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Original Research Article

Bacterial profile and current distribution of antimicrobial susceptibility patterns of uropathogens from pregnant women with urinary tract infections

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Abstract

Background: Urinary tract infections (UTIs) are the most frequently encountered bacterial infections among pregnant women. Untreated UTIs increase both maternal and perinatal morbidity and mortality.
Objective: To determine the uropathogens profile of pregnant women with urinary tract infections and their susceptibility pattern to commonly used antimicrobials.
Methods: A total of 358 urine samples from pregnant women with urinary tract infections at different trimesters were collected and processed for the isolation of uropathogens and tested against six groups of commonly used antibiotics.
Results: A total of 358 pregnant women were recruited for the study over the study period. Of these, 120 (33.5%) had positive urine culture and varying antibiotic sensitivity pattern. *Escherichia coli* was the most common bacteria isolated with a percentage of 56.7%. Other isolated microorganisms included *Staphylococcus aureus* (21.7%), *Klebsiella spp.* (4.2%), *Pseudomonas spp.* (3.3%), *Enterococcus spp*. (1.7%), *Enterobacter spp*. (1.7%), *Proteus spp.* (1.7%) and *Citrobacter spp.* (1.7%). Levofloxacin had the highest overall antibiotic sensitivity of 83.0%. Others with overall antibiotic sensitivity pattern greater than 50% included ciprofloxacin (82.5%), streptomycin (70.0%), perfloxacin (61.6%), ceftriaxone (69.2%), cefixime (65.0%), amoxicillin (61.6%) and gentamicin (60.0%). There was strong resistance to nalidixic acid, cotrimoxazole and chloramphenicol.
Conclusion: Uropathogens causing UTIs in pregnancy were the usual known organisms but the antibiotic resistance patterns varied. Fluoroquinolone, Cephalosporin and aminoglycosides were shown to be very effective against the organisms causing UTIs in these pregnant women.
Keywords: antibiotic sensitivity pattern, pregnancy, urinary tract infection, uropathogens.

1. Introduction

Urinary tract infections (UTIs) are the most frequently encountered bacterial infections among pregnant women. [1] While not thought to cause significant sequelae, if left untreated or undertreated can result in life threatening complications. Untreated UTI increases both maternal and perinatal morbidity and mortality.[2,3] Maternal sequelae include maternal anaemia, hypertension, preeclampsia, chronic renal failure, septicaemia, preterm labour, preterm delivery and adult respiratory syndrome.[4-6] Possible foetal complications are miscarriages, intra-uterine growth retardation (IUGR), low birth-weight, foetal death, acute respiratory distress and prematurity and its attendant complications.[7-9] Impairment of mental and motor development is seen more in children born with mothers having pyelonephritis.[10] There is a significant statistical correlation between UTIs and mental retardation.[10]

Pregnant women are more susceptible to urinary tract infections due to anatomical and physiological changes of pregnancy in the urogenital system in addition to short urethra and easy contamination of urinary tract with faecal flora. [11,12] These changes include urethral dilatation, increased bladder volume and decreased bladder tone, along with decreased ureteral tone which contributes to increased urinary stasis and vesico-ureteric reflux. The alterations in urine chemical composition with elevated

glucose and amino acids levels facilitate bacterial growth.[13] Up to 70 % of pregnant women develop glycosuria, which encourages bacterial growth in the urine.[14]

These modifications usually begin in the 6th week and peaks during weeks 22 to 24 of pregnancy. [1,4,13,15] Other risk factors identified are low socioeconomic status, increasing age, high parity, poor perineal hygiene, history of recurrent UTIs, diabetes mellitus, neurogenic bladder retention, anatomic or functional urinary tract abnormality, and increased frequency of sexual activity.[2,16]

Typical symptoms of urinary tract infection include the triad of dysuria, urgency and urinary frequency. Pregnant women may manifest other symptoms such as haematuria, nausea, vomiting, preterm contractions, fever, flank pain, and tenderness in addition to significant bacteriuria.[15-17] It could also manifest as asymptomatic bacteriuria in 2% to 13% of pregnant women.[15]

Although several different microorganisms can cause UTIs, including fungi and viruses, bacteria are the major causative organisms and are responsible for more than 95% of UTI cases.[18]Organisms that cause UTIs are those from the normal vaginal, perineal, and faecal flora.[11,12,19] The vast majority of uncomplicated UTIs are caused by the Gram negative bacillus *Escherichia coli*, with other pathogens including *Enterococci, Staphylococcus spp., Klebsiella spp.* and *Proteus mirabilis.*[20] *Escherichia coli* is the most prevalent causative organism of UTI and is solely responsible for more than 80% of these infections.[21]

An accurate and prompt diagnosis of UTI is important in shortening the disease course and for preventing the ascent of the infection to the upper urinary tract and renal failure. Treatment of UTI is often started empirically and therapy is based on local antimicrobial sensitivity pattern of the urinary pathogens. There have been reported cases of resistance to antibiotics by these UTI causing organisms.[22,23] The extensive and inappropriate use of antimicrobial agents has invariably resulted in the development of antibiotic resistance which, in recent years, has become a major problem worldwide.[21]

Distribution of urinary pathogens and their susceptibility to antibiotics varies regionally so it becomes necessary to have knowledge of distribution of these pathogens and their susceptibility to antibiotics in a particular setting to ensure appropriate and adequate treatment.[2, 21]

Also due to the evolving and continuing antibiotic resistance phenomenon, a continuous review of antibiograms is therefore necessary to track changes in aetiological agents and antimicrobial patterns to improve guidelines for effective empirical antibiotic therapy.[21,24] This study aimed at identifying the bacterial agents, including their antibiotic susceptibility pattern isolated from pregnant women with urinary tract infection at Fertile Ground Hospital, Jos north-central Nigeria. The private hospitals and clinics are not usually involved in studies and reviews of these indices. There is limited available information on prevalence of UTI and causative agents in the private healthcare sector.[24]

2. Materials and Methods

2.1 Study Area

The study was conducted at Fertile Ground Hospital, a multi-specialist private hospital located in Jos, Plateau State North-central Nigeria. A 30 bed space capacity hospital with state of the art IVF-ET/ICSI facility. The study was undertaken reviewing the case notes of patients from January 2014 to June 2017.

2.2 Study population

The study population comprised of pregnant women age 18 to 45 years who presented with symptoms suggestive of urinary tract infections (e.g. dysuria, urgency, urinary frequency, flank pain and tenderness) and were managed as such. Ethical approval from institutional research ethical committee was obtained before starting the study. Pregnant women who had taken antibiotics prior to presentation were excluded.

2.3 Sample collection and processing

The women were trained and instructed adequately on how to collect clean catch midstream urine by standard method. Clean catch midstream urine samples were collected into sterile screw capped universal containers. The samples were labelled and 0.5 mg of boric acid was added to prevent the bacterial growth in urine samples. The samples were cultured on cysteine-lactose electrolyte deficient agar and blood agar using a sterile 4 mm platinum wired calibrated loop for the isolation of microorganisms. The plates were incubated for 24 hours at 37 °C and the samples were considered positive when an organism was cultured at a concentration of 10^5 CFU/mL which was estimated through multiplying the isolated colonies by 1000. The isolates were identified up to the species level by standard biochemical tests.

2.3 Antibiotic sensitivity assay

Kirby-Bauer disk diffusion test was used to perform antimicrobial susceptibility testing for all the isolates as recommended by Clinical and Laboratory Standard Institute (CLSI 2006). Antibiotic disks (Oxoid) were applied to each plate. Inhibition zone sizes were measured and interpreted according to CLSI guidelines. Antimicrobial drug susceptibility testing was done for six groups of commonly used antimicrobials (penicillin, cephalosporin, fluoroquinolone, aminoglycosides, macrolides, and sulphonamides). Among the group, the antibiotics tested were amoxicillin (10 µg), amoxicillin-clavulanic acid (20 µg), cefixime (10 µg), ceftriaxone (30 µg), nalidixic acid (30 µg), ciprofloxacin (5 µg),

levofloxacin (10 µg), perfloxacin (10µg), gentamicin (10 µg), erythromycin (10 µg), chloramphenicol (30 µg), streptomycin (10 µg) and co-trimoxazole (30 µg).

2.4 Data management and analysis

All information about the clients was entered into the study proforma. The data were entered and analysed using 2017 Epi Info™ statistical software (version 7.2.2.2, Centres for Disease Control, Atlanta, GA, USA). Descriptive analysis was used for the socio-demographic characteristic and other variables. Bivariate analysis and multivariate analysis were done by stratification of variables and this was used to identify the level of antibiotic sensitivity pattern of the isolated uropathogens.

3. Results

The mean and median ages of women with suspected cases of UTI were 30.2±5.9 and 30 years respectively. Majority (44.7%) of the study participants were in the age group of 20-29 years.

Majority (41.6%) of the pregnant women with suspected UTIs were in their third trimester of pregnancy. UTI was seen more frequently among the multigravidas.

Table 1: Characteristics of UTI in Pregnancy

Characteristics	Frequency n=358	Percent
Age group		
>20	4	1.1
20-29	152	42.5
30-39	160	44.7
40	42	11.7
Parity		
0	6	1.7
1-2	254	70.9
3-4	92	25.7
5	6	1.7
Trimester		
1	75	21.0
2	134	37.4
3	149	41.6

Among the 358 samples collected, 120 were laboratory confirmed cases of UTI with a positive culture percentage of 33.5%.

Table 2: Positive Urine Culture among pregnant women with suspected cases of UTI

Significant growth	Frequency	Percent
Present	120	33.5
Absent	238	66.5
Total	**358**	**100**

The highest laboratory diagnosed UTIs were observed at second trimester of pregnancy (n=47; 39.2%)

Table 3: Significant growth according to trimester, age group and parity

Characteristics	Significant growth n= 120 (%)
Trimester	
1	30 (25.0)
2	47 (39.2)
3	43 (35.8)
Age group	
>20	2 (1.6)
20-29	57 (47.5)
30-39	55 (45.9)
40	6 (5.0)
Parity	
0	3 (2.5)
1-2	94 (78.4)
3-4	22 (18.3)
5	1(0.8)
Total	**120 (100)**

The uropathogens isolated are presented in Table 4. There were 120 bacterial isolates. *Escherichia coli* was the most common organism isolated accounting for 68 (56.7%) of the total isolates. This was followed by *Staphylococcus aureus* which accounted for 26 (21.7%) of the isolates. The frequency of occurrence of the remaining bacteria isolates included: *Klebsiella Spp.,* 5 (4.2%); *Pseudomonas Spp.,* 4 (3.3%); *Enterococcus Spp.,* 2 (1.7%); *Enterobacter Spp.,* 2 (1.7%); *Klebsiella Spp.,* 2 (1.7%); and *Citrobacter Spp.,* 2 (1.7%).*Candida spp.,* a fungus accounted for 9 (7.5%).

Table 4: Distribution of bacterial population in pregnant women with UTI

Pathogens	Frequency	Percent
Escherichia coli	68	56.7
Staphylococcus aureus	26	21.7
Candida spp.	9	7.5
Klebsiella spp.	5	4.2
Pseudomonas spp.	4	3.3
Enterococcus spp.	2	1.7
Enterobacter spp.	2	1.7
Proteus spp.	2	1.7
Citrobacter spp.	2	1.7
Total	120	100.0

The isolated uropathogens revealed the presence of high levels of single and multiple antimicrobial sensitivity against commonly prescribed drugs as shown in Table 3. Levofloxacin had the highest overall sensitivity of 83.0%. This was closely followed by ciprofloxacin with 82.5%against commonly prescribed drugs as shown in Table 3. Gentamicin had a sensitivity of 60.0% against the 120 isolates tested. Amoxicillin, perfloxacin, cefixime, ceftriaxone and streptomycin had overall sensitivities above 60.0% but below 80.0%.

The other antibiotics had lesser than 50% sensitivity against the isolates as follows: nalidixic acid 43.0%, erythromycin 55.8%, cotrimoxazole 35.0% and chloramphenicol 44.2%.

Table 5: Antibiotic sensitivity pattern of the isolates

Antibiotics	Frequency	Percentages (%)	
		S	R
Amoxicillin	74	61.6	38.4
Ciprofloxacin	99	82.5	17.5
Levofloxacin	100	83.0	17.0
Perfloxacin	74	61.6	38.4
Cefixime	78	65.0	35.0
Ceftriaxone	83	69.2	30.8
Gentamicin	80	60.0	40.0
Streptomycin	84	70.0	30.0
Nalidixic acid	52	43.0	57.0
Erythromycin	67	55.8	44.2
Cotrimoxazole	42	35.0	65.0
Chloramphenicol	53	44.2	55.8

Table 6 shows the antibiotic sensitivity pattern of the bacterial isolates from pregnant women with UTI. Among the women in which *Escherichia coli* was isolated, 93% showed sensitivity to ciprofloxacin, 90% to ciprofloxacin and 76% to gentamicin. The sensitivity patterns of *Escherichia coli* to nalidixic acid, erythromycin, co-trimoxazole and chloramphenicol were much lower (29%, 49%, 44% and 43% respectively). Among the women in which *Staphylococcus aureus* was isolated, 88% showed sensitivity to ceftriaxone and 81% to ciprofloxacin, levofloxacin and cefixime. Gross 100% sensitivity was noted in the sensitivity pattern of *Klebsiella spp.* to levofloxacin, ciprofloxacin, perfloxacin, cefixime, ceftriaxone, gentamicin, streptomycin, erythromycin and chloramphenicol. *Pseudomonas spp.* was 100% sensitive to amoxicillin ciprofloxacin, cefixime and gentamicin. *Pseudomonas spp.* showed 100% resistance to nalidixic acid, cotrimoxazole and chloramphenicol. The antibiotic sensitivity pattern of other uropathogens (*Enterococcus spp., Enterobacter spp., Proteus spp., Citrobacter spp.*) isolated are as shown in Table 6.

Table 6: Antibiotic sensitivity pattern of the isolates

Pathogens	*E. coli* (%)	*Staph. A* (%)	*Klebsiell spp.*(%)	*Pseudo spp.*(%)	*Enteroco spp.*(%)	*Enterobac spp.*(%)	*Proteus spp.*(%)	*Citrobacter spp.*(%)
Antibiotics								
Amoxicillin	**S**(66) **R** (34)	**S** (73) **R** (27)	**S** (20) **R** (80)	**S** (100) **R** (0)	**S** (50) **R** (50)	**S** (100) **R** (0)	**S** (0) **R** (100)	**S** (100) **R** (0)
Ciprofloxacin	**S** (90) **R** (10)	**S** (81) **R** (19)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)
Levofloxacin	**S** (93) **R** (7)	**S** (81) **R** (19)	**S** (100) **R** (0)	**S** (75) **R** (25)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)
Perfloxacin	**S** (71) **R** (29)	**S** (50) **R** (50)	**S** (100) **R** (0)	**S** (50) **R** (50)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)
Cefixime	**S** (65) **R** (35)	**S** (81) **R** (19)	**S** (100) **R** (0)	**S**(100) **R** (0)	**S** (100) **R** (0)	**S** (0) **R** (100)	**S** (100) **R** (0)	**S** (0) **R** (100)
Ceftriaxone	**S** (69) **R** (31)	**S** (88) **R**(12)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (0) **R** (100)	**S** (100) **R** (0)	**S** (0) **R** (100)
Gentamicin	**S** (76) **R** (24)	**S** (62) **R** (38)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (50) **R** (50)	**S** (0) **R** (100)	**S** (100) **R** (0)	**S** (0) **R** (100)
Streptomycin	**S** (75) **R** (25)	**S** (69) **R** (31)	**S** (100) **R** (0)	**S** (50) **R** (50)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)
Nalidixic Acid	**S** (29) **R** (71)	**S** (73) **R** (27)	**S** (0) **R** (100)	**S** (0) **R** (100)	**S** (50) **R** (50)	**S** (100) **R** (0)	S (0) **R** (100)	**S** (100) **R** (0)
Erythromycin	**S** (49) **R** (51)	**S**(73) **R** (27)	**S** (100) **R** (0)	**S**(50) **R** (50)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)	**S** (100) **R** (0)
Cotrimoxazole	**S** (44) **R** (56)	**S** (27) **R** (73)	**S** (20) **R** (80)	**S** (0) **R** (100)	**S** (0) **R** (100)	**S** (100) **R** (0)	**S** (0) **R** (100)	**S** (100) **R** (0)
Chlorampheni	**S** (43) **R** (57)	**S** (54) **R** (46)	**S** (100) **R** (0)	**S** (0) **R** (100)	**S** (50) **R** (50)	**S** (0) **R** (100)	**S** (100) **R** (0)	**S** (100) **R** (0)

S= sensitivity; R= resistance

4. Discussion

A total of 358 cases were reviewed, of which 120 cases i.e. 33.5% were UTI positive. The 33.5% positive culture rate obtained in this study is comparable with 32.7% in Benin, southern Nigeria [25], 31.6% in Kano, northern Nigeria[26] and 35.5% in Ilorin, western Nigeria.[27] It is lower than the rate reported at Lafia, Nigeria.[28]

Pregnant women of the age group 20-29 years were more susceptible to UTIs (47.5%) than the elderly ones and is comparable to a study in India.[1] This may be connected to high sexual activities in the younger women. Another possibility is recent use of diaphragm with spermicide.[1]

UTI in pregnancy occurs in higher gestational ages as observed in 39.2% of second trimester gestations and 35.8% in third trimester. This is similar to the result of a study by Sibi *et al* in which 31.1% and 57.2% were reported in second and third trimester respectively.[1] This may be due to a well-established or pronounced pregnancy hormonal effect on the urinary system in second and third trimesters of pregnancy.

This study observed that most of the uropathogens were same as over the years but the antibiotic resistance patterns were varying and increasing. Gram negative bacteria predominated the isolates with *Escherichia coli* being the most common pathogen (56.7%) followed by *Klebsiella spp*. (4.2%) and this is similar to most other studies.[29-32] *Escherichia coli* and *Klebsiella spp.* are most common in each of three trimesters of pregnant women with UTI. This supports the fact that most organisms causing UTI are from the lower gastrointestinal tract which acts as a reservoir for organisms like *Escherichia coli* and uropathogenic strains of *Escherichia coli* have adherence factor called the P-fimbriae which mediate their attachment to uroepithelial cells.[33]

Among the Gram positive organisms, *Staphylococcus aureus* formed the majority accounting for 21.7% of isolated uropathogens and is comparable with 20.6% in a study by Onoh *et al*.[2] This is also similar to findings in Enugu[34], Benin[25] and Ilorin[27], although it is at variance with other studies.[27,28]

The antibiotic with the overall highest sensitivity pattern in this study was levofloxacin which is a fluoroquinolone. This is similar to other reports where quinolones were the most effective and sensitive antibiotics to the organisms causing UTI.[28,35] All fluoroquinolones used in this study had good antibiotic sensitivity pattern except nalidixic acid with poor sensitivity pattern: 83.0% for levofloxacin, 82.5% for ciprofloxacin, and 61.6% for perfloxacin. An overall sensitivity pattern of 61.6% was demonstrated by amoxicillin, a penicillin. This finding was higher than that reported by Saraswathi *et al*.[36]

Streptomycin, an aminoglycoside had a sensitivity of 70.0% across all isolates. This is unusually higher compared with findings from other studies.[2,24] This may have been duet infrequent use of streptomycin due to availability alternatives especially oral drugs. Parenteral route of administration and pain at the site of injection are its major disadvantages. It is mostly used when uropathogens are resistant to most available drugs and culture shows sensitivity to streptomycin. Gentamicin, another aminoglycoside had an overall good sensitivity pattern of 60.0%.

In this study, cephalosporin had a remarkable antibacterial activity, 69.2% for ceftriaxone and 65.0% forcefixime. This sensitivity pattern is however lower than that seen in previous studies.[2,13] This may be due to wide spread use with development of resistant strains.

This study demonstrated poor antibiotic sensitivity pattern to other antibiotics used. They include nalidixic acid, chloramphenicol, erythromycin and cotrimoxazole. This findings is in contrast to 100% and 83% reported for nalidixic acid and cotrimoxazole reported by Sibi *et al* in India.[1] The poor antibiotic sensitivity pattern of the above commonly available drugs could be due to the practice of self-medication, use of substandard medications, patronage of pharmacy shops manned by non-professionals leading to under dosage and indiscriminate abuse of drugs in our environment. The above practice leads to emergence of resistant strains among the UTI causing bacteria. This invariably increases the cost of treatment because the quinolones and cephalosporin, which have excellent antibacterial effects are expensive.

5. Conclusion

Uropathogens causing UTI in pregnancy remain essentially the same over the years but they have become increasingly resistant to the usual antibiotics. *Escherichia coli* was the most common aetiological agent of UTI in pregnancy with *Staphylococcus aureus* gaining prominence. Fluoroquinolone, Cephalosporin and aminoglycosides were shown to be very effective against the organisms causing UTI in these pregnant women. Regular monitoring of antimicrobial susceptibility for *Escherichia coli* is recommended to improve treatment.

Limitations

The study was Anurban hospital based study and may not truly reflect findings in the rural areas and the entire state. The antibiotic sensitivity test against bacteria in the laboratory is an in-vitro activity and may not exactly reflect the *in-vivo* activity.

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