Uropathogens of Urinary Tract Infection in Pregnancy and Maternal-Fetal Outcomes at the Douala Referral Hospital, Cameroon: A Case-Control Study

Thomas Obinchemti Egbe¹,²*, Njimanted Omarine³, Essome Henri⁴,⁵, Wague Wague Christiane Dayas Francine⁶, Doretta Nzele Egbe⁴, George Enonchong Enow-Orock⁶

¹Faculty of Health Sciences, University of Buea, Buea, Cameroon
²Department of Obstetrics and Gynecology, Douala Referral Hospital, Douala, Cameroon
³Faculty of Health Sciences, University of Bamenda, Bamenda, Cameroon
⁴Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon
⁵Department of Obstetrics and Gynecology, Laquintinie Hospital Douala, Douala, Cameroon
⁶Department of Pathology, Faculty of Health Sciences, University of Buea, Buea, Cameroon

Email: *toegbe@gmail.com, *obinchemti@yahoo.com, omarinenlinwe@yahoo.com, essometocky@yahoo.com, waguedayas237@gmail.com, dorettaegbe@gmail.com, enoworock24@yahoo.com

Abstract

Background: Urinary tract infection (UTI) is common in pregnancy and accounts for a high burden of maternal and perinatal morbidity/mortality and health expenditure. The burden of this condition has been understudied in Cameroon. We aimed to determine the uropathogens of urinary tract infection in pregnancy, and the maternal-fetal outcomes of UTI at the Douala Referral Hospital. Methods: We conducted an analytic matched case-control study of 206 pregnant women with evidence of urinary tract infection (103 cases) and those without (103 controls) who underwent antenatal care and gave birth at the DRH from January 2019 to April 2019. Socio-demographic, laboratory and maternal-fetal outcome data were collected using a pre-tested structured questionnaire and analyzed with SPSS version 23. Statistical significance was set at p < 0.05. Results: Escherichia coli (51.5%), Proteus mirabilis (15.5%), Staphylococcus aureus (11.7%) and Klebsiella sp. (6.8%) were the predominant uropathogens of UTI. Maternal outcomes of UTI were puerperal pyelonephritis (AOR 3.1; 95% CI: 1.11 - 3.55, p = 0.0023), preterm labor (AOR 4.4; 95% CI: 1.0 - 2.7, p = 0.008) and preterm birth (AOR 4.6; 95% CI 1.9 - 22.9, p = 0.05). Furthermore, low birth weight (AOR 2.1; 95% CI: 0.8 - 5.6, p = 0.05),
neonatal infection (AOR 13; 95% CI: 0.9 - 191.6, p = 0.04) and neonatal intensive care unit admission (AOR 2.5; 95% CI: 1.7 - 3.6, p = 0.003) were fetal outcomes of UTI. Conclusion: Escherichia coli was the main uropathogenic agent of UTI during pregnancy. Maternal outcomes of UTI were puerperal pyelonephritis, preterm labor and delivery while fetal outcomes include: low-birth weight, neonatal infection and neonatal intensive care admission. Prompt diagnosis of this condition is the cornerstone to avoid adverse outcomes.

Keywords
Escherichia coli, Urinary tract Infection, Maternal-Fetal Outcomes, Neonatal Infection, Neonatal Intensive Care

1. Background
Urinary tract infection (UTI) is a common clinical problem and is an infection caused by the presence and growth of microorganisms in the urinary tract and may involve the lower urinary tract or both the lower and upper urinary tracts [1]. Anatomically the infection can involve the urethra, bladder and kidney. It affects all age groups but women are more susceptible than men due to their short urethra, absence of prostatic secretion, pregnancy and easy contamination of the urinary tract with fecal flora [2]. Urinary tract infection and its associated complications are the cause of nearly 150 million deaths per year worldwide and the disease can develop in 40% - 50% of women and 5% of men [3]. UTI is the second common infection occurring during pregnancy [4].

UTI’s are usually sub-divided into asymptomatic bacteriuria (ASB), which can lead to the development of cystitis and pyelonephritis and symptomatic bacteriuria (SB). Asymptomatic bacteriuria is defined as the presence of significant bacteriuria without symptoms of acute urinary tract infection [5]. Symptomatic urinary tract infections are divided into the lower urinary tract (acute cystitis) or upper urinary tract (acute pyelonephritis) infections. Cystitis is defined as significant bacteriuria with associated bladder mucosal invasion, whereas pyelonephritis is defined as significant bacteriuria with associated inflammation of the renal parenchyma, calyces and pelves [6].

Several microorganisms have been associated with UTI although Escherichia coli is the most frequent accounting for 80% to 90% of UTI’s in pregnancy. Other agents responsible for UTI are Proteus mirabilis, Klebsiella sp., Staphylococcus saprophyticus, and Staphylococcus aureus, etc. [7]. UTI or neglected asymptomatic bacteriuria has significant fetal morbidity including intrauterine growth restriction (IUGR), neonatal sepsis, preterm labor, prematurity, acute respiratory distress, mental retardation and fetal death and maternal morbidities like anemia, sepsis, acute pyelonephritis, renal failure and preeclampsia [8]. UTI is therefore associated with high neonatal morbidity and mortality as well as maternal morbidity and mortality especially in low resource settings.
The diagnosis of UTI is usually based on clinical suspicion (urinary frequency, dysuria, fever, rigors etcetera) and confirmed by urine culture and antimicrobial susceptibility testing (gold standard) or the new technologies such as high-throughput DNA sequence-based (HTS) analyses, should be used in order to improve antenatal screening of pregnant women [9].

Urinary tract infections are the most common infections in hospitals causing several complications including death [4]. There is a paucity of data regarding the uropathogens and the maternal-fetal outcomes of UTI in pregnancy in Cameroon. Therefore, there is need to conduct additional studies that will identify the uropathogens causing UTI and the maternal-fetal outcomes. This study will provide baseline data wherein valuable information will be used to improve the management of pregnant women with urinary tract infection especially in Cameroon where many laboratories are not equipped to do specimen cultures and antibiotic susceptibility testing and where the syndromic approach in diagnosis and treatment is the mainstay in many centres despite its pitfalls [10].

The goal of this study is to reduce perinatal and maternal morbidity/mortality and prevent further complications both on the babies and the mother in future pregnancies. We, therefore, asked the following research questions:

1) What are the pathogens that cause urinary tract infection at the Douala Referral Hospital?

2) What are the maternal-fetal outcomes of UTI among pregnant women at the Douala Referral Hospital?

We hypothesize that the uropathogens of urinary tract infection are polymicrobial and that there are severe unidentified maternal-fetal outcomes of UTI amongst pregnant women at the DRH.

The objectives of this study were to determine the uropathogens of UTI and the maternal-fetal outcomes of UTI among pregnant women at the Douala Referral Hospital, Cameroon.

2. Materials and Methods

2.1. Study Design and Duration

This was a hospital-based matched case-control study of files of patients from January 1, 2019, to April 30, 2019. We studied patient's files from January 1, 2014, to December 31, 2018.

2.2. Study Area and Setting

We enrolled for study, participants who came for antenatal care at the outpatient unit and those admitted at the maternity of the Douala Referral Hospital.

The DRH is a tertiary care health facility that offers emergency obstetrics care, scientific treatment, teaching and research to a population of over three million inhabitants of the Littoral region and its environs. The hospital is located in Douala, an urban town, and also the economic capital of Cameroon. The Obstetrics and Gynecology department offers the following services: outpatient con-
sultations, antenatal care (ANC), hospitalization, labor, delivery and gynecologic and obstetric surgery including laparoscopic and hysteroscopic surgery and colposcopy. The service is made up of eight obstetricians and gynecologists, one general medical practitioner and 39 midwives and nurses/assistant nurses. The outpatient department receives over 300 patients per week. There are thirty beds that assure in-service admission care of patients that are shared as eight common rooms and six private rooms and a nurse’s station. The labor room has four beds and there are two delivery rooms totaling two beds and a room for neonatal resuscitation. Averagely, there are 1250 births per year in the service.

The neonatology unit has a capacity of ten incubators, and there are six pediatricians and 15 specialized nurses that take charge of the neonatal intensive care unit. The service runs 24/7 and there is always one obstetrician/gynecologist and one pediatrician that take charge of call duties.

2.3. Study Population

Files of pregnant women who came to the outpatient unit and those admitted to the maternity of the DRH were enrolled for the study.

Inclusion criteria

- Cases were files of consenting pregnant women who came for antenatal care and those admitted or gave birth at the maternity of the DRH and had a positive diagnosis of urinary tract infection by urine culture during the period of study.
- Controls were also files of consenting pregnant women without symptomatic/asymptomatic UTI with negative urine culture at the OPD and those admitted or gave birth at the maternity of the DRH during the study period.

Exclusion criteria

- We excluded from the study all the files of pregnant women who did not give birth at the DRH and those who were receiving antibiotics for an infectious condition.

Matching criterion

A file of a woman in the case group was matched by age to one file (woman) in the control group giving a 1:1 ratio and participants were enrolled using the consecutive and convenience sampling method.

2.4. Study Procedure

Ethical clearance for this study was obtained from the Institutional Review Board of the University of Bamenda and Administrative Authorization was obtained from the Delegation of Public Health for the Littoral Region and the Managing Director of the DRH (Ref. No. 044 AP/MINSANTE/HGD/DM/03/19). Furthermore, we carried-out pre-testing of the questionnaire on 15 pregnant women from the Bambui Health unit and adjustments were made on the questionnaire. Data was collected from patient’s files after obtaining verbal consent through phone calls to complete the questionnaires in case of missing information.
The data collection form contained information regarding:

- Socio-demographic characteristics: Profession, age, marital status, and residence.
- Laboratory tests: Urine culture and uropathogens isolated.
- Maternal-fetal outcome: Pyelonephritis, recurrent urinary tract infection during pregnancy, threatened preterm birth, threatened preterm labor, premature rupture of membranes, gestational age at delivery, birth weight, Apgar scores, sex, neonatal infection, neonatal jaundice, neonatal intensive care unit admission.

2.5. Data Management and Analysis

Data collected were double-checked, coded and entered into CSPro version 7.2 and exported and analyzed with SPSS version 23. The baseline characteristics of the study population were summarized using frequencies, mean and standard deviation. A comparison was made using binary logistic regression to determine the independent effect of the variables by calculating the strength of the association between UTI and adverse maternal-fetal outcomes of UTI using odds ratio (OR) and 95% confidence interval (CI). Adjusted OR (for variables which were statistically significant in binary logistic analysis) was computed using multivariable logistic regression to control the confounding variables. Statistical significance two-tailed was set at p < 0.05.

Cases were those with laboratory confirmation of UTI while those with negative laboratory tests served as controls. We respected the ethical principles of the Helsinki declaration while carrying out this study [11] and reported according to Strobe checklist for case-control studies.

3. Results

We reviewed a total of 305 files with the diagnosis of UTI or without UTI during pregnancy but only 206 were eligible for the study. Seventy-three files were excluded because they gave birth out of the Douala Referral Hospital and 26 were unreachable by phone or did not give consent. A total of 103 participants (cases) and 103 (controls) enrolled, completed the study.

As shown in Table 1, the mean age of both cases and controls 29.61 ± 4.69 was similar (P = 1.0). Participants working in the private sector (13.6% cases versus 30.1% controls, p = 0.001), civil servants (35% cases versus 22.3% controls, p = 0.03) were different while those who were single (24.3% cases versus 35% controls, p = 0.06) were only slightly different in both groups.

As shown in Table 2, the leading uropathogens of urinary tract infection in this study were Escherichia coli (51.5%), Proteus mirabilis (15.5%), Staphylococcus aureus (11.7%) and Klebsiella species (7.8%).

As shown in Table 3, participants with UTI in pregnancy were more likely to develop pyelonephritis, recurrent urinary tract infection, preterm labor, amnionitis and premature rupture of fetal membranes.
The other characteristics studied were not statistically significant.

As shown in Table 4 participants with UTI in pregnancy were more likely to have preterm delivery and the babies were prone to have low Apgar scores < 7 at the 1st, 5th and 10th minute, low-birth weight, develop neonatal infection and admitted to the neonatal intensive care unit.

As shown in Table 5, after multivariate analysis by logistic regression, participants with UTI in pregnancy were more likely to have; pyelonephritis, amnionitis, preterm labor, preterm delivery, low birthweight < 2500 g, neonatal infection and neonatal intensive care unit admission.

Table 1. Socio-demographic characteristics of study population.

| Variable          | Cases N = 103 (%) | Controls N = 103 (%) | Total N = 206 (%) | p-value |
|-------------------|-------------------|---------------------|-------------------|---------|
| **Age (years)**   |                   |                     |                   |         |
| <19               | 1 (1)             | 1 (1)               | 2 (1)             | 0.75    |
| 19 - 25           | 15 (14.6)         | 15 (14.6)           | 30 (14.6)         | 0.58    |
| 26 - 30           | 43 (41.7)         | 43 (41.7)           | 86 (41.7)         | 0.56    |
| 31 - 35           | 35 (34)           | 35 (34)             | 70 (34)           | 0.56    |
| >35               | 9 (8.7)           | 9 (8.7)             | 18 (8.7)          | 0.6     |
| Mean ± SD         | 29.61 ± 4.69      | 29.61 ± 4.69        | -                 | 1.0     |
| **Profession**    |                   |                     |                   |         |
| Civil servant     | 36 (35)           | 23 (22.3)           | 59 (28.6)         | 0.03    |
| Self employed     | 12 (11.7)         | 9 (8.7)             | 21 (10.2)         | 0.3     |
| Housewife         | 14 (13.6)         | 15 (14.6)           | 29 (14.1)         | 0.5     |
| Private sector    | 14 (13.6)         | 31 (30.1)           | 45 (21.8)         | 0.001   |
| Student           | 27 (26.2)         | 25 (24.3)           | 52 (25.2)         | 0.4     |

| Level of education|                   |                     |                   |         |
| No formal education| 0 (0)             | 1 (1)               | 1 (0.5)           | 0.5     |
| Primary           | 3 (2.9)           | 5 (4.9)             | 8 (3.9)           | 0.36    |
| Secondary         | 21 (20.4)         | 26 (25.2)           | 47 (22.8)         | 0.25    |
| Tertiary          | 78 (75.7)         | 70 (68)             | 148 (71.8)        | 0.14    |
| **Marital status**|                   |                     |                   |         |
| Married           | 77 (74.8)         | 66 (64.1)           | 143 (69.4)        | 0.07    |
| Single            | 25 (24.3)         | 36 (35)             | 61 (29.6)         | 0.06    |
| **Religion**      |                   |                     |                   |         |
| Christian         | 96 (93.2)         | 94 (91.3)           | 190 (92.2)        | 0.4     |
| Muslim            | 5 (4.9)           | 4 (3.9)             | 9 (4.4)           | 0.5     |
| Jehovah witness   | 1 (1)             | 5 (4.9)             | 6 (2.9)           | 0.11    |

SD: Standard deviation.
## Table 2. Pathogens isolated after urine culture of study participants.

| Bacterial pathogens | N = 130 | Percentage |
|---------------------|---------|------------|
| *Escherichia coli*   | 53      | 51.5       |
| *Proteus mirabilis*  | 16      | 15.5       |
| *Staphylococcus aureus* | 12   | 11.7       |
| *Klebsiella species* | 8       | 7.8        |
| *Enterobacter species* | 7    | 6.8        |
| *Staphylococcus aureus + Streptococcus* | 2    | 1.9        |
| *Acinobacter baumanii* | 2     | 1.9        |
| *S. aureus + Pseudomonas* | 1 | 1.0        |
| *Ureaplasma urealyticum* | 1     | 1.0        |
| *Morexella catarralis* | 1     | 1.0        |
| Total               | 103     | 100        |

## Table 3. Maternal outcomes of UTI in the study population (univariate analysis).

| Variable                                      | Cases N = 103 (%) | Controls N = 103 (%) | Total N = 206 (%) | OR (95% CI) p-value |
|-----------------------------------------------|-------------------|----------------------|-------------------|---------------------|
| **Pyelonephritis**                            |                   |                      |                   |                     |
| Yes                                           | 14 (13.6)         | 2 (2)                | 14 (6.8)          | 4.6 (3.7 - 17.2)    | <0.001              |
| No                                            | 89 (86.4)         | 103 (100)            | 192 (93.2)        | Ref.                |                     |
| **Recurrent urinary tract infection during the pregnancy** |                   |                      |                   |                     |
| Yes                                           | 19 (18.4)         | 1 (1)                | 20 (9.7)          | 23.07 (4.1 - 488.6) | <0.001              |
| No                                            | 84 (81.6)         | 102 (99)             | 186 (90.3)        | Ref.                |                     |
| **Threatened abortion**                       |                   |                      |                   |                     |
| Yes                                           | 14 (13.6)         | 0 (0)                | 14 (6.8)          | -                   | <0.001              |
| No                                            | 89 (86.4)         | 103 (100)            | 192 (93.2)        | Ref.                |                     |
| **Preterm labor**                             |                   |                      |                   |                     |
| Yes                                           | 38 (36.9)         | 2 (1.9)              | 40 (19.4)         | 29.52 (7.94 - 184.95) | <0.001              |
| No                                            | 65 (63.1)         | 101 (98.1)           | 166 (80.6)        | Ref.                |                     |
| **Premature rupture of membranes**            |                   |                      |                   |                     |
| Yes                                           | 38 (36.9)         | 2 (1.9)              | 40 (19.4)         | 29.52 (7.94 - 184.95) | <0.001              |
| No                                            | 65 (63.1)         | 101 (98.1)           | 166 (80.6)        | Ref.                |                     |
| **Amnionitis**                                |                   |                      |                   |                     |
| Yes                                           | 33 (29.1)         | 4 (2.3)              | 37 (16.3)         | 18.33 (3.1 - 44.2)  | 0.001               |
| No                                            | 70 (70.9)         | 99 (97.7)            | 169 (83.7)        | Ref.                |                     |
| **Vaginal birth**                             |                   |                      |                   |                     |
| Yes                                           | 82 (79.6)         | 79 (76.7)            | 161 (78.2)        | 1.19 (0.61 - 2.32)  | 0.37                |
| No                                            | 21 (20.4)         | 24 (23.3)            | 45 (21.8)         | Ref.                |                     |
| **Cesarean section**                          |                   |                      |                   |                     |
| Yes                                           | 21 (20.4)         | 24 (23.3)            | 45 (21.8)         | 0.84 (0.43 - 1.64)  | 0.37                |
| No                                            | 82 (79.6)         | 79 (76.7)            | 161 (78.2)        | Ref.                |                     |

OR = Odd Ratio, CI = Confidence interval.
Table 4. Fetal outcomes of urinary tract infection in study population (univariate analysis).

| Variable                        | Case N = 103 (%) | Control N = 103 (%) | Total N = 206 (%) | OR (95% CI) | p-value |
|---------------------------------|------------------|---------------------|-------------------|-------------|---------|
| GA at delivery                  |                  |                     |                   |             |         |
| Abortion                        |                  |                     |                   |             |         |
| Yes                             | 3 (2.9)          | 1 (1)               | 4 (1.9)           | 3.1 (0.3 - 81.3) | 0.31    |
| No                              | 100 (97.1)       | 102 (99)            | 202 (98.1)        | Ref.        |         |
| Preterm delivery                |                  |                     |                   |             |         |
| Yes                             | 44 (42.7)        | 8 (7.8)             | 52 (25.2)         | 8.9 (4.0 - 21.2) | 0.001   |
| No                              | 59 (57.3)        | 95 (92.2)           | 154 (74.8)        | Ref.        |         |
| Term                            |                  |                     |                   |             |         |
| Yes                             | 56 (54.4)        | 94 (91.3)           | 150 (72.8)        | 0.11 (0.05 - 0.3) | 0.001   |
| No                              | 47 (45.6)        | 9 (8.7)             | 56 (27.2)         | Ref.        |         |
| 1st minute Apgar score          |                  |                     |                   |             |         |
| <7                              | 23 (21.5)        | 2 (1.9)             | 25 (11.8)         | 14.0 (3.7 - 89.2) | 0.001   |
| ≥7                              | 9 (8.4)          | 1 (1)               | 10 (4.7)          | 9.5 (1.5 - 210.9) | 0.01    |
| 5th minute Apgar score          |                  |                     |                   |             |         |
| <7                              | 14 (13.1)        | 1 (1)               | 15 (7.1)          | 15.5 (2.64 - 333.9) | 0.001   |
| ≥7                              | 9 (8.4)          | 0 (0)               | 9 (4.3)           | Ref.        | 0.001   |
| 10th minute Apgar score         |                  |                     |                   |             |         |
| <7                              | 12 (11.2)        | 0 (0)               | 12 (5.7)          | -           | 0.02    |
| ≥7                              | 78 (72.9)        | 102 (98.1)          | 180 (85.3)        | 0.05 (0.01 - 0.2) | 0.001   |
| Sex                             |                  |                     |                   |             |         |
| Male                            | 60 (56.1)        | 60 (57.7)           | 120 (56.9)        | 0.94 (0.54 - 1.6) | 0.5     |
| Female                          | 45 (42.1)        | 44 (42.3)           | 89 (42.2)         | 1.0 (0.57 - 1.71) | 0.54    |
| Birth weight of the baby (grams)|                  |                     |                   |             |         |
| <2500                           | 25 (23.4)        | 8 (7.7)             | 33 (15.6)         | 3.7 (1.59 - 9.0) | 0.001   |
| >2500                           | 79 (73.8)        | 96 (92.3)           | 175 (82.9)        | 0.24 (0.1 - 0.54) | 0.001   |
| Neonatal infection              |                  |                     |                   |             |         |
| Yes                             | 35 (32.7)        | 7 (6.7)             | 42 (19.9)         | 6.7 (2.9 - 17.1) | 0.001   |
| No                              | 72 (67.3)        | 97 (93.3)           | 169 (80.1)        | Ref.        |         |
| Neonatal Jaundice               |                  |                     |                   |             |         |
| Yes                             | 5 (4.7)          | 3 (2.9)             | 8 (3.8)           | 1.7 (0.4 - 8.6) | 0.4     |
| No                              | 102 (95.3)       | 101 (97.1)          | 203 (96.2)        | Ref.        |         |
| Neonatal intensive care unit admission |             |                     |                   |             |         |
| Yes                             | 34 (31.8)        | 9 (8.7)             | 43 (20.4)         | 4.9 (2.3 - 11.4) | 0.001   |
| No                              | 73 (68.2)        | 95 (91.3)           | 168 (79.6)        | Ref.        |         |

OR = Odd Ratio, CI = Confidence interval.
Table 5. Maternal-fetal outcomes of urinary tract infection (multivariate analysis).

| Variable                        | AOR (95% CI)  | p-value |
|---------------------------------|---------------|---------|
| Pyelonephritis                  | 3.1 (1.1 - 3.6) | 0.002   |
| Amnionitis                      | 1.1 (1.7 - 2.5) | 0.002   |
| Preterm labor                   | 4.4 (1.0 - 12.7) | 0.008   |
| Preterm delivery                | 4.6 (1.9 - 22.9) | 0.05    |
| Weight < 2500                   | 2.1 (0.8 - 5.6)  | 0.05    |
| Neonatal infection              | 13.0 (0.9 - 191.6) | 0.04    |
| Neonatal intensive care unit admission | 2.46 (1.7 - 3.6) | 0.003   |

AOR = Adjusted odd ratio.

4. Discussion

The aim of this study was to determine the uropathogens of UTI during pregnancy and the maternal-fetal outcomes at the Douala Referral Hospital. The most frequently occurring uropathogens of UTI during pregnancy in this study were *Escherichia coli*, *Proteus mirabilis*, *Staphylococcus aureus* and *Klebsiella* species. The adverse maternal-fetal outcomes of UTI in pregnancy were pyelonephritis, amnionitis, preterm labor, preterm delivery, low birth weight < 2500, neonatal infection, and neonatal intensive care unit admission.

4.1. Uropathogens Identified during Urine Culture in Pregnancy

The most commonly isolated bacterial pathogens in this study were Gram-negative bacteria: *Escherichia coli* (51.5%), *Proteus mirabilis* (15.5%), and *Klebsiella spp* (7.8%). This is consistent with others authors; Mohamed et al., Elzayat et al., Masinde et al., Amira et al. who reported a predominance of gram-negative microorganism and precisely *Escherichia coli* at a frequency of 47.4%, 70%, 47.2%, and 67.2% respectively [3] [12] [13] [14]. Furthermore, a study in Ethiopia reported that the most common isolates detected were *E. coli* (45.7%) followed by coagulase-negative *Staphylococcus* (17.1%) and *S. aureus* (8.6%) [15]. Also, Kim et al. reported that the predominant uropathogen isolated in their study was *E. coli* in 756/862 (87.7%) [16]. Besides UTI is common in pregnancy mostly because of stasis from the gravid uterus and elevated levels of progesterone secreted by the placenta that causes smooth muscle relaxation resulting in decreased peristalsis of the ureters, increased bladder capacity and urinary stasis. Furthermore, differences in urine pH and osmolality and pregnancy-induced glycosuria and aminoaciduria may facilitate bacterial growth [17] [18]. Besides, it may also result from poor hygiene methods of cleaning the anus after defecation and urogenital organs after micturition [19] [20]. The relatively short female urethra is frequently colonized with organisms from the gastrointestinal tract [21] [22]. Besides, most of these uropathogens like *Escherichia coli* are present in the gastrointestinal tract.
4.2. Maternal-Fetal Outcomes of Urinary Tract Infection in Pregnancy

In this study, we found that women exposed to UTI in pregnancy were independently associated with pyelonephritis during the puerperal period, amnionitis, premature labor, and preterm delivery. These findings are consistent with those reported by Matuszkiewiez et al. [4]. It has been postulated that specific virulence determinants in uropathogenic strains of *E. coli* are associated with invasive infection and pyelonephritis in pregnancy. These include toxins and adhesions. The short attachment pili or fimbriae are organelles of adhesion allowing bacteria to colonize (multiplication and tissue invasion) the uroepithelial cells and prevent bacteria from urinary lavage or resist flushing. The frequencies of virulence-associated determinants are significantly high in case of pyelonephritis [23]. The pyelonephritis presented by women after delivery may also be due to inappropriate treatment of ASB or cystitis during pregnancy or to an undiagnosed ASB which led to renal tissue damage caused by bacterial endotoxins and systemic inflammatory response with endothelial injury [24]. Other studies have reported that women with urinary tract infection are independently associated with adverse pregnancy outcomes (preterm premature rupture of fetal membranes that ended up in preterm labor, and preterm birth of low birth weight neonates and amnionitis [25]. Furthermore, amnionitis may result from the premature rupture of membranes thereby favouring ascending infection (uropathogens) from the vagina into the uterus and therefore causing amniotic fluid contamination and infection. Later on, the heavily colonized birth canal may favour the transmission of microorganisms to the baby causing neonatal infection and neonatal intensive care unit admission [25]. This is consistent with our findings. The significant association between preterm labor and UTI has been well documented and the pathogenesis includes several theories as; uterine contractions may be induced by cytokines and prostaglandins, which are released by the microorganisms. Urinary tract infection affects premature labor directly through the development of amnionitis. Furthermore, bacterial enzymes such as collagenase may weaken the fetal membrane. It was also postulated that bacterial products such as phospholipase A and C or endotoxins might stimulate prostaglandin biosynthesis by the fetal membranes, which initiate labor [26] [27].

Our study furthermore strengthens the association between urinary tract infections and adverse maternal-fetal outcomes. Health education about personal hygiene, urine cultures early in pregnancy and during the third trimesters especially among pregnant women in low-resource settings like Cameroon should be considered in routine obstetric practice.

4.3. Strengths and Limitations of the Study

This is one of the few studies regarding UTI during pregnancy in our environment. However, the limitations of being a retrospective study may lead to recall bias, and selection of cases and controls by convenience sampling may make the results not be representative of the general population in Cameroon.
5. Conclusion

The main uropathogenic agent of UTI during pregnancy is *Escherichia coli*. Furthermore, urinary tract infection has major adverse maternal-fetal outcomes (pyelonephritis, amnionitis, preterm labor, preterm delivery, low birth weight < 2500, neonatal infection, and neonatal intensive care admission) during pregnancy that could increase perinatal morbidity/mortality. We, therefore, recommend screening and treatment of UTI early in pregnancy and also in the third trimester of pregnancy. Health education regarding personal hygiene should be emphasized to pregnant women by the obstetrician or caregiver.

Acknowledgements

We are grateful to the staff of the Douala Referral Hospital for the assistance they gave us during the study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Rowe, T.A. and Juthani-Mehta, M. (2013) Urinary Tract Infection in Older Adults. *Aging Health*, 9, 519-528. https://doi.org/10.2217/ahe.13.38

[2] Foxman, B. (2010) The Epidemiology of Urinary Tract Infection. *Nature Reviews Urology*, 7, 653. https://doi.org/10.1038/nrurol.2010.190

[3] Amiri, M., Lavasani, Z., Norouzirad, R., Najipour, R., Mohamadpour, M., Nikpoor, A.R., et al. (2015) Prevalence of Urinary Tract Infection among Pregnant Women and Its Complications in Their Newborns during the Birth in the Hospitals of Dezful City, Iran, 2012-2013. *Iranian Red Crescent Medical Journal*, 17, e26946. https://doi.org/10.5812/ircmj.26946

[4] Matuszkiewicz-Rowińska, J., Małyszko, J. and Wieliczko, M. (2015) Urinary Tract Infections in Pregnancy: Old and New Unresolved Diagnostic and Therapeutic Problems. *Archives of Medical Science: AMS*, 11, 67. https://doi.org/10.5114/aoms.2013.39202

[5] Ansari, H.Q.F. and Rajkumari, A. (2011) Prevalence of Asymptomatic Bacteriuria and Associated Risk Factors among Antenatal Patients Attending a Tertiary Care Hospital. *Journal of Medical and Allied Sciences*, 1, 74.

[6] Rahiman, F., Balasubramanian and Musambil, M. (2015) A Review on Urinary Tract Infection in Pregnancy. *International Journal of Pharma and Bio Sciences*, 4, 42.

[7] Alemu, A., Moges, F., Shiferaw, Y., Tafess, K., Kassu, A., Anagaw, B., et al. (2012) Bacterial Profile and Drug Susceptibility Pattern of Urinary Tract Infection in Pregnant Women at University of Gondar Teaching Hospital, Northwest Ethiopia. *BMC Research Notes*, 5, 197. https://doi.org/10.1186/1756-0500-5-197

[8] Gilbert, N.M., O’brien, V.P., Hultgren, S., Macones, G., Lewis, W.G. and Lewis, A.L. (2013) Urinary Tract Infection as a Preventable Cause of Pregnancy Complications: Opportunities, Challenges, and a Global Call to Action. *Global Advances in Health and Medicine*, 2, 59-69. https://doi.org/10.7453/gahmj.2013.061
[9] Kalinderi, K., Delkos, D., Kalinderis, M., Athanasiadis, A. and Kalogiannidis, I. (2018) Urinary Tract Infection during Pregnancy: Current Concepts on a Common Multifaceted Problem. *Journal of Obstetrics and Gynaecology, 38*, 448-453. https://doi.org/10.1080/01443615.2017.1370579

[10] Romoren, M., Valauthapillai, M., Rahman, M., Sundby, J., Klouman, E. and Hjortdahl, P. (2007) Trichomoniasis and Bacterial Vaginosis in Pregnancy: Inadequately Managed with the Syndromic Approach. *Bulletin of the World Health Organisation, 85*, 297-304. https://www.scielosp.org/article/bwho/2007.v85n4/297-304/en https://doi.org/10.2471/BLT.06.031922

[11] World Medical Association (2014) World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *Journal of the American College of Dentists, 81*, 14. https://doi.org/10.1515/9783110208856.233

[12] Mohamed, N.R., Omar, H.H. and Abdallah, I.M. (2017) Prevalence and Risk Factors of Urinary Tract Infection among Pregnant Women in Ismailia City, Egypt. https://doi.org/10.9790/1959-0603076272

[13] Elzayat, M.A.-A., Barnett-Vanes, A., Dabour, M.F.E. and Cheng, F. (2017) Prevalence of Undiagnosed Asymptomatic Bacteriuria and Associated Risk Factors during Pregnancy: A Cross-Sectional Study at Two Tertiary Centres in Cairo, Egypt. *BMJ Open, 7*, e013198. https://doi.org/10.1136/bmjopen-2016-013198

[14] Masinde, A., Gumodoka, B., Kilonzo, A. and Mshana, S.E. (2009) Prevalence of Urinary Tract Infection among Pregnant Women at Bugando Medical Centre, Mwanza, Tanzania. *Tanzania Journal of Health Research, 11*, 154-159. https://doi.org/10.4314/thrb.v11i3.47704

[15] Demilie, T., Beyene, G., Melaku, S. and Tsegaye, W. (2012) Urinary Bacterial Profile and Antibiotic Susceptibility Pattern among Pregnant Women in North West Ethiopia. *Ethiopian Journal of Health Sciences, 22*, 121-128.

[16] Kim, W.B., Cho, K.H., Lee, S.W., Yang, H.J., Yun, J.H., Lee, K.W., et al. (2017) Recent Antimicrobial Susceptibilities for Uropathogenic *Escherichia coli* in Patients with Community Acquired Urinary Tract Infections: A Multicenter Study. *Urinary Tract Infection, 12*, 28-34. https://doi.org/10.14777/uti.2017.12.1.28

[17] Thadhani, R.I., Maynard, S.E. and Sterns, R.H. (2018) Maternal Adaptations to Pregnancy: Renal and Urinary Tract Physiology.

[18] Nwachukwu, E., Onyebuchi, O. and Michael, O. (2018) Prevalence of Urinary Tract Infections in Pregnant Women in Onitsha, Nigeria. *Journal of Bacteriology & Mycology: Open Access, 6*, 284-285. https://doi.org/10.15406/jbmoa.2018.06.00219

[19] Amiri, F.N., Rooshan, M.H., Ahmady, M.H. and Soliamani, M.J. (2009) Hygiene Practices and Sexual Activity Associated with Urinary Tract Infection in Pregnant Women. *Eastern Mediterranean Health Journal, 151*, 104-110. https://doi.org/10.26719/2009.15.1.104

[20] Badran, Y.A., El-Kashef, T.A., Abdelaziz, A.S. and Ali, M.M. (2015) Impact of Genital Hygiene and Sexual Activity on Urinary Tract Infection during Pregnancy. *Urology Annals, 7*, 478. https://doi.org/10.4103/0974-7796.157971

[21] Parveen, K., Momen, A., Begum, A.A. and Begum, M. (2011) Prevalence of Urinary Tract Infection during Pregnancy. *Journal of Dhaka National Medical College & Hospital, 17*, 8-12. https://doi.org/10.3329/jdnmch.v17i2.12200

[22] Finer, G. and Landau, D. (2004) Pathogenesis of Urinary Tract Infections with Normal Female Anatomy. *The Lancet Infectious Diseases, 4*, 631-635. https://doi.org/10.1016/S1473-3099(04)01147-8
[23] Subashchandrabose, S. and Mobley, H.L.T. (2015) Virulence and Fitness Determinants of Uropathogenic Escherichia coli. Microbiology Spectrum, 3. https://doi.org/10.1128/microbiolspec.UTI-0015-2012

[24] Kazemier, B.M., Koningstein, F.N., Schneeberger, C., Ott, A., Bossuyt, P.M., de Miranda, E., Vogelvang, T.E., Verhoeven, C.J., Langenveld, J., Woiski, M., Oudijk, M.A., van der Ven, J.E., Vlegels, M.T., Kuiper, P.N., Feiertag, N., Pajkrt, E., de Groot, C.J., Mol, B.W., and Geerlings, S.E. (2015) Maternal and Neonatal Consequences of Treated and Untreated Asymptomatic Bacteriuria in Pregnancy: A Prospective Cohort Study with an Embedded Randomised Controlled. The Lancet Infectious Diseases, 15, 1324-1333. https://doi.org/10.1016/S1473-3099(15)00070-5

[25] Dray, E.M., Levy, A., Schlaeffer, F. and Sheiner, E. (2009) Maternal Urinary Tract Infection: Is It Independently Associated with Adverse Pregnancy Outcome? Journal of Maternal-Fetal and Neonatal Medicine, 22, 124-128. https://doi.org/10.1080/14767050802488246

[26] Lappas, M., Permezel, M., Holdsworth, S.J., Zanoni, G., Porta, A., and Rice, G.E. (2007) Antiinflammatory Effects of the Cyclopentenone Isoprostane 15A (2)-IsoP in Human Gestational Tissues. Free Radical Biology & Medicine, 42, 1791-1796. https://doi.org/10.1016/j.freeradbiomed.2007.03.009

[27] Lappas, M. and Rice, G.E. (2009) Transcriptional Regulation of the Processes of Human Labour and Delivery. Placenta, 30, 90-95. https://doi.org/10.1016/j.placenta.2008.10.005
# Data Entry Form

| N° | VARIABLE | CLASS |
|----|----------|-------|
| 1  | Number of the copy | |
| 2  | Date of enlistment | |
| 3  | Group | 1 = Case, 2 = Control |
| 4  | Site of the study | 1 = DRH |

## Section I: Identification/Socio-demographic Characteristics

| N° | VARIABLE | CLASS |
|----|----------|-------|
| 1  | Initials of the names | |
| 2  | Age (in year) | 1 = Civil servant, 2 = Trader, 3 = Housewife, 4 = Private worker, 5 = Student, 6 = Other |
| 3  | Profession: | 1 = Civil servant, 2 = Trader, 3 = Housewife, 4 = Private worker, 5 = Student, 6 = Other |
| 4  | Other occupation precise | 1 = None, 2 = Primary, 3 = Secondary, 4 = University |
| 5  | Level of education | 1 = None, 2 = Primary, 3 = Secondary, 4 = University |
| 6  | Marital Status: | 1 = Married, 2 = Single, 3 = Concubine, 4 = Widow |
| 7  | Nationality | 1 = Cameroonian, 2 = Other |
| 8  | Other nationality precise | 1 = West, 2 = Centre, 3 = Littoral, 4 = Nord, 5 = Nord-west, 6 = South-west, 7 = South, 8 = Extreme-north, 9 = Adamawa, 10 = East |
| 9  | If Cameroonian region of origin | 1 = West, 2 = Centre, 3 = Littoral, 4 = Nord, 5 = Nord-west, 6 = South-west, 7 = South, 8 = Extreme-north, 9 = Adamawa, 10 = East |
| 10 | Religion | 1 = Christian, 2 = Muslim, 3 = Other |
| 11 | If other religion precise | |

## Section II: Obstetrical History

| N° | VARIABLE |
|----|----------|
| 12 | Gravidity |
| 13 | Parity |
| 14 | Number of preterm |
| 15 | Number of abortion |
| 16 | Number of children alive |
### Gynecological History

|   | Question                                      | Options                  |
|---|-----------------------------------------------|--------------------------|
| 17| Genital infection                             | 1 = yes, 2 = no          |
| 18| Past toxicological history                    |                          |
| 19| Alcohol                                       | 1 = yes, 2 = no          |
| 19| Tabaco                                        | 1 = yes, 2 = no          |

### Present pregnancy

|   | Question                                      | Options                  |
|---|-----------------------------------------------|--------------------------|
| 20| Gestational age (day)                         | 1 = one                  |
| 21| Number of fetuses                             | 2 = two, 3 = three       |
| 22| Number of prenatal consultations              |                          |
| 23| ANC done by:                                  | 1 = Gynecologist, 2 = General practitioner, 3 = Mid-wife, 4 = Other |
| 24| If CPN done by other precise                 |                          |
| 25| HTA during pregnancy (ANC)                    | 1 = yes, 2 = no          |
| 26| Gestational diabetes                          | 1 = yes, 2 = no          |
| 27| Urinary infection during pregnancy            | 1 = yes, 2 = no          |
| 28| Frequency of sexual intercourse per week      |                          |

### Medical History

|   | Question                                      | Options                  |
|---|-----------------------------------------------|--------------------------|
| 29| Chronic hypertension                          | 1 = yes, 2 = no          |
| 30| Diabetes                                      | 1 = yes, 2 = no          |
| 30|                                             | 1 = Positive             |
| 31| HIV serology                                  | 2 = Negative, 3 = Not known |
| 32| Urinary malformation                          | 1 = yes, 2 = no          |
| 33| Kidney failure                                | 1 = yes, 2 = no          |
| 34| Cardiac insufficiency                         | 1 = yes, 2 = no          |
| 35| Past urinary tract infection                  | 1 = yes, 2 = no          |

### Section III: Laboratory Test

|   | Question                                      | Options                  |
|---|-----------------------------------------------|--------------------------|
| 36| Dipstick done                                 | 1 = yes, 2 = no          |
| 37| Dipstick                                      | 1 = Positive, 2 = Negative |
| 38| Leucocyturia                                  | 1 = yes, 2 = no          |
| 38|                                             | 1 = Trace                |
| 38|                                             | 2 = +                    |
| 38|                                             | 3 = +++                  |
| 39| If leucocyturia                               | 4 = +++                  |
| 40| Proteinuria                                   | 1 = Yes, 2 = No          |
| 41| If proteinuria                                | 1 = Traces               |
| 41|                                             | 2 = +                    |
| 41|                                             | 3 = +++                  |
| 41|                                             | 4 = +++                  |
|   | Nitrites                                      | 1 = yes, 2 = no |
|---|------------------------------------------------|-----------------|
| 42| Culture done                                  |                 |
| 43| If yes culture results                        | 1 = Normal urine|
| 44| Number of colony unit                         | 1 = >10^5, 2 = <10^5 |
| 45| If urinary infection during culture           |                 |
| 46| - E. coli                                     | 1 = yes, 2 = no |
| 47| - Proteus mirabilis                           | 1 = yes, 2 = no |
| 48| - Enterobacter                                | 1 = yes, 2 = no |
| 49| - Other microorganisms                        | 1 = yes, 2 = no |
| 50| If other microorganisms (precise)             |                 |

**Section IV: Maternal Outcomes**

|   | Pyelonephritis                                | 1 = yes, 2 = no |
|---|------------------------------------------------|-----------------|
| 51| Amnionites                                    | 1 = yes, 2 = no |
| 52| Recurrent urinary tract infection during same pregnancy | 1 = yes, 2 = no |
| 53| Threatened abortion                           | 1 = yes, 2 = no |
| 54| Threatened preterm labor                      | 1 = yes, 2 = no |
| 55| Premature of rupture of fetal membranes       | 1 = yes, 2 = no |
| 56| Genital infection                             | 1 = yes, 2 = no |
| 57| Delivery method                               | 1 = NVD, 2 = Cesarean section |
| 58| Gestational age at delivery                   |                 |

**Fetal Outcomes**

|   | Birth Weight of the baby (grams)             | 1 = 1st baby, 2 = 2nd baby, 3 = 3rd baby |
|---|------------------------------------------------|----------------------------------------|
| 60| Apgar Score                                   | 1 = male, 2 = female                  |
| 61| Sex                                           | 1 = yes, 2 = no                       |
| 62| Neonatal infection                            | 1 = yes, 2 = no                       |
| 63| Neonatal jaundice                             | 1 = yes, 2 = no                       |
| 64| Neonatal intensive unit admission             | 1 = yes, 2 = no                       |