Antimicrobial Susceptibility of Common Bacterial Pathogens Isolated from a New Regional Hospital in Southern Taiwan

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Background: Antimicrobial resistance has become a major health problem in Taiwan. While some trends in antimicrobial resistance are universal, others appear to be unique for specific regions.

Methods: To determine the distribution and antimicrobial drug resistance of bacterial pathogens in a new hospital in southern Taiwan, surveillance data on major bacterial pathogens isolated from Chang Gung Memorial Hospital at Chia-Yi from January 2002 through December 2002 were retrospectively analyzed.

Results: The most common gram-positive isolate was *Staphylococcus aureus*. *Escherichia coli* and *Klebsiella pneumoniae* were the two most common gram negative isolates. *Pseudomonas aeruginosa* ranked the first among gram-negative, glucose non-fermenting isolates, followed in the order of frequency by *Acinetobacter baumannii*. Oxacillin resistance rate of *S. aureus* was 58%, while vancomycin and teicoplanin remained effective against all of the isolates. The penicillin non-susceptibility rate of *Streptococcus pneumoniae* was 52%, and it is notable that the rate of resistance to erythromycin was 87%. Resistance to various antimicrobial agents for *P. aeruginosa*, *Aeromonas hydrophila*, and gram-negative enteric bacilli was very common in our study. Infections caused by multidrug-resistant *A. baumannii* was not uncommon in this hospital but fortunately, imipenem resistant *A. baumannii* was rarely encountered. Antimicrobial resistance was common in nontyphoid *Salmonella*, *S. choleraesuis* and serogroup B isolates in particular.

Conclusion: The high rates of antimicrobial resistance among these major bacterial pathogens in this new hospital are impressive and alarming. Judicious use of antimicrobial agents can never be overemphasized. Continued surveillance of the changes of resistance patterns over time is necessary.

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Key words: **antimicrobial resistance, bacterial pathogens, regional hospital.**

The emergence of resistance to antimicrobial agents in bacterial pathogens is a global public health problem.(1-3) Antimicrobial resistance results in increased illness, deaths, and healthcare costs.(1) The distribution of pathogens causing infections, especially antimicrobial-resistant pathogens, changes

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with time and varies among hospitals and among different locations in the same hospital.[4] The increasing number of immunocompromised patients and increased use of indwelling devices, as well as widespread use of antimicrobial agents in both hospital and community settings contributes to antimicrobial resistance among bacterial pathogens causing infections.

Chang Gung Memorial Hospital at Chia-Yi opened for service in December 2001. This new hospital serves patients living in the coastal region of Yun-Lin, Chia-Yi, and Tainan counties. We describe the distribution of major bacterial pathogens causing infections as well as the antimicrobial drug resistance patterns of the isolates collected during the first year of service at this hospital. The data obtained highlight the seriousness of antimicrobial drug resistance among the common bacterial pathogens in southern Taiwan.

METHODS

Data collection

Chang Gung Memorial Hospital is a 700-bed referral regional hospital in Chia-Yi, Taiwan. Available data for inpatient-days at the hospital was 154,856 (including 13,763 for ICUs) in 2002. The number of ICU beds was 50. All bacterial isolates were identified using the standard methods and confirmed using Vitek or API products (bioMerieux Vitek, Inc., Hazelwood, Mo). For determining the percentage of resistance, the same organisms from multiple blood cultures or from the same sources with an identical antibiotype were considered as a single isolate.

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing of the bacterial isolates was performed using the disk diffusion method as described by the National Committee for Clinical Laboratory Standards (NCCLS).[5] *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were included as the control strains. The interpretive criteria for susceptibility or resistance followed the NCCLS guidelines.[5] For this report, we present susceptibility data for penicillin, oxacillin, vancomycin, gentamicin, cefotaxime, ceftazidime, imipenem, and ciprofloxacin. The double-disk diffusion assay was used to screen for the presence of extended-spectrum β-lactamases (ESBL) in *Enterobacteriaceae*, except for *Serratia marcescens* according to the published method.[6]

RESULTS

In Tables 1-5, we describe the frequency of bacterial pathogens identified in this hospital. The most commonly found gram-positive isolate was *S. aureus*. *Escherichia coli* and *Klebsiella pneumoniae* were the two most commonly found gram-negative isolates. *Pseudomonas aeruginosa* ranked first among the gram-negative, glucose non-fermenting isolates, followed in the order of frequency by *Acinetobacter baumannii*.

Antibiotic resistance patterns of the major gram-positive pathogens isolated from this hospital are described in Table 1. The oxacillin resistance rate of *S. aureus* was 58%, while vancomycin and teicoplanin remained effective against all of the isolates. The penicillin non-susceptibility rate of

Table 1. Antimicrobial Susceptibility of Common Gram-positive Bacteria Isolated.

Bacteria	Isolate No.	Resistance rates of antibiotics (%)											
		SXT	AM	H-GM	C	CC	E	OX	P	CXM	CRO	Tei	Van
S. aureus	1383	30	—	—	36	68	74	58	97	—	—	0	0
S. pneumoniae	106	—	—	—	—	40	87	—	52	3	0	0	0
β-strep. Group A	35	—	—	—	50	30	24	—	0	—	—	0	0
β-strep. Group B	139	—	—	—	33	57	54	—	2	—	—	0	0
E. faecalis	498	—	1	57	—	—	—	—	—	—	—	0	0
E. faecium	17	—	47	38	—	—	—	—	—	—	—	0	0

Abbreviations: SXT: sulfamethoxazole-trimethoprim; AM: ampicillin; H-GM: high level gentamicin; C: chloramphenicol; CC: clindamycin; E: erythromycin; OX: oxacillin; P: penicillin-G; CXM: cefuroxime; CRO: ceftriaxone; Tei: teicoplanin; Van: vancomycin; Footnote: —: not tested or not available; β-strep. Group A: β-streptococcus Group A; β-strep. Group B: β-streptococcus Group B

Streptococcus pneumoniae was 52%, and it is notable that the rate of resistance to erythromycin was 87%. All *S. pneumoniae* isolates were susceptible to ceftriaxone. Group A streptococci remained susceptible to penicillin, but the resistance rate to erythromycin was as high as 24%. It was also the case for group B streptococci, the penicillin resistance rate was 2% and the rate to erythromycin was 54%. Of the *Enterococcus faecalis* isolates, 1% was ampicillin resistant and 57% was high-level gentamicin resistant; however, in terms of *Enterococcus faecium*, 47% was ampicillin resistant and 38% was high-level gentamicin resistant. All were susceptible to vancomycin and teicoplanin.

The antibiotic resistance patterns of six common enteric bacilli are described in Table 2. Amikacin, ceftriaxone, ceftazidime, cefepime, imipenem, and ciprofloxacin remained fairly active against these gram-negative pathogens, except for the ESBL-producing strains. The general effectiveness of antibiotics against *Enterobacteriaceae* varied with the species and the antibiotic. Notably, *Citrobacter freundii* and *S. marcescens* were generally more resistant. We found that 28% of *C. freundii* were resistant to ceftriaxone, 29% to ceftazidime, and 18% to aztreonam. Furthermore, 51% of *S. marcescens* were resistant to ceftriaxone, 9% to ceftazidime, and 36% to aztreonam. The resistance to cefepime was found the highest in *S. marcescens*, which was 73%. The resistance rate to ciprofloxacin was 13% in *C. freundii*, 16% in *E. coli*, 20% in *Morganella morganii*, and the highest at 43% in *S. marcescens*. The rate of ESBL production among the seven *Enterobacteriaceae* were 5.1% in *E. coli*, 5.8% in *M. morganii*, 7.5% in *Citrobacter diversus*, 8.6% in *K. pneumoniae*, 12% in *C. freundii*, and 21.9% in *Enterobacter cloacae*. None of the *Proteus mirabilis* isolates produced ESBL.

Table 3 shows the list of susceptibilities of the major enteric pathogens isolated during this period. Nearly 100% of nontyphoid *Salmonella* isolates were sensitive to ceftriaxone and cefixime. Resistance to ampicillin, sulfamethoxazole-trimethoprim, and chloramphenicol was high, especially in serogroups B and C1 and *Salmonella choleraesuis* isolates. Serogroups C2 and D isolates appeared relatively less resistant. The most worrisome situation was that 85% of *S. choleraesuis* isolates were resistant to ciprofloxacin. Such resistance has not yet been found in any nontyphoid *Salmonella* except for *S. choleraesuis*. Another enteric pathogen, *Vibrio vulnificus*, though only nine isolates tested, showed susceptibility to the third and fourth generation cephalosporins, piperacillin, imipenem, cipro-

Table 2. Antimicrobial Susceptibility of Common Gram-negative Enteric Bacilli Isolated.

Bacteria	Isolate No.	Resistance rates of antibiotics (%)												
		AN	GM	AM	CZ	CXM	CRO	CAZ	FEP	PIP	ATM	IPM	SXT	CIP
C. diversus	53	0	4	100	6	19	4	4	0	19	4	0	4	0
C. diversus-ESBL	4	75	100	100	100	100	100	100	75	100	100	0	100	0
C. freundii	83	5	30	96	89	39	28	29	0	47	18	0	41	13
C. freundii-ESBL	10	60	80	100	100	100	100	100	20	100	100	0	80	10
E. coli	1774	1	34	83	24	16	7	7	3	72	5	0	62	16
E. coli-ESBL	90	34	94	100	100	100	100	82	53	100	90	0	86	46
E. cloacae	187	5	11	98	97	85	14	11	11	19	13	1	15	2
E. cloacae-ESBL	41	44	95	100	100	100	100	97	13	100	100	0	80	5
K. pneumoniae	717	1	8	100	7	6	1	1	33	27	1	0	21	6
K. pneumoniae-ESBL	62	55	90	100	100	100	98	95	73	100	97	2	90	53
M. morganii	139	6	42	99	96	93	7	8	17	22	5	2	60	20
M. morganii-ESBL	8	100	100	100	100	100	100	100	43	100	100	0	100	75
P. mirabilis	350	3	33	55	28	5	1	0	0	21	0	0	64	14
S. marcescens	155	41	54	99	98	98	51	9	73	53	36	0	52	43

Abbreviations: AN: amikacin; AM: ampicillin; CZ: cephazolin; CAZ: ceftizoxime; CXM: cefuroxime; CIP: ciprofloxacin; GM: gentamicin; IPM: imipenem; PIP: piperacillin; SXT: sulfamethoxazole-trimethoprim; ATM: aztreonam; FEP: cefepime; CFM: cefixime; CRO: ceftriaxone; C: chloramphenicol; TE: tetracycline; M: metronidazole; P: penicillin-G; CC: clindamycin; Footnote: —: not tested or not available

Table 3. Antimicrobial Susceptibility of Common Enteric Pathogens Isolated.

Bacteria	Isolate No.	Resistance rates of antibiotics (%)															
		AN	GM	AM	CZ	CXM	CAZ	CRO	CFM	FEP	PIP	ATM	IPM	SXT	CIP	C	TE
Sal. choleraesuis	13	−	−	85	−	−	−	0	0	−	−	−	−	85	85	92	−
Sal. enteritidis B	58	−	−	55	−	−	−	2	2	−	−	−	−	45	0	69	−
Sal. enteritidis C1	12	−	−	0	−	−	−	0	0	−	−	−	−	8	0	8	−
Sal. enteritidis C2	11	−	−	18	−	−	−	0	9	−	−	−	−	18	0	18	−
Sal. enteritidis D	20	−	−	20	−	−	−	0	0	−	−	−	−	20	0	20	−
Vibrio vulnificus	9	22	0	33	100	22	0	0	−	0	0	67	0	0	0	−	0

Abbreviations are same as Table 2.

Table 4. Antimicrobial Susceptibility of Major Glucose-nonfermenting Bacteria Isolated.

Bacteria	Isolate No.	Resistance rates of antibiotics (%)										
		AN	GM	CXM	CAZ	CRO	FEP	PIP	ATM	IPM	SXT	CIP
A. baumannii	548	79	82	−	84	−	81	88	96	2	−	83
A. calcoaceticus	23	61	74	−	43	−	43	70	91	4	−	65
A. hydrophila	77	0	0	5	3	3	0	35	0	43	16	6
Ps. aeruginosa	925	11	20	−	5	−	5	10	11	9	−	11

Abbreviations are same as Table 2.

floxacin, and tetracycline.

Antimicrobial susceptibility of glucose-nonfermenting bacteria is shown in Table 4. For *P. aeruginosa*, the resistance rates to gentamicin and amikacin were 20% and 11%, respectively. The resistance rates to ceftazidime and cefepime were both 5%, and to piperacillin, aztreonam, imipenem, and ciprofloxacin were approximately 10%. As for *A. baumannii* and *Acinetobacter calcoaceticus*, only imipenem showed good activity, with susceptibility rates of 98% and 96%, respectively. *Aeromonas hydrophila* remained highly susceptible to aminoglycosides, the third and fourth generation cephalosporins, sulfamethoxazole-trimethoprim, and ciprofloxacin; however, the resistance rates of *A. hydrophila* isolates to piperacillin and imipenem were approximately 40%.

Antimicrobial susceptibilities of seven common anaerobic pathogens are summarized in Table 5. *Bacteroides fragilis* and other species were the most commonly encountered clinically significant isolates among the gram-negative anaerobes. These isolates were uniformly resistant to penicillin, but remained susceptible to metronidazole. The resistance rate to clindamycin was 58% in this study. The most common respiratory anaerobic pathogens isolated were *Peptostreptococcus, Prevotella*, and *Veillonella* species. Resistance to penicillin was high in *Prevotella* (67%) and *Veillonella* (73%). All of these isolates remained susceptible to metronidazole. *Clostridium perfringens* appeared to be more susceptible to chloramphenicol, metronidazole, and piperacillin, but 37% and 50% of the isolates were resistant to clindamycin and penicillin, respectively.

Table 5. Antimicrobial Susceptibility of 7 Common Anaerobic Bacteria Isolated.

Bacteria	Isolate No.	Resistance rates of antibiotics (%)				
		C	CC	M	P	PIP
Bacteroides spp.	64	27	58	0	86	59
B. fragilis	170	22	51	4	96	48
C. perfringens	30	17	37	0	50	7
Peptostreptococcus spp.	210	13	20	1	9	2
Prevotella spp.	151	9	36	0	67	30
P. acnes	63	2	3	100	3	0
V. alcalescens	37	8	22	0	73	24

Abbreviations are same as Table 2.

DISCUSSION

Hospitals worldwide are continuing to face the crisis of the upsurge and dissemination of antimicrobial-resistant bacteria, particularly those causing nosocomial infections in ICU patients.[1] Among resistant bacteria, MRSA, VRE, third-generation cephalosporin-resistant *Enterobacteriaceae*, and imipenem- or ciprofloxacin-resistant *P. aeruginosa* and *A. baumannii* are of great concern because these bacteria have spread worldwide and ultimately will compromise the antimicrobial therapy of infections caused by these organisms.[1]

In this report, we describe the distribution of major bacterial pathogens and their antimicrobial susceptibilities during a 1-year period in a newly-opened regional hospital in southern Taiwan. The data generally reflect the seriousness of the antimicrobial resistance among bacterial pathogens in Taiwan. MRSA is common in southern Taiwan. Even in this new hospital, more than 50% of *S. aureus* isolates were resistant to oxacillin. In this study, we did not further divide these isolates based on their community or hospital of origin for analysis. However, a recent study showed that the rate of community-acquired MRSA was approximately 30% of overall *S. aureus* isolates, indicating that the prevalence of MRSA in the hospital settings was even higher than the 50%. The present study also confirmed a high prevalence of penicillin resistance in *S. pneumoniae*, which was 58%, a rate about the same as the rates reported in earlier studies.[7,8] Previous studies from different parts of Taiwan have reported high rates of macrolide resistance among *S. pneumoniae*,[7,9,10] which is consistent with findings from the present study. It is also the case in group A and B streptococci. Both groups of organisms showed considerable rates of resistance to macrolide. As for enterococcus, the most important problem is gentamicin resistance. High-level gentamicin resistance was found to be 57% in *E. faecalis* and 38% in *E. faecium*. The rates are similar to those of previous reports, which showed high prevalence of high-level gentamicin resistance in Taiwan.[7,11]

Resistance to various antimicrobial agents in *P. aeruginosa, A. hydrophila*, and gram-negative enteric bacilli was very common in our study, which is consistent with reports from elsewhere in Taiwan or other countries.[7,12] We believe most of these isolates were from patients with nosocomial infections or colonization. The high rate of antimicrobial resistance could be a result of antibiotic pressure in the hospital settings. However, the resistance rates were still higher than those of most western countries for many of the antimicrobial agents tested, including gentamicin, anti-pseudomonal β-lactams and ciprofloxacin in *P. aeruginosa* and *A. hydrophila*. Continued increases of antimicrobial resistance among these organisms could pose a big problem in Taiwan and the trend should be monitored closely.

The emergence and rapid spread of multidrug-resistant isolates causing nosocomial infections are of great concern worldwide; among them, extended-spectrum β-lactamase-producing *Enterobacteriaceae* has been the subject of concern. The proportion of isolates of *K. pneumoniae* exhibiting the ESBL phenotype has increased progressively from 3.4% in 1993 to 10.3% in 1997 at the National Taiwan University Hospital.[13] In this study, the average rate of ESBL production among gram-negative enteric bacilli was 10.2%, with a higher rate of 21.9% found in *E. cloacae* and 12% in *C. freundii*. Except for carbapenems, there are virtually no other antimicrobial agents available for the treatment of severe infections caused by these organisms. It has been suggested that the confirmatory double-disk test to detect ESBL production should be routinely performed in all clinical isolates of enteric bacilli in clinical microbiology laboratories.

Another emerging resistance trend that warrants attention is the high prevalence of multidrug resistant *A. baumannii* and *A. calcoaceticus* in Taiwan. During the last decade, nosocomial infections caused by multidrug resistant *A. baumannii* have been reported.[14,15] A feared fact is that an emergence of pandrug-resistant *A. baumannii* has been reported at a university hospital in Taiwan.[15] Fortunately, imipenem resistant *A. baumannii* has not been a problem in our hospital. Increasing the use of carbapenems and ciprofloxacin has been shown to contribute to the emergence and wide spread of pandrug resistant *A. baumannii*. Therefore, actions, including rigorous restriction of the use of these extended-spectrum antibiotics and reinforcement of infection control measures, should be taken to prevent its emergence and spread.

High resistance rates to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole in clinical isolates of nontyphoid *Salmonella* species were found in this as well as other reports from Taiwan.[16-18] It appears that resistance problems were more severe in serogroup B and *S. choleraesuis* isolates. Resistance to third generation cephalosporins and fluoroquinolones was estimated to be low (1% to 3%) in Taiwan.[16,17] However, an emergence of fluoroquinolone resistance among *S. choleraesuis* has been observed since 2000.[19] The current study from southern Taiwan confirms the trend. This islandwide situation has serious clinical as well as public health implications and deserves further study. Third generation cephalosporins become the only agent reliable for the treatment of invasive nontyphoid salmonellosis, especially those caused by *S. choleraesuis*.

Rates of resistance among anaerobic bacteria isolated from our hospital were slightly different from findings of other studies.[20] *Bacteroides* species and *C. perfringens* appeared to be more resistant to either chloramphenicol or clindamycin, and penicillin resistance among respiratory anaerobes was common for *Prevotella* and *Veillonella* species in particular. Metronidazole remains the most active agent against all anaerobic pathogens.

In summary, surveillance of the bacteria isolated from patients over prolonged periods not only can provide important information for day-to-day decision-making in antimicrobial therapy in individual hospitals but can also reflect local trends and shifts in etiology and antimicrobial drug resistance. The distribution of bacterial species isolated from a new hospital and their antimicrobial resistance patterns are generally consistent with what have been observed and reported from other older hospitals in Taiwan. It is agreed that bacterial pathogens, either community-based or hospital-based, have shifted away from the easily treated bacteria toward more resistant bacteria. These shifts continue to present challenges for infection control and prevention no matter whether the hospital is new or old. Continued surveillance of the changes of resistance over time is necessary.

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南台灣一所新區域醫院常見菌株之抗藥性分布

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背 景： 抗生素的研發及使用，使抗藥性菌株在台灣已成重要課題，然而各地區之抗藥性又有其獨特性。

方 法： 爲了探討南台灣細菌菌種及抗藥性分布之特色，針對嘉義長庚醫院自91年1月至同年12月所分離出之菌株採取回溯性的研究。

結 果： 最常見的格蘭氏陽性菌是*Staphylococcus aureus*，*E. coli* 和*Klebsiella pneumoniae* 則是最常見之兩種格蘭氏陰性菌。最常見之葡萄糖不發酵格蘭氏陰性菌是*P. aeruginosa*，其次則是*A. baumannii*。對oxacillin 抗藥性之*S. aureus*雖佔有58%，但對vancomycin和teicoplanin全無抗藥性；至於*S. pneumoniae* 對penicillin 非感受性之比例爲52%，但對erythromycin 抗藥性比例則高達87%。多重抗藥性之*P. aeruginosa, A. hydrophila* 和格蘭氏腸道陰性菌在此很常見之外，多重抗藥性之*A. baumannii* 亦不少見，所幸對imipenem 抗藥性仍很低。至於non-typhoid *Salmonella*的抗藥菌株亦很常見，特別是以*S. choleraesuis* 和 serogroup B 最多。

結 論： 嘉義長庚醫院所分離出之細菌菌種及抗藥性分布與台灣其他醫院的結果大致相似，可見即使是在新成立醫院仍可發現很高比率的抗藥性菌株，因此強調抗生素的適當使用是絕對不容忽視的，未來仍然需要繼續監測這些菌種及抗藥性的變遷。
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關鍵字： 抗藥性，細菌菌種，區域醫院。

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