Antimicrobial Susceptibility of Enterococci in Thailand from 2000 to 2005

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Objective: *To determine the trends of antimicrobial susceptibility of enterococci in Thailand from 2000 to 2005*
Material and Method: *All enterococcal isolates from sterile site obtained from 28 hospitals in Thailand from 2000 to 2005 were tested for their susceptibility to ampicillin, high-level gentamicin, and vancomycin by the disk diffusion (Kirby Bauer) method. The relevant data were collected and analyzed by WHONET software program supported by the World Health Organization.*
Results: *Enterooccus faecalis (47%) and E. faecium (23%) were the two most frequent enterococcal isolates. There was no trend of increasing resistance to ampicillin, high level gentamicin, and vancomycin among E. faecalis isolates during the study period. There was a trend of an increasing resistance to ampicillin and high-level gentamicin among E. faecium isolates. Among E. faecium, the rates of vancomycin resistance were very low, ranging from 0.5% to 1.9%, and there was no trend of increasing rates of resistance.*
Conclusion: *In the present study, there is a trend of decreasing susceptibility to ampicillin and high-level gentamicin in E. faecium. In contrast, there is no trend of increasing resistance to vancomycin. This would have effects on selection of empirical antimicrobial treatment on enterococcal infections especially a decision to use ampicillin or gentamicin.*

Keywords: *Anti-infective agents, Drug resistance, microbial, Enterococcus, Microbial sensitivity tests, Thailand, Vancomycin resistance*

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Enterococci (most are *E. faecalis*, which accounts for ~80% of all enterococcal infections) cause many infections including urinary tract infections, bacteremia, intra-abdominal infections, and endocarditis[1-3]. Enterococci are also prominent nosocomial pathogens, ranked second or third in frequency as causes of nosocomial infections in some countries[4]. Enterococci are concerned not only as the frequent causes of infections but also because of having acquired numerous resistance to antimicrobial agents including new agents including linezolid[5,6]. The resistance patterns of highest concern include ampicillin resistance[1], high-level resistance to the aminogly-cosides (gentamicin and streptomycin)[2], and glyco-peptides[3]. Some countries have reported the increasing occurrence of vancomycin-resistant enterococci (VRE)[2]. In Thailand, only rates of resistance to vancomycin among enterococci between 2000 and 2003 were available from the National Antimicrobial Resistance Surveillance, Thailand (NARST) surveillance program. The present study aimed to determine the susceptibility of vancomycin, ampicillin, and high-level gentamicin among enterococcal isolated from clinical specimens in Thailand from 2000 to 2005.

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Material and Method

There were 28 hospitals participating in the NARST program; these included 9 small hospitals (fewer than 500 beds) and 19 large hospitals (equal to more than 500 beds). Isolation and primary identification of enterococci were performed in each hospital according to the standard guidelines. At the National Institute of Health of Thailand (Thai NIH), the confirmation was performed according to Facklam and colleagues[8] and antimicrobial susceptibility was determined by the disk diffusion (Kirby Bauer) method according to the Clinical Laboratory Standards Institute (CLSI) [formerly National Committee for Clinical Laboratory Standards (NCCLS)] guidelines. Vancomycin resistance screening test was also carried out at the Thai NIH.

Data collection

NARST program has been organized since 1998 to strengthen and standardize laboratory practices as well as to investigate the antimicrobial susceptibility of various microorganisms in Thailand. The program was supported by the World Health Organization (WHO). All data were recorded in the WHONET software program and sent back to the Thai NIH every 3 months.

Results

Among all enterococcal isolates, *E. faecalis* was the most common species found (47%, range 30% to 49%), followed by *E. faecium* (23%, range 22% to 28%). Most patients with positive enterococcal cultures were in the age group of less than 1 year and more than 60 years. Both *E. faecalis* and *E. faecium* were commonly isolated from out-patients and in-patients, whereas *E. faecalis* was more commonly isolated than *E. faecium* in the intensive care units (ICUs).

There was no trend of an increasing resistance of ampicillin, high-level gentamicin, and vancomycin among *E. faecalis* isolates, while there was a trend of increasing resistance of ampicillin and high-level gentamicin among *E. faecium* (Table 1 and Fig. 1). Ampicillin-resistant *E. faecium* was still more problematic than *E. faecalis.* The rates of ampicillin resistance among *E. faecium* significantly increased from 52% in 2000 to 84% in 2005. The high-level gentamicin resistance rates among *E. faecium* significantly increased from 47% in 2000 to 75% in 2005.

A comparison of the trends of resistance among *E. faecalis* and *E. faecium* isolated from small (less than 500 beds) and large (equal or more than 500 beds) hospitals.

Table 2 shows the rates of ampicillin high-level gentamicin, and vancomycin resistance among enterococcal isolates from small and large hospitals No different in the rates to all three antibiotics was found.

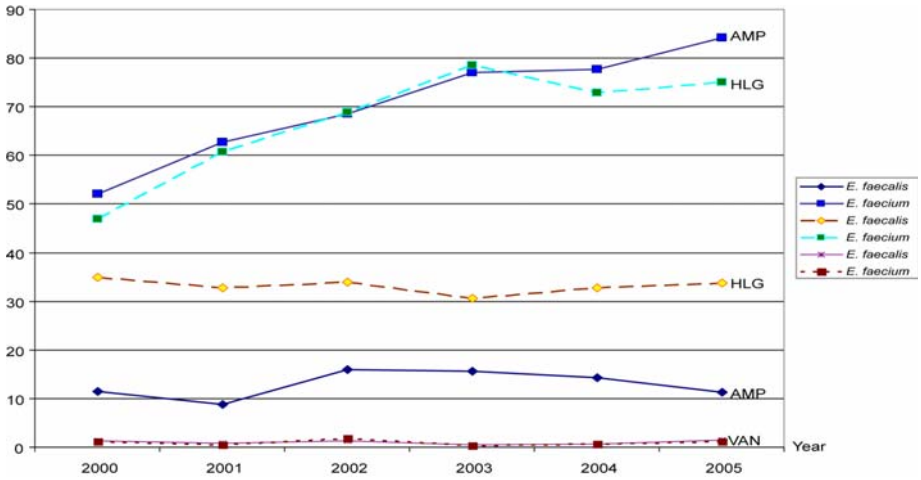
The resistance rates of ampicillin and high-level gentamicin were increased among *E. faecium* isolates from both types of hospitals; the higher rates were noted in the isolates from the large hospitals more than small hospitals. There were no trends of increasing resistance rates of vancomycin among *E. faecium* isolated from both types of hospitals (Table 3 and Fig. 3).

The resistance rates of enterococci isolated from the blood, cerebrospinal fluid (CSF), and urine

The rates of both ampicillin and high-level gentamicin resistance among isolates from blood were not increased among *E. faecalis.* In contrast, *E. faecium* had a trend of increasing resistance rates of both ampicillin and high-level gentamicin from 32% to 86% and from 42% to 69%, respectively (Table 4). The rates

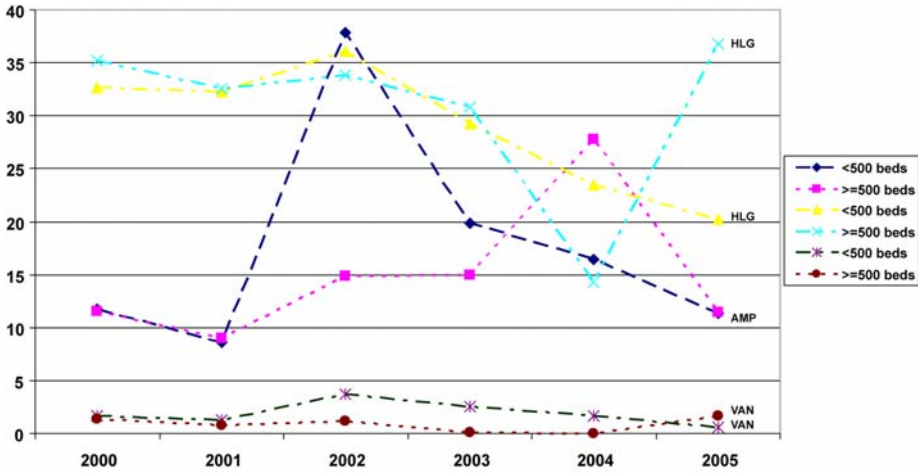
Table 1. Tendency of the antimicrobial resistance rates of resistant *Enterococcus faecalis* and *Enterococcus faecium* from 2000 to 2005

Year	Ampicillin		High-level gentamicin		Vancomycin	
	E. faecalis	*E. faecium*	*E. faecalis*	*E. faecium*	*E. faecalis*	*E. faecium*
2000	11.5%	52.0%	35.0%	46.9%	1.4%	1.1%
2001	8.9%	62.8%	32.7%	60.8%	0.9%	0.5%
2002	15.9%	68.6%	33.9%	68.8%	1.4%	1.9%
2003	15.6%	77.0%	30.6%	78.6%	0.5%	0.4%
2004	14.3%	77.7%	32.7%	72.8%	0.6%	0.6%
2005	11.3%	84.1%	33.7%	75.0%	1.5%	1.2%



AMP: ampicillin, HLG: high-level gentamicin, VAN: vancomycin

Fig. 1 The percentage of drug-resistant enterococci from 2000 to 2005 from 28 hospitals

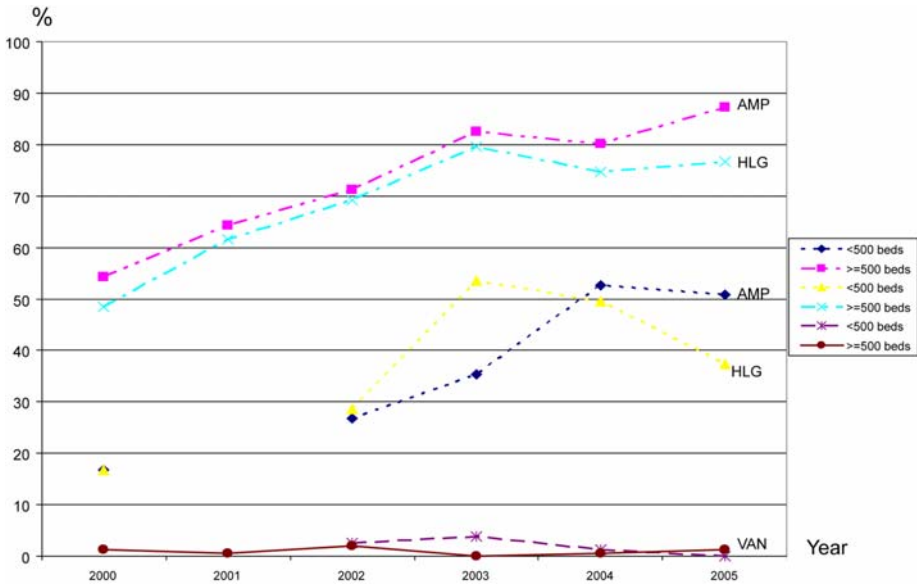


AMP: ampicillin, HLG: high-level gentamicin, VAN: vancomycin

Fig. 2 Comparison of the resistance rates of *Enterococcus faecalis* isolated from small (less than 500 beds) and large (equal or more than 500 beds) hospitals from 2000 to 2005

Table 2. Comparison of the resistance rates of *Enterococcus faecalis* isolated from small (less than 500 beds) and large (equal or more than 500 beds) hospitals from 2000 to 2005

Year	Ampicillin		High-level gentamicin		Vancomycin	
	Small hospital	Large hospital	Small hospital	Large hospital	Small hospital	Large hospital
2000	11.7%	11.5%	32.7%	35.2%	1.7%	1.4%
2001	8.6%	9.0%	32.3%	32.6%	1.3%	0.8%
2002	37.8%	14.9%	36.1%	33.8%	3.7%	1.2%
2003	19.9%	15.0%	29.2%	30.8%	2.5%	0.1%
2004	16.4%	27.8%	23.5%	14.3%	1.7%	0.0%
2005	11.3%	11.4%	20.2%	36.8%	0.6%	1.7%



AMP: ampicillin, HLG: high-level gentamicin, VAN: vancomycin

Fig. 3 Comparison of the resistance rates of *Enterococcus faecium* isolated from small (less than 500 beds) and large (equal or more than 500 beds) hospitals from 2000 to 2005

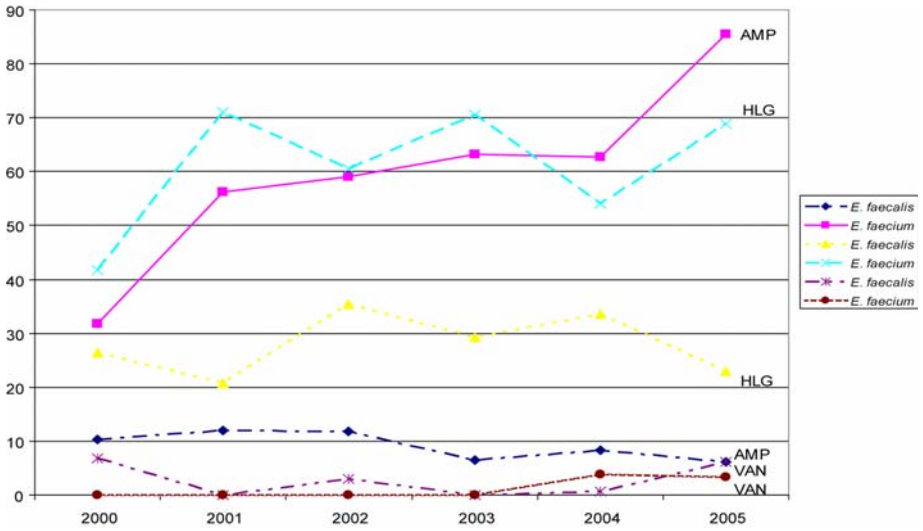
Table 3. Comparison of the resistance rates of *Enterococcus faecium* isolated from small (less than 500 beds) and large hospitals (equal or more than 500 beds) from 2000 to 2005

Year	Ampicillin		High-level gentamicin		Vancomycin	
	Small hospital	Large hospital	Small hospital	Large hopital	Small hospital	Large hospital
2000	16.7%	54.3%	16.7%	48.5%	ND	1.2%
2001	ND	64.3%	ND	61.6%	ND	0.5%
2002	26.8%	71.2%	28.6%	69.3%	2.6%	2.0%
2003	35.3%	82.6%	53.6%	79.6%	3.9%	0.0%
2004	52.7%	80.2%	49.6%	74.7%	1.3%	0.5%
2005	50.9%	87.3%	37.7%	76.7%	0.0%	1.2%

ND: not determined

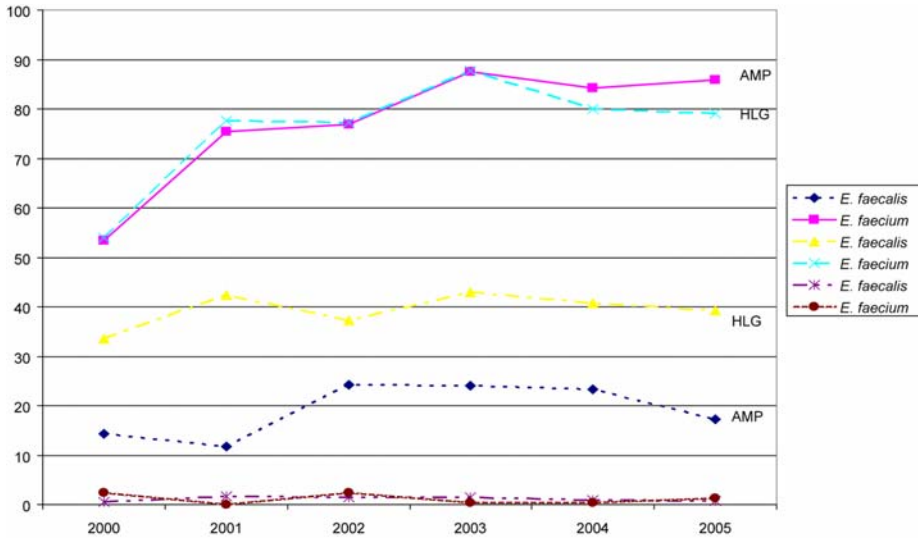
Table 4. Tendency of resistance rates of *Enterococcus faecalis* and *Enterococcus faecium* isolated from blood (2000 to 2005)

Year	Ampicillin		High-level gentamicin		Vancomycin	
	E. faecalis	*E. faecium*	*E. faecalis*	*E. faecium*	*E. faecalis*	*E. faecium*
2000	10.3%	31.8%	26.4%	41.7%	6.8%	0.0%
2001	11.9%	56.2%	20.8%	71.0%	0.0%	0.0%
2002	11.8%	59.0%	35.5%	60.6%	3.0%	0.0%
2003	6.5%	63.2%	29.2%	70.6%	0.0%	0.0%
2004	8.4 %	62.8%	33.6%	54.1%	0.6%	3.9%
2005	6.2%	85.5%	22.9%	68.8%	6.2%	3.4%



AMP: ampicillin, HLG: high-level gentamicin, VAN: vancomycin

Fig. 4 Comparison tendency of resistance rates of enterococci isolated from the blood (2000 to 2005)



AMP: ampicillin, HLG: high-level gentamicin, VAN: vancomycin

Fig. 5 Comparison of tendency of resistance rates of enterococci isolated from the urine (2000 to 2005)

of vancomycin resistance were 6.8% in 2000, 6.2% in 2005 among *E. faecalis*, as well as from 3.9% in 2004 to 3.4% in 2005 among *E. faecium*, respectively (Fig. 4). The isolates from the CSF were susceptible to vancomycin during the study period.

Enterococci isolated from the urine showed that *E. faecium* was more resistant to ampicillin, high-level gentamicin, and vancomycin than *E. faecalis*. *E. faecalis* had not increasingly resisted to ampicillin and high-level gentamicin (Table 5). The resistance rates of ampicillin and high-level gentamicin among *E. faecium* had been significantly increasing from 53% to 86% and 54% to 88%, from 2000 to 2005, respectively (Fig. 5). The resistance rates of vancomycin was 1.6% in 2001 among *E. faecalis*, and 2.4% in 2000 and 2002 among *E. faecium*.

Table 5. Tendency of resistance rates of enterococci isolated from urine (2000 to 2005)

Year	Ampicillin		High-level gentamicin		Vancomycin	
	E. faecalis	*E. faecium*	*E. faecalis*	*E. faecium*	*E. faecalis*	*E. faecium*
2000	14.3%	53.4%	33.6%	53.9%	0.6%	2.4%
2001	11.7%	75.4%	42.4%	77.7%	1.6%	0.0%
2002	24.3%	76.9%	37.3%	77.2%	1.4%	2.4%
2003	24.0%	87.6%	43.0%	87.7%	1.4%	0.4%
2004	23.3%	84.2%	40.7%	80.0%	1.0%	0.4%
2005	17.3%	85.9%	39.2%	79.0%	0.7%	1.2%

Discussion

The present study showed that *E. faecalis* was the most commonly isolated enterococci, followed by *E. faecium*, in consistent with the previous study[2,3]. Among *E. faecalis* isolates. There was no trend of increasing resistance of ampicillin and high-level gentamicin during the study period. In contrst, among *E. faecium* isolates, there were increasing resistance rates of both ampicillin and high-level gentamicin. The present results did not show the high frequency of VRE; this is in contrast to the previous study carried out in other countries[2]. The authors anticipated that the large hospitals would have more and increasing occurrences of VRE, due to more risk factors predisposing to VRE including the frequent use of antimicrobials (third-generation cephalosporins, metronidazole, and fluoroquinolones) and higher number of patients with compromised conditions[9]. However, there were no differences in the prevalence rates of VRE isolated from both types of hospitals. In addition, both types of hospitals had the same antimicrobial resistance patterns, except the higher resistance rates of ampicillin and high-level gentamicin among *E. faecium* isolated from large hospitals compared to small hospitals.

Blood and CSF isolates of *E. faecium* had a trend of increasing rates of ampicillin and high-level gentamicin-resistant. However, nearly all of them were still susceptible to vancomycin.

Both *E. faecalis* and *E. faecium* isolated from the urine had the trends of increasing resistance to ampicillin and high-level gentamicin. These results may cause a problem while using ampicillin or gentamicin for empirical treatment of urinary tract infections caused by suspected *Enterococcus*.

Conclusion

There was no trend of an increasing resistance of vancomycin among enterococci isolated from 2000 to 2005 in Thailand. The problems of antimicrobial resistance were noted among *E.faecium*, both ampicillin and high-level gentamicin. These high resistance rates made the combination of ampicillin and gentamicin for the treatment of serious infections especially endocarditis and meningitis ineffective. Even though the resistance rates of vancomycin among enterococci in the present study remained relatively low, the authors still need to continue an active surveillance for the occurrence of VRE in Thailand in order to reduce the colonization and infections caused by this organism which are much more difficult to treat.

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การศึกษาความไวต่อยาต้านจุลชีพของเชื้อ Enterococci ในประเทศไทยระหว่างปี พ.ศ. 2543-2548

ลีลาวดี แสงสุก, สุรางค์ เดชศิริเลิศ, ปฐม สวรรค์ปัญญาเลิศ, นลินี อัศวโภคี, ธวัชชัย จริยะเศรษฐพงศ์

วัตถุประสงค์*: เพื่อศึกษาแนวโน้มของความไวต่อยาต้านจุลชีพของเชื้อ enterococci ในปี พ.ศ. 2543-2548*
วัสดุและวิธีการ*: เชื้อ Enterococci ที่แยกได้จากเลือด น้ำไขสันหลัง และปัสสาวะในระหว่างปี พ.ศ. 2543-2548 จากโรงพยาบาล 28 แห่ง ทำการทดสอบความไวของเชื้อต่อยาต้านจุลชีพ 3 ชนิด แอมพิซิลิน (ampicillin), เจนตามิซิน ที่ความเข้มข้นระดับสูง (high-level gentamicin) และ แวนโฆมัยซิน (vancomycin) ด้วยวิธี disk diffusion (Kirby-Bauer) และทำการวิเคราะห์ข้อมูลด้วยโปรแกรม WHONET ที่ได้รับการสนับสนุนจากองค์การอนามัยโลก (WHO)*
ผลการศึกษา*: สายพันธุ์ Enterococci ที่พบมากที่สุดคือ E. faecalis (46.5%) E. faecium (23%) ตามลำดับ ในระหว่างปี พ.ศ. 2543-2548 ไม่พบแนวโน้มความเปลี่ยนแปลงของการดื้อยาแอมพิซิลลิน และเจนตามิซิน ที่มีความเข้มข้นระดับสูง ในเชื้อ E. faecium ในขณะเดียวกันเชื้อสมาชิกในกลุ่ม Enterococci มีการดื้อยาแวนโฆมัยซิน อยู่ในระดับ 0.5-1.9% ซึ่งพบ VRE ของ E. faecalis 6.8%,6.2% ในปี พ.ศ. 2543-2548 ตามลำดับ*
สรุป*: กลุ่มเชื้อ Enterococci ในประเทศไทยสายพันธุ์ E. faecium มีอัตราความไวต่อยาต้านจุลชีพ แอมพิซิลิน, เจนตามิซินที่ความเข้มข้นระดับสูงลดลง ซึ่งพบได้เช่นเดียวกับประเทศอื่น ๆ แต่สำหรับประเทศไทยกลุ่ม Enterococci ยังคงไม่มีปัญหาแนวโน้มการดื้อต่อยาแวนโฆมัยซินสูงขึ้นมากเหมือนกับประเทศอื่น ๆ จึงทำให้มีผลทางการแพทย์ ต่อการตัดสินใจในการใช้ยารักษาเบื้องต้น (empirical treatment) ในคนไข้ที่ติดเชื้อ Enterococci โดยเฉพาะในยาแอมพิซิลิน หรือ เจนตามิซิน*