ASSESSMENT OF THE EFFECT OF HORMONAL CONTRACEPTIVES ON URINARY TRACT INFECTION IN WOMEN IN PORT HARCOURT

ABSTRACT

Increasing trend in unwanted pregnancy, economic factor, maternal-child and other health conditions are the rationales for fertility regulation and family planning; hence, an essential element of preventive care. However, contraception has been implicated with risk of Urinary Tract Infection (UTI) which is a cause of morbidity, mortality and great economic loss. This descriptive cross-sectional study investigated the bacteria associated with UTI in women on hormonal contraceptives in Rivers State. A total of 250 subjects grouped as contraceptive users and controls were recruited excluding those who did not consent, less than 18 years of age as well as those pregnant or on treatment for UTI using well-structured questionnaire. Blood and urine samples were collected and analyzed following standard microbiological methods. Estimation of the Progesterone and estradiol as done using Enzyme Linked Immunosorbent Assay method. The result obtained in this study revealed prevalence of 80% and 20% for contraceptive users and control subjects respectively. The predominant uropathogens isolated include;*Esherichia. coli* (55.6%), *Klebsiella* spp (17.6%), *Staphylococcus auerus* (3.2%), *Pseudomonas* spp (2.0%) and *Staphylococcus*Spp (1.6%). *E. coli* was the most prevalent and *Staph*Sppthe least prevalent pathogen. UTI was significantly correlated with the use of contraceptives. The study therefore suggests that contraceptive users be routinely checked for urinary tract infection.

Keywords: Contraceptives, Hormones, Urinary tract infection, Bacteria.

Introduction

The negative impact of fertility rate on ladies and their kids and the advantages of richness control are becoming worrisome. Too many or too closely spaced pregnancies, pregnancies of a woman at too young or too old an age, give rise to health risks with associated higher maternal and neonatal mortality rates to both mothers and the infants (1). These elements, among others, give wellbeing method of reasoning to richness guideline and family planning, which is presently viewed as a fundamental component of preventive medical care. The advantages of fertility guideline identify with a more extensive issue of the status of women. The capacity of a woman to control her very own fruitfulness is one of her essential and critical rights. It is presumed that better-regulated sexuality and fertility affects the status of women socially and economically.

This is perceived to be reflected in their educational, health, and economic status coupled with independence to take decisions on their role and be responsible for the total well-being (1).

Among the most common infectious diseases, urinary tract infections (UTIs) are commonly encountered diseases in developing countries which are estimated to affect at least 250 million all around the world each year (2). UTIs refer to the presence of microbial pathogens within the urinary tract and it is usually classified by the infection site:-bladder (cystitis), kidney (pyelonephritis), or urine (bacteriuria) and also can be asymptomatic or symptomatic, UTIs that occur in a normal genitourinary tract with no prior instrumentation are considered as "uncomplicated," whereas "complicated" infections are diagnosed in genitourinary tracts that have basic or practical irregularities, including instrumentation, for example, inhabiting urethral catheters, and are much of the time asymptomatic(3). It has been estimated that globally symptomatic UTIs result in as many as 7 million visits to outpatient clinics, one million visits to emergency departments, and 100,000 hospitalizations every year (4). Urinary tract infections have been linked to several predisposing factors. The effect of hormonal contraceptive as one of the factors is scarcely documented. Hormonal contraceptives are compelling at counteracting unintended pregnancy (4b). Between zero to nine in every hundred individuals depending on these will get pregnant through the span of a year, contingent upon which type of hormonal prophylactic they use (4b). This number is lower in individuals who utilize hormonal contraceptives superbly. In an examination, 18 of every 100 individuals depending on male condoms will get pregnant through the span of a year (4b). The implantable bar, or simply the embed, is the best type of hormonal preventative (4b) and is normally put in your arm by your social insurance supplier. Under one of every hundred individuals utilizing this strategy will get pregnant throughout a year (4b).

Strategies for contraception can be named non-hormonal or hormonal. Non-hormonal types of contraception, similar to condoms or the copper intrauterine gadget (IUD), don't change the regular dimensions or elements of hormones inside the body.

Notwithstanding, hormonal contraceptives change the ordinary dimensions of estrogen, progesterone, just as different hormones

There is, therefore, the need to scientifically establish the relationship between hormonal contraception and UTI. The information from this study will aid individuals and health caregivers on better ways of managing women on hormonal contraceptive to avoid the inherent risk associated with such infections. It will also assist in shaping government policies and guidelines in treatment, prevention and control of urogenital infections among women using

contraceptives in Port Harcourt, and beyond. The aim of this study was to determine the effect of hormonal contraceptives on urinary tract infection in women in Port Harcourt, Nigeria.

Materials and Methods

Study design: The study was a (descriptive) study that employed a cross-sectional approach, blood and urine specimens were collected following standard microbiological methods, for the assessment of the effect of hormonal contraceptives on urinary tract infection in women in Port Harcourt. There were two groups of subjects; 200 of those using hormonal birth control contraceptives (test subjects) and 50 of those not using birth control contraceptives at all (control subjects) who have met the set inclusion criteria. Women undergoing treatment for UTI or pregnant as at the time of the study were excluded from this study. Diabetic patients, patients experiencing vaginal discharge, dysuria, lower abdominal pains, loin pains; patients identifying with antimicrobial use during the previous 14 days; patients who have participated in sexual intercourse within the last 24 hours and those hospitalized during the four weeks before enrolment, were excluded from the study.

Ethical approval: this was obtained from the Rivers State Hospital Management Board, Rivers State University Teaching Hospital and University of Port Harcourt Teaching Hospital ethical committees before the commencement of the study.

Informed written consents were obtained from participants who met the inclusion criteria.

Sample collection: Blood and clean-catch mid-stream urine samples were obtained from consenting subjects for analysis using standard laboratory methods. Venipuncture blood (3ml) was collected into plain (anti-coagulant-free) bottles. The site of the venipuncture was swabbed

with 70% alcohol. A tourniquet was tied on the forearm and a venipuncture was carried out. Approximately 10 ml of urine was collected. The blood and urine samples collected were transported to the laboratory for hormones estimation and urine culture. Clinical data and laboratory values were collected using the procedure as stated above with well-structured questionnaire

Analytical procedures: Urine culture in CLED, Gram staining, Biochemical tests were done. All urine samples were cultured on Cysteine Lactose Electrolyte Deficient Agar (CLED) and incubated at 37^0C for 24 hours. Pure cultures of all isolates were obtained and biochemical tests are done to identify the isolates. The confirmation of various microorganisms isolated was achieved by Gram staining procedure and Biochemical tests which include: catalase test, coagulase test, indole test, oxidase test, citrate test, urease test and motility test.

Estimation of Estradiol (Performed ELISA) and Estimation of Progesterone (Performed ELISA) were performed. The following materials were used: Enzyme-Linked Immunosorbent Assay Machines, Apdia Reader (AD Touch), Apdia washer (AD Wash), Apdia shaker/incubator, Perfemed ELISA reagents (Lot No.: 118021403) for estradiol, Perfemed ELISA reagent (Lot No.: 118020704) for progesterone, Capp pipette ,Agar and other culture materials and Biochemical test kits

Statistical Analysis: The data collected from this study was analyzed using predictive Statistical Package for Social Sciences (SPSS IBM version 21). Prevalence rate, odd ratio, were estimated. Discrete variables were expressed as percentages and proportions were compared using the Chi-square test. Statistical significance difference was considered at the value of $p<0.05$ while quantitative data were analyzed using t-test and ANOVA, regression, following a parametric test for normal distribution using S-K test with $p>0.05$ as normally distributed.

Results

This study included a total of 250 female subjects categorized into two of which 80% were contraceptive users test subjects and 20% non-contraceptive users (control subjects)respectively. The study subjects had a mean age of 35.48±5.237 and a greater percentage of the study participants were mainly married 233 (92%). Also, 139 (55.6%) were professionals/skilled in terms of occupation with 167 (66.8%) tertiary level education; only 7 (2.8%) had no formal education. In addition, the bacteria count showed that 181 (72.4%) had counts <105 CFU/ml while 69 (27.6%) had count ≥105cfu/ml respectively. Basically, five different species of bacteria were isolated namely; *Escherichia coli, Klebsiella* spp, *Pseudomonas* spp, *Staphylococcus* spp and *Staphylococcus auerus with a bacteria* frequency *of* 169 (67.6%), 58 (23.2%), 6 (2.4%), 6 (2.4%) and 11 (4.4%)

Table 1 shows the prevalence of UTI in the study population. 65 (26.0%) subjects of the contraceptive users were positive while the non-contraceptive users were 4 (1.6%) subjects. The prevalence of 69 (28.0%) and 181 (72.4%) was recorded for positive and negative respectively.

Table 1: Prevalence of Urinary Tract Infection among Study Population

	Population	Number Positive (%)	Number Negative (%)	X^2value	DF	P-value
Contraceptive users	200	65 (26.0%)	135			
Non-contraceptive Users	50	4 (1.6%)	46	12.016	1	0.00
Total	250	69	181			

Table 2 shows the prevalence of the risk factor. Of all the subjects 24.0% were married, while 2.0% were either separated or divorced. As regards to the occupation distribution, the highest prevalence was recorded within the skilled/professional subjects which amounted to 14.8% for users and 0 (0%) non-users. 19.2% of the study population for users and 1.6% for non-users had tertiary education.

Table 2: Prevalence of Risk Factors

Variables	Classification (N=250)	Contraceptive users Prevalence (%)	Non-contraceptive users prevalence (%)
	Single	0.0	0.0
Marital status	Married	24.0	1.6
	Separated/ divorced	2.0	0.0
	20 - 29 years	2.4	0.4
	30 - 39 years	16.4	1.2
Age	40 - 49years	7.2	0.0
	50 years and above	0	0.0

	Student/ Applicants	0.0	0.8
	Public/ Civil servants	4.8	0.8
Occupation	Skilled/professional	14.8	0.0
	Business	4.4	0.0
	Unskilled	2.0	
	No formal education	0.4	0.0
Education	Primary	0.4	0.0
	Secondary	6.0	0.0
	Tertiary	19.2	1.6

Table 3 present the age-related occurrence of the study population. The study revealed that 44% of the study population was between the age bracket of 30 - 39 years for both users and non-users, while 7% of the population fell between the age brackets of 20-29 years respectively. The chi-square distribution showed no evidence of a statistically significant relationship.

Table 3: Age Related Occurrence

Age group	Control	contraceptive	Total Users	X^2 value	DF	P-value	remarks
20 - 29 years	1 (14.29%)	6(85.71)	7(100%)				
30 - 39years	3 (6.82%)	41(93.18%)	44(100%)				
40 - 49 years	0 (0.0%)	18(100%)	18(100%)	1.037	3	0.59	N/S
50 years & above	0(0.0%)	0(0.0%)	0(0.0%)				
Total	4(5.79%)	65(94.20%)	69(100%				

Table 4 illustrates the percentage of occurrence of isolates in the study population. *E.coil* had the highest occurrences for both (contraceptive users and non -users) groups with 69.57% while *staph auerus* had the lowest of 1.45%.

Table 4: Percentage Occurrence of Isolate among Study Population

S/N	Isolates	Contraceptive Users (%)	Non-contraceptive Users (%)	Total
1	*E.coil*	46 (66.67%)	2 (2.89%)	48 (69.57%)
2	*Kleb*.spp	14 (20.29%)	1 (1.45%)	15 (21.74%)
3	*Pseudo*.spp	1 (1.45%)	0 (0.0%)	1 (1.45%)
4	*Staph*.spp	3 (4.35%)	1(1.45%)	4(5.79%)
5	*Staph. auerus*	1(1.45%)	0(0.0%)	1(1.45%)
Total		65(94.21%)	4(5.79%)	69(100%)

E.coli= *Escherichia coli*

Kleb spp = *Klebsiella pneumoniae*

Pseudo spp = *Pseudomonas aeruginosa*

Staph spp = coagulase negative Staphylococcus

Staph aureus = *Staphylococcus aureu*

Table 5: relationship between Hormonal contraceptives (Progesterone and Estradiol) and bacterial count

Variables	X^2	DF	P-value	Remark
Progesterone * Bacterial count	3.450	2	>0.05	Non-significant
Estradiol * Bacterial count	-0.052	2	0.05	Non-significant

Discussion: UTI among women has been a subject of revolving research interest over the past decade because of its high prevalence (3). This research was centred on investigating the urinary tract infection

in a relationship with hormonal estrogen and progesterone levels in women using such as birth controls. This result had shown, however, that there is a high incidence of Gram-negative enterobacteria infection among women using hormonal contraceptives compared to those that do not use hormonal contraceptives. There was also an observed high incidence of *Escherichia coli* infection among this study group compared to the control group. This is in consonance with the report of Takasashi and Loveland (2014) (5) but there was an observed five per cent (5%) increased rate to that study. Also, this may have been the case due to the fact that the use of hormonal contraceptives according to Walter, (2011) (6), has made the lower vaginal and periurethral areas vulnerable to infection due to the exacerbating effect of these contraceptives.

Furthermore, the high incidence of urinary tract infection among women using hormonal contraceptive may have been facilitated by the underlying mechanism of contraception which was described by Johnson *et al*. (2017)(7) to contribute to the process of vulnerability since there is repressive ovulation, thickening of cervical mucus, variation in muscle tone and cervical endometrium. This position was also held by Remis *et al*. (2007) (8) with significant correlation established between urinary tract infection and contraceptives usage. Foxman and Frerichs (2015)(9) had also held strongly that there is association between UTI & contraceptive use Nevertheless, despite the above correlation, this phenomenon could be also be attributed to some socio-demographic statistics like history of contraceptive usage, antibiotic usage as a method of contraception as well as age and progesterone levels (table 5). The risk estimates obtained from this study which reportedly did not attribute individual disparities like demographics with urinary tract infection.

Age distribution of infection among the studied population was observed to have no significant difference with $p>0.05$ while the highest prevalence was seen among the young and mid-adult

(30-39years & 40-49years) population. This was comparable with the reports of Kazi (10). Although, in contrast to this present study that had *Escherichia coli* as the most prevalent pathogen, Kazi (10) reported *Lactobacillus fermentum* as the most population prevalent pathogen among their studied population. However, this study is in conformity with the conclusion which affirmed that the infection rate was related to the use of contraceptive and age (11).

Similarly, an attempt to evaluate hormonal relationships with the isolates showed that in this study, there was observed a significant marked disparity in the prevalence of each isolated pathogen among contraceptive users and the control subjects. Similarly, there was observed a five increase in the risk of contracting urinary tract infection for those exposed to contraceptive usage compared with non - contraceptive users (controls) (12,9).

Vaginal colonization with *E. coli* as significantly higher in contraceptive users (13), this is evident in the high rate of *E.coli* isolated in this study. In the same way, another study (14) observed *E.coli* as the most predominantly isolated uropathogen in their study despite the fact that the prevalence rate of *E.coli* is less than the one noted in this study. Another study also showed high colonization of the vagina with bacteria and a marked prevalence of *E.coli* similar to what was observed in this study (15).

In addition, this present study is contrary to another study which reported a low prevalence (5), this could, however, be due to the selection and diagnostic criteria that backed the study. Nonetheless, Takahashi & Loveland (2014) share agreement in the type of organisms isolated revealing *Escherichia coli* and the absence of effect of period/duration of contraceptive on the risk of urinary tract infection among contraceptive users. This present study reported a higher prevalence of urinary tract infections than a previous work done in the same region for both contraceptive users and control subjects (16).

Gram-positive bacteria isolated in this study had low prevalence and mainly *Staphylococcus* species (*Staphylococcus arueus and other Staphylococcus* spp). The prevalence of Gram-positive organisms, as well as *Staphylococcus arueus and other Staphylococcus* sppobtained in this study, showed less than ten per cent as opposed to the account of Seifu and colleague (2018)(14) which is about twenty per cent. A different study also reported similar isolates (*E.coli and Staph.* spp) with high frequency in their study (10).

The high infection rate and prevalence of urinary tract infections seen in this study can be explained by the susceptibility ofthe female reproductive system to microorganisms thus, a good pointer apart from the use of contraceptives. On the other hand, the use of contraceptive has made the lower vaginal and periurethral areas vulnerable to infection due to the exacerbating effect of these contraceptives (6). The underlying mechanism of contraception on causation of urinary tract infection shows that repressive ovulation, thickening of cervical mucus, variation in muscle tone and cervical endometrium all contributes to the process of vulnerability to microbes as published by one of the researchers in this area of study(7). This biological plausibility established the rationale behind the increased risk of urinary tract infections among contraceptive user with a considerable indication.

Further investigation revealed an association of UTI (measured using the bacteria count) with contraceptive use was statistically significant with the exception of the type of pathogens isolated, this association is synonymous to the study of Paul and Precious (2011)(16) which reported contraception as a predisposing factor of urinary tract infection. Similarly, there was a report of an extensive association between urinary tract infections with contraception even after controlling for confounders (8).

Conclusion: Contraception is beneficial with an inherent risk of urinary tract infections for users as established in this study. Generally, urinary tract infections were highly prevalent in the study population and more prevalent among contraceptives users. Age distribution had no influence on the risk of urinary tract infections.

Conflict of interest: there was no conflict of interest in this study.

Ethical approval: this was obtained from the Rivers State Hospital Management Board, Rivers State University Teaching Hospital and University of Port Harcourt Teaching Hospital ethical committees before the commencement of the study.

Informed written consents were obtained from participants who met the inclusion criteria.

REFERENCES

1. Akani CI, Enyindah CE, Babatunde S. Emergency contraceptives, knowledge and perception of female undergraduates in the Niger Delta of Nigeria. Ghana Medical Journal. 2008; 42(2): 68-70.
2. Gonzalez CM, Schaeffer AJ. Treatment of urinary tract infection, what is old and what is new?. World Journal of Urology. 1999; 17(6): 372-382.
3. Stamm WE, Hooton TM. Management of urinary tract infection in adults. New England Journal of Medicine. 1993; 329: 1328-1334.
4. Wilson MI, Giado L. Laboratory diagnosis of urinary tract infection. Clinical Infectious Diseases. 2004; 38: 1150-1151.

Centers for Disease Control and Prevention. (2016). Reversible methods of birth control. Retrieved on November 29, 2016 fromhttps://www.cdc.gov/reproductivehealth/contraception/

5. Takasashi M, Loveland DB. Bacteriuria and oral contraceptives routine health examination of middle case women. Journal of American Association. 2014; 227(7): 762-765.

6. Walter ES. Urinary tract infections and pyelonephritis. In: Braunwald E, Hauser S, Longo D, Kasper D, Jameson L, editors. Harrison's Principles of Internal Medicine. 15th ed. New York: McGraw-Hill; 2011, Pp 1620-1625.

7. Johnson JV, Gurb GS, Constantine GD. Endometrial histology following 1 year of continuous daily regimen of levonorgesterol 90µg/ethiny/estradiol 20µg. Contraception. 2017; 75:23-26.

8. Remis RS, Gurwith MJ, Gurwith D, Hargrett-Bean NT, Layde PM. Risk factors for urinary tract infection. American Journal of Epidemiology. 2007; 126(4): 685-694.

9. Foxman B, Frerichs RR. Epidemiology of urinary tract infections: Incidence, morbidity and economic costs. American Journal of Public Health. 2015; 75(11): 1308-1313.

10. Kazi YF, Saleem S, Kazi, N. Investigation of Vaginal microbiota in sexually active women using hormonal contraceptives in Pakistan. Urology. 2012; 12: 22-23.

11. Julius S, Eileen S, Moncade J. Screening of chlamydial infections in women attending family planning clinics – Evaluation of presumptive indicators of therapy. West Journal of Medicine. 2009; 138(3): 375-379.

12. Townsend MK, Curhan GC, Resnick NM, Grodstein F. Oral contraceptives use and incident urinary incontinence in premeno pausal women. Journal of Urology. 2014; 2175-2176.

13. Fihn SD, Latham RH, Roberts P, Running K, Stamm WE. Association between diaphragm use and urinary tract infection. Journal of America Medical Association. 2015; 254(2): 240-245.

14. Seifu WD, Gebissa AD. Prevalence and antibiotic susceptibility of uropathogens from cases of urinary tract infections in shashemene referral hospitals, Ethiopia. Biomedical Central Journal of Infectious Diseases. 2018; 18(1):30-31.

15. Percival-Smith R, Bartlett KH, Chow AW. Vaginal colonization of *Escherichia coli* and its relation to contraceptive methods. Contraception. 2013; 27(5): 497-504.

16. Paul OD, Precious KG. contraception as a risk factor for urinary tract infection in Port Harcourt, Nigeria: A case control study. African Journal of Primary Health Family Medicine. 2011; 3(1): 207-208.

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