OUTCOME OF TREATMENT OF VULVOVAGINAL CANDIDIASIS IN AMINU KANO TEACHING HOSPITAL (AKTH); A RANDOMIZED CONTROLLED TRIAL OF TOPICAL CLOTRIMAZOLE VERSUS ORAL FLUCONAZOLE

BY

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Ethical Clearance
DECLARATION

I hereby declare that this work is the product of my own research effort under the supervision of Drs. Zakari Muhammad and Hadiza Galadanci and has not been presented and will not be presented elsewhere for the award of a degree or certificate. All sources have been duly acknowledged.

…………………………………..

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CERTIFICATION

This is to certify that the work of this dissertation and its subsequent preparation was carried out by Dr Emmanuel Ajuluchukwu Ugwa under our supervision.

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ABBREVIATIONS

**AKTH:** Aminu Kano Teaching Hospital

**E.G:** Example

**FMOH:** Federal Ministry of Health

**RCT:** Randomized Controlled Trial

**UNISAID:** United States Agency for International Development

**VVC:** Vulvovaginal Candidiasis
ABSTRACT

**Background:** Despite therapeutic advances, vulvovaginal candidiasis remains a common problem worldwide, affecting all strata of society. Vulvovaginal candidiasis (VVC) is very common and a frequent cause of vaginosis. It has a high prevalence. A randomized controlled trial of topical clotrimazole versus oral fluconazole for treatment of vulvovaginal candidiasis was done at Aminu Kano Teaching Hospital between 30th December, 2011 and 23rd February, 2012. Ethical approval for the research was obtained from the ethical committee of Aminu Kano Teaching Hospital

**Objective:** To determine the more effective anti-candidal agent between topical clotrimazole and oral fluconazole in Aminu Kano Teaching Hospital (AKTH).

**Method:** This was a prospective study of 300 patients who presented at the gynaecologic and general outpatients clinics of AKTH with clinical and laboratory evidence of vulvovaginal candidiasis who fulfilled the inclusion criteria. A subset of the study population (group A) comprising 150 subjects received topical clotrimazole 200mg intravaginally at bedtime for 3 days. Another subset (group B) comprising 150 subjects received fluconazole capsule 150mg statim. Research structured questionnaires were administered to all the 300 subjects before and after treatment. These gave various sociodemographic and clinical information. At the test-of-cure visit, clinical history and vaginal examination were carried out. Symptoms/signs numerical score after treatment was compared to the score at entry. The data obtained was analyzed using SPSS version 16.0 statistical software.
Statistical significance of differences between means was determined using ANOVA. Significant association between sociodemographic factors and vulvovaginal candidiasis were tested using chi-square test and p<0.05 was considered significant.

**Results:** *Candida albicans* was responsible for 84.5% of positive high vaginal swabs. Vulvovaginal candidiasis was commonest in those aged 26-35 years (53%). The mean age was 27.7±7.8 years. There was no statistically significant difference in the mean age of the clotrimazole and fluconazole groups. Those of para 1-2 had the highest prevalence (41.9%) compared to others. There was no statistically significant difference in the mean parities of women in the two groups. Vulvovaginal candidiasis was more prevalent among those who were married (80%) than those who were unmarried (20%) in the two groups. Cheesy vaginal discharge was the commonest presentation in patients with vulvovaginal candidiasis occurring in 47.4% of cases. Most of the patients presented at 8-14 days (38.9%) after the onset of symptoms. The mean duration of symptoms before presentation was 13.3±7.4 days. There was no statistically significant difference in the mean duration of symptoms before presentation between the clotrimazole and fluconazole groups. About 42% of the patient believed that they contracted vulvovaginal candidiasis from the toilet. Douching was the most common risk factor responsible for vulvovaginal candidiasis prevalence occurring in 42.6% of the patients. The mean symptoms/signs numerical score at entry was 6±3. There was no difference in scores between patients in the clotrimazole and fluconazole group. One week after treatment, 85% of patients in the fluconazole group and 83.3% in the clotrimazole
group were satisfied with their treatment. This difference was not statistically significant (p=0.890). Three weeks after treatment, 80% of the fluconazole group and 77.7% of the clotrimazole group were satisfied with their treatment. The difference was not statistically significant (p=0.90). Clinical and mycological cure rates for the fluconazole and clotrimazole groups were 80%, 72.1% and 76.2%, 70% respectively. The differences were not statistically significant (p=0.90 and 0.890 respectively).

**Conclusion:** The overall result of this study rejects the hypothesis that topical clotrimazole is more effective than oral fluconazole in treatment of vulvovaginal candidiasis. There was no difference statistically between topical clotrimazole and oral fluconazole in the treatment of vulvovaginal candidiasis. Therefore treatment of VVC should be individualized based on a comparison of convenience, potential side effects, and costs.

**Keywords:** Outcome, Treatment, Vulvovaginal Candidiasis, Teaching Hospital, Randomized Controlled Trial, Topical Clotrimazole, Oral Fluconazole
CHAPTER ONE

1.0 Introduction

Despite therapeutic advances, vulvovaginal candidiasis remains a common problem worldwide, affecting all strata of society. The absence of rapid, simple, and inexpensive diagnostic tests continues to result in both overdiagnosis and underdiagnosis of vulvovaginal candidiasis. Although commonly caused by *Candida albicans*, non-albicans species and immunosuppression have led to development of recurrent diseases some of which are nonresponsive to conventional antifungal regimes.

Complete information on the incidence of vulvovaginal candidiasis is lacking, since the disease is not a reportable entity and data collection is in jeopardy by inaccuracies of diagnosis and the use of non-representative study populations. The infection is caused by *candida* spp and affects 70–75% of women at least once during their lives, most frequently young women of childbearing age. Research has shown that 40–50% of women will experience a recurrence.\(^1\) Another study showed that 5–8% of adult women have recurrent vulvovaginal candidiasis, defined as four or more episodes every year.\(^2\) Almost 30% of the women with symptoms of vulvovaginitis had yeast isolated, confirming the diagnosis of vulvovaginal candidiasis.\(^3\) Other authors indicate that vulvovaginal candidiasis is responsible for 15–30% of vulvovaginal symptoms.\(^4,5\) Unfortunately, the availability of over-the-
counter antimycotics will further limit the ability to measure asymptomatic candida carriage and vulvovaginal candidiasis. Point-prevalence studies indicate that *candida* spp can be isolated from the vagina of about 20% (range 10–80%) of asymptomatic healthy women.⁶⁻⁸ Higher cumulative incidence of candida colonisation is reported.⁹ The incidence of vulvovaginal candidiasis caused by non-albicans strains is thought to be increasing because of single-dose treatment, low-dosage azole maintenance regimens, and the use of over-the-counter antimycotics.¹⁰ The cost of diagnosis, treatment and maltreatment, effect on the quality of life and sexual disharmony call for commitment to prevention and correct treatment at all levels.

Clinically, candidiasis is broadly divided into three groups as cutaneous, superficial and systemic candidiasis. Superficial (mucosal) candidiasis consists of chronic mucocutaneous candidiasis, oral candidiasis (oral thrush) and vulvo-vaginal candidiasis or vaginal thrush.¹¹ Vulvovaginal candidiasis or vaginal thrush occurs in the epithelial surfaces of the vulva, vagina and cervix of the female. Candida burrows into the cells lining the vagina and the epithelial cells of the vulva. The infected superficial cells are shed into the vagina causing thick discharge. Vulvovaginal candidiasis is commonly associated with pregnancy, immunosuppression, use of steroids, diabetes mellitus, vaginal douching, increased oestrogen, high doses of oral contraceptive pills, underlying dermatosis, use of broad spectrum antibiotics, dietary factors and poor hygiene.¹²,¹³ However, the presence of predisposing factors does not necessarily define vulvovaginal candidiasis, but culture of samples from the vaginal content followed by identification of the micro-organism
Systemic candidiasis is defined as spread of the candida organism through the bloodstream and it is characterized by a positive blood culture. It usually occurs in immunosuppressive patients and may involve the heart valve, liver, lungs and kidneys. Some workers have suggested that since clinical diagnosis has a sensitivity of 85-88% it may be safe and cost effective to restrict vaginal microscopy to a subgroup of women presenting with vaginal discharge, especially for complicated cases as a key to rational selection of antifungal treatment. Microscopy may still remain valuable but it is important to avoid overtreatment based on microscopy alone because positive culture of as much as 40.78% for *candida species* and 38.1% for *candida albican* has been isolated from high vaginal swabs specimens of asymptomatic females. In this study, intravaginal clotrimazole 200mg daily for three days and oral fluconazole 150mg statim were used for treatment of vulvovaginal candidiasis.

1.1. Justification for the research

Despite therapeutic advances, vulvovaginal candidiasis remains a common problem worldwide, affecting all strata of society. There is evidence that the incidence of vulvovaginal candidiasis is increasing. Topical clotrimazole or oral fluconazole are commonly used drugs for treatment of vulvovaginal candidiasis by clinicians in AKTH but no study has been done to determine their comparative effectiveness and patients’ compliance. This has informed the choice of the research. The outcome of the research will therefore form the basis for recommending the choice of treatment for vulvovaginal candidiasis in AKTH.
1.2. Aims

To determine the more effective anti-candidal agent between topical clotrimazole and oral fluconazole in Aminu Kano Teaching Hospital (AKTH).

1.3 Specific Objectives

1. To determine the demographic and social characteristics of women with vulvovaginal candidiasis in AKTH.
2. To determine the outcome of treatment of vulvovaginal candidiasis with topical clotrimazole in AKTH
3. To determine the outcome of treatment of vulvovaginal candidiasis with oral fluconazole in AKTH
4. To compare the outcome of treatment of vulvovaginal candidiasis in AKTH with topical clotrimazole and oral fluconazole.
CHAPTER TWO

2.0 Literature Review

2.1 Epidemiology

Vulvovaginal candidiasis (VVC) is very common and a frequent cause of vaginosis. It has a high prevalence. Various studies have reported the prevalence of vulvovaginal candidiasis as 25%\textsuperscript{19}, 24%\textsuperscript{20.21} and 18.5%\textsuperscript{22}. Other authors indicate that vulvovaginal candidiasis is responsible for 15–30% of vulvovaginal symptoms\textsuperscript{4,5}. Parveen et al., Maccato and Kaufman reported a high rate among pregnant women\textsuperscript{23,24} and Okonofua et al., reported a high carriage of *Candida albicans* in Nigeria infertile women compared with controls\textsuperscript{25}. It is estimated that 72% of women will have at least one episode of vulvovaginal candidiasis in their life, and recurrence is not unusual\textsuperscript{26}. By the time women reach their mid-20’s, half of them will have had one episode of vulvovaginal candidiasis, and up to 25% of these women will suffer recurrent vulvovaginal candidiasis (defined as four or more episodes a year)\textsuperscript{27}.

2.2 Aetiology and predisposing factors
Vulvovaginal candidiasis is commonly caused by *Candida albicans*, but some cases of non-albican candidiasis exist especially in recurrent disease. Although vulvovaginal candidiasis is monomicrobial, causation is multifactorial. Factors that predispose to vaginal colonisation can differ from those that facilitate transformation from asymptomatic colonisation to symptomatic vaginitis.

Report shows familial susceptibility to vulvovaginal candidiasis and increased prevalence in African-American women\textsuperscript{28} and people with blood group ABO-Lewis non-secretor phenotype all suggest that there could be genetic factors that predispose individuals to colonisation or vaginitis.\textsuperscript{29} Recently, in-vivo polymorphism studies involving mannose-binding lectin and experimental vaginitis in inbred and outbred mice further suggest that some individuals could have a genetic susceptibility to *candida* colonisation or vaginitis.\textsuperscript{30}

A higher prevalence of vaginal colonisation and symptomatic vaginitis is more often seen in pregnant women than in those who are not pregnant\textsuperscript{31,32} and recurrences are more common and therapeutic response is reduced compared with women who are not pregnant.\textsuperscript{36} High concentrations of reproductive hormones which increase the glycogen content in the vaginal tissue have been reported to provide a carbon source for candida organisms.\textsuperscript{33,34} Oestrogen also enhances adherence of yeast to vaginal epithelial cells. A cytosol receptor or binding system for female reproductive hormones has been documented in *C. albicans*, resulting in enhanced mycelial formation.\textsuperscript{35}
Many small, poorly controlled studies of the effect of contraceptives on predisposition to vulvovaginal candidiasis have produced conflicting data. Some studies indicate increased vaginal colonisation with candida after the use of oral contraceptives with high oestrogen content.36-38 Contradictory results from studies of women using low-oestrogen oral contraceptives have been reported.39 Nevertheless, most investigators believe that oral contraceptives predispose women to recurrent vulvovaginal candidiasis.

Increased carriage of yeast is reported in users of intrauterine contraceptive devices, contraceptive sponges, diaphragms, and condoms, with or without spermicides.40,41 However, an extensive study in college students did not show an increase in the risk of symptomatic vulvovaginal candidiasis in users of oral contraceptives, diaphragms, condoms, or spermicides.37

Vaginal colonisation with candida is more frequent in diabetic women than in non-diabetics. Women with type 2 diabetes are more prone to colonisation with *candida glabrata*.42,43 Although uncontrolled diabetes predisposes to symptomatic vaginitis, the prevalence of vulvovaginal candidiasis is not increased in individuals with well-controlled diabetes.44

Symptomatic vulvovaginal candidiasis frequently follows use of vaginal or systemic antibiotics.45,46 All antimicrobials seem to exert this effect. Estimates of how
frequently vulvovaginal candidiasis follows antibiotic use range from 28% to 33%.\textsuperscript{47,48} Vaginal colonisation rate increases from about 10% to 30%.\textsuperscript{49} Antibiotics are thought to predispose women to vulvovaginal candidiasis by eliminating the protective bacterial flora, thus allowing candida overgrowth in the gastrointestinal tract, vagina, or both.\textsuperscript{50} In particular, \textit{lactobacillus spp} could provide colonisation resistance and prevent germination, maintaining low numbers of yeast. Auger and Joly\textsuperscript{51} found low numbers of lactobacilli in vaginal cultures obtained from women with symptomatic vulvovaginal candidiasis. Lactobacilli and yeast cells can interact in several ways, including competition for nutrients, stearic interference with candida adherence, and elaboration of hydrogen peroxide and inhibitory bacteriocins by lactobacilli. Studying adult mice, Pultz and colleagues\textsuperscript{52} reported that antibiotics that inhibit intestinal anaerobes promote \textit{candida glabrata} gut colonisation. Some studies have failed to show a link between the occurrence of vulvovaginal candidiasis and antibiotic treatment.\textsuperscript{53} Most women who receive antibiotics do not develop symptomatic vulvovaginal candidiasis; moreover, most women with acute vulvovaginal candidiasis have not been recent recipients of antibiotics. Only those women who are already colonised with candida are at risk of vaginitis following antimicrobial treatment.\textsuperscript{54}

The role of sexual behaviour in causing symptomatic, often recurrent, vulvovaginal candidiasis has been underestimated.\textsuperscript{39,55} Although women who are not sexually active often develop vulvovaginal candidiasis, the incidence of the disease increases dramatically in the second decade of life, corresponding with the onset of sexual
activity. Occurrence peaks in the third decade of life, declining in women older than 40 years, until the permissive effect of oestrogen replacement therapy becomes apparent. There is some evidence to suggest that the frequency/periodicity of sexual intercourse is associated with acute vaginitis.\textsuperscript{38,39}

Douching has been shown to be a risk factor for candida vulvovaginitis for some women, and for others, there was no relationship found.\textsuperscript{56,57} The douche liquid irrigates the vagina and washes away any material there, such as blood, mucus, and microorganisms. Current thinking posits that the douche process clears away the hydrogen peroxide producing lactobacillus that prevent overgrowth of candida, thus leaving women more open to candida vulvovaginitis.

In spite of some reports, there is no evidence to suggest that female hygiene habits are risk factors for vulvovaginal candidiasis.\textsuperscript{37} The use of well-ventilated clothing and cotton underwear could be of value in preventing infection. However, no increased risk for vulvovaginal candidiasis has been found among wearers of tight clothing or non-cotton underwear.\textsuperscript{37}

Although the gut could well be the initial source of vaginal colonisation by candida organisms, there is some controversy with regard to the role of the intestinal tract as a source of reinfection in women with recurrent vulvovaginal candidiasis. Candida isolated from rectal cultures of women with recurrent vulvovaginal candidiasis were found to be identical to candida isolated from vaginal cultures suggesting that there is
a persistent intestinal reservoir of yeast. Re-inoculation of the vagina might occur from the persistent rectal focus following apparent eradication of vaginal yeast by topical treatments.

Chemical contact, atopy, local allergy, or hypersensitivity reactions could alter the vaginal milieu and facilitate transformation from asymptomatic colonisation to symptomatic vaginitis.58

**2.3 Microbiology**

Between 85% and 95% of yeast strains isolated from the vagina belong to the species *candida albicans*59-61 while the remainder comprise of non-albicans *candida spp*, the most common of which is *candida glabrata*. In many parts of the world, non-albicans isolates, notably *candida glabrata*, affect 10–20% of women.62-64 Vaginitis is infrequently caused by *candida parapsilosis*, *candida tropicalis*, and *candida krusei*, although most species of candida have been associated with the condition.65,66 Vaginitis induced by non-albicans species is clinically indistinguishable from that caused by *candida albicans*; moreover, such species are often more resistant to treatment.59,67-69 Non-albicans *candida spp*, especially *candida glabrata*, often cause recurrent vulvovaginal candidiasis. Germinated yeast, which has produced mycelia (hyphae), are found most commonly in symptomatic vaginitis. Colonisation of the vagina requires yeast adherence to vaginal epithelial cells. *C albicans* adheres in significantly higher numbers to such cells than do non-albicans species.70 Factors that enhance or facilitate germination promote symptomatic vaginitis, whereas
inhibition of germination could prevent vaginitis in asymptomatic yeast carriers. Virulence is enhanced by proteolytic enzymes, toxins, and phospholipase elaborated by yeast. Secreted aspartyl proteinases elaborated by pathogenic *candida* spp have been identified in vaginal secretions in women with symptomatic vaginitis but not in those with asymptomatic colonisation.71,72 These proteolytic enzymes, with broad substrate specificity, destroy free and cell-bound proteins that impair fungal colonisation and invasion. Several genes that govern proteinase production (sap1, sap2, and sap3) have been cloned, and a strong correlation exists both in vitro and in experimental vaginitis between gene expression, aspartyl proteinase secretion, and the ability to cause disease.73-75 Mycotoxin such as gliotoxin identified in the vagina could act to inhibit phagocytic activity or suppress the local immune system.76 Iron binding by candida organisms has also been reported to facilitate yeast virulence.77

Candida organisms gain access to the vaginal lumen and secretions mainly from the adjacent perianal area.78 Effective anti-candida defence mechanisms in the vagina allow long-term persistence of candida organisms as vaginal commensals in an avirulent phase. Most, if not all women carry candida in the vagina at some point in their lives, yet without symptoms or signs of vaginitis and usually with a low concentration of yeast organisms.9 Candida can be either a commensal organism or a pathogen in the vagina, and it is believed that changes in the host vaginal environment are necessary before the organism induces pathological effects.

2.4 Diagnosis
Although acute pruritus and vaginal discharge are the usual presenting complaints associated with vulvovaginal candidiasis, neither is specific to this infection.\textsuperscript{79,80} The differential diagnosis of vulvovaginal candidiasis are, vulval dermatitis, genital herpes, bacterial vaginosis, \textit{lichen sclerosis}, urinary tract infection and vestibulitis the typical cottage-cheese-like discharge, which can vary from watery to homogeneously thick may aid diagnoses. Vaginal soreness, irritation, vulvar burning, dyspareunia, and external dysuria are common. Odour, if present, is slight and inoffensive. Examination reveals erythema and swelling of the labia and vulva, often with fissures and pustule-papular peripheral lesions. The cervix is normal, and vaginal erythema is present together with an adherent off-white discharge. Characteristically, symptoms are exacerbated in the week before menses. Several surveys indicate the unreliability of patient self-diagnosis. Since the symptoms and signs of vulvovaginal candidiasis are not specific to the infection, diagnosis cannot be made solely on the basis of history and physical examination.\textsuperscript{4,5} A wet mount or saline preparation should be done routinely to identify the presence of yeast cells and mycelia but also to exclude the presence of so-called clue cells indicative of \textit{Bacterial vaginosis} and motile trichomonads. A 10% potassium hydroxide preparation is more sensitive than a saline preparation in identifying yeast or hyphae (65–85% sensitivity). Vaginal pH is normal (4.0–4.5) in vulvovaginal candidiasis, and pH in excess of 4.7 usually indicates \textit{Bacterial vaginosis}, \textit{Trichomoniasis}, or a mixed infection. Unfortunately, up to 50\% of patients with culture-positive symptomatic vulvovaginal candidiasis will have negative microscopy.\textsuperscript{5} Thus, although routine cultures are not necessary if microscopy is positive, vaginal culture
should be done in symptomatic women with negative microscopy and a normal pH. The \textit{Papanicolaou}'s smear, although specific, is insensitive, being positive in only about 25% of patients with culture-positive symptomatic vulvovaginal candidiasis. There is no difference in using Sabouraud agar, Nickerson’s medium, or microstix-candida medium for culture. A positive culture alone does not necessarily indicate that the yeasts so identified are responsible for vaginal symptoms, since 10–15% of asymptomatic women are colonised with \textit{candida} and hence are culture positive. Diagnosis of vulvovaginal candidiasis requires a correlation of clinical findings, microscopic examination, and vaginal culture. There is no reliable serological or antigen detection technique available for the diagnosis of vulvovaginal candidiasis. Because most clinicians are unable or unwilling to measure vaginal pH and do microscopy, most women with vulvovaginal symptoms remain incorrectly diagnosed and treated. Polymerase chain reaction detection of \textit{candida} spp in vaginal samples is possible but is not available as a diagnostic test and might not prove to be a clinically useful test. Unfortunately, the availability of over-the-counter antimycotics will limit the ability to measure asymptomatic candida carriage and vulvovaginal candidiasis.

\textbf{2.5. Treatment}

The optimal treatment of VVC has not yet been defined. Consequently, treatment must be
individualized based on a comparison of effectiveness, convenience, potential side effects, and costs. Uncomplicated vaginitis is seen in 90% of patients and responds readily to short-course oral or topical treatment with azoles. In contrast, the complicated vaginitis seen in about 10% of patients requires antifungal therapy for >7 days. Azole therapy is unreliable for non-albicans species of candida. C. glabrata and the other non-albicans infections.

Treatment of the acute episode usually involves topical application of azoles drugs or nystatin or systemic oral antifungal agents. Whether individuals who are asymptomatic carriers of candida should receive treatment is controversial. In otherwise healthy women, treatment with an antifungal is not advised. Treatment of acute vulvovaginal candidiasis should be assessed on an individual basis.

The first agent with antifungal activity, griseofulvin, was isolated in 1939 and the first azole and polyene antifungal agents were reported in 1944 and 1949, respectively. It was not until 1958 that oral griseofulvin and topical chlormidazole became available for clinical use. The introduction of griseofulvin was followed in 1960 by that of amphotericin B, which is still the “gold standard” for the treatment of severe systemic mycoses. Two topical azole antifungal agents, miconazole and clotrimazole, were introduced in 1969; this was followed by the introduction of econazole in 1974 and a parenteral formulation of miconazole in the late 1970s. Today, these three agents remain the mainstay of topical therapy for many dermatophytoses.
Progress in the development of both topical and systemic antifungal agents lagged, due in part to the intensive research efforts in the area of antibacterial therapy which began in the 1940s following the large-scale production of penicillin and also to the relatively low incidence of serious fungal infections compared with that of bacterial infections. By 1980, members of the four major classes of antifungal agents which include polyenes, azoles, morpholines, and allylamines had been identified, yet the only new drug introduced for the treatment of systemic fungal infections was oral ketoconazole. It would be more than 10 years before either fluconazole or itraconazole became available for the treatment of systemic mycoses.

However, with 15 different marketed drugs worldwide, the azoles are currently the most widely used and studied class of antifungal agents. Azoles inhibit ergosterol synthesis by blocking lanosterol 14-demethylase, which converts lanosterol to ergosterol. This leads to increased membrane fluidity and permeability and inhibition of fungal cell growth and replication. The azole antifungal agents in clinical use contain either two or three nitrogens in the azole ring and are thereby classified as imidazoles (e.g., ketoconazole and miconazole, clotrimazole) or triazoles (e.g., itraconazole and fluconazole), respectively. With the exception of ketoconazole, use of the imidazoles is limited to the treatment of superficial mycoses, whereas the triazoles have a broad range of applications in the treatment of both superficial and systemic fungal infections. Another advantage of the triazoles is their greater affinity for fungal rather than mammalian cytochrome p-450 enzymes, which contributes to an improved safety profile.
Research has concluded that intravaginal imidazoles (including clotrimazole) are beneficial in non-pregnant women with vulvovaginal candidiasis.\textsuperscript{26} Compared with placebo, intravaginal imidazoles (including clotrimazole) reduced persistent symptoms of vulvovaginal candidiasis 1–5 weeks after treatment.\textsuperscript{26} Adverse effects such as vulval irritation was reported.\textsuperscript{26} It also found no clear or consistent difference in the effectiveness between different imidazoles.

Topical azole have been suggested as the first-line of therapy, but oral agents are sometimes associated with better compliance and are found to be the preferred route of treatment by patients.\textsuperscript{94} Topical azole are the most commonly used for initial treatment of uncomplicated vulvovaginal candidiasis. Several effective topical azole agents are available in a variety of formulations. Topical azoles are remarkably safe and well tolerated, although patients may report occasionally, local effects such as vaginal burning, stinging or irritation may occur.\textsuperscript{95} No evidence exists to suggest that any one formulation of topical azole results in better cure rates, nor is there any evidence of any specific azole being better than any other. Overall cure rates for topical azoles range from 80\% to 90\%. Topical antifungal agent is the therapeutic agent of choice in pregnancy. Both intravaginal azoles and intravaginal nystatin can be used in the first trimester of pregnancy.\textsuperscript{96} Oral azole agents on the other hand achieve comparable or marginally higher cure rates than do topical agents.

In a study comparing single oral dose of fluconazole versus conventional topical clotrimazole therapy of candida vaginitis, responses were similar in both groups and
side effects were mild in both groups. Hence single dose of 150mg fluconazole was concluded to be as safe and as effective as conventional 7 days of topical clotrimazole therapy. A recent randomised controlled trial also found no statistically significant differences in the clinical and mycological efficacy between topical clotrimazole (200mg for 3 days) and fluconazole (150mg single dose) in the treatment of both uncomplicated and recurrent vulvovaginal candidiasis. However, the onset of symptomatic relief in the first 24 hours of treatment was significantly higher in the fluconazole than in the clotrimazole group. In a study by Sobel et al. on 429 patients with vaginal candidiasis, the efficacy and safety of a single oral dose of fluconazole was compared with a 7-day clotrimazole (100mg) regimen. At day 14, clinical cure or improvement was found in 94% of fluconazole and 97% of clotrimazole-treated patients, however, after 35 days, 75% of both groups remained clinically cured, therefore, the cure rate was similar in both groups. Indeed, in a meta-analysis of 17 trials that assessed the effect of antifungal treatments on uncomplicated vulvovaginal candidiasis, treatment was similarly effective when administered by either the oral or vaginal route.

A Cochrane review comparing oral versus intra-vaginal imidazole and triazole antifungal treatments found no differences between clotrimazole and fluconazole or itraconazole for clinical cure at long (2 to 12 weeks) or short term (5-15 days) follow up. Most patients prefer the convenience of oral administration, which eliminates local side-effects and messiness. Consequently, compliance with topical form of treatment is poor, as women often stop the treatment as soon as their symptoms

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disappear, but prematurely before eradication of the fungi. However, oral azoles have a potential side effect of systemic toxicity, which has dramatically restricted the use of ketoconazole however, the better safety of fluconazole and clotrimazole means that ketoconazole is rarely used.

In a double-blind study by Sadovsky, the treatment of acute episode of vaginal candidiasis by fluconazole in 2 divided doses within 2 hours was compared with fluconazole single dose therapy. In this study, a better cure rate was achieved by divided doses, but because of popularity of single dose method, the authors reported that this method was more effective. Thus, patient’s acceptance of drug type and consumption route is of utmost importance.

One systematic review found that persistence of symptoms at 5–15 days was similar with intravaginal azoles ( clotrimazole, miconazole or econazole) compared with oral fluconazole or itraconazole. It found no significant difference in the persistence of symptoms measured at 5–15 days between intravaginal imidazoles and oral fluconazole or itraconazole. Two large randomized controlled trials (RCTs) evaluated adverse effects of intravaginal imidazoles compared with oral fluconazole or ketoconazole. One of the RCTs included a comparison with clotrimazole. Intravaginal clotrimazole had significantly lower incidence of adverse effects than oral fluconazole and frequencies were higher with oral fluconazole for individual adverse effects including headache (12% v 9%), abdominal pain (7% v 3%) and nausea (4% v 0%).
In the United States comparison of drug treatment costs for vaginal candidiasis revealed that the single dose treatment with fluconazole (150 mg) is less expensive than intravaginal treatment with clotrimazole, miconazole, or terconazole. On the contrary, in Japan, the National Health Insurance (NHI) price of 150 mg of fluconazole is 2,882 yen, while a 6-day course of intravaginal clotrimazole, 100 mg daily, costs 477.6 yen. Nevertheless, cost reductions resulting from decreases in physician office visits and associated laboratory tests may result if recurrences and relapses can be reduced with fluconazole treatment. Therefore it has been suggested that the treatment of vaginal candidiasis with oral fluconazole is effective and that a single oral fluconazole dose might be one choice in the treatment of vaginal candidiasis.

However, women with severe vulvovaginal candidiasis do not respond adequately to single dose and short-course treatment and may therefore require treatment for 5–7 days. Because many agents have comparable efficacy, selection depends on other factors such as the severity and duration of symptoms, the extent of inflammation, and the causative organism versus its known susceptibility pattern. Additional considerations include drug delivery to the infection site, safety issues, relative resistance rates in cases requiring long-term therapy, and patient preferences to maximize compliance. It is possible that the use of short-duration narrow-spectrum agents may increase selection of more resistant organisms which will result in an increase of recurrent VVC (RVVC). Women who are known or suspected to
be pregnant and women of childbearing age who are not using a reliable means of contraception should receive topical therapy, as should those who are breast-feeding or receiving drugs that can interact with an oral azole and those who have previously experienced adverse effects during azole therapy.\textsuperscript{106}

A number of promising new azole and triazole derivatives are currently being developed by several pharmaceutical companies. Three of these agents namely, voriconazole, ER-30346, and D0870 are derivatives of fluconazole, and another agent, SCH 56592, is a hydroxylated analogue of itraconazole.\textsuperscript{107} All of these new agents are active following oral administration; voriconazole may also be administered intravenously, and SCH 56592 shows topical activity.\textsuperscript{107}

In most developing countries, topical and systemic azoles are available over-the-counter, that is, the patient does not need a prescription from a physician. Of concern is the use of these readily available topical antifungal agents for self-diagnosed vulvovaginal candidiasis. Women are unable to correctly self-diagnose vulvovaginal candidiasis in the presence of vulvovaginal symptoms. Ready access to these products is associated with wasted financial expenditures, unfulfilled expectations, and delay in correct diagnosis. This problem could be resolved if a simple, inexpensive candida detection diagnostic test was available.

\textbf{2.6. Prevention of vulvovaginal candidiasis}

In majority of women who take oral antibiotics, symptomatic vulvovaginal candidiasis does not develop. However, for the patient who has had confirmed
antibiotic induced vulvovaginal candidiasis episodes in the past, it is reasonable to prescribe prophylactic antimycotic therapy along with antibiotics. New immunotherapeutic strategies to control vaginal candidiasis is currently being studied. Anti-candida vaccines and systemically administered antibodies have been effective in preventing vaginal candidiasis in rodents, but no data are available in human beings. Further progress is dependent upon delineation of host genetic susceptibility, anti-candida defence mechanisms in the vagina, and yeast genetic factors that induce host inflammation and facilitate vaginal persistence. There is some evidence to suggest that suppression of recurrence is possible with other agents. Dennerstein reported a reduced rate of recurrence in 15 patients with recurrent vulvovaginal candidiasis when treated with depo-medroxyprogesterone acetate for 3 months. In a small study using patients as their own controls, it was reported that fewer episodes of vulvovaginal candidiasis occurred in women who ate live yoghurt daily. However, in view of the small number of patients and absence of controls in this unblinded study, the role of yoghurt in preventing candida vaginitis remains questionable. Occasionally, women on fluconazole with persistent pruritus benefit from addition of antihistamines. Treatment of male sexual partners is of no benefit.
CHAPTER THREE

3.0 Materials and Method

3.1 Ethical Approval and Informed Consent

Ethical approval for the research was obtained from the ethical committee of Aminu Kano Teaching Hospital (AKTH), Kano and informed consent was obtained from the patient in compliance with the Lisbon Declaration on the Rights of the patient.\textsuperscript{112}

3.2 Study Setting

Aminu Kano Teaching Hospital is one of the tertiary health facilities in Kano. It was established in August 1988 as the Teaching Hospital for Bayero University Medical School. The hospital was established to serve as a fully functional 500-bed teaching hospital with state of the art facilities for provision of service, teaching and research to cater for the needs of the local and wider community. Patients from other hospitals and clinics are referred here. It also serves as a referral centre for other neighbouring states such as Bauchi, Katsina and Jigawa. Training covers medical
students, resident doctors, house officers, intern medical laboratory scientists, pharmacists, physiotherapists, medical imaging scientists, optometrists and dentists. The hospital also trains community health officers, health information management officers and post basic nursing training in accident and emergency in collaboration with National Orthopedic Hospital, Dala, Kano state. The hospital currently has sixteen (16) clinical departments offering services, conducting trainings and research as well as over 10 support service departments including a diagnostic centre. The hospital provides various services to the community in the field of health and social services through its clinical and service departments. The para-clinical departments include haematology and blood bank, microbiology, pathology, chemical pathology, anaesthesia, radiology, physiotherapy and the pharmacy. The other supporting departments are the medical records, social welfare, the medical library and the catering services.

3.2.1 Obstetrics and Gynaecology Department

The department of Obstetrics and Gynaecology is one of the clinical departments of AKTH with twelve consultants and 28 resident doctors. There are eight outpatient clinics in a week. The antenatal clinics operate on Mondays, Tuesdays, Wednesdays and Thursdays from 8.00am – 1.00pm. The four Gynaecological clinics are held on Mondays, Tuesdays, Wednesdays and Thursdays at 2.00 – 6.00pm where an average of 50 gynaecologic patients are seen at each gynaecologic clinic day. All new gynaecologic patients obtain cards from the general outpatient department and are subsequently referred to the gynaecology clinic or to gynaecology emergency room.
A detailed history is obtained from all patients. This is followed by general, systemic and pelvic examination. The common conditions encountered in this clinic are pelvic inflammatory disease (PID), vulvovaginal candidiasis, infertility, uterine fibroids, and gynaecologic malignancies especially of the cervix. The extent of the investigations done on each patient depends on the diagnosis. The tests that are necessary are indicated by the patient’s diagnosis.

3.3 Study Design

This was a prospective study of 300 patients who presented at the gynaecologic and general outpatients clinics of AKTH with clinical and laboratory evidence of vulvovaginal candidiasis who fulfilled the inclusion criteria.

Postmenarchal females with a diagnosis of vulvovaginal candidiasis were included in the study. The patients had a clinical diagnosis of VVC based on history and physical examination (including vaginal examination).

Signs and symptoms to be evaluated include: itching, burning, irritation, edema, erythema and/or excoriation of the vagina/vulva. Each evaluated sign and/or symptom was given a numerical rating based on severity (absent = 0; mild = 1; moderate = 2; severe = 3).\textsuperscript{113} The patients had a minimum composite signs/symptoms score equal to 2. It is recommended that 50% or more of the evaluable patients had clinical evidence of disease of at least moderate severity at entry, defined as having a minimal composite score of 7. Severe disease was defined as a minimal composite sign/symptom score of 13. Patients with VVC may have a vaginal discharge, which is usually described as white, creamy, and cottage cheese-
like in appearance and adherent to the epithelium. A screening 10% KOH preparation from the inflamed vaginal mucosa or vaginal discharge should reveal yeast forms (hyphae/pseudohyphae) or budding yeasts and sample culture was performed for cases in which the result of direct examination was negative but there was high clinical suspicion of the disease. This entry culture was positive for *Candida albicans* for patient included in the study. The patient received no additional vulvovaginal or systemic antifungal drug during the study period covering days 1 to 30.

Exclusion criteria were females less than 16 years of age, those who were menstruating, those who had any immunosuppressive illness, those with history of diabetes mellitus, those with recurrent vulvovaginal candidiasis, those with premalignant or malignant cervical lesions, those who were pregnant, those with reported sensitivity to oral fluconazole or topical clotrimazole and those who could not be fully monitored during the period of the study.

### 3.3.1 Null Hypothesis (H₀)

H₀ = Topical clotrimazole is more effective than oral fluconazole in treatment of vulvovaginal candidiasis.

### 3.4. Work Plan

#### 3.4.1. Personnel
This research involved the researcher, who is a clinician and, who carried out structured interview and made clinical diagnosis with the assistance of other resident doctors in Obstetrics and Gynaecology Department of AKTH, a microbiologist who examined the high vaginal swab specimens and made laboratory diagnosis, an attendant who conveyed the specimens to the laboratory and a statistician who carried out statistical analysis.

### 3.4.2. Time Frame

<table>
<thead>
<tr>
<th>Activity</th>
<th>Time Frame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proposal Development</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Proposal Review by Supervisors</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Departmental Research Proposal Defense</td>
<td>A day</td>
</tr>
<tr>
<td>Ethical Clearance</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Proposal Submission to College/return</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Data Collection/ Laboratory Analysis</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Data Analysis</td>
<td>1 weeks</td>
</tr>
<tr>
<td>Writing of Draft Chapters and Submission</td>
<td>1 weeks</td>
</tr>
<tr>
<td>Revision</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Dissertation Defense</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Final Approval And Completion</td>
<td>1 week</td>
</tr>
</tbody>
</table>

### 3.5. Sample Size Determination and Sampling Technique

Sample size was determined by using the formula:

\[ n = z^2 \frac{pq}{d^2} \]

\(n=\) Sample Size, \(z = \) Standard Normal Deviation = 1.96 at 95% Confidence Limit, \(p = \) Prevalence Rate = 22.5%, \(q = 1-P = 1-22.5\% = 0.775, d = \) Error Margin = 5%)

\[ n = \frac{1.96^2 \times 0.225 \times 0.775}{0.05^2} = 268 \]
Documented prevalence of vulvovaginal candidiasis are 25\%\(^5\), 24\%\(^2,6\) and 18.5\%\(^7\). Twenty-two and half percent (22.5\%), being the average of the above reported prevalence, was used for this study. The calculated minimum sample size was 268. Ten percent of minimum sample size was added to take care of attrition. Therefore the sample size of 300 patients was used for this study.

Letters A and B was written on 300 pieces of paper shared equally among groups A and B. These were placed in sealed identical envelopes. Each patient picked one envelope, when it was opened the option in her envelope was the treatment she received. A subset of the study population (group A) comprising 150 subjects received topical clotrimazole 200mg intravaginally at bedtime for 3 days. Another subset (group B) comprising 150 subjects will receive fluconazole capsule 150mg statim.

3.6. Data and Specimen Collection

Research structured questionnaires were administered to all the 300 subjects before and after treatment. These gave various sociodemographic and clinical information. The after treatment questionnaires gave information if any doses were missed, the reason(s) for noncompliance, patient’s subjective assessment of efficacy of treatment and side effects.

All the recruited patients were examined by the researcher. They were put in lithotomy position and the vulva was inspected. Under good light, a sterile Cusco’s bivalve speculum was used to expose the vagina after swabbing the vulva with sterile water. A female chaperon was available to gain the patient’s confidence since the investigator was a male. Specimens of secretions were taken from the posterior
fornix with a sterile cotton swab which were immediately put into a sterile tube containing about 3cc of saline. A screening 10% KOH preparation from the inflamed vaginal mucosa or vaginal discharge was done to identify yeast forms (hyphae/pseudohyphae) or budding yeasts. A drop of 10% potassium hydroxide (KOH) on the pool of the secretion on the speculum when it produced a fishy smell denoted a positive test for *Trichomonas vaginalis* (TV). The tube was labeled with the patient’s initials and case form number and taken to the laboratory for further investigations which included wet microscopy and preparation of a dry Gram stain slide for microscopy. A Gram stain slide can reveal candida (pseudohyphae) or *Bacteria vaginosis* (clue cells and proportions of lactobacilli and other organisms). Wet microscopy was prepared in the laboratory by dipping a small amount of discharge (from a HVS) into saline on a microscope slide. This was useful in identifying protozoa in TV and pseudohyphae in candida. Culture in Sabouraud’s medium was used to detect candida when microscopy was inconclusive. Whenever the HVS was not transported immediately to the laboratory, it was stored at 4°C for no longer than 48 hours.

3.7 Treatment Precautions

The patients began using the study drug within 2 days of the entry visit to be considered evaluable. The patients were encouraged to refrain from sexual intercourse and the use of intravaginal products during the treatment period (e.g.,
douches, spermicides, condoms, tampons, diaphragms) because use of such products may preclude accurate assessment of the study drug’s efficacy as well as safety. In the consent form and before leaving the study facility, the patient was told that if her symptoms did not improve within 2 to 3 days, she should contact the investigator and be reassessed. Similarly, if other adverse events occurred that concerned the patient, she was encouraged to contact the researcher.

3.8. Evaluation and Assessment of Efficacy

Most of the patients randomized were followed throughout the study period. Only patients who had adhered to complete treatment prescription were evaluated for therapeutic outcome. It was recommended that a patient attended two study visits. These visits included the entry visit and the test-of-cure visit at 21 to 30 days of the study. An interim telephone contact was considered for evaluation of clinical response. Post-treatment telephone contact was initiated by the researcher 7 to 10 days after the beginning of therapy. The purpose of this call was to ensure patient compliance with the protocol and to evaluate the patient’s response to therapy, as well as to inquire about possible adverse events. If during the telephone interview the patient’s clinical response was considered inadequate, the investigator asked the patient to come to the clinic for further evaluation. At the test-of-cure visit, clinical history and vaginal examination were carried out. Symptoms/signs numerical score after treatment was compared to the score at entry. If a patient used other vaginal products (e.g., douche and tampons) during the treatment phase of the study she was considered non evaluable. Patients who used these vaginal products after completing
treatment will be evaluated. Resolution of signs and symptoms of vulvovaginal infection during treatment and by the time of the 21 to 30 test-of-cure visit and without further antifungal treatment will be regarded as clinical cure. Specifically, any sign or symptom with a score of 1 or 2 at entry were absent (score = 0) by the test-of-cure visit. Any sign or symptom with a score of 3 at entry had a score of 0 or 1 by the test-of-cure visit. If there was no response to therapy or incomplete resolution of signs and symptoms, it was considered clinical failure otherwise it was a clinical success. Mycological eradication was considered if a patient had negative culture (no growth) for *Candida albicans* (or baseline yeast pathogen) at the test-of-cure visit, days 21 to 30 of the study.

3.9. **Statistical analysis**

The data obtained was analyzed using SPSS version 16.0 statistical software. Absolute numbers and simple percentages were used to describe categorical variables. Similarly, quantitative variables were described using measures of central tendency (mean, median) and measures of dispersion (range, standard deviation) as appropriate. Statistical significance of differences between means will be determined using ANOVA. Significant association between sociodemographic factors and vulvovaginal candidiasis were tested using chi-square test and p<0.05 was considered significant.
3.10. Limitation of the study

Patients who did not understand English had the questionnaire translated to them in their own language.
CHAPTER 4
Results

A randomized controlled trial of topical clotrimazole versus oral fluconazole for treatment of vulvovaginal candidiasis was done at Aminu Kano Teaching Hospital between 30\textsuperscript{th} December, 2011 and 26\textsuperscript{th} February, 2012. A total of 374 high vaginal swab specimens were culture positive and of which 316 were positive for \textit{Candida albicans} during this period. Of these \textit{candida albican} positive patients, 300 were included in the study. At the end of the study 270 patients were found evaluable. This gave a response rate of 90%. One hundred and thirty responded in group A (topical clotrimazole group), while 140 responded in group B (oral fluconazole group). Non-evaluable was due to irregular visits, wrong telephone contacts and missing drug use. The reason for missing drug were forgetfulness and subjective feeling of cure before the end of the course of clotrimazole. The non-evaluable patients in the oral fluconazole group was due to irregular visits or wrong telephone contact. There was no reported case of treatment-related adverse effects of both drugs.

4.1 Microbiological pattern in 374 positive high vaginal swabs specimens in AKTH.

As shown in table 1, \textit{Candida albicans} was responsible for 316 infections (84.5%), \textit{Streptococci species} 20 (5.35%), \textit{Staphylococci species} 14 (3.74%), \textit{Escherichia coli} 14 (3.74%), \textit{Bacterial vaginosis} 8(2.14%) and \textit{Proteus vulgaris} 2 (0.53%).
4.2 Distribution of socio demographic characteristics

As shown in table 2, vulvovaginal candidiasis was commonest in those aged 26-35 years (53%), followed by 16-25 years (33.3%) and lowest among those 36-45 years of age (13.7%). The mean age was 27.7±7.8 years. There was no statistically significant difference in the mean age of the clotrimazole and fluconazole groups. Those of parities 1-2 had the highest prevalence (41.9%) compared to others. There was no statistically significant difference in the mean parities of women in the two groups. Vulvovaginal candidiasis was more prevalent among those who were married (80%) than those who were unmarried (20%) in the two groups. There was no difference in educational and employment status between the two groups.

4.3 Distribution of clinical presentations of vulvovaginal candidiasis in the study

As shown in table 3, cheesy vaginal discharge was the commonest presentation in patients with vulvovaginal candidiasis occurring in 47.4% of cases. This was followed by vulval itching or pruititus which occurred in 30.4% of cases. Vulval redness occurred in 12.2% and vulval burning sensation in 10% of cases. Most of the patients presented 8-14 days (38.9%) after the onset of symptoms compared to those who presented at 0-7days (26.3%), 15-21 days (21.1%) and 22-29 days (13.7%) after the onset of symptoms. The mean duration of symptoms before presentation was 13.3±7.4 days. There was no statistically significant difference in
the mean duration of symptoms before presentation between the clotrimazole and fluconazole groups.

**Table 1**: Microbiological pattern in 374 positive high vaginal swabs specimens in AKTH.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Candida albicans</em></td>
<td>316</td>
<td>84.5</td>
</tr>
<tr>
<td><em>Streptococcus species</em></td>
<td>20</td>
<td>5.35</td>
</tr>
<tr>
<td><em>Staphylococcus species</em></td>
<td>14</td>
<td>3.74</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>14</td>
<td>3.74</td>
</tr>
<tr>
<td><em>Bacterial vaginosis</em></td>
<td>8</td>
<td>2.14</td>
</tr>
<tr>
<td><em>Proteus vulgaris</em></td>
<td>2</td>
<td>0.53</td>
</tr>
</tbody>
</table>
Table 2: Distribution of socio demographic characteristics

<table>
<thead>
<tr>
<th>parameters</th>
<th>Fluconazole N=140</th>
<th>Clotrimazole N=130</th>
<th>All groups (%) N=270</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-25</td>
<td>47</td>
<td>43</td>
<td>90 (33.3)</td>
<td></td>
</tr>
<tr>
<td>26-35</td>
<td>78</td>
<td>65</td>
<td>143 (53)</td>
<td></td>
</tr>
<tr>
<td>36-45</td>
<td>15</td>
<td>22</td>
<td>37 (13.7)</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>28±8.5</td>
<td>27±7.5</td>
<td>27.7±7.8</td>
<td>0.84755</td>
</tr>
<tr>
<td><strong>Parity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>31</td>
<td>29</td>
<td>60 (22.2)</td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>62</td>
<td>51</td>
<td>113 (41.9)</td>
<td></td>
</tr>
<tr>
<td>3-4</td>
<td>31</td>
<td>31</td>
<td>62 (23.0)</td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>16</td>
<td>19</td>
<td>35 (13.0)</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>2±2</td>
<td>2±2</td>
<td>2±2</td>
<td>n.d</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>112</td>
<td>104</td>
<td>216 (80)</td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>28</td>
<td>26</td>
<td>54 (20)</td>
<td></td>
</tr>
<tr>
<td><strong>Educational status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>32</td>
<td>32</td>
<td>64 (23.7)</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>18</td>
<td>16</td>
<td>34 (12.6)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>39</td>
<td>33</td>
<td>72 (26.7)</td>
<td></td>
</tr>
<tr>
<td>tertiary</td>
<td>51</td>
<td>49</td>
<td>100 (37.0)</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td>Fluconazole</td>
<td>Clotrimazole</td>
<td>All groups</td>
<td></td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------</td>
<td>--------------</td>
<td>------------</td>
<td></td>
</tr>
<tr>
<td>House wife</td>
<td>61</td>
<td>58</td>
<td>119 (44.1)</td>
<td></td>
</tr>
<tr>
<td>Employee</td>
<td>32</td>
<td>29</td>
<td>61 (22.6)</td>
<td></td>
</tr>
<tr>
<td>Trader</td>
<td>15</td>
<td>14</td>
<td>29 (10.7)</td>
<td></td>
</tr>
<tr>
<td>students</td>
<td>32</td>
<td>29</td>
<td>61 (22.6)</td>
<td></td>
</tr>
</tbody>
</table>

(N= Total sample size, Na= sample size for group A, Nb= sample size for group B, %=Percent, SD= Standard Deviation at 95% confidence interval, nd=no difference)

### Table 3: Distribution of clinical presentations of vulvovaginal candidiasis in the study

<table>
<thead>
<tr>
<th>parameters</th>
<th>Fluconazole</th>
<th>Clotrimazole</th>
<th>All groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na=140</td>
<td>Nb=130</td>
<td>(%) N=270</td>
</tr>
<tr>
<td><strong>Presenting Clinical features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheesy vaginal discharge</td>
<td>70</td>
<td>58</td>
<td>128 (47.4)</td>
</tr>
<tr>
<td>itching</td>
<td>30</td>
<td>52</td>
<td>82 (30.4)</td>
</tr>
<tr>
<td>burning</td>
<td>20</td>
<td>7</td>
<td>27 (10)</td>
</tr>
<tr>
<td>redness</td>
<td>20</td>
<td>13</td>
<td>33 (12.2)</td>
</tr>
<tr>
<td><strong>Duration of symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-7days</td>
<td>32</td>
<td>39</td>
<td>71 (26.3)</td>
</tr>
<tr>
<td>8-14</td>
<td>53</td>
<td>52</td>
<td>105 (38.9)</td>
</tr>
<tr>
<td>15-21</td>
<td>31</td>
<td>26</td>
<td>57 (21.1)</td>
</tr>
<tr>
<td>22-29</td>
<td>24</td>
<td>13</td>
<td>37 (13.7)</td>
</tr>
<tr>
<td><strong>Mean±SD</strong></td>
<td>14.2±8</td>
<td>12.4±6.7</td>
<td>13.3±7.4</td>
</tr>
</tbody>
</table>

0.98171
4.4 Distribution of perception of the source of infection and some risk factors

As shown in table 4, 41.9% of the patient believed that they contracted vulvovaginal candidiasis from the toilet, 31.1% did not know the source of the infection and 27% believed that it was sexually transmitted. Douching was the most common risk factor responsible for vulvovaginal candidiasis prevalence occurring in 42.6% of the patients, followed by use of contraceptives (combined oral contraceptive pills and intrauterine devices) in 28.9% of cases and antibiotics use in 19.3% of cases. In 9.3% of cases, no apparent risk factor was discovered.

4.5 Distribution of pre-treatment scores and assessment of effectiveness after treatment

As shown in table 5, 48.5% of the patients had pre-treatment numerical symptom scores of 2-6 (mild) and 51.5% of the patients had scores of 7-12 (moderate). The mean score was 6±3. There is no difference in scores between patients in the clotrimazole and fluconazole group. One week after treatment, 85% of patients in the fluconazole group and 83.3% in the clotrimazole group were satisfied with their
treatment. This difference was not statistically significant (p=0.890). Three weeks after treatment, 80% of the fluconazole group and 77.7% of the clotrimazole group were satisfied with their treatment. The difference was not statistically significant (p=0.90). Clinical and mycological cure rates for the fluconazole and clotrimazole groups were 80%, 72.1% and 76.2%, 70% respectively. The differences were not statistically significant (p=0.90 and 0.890 respectively).

Table 4: Distribution of perception of the source of infection and some risk factors
**Table 5:** Distribution of pre-treatment scores and assessment of effectiveness after treatment

<table>
<thead>
<tr>
<th>infection</th>
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<tbody>
<tr>
<td>Sex</td>
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<td>33</td>
<td>73 (27)</td>
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<tr>
<td>toilet</td>
<td>80</td>
<td>33</td>
<td>113 (41.9)</td>
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<tr>
<td>unknown</td>
<td>20</td>
<td>64</td>
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<table>
<thead>
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<td>contraceptive</td>
<td>42</td>
<td>36</td>
<td>78 (28.9)</td>
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<tr>
<td>Antibiotics</td>
<td>28</td>
<td>24</td>
<td>52 (19.3)</td>
</tr>
<tr>
<td>Douching</td>
<td>56</td>
<td>59</td>
<td>115 (42.6)</td>
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<tr>
<td>None</td>
<td>14</td>
<td>11</td>
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<tr>
<td>Parameters</td>
<td>Fluconazole Frequency(%)</td>
<td>Clotrimazole Frequency(%)</td>
<td>All frequency(%)</td>
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<td>--------------------------</td>
<td>---------------------------</td>
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</tr>
<tr>
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<td>63</td>
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<td>≥13</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
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<td>mean±SD</td>
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### Pre-treatment Score

<table>
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<tr>
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<th>Clotrimazole</th>
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<th>P-value</th>
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<tbody>
<tr>
<td>2-6</td>
<td>119(85)</td>
<td>108(83.1)</td>
<td>-</td>
<td>0.890</td>
</tr>
<tr>
<td>7-12</td>
<td>112(80)</td>
<td>101(77.7)</td>
<td>-</td>
<td>0.90</td>
</tr>
<tr>
<td>≥13</td>
<td>112(80)</td>
<td>99(76.2)</td>
<td>-</td>
<td>0.90</td>
</tr>
</tbody>
</table>

### Satisfaction Rating 1<sup>st</sup> Week

| Satisfied | 119(85) | 108(83.1) | - | 0.890 |
| undecided | 1(0.7)  | 1(0.77)   | - |       |
| dissatisfied | 20(14.3) | 21(16.2) | - |       |

### Satisfaction Rating 3<sup>rd</sup> Week

| Satisfied | 112(80) | 101(77.7) | - | 0.90 |
| undecided | -       | -         | - |       |
| dissatisfied | 28(20)  | 29(22.3)  | - |       |

### Clinical Effectiveness

| Cure | 112(80) | 99(76.2) | - | 0.90 |
| Failure | 28(20)  | 31(23.8) | - |       |

### Mycological Effectiveness

| Cure | 101(72.1) | 91(70) | - | 0.890 |
| failure | 39(27.9)  | 39(30) | - |       |

**Pre-treatment Scoring guide:**

- 2-6 (mild)
- 7-12 (moderate)
- ≥13 (severe)

**Post-treatment Scoring guide:**

- 0 or 1 (clinical cure)
- >1 (clinical failure)

**Mycological effectiveness**

- No growth of *Candida albican* (mycological cure)
- Growth of *Candida albican* (mycological failure)

**CHAPTER 5**
Discussion, Conclusion, Recommendation

5.1 Discussion

Vulvovaginal candidiasis (VVC) is very common and a frequent cause of vaginosis. The prevalence of VVC among patients with positive high vaginal swab specimens culture in this study (table 1) was 84.5%. This was comparable to that reported by Onifade and Olorunfemi in Ondo State (81.5%)\(^1\). Other studies have reported a lower prevalence of 25%\(^1\), 24%\(^2\)-\(^5\), 15-30%\(^4\)-\(^5\) and 18.5%\(^2\). Parveen et al., Maccato and Kaufman reported a high rate among pregnant women\(^2\)-\(^4\) and Okonofua et al., reported a high carriage of *Candida albicans* in Nigeria infertile women compared with controls.\(^2\) Studies have shown that fungal infections of the female genital tract including candidiasis are presently becoming more prevalent.\(^2\)-\(^4\)

This study showed that vulvovaginal candidiasis is commonest among women in the age group 16-45 years (table 2). This was also similarly reported in previous studies.\(^1\)-\(^5\) The reason for this is because of high oestrogen levels in this group of women resulting in a favourable pH for candida colonization. The mean age of women with VVC in this study was 27.7±7.8. There was no statistically significant age difference between the topical clotrimazole and oral fluconazole groups (p=0.84755). The condition was more prevalent in women who were aged 26-35 years (53%) and lowest in those aged 36-45 years (13.7%). This report is a replication of that of other studies\(^3\)-\(^5\),\(^6\) that showed that the occurrence of VVC peaks in the third decade of life, declining in women older than 40 years. It is
however contrary to highest incidence among women 20-25 years of age reported by Ako-Nai et al\textsuperscript{115} and UNAID. \textsuperscript{116}

The result of this study has shown that the highest incidence of VVC was among women of parities 1-2. Jindall, \textit{et al} reported that Women with parity of more than one and those using oral contraceptives showed significantly higher rate of candida culture positivity than women of parity one or nil.\textsuperscript{117}

This present study has shown that marital factor affects the prevalence of vulvovaginal candidiasis. Although Enweani et al\textsuperscript{118} reported that marital factor had no effect on the prevalence of vulvovaginal candidiasis, FMOH\textsuperscript{114} and Okungbowa,\textit{et al}\textsuperscript{63} are of the view that marital factor was important. This study showed higher incidence among the married (69.6\%) compared to the unmarried (30.4\%). The report of this study agrees with that of Okongbowa,\textit{et al}\textsuperscript{63} that vulvovaginal candidiasis is commoner among the married women.

The result of this study showed that VVC affects all strata of women despite their educational and employment status. This support earlier findings.\textsuperscript{117}

The result of this study has shown that cheesy vaginal discharge was the commonest presentation in patients with vulvovaginal candidiasis occurring in 47.4\% of cases (table 3). This was followed by vulval itching or pruritus which occurred in 30.4\% of cases. Vulval redness occurred in 12.2\% and vulval burning sensation in 10\% of
cases. This is compatible with the reported symptoms for vaginal candidiasis including vaginal discharge, burning and pruritus\textsuperscript{118,119}. Vaginal discharge is a common presentation in gynaecological patients\textsuperscript{120}. Two studies\textsuperscript{117,121} however reported that vulval itching was the most frequent clinical manifestation of VVC. Although acute pruritus and vaginal discharge are the usual presenting complaints associated with vulvovaginal candidiasis, neither is specific to this infection.\textsuperscript{79,80} Other differential diagnosis such as vulval dermatitis, genital herpes and bacterial vaginosis should be considered.

Most of the patients presented 8-14 days (38.9\%) after the onset of symptoms compared to those who presented at 0-7 days (26.3\%), 15-21 days (21.1\%) and 22-29 days (13.7\%) after the onset of symptoms. The mean duration of symptoms before presentation was 13.3±7.4 days. There was no statistically significant difference in the mean duration of symptoms before presentation between the clotrimazole and fluconazole groups.

As shown in table 4, 41.9\% of the patient believed that they contracted vulvovaginal candidiasis from the toilet, 31.1\% did not know the source of the infection and 27\% believed that it was sexually transmitted. Most women in this study believed that they contacted the disease from the toilet rather than sexual intercourse. This was comparable to the reports of Rabiu et al\textsuperscript{122} from Lagos, Nigeria, that 44.6\% of women perceived that they contracted reproductive tract infection was from the toilet, followed by sexual intercourse and poor hygiene. The role of sexual behaviour
in causing symptomatic, often recurrent, vulvovaginal candidiasis has been underestimated because women who are not sexually active often develop vulvovaginal candidiasis.\textsuperscript{39,55} Although vulvovaginal candidiasis is not a sexually transmitted disease, there are some evidences to suggest that the frequency/periodicity of sexual intercourse is associated with acute vaginitis.\textsuperscript{38,39}

Douching was the most common risk factor responsible for vulvovaginal candidiasis prevalence occurring in 42.6\% of the patients in this study, followed by use of contraceptives (combined oral contraceptive pills and intrauterine devices) in 28.9\% of cases and antibiotics use in 19.3\% of cases. Douching has been shown to be a risk factor for candida vulvovaginitis for some women, and for others, there was no relationship found.\textsuperscript{56,57,123} The douche liquid irrigates the vagina and washes away any material there, such as blood, mucus, and microorganisms. Current thinking posits that the douche process clears away the hydrogen peroxide producing lactobaccillus that prevent overgrowth of candida, thus leaving women more open to candida vulvovaginitis.

As in this study, most investigators believe that oral contraceptives predispose women to recurrent vulvovaginal candidiasis.\textsuperscript{40,41} Increased carriage of yeast was reported in users of intrauterine contraceptive devices, contraceptive sponges, diaphragms, and condoms, with or without spermicides.\textsuperscript{40,41} However, an extensive study in college students did not show an increase in the risk of symptomatic
vulvovaginal candidiasis in users of oral contraceptives, diaphragms, condoms, or spermicides.\textsuperscript{37}

Symptomatic vulvovaginal candidiasis frequently follows use of vaginal or systemic antibiotics.\textsuperscript{45,46} Antibiotics are thought to predispose women to vulvovaginal candidiasis by eliminating the protective bacterial flora, thus allowing candida overgrowth in the gastrointestinal tract, vagina, or both.\textsuperscript{50} In particular, \textit{lactobacillus spp} could provide colonisation resistance and prevent germination, maintaining low numbers of yeast. Some studies have however failed to show a link between the occurrence of vulvovaginal candidiasis and antibiotic treatment.\textsuperscript{53}

As shown in table 5, 48.5\% of the patients had pre-treatment numerical symptom scores of 2-6 (mild) and 51.5\% of the patients had scores of 7-12 (moderate). The mean score was 6±3. It has been recommended that for RCT of antifungal agents 50\% or more of the evaluable patients should have clinical evidence of disease of at least moderate severity at entry, defined as having a minimal composite score of 7.\textsuperscript{113} There was no difference in scores between patients in the clotrimazole and fluconazole group. One week after treatment, 85\% of patients in the fluconazole group and 83.3\% in the clotrimazole group were satisfied with their treatment. This difference was not statistically significant (p>0.05). Three weeks after treatment, 80\% of the fluconazole group and 77.7\% of the clotrimazole group were satisfied with their treatment. The difference was not statistically significant (p>0.05). Clinical and mycological cure rates for the fluconazole and clotrimazole groups were
80%, 72.1% and 76.2%, 70% respectively. The differences were not statistically significant (p>0.05). These rates were higher than those reported by Mikano et al\textsuperscript{124} but lower than those reported by Skrodeniene et al\textsuperscript{125}. The current study also agrees with a previous study which found no statistically significant differences in the clinical and mycological efficacy between topical clotrimazole (200mg for 3 days) and fluconazole (150mg single dose) in the treatment of both uncomplicated and recurrent vulvovaginal candidiasis.\textsuperscript{97} In another study by Sobel et al on a larger sample size of 429 patients with vaginal candidiasis, the efficacy and safety of a single oral dose of fluconazole was compared with a 7-day clotrimazole (100mg) regimen he reported that cure rate was similar in both groups.\textsuperscript{96} Again, in a meta-analysis of 17 trials that assessed the effect of antifungal treatments on uncomplicated vulvovaginal candidiasis, treatment was similarly effective when administered by either the oral or vaginal route.\textsuperscript{98} A Cochrane review\textsuperscript{99} comparing oral versus intra-vaginal imidazole and triazole anti-fungal treatments found no differences between clotrimazole and fluconazole or itraconazole for clinical cure at long (2 to 12 weeks) or short term (5-15 days) follow up.

As shown in this study, compliance with oral fluconazole was better than with topical clotrimazole. Studies have shown that most patients prefer the convenience of oral administration, which eliminates local side-effects and messiness.\textsuperscript{100} Consequently, compliance with topical form of treatment is poor, as women often stop the treatment as soon as their symptoms disappear, but prematurely before eradication of the fungi.\textsuperscript{101} Side effects of use of both drugs were
uncommon in this study and another study, however some have reported mild side effects in both groups. The reported side effects include headache, abdominal pain, nausea and vulval irritation (with topical clotrimazole).

5.1 Conclusion

The overall result of this study rejects the hypothesis that topical clotrimazole is more effective than oral fluconazole in treatment of vulvovaginal candidiasis. As reported from reports of several studies, this study agrees that there is no difference statistically between topical clotrimazole and oral fluconazole in treatment of vulvovaginal candidiasis.

Besides, douching was a very prevalent practice which may have been responsible among other factors for the high prevalence of vulvovaginal candidiasis in the group of women studied.

5.2 Recommendation

Because both oral fluconazole and topical clotrimazole are equally effective for treatment of vulvovaginal candidiasis as shown by this study, treatment should be individualized based on a comparison of effectiveness, convenience, potential side effects, and costs. Women who are known or suspected to be pregnant, breastfeeding or women of childbearing age who are not using a reliable means of contraception or receiving drugs that can interact with an oral azole and those who have previously experienced adverse effects during azole therapy should receive topical clotrimazole.
Furthermore, women with severe or complicated vulvovaginal candidiasis who do not respond adequately to single dose and short-course treatment may require treatment for 5–7 days.

Douching is a significant predisposing factor for development of vulvovaginal candidiasis in our environment, therefore this practice should be discouraged. In majority of women who take oral antibiotics, symptomatic vulvovaginal candidiasis does not develop. However, for the patient who has had confirmed antibiotic induced vulvovaginal candidiasis episodes in the past, it is reasonable to prescribe prophylactic antmycotic therapy along with antibiotics.

In most developing countries, including Nigeria, topical and systemic azoles are available over-the-counter, that is, the patient does not need a prescription from a physician. Of concern is the use of these readily available topical antifungal agents for self-diagnosed vulvovaginal candidiasis. Women are unable to correctly self-diagnose vulvovaginal candidiasis in the presence of vulvovaginal symptoms. Ready access to these products is associated with wasted financial expenditures, unfulfilled expectations, and delay in correct diagnosis. This problem could be resolved if a simple, inexpensive candida detection diagnostic test was available.

The limitation of this study was that being a questionanaire-based study it was challenging to use in respondents who are uneducated and uncooperative. The use of interpreter in this respect may not have conveyed the full intent of the researcher.
Further study to assess the effectiveness of topical and oral fluconazole for recurrent vulvovaginal candidiasis are needed.

References


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APPENDIX A

PARTICIPANTS’ INFORMATION SHEET

I am Dr. Ugwa Emmanuel Ajuluchukwu of Department of Obstetrics and Gynaecology, Aminu Kano Teaching Hospital. I am conducting a research whose details are provided below. I can be reached on my email drajulugreatgod@hotmail.com, or via telephone on 08035851872

1. Study Title

Outcome of treatment of vulvovaginal candidiasis in Aminu Kano Teaching Hospital; A Randomized Controlled Trial of Topical Clotrimazole Versus Oral Fluconazole.

2. Invitation
I am inviting you to participate in a research with the above study title. I am providing this information in order to let you know what the research is about, and how it will be conducted. I will very much appreciate it if you can read this information thoroughly before making a decision about participation in the research. I will be happy to provide any additional details you may require after reading this, or at any other time.

3. Research purpose.

The purpose of this research is to determine the demographic and social characteristics of women with vulvovaginal candidiasis and to compare the outcome of treatment with topical clotrimazole and oral fluconazole.

4. Why have I been chosen?

You have been chosen after careful consideration that based on your complaints and laboratory test you have vulvovaginal candidiasis.

5. Do I have to take part?

Please note that participation in this research is entirely voluntary. Upon agreeing to take part in this study, you will be required to sign two consent forms, one of which will be for your own reference and record. You also have the option of withdrawing from the study at any time or stage, without the need to give reasons. If for any reason you decide to withdraw from the study before completion, your decision will not affect the quality of care you receive in any way.
6. What will happen to me if I take part?

If you agree to take part in this study, you will be assigned to a consulting room as was always previously done. After your visit, we will ask you to fill a very brief questionnaire that will last for about 10 minutes.

7. What do I have to do?

There are no special preparations you have to make upon agreeing to participate in this study.

8. What are the harms of participation?

No known harm is associated with taking part in the study. Those who are hypersensitive to any of the drugs in this study will be excluded from taking part. You will however be required to sacrifice part of your time for filling the questionnaire after the consultation. All information provided by you on the questionnaire cannot be linked to you, and I will accept the filled questionnaire in to a locked box that will be opened only at the end of the day, and no questionnaire can be linked to any one.

9. What are the benefits of participation?

This study will help by giving information about effectiveness of vulvovaginal candidiasis treatment using the drugs under study. These treatments are used by clinicians in AKTH but no study has been done to determine their comparative effectiveness and patients’ compliance. The
Findings will therefore help recommendations on acceptable treatment modality.

10. Payments

You will not be paid for participation in this study.

11. Use of the results of the study

At the end of the study, copies of the study findings will be submitted to the National Postgraduate Medical College of Nigeria and Aminu Kano Teaching Hospital, Kano. The study may be published in a journal purely for academic purposes only, and will be disseminated at scientific forums and conferences without identifying participants, and without providing any information that will lead to their individual identification.

12. Data handling and confidentiality

All information will be kept in secure pass-worded files only accessible to the principal investigator who will ensure anonymity before analysis. Analysed data will be checked again for both anonymity and confidentiality.

13. Who certified the safety of this study?
The study has been reviewed and approved by the Ethical Committee of Aminu Kano Teaching Hospital, and has been accepted as useful by the National Postgraduate Medical College of Nigeria.

Please do not hesitate to contact me if you have any further questions.

Thank you.

Dr. Ugwa Emmanuel Ajuluchukwu

Telephone: 08035851872

Email: drajulugreatgod@hotmail.com

APPENDIX B

CONSENT FORM

GENERAL CONSENT FORM

Title of Project: Outcome of treatment of vulvovaginal candidiasis in Aminu Kano Teaching Hospital (AKTH); A randomized controlled trial of topical clotrimazole and oral fluconazole.
Name of Researcher- Dr. Ugwa Emmanuel Ajuluchukwu, Department of Obstetrics and Gynaecology, Aminu Kano Teaching Hospital.

Telephone number: 08035851872;

E-mail: drajulugreatgod@hotmail.com

Please tick box

1. I have read the attached information sheets (or have appreciated the oral explanation) and I understand what will be required and what will transpire if I participate in the study

2. My questions concerning this study have been answered

3. I understand that at any time I may stop further participation in the study without giving reason(s) and without affecting my health care

4. I understand that my involvement is voluntary and that I am free withdraw at any time, without having to give any reason.

5. I understand that all information I will provide will be treated with outmost Confidentiality
6. I consent to participate in this study

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<th>Date</th>
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<table>
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Signed ____________________________ ………Date

| __________________________________________________________________________ |

APPENDIX C

QUESTIONNAIRE
Instruction: Tick clearly within the parenthesis as appropriate or specify where required.

SECTION ONE- BIODATA

Unit Number:…………………… Last Menstrual Period:……………………

Address: ……………………… Telephone
Number(GSM):…………………

1. Parity:…………………………


4. Age:…………………………


4. ( )Student 5.( )others……………………(specify)

7. Educational Status: 1.( )None 2.( )Qur’anic only 3.( )Primary 4.( )Secondary

5.( )Tertiary

SECTION TWO- HISTORY OF PRESENT COMPLAINTS

8. What are your present complaints?: 1.( )Cheese-like vaginal discharge 2.( )Vulval itching

3.( )Burning sensation 4.( )Vulval swelling 5.( )Vulval redness/excoriation

9. How long have you had the complaints?…………………………

10. How many times do you have the complaints in one year?…………………

11. How many times have you treated the complaints in one year?………………

12. Was the diagnosis made before treatment?: 1.( )Yes 2.( )No

13. Who treated you?: 1.( )patent medicine dealer-“chemist” 2.( )Traditional herbalist

14. Through which route was the treatment administered?: 1. ( )Mouth 2. ( )Inside the vagina 3. ( )Mouth and vagina at the same time 4. ( )Others………………………(specify)

15. Did you get relieved of your complaints?: 1. ( )Yes 2. ( )No 3. ( )Fairly

16. Was your husband treated with you?: 1. ( )Yes 2. ( )No

17. Did your husband have similar complaints?: 1. ( )Yes 2. ( )No


SECTION THREE- GYNAECOLOGICAL/CONTRACEPTIVE/SEXUAL HISTORY

20. At what age did you start menstruating?:…………………………

21. Did you have a regular monthly cycle?: 1. ( )Yes 2. ( )No

22. What is the duration of your menstrual period?:…………………………

23. How is your menstrual flow?: 1. ( )Normal 2. ( )Heavy 3. ( )Scanty

24. What premenstrual symptom do you have?:…………………………

25. Did you have abdominal/waist pain during menstruation?: 1. ( )Yes 2. ( )No

26. Have you done a dilatation/curettage (D/C) before?: 1. ( )Yes 2. ( )No

27. If your response to 26 above is yes, who did the dilatation/curettage for you?: 1. ( )Patent medicine dealer-“chemist” 2. ( )Traditional herbalist 3. ( )Laboratory scientist 4. ( )Pharmacist 5. ( ) 6. ( )Doctor

83
28. Mention complications you developed after the dilatation/curettage (if any)…………………………

29. Have you done cervical screening test (Pap smear) before?: 1.( )Yes 2.( )No

30. Do you usually wash your vagina with antiseptics?:  1.( )Yes 2.( )No

31. Have you any knowledge of contraception?:  1.( )Yes 2.( )No

32. Which of these methods have you used in the last six months or currently?:1.( )COCP (pills) 2.( )Condoms 3.( )Injectable 4.( )Douching 5.( )Tampoon 6.( )Spermicide

7.( )Loop

33. Are you sexually active?: 1.( )Yes 2.( )No

34. How many sexual partners do you have……………………..

SECTION FOUR- PAST MEDICAL/DRUG HISTORY

35. Do you have any medical conditions?..........................(specify)

36. Are you currently taking any drug?:………………………..(specify)

37. Do you have any history of drug allergy?………………………..(specify)

SECTION FIVE- POST-TREATMENT EVALUATION

37. What treatment route was administered to you?:  1.( )Oral floconazole  2.( )Topical clotrimazole

38. Describe your symptoms after using the medication: 1.( )Completely cured 2.( )Much improvement 3.( )Little improvement 4.( )No improvement 5.( )Worse

39. When did you start observing an improvement in your symptoms?: 1.( )1st day of treatment 2.( )2nd day 3.( )3rd day 4.( )4th day 5.( )5th day 6.( )6th day

40. If your symptoms completely disappeared state how long it took to happen:………………

41. If your symptoms re-occurred state how many days after treatment this occurred………

42. Please record number of days drug was not correctly taken(if any)…………………………
45. Why was drug not taken correctly?: 1.( )Forgot  2.( )Inconveniencing  3.( )Drugs are too much  4.( )It’s messy  5.( )My partner doesn’t like it  6.( )Side effects…………..(specify)

46. What was your major concern with the drug?: 1.( )Soils my underwear
   2.( )Nausea/vomiting  3.( )Diarrhoea  4.( )Abdominal discomfort/pain  5.( )Headache
   6.( )Dizziness  7.( )Sexual dissatisfaction  8.( )None

47. Indicate if you used any of the following during treatment:  1.( )Condoms
   2.( )Spermicide  3.( )Douching  4.( )COCP(pills)  5. Loop  6.( )None

48. How would you rate your satisfaction with the treatment?:  1.( )Excellent  2.( )Very good  3.( )Good  4.( )Fair  5.( )Poor

Thank you. Kindly return this questionnaire to the researcher as soon as it has been completed.