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Widespread antibiotic resistance in savannah Nigeria+

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Summary
There is minimal data on antibiotic resistance from savannah northern Nigeria. A retrospective study of 438 patients seen in 12 months (2000) with microbial pathogens from urinary and respiratory tracts was undertaken. Antibiotic susceptibilities were determined using stokes disc diffusion technique. Resistance in Escherichia coli (E.coli) reached 91-96% to cotrimoxazole, tetracycline and ampicillin but was 11%, 17% and 28% to colistin, nitrofurantoin and nalidixic acid. Resistance of other uropathogens (Klebsiella and Proteus spp) reached 83-99% to cotrimoxazole, tetracycline and ampicillin but was14-40% to colistin, nitrofurantoin and nalidixic acid. Pneumococci were non-susceptible to penicillin (93%), cotrimoxazole (92%), tetracycline (84%), ampicillin (53%), chloramphenicol (21%) and cefazolin (8%). Antibiotic resistance is widespread in savannah northern Nigeria. Resistance is less to chloramphenicol, colistin, nalidixic acid, nitrofurantoin and the latter generation cephalosporins and quinolones than to penicillin, ampicillin, cotrimoxazole and tetracycline.

Keywords: *Infections, anti-microbial resistance, savannah, sub-Saharan Africa, Nigeria.*

Résumé 2457
Il y a moins des données sur la résistance des antibiotiques dans la savane au Nord du Nigéria. Une étude retrospective sur 438 patients en 12 mois (2000) infectés des microbes pathogénes des voies urinaires et respiratoires etait entreprisée Les susceptibilités des antibiotiques étaient determinées en utilisant la technique du disque de diffusion de Stokes. La résistance de *l'Escherichia coli (E.coli)* variait entre 91-96% au cotrimoxazole, tetracycline et amplicilline mais etait de 11% , 17%, et 28% au colistrine, nitrofurantoine et l'acide nalidixique. La résistance d autres uropathogénes (*Klebsiella et Proteus spp*) étaient de 83-99% au cotrimoxazole, tétracycline et amplicilline cependant était de 14-40% au colistrine, nitrofurantoine et l'acide nalidixique.Les pneumocoques étaient pas susceptible au penicilline (93%), cotrimoxazole(92%), tetracycline(84%), Amplicilline(53%), chlorammphenicole (21%) et Cefazoline(8%). La résistance des antibiotiques est répandue dans le nord savanien du Nigéria. Cette résistance est moins au chloramphénicole, colistine, l'acide nalidixique, nitrofurantoine et la seconde géneration des cephalosporines et quinolones qu' au penicilline, amplicilline, cotrimoxazole et tetracycline

Introduction

Anti-microbial drug resistance has been reported from different parts of sub-Saharan Africa [1] but there is no data on resistance from northern Nigeria. Conditions promoting antibiotic resistance such as lack of functional regulatory institutions, widespread availability of substandard formulations, poverty and general inadequacy of health care services exist in many of the populated cities of savannah, Nigeria. Respiratory and urinary tract infections are among the major causes of infectious diseases morbidity and mortality in sub-Saharan Africa [2], and significant antibiotic resistance in the causative organisms of these conditions will have great public health consequences. Thus the present preliminary study was undertaken to determine the prevalence of antibiotic resistance among clinical bacterial isolates from patients with respiratory and urinary tract infections in a new teaching hospital (AKTH) in Kano, Nigeria.

Patients and methods

Study and Methods- The study was carried out in Kano (population 7.26 million: *National Population Commission, Abuja, Nigeria*) situated in the sudan savannah of northern Nigeria. It is a retrospective study of patients (both hospitalized and outpatients) who presented over a 12 months period (January to December 2000), and who had culture positive respiratory and urinary tract isolates. Basic clinical data of patients with relevant symptoms and signs were obtained from the records. Respiratory samples mainly sputum were collected and brought to the laboratory in a sterile container.

Urine specimens were obtained by clean catch method. The urine samples were collected in sterile universal containers containing boric acid crystals and examined immediately. Microscopic examination using Gram's and Ziehl-Neelson's staining was done on the urine and sputum samples. The samples were processed and innoculated onto Chocholate agar, MacConkey's agar, Blood agar and Cysteine-lactose-electrolyte-deficient (CLED) medium, as the case may be, and incubated aerobically overnight or for 24 hours at 37C. In the case of urine, samples showing at least 5 log colony-forming units per ml of urine after overnight incubation were considered indicative of significant bacteriuria. Colonies with characteristic morphologies were sub-cultured onto fresh plates and identification of the organism to species level was confirmed by conventional tests. Antimicrobial sensitivity tests were carried out using the Stokes disc diffusion method [3, 4].

Analysis-Data was analysed using the statistical programme SPSS version 10.0.1 (SPSS Inc, Chicago IL, USA) for Windows operating system 1998 (Win98NT). Student's t-test was used to compare quantitative data. Results were expressed as proportions.

Results

A total of 2649 urine and 497 respiratory samples were processed. Three hundred and twelve (312) and 126 patients with non-duplicative urinary and respiratory tract isolates were seen. Table 1 gives the distribution of sources of clinical isolates. The mean ages for patients with positive urine and respiratory cultures were 28.4 and 29.6 years ($P > 0.05$) respectively, and the mean ages for patients with hospital and community acquired isolates were 30.6 and 28.0 years ($P > 0.05$) respectively. Pneumococci (69), *Klebsiella* spp (23) and *Staphylococcus aureus* (13) accounted for 83% of all respiratory

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isolates. In urine, *Escherichia coli (E. coli)* (119), *Klebsiella* spp (73), *Proteus* spp (37) and *Pseudomonas aeruginosa (P. aeruginosa)* (35) accounted for 85% of pathogens in urinary tract infection (Table 1). At least 64% of all urinary isolates were responsible for community acquired urinary tract infections (Table 2).

Table 1. Distribution of sources of clinical isolates

Urinary (n = 312)	Respiratory (n = 126)
Escherichia coli (119)	Pneumococcus (69)
Klebsiella spp (73)	*Klebsiella* spp (23)
Proteus spp (37)	*Staphylococcus aureus* (13
Pseudomonas aeruginosa (35)	*Pseudomonas aeruginosa* (5)
Streptococcus spp (21)	*Escherichia coli* (5)
(*E. faecalis* –7)	*Streptococcus* spp (4)
Staphylococcus spp (11)	*Proteus vulgaris* (2)
(*S. saphrophyticus* – 4)	*Candida albicans* (1)
Other Coliforms (8)	Others (4)
Candida albicans (8)	

Table 2: Pathogens in Community Acquired Urinary Tract infections (UTI[1]) (199 patients and isolates)

Escherichia coli	77
Klebsiella species*	42
Pseudomonas aeruginosa	26
Proteus species~	25
Streptococcus species+	15
Staphylococcus species!	9
Other coliforms	4
Candida albicans	1

*(*Klebsiella pneumoniae*-17; *K. rhinoscleromatis*-2; unspeciated-23)
~(*Proteus mirabilis*- 14; *P. vulgaris*- 5; unspeciated- 6)
+(*Enterococcus faecalis*- 4; rest unspeciated)
!(*Staphylococcus aureus*- 5; *S. saphrophyticus*- 3; *S. epidermidis*-1)
1 (Community acquired UTI is defined as symptomatic bacteriuria among outpatients)

Pneumococcal resistance was found to penicillin (93%), cotrimoxazole (92%), tetracycline (84%), ampicillin (53%), chloramphenicol (21%) and cefazolin (8%).
Resistance in *E.coli* reached 91-96% to cotrimoxazole, tetracycline and ampicillin but was 11%, 17% and 28% to colistin, nitrofurantoin and nalidixic acid. Resistance of other pathogens (*Klebsiella* and *Proteus* spp) reached 83-99% to cotrimoxazole, tetracycline and ampicillin but was 14-40% to colistin, nitrofurantoin and nalidixic acid (Tables 3 and 4). Cefuroxime resistance was found in *E.coli* (25%), *Klebsiella* spp (20%) and *Proteus* spp (20%). All *P.aeruginosa* tested were susceptible to ceftazidime and ciprofloxacin.

Table 3. Bacterial resistance to commonly used antibiotics in proportion and percentage (%)

	Ampicillin	Cotrimoxazole	Tetracycline
Escherichia coli	98/102 (96.1)	72/79 (91.1)	94/102 (92.2)
Klebsiella spp	74/75 (98.7)	55/60 (91.7)	61/72 (84.7)
Proteus spp	23/26 (88.5)	19/23 (82.6)	27/30 (90)
Pneumococcus	27/51 (52.9)	12/13 (92.3)	51/61 (83.6)
Staphylococcus spp	16/17 (94.1)	5/5 (100)	14/18 (77.8)

Table 4. Bacterial resistance to less commonly used antibiotics in proportion and percentage (%)

	Nalidixic acid	Nitrofurantoin	Colistin	Chloramphenicol
Escherichia coli	22/78 (28.2)	17/98 (17.3)	8/74 (10.8)	6/8 (75)
Klebsiella spp	16/49 (32.7)	19/50 (38)	9/63 (14.3)	6/9 (66.7)
Pseudomonas aeruginosa	10/26 (38.5)	10/25 (40)	8/26 (30.8)	2/3 (66.7)
Proteus spp	7/20 (35)	10/25 (40)	5/19 (26.3)	2/3 (66.7)
Pneumococcus	NT	NT	NT	10/47 (21.3)

NT=Not tested

Discussion

Antibiotic bacterial resistance is widespread in savannah northern Nigeria with *E.coli* resistance of over 90% to cotrimoxazole, tetracycline and ampicillin, and penicillin resistant in 93% of pneumococci. Similar levels of antibitiotic resistance have been reported from southern Nigeria; *E.coli* resistance (80-100%) to ampicillin and tetracycline was recently reported for isolates collected in 1998 from healthy students in south-western Nigeria [5]. Pneumococcal non-susceptibility (intermediate and full resistance) to penicillin reported in our study alarmingly surpasses previous reports from West Africa; 62% from Dakar, Senegal and 67% in isolates from northeastern, Nigeria [6,7].

Resistance is less to chloramphenicol, colistin, nalidixic acid and nitrofurantoin than to penicillin, ampicillin, cotrimoxazole and tetracycline, and the former antibiotics may be useful in certain circumstances. Resistance to relatively newly introduced antibiotics like cephalosporins and quinolones is less but could emerge rapidly if appropriate control measures are not taken.

The widespread resistance in Nigeria may be partly due to availability of substandard antibiotic formulations, lack of functional regulatory institutions and deterioration in health care services. Our findings if re-confirmed in a prospective study would have serious clinical and therapeutic implications for the management of common infections in Nigeria, and appropriate measures should be undertaken to prevent dissemi-

nation of resistance to the new anti-microbials.

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