Full Length Research Paper

Anti-microbial susceptibility pattern of microorganisms associated with urinary tract infections in a tertiary health institution in the Niger Delta Region of Nigeria

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Accepted 21 March, 2012

In order to assess the prevalence and sensitivity pattern of urinary pathogens, 634 midstream urine samples from patients at the Niger Delta University Teaching Hospital, Okolobiri, Nigeria were analysed. Samples were examined microscopically and cultured on blood agar, MacConkey agar and CLED agar. Standard techniques were used for identification of micro-organisms and the Kirby-Bauer disk diffusion method was used for antibiotic testing. Of the 634 urine samples, 237 yielded significant growth meaning a prevalence of 37.38%. There was female preponderance of urinary tract infection. The prevalence increased with age in the female patients peaking in the 21 to 30 years age group. Gram negative bacteria accounted for 82.28% of isolates, with E. coli being the predominant microorganism isolated. The bacterial isolates were most sensitive to nitrofurantoin and most resistant to amoxicillin-clavulanate and cloxacillin. There was a significant proportion of isolates that were resistant to multiple antibiotics, and the resistance levels to most antibiotics was above 50%. There were no differences in resistance pattern between age groups and sex. We recommend periodic assessment of sensitivity patterns of urinary pathogens, rational drug use and institution of infection control measures in the Niger Delta area of Nigeria. We also recommend the use of nitrofurantoin in the treatment of uncomplicated UTI.

Key words: Antibiotics, bacterial, resistance.

INTRODUCTION

Urinary tract infection (UTI) is one of the most frequently encountered diseases in the health care settings. Prevalence rates are unknown in the Niger Delta region of Nigeria. The definition of UTI and the criteria for diagnosis are still controversial (Kolawole et al., 2009; Obiogbolu et al., 2009). The gold standard for diagnosis should be the detection and identification of the causative pathogen in the urine (Schmiemann et al., 2010). The minimum level of bacteriuria ranges between 10³ to 10⁵ pure colony forming units/ml of urine. There is the possibility that many relevant infections could be missed using such criteria, as UTI has been shown to occur with counts as low as 100 cfu/ml (Akinyemi et al., 1997).

In resource poor settings as the Niger Delta region of Nigeria, suspected cases of UTI are treated empirically
due to the unavailability and non-affordability of tests like urine microscopy, culture and sensitivity. Diagnosis of UTI by clinical criteria has been shown to have an error rate of 33% (Schmiemann et al., 2010). This is of importance in settings such as ours where there are no clear evidence-based clinical practice guidelines for UTI. Also, there is the paucity of epidemiological data on UTI which could guide treatment.

These local problems are further compounded by the emergence of widespread antimicrobial resistance. Antimicrobial resistance is believed to be aided by poor prescription practices and antibiotic abuse including self-medication. Primary treatment of presumed UTI with fluoroquinolones has been shown to often lead to antimicrobial resistance (Schmiemann et al., 2010).

Antibiotic resistance increases both morbidity and mortality and has a bearing on length of hospital stay and costs (Butler et al., 2007). The emergence of extended-spectrum beta-lactamases (ESBL) has threatened the empirical use of cephalosporins and ciprofloxacin (Potz et al., 2006). Incidentally, these drugs are rarely affordable in resource-limited settings like the Niger delta region of Nigeria.

With the diagnostic and treatment difficulties facing the physician in the Niger Delta in mind, we sought to determine the distribution and antibiotic sensitivity of bacterial strains isolated from the urine of patients at the NDUTH.

### MATERIALS AND METHODS

#### Sample collection and analysis

Freshly voided midstream urine samples were received at the Medical microbiology department of Niger Delta University Teaching Hospital (NDUTH), Okolobiri between May 2010 and July 2011. The NDUTH is a tertiary health institution in Bayelsa State, in the Niger Delta region of Nigeria. The general population of Bayelsa State is about 1.5 million people, made up mostly of farmers and fishermen. Patients were enrolled from all clinics and wards for the study. Only patients who had not been on antibiotic treatment in the two weeks preceding sample collection were enrolled. The reasons for requesting urine m/c/s and the number of patients are shown in Table 1. 15-20 ml of clean catch midstream urine samples were collected after clear instructions on collection (including cleaning the genitalia before voiding of urine). The colour, turbidity/cloudiness was noted and duly recorded. 10 ml of the urine sample was centrifuged at 1500 rpm for 5 min and the residue examined under the microscope. Urine containing more than 5 pus cells/high power field was cultured.

A loopful of each sample was inoculated on cystine lactose electrolyte-deficient (CLED). MacConkey and Blood agar respectively, and incubated at 37°C for 18-24 h. Significant bacteriuria was defined as culture of a single bacterial species from the urine sample at a concentration of >10<sup>5</sup> colony forming units/ml of urine. Biochemical tests were performed on each organism isolated for proper identification. Unclassified coliforms were lactose fermenting on MacConkey agar, yielding pink-coloured colonies, and were uniform Gram negative rods.

### Antibiotic susceptibility testing

Antimicrobial sensitivity was tested for each isolated organism using the disk diffusion method of Kirkby-Bauer as described by the National Committee for Clinical laboratory Standards (Clinical Laboratory Standard Institute) (National Committee for Clinical Laboratory Standards, 2001).

### Statistical analysis

Differences in the prevalence of UTI and antibiotic resistance between groups were analysed using χ<sup>2</sup> test and the Wilcoxon signed-rank test. Significant difference was observed if there was a less than 5% (p<0.05) probability that the results were due to chance.

### RESULTS

#### Incidence of UTI

A total of 634 midstream urine samples were received at the Medical Microbiology department of NDUTH between May 2010 and July 2011. 237 samples (37.38%) had significant bacterial growth suggestive of urinary tract infection. 195 of these isolates were Gram negative bacteria (82.28%). This is reflected in Table 1.

#### Incidence according to age

The incidence of UTI was higher in male children compared with females. The female preponderance rises and peaks in the 21 to 30 years age group and then begins to drop. Male prevalence rises steeply in the 5<sup>th</sup> decade and by the 7<sup>th</sup> decade there is male preponderance (Figure 1).

#### Incidence according to risk factors

There was relatively high incidence of UTI among patients at high risk of UTI. 41.6% of patients with renal pathology, 39% of the pregnant patients, 33.3% of patients with benign prostatic hypertrophy and 16% of

### Table 1. Proportion of patients and the reasons for urine m/c/s investigations. The frequency of positive cultures is indicated.

<table>
<thead>
<tr>
<th>Reasons for urine m/c/s</th>
<th>Total</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ante-natal clinic</td>
<td>123</td>
<td>48</td>
<td>75</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>25</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>? UTI</td>
<td>55</td>
<td>15</td>
<td>40</td>
</tr>
<tr>
<td>Renal pathology</td>
<td>12</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Benign Prostatic Hypertrophy</td>
<td>12</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Fertility investigation.</td>
<td>49</td>
<td>18</td>
<td>31</td>
</tr>
<tr>
<td>Gynaecological problems</td>
<td>43</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>Others</td>
<td>315</td>
<td>129</td>
<td>186</td>
</tr>
<tr>
<td>Total</td>
<td>634</td>
<td>237</td>
<td>397</td>
</tr>
</tbody>
</table>
diabetic patients, respectively, had significant bacterial growth suggestive of UTI.

**Resistance according to organism**

Generally, the Gram negative bacteria were most resistant to cloxacillin and amoxicillin-clavulanate. *E. coli*, *K. pneumoniae* and *P. mirabilis* isolates were more sensitive to nitrofurantoin and least sensitive to cloxacillin and amoxicillin-clavulanate (Table 2). *Staphylococcus* was most sensitive to ceftazidime and least sensitive to cloxacillin, lincomycin and oxacillin.

**Resistance according to antibiotic**

Resistance levels above 20% are considered serious enough to discontinue treatment with such antibiotics. The least resistance by all the isolates was to nitrofurantoin (Figure 2 and Table 3). *P. mirabilis* was the most sensitive to nitrofurantoin and together with *E. coli* and *K. pneumoniae* had resistance of less than 20%. *P. aeruginosa* had the greatest resistance.

The greatest resistance by all the isolates was to cloxacillin as shown in Figure 3. *K. pneumoniae*, *P. Mirabilis*, and the coliforms were absolutely resistant (100%) to cloxacillin. The least resistance to cloxacillin was 75% by *S. aureus*.

**Resistance according to age and sex**

There were no discernible significantly different patterns in antimicrobial resistance between the different age groups (p<0.98). There was also no difference in
Figure 2. Susceptibility pattern of isolates to Nitrofurantoin. Nitrofurantoin was the most effective antibiotic against the bacterial isolates.

Figure 3. Sensitivity pattern of isolates to cloxacillin. Some isolates were absolutely resistant to cloxacillin.
Resistance pattern of *E. coli* isolates according to sex. There was little difference in the resistance pattern according to sex for all the antibiotics tested, as exemplified by the resistance of *E. coli*.

### Table 3. Degree of sensitivity of microbial isolates to antibiotics expressed in percentage resistance.

<table>
<thead>
<tr>
<th>Organism</th>
<th>CAZ</th>
<th>CTX</th>
<th>NIT</th>
<th>CXC</th>
<th>AMX-CLA</th>
<th>GEN</th>
<th>CRX</th>
<th>OFL</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>45</td>
<td>55</td>
<td>16</td>
<td>95.8</td>
<td>82.2</td>
<td>45</td>
<td>61.7</td>
<td>49.6</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>57.4</td>
<td>59.3</td>
<td>14.8</td>
<td>100</td>
<td>98.1</td>
<td>66.7</td>
<td>72.2</td>
<td>44.4</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>19.5</td>
<td>48</td>
<td>44</td>
<td>75</td>
<td>48.7</td>
<td>46.3</td>
<td>36.6</td>
<td>36.6</td>
</tr>
<tr>
<td><em>Coliform</em></td>
<td>64</td>
<td>48</td>
<td>44</td>
<td>100</td>
<td>88</td>
<td>56</td>
<td>72</td>
<td>52</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>33.3</td>
<td>33.3</td>
<td>11.1</td>
<td>88.9</td>
<td>66.7</td>
<td>33.3</td>
<td>44.4</td>
<td>55.6</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>57.1</td>
<td>42.9</td>
<td>71.4</td>
<td>100</td>
<td>71.4</td>
<td>28.6</td>
<td>57.1</td>
<td>28.6</td>
</tr>
</tbody>
</table>

CAZ – ceftazidime; CTX – cefotaxime; NIT – nitrofurantoin; CXC – cloxacillin; AMX-CLA – amoxicillin-clavulanic acid; GEN – gentamicin; CRX – cefuroxime; OFL – ofloxacin.

There were 18 isolates resistant to all antimicrobials tested. This represented 7.59% of all isolates. *E. coli* had 6 of these isolates (33.3%), coliforms and *Staphylococcus* 4 isolates each (22.2%, respectively), whilst *Proteus*, *Klebsiella* and *Pseudomonas* had one isolate each (5.5%, respectively). 35 isolates (14.76% of all isolates) were sensitive to only one antimicrobial agent tested. 28 of these isolates were sensitive only to nitrofurantoin, 4 isolates sensitive to only ofloxacin, whilst three isolates were sensitive only to gentamicin.
DISCUSSION

A UTI prevalence of 37.38% was observed in this study. This is very different from the prevalence of 60% obtained in another study in the North-Central region of Nigeria (Kolawole et al., 2009). Incidence and prevalent rates of UTI have differed among studies. Prevalence rates as low as 14% have also been observed, although the study was among pregnant women and geographical differences could have contributed (Hamdan et al., 2011). A high incidence of 47.5% was observed among pregnant women in South-Western Nigeria (Okonko et al., 2010).

The highest prevalence was among the 21 to 30 years age group, similar to what was obtained in another study (Oladeinde et al., 2011). This age group has reproductively active women, and UTI is known to be common among pregnant women.

Gram-negative bacilli were identified as the predominant organisms causing UTI, similar to findings in another study (Laupland et al., 2007). E.coli was the commonest organism isolated and conforms with previous observations (Hamdan et al., 2011).

Antimicrobial resistance is a growing global problem. The use of antibiotics can provide selective pressure favouring resistant microbial strains. Contributing factors to resistance include inappropriate and irrational drug misuse by physicians in clinical practice, unskilled practitioners and the public. Drug treatment is usually started before identification of the causative microorganism or the antimicrobial agent most suited for treatment. Other factors are poor quality of drugs, poor storage, counterfeit drugs, expired drugs (Okeke et al., 1999). Drug misuse by the public has been surveyed in Nigeria, with Ampicillin and Tetracycline being the most abused antibiotics (Obaseiki-Ebor et al., 1987; Yah et al., 2008).

The least resistance by the bacterial isolates to antimicrobial agents was to nitrofurantoin. This result was also obtained in a UK-based study (Bean et al., 2008). Nitrofurantoin is not a frequently prescribed drug and in some countries prescription is restricted (Schmiemann et al., 2010). It is thus not a commonly abused antibiotic. This could be responsible for the the little resistance by bacterial isolates to nitrofurantoin. This is different from the observation in previous studies in which nitrofurantoin was poorly effective against organisms causing UTI (Akram et al., 2007; Kolawole et al., 2009). In contrast, most of the isolates exhibited high resistance to cloxacillin. Cloxacillin is a component of Ampiclox, which is one of the most popular antibiotics involved in self-medication in Nigeria (Yah et al., 2008). The high resistance to the cephalosporins is indeed worrisome as this class of antibiotics cannot be afforded by the average patient and is used when other antibiotics have failed. High levels of resistance to oral cephalosporins have been reported in the UK (Farrell et al., 2003). Our study reports a similar high level of resistance to cephalosporins in Bayelsa State, Nigeria.

The prevalence of multi-drug resistant strains (7.59%) and isolates sensitive to only one antibiotic (14.76%) is indicative of serious antimicrobial resistance in the populace. This proportion of isolates which are potentially unresponsive to antibiotics could lead to increased morbidity and mortality. It could mean increased costs of treatment among an already indigent population.

With the emergence of new resistance mechanisms like the Extended spectrum beta lactamases (ESBL) and the New Delhi metallo-beta-lactamase 1 (NDM-1), there is an urgent need to adddress the problem of antimicrobial resistance. Antibiotics should be rationally and specifically used in the treatment of UTI (Schmiemann et al., 2010). Reducing antibiotic prescription and dispensing has been associated with reduced local antibiotic resistance (Schmiemann et al., 2010).

Poor manufacturing practices are common in the third World and may contribute significantly to resistance. Unless measures are taken to provide good healthcare and make quality drugs available and affordable, most people in the Third World would obtain drugs from sources outside the hospital further fuelling antimicrobial resistance.

This is the appropriate time to institute infection control measures which are largely lacking in most healthcare institutions in Subsaharan Africa. Also, there is a need to establish disease control and surveillance agencies like the Centres for Disease control and Prevention (CDC) and the Health Protection Agency (HPA) as obtains in the USA and the UK, respectively.

There is a need for greater interaction between physicians and the microbiology department. There have been occasions where the antibiotics tested are different from those frequently prescribed, since the laboratories use only the susceptibility diffusion disks available to them.

Conclusion

Nitrofurantoin is the most active chemotherapeutic agent against microorganisms causing UTI and is the most appropriate for use in uncomplicated UTI in Bayelsa State, Nigeria. These results will hopefully serve as baseline data for management of UTI and surveillance of antimicrobial resistance in Bayelsa State of Nigeria.

REFERENCES


