

Antibiotics Susceptibility Patterns of some Uropathogens to Nitrofurantoin and Nalidixic Acid among Pregnant Women with Urinary Tract Infections in Federal Medical Centre, Bida, Niger-State, North Central, Nigeria

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Abstract Background: Antimicrobial drug resistance is a worldwide problem that is exacerbated by the diminishing number of new antimicrobial drugs. Developing countries face substantial problems of antimicrobial resistance as a result of emerging and re-emerging resistant organisms. **Aim:** This study was design to reports on antibiotic susceptibility and resistance pattern of bacteria pathogens of UTIs among pregnant women in Bida, North Central, Nigeria, and to determine the extent of resistance of these bacteria pathogens to these drugs in the community. **Materials and Methods:** The research was a retrospective studies carried out between August 2012 to December 2013 and were exempted from ethical approval. Five hundred and sixteen (516) bacterial pathogens were selected for this study as isolated at the Medical Microbiology Department of Federal Medical Centre, Bida, Niger State, North Central, Nigeria. Data was coded, computed and analyzed using SPSS version 16.0 and p-values ≤ 0.05 was considered to be statistically significant. **Result:** Out of this 516 bacteria isolates, Escherichia coli 342(66.3%) was the most predominant followed by Staphylococcus aureus 162(31.4%), Klebsiella specie 6(1.2%), Serratia marcescens 4(0.8%) and the least prevalence Proteus specie 2(0.4%). Overall susceptibility pattern of uropathogens to Nitrofurantoin was (58.5%) and Nalidixic acid (34.5%) and both were statistically significant (Nitrofurantoin $p=0.000$, Mean value 75.5 and Nalidixic acid $p=0.000$, Mean value 44.5). Escherichia coli the highest in predominance shows susceptibility rate of 61.4% and 42.1% to Nitrofurantoin and Nalidixic acid respectively. **Conclusion:** Routine microbiological analysis and susceptibility test should be carried out before administration of drugs to patient. Government should make policy that will discourage over the counter sales and use of antimicrobials without prescription from authorized Medical personnel.

Keywords: Antibiotics susceptibility, Uropathogen, Urinary tract infections

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1. Introduction

Bacterial antimicrobial drug resistance is a worldwide problem that is exacerbated by the diminishing number of new antimicrobial drugs [1,2,3]. Developing countries face substantial problems of antimicrobial resistance. Contributing factors include those involving the public

(e.g. self-medication), prescriber (e.g. misinformation, absence of diagnostic tools) and dispenser (e.g. over the counter use, inadequate storage, use of expired drugs) [4,5]. The current discourse on infectious disease and drug resistance, as it affects Sub-Saharan Africa is limited to the pressing problems associated with emerging and re-emerging resistant organisms [6,7]. Worldwide, the prevalence of antimicrobial resistance limits the

therapeutic options for treatment of infections, and increases the social benefit from disease prevention [8].

In Africa, about 90.1% individuals seek care outside the home, of these, 94.7% take medicines and 36.2 % receive antibiotics. Of all those who receive antibiotics, 31.7 % do not receive a prescription from a doctor and about 26.4% obtain antibiotics from an informal dispenser [9].

Evidently, antibiotics are widely and inappropriately used in Africa resulting to antibiotic resistance. This situation impinges on the quality of patient care through its associated mortality, morbidity, and significant economic consequences [10]. The emergence of antimicrobial resistance is primarily due to excessive and often unnecessary use of antibiotics in humans and animals [8,11,12]. Increasing antimicrobial resistance in Africa has been exacerbated by multiple factors.

For instance, misdirected human resource and training policies, weak institutions, and inappropriate structures [13]. Conspicuously, there are no adequate laboratory facilities [14] and enough trained staff to isolate pathogens and perform sensitivity tests so that infectious diseases are treated empirically [15].

The prevalent pathogens of UTIs have been found to be resistant to most chemotherapeutic agents, though the antimicrobial susceptibilities of these pathogens are highly predictable [16].

Development of resistance to these antimicrobial agents in UTI cases will therefore affect future treatment and management of the infection with these drugs. Adequate treatment and control of these conditions need a good knowledge of the bacteria species involved and their susceptibility to antimicrobial agents [17]. In the UK, Trimethoprim or Nitrofurantoin are usually recommended for empirical treatment of episodes of uncomplicated cystitis in the community [18], while parenteral cephalosporin and aminoglycosides are reserved for complicated infections or pyelonephritis [19]. According to the Infectious Diseases Society of America (IDSA) guidelines, the agents used in the treatment of UTI include Fluoroquinolones, Cephalosporins and other β -lactams with or without β -lactamase inhibitors and Nitrofurantoin [20]. Treatment of a UTI with an antibiotic to which the organism is resistant results in high rates of microbiologic and clinical failure and leads to additional morbidity and costs [21,22], resistance rates vary geographically [23]. The structure of the female's urethra and vagina makes it susceptible to trauma during sexual intercourse as well as bacteria being massaged up the urethra and into the bladder during pregnancy and/or child birth [24]. Majority of UTIs are not life threatening and do not cause any irreversible damage. However, when the kidneys are involved, there is a risk of irreparable tissue damage with an increased risk of bacteraemia [25]. The emergence of antibiotic resistance in the management of UTIs is a serious public health issue, particularly in the developing world where apart from high level of poverty, ignorance and poor hygienic practices, there is also high prevalence of fake and spurious drugs of questionable quality in circulation [26].

AIM: This current study therefore, reports on antibiotic susceptibility and resistance of bacteria pathogens of UTIs among pregnant women in Bida, North Central, Nigeria

and to determine the extent of resistance of these bacteria pathogens to these drugs in the community.

2. Materials and Methods

2.1. Study Population

The research was a retrospective study carried out between August 2012 to December 2013 and was exempted from ethical approval.

Selection of Isolates: Five hundred and sixteen (516) bacterial pathogens were selected for this study as isolated at the Medical Microbiology Department of Federal Medical Centre, Bida, Niger State, according to the standard bacteriological methods described by Baur *et al.* [6] and Ebie *et al.* [7]. The agar diffusion method as described by Baur *et al.* [6] and Ebie *et al.* [7] was used. Discrete colonies were inoculated into 5 ml of sterile nutrient broth and incubated at 37°C over night. The broth culture was then diluted 1:10 with a freshly prepared nutrient broth to give a count of approximately 10^5 colonies per millimetre. A sterile cotton wool was allowed to soak in the broth culture, squeezed by the side of the bottle before streaking over the sensitivity plates and incubated at 37°C for 18 h. Interpretation of results was done using the zone of inhibition sizes. Zones of inhibition of > 13 mm were considered sensitive and < 13 mm resistant. Nitrofurantoin (50 mcg) and Nalidixic acid (300 mcg) antimicrobial discs were used. SPSS version 16.0 was used for statistical analysis.

Table 1. Antibiotics Susceptibility Pattern of Bacterial Pathogen to Nitrofurantoin and Nalidixic Acid. ISOLATES NO. OF OCCURENCE NITROFURANTOIN (%) NALIDIXIC ACID (%)

<i>Escherichia coli</i>	342(66.3 %)	210(61.4%)	144(42.1%)
<i>Staphylococcus aureus</i>	162(31.4%)	84(51.9%)	28(17.3%)
<i>Klebsiella</i> specie	6(1.2%)	4(66.7%)	2(33.3%)
<i>Proteus</i> specie	2(0.4%)	0	0
<i>Serratia marcescens</i>	4(0.8%)	4(100%)	4(100%)
Total	516(100%)	302(58.5%)	178(34.5%)

Mean susceptibility = Sum of susceptibility of individual organisms/total no of organisms.

3. Result

Five hundred and sixteen (516) bacteria pathogens were used for this study (Table 1). Out of this 516 bacteria isolates, *Escherichia coli* 342(66.3%) was the most predominant isolates followed by *Staphylococcus aureus* 162(31.4%), *Klebsiella* specie 6(1.2%), *Serratia marcescens* 4(0.8%) and the least prevalence *Proteus* specie 2(0.4%). This bacterial isolates were tested against Nitrofurantoin and Nalidixic acid to determine their antibiotic susceptibility pattern. The in-vitro antibiotics susceptibility of the two [2] common antimicrobial agents is shown in Table 1. The overall susceptibility pattern of Nitrofurantoin to all the bacteria isolated was (58.5%) and Nalidixic acid (34.5%). *Escherichia coli* the highest in predominance shows susceptibility rate of 61.4% and 42.1% to Nitrofurantoin and Nalidixic acid respectively. The susceptibility of *Staphylococcus aureus* to Nitrofurantoin was (51.9%) and Nalidixic acid (17.3%). The susceptibility of *Klebsiella* specie to Nitrofurantoin was (66.7%) and Nalidixic acid (33.3%). *Serratia marcescens* was (100%) susceptible to both Nitrofurantoin

and Nalidixic acid. While *Proteus* specie was not susceptible to the two [2] antimicrobial agents.

4. Discussion

Antimicrobial resistance among uropathogens to commonly used antibiotics is becoming increasing.

This phenomenon is giving clinicians few choices of drugs for the treatment of urinary tract infections [27].

In this research, the overall susceptibility patterns of uropathogens to Nitrofurantoin was (58.5%) and Nalidixic acid (34.5%) and both were statistically significant (Nitrofurantoin $p=0.000$, Mean value 75.5 and Nalidixic acid $p=0.000$, Mean value 44.5). This report is higher than Mokube *et al*, (28) who reported overall susceptibility rate of Nitrofurantoin (29.2%), Onoh *et al*, [29] reported susceptibility rate of Nitrofurantoin (33.7%), our report is relatively lower than David *et al*, (30) in London, who reported susceptibility rate of Nitrofurantoin (94%) and Okonko *et al*, [31] reported susceptibility rate of Nitrofurantoin (84.2%) in Nigeria.

The overall susceptibility pattern of Nalidixic acid (34.5%) in this present study is lower than Mokube *et al*, [28] who reported Nalidixic acid (95.8%) in Buea, South West, Cameroon and Okonko *et al*, [31] reported Nalidixic acid (60.5%) at Ibadan, South West, Nigeria. The report in this study is higher than Onoh *et al*, [29] who reported overall susceptibility rate of Nalidixic acid (21.4%) against all uropathogen in Abakaliki, South East, Nigeria.

In this study, *Escherichia coli* the highest uropathogen exhibited (61.4%) and (42.1%) susceptibility rate to Nitrofurantoin and Nalidixic acid respectively. This report is relatively higher than Kalantar *et al*, [32], who reported *Escherichia coli* (29.1%) susceptible to Nitrofurantoin and Nalidixic acid (18.9%) susceptible in Iran.

Onoh *et al*, [29] reported *Escherichia coli* (21.1%) susceptible to Nitrofurantoin and Nalidixic acid (12.5%), while Mohemid M. Al-Jebouri *et al*, [33] had similar report, with *Escherichia coli* (60%) susceptible to Nitrofurantoin in Iraq. However, this report is contrary to Igwegbe *et al*, [34] who reported *Escherichia coli* (100%) susceptible to Nitrofurantoin and Nalidixic acid respectively. Also, Sevki *et al*, [35] reported *Escherichia coli* (95.4%) susceptible to Nitrofurantoin in Turkey.

Staphylococcus aureus second uropathogen was (51.9%) susceptible to Nitrofurantoin and Nalidixic acid (17.3%) susceptible. Our report is lower than Okonko *et al*, [31] who reported *Staphylococcus aureus* (72.7%) susceptible to Nitrofurantoin and Nalidixic acid (36.4%), Iram *et al*, [37] reported *Staphylococcus aureus* (66.7%) susceptible to Nitrofurantoin and Nalidixic acid (100%) susceptible.

However, our report is similar to Onoh *et al*, [29] who reported *Staphylococcus aureus* (57.7%) susceptible to Nitrofurantoin in Abakaliki, Nigeria. However, our present report is higher than May Mohammed Ali [44], who reported *Staphylococcus aureus* not susceptible to Nitrofurantoin. Also, Awonuga *et al*, [36] and Onuoha *et al*, [48] both reported *Staphylococcus aureus* not susceptible to Nalidixic acid.

In this study, the susceptibility rate of *Klebsiella* species was (66.7%) susceptible to Nitrofurantoin and Nalidixic acid (33.3%). This report is higher than Kalantar

et al, [32] who reported *Klebsiella* specie (44.4%) susceptible to Nitrofurantoin, May Mohammed Ali, [44] reported *Klebsiella* specie (50%) susceptible to Nitrofurantoin, Onoh *et al*, [29] reported *Klebsiella* specie (25%) susceptible to Nitrofurantoin and Nalidixic acid (25%) in Abakaliki, Nigeria. Sevki *et al*, [35] reported *Klebsiella pneumoniae* (36%) susceptible to Nitrofurantoin in Ankara, Turkey, and Das *et al*, [38] reported *Klebsiella* specie (2.1%) susceptible to Nitrofurantoin While Onoh *et al*, [29] reported *Klebsiella* specie (25%) susceptible to Nalidixic acid.

Our report is relatively lower than Awonuga *et al*, [36] who reported *Klebsiella* specie (75%) susceptible to Nitrofurantoin and Nalidixic acid (50%), Okonko *et al*, [31] reported *Klebsiella* specie (85.7%) susceptible to Nitrofurantoin and Nalidixic acid (71.4%) and Mohemid M. Aljebouri *et al*, [33] reported *Klebsiella* specie (88%) susceptible to Nitrofurantoin and Nalidixic acid (70%). However, our report is contrary to Selimuzzaman *et al*, (43) who reported *Klebsiella* specie (90%) susceptible to Nitrofurantoin and Nalidixic acid (100%) susceptible.

Serratia marcescens was (100%) susceptible to Nitrofurantoin and Nalidixic acid respectively. Our report is similar to Rahman *et al*, [49] who reported *Serratia marcescens* (100%) susceptible to Nitrofurantoin but higher than Mohemid M. Aljebouri *et al*, [33] who reported *Serratia marcescens* (80%) susceptible to Nitrofurantoin and Nalidixic acid (90%). However, Lin-Hui *et al*, [39] reported *Serratia marcescens* (2.3%) susceptible to Nitrofurantoin and Nalidixic acid (11.5%) susceptible among nosocomial urinary tract infection. Drug resistance is one of the nature's never ending process whereby organisms develop tolerance for new environmental condition. These may be due to pre-existing factor in the organisms or it may result from the acquired factor(s). Some naturally susceptible strains of bacteria may acquire resistance [40].

However, in this study, the *Proteus* specie isolated was not susceptible to both Nitrofurantoin and Nalidixic acid. This finding is in agreement with Stanley *et al*, [41], who reported *Proteus mirabilis* not susceptible to Nalidixic acid. Our findings is similar to Das *et al*, [38] who reported *Proteus mirabilis* (13.4%) susceptible to Nitrofurantoin and Onoh *et al*, [29] reported *Proteus* specie (20.8%) susceptible to Nalidixic acid. Our report is contrary to Sevki *et al*, [35] who reported *Proteus* specie (100%) susceptible to Nitrofurantoin, Akinola *et al*, [42] reported *Proteus* specie (100%) susceptible to Nalidixic acid, Selimuzzaman *et al*, [43] reported *Proteus* specie (80%) susceptible to Nitrofurantoin and Nalidixic acid respectively. Also, May Mohamed Ali *et al*, [44] reported *Proteus* specie (83.3%) susceptible to Nitrofurantoin and Nalidixic acid (50%) susceptible in Karbala.

The overall susceptibility pattern of Nitrofurantoin (58.5%) and Nalidixic acid (34.5%) to all isolated clinical uropathogen. This is no doubt a public health concern in Bida, North Central, Nigeria. Karlowsky *et al*, [45] stated that the increasing antimicrobial resistance in bacteria pathogen is a worldwide concern, and resistance rates vary from country to country (Gales *et al*, 2002), [46].

The prevalence of antimicrobial resistance among UTI agents is increasing and its treatment has become more complicated due to increasing resistance and empirical

therapy leading to treatment failures mostly associated with gram-negative bacteria (Blondeau *et al*, 1999), [47].

5. Conclusion

The overall susceptibility rate of Nitrofurantoin (58.6%) and Nalidixic acid (34.5%) to all isolated uropathogen is of public health concern in this community. Increasing antibiotic resistance is a burden in health industry and the outcome increases mortality and morbidity rate in health statistics.

It is therefore recommended, that routine microbiological analysis and susceptibility test should be carried out before administration of drugs to patient. Government should make policy that will discourage over the counter sales and use of antimicrobials without prescription from authorized Medical personnel.

Africa, is home of unlawful street drug hawkers and counterfeit drugs. Governments need to make policy to control and eradicate this menace through public enlightenment programmes.

Conflict of Interest

No conflict of interest.

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