

National Antimicrobial Resistance Surveillance, Thailand (NARST) Data among Clinical Isolates of *Pseudomonas aeruginosa* in Thailand from 2000 to 2005

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Objective: To determine the prevalence, clinical epidemiology, and antimicrobial susceptibility of *Pseudomonas aeruginosa* in Thailand from 2000 to 2005.

Material and method: Using WHONET data from 28 hospitals participating in the National Antimicrobial Resistance Surveillance Thailand (NARST) program, all data were reviewed and analyzed for the prevalence, clinical epidemiology, and antimicrobial susceptibility of clinical isolates of *P. aeruginosa* from 2000 to 2005.

Results: During the six-year surveillance, the prevalence of *P. aeruginosa* in clinical isolates was constant among 28 hospitals. The most common sites of isolation included sputum, pus, and urine. The most active antimicrobials were netilmicin (88% to 90.8%), cefoperazone/sulbactam (85.1% to 89.5%), imipenem (84.6% to 87.2%), and meropenem (84.5%). The resistance to ceftazidime was very high, ranging from 24.6-27.4%. The prevalence of multidrug-resistant (MDR) *P. aeruginosa* (resistance to amikacin, ciprofloxacin, and ceftazidime) was constant. Some hospitals in Central and Eastern regions had the prevalence of MDR up to 20% to 30% of the isolates.

Conclusion: According to NARST data, the antimicrobial resistance rates of *P. aeruginosa* remains constant with the exception of relatively high rates in ceftazidime. The prevalence of MDR *P. aeruginosa* is generally low with a moderately high prevalence in some hospitals.

Keywords : Anti-infective agents, Drug resistance microbial, Microbial sensitivity tests, Population surveillance, *Pseudomonas aeruginosa*, Thailand

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Pseudomonas aeruginosa is primarily encountered as a nosocomial pathogen in adult clinical medicine⁽¹⁾. Outside the hospital, it is commonly found in soil, water, and plants and can on occasion, be associated with a colonization of otherwise healthy

humans and animals⁽²⁾. Within the hospitals, it can colonize moist surfaces including inanimate environment like water in sinks and drains^(2,3). Hospital equipment that comes in contact with water such as ventilators can be the source of *P. aeruginosa*^(2,3). Prior colonization with *P. aeruginosa* is frequently associated with later invasive infection⁽²⁾.

Although a change in the epidemiology and incidence of various nosocomial organisms was observed lately, infections caused by *P. aeruginosa*

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have remained relatively constant over the past ten years according to the National Nosocomial Infections Surveillance (NNIS)⁽¹⁾ system data of the United States. It causes about 3% of blood stream infections, 21% of pneumonia (making it be the most common isolate from the lung), 10% of urinary tract infections (fourth most common pathogen), 13% of head-eye-ear-nose-throat infections (third most common pathogen), and 5% of cardiovascular infections⁽⁴⁾.

With this perspective, the authors examined WHONET data from 28 hospitals participating in the National Antimicrobial Resistance Surveillance Thailand (NARST) program to determine the prevalence, clinical epidemiology, and antimicrobial susceptibility of clinical isolates of *P. aeruginosa* in Thailand from 2000 to 2005.

Material and Method

The NARST program was founded in Thailand in 1998 with the support from the World Health Organization (WHO). The program was designed for investigating the antimicrobial susceptibility of various microorganisms in Thailand. With 33 hospitals initially included in the network, data from 28 hospitals from the year 2000 to 2005 were analyzed because of availability of continuous data. The representing

hospitals were 6 hospitals from the Northeast, 5 from the North, 5 from the Center, 4 from the East, 4 from the South, and 4 from Bangkok

Isolation and identification of *P. aeruginosa* were performed following the conventional culture at each participating hospital. Antimicrobial susceptibility test was determined by the disk diffusion method as recommended by the Clinical Laboratory Standards Institute (CLSI) [formerly National Committee for Clinical Laboratory Standards (NCCLS)] was performed at each hospital. The antimicrobial agents to be analyzed were amikacin, netilmicin, gentamicin, ampicillin/sulbactam, cefoperazone/sulbactam, piperacillin/tazobactam, ceftazidime, imipenem, meropenem, ciprofloxacin, and levofloxacin. There was a proficiency test with a panel of bacterial samples for both identification and antimicrobial susceptibility every four months at each hospital provided by the NARST that served as a WHO Collaborating Center.

Epidemiologic and microbiologic data were obtained and analyzed by the WHONET software program. Multiple isolates from different sites of each patient were counted only one time and antimicrobial susceptibility determination of the first isolate was used in the present study. A descriptive analysis was presented in terms of number and percentage.

Table 1. The overall rate of the antimicrobial resistance in *Pseudomonas aeruginosa* from 2000 to 2005

Antibiotic	2000		2001		2002		2003		2004		2005	
	% R	Number*	% R	Number								
AMK	23.6	17,226	22.4	18,725	19.4	17,111	19.3	17,069	18.0	18,112	17.9	19,781
AMP	98.3	751	98.2	1,027	97.8	1,230	94.5	238	93.6	470	89.1	385
CFP	22.2	976	24.8	2,872	25.1	3,770	24.1	4,287	21.6	5,687	22.4	7,731
CPS	14.9	11,822	14.5	12,217	12.7	11,959	11.7	11,939	11.4	13,165	10.5	16,034
CAZ	26.2	15,561	27.4	17,374	25.2	15,561	25.6	16,117	24.6	16,999	24.6	19,364
CIP	26.8	14,646	24.2	16,370	22.1	14,386	20.6	15,099	20.5	16,263	21.8	18,126
GEN	32.8	16,869	31.3	18,180	28.7	16,893	27.1	16,723	25.3	17,022	24.7	18,097
IPM	12.8	12,051	13.2	13,781	14.3	13,150	14.3	13,538	15.4	14,455	14.4	16,158
LVF	-	-	53.3	15	23.4	1,139	27.4	1,882	25.1	2,221	26.4	2,482
MEM	8.5	3,917	10.0	4,812	13.0	5,508	11.7	5,731	15.4	7,544	15.5	9,349
NET	12.0	11,950	11.3	12,865	10.2	10,740	10.5	9,352	9.6	10,328	9.2	11,926
PIP	18.9	2,440	25.2	3,024	22.0	4,038	22.1	4,668	20.5	4,807	17.3	9,489
MDR	44.6	2,438	42.9	2,691	38.3	1,982	33.0	2,087	37.9	2,151	41.3	2,550

R: resistance (denoted by percentage), number: number of total isolates tested, MDR: multidrug-resistant (resistance to amikacin, ciprofloxacin, and ceftazidime)

AMK: amikacin, GEN: gentamicin, NET: netilmicin, AMP: ampicillin, CAZ: ceftazidime, CFP: cefepime, CPS: cefoperazone-sulbactam, PIP: piperacillin/sulbactam, IPM: imipenem, MEM: meropenem, CIP: ciprofloxacin, LVF: levofloxacin

Table 2. The rate of the antimicrobial resistance of pseudomonas aeruginosa isolated from ICU and non-ICU 2000-2005

Antibiotic	2000		2001		2002		2003		2004		2005														
	ICU	Non ICU	ICU	Non ICU	ICU	Non ICU	ICU	Non ICU	ICU	Non ICU	ICU	Non ICU													
% R	No.	% R	No.	% R	No.	% R	No.	% R	No.	% R	No.	% R	No.												
AMK	20.8	645	17.6	3,899	27.1	627	19.7	6,520	29.0	794	18.7	5,951	18.2	786	18.8	6,296	14.4	748	18.0	4,791	18.7	493	22.5	4,337	
AMP	100.0	4	83.3	6	-	-	-	-	-	-	-	-	100.0	18	89.5	38	100.0	34	88.0	13	88.0	34	-	100.0	1
CFP	11.8	34	21.6	703	32.6	86	19.1	844	48.2	338	20.8	1,579	28.2	347	19.8	2,205	25.8	353	23.0	1,035	57.6	92	51.3	493	
CPS	12.7	503	9.1	3,135	13.0	300	10.8	3,926	10.2	283	12.0	4,000	4.9	364	9.6	3,963	9.3	364	11.0	3,303	9.3	257	12.9	2,989	
CAZ	27.8	643	21.5	3,862	41.8	625	24.5	6,482	39.7	781	23.2	5,894	29.9	790	25.3	6,283	28.5	755	25.0	4,828	24.5	493	26.7	4,325	
CIP	23.7	558	22.6	3,294	22.2	567	21.6	5,908	27.6	644	20.5	5,052	23.1	732	20.9	5,743	24.9	690	22.0	4,630	17.9	485	22.4	4,264	
GEN	24.1	585	24.7	3,615	34.8	630	25.7	6,524	40.3	791	26.4	5,952	28.5	747	25.6	6,010	27.7	729	25.0	4,771	22.9	489	26.2	4,308	
IPM	16.1	558	6.3	3,286	24.1	580	10.3	5,738	33.1	532	11.3	5,065	18.9	581	14.1	5,193	19.6	557	14.0	3,536	26.8	310	14.8	2,614	
LVF	-	-	-	-	-	-	-	-	-	-	22.3	503	0	2	31.6	364	-	-	24.0	-	372	80.0	5	25.0	8
MEM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	38.8	147	20.0	2,006
NET	5.5	542	10.4	3,012	17.5	475	9.4	5,383	24.9	450	9.5	4,263	10.7	326	9.9	3,465	12.6	420	7.4	2,216	11.3	248	5.7	1,459	
PIP	0	4	18.2	501	-	-	19.4	780	30.1	113	18.3	1,417	7.8	193	16.1	1,637	9.9	222	16.0	1,222	19.0	247	15.3	2,882	

R: resistance (denoted by percentage), number: number of total isolates tested, MDR: multidrug-resistant (resistance to amikacin, ciprofloxacin, and ceftazidime)
 AMK: amikacin, GEN: gentamicin, NET: netilmicin, AMP: ampicillin/sulbactam, CAZ: ceftazidime, CFP: ceftipime, CPS: ceftiofloxacin-sulbactam, PIP: piperacillin/sulbactam, IPM: imipenem, MEM: meropenem, CIP: ciprofloxacin, LVF: levofloxacin

Results

A total of 17,971, 19,008, 18,057, 18,532, 19,202, and 21,119 non-duplicate isolates of *P. aeruginosa* were collected in 2000, 2001, 2002, 2003, 2004, and 2005, respectively. The five most common sites of isolation included sputum (8,116-9,270 isolates, 43.4% to 47.4%), pus (2,252-4,300 isolates, 10.6% to 23.9%), urine (1,937-2,863 isolates, 11.5% to 15.9%), blood (514-834 isolates, 2.8% to 3.9%), and wound (189-608 isolates; 1.1% to 3.1%), respectively. There was no significant difference among hospitals in each region regarding *P. aeruginosa* prevalence.

The overall rate of antimicrobial susceptibility of *P. aeruginosa* is shown in Table 1. The susceptibility pattern of *P. aeruginosa* to most antibiotics remained constant with best susceptibility to netilmicin (88% to 90.8%), cefoperazone/sulbactam (85.1% to 89.5%), imipenem (84.6% to 87.2%), and meropenem (84.5%) However, meropenem susceptibility was determined only in 2005. The susceptibility patterns of *P. aeruginosa* from the intensive care units (ICUs) and non-ICU isolates are shown in Table 2. The resistance generally was observed with the high rates among the ICU strains. The patterns of antimicrobial susceptibility of ceftazidime-resistant *P. aeruginosa* are shown in Table 3. The resistance rates to all antimicrobials tested were very high with the three least resistance in imipenem (29.7% to 39%), meropenem (22.6% to

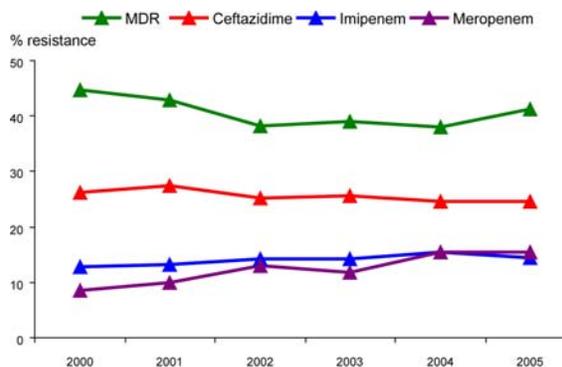


Fig. 1 Trends of antimicrobial resistance of *Pseudomonas aeruginosa* isolated by 28 hospitals from 2000 to 2005

38.8%), and netilmicin (28.5% to 30.8%). The prevalence of multidrug-resistant (resistance to amikacin, ciprofloxacin, and ceftazidime) *P. aeruginosa* among regions shown in Tables 4-8 (by the rate and number of isolates) and Fig. 1. The prevalence was generally constant although some hospitals in the central and eastern regions had prevalence of up to 20% to 30% of the isolates.

Discussion

The present study has shown the overall data from the NARST system for the prevalence, clinical

Table 3. The rates of antimicrobial resistance in ceftazidime-resistant *Pseudomonas aeruginosa* from 2000 to 2004

Antibiotic	2000		2001		2002		2003		2004	
	% R	Number								
AMK	70.2	4,042	67.7	4,744	65.9	3,896	67.7	4,078	62.9	4,125
AMP	98.7	151	98.3	238	99.6	243	96.8	62	100.0	146
CFP	81.7	191	74.9	845	79.5	986	80.7	1,188	81.2	1,362
CPS	48.4	3,049	44.7	3,179	45.8	2,884	42.0	3,049	41.6	3,136
CAZ	100.0	4,083	100.0	4,766	100.0	3,924	100.0	4,124	100.0	4,178
CIP	73.4	3,780	67.6	4,457	64.1	3,630	62.5	3,857	63.1	3,971
GEN	83.0	3,985	81.5	4,571	80.7	3,838	81.9	4,017	78.0	3,961
IPM	29.7	3,228	33.2	3,885	37.6	3,202	37.3	3,430	39.0	3,430
LVF	-	-	88.9	9	60.2	339	55.1	717	56.6	700
MEM	22.6	1,104	25.7	1,383	34.5	1,468	28.5	1,749	38.8	2,157
NET	28.5	2,963	27.2	3,435	29.2	2,717	30.6	2,413	30.8	2,463
PIP	47.5	712	60.3	1,048	62.0	1,042	58.1	1,502	54.9	1,430

R: resistance (denoted by percentage), number: number of total isolates tested, MDR: multidrug-resistant (resistance to amikacin, ciprofloxacin, and ceftazidime)

AMK: amikacin, GEN: gentamicin, NET: netilmicin, AMP: ampicillin, CAZ: ceftazidime, CFP: cefepime, CPS: cefoperazone-sulbactam, PIP: piperacillin/sulbactam, IPM: imipenem, MEM: meropenem, CIP: ciprofloxacin, LVF: levofloxacin

Table 4. The rates and number of multidrug resistant (resistance to amikacin, ciprofloxacin, and ceftazidime) *Pseudomonas aeruginosa* isolates from northeastern region from 2000 to 2005

Year	Code of hospital name in the Northeast											
	NE1		NE2		NE3		NE4		NE5		NE6	
	% R	Number	% R	Number	% R	Number	% R	Number	% R	Number	% R	Number
2000	-	-	5.28	13	17.25	44	15.18	116	11.83	40	16.90	85
2001	-	-	12.37	23	12.65	31	13.38	89	9.73	44	16.34	84
2002	-	-	12.65	93	9.65	25	13.86	111	9.20	30	17.15	83
2003	-	-	8.18	48	6.64	19	13.57	109	13.37	46	10.27	30
2004	-	-	4.32	23	14.01	29	10.19	91	9.04	33	9.25	36
2005	-	-	15.81	135	11.31	38	11.71	150	12.36	68	8.48	58

R: resistance (denoted by percentage), number: number of total isolates tested

Table 5. The rates and number of multidrug-resistant (resistance to amikacin, ciprofloxacin, and ceftazidime) *Pseudomonas aeruginosa* isolates from northern region from 2000 to 2005

Year	Code of hospital name in the North									
	N1		N2		N3		N4		N5	
	% R	Number	% R	Number	% R	Number	% R	Number	% R	Number
2000	15.45	188	-	-	7.64	62	-	-	16.18	30
2001	13.01	160	12.92	42	6.26	48	-	-	17.41	88
2002	12.47	94	16.85	62	9.49	70	-	-	13.64	39
2003	20.86	145	11.82	48	3.43	15	-	-	10.53	58
2004	21.35	149	12.62	40	4.89	23	50.00	3	5.79	53
2005	18.15	280	9.21	21	8.73	69	100.00	1	-	-

R: resistance (denoted by percentage), Number: number of total isolates tested

Table 6. The rates of and number multidrug-resistant (resistance to amikacin, ciprofloxacin, and ceftazidime) *Pseudomonas aeruginosa* isolates from the central region 2000 to 2005

Year	Code of hospital name in the Central															
	C1		C2		C3		C4		C5		C6		C7		C8	
	% R	Number	% R	Number	% R	Number	% R	Number	% R	Number	% R	Number	% R	Number	% R	Number
2000	7.41	2	21.13	61	10.37	25	18.40	129	6.73	33	20.12	33	19.00	22	20.95	97
2001	6.06	2	24.93	47	6.81	13	17.10	113	6.99	43	7.27	12	17.00	23	19.85	109
2002	4.55	2	24.07	9	7.28	31	12.19	68	3.99	27	9.09	10	11.00	11	14.12	48
2003	3.23	1	16.67	12	10.68	30	11.67	74	4.46	32	6.21	11	11.00	10	14.84	69
2004	4.08	2	16.46	11	7.85	49	12.83	97	4.36	31	18.18	34	9.00	11	17.84	81
2005	18.18	12	21.28	100	12.61	148	20.68	278	7.00	78	20.54	53	4.80	9	11.61	86

R: resistance (denoted by percentage), Number: number of total isolates tested

Table 7. The rates and number of multidrug-resistant (resistance to amikacin, ciprofloxacin, and ceftazidime) *Pseudomonas aeruginosa* isolates from the eastern region from 2000 to 2005

Year	Code of hospital name in the East							
	E1		E2		E3		E4	
	% R	Number	% R	Number	% R	Number	% R	Number
2000	14.09	52	33.48	154	13.28	81	17.89	39
2001	18.45	93	22.01	94	20.36	137	6.36	22
2002	20.38	97	19.71	67	15.08	89	8.15	34
2003	13.14	72	21.43	69	22.75	167	7.73	30
2004	15.50	97	24.58	74	17.49	128	6.86	24
2005	15.23	161	36.42	220	21.21	204	8.44	26

R: resistance (denoted by percentage), Number: number of total isolates tested

Table 8. The rates and number of multidrug-resistant (resistance to amikacin, ciprofloxacin and ceftazidime) *Pseudomonas aeruginosa* isolates from the southern region from 2000 to 2005

Year	Code of hospital name in the South							
	S1		S2		S3		S4	
	% R	Number	% R	Number	% R	Number	% R	Number
2000	-	-	7.13	34	11.79	77	10.29	21
2001	13.74	43	7.77	31	17.61	110	6.77	18
2002	12.93	19	49.85	16	11.47	43	6.93	21
2003	6.25	14	4.68	27	4.76	28	5.52	19
2004	5.70	9	7.52	43	7.43	53	10.45	28
2005	5.75	21	10.94	105	10.18	111	17.71	82

R: resistance (denoted by percentage), Number: number of total isolates tested

epidemiology, and antimicrobial susceptibility of *P. aeruginosa* in Thailand from 2000 to 2005. The presented data suggested that *P. aeruginosa* was commonly isolated from the sputum, pus and urine specimens. As compared to the data of the NNIS (National Nosocomial Infection Surveillance) of the United States, *P. aeruginosa* was the most frequent nosocomial pathogen isolated from the lung⁽⁴⁾.

The presented data suggest that netilmicin, cefoperazone/sulbactam, imipenem, and meropenem were the most active agents against *P. aeruginosa*, with the resistance rate ranging from 9.2% to 15.4%. As compared to the Spanish MYSTIC program, meropenem and piperacillin/tazobactam were the most active agents against *P. aeruginosa*⁽⁵⁾. Accordingly, the SENTRY program has shown the lowest rates of antimicrobial resistance among *P. aeruginosa* in amikacin, meropenem,

and cefepime⁽⁶⁾. In the present study, the resistance rates of meropenem ranged from 10% to 15.5%. Although the patterns of resistance were constant in most of the antimicrobials, we observed the overall but nonsignificant decrease in the resistance rate of *P. aeruginosa* to all aminoglycosides (amikacin, gentamicin, and netilmicin) from 2000 to 2005. The resistance rates had decreased from 23.6% to 17.9% in amikacin, from 32.8% to 24.7% in gentamicin, and from 12% to 9.2% in netilmicin. These phenomena may be related to a general decrease in the use of aminoglycosides during the past five years.

Although *P. aeruginosa* isolates from the ICUs were generally more resistant to most antimicrobials tested, as compared to the non-ICU isolates, there were some reverse data observed in Table 2. These features may be associated with the epidemics

**การเฝ้าระวังเชื้อดื้อยาต้านจุลชีพของเชื้อ *Pseudomonas aeruginosa* ที่แยกได้จากผู้ป่วย
ในประเทศไทยระหว่าง พ.ศ. 2543-2548**

สุรางค์ เดชศิริเลิศ, ชุษณา สอนกระต่าย, สุวรรณา ตระกูลสมบูรณ์, อรทัย ทองมะลิ, ปฐม สวรรค์ปัญญาเลิศ,
นลินี อัสวโกติ, วรพจน์ ตันติศิริวัฒน์

จุดประสงค์: ศึกษาอุบัติการณ์ ระบาดวิทยา และความไวของเชื้อ *Pseudomonas aeruginosa* ต่อยาต้านจุลชีพ
ในประเทศไทยระหว่าง พ.ศ. 2543-2548

วัตถุประสงค์: รวบรวมข้อมูลการทดสอบความไวของเชื้อต่อยาจากโปรแกรม WHONET ที่ส่งจากโรงพยาบาลใน
เครือข่ายเฝ้าระวังเชื้อดื้อยาต้านจุลชีพแห่งชาติ (NARST) และทำการวิเคราะห์อุบัติการณ์, ระบาดวิทยาทางคลินิก
และผลการทดสอบความไวของเชื้อ *Pseudomonas aeruginosa* ต่อยา ในช่วงปี พ.ศ. 2543-2548

ผลการศึกษา: จากการเฝ้าระวังใน 28 โรงพยาบาล ในระยะเวลา 6 ปี พบว่า อุบัติการณ์ของ *P. aeruginosa* คงที่
โดยพบเชื้อมากในเสมหะ หนอง และปัสสาวะ ตามลำดับ เชื้อไวต่อยา netilmicin มากที่สุด (88%-90.8%)
cefoperazone/sulbactam ไว 85.1%-89.5% และ imipenem (84.6%-87.2%)
