Toole *et al.*, 2000; Keele *et al.*, 2001; Costerton *et al.*, 2005; Ghannoum *et al.*, 2013). As a result, bacteria in biofilms have a stable habitat and also can survive extremely high antibiotic doses. Biofilms have a significant impact on public health because cells discharged from them can migrate into the circulation and produce systemic illnesses with high fatality rates (Finkel and Mitchell, 2011). Importantly, the rise in drug resistance has fueled research into the processes underlying biofilm-associated illnesses' increased resistance to antimicrobial therapy (Tournu and Van Dijck, 2012).

Biofilm production is associated to the majority *of C. albicans* infections (Kruppa and Jabra-Rizk, 2004; Nett and Andes, 2006; Finkel and Mitchell, 2011; Tournu and Van Dijck, 2012; Mathe and Van Dijck, 2013). Biofilm growth comprises a series of steps over the period of 24– 48 hours, according to in vitro experiments (Ricicova *et al.*, 2010; Mathe and Van Dijck, 2013).

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The initial stage (adherence step) involves adhering single fungal yeast cells to the substrate, laying the groundwork for a basal yeast cell layer (Nett and Andes, 2006; Finkel and Mitchell, 2011; Nobile *et al*, 2012; Tournu and Van Dijck, 2012). Cells create elongated projections that continue to proliferate into filamentous hyphal forms after a phase of cell proliferation across the surface and filamentation (initiation step). The formation of hyphae signifies the beginning of biofilm formation, which is followed by the deposition of an extracellular polysaccharide matrix as the biofilm grows (maturation stage). In the last stage, non-adherent yeast cells are freed from the biofilm and permitted to colonize various surfaces (dispersal step). Released biofilm-associated cells can cause new biofilms to form or spread into host tissues, making them associated to candidemia and widespread invasive disease (Uppuluri *et al.*, 2010; Tournu and Van Dijck, 2012).

C. albicans capacity to cling to host surfaces, like that of other microbial pathogens, is required for effective colonization and infection persistence. Critical elements of the host's defense against Candida overgrowth include the physical flushing of loosely attached Candida albicans and the sloughing off of epithelial cells from mucosal surfaces. As a result, the capacity to get around these elimination processes can be considered a virulence trait. Importantly, *C. albicans* adherence to host tissues is a need for infection. The production of a class of cell-wall adhesins known as agglutinin-like sequences (ALS), which have been demonstrated to be differently regulated in biofilm-grown cells (Hoyer, 2001; Lewis, and Williams, 2011), aids *C. albicans* attachment to receptors on host tissues.

CHAPTER THREE

METHODOLOGY

3.1 STUDY AREA

The samples were collected from male and female toilet in hostels of a tertiary institution in Ogun state, Nigeria. The rooms had 4 occupants on average using the same toilet.

3.2 SAMPLE COLLECTION

A total of 92 swab samples were aseptically obtained from volunteering students' toilet in an institution in Ogun state, Nigeria. The sample collection was done in the early hours of the day. Sample were collected from the toilet using swab stick preserved in normal saline to keep the pathogens alive. 2ml of normal saline was dispensed into each swab bottle. The swab stick was used to swab the toilet bowl area and then inserted back into the bottle containing normal saline. The swab stick was sealed labeled, and transported to the laboratory under aseptic condition.

3.3 CULTURE MEDIA

Normal saline was prepared following the manufacturer's instruction using Saline tablets (Oxoid Limited, England)

1. Sabouraud dextrose agar: a selective medium for the culture of fungi and is largely employed for the isolation of dermatophytes, yeasts, and different pathogenic and non-pathogenic fungi. Low pH (5.6) is used in the conventional formula to stop the development of

bacteria. However, contemporary versions frequently include antibiotics to the acid medium to inhibit bacteria. The growth of (osmotically stable) fungus is also facilitated by the high glucose concentration, whereas most bacteria cannot handle the high sugar concentration.

2. CHROMAGAR[™]: The recommendation is to quickly isolate and identify Candida species from mixed cultures in clinical and non-clinical samples using CHROMagarTM Candida or HiCrome Candida differential agar. According to Rousselle et al., incorporation of chromogenic or fluorogenic hexosaminidase substrates into the growth medium aids in the direct identification of Candida albicans isolates after primary isolation. Perry and Miller reported that Candida albicans produces the enzyme b-N-acetyl-galactosaminidase. Using the selective and differentiating medium known as HiCrome Candida Differential Agar, yeasts from mixed cultures may be quickly isolated, and Candida species can be differentiated namely *C. albicans, C. krusei, C. tropicalis* and *C. glabrata* based on colony morphology and coloring. Results are achieved on these mediums in 48 hours, and they are helpful for the quick and speculative identification of common yeasts in mycology and clinical microbiology laboratories.

Yeast extract and Peptone Special both provide nitrogenous, carbonaceous, and other vital growth ingredients. The medium is well-buffering by phosphate. Chloramphenicol reduces the bacterial flora that is present. C. tropicalis appears as elevated colonies that are blue to metallic blue in hue, while C. albicans appears as smooth colonies that are light green in color. *C. glabrata* colonies appear as cream to white smooth colonies, while *C. krusei* appear as purple fuzzy colonies.

3.4 ISOLATION OF CANDIDA

Candida spp were extracted from the swab stick following the following methods:

- The swab bottle containing the swab stick and normal saline was first vortexed for 1 minute.
- A 3000 rpm vortex was used to spin the urine sample for one minute after which the supernatant was decanted and the sediment was reconstitute with 1 ml normal saline.
- Serial dilution is done from 10-1 to 10-4. 1ml of the normal saline from the swab stick bottle was inoculated into a test tube containing 9ml of sterile normal saline. This was done for the test tubes labeled 10-1 to 10-4.

- Sample was inoculated into plates containing sabouraud dextrose agar (SDA) and incubated at 37°C for 72 h.
- To prepare SDA medium, 3g of SDA power was diluted in 46ml of distilled water. It was autoclaved for 15 minutes at 15 pounds of pressure (121°C) to 45–50 °C. Chloramphenicol was added to the medium and then mixed together to allow the growth of *Candida* spp. The medium was then poured into the labeled petri dish after cooling.
- After 72h, plates that had growths identified as *candida* was separated.
- Isolates from positive plates were picked using inoculating loop and inoculated into Eppendorf tubes containing SDA broth and 20% sterile glycerol to store.

Resuscitation of Isolate

0.38g of SDA was measured using weighing balance and then added into 10.4ml of distilled water in an Eppendorf tube. 500µl was pipetted into the Eppendorf tube and it was autoclaved for 15 minutes. 100µl of the isolates was inoculated into each Eppendorf tubes using inoculating loop. Incubation was done at 30°c.

3.5 Assay for identification of Candida:

Growth at 45°C

Growth at 45 °C has been regarded as a helpful test for separating Candida dubliniensis (no growth) from Candida albicans (growth). The 55 positive samples for growth on SDA were subjected to this assay. All isolates were incubated at 45°C, and growth was assessed daily for 10 days.

Germ tube test

It serves as a preliminary test to distinguish candida albicans from other yeast. Reynolds and Braude published the first study on germ tube development in 1956. The germ tubes that emerge when candida is cultured on human or sheep serum at 37° C for three hours can be seen as filamentous outgrowths extending from yeast cells on wet KOH films. This is a rapid test for the presumptive identification of *C. albicans*.

Procedure for identification of candida

- Three drops of fresh human serum were dispensed into labeled test tubes.
- Using a sterile inoculating loop, a colony of yeasts was transferred into the serum in the labeled test tubes.
- The colony was emulsified in the serum.
- The set up was incubated at 37°C for about 3 h.
- A drop of the suspension taken from the test tube after incubation was placed on a clean dry slide.
- The suspension was covered with a clean cover glass.
- The slide was examined under a microscope for germ tubes on the yeasts.
- A germ tube is a tube-like outgrowth that arises from the yeast cell

3.6 BIOCHEMICAL TESTS.

Chromogenic agar culture

For the quick isolation and identification of Candida species from mixed cultures in clinical and non-clinical samples, CHROMagar Candida or HiCrome Candida differential agar is advised. For 48 hours, each isolate was grown on SDA at 30°C. After this, they were seeded on CHROMAgarTM *Candida* and incubated at 30°C for 48 h. Utilizing the CHROMAgarTM, C. albicans, C. dubliniensis, C. tropicalis, and C. krusei colonies can be identified through selective yeast isolation by morphology and color reaction. The strains were identified according to the manufacturer's instructions, which defines: In accordance with the manufacturer's instructions, the following strains were identified:

- I. Green colonies indicative of *c. albicans* or *C. dubliniensis*,
- II. *C. tropicalis* as steel blue colonies,
- III. C. krusei colonies as showing rose color and rough aspect,
- IV. Other species as developing colonies from white to rose.

CHAPTER FOUR

RESULTS

A total of 92 samples were analyzed in this study, out of which 51 (55.4%) isolates were identified on Sabouraud Dextrose Agar (SDA) (Titan Biotech Limited) showing white colored, smooth colonies. 28 (54.9%) of the isolates were male and 23 (45.1%) were female (table 4.0) (table 4.1).

For some positive plates that had more than one positive isolates, the positive isolates were picked and inoculated into different Eppendorf tubes, labeled with similar codes. Three tests were done to characterize the different Candida species. The first test was growth utilizing the positive isolates found on SDA at 45 oC. Growth at 45 °C has been regarded as a helpful test for separating Candida dubliniensis (absence of growth) from Candida albicans (growth). Total number of Female isolates positive 41 (74.5%) (table 4.0) and 14 (25.5%) positive male isolates (table 4.1). Germ tube test was then carried out for the positive isolates. Candida albicans forms germ tubes can be distinguished from other yeasts using the Germ Tube Test. Total number of isolates was 9 (16.4%) from the female samples collected (table 4.0). All male isolates were negative for germ tube test. The 55 isolates from growth at 45°c were then inoculated on CHROMAgar[™] (Kanto Chemical Co., Inc group). The CHROMAgarTM enables for the selective isolation of yeast and the detection of C. albicans colonies, C. dubliniensis, C. tropicalis and C. krusei by morphology and color reaction. Total number of isolates positive from the female samples were 30 (54.5%) (plate 4.0). Male positive isolates, 7 (12.73%) (table 4.1). On CHROMAgarTM, identification of isolates strain for females isolates, 14 (25.5%) isolates appeared green, 13 (23.6%) isolates appeared steel blue, 2 (3.6%) isolates appeared as other color (table 4.0).

The 14 isolates that appeared green are positive for *Candida albicans*. 13 that appeared steel blue are positive for *Candida tropicalis*. Positive isolates for male, were 7 (12.73%), 3 (5.5%) appeared steel blue, 3 (5.5%) appeared as other colors, 1 (1.8%) appeared as a mixed culture. The 3 that appeared steel blue are positive for *Candida tropicalis* (table 4.1).

Table 4.0: Candida *spp*. identification using the germ-tube test (GT), a culture in CHROMAgarTM, and growth at 45 °C in female hostel

Strain	Growth at 45°c	Germ tube	СHROMAgar™	Presumptive identification
F1	+		-	
F2		+	GREEN	C. albicans
F3	+		GREEN	C. albicans
F4	+		BLUE	C. tropicalis
F5	+			
F6	+	+	GREEN	C. albicans
F7	+		GREEN	C. albicans
F8	+			
F9		+	GREEN	C. albicans
F10	+		GREEN	C. albicans
F11	+		BLUE	C. tropicalis
F12	+		GREEN	C. albicans
F13	+		GREEN	C. albicans
F14	+		BLUE	C. tropicalis
F15	+		GREEN	C. albicans
F16	+		BLUE	C. tropicalis
F17		+	BLUE	C. tropicalis
F18	+		YELLOW	

F19	+			
F20	+		BLUE	C. tropicalis
F21	+		GREEN	C. albicans
F22	+			
F23		+	GREEN	C. albicans
F24	+			
F25	+		GREEN	C. albicans
F26		+	GREEN	C. albicans
F27	+			
F28	+		YELLOW	
F29	+			
F30			GREEN	C. albicans
F31	+			
F32		+	BLUE	C. tropicalis
F33	+			
F34			BLUE	C. tropicalis
F35	+			
F36			BLUE	C. tropicalis
F37	+		BLUE	C. tropicalis
F38		+		
F39		+	BLUE	C. tropicalis
F40	+		BLUE	C. tropicalis
F41	+		BLUE	C. tropicalis

Strain	Growth at 45°C Germ tube	ChromAgar TM	Presumptive identification
M1	+	YELLOW	
M2	+		
M3	+	YELLOW	
M4	+	MIXED	
M5	+		
M6	+		
M7	+		
M8	+		
M9	+	BLUE	C. tropicalis
M10	+	BLUE	C. tropicalis
M11	+		
M12	+	BLUE	C. tropicalis
M13	+		
M14	+	YELLOW	

Table 4.1: Candida *spp*. identification using the germ-tube test (GT), a culture in CHROMAgarTM, and growth at 45 °C in male hostel.

DISCUSSION

The relative incidence of the common *Candida* species has been documented in recent epidemiological studies of candidiasis, and *C. albicans* the species that is still most frequently isolated globally. (Silva *et al.*, 2012). In 20–50% of healthy, asymptomatic women, the lower vaginal tract flora contains Candida species (McClelland *et al.*, 2009; Akah *et al.*, 2010). C. albicans is the most common strain of candida in this study among females (25.5%). According to (Pfaller and Diekema., 2012), the most common fungus in humans, *Candida albicans*, can cause everything from minor mucosal infections to fatal systemic infections.

Research so far has shown that the percentage of *Candida albicans* that affects the urinary tract is more prevalent than any other *candida spp* in existence. The presence of ideal conditions and a supply of nutrients required for growth are responsible for the widespread presence of *candida*. Additionally, microbial growth is favored by the female genitals' moist environment as fungi and bacteria thrive in moist environment (Nicolle, 2005). The fimbrial adhesions expressed by uropathogenic organisms allow them to bind to the glycolipids and glycoproteins on the epithelial surface. Thus, bacteria can survive the transit of urine in the urinary tract and continue to grow there. The percentage of *c. albicans* recorded in this study is (25.5%). Compared to a study conducted at Milad hospital, Tehran, Iran, 50 patients who were hospitalized to Milad ICUs between April and September 2013 provided Candida isolates. 28.3% were C. albicans. The prevalence of C. albicans was higher (Alimehr *et al.*, 2015). In contrast with another research at Nasarawa State University, Keffi, a north central state in Nigeria, a total of 56 (38.89%) *Candida* species were isolated from 144 samples in the study of candiduria among students. (12.5%) of unmarried women were positive for *C. albicans* (Tsaku *et al.*, 2019). A study was conducted Ihiala community, Ihiala Local Government Area, Anambra State,

Southeastern Nigeria. 734 women were selected, the results revealed that 150 (20.4%) tested positive for *C. albicans*, demonstrating the high frequency of the strain in the area. The significant frequency of C. albicans, reported by this study could be a result of the ability of the pathogen as a frequent colonizer and responsible for most cases of vulvovaginitis (Donbraye *et al.*, 2010; Alli *et al.*, 2011). The result is higher than some studies (Konje *et al.*, 1991; Cronje *et al.*, 1994; Di Bartolomeo *et al.*, 2002; Nwokedi *et al.*, 2003; Choudhry *et al.*, 2010) who reported 2.0%, 2.20%, 12.0%, 2.6%, and 17.8% respectively. However, this is lower than other studies (Khan, Amir, 2009), (Adeoye 2007; Muvunyi *et al.*, 2010) who reported the prevalence rate of 28.0%, 52.5% and 33.6% respectively. It has previously been observed that high incidence of *C. albicans* could be associated with severe immunosuppression or illness, and sexual activities of a woman (Horn, Neofytos, 2019). Some studies noted that *Candida* species are part of the lower genital tract flora in 20-50% of healthy asymptomatic women and may spread due to sexual activities or immunosuppression (McClelland *et al.*, 2009; Akah *et al.*, 2010).

A two-year research conducted at the Dr. Shariati Hospital's Central Laboratory, (April 2006-April 2008), findings revealed that out of the 4136 (100%) patients engaged, 1557 (37.6%) were men and 2579 (62.4%) were women. 283 (6.8%) of the 4136 instances of candiduria overall were caused by *Candida albicans* (Behzadi and Behzadi, 2008). In an experiment carried out to identify Candida on Chromagar by a university in Niger state, the species with the highest frequency (64.7%) was C. albicans (Yang et al., 2003; Marinho et al., 2010) which conforms with the rate of prevalence gotten in this study. Therefore, Candida albicans is the most prevalent strain of Candida specie that causes Urinary tract disease. The Candida-non-albicans group's most common pathogenic yeast species has been identified as Candida tropicalis. (Kothavade et al., 2010). In neutropenic patients, such as those with acute leukemia or those who have had bone marrow transplantation, C. tropicalis has increasingly been found to be the most common cause of invasive candidiasis (Wingard et al., 1979; Sandford et al., 1980;). C. tropicalis displayed a modest level of fluconazole resistance in a significant monitoring investigation by (Pfaller et al., 2009). This suggests that exposure to higher fluconazole concentrations may increase the development of fluconazole resistance through the activation of efflux transporters (Barchiesi et al., 2000). In the female samples, C. tropicalis (blue) accounted

for 13 (23.6%) out of 30 (54.5%) positive isolates on Chromagar. For the male samples, *C. tropicalis* (blue) was 3 (5.5%).

UTIs are uncommon in adult males under the age of 50, but they become more common beyond that. In studies conducted at Colombian intensive care units between 2010 and 2013, Candida isolates made up 94.5% of the 2680 fungal isolates considered, with comparable percentages for Candida species that are not Candida albicans (48.3% and 51.7%, respectively). The latter included Candida tropicalis (38.6%) and Candida parapsilosis (28.5%). According to several studies (Sellami et al., 2011, Chakrabarti et al., 2014, Megri et al., 2020), Candida tropical is the main cause of candidemia in India, Algeria, and Tunisia and ranks second to third in South Asian nations (Xiao et al., 2018; Liu et al., 2019). *C. tropicalis* is among the most azole-tolerant *Candida* species (Rueda *et al.*, 2017; Arthington-Skaggs *et al.*, 2002). Compared to the prevalence found in this study, the prevalence of Candida tropicalis in the research is higher (38.8%). This is due to the sample being taken from male students under the age of 30.

High prevalence of *Candida tropicalis* and *Candida albicans* in this study is due to the excessive intake of antibiotics among students of the institution. *Candida* spp survive in the urinary tract due to their resistance to antibiotics. Biofilm growth is a characteristic of several *Candida albicans* disease states. Because biofilm-associated organisms have a drastically decreased resistance to antifungal medication, these infections have a significant negative influence on public health (Nett and Andes, 2006). The development of medication tolerance, which could enable the fungus to acquire persistent genetic modifications leading to antifungal resistance and which may be associated with azole therapeutic failure and mortality, is another issue of concern (Rosenberg *et al.*, 2018; Berman and Krysan, 2020).

CHAPTER FIVE

5.1 CONCLUSIONS

This research shows the occurrence of *Candida spp*. in the student's hostels. It was also noted that *Candida albicans* was the species that was most prevalent. More females than males have the prevalence of *Candida spp*. Urinary tract infection can be prevented by maintaining good personal hygiene, proper treatment of infection on first occurrence, avoid wearing of damp clothes, wiping of the anus from the vaginal side to the anal side and not the other way, use of probiotics to increase the number of good bacteria in the urinary tract.

5.2 RECOMMENDATIONS

- University officials should ensure that hostels toilet are properly taken care of.
- Students who showed any signs of UTI should visit the Medical Centre for proper care.

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APPENDIX 1

REAGENTS AND EQUIPMENTS USED

REAGENTS: Sabouraud dextrose agar (Titan Biotech Ltd, India), Sabouraud dextrose agar broth, glycerol, chloramphenicol, CHROMAgarTM, blood serum, distilled water, normal saline (Oxoid, England).

EQUIPMENTS USED: Petri-dish, Beakers, Flasks, Eppendorf tubes, Micro pipette, Test tube, thin foil, Weighing balance, Bunsen burner, incubator, centrifuge, microscope, glass slides, cover slide inoculating loop. Swab bottles and swab sticks.

APPENDIX 2

ABBREVATIONS

SDA- Sabouraud dextrose agar

UTI- Urinary tract infection

GT- Germ tube test

UPC- Uropathogenic Candida

C. albicans- Candida albicans

C. tropicalis - Candida tropicalis

C krusie – Candida krusie

C. glabrata- Candida glabrata