

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

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

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

61

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

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

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

71 **Materials and Methods**

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

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

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

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

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

95 **Analytical procedures:** Urine culture in CLED, Gram staining, Biochemical tests were done. All urine
96 samples were cultured on Cystein Lactose Electrolyte Deficient Agar (CLED) and incubated at 37°C for 24
97 hours. Pure cultures of all isolates were obtained and biochemical tests done to identify the isolates.
98 The confirmation of various microorganisms isolated was achieved by Gram staining procedure
99 and Biochemical tests which include: catalase test, coagulase test, indole test, oxidase test, citrate
100 test, urease test and motility test.
101

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

107
108 **Statistical Analysis:** The data collected from this study was analyzed using predictive Statistical
109 Package for Social Sciences (SPSS IBM version 21). Prevalence rate, odd ratio, were estimated.
110 Discrete variables were expressed as percentages and proportions were compared using the Chi-
111 square test. Statistical significance difference were considered at value of $p < 0.05$ while
112 quantitative data were analyzed using t-test and ANOVA, regression, following a parametric test
113 for normal distribution using S-K test with $p > 0.05$ as normally distributed.

114

115 **Results**

116 This study included a total of 250 female subjects categorized into two of which 80% were
117 contraceptive users test subjects and 20% non-contraceptive users (control subjects) respectively.

118 The study subjects had a mean age of 35.48 ± 5.237 and greater percentage of the study
119 participants were mainly married 233 (92%). Also, 139 (55.6%) were professionals/skilled in
120 terms of occupation with 167 (66.8%) tertiary level education; only 7 (2.8%) had no formal
121 education. In addition, the bacteria count showed that 181 (72.4%) had counts <105 cfu/ml while
122 69 (27.6%) had count ≥ 105 cfu/ml **respectively**. Basically, five different species of bacteria were
123 isolated namely; *Escherichia coli*, *Klebsiella* spp, *Pseudomonas* spp, *Staphylococcus* spp and
124 *Staphylococcus auerus* with a bacteria frequency of 169 (67.6%), 58 (23.2%), 6 (2.4%), 6
125 (2.4%) and 11 (4.4%)

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

129 Table 1: Prevalence of Urinary Tract Infection among Study Population

130	Population	Number	Number	X ² value	DF	P-value
131		Positive (%)	Negative (%)			
132						
133	Contraceptive users	200	65 (26.0%)	135		
134	Non-contraceptive	50	4 (1.6%)	46	12.016	1 0.00
135	Users					
136	Total	250	69	181		

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

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155 Table 2: Prevalence of Risk Factors

156	Variables	Classification (N=250)	Contraceptive users	Non-contraceptive
157	users		Prevalence (%)	prevalence (%)
158				
159		Single	0.0	0.0
160	Marital status	Married	24.0	1.6
161		Separated/ divorced	2.0	0.0
162		20 - 29 years	2.4	0.4
163		30 - 39 years	16.4	1.2
164	Age	40 - 49years	7.2	0.0
165		50 years and above	0	0.0

166				
167		Student/ Applicants	0.0	0.8
168		Public/ Civil servants	4.8	0.8
169	Occupation	Skilled/professional	14.8	0.0
170		Business	4.4	0.0
171		Unskilled	2.0	
172				
173		No formal education	0.4	0.0
174	Education	Primary	0.4	0.0
175		Secondary	6.0	0.0
176		Tertiary	19.2	1.6
177	<hr/>			
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179

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

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186 Table 3: Age Related Occurrence

187	Age group	Control	contraceptive	Total	X ² value	DF	P-value	
188	remarks			Users	Occurrence			
189	20 - 29 years	1 (14.29%)	6(85.71)	7(100%)				
190	30 - 39years	3 (6.82%)	41(93.18%)	44(100%)				
191	40 - 49 years	0 (0.0%)	18(100%)	18(100%)	1.037	3	0.59	N/S
192	50 years & above	0(0.0%)	0(0.0%)	0(0.0%)				
193	Total	4(5.79%)	65(94.20%)	69(100%)				

194

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

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200 Table 4: Percentage Occurrence of Isolate among Study Population

201	S/N	Isolates	Contraceptive Users (%)	Non-contraceptive Users (%)	Total
202					
203	1	<i>E.coil</i>	46 (66.67%)	2 (2.89%)	48 (69.57%)
204	2	<i>Kleb.spp</i>	14 (20.29%)	1 (1.45%)	15 (21.74%)
205	3	<i>Pseudo.spp</i>	1 (1.45%)	0 (0.0%)	1 (1.45%)
206	4	<i>Staph.spp</i>	3 (4.35%)	1(1.45%)	4(5.79%)
207	5	<i>Staph. auerus</i>	1(1.45%)	0(0.0%)	1(1.45%)
208		Total	65(94.21%)	4(5.79%)	69(100%)

209 *E.coli*= *Escherichia coli*

210 *Kleb spp* = *Klebsiella pneumoniae*

211 *Pseudo spp* = *Pseudomonas aeruginosa*

212 *Staph spp* = coagulase negative Staphylococcus

213 *Staph aureus* = *Staphylococcus aureu*

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

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

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221 **Discussion:** UTI among women has been a subject of revolving research interest over the past decade

222 because of its high prevalence (3). This research was centered on investigating the urinary tract infection

223 in relationship with hormonal estrogen and progesterone levels in women using such as birth controls.
224 This result had shown, however, that there is high incidence of Gram negative enterobacteria infection
225 among women using hormonal contraceptives compared to those that do not use hormonal
226 contraceptives. There was also an observed high incidence of *Escherichia coli* infection among this study
227 group compared to the control group. This is in consonance with the report of Takasashi and Loveland
228 (2014) (5) but there was an observed five percent (5%) increased rate to that study. Also, this may have
229 been the case due to the fact that, the use of hormonal contraceptives according to Walter, (2011) (6),
230 has made the lower vaginal and periurethral areas vulnerable to infection due to the exacerbating effect
231 of these contraceptives.

232 Furthermore, the high incidence of urinary tract infection among women using hormonal
233 contraceptive may have been facilitated by the underlying mechanism of contraception which
234 was described by Johnson *et al.* (2017)(7) to contribute to the process of vulnerability since there
235 is repressive ovulation, thickening of cervical mucus, variation in muscle tone and cervical
236 endometrium. This position was also held by Remis *et al.* (2007) (8) with significant correlation
237 established between urinary tract infection and contraceptives usage. Foxman and Frerichs
238 (2015)(9) had also held strongly that there is association between UTI & contraceptive use
239 Nevertheless, despite the above correlation, this phenomenon could be also be attributed to some
240 socio-demographic statistics like history of contraceptive usage, antibiotic usage as a method of
241 contraception as well as age and progesterone levels. The risk estimates obtained from this study
242 which reportedly did not attribute individual disparities like demographics with urinary tract
243 infection.

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

246 (30-39years & 40-49years) population. This was comparable with the reports of Kazi (10).
247 Although, in contract to this present study that had *Escherichia coli* as the most prevalent
248 pathogen, Kazi (10) reported *Lactobacillus fermentum* as the most population prevalent pathogen
249 among their studied population. However, this study is in conformity with the conclusion which
250 affirmed that the infection rate was related to the use of contraceptive and age (11).
251 Similarly, an attempt to evaluate hormonal relationships with the isolates showed that in this
252 study, there was observed a significant marked disparity in the prevalence of each isolated
253 pathogen among contraceptive users and the control subjects. Similarly there was observed a five
254 increase in the risk of contracting urinary tract infection for those exposed to contraceptive usage
255 compared with non - contraceptive users (controls) (12,9).
256 Vaginal colonization with *E. coli* as significantly higher in contraceptive users (13), this is
257 evident in the high rate of *E.coli* isolated in this study. In the same way, another study (14)
258 observed *E.coli* as the most predominantly isolated uropathogen in their study despite the fact
259 that the prevalence rate of *E.coli* is less than the one noted in this study. Another study also
260 showed high colonization of the vagina with bacteria and a marked prevalence of *E.coli* similar
261 to what was observed in this study (15).
262 In addition, this present study is contrary to another study which reported a low prevalence (5),
263 this could however be due to the selection and diagnostic criteria that backed the study.
264 Nonetheless, Takahashi & Loveland (2014) share agreement in the type of organisms isolated
265 revealing *Escherichia coli* and the absence of effect of period/duration of contraceptive on risk of
266 urinary tract infection among contraceptive users. This present study reported a higher
267 prevalence of urinary tract infections than a previous work done in same region for both
268 contraceptive users and control subjects (16).

269 Gram positive bacteria isolated in this study had low prevalence and mainly *Staphylococcus*
270 species (*Staphylococcus aureus* and other *Staphylococcus* spp). The prevalence of Gram positive
271 organisms, as well as *Staphylococcus aureus* and other *Staphylococcus* spp obtained in this study
272 showed less than ten percent as opposed to the account of Seifu and colleague (2018)(14) which
273 is about twenty percent. Different study also reported similar isolates (*E.coli* and *Staph.* spp)
274 with high frequency in their study (10).

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

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

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

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

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