ANTIMICROBIAL RESISTANCE PATTERN OF BACTERIA ISOLATED FROM PATIENTS SEEN BY PRIVATE PRACTITIONERS IN THE KLANG VALLEY

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ABSTRACT

Data on bacterial resistance in patients seen by general practitioners are usually not readily available. The objective of this paper is to present the antimicrobial resistance pattern of bacteria isolated from patients seen by private practitioners in the Klang Valley. A total of 18 clinics participated in this study. From mid August 1991 to end of June 1993, 2,823 specimens were received. Throat swabs and urine specimens constituted 56% of all the specimens. A large proportion of the specimens (55%) yielded no growth or just normal flora. The common bacteria encountered were Staphylococcus aureus (18.4%), Escherichia coli (16.2%), Klebsiella spp (13.7%) and Neisseria gonorrhoeae (9.3%). The S. aureus strains were mainly isolated from wound, pus and ear swabs. Not one out of the 218 strains tested was resistant to methicillin. In vitro susceptibility tests showed that 91% were resistant to penicillin while 23% were resistant to tetracycline and 13% to erythromycin. Eighty-two percent of the E. coli were isolated from urine. It was also the most common isolate from urine. Fifty percent of these strains were resistant to ampicillin, 33% to cotrimoxazole, 17% to cephalothin, 21% to ampicillin-sulbactam, 18% to amoxycillin-clavulanic acid while only 2.3% were resistant to nalidixic acid and nitrofurantoin and none to cefuroxime. Generally the gram negative bacilli encountered in general practice are less resistant to the third generation cephalosporins and aminoglycosides when compared to the hospital strains.

Keywords: *antimicrobial resistance, general practice*

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INTRODUCTION

Data on the epidemiology of antimicrobial resistance are usually gathered from hospital laboratories where such records are easily available for surveillance and monitoring purposes[1-3]. However, information on bacterial isolates from patients seen by general practitioners are not that easily available. The reasons are probably due to the fact that most general practitioners have logistic problems in sending fresh clinical specimens for culture and sensitivity and even if they do, it would be sent to different private laboratories where the data are difficult to access to. Therefore we decided to do a prospective study on the antimicrobial susceptibility pattern of bacteria isolated from patients seen by private practitioners in the Klang Valley. This information would be useful as baseline epidemiological data for doctors in their empirical choice of antimicrobials.

MATERIALS AND METHODS

Sources of specimens

Doctors from eighteen clinics in the Klang Valley agreed to participate in this study. Two of the clinics were specialist clinics; one, a chest clinic and, the other, an Ear, Nose and Throat clinic. Relevant clinical specimens from patients with suspected infections were taken and sent to the Bacteriology Division of the Institute for Medical Research accompanied by a form with relevant clinical history. Specimens from patients who had been hospitalised in the last one month and had antibiotics in the last one week prior to seeing the doctor were excluded. Appropriate instructions and transport media were given to the doctors. Specimens were only collected from the clinics everyday from 11.30 am to 2.30 pm except for weekends and public holidays when there was no collection at all.

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Processing of specimens

When the specimens arrived at the laboratory, they were all processed immediately. The isolation and identification of recognised bacterial pathogens were done according to standard bacteriological techniques. No attempt was made to isolate anaerobes.

However, gram negative bacilli and *Staphylococcus aureus* present in throat swabs and sputum specimens were also isolated and identified and the susceptibility tests done; even though they may not be clinically significant.

Susceptibility Test

The agar diffusion method according to the National Committee for Clinical Laboratory Standards (NCCLs) were followed for the antimicrobial susceptibility test[4]. The antimicrobial-discs used were amikacin, ampicillin, aztreonam, carbenicillin, cefoperazone, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, cephalothin, chloramphenicol, ciprofloxacin, clindamycin, cotrimoxazole, erythromycin, gentamicin, imipenem, kanamycin, oxacillin, nalidixic acid, netilmicin, nitrofurantoin, norfloxacin, ofloxacin, penicillin G, pefloxacin, piperacillin, spectinomycin tetracycline, ticarcillin, tobramycin, trimethoprim, vancomycin, amoxycillin-clavulanic acid and ampicillin-sulbactam. The choice of antibiotic disc used depends on the bacteria. Both the first line and second line antibiotics were tested but only the results of the first line drugs were reported back to the doctors.

All bacteria were tested for beta-lactamase production using the nitrocefin disc as the substrate.

Antibiotics used by doctors

The form that accompanied the specimens also specify the antibiotics that the doctors would use after collecting the specimen. This data was gathered to see what are the common antibiotics used in private practice.

Analysis of data

All the data were entered into a 386 personal computer using a menu driven programme written in the Clipper language for the purpose of generating individual reports back to the doctors and for final analyses.

RESULTS

From mid August 1991 to end of June 1993, 2,823 specimens were received. Most of the specimens (63%) were from patients between the age of 20 to 40 years. The frequency distribution of the types of specimens received is shown in Table I. Throat swabs and urine specimens constituted 56% of all the specimens. A total of 1,352 bacteria were isolated from 1,182 (42%) specimens and their frequency distribution is shown in Table II. A large proportion (55%) of the specimens yielded no growth or normal flora. The common bacteria encountered were *Staphylococcus aureus* (18.4%), *E. coli* (16.2%), *Klebsiella spp* (13.7%) and *Neisseria gonorrhoeae* (9.5%).

Table I – Frequency distribution of types of specimens

Specimen	Frequency	Percentage
Throat swab	1,014	35.9
Urine	568	20.1
Sinus washout/aspirate	241	8.5
Ear swab	211	7.5
Urethral discharge	210	7.4
Sputum	183	6.5
Pus/wound swabs	183	6.5
Endocervical/vaginal swab	143	5.1
Stool	36	1.3
Eye swab	22	0.8
Body Fluid	7	0.3
Blood	5	0.2
Total	2,823	100

The frequency distribution of organisms isolated from throat swabs, urine and sputum are shown in Tables III, IV and V respectively. The total numbers here do not reflect the number of specimens tested but indicate the number of organism types isolated from the specimens. For the throat swab and sputum specimens, the predominant gram negative bacteria were identified even though they may not be clinically significant. Only 3.7% of the throat swabs examined were positive for Group A beta haemolytic *streptococci*. The rest of the bacteria identified were possibly part of the throat flora. *E. coli* was the most common pathogen isolated from urine (27.5%).

Nineteen percent of the urine samples showed mixed growth in low numbers indicating improper collection. The majority of the sputum specimens yielded normal flora. Only 5.4%, 3.4% and 2.5% of the sputum specimens were positive for *H. influenzae, S. pneumoniae* and *M. catarrhalis* respectively.

Out of the 241 sinus washout and aspirates examined, only 2.9% and 2.4% of the specimens were positive for *H. influenzae* and *S. pneumoniae* respectively. *S. aureus* (31.5%) was the most common bacteria isolated from pus and swabs from skin lesions. Forty-eight percent of the urethral discharge were positive for *N. gonorrhoeae* while 7.7% of the endocervical specimens were positive. Group B beta haemolytic *streptococci* were present in 18.9% of the endocervical or vaginal swabs examined. Only 36 samples of stools were sent for culture; of which 2 were positive for *Salmonella spp.* and one for *Shigella boydii.*

Table II – Frequency distribution of organisms isolated from 1,182 specimens

Organism	Frequency	Percentage
Gram negative	**765**	**56.5**
E. coli	191	14.1
Klebsiella spp	162	12.0
N. gonorrhoeae	112	8.3
Pseudomonas spp	84	6.2
Enterobacter spp	53	3.9
H. influenzae	44	3.3
Acinetobacter spp	42	3.1
Proteus spp	22	1.6
Moraxella catarrhalis	11	0.8
Citrobacter spp	10	0.7
Others	34	2.5
Gram positive	**540**	**40.0**
S. aureus	218	16.1
Gp.B streptococci	101	7.5
Gp.A streptococci	50	3.7
Other beta haemolytic *streptococci*	78	5.8
Coagulase negative *Staphylococci*	47	3.5
S. pneumoniae	24	1.8
Viridan group of *streptococci*	15	1.1
Enterococci	7	0.5
Candida spp	**47**	**3.5**

Table III – Frequency distribution of organisms in throat swabs

Organism	Frequency	Percentage
Normal flora	703	65.0
No growth	15	1.4
Gp. A *streptococci*	38	3.5
Gp. B *streptococci*	38	3.5
Gp. C *streptococci*	6	0.6
Gp. G *streptococci*	46	4.3
S. aureus	61	5.6
S. pneumoniae	7	0.7
H. influenzae	21	1.9
Moraxella catarrhalis	4	0.4
Enterobacteriaceae	121	11.2
Pseudomonas spp & other non-fermentative gram negative bacilli	21	1.9
Total	1,081	100

Out of the 1,489 isolates tested for beta lactamase production, 47% were positive (42% with gram positive bacteria and 49% with gram negative bacteria).

The commonly prescribed antibiotics were ampicillin (29.7%), cotrimoxazole (15.6%), amoxycillin (6.5%), ampicillin-

cloxacillin (5.9%), erythromycin (5.6%) and doxycycline (5.1%), out of the total of 2,130 antibiotics prescribed.

Table IV – Frequency distribution of organisms in urine specimens

Organism	Frequency	Percentage
No growth	166	27.3
Mixed growth in insignificant numbers	113	18.6
Enterobacteriaceae	200	32.8
Pseudomonas spp and other gram negative non-fermentative bacilli	20	3.3
S. aureus	22	3.6
S. epidermidis	22	3.6
S. saprophyticus	17	2.8
Gp. B streptococci	25	4.1
Gp. D streptococci	6	1.0
Viridan group of *streptococci*	13	2.1
Enterococci	5	0.8
Total	609	100

Table V – Frequency distribution of organisms in sputum

Organism	Frequency	Percentage
Normal flora	125	61.6
H. influenzae	11	5.4
S. pneumoniae	7	3.4
Beta haemolytic *streptococci*	10	4.9
M. catarrhalis	5	2.5
Enterobacteriaceae	30	14.8
Pseudomonas spp & other gram negative non fermentative bacilli	15	7.4
Total	203	100

The percentages of the Enterobacteriaceae family, *E. coli, Ps. aeruginosa* and *S. aureus* resistant to the various antimicrobials are shown in Tables VI and VII. Although the results of *E. coli* have already been grouped under the Enterobacteriaceae, it was specially shown in Table VI as it is the most common gram negative bacteria isolated and more than 80% of these strains were isolated from urine specimens. The results of other bacterial species were not tabulated because the total number tested was too few.

Fifty percent of the *E. coli* was resistant to ampicillin while 33.5% was resistant to cotrimoxazole, 2.6% resistant to nalidixic acid and nitrofurantoin, 21.1% to ampicillin-sulbactam, 18.0% to amoxycillin-clavulanic acid, 17.3% to cephalothin and 0.0% to cefuroxime. Generally, the resistance of the gram negative bacteria to the third generation cephalosporins and aminoglycosides was very low (Table VI). None of the *S. aureus* tested was resistant to methicillin while 91.3% were resistant to penicillin G, 23.4% to tetracycline and 13.3% to erythromycin.

Five out of 43 *H. influenzae* strain, (12%) were resistant to ampicillin and one was also resistant to chloramphenicol.

Two out of 22 *S. pneumoniae* were resistant to penicillin. Of the 50 strains of Group A *streptococci* and 101 Group B *streptococci* tested, all were susceptible to penicillin. All the Gp A *streptococci* were susceptible to erythromycin, however 3% of the Gp B *streptococci* were resistant. Of the 112 strains of *N. gonorrhoeae* tested, 59% were resistant to penicillin, 81% to tetracycline and none to ceftriaxone and spectinomycin.

Table VI – Percentage of gram negative bacteria resistant to antimicrobials

Antimicrobials \ Bacteria	*Entero-bacteriaceae*	*E. coli*	*Ps. aeruginosa*
Amikacin	1.3(445)	0.0(187)	4.2(71)
Ampicillin	71.1(453)	50.3(191)	–
Ampicillin-sulbactam	19.4(433)	21.1(185)	–
Amoxycillin-clavulanic acid	22.1(389)	18.0(161)	–
Aztreonam	3.6(442)	2.7(186)	7.0(71)
Carbenicillin	51.6(438)	46.0(187)	8.3(72)
Cefoperazone	3.4(443)	5.3(187)	4.1(73)
Cefotaxime	0.2(450)	0.0(190)	20.0(70)
Ceftazidime	0.7(449)	0.5(189)	4.1(73)
Ceftriaxone	0.3(293)	0.0(188)	22.9(70)
Cefuroxime	3.3(448)	0.0(190)	–
Cephalothin	21.8(450)	17.3(191)	–
Chloramphenicol	16.2(451)	25.4(189)	–
Ciprofloxacin	0.7(451)	0.0(190)	1.4(71)
Cotrimoxazole	18.8(453)	33.5(191)	–
Gentamicin	1.7(451)	0.5(191)	5.6(72)
Imipenem	0.7(437)	1.1(187)	1.4(72)
Kanamycin	9.5(452)	15.2(191)	–
Nalidixic acid	3.0(198)	2.6(152)	–
Netilmicin	1.3(447)	0.0(189)	5.5(73)
Nitrofurantoin	2.6(192)	2.6(154)	–
Norfloxacin	1.1(450)	1.6(190)	0.0(72)
Ofloxacin	0.9(446)	1.6(185)	8.3(72)
Pefloxacin	1.6(449)	1.6(188)	19.7(71)
Piperacillin	23.9(444)	40.9(186)	1.4(70)
Tetracycline	38.9(463)	61.8(191)	–
Ticarcillin	52.0(304)	47.5(141)	11.9(42)
Tobramycin	1.4(437)	1.1(182)	2.9(70)
Trimethoprim	33.1(166)	37.1(124)	–

( ) Total no. tested

Table VII – Percentage of *S. aureus* resistant to antimicrobials

Antimicrobials	No. tested	Percentage
Chloramphenicol	207	3.4
Clindamycin	218	1.8
Cotrimoxazole	218	2.8
Erythromycin	218	13.3
Fusidic acid	216	6.5
Methicillin	217	0.0
Penicillin G	218	91.3
Tetracycline	218	23.4

DISCUSSION

This study is probably the first of its kind to be conducted in the Klang Valley. Initially, it was targeted to be completed in one year with about 5,000 specimens to be processed in that period. Unfortunately when the project started a number of patients had to be excluded because collection services to these clinics was confined to 11.30 am to 2.30 pm during the weekdays due to logistic problems. This reflects the difficulty in collecting such data.

The most common specimens sent for culture from the private

clinics were throat swabs and urine specimens which constituted more than half the specimens. From the culture results, only a low percentage ie 3.5% of the throat swabs were positive for group A *streptococci*, implicating that the majority of pharyngitis cases could be due to viral or other causes. The aetiological significance of the other bacteria isolated was doubtful.

Nineteen percent of the urine specimens showed mixed growth in insignificant numbers. This indicated the problem of ensuring proper urine collection in private clinics for culture. The resistance of *E. coli*, the commonest isolate from urine, to ampicillin and cotrimoxazole was relatively high ie 50% and 34% respectively. These results are quite comparable to two other studies, one done in the United Kingdom where 38.4% of the coliforms isolated from urine of patients in the community in 1991 were resistant to ampicillin, and another in Spain where 56% of the *E. coli* were resistant to ampicillin and 37% to cotrimoxazole[3,5]. These two antibiotics also happen to be the most commonly prescribed antibiotics in the study. Alternative empirical antibiotic for the treatment of urinary tract infection in the community need to be considered in the light of these results.

Although the prevalence of methicillin resistant *S. aureus* (MRSA) is high in our local hospitals and other studies have reported the occurrence of MRSA in some outpatient intravenous drug addicts, this study did not detect any isolate of MRSA out of the 217 *S. aureus* strains tested[6,7]. However resistance to penicillin and tetracycline was high (91.3% and 23.4% respectively).

Increasing incidence of penicillin resistant *Streptococci pneumoniae* and ampicillin resistant *Haemophilus influenzae* have been reported worldwide[8,9]. Only 24 strains of *S. pneumoniae* and 44 strains of *H. influenzae* were isolated from specimens of the respiratory tract. Therefore, it is difficult to comment on the significance of the resistance rates of 8% and 12% obtained respectively.

The high resistance of *N. gonorrhoeae* to penicillin (59%) and tetracycline (81%) was expected. This is consistent with the results of the surveillance programme conducted by the Institute for Medical Research[10].

All the Group A and B *streptococci* tested were susceptible to penicillin and all the Group A *streptococci* were also susceptible to erythromycin, an alternative antibiotic for patients allergic to penicillin. However, reports of erythromycin resistance have been published in other countries as well as locally where a resistance rate of 4% was reported in a national surveillance programme[11-13].

Twenty-six percent of the *Ps. aeruginosa* isolated from the local hospitals were resistant to gentamicin compared to this study where only 5.6% were resistant[1]. Similarly, most gram negative bacteria isolated in this study are highly susceptible to the third generation cephalosporins which is in marked contrast to the hospital isolates where resistance to these cephalosporins varied from 4% to 51.1%[1].

The production of beta lactamase enzyme is one of the major mechanism of resistance amongst bacteria and these can be transmitted easily from one bacteria to another via plasmids. Almost half of the isolates tested in this study produced beta lactamases, despite the fact that the method employed was only suitable for detecting extracellular enzyme. Hence, there is a place for the use of the beta lactam antibiotics together with a beta lactamase inhibitor like sulbactam and clavulanic acid or a cephalosporin that is stable to beta lactamases.

The relatively small number of specimens received in two years from private clinics reflect the logistic problems that doctors face in sending suitable specimens for bacteriological culture. To increase the number of samples, more clinics would need to be enrolled in such a study. Perhaps in the future a larger study can be conducted so that more representative samples can be collected. Nevertheless this study did yield some useful basic epidemiological data regarding antimicrobial resistance amongst bacteria isolated from patients in the community.

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