

Prevalence and Antimicrobial Resistance of Enterococcus species in a Tertiary Center Children's Hospital in Korea

Hyejin So^{1,2}, Junghwa Kim¹, Jina Lee³

¹ Department of Pediatrics, Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, Republic of Korea

² Department of Pediatrics, Chungnam National University Sejong Hospital, Sejong, Republic of Korea

³ Department of Pediatrics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Contact Information:
Hyejin So
e-mail: twinkler@hanmail.net



Background

- Current EUCAST¹ and CLSI² guidelines regarding *Enterococcus* species state that;
 - **Susceptibility to ampicillin, amoxicillin and piperacillin with and without beta-lactamase inhibitor can be inferred from ampicillin¹**
 - *E. faecalis*: **Ampicillin susceptibility can be used to predict imipenem susceptibility²**
- Ampicillin-susceptible Penicillin-resistant (ASPR) *E. faecalis* strains are recently emerging³

Purpose

- This study is a pioneer research which was designed to investigate the newly emerging antibiotics sensitivity patterns of enterococcal strains in the pediatric age.

Methods

- Study design:** Retrospective study, during March 2014 through September 2020 at Asan Medical Center Children's Center
- Enterococcal strains isolated from normally sterile body sites
- Duplicate results from same patient ≤ 4 weeks were excluded
- Strain identification & antimicrobial susceptibility testing (AST)**
 - MicroScan WalkAway 96-Combo Pos 28 panels (Siemens, West Sacramento, CA, USA)
 - Etest (bioMérieux SA, France) for minimal inhibitory concentration (MIC) of MicroScan-detected ASPR enterococcal strains
 - 1) Isolated strains were maintained frozen at -70°C and recovered for Etest
 - 2) Added to cation-adjusted Mueller-Hinton broth (Becton Dickinson)
 - 3) Ampicillin, penicillin, imipenem, meropenem, and piperacillin were tested
- Analysis of results**
 - Categorical interpretations for all the AST methods were interpreted according to the CLSI guideline
 - But no CLSI breakpoints available for *E. faecalis* in the interpretation of imipenem, meropenem, and piperacillin currently
 - * Imipenem and meropenem: United States Food and Drug Administration(FDA)
 - * Piperacillin: EUCAST non-species related breakpoints were used for piperacillin

	Susceptible (µg/ml)	Intermediate (µg/ml)	Resistant (µg/ml)
Ampicillin & Penicillin	≤ 8	-	≥ 16
Imipenem & Meropenem	≤ 4	8	≥ 16
Piperacillin	≤ 4	-	>16

Results

Figure 1. Flow Chart

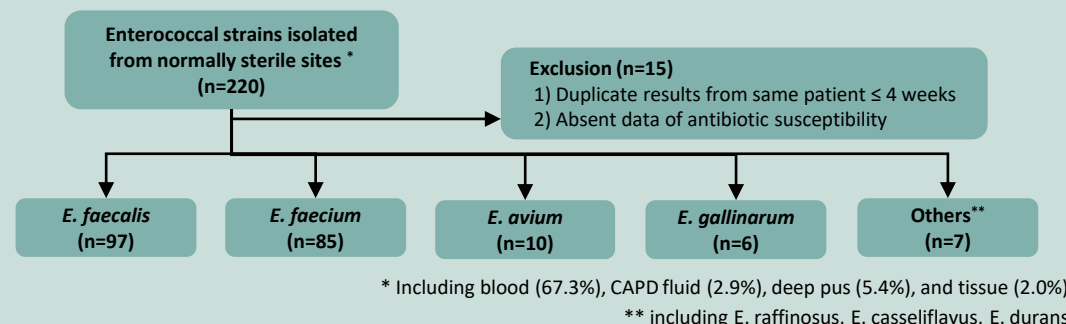


Table 1. Antibiotic Resistance pattern of Enterococcus species by Microscan

	Ampicillin	Penicillin	Vancomycin	GM-synergy	SM-synergy
<i>E. faecalis</i> (n=97)	0	6 (6.2%)	0	39 (40.2%)	16 (16.5%)
<i>E. faecium</i> (n=85)	72 (84.7%)	74 (87.1%)	28 (32.9%)	30 (35.3%)	7 (8.2%)
<i>E. avium</i> (n=10)	4 (40.0%)	5 (50.0%)	0	0	3 (30.0%)
<i>E. gallinarum</i> (n=6)	0	1 (16.7%)	6 (100%)	0	1 (16.7%)
Others (n=7)	4 (57.1%)	4 (57.1%)	1 (14.3%)	0	0
Overall R (%)	39.0%	43.9%	17.1%	33.7%	13.2%

* All strains were susceptible to linezolid

Table 2. MIC of ASPR Enterococcus species by Etest*

No.	Sex/Age	Year of isolation	Species	MIC (µg/ml) by Etest				
				Penicillin	Ampicillin	Imipenem	Meropenem	Piperacillin
1	F / 21d	2014	<i>E. faecalis</i>	>32	>256	>32	>32	>256
2	F / 15Y	2016	<i>E. faecalis</i>	>32	>256	>32	>32	>256
3	M / 4Y	2017	<i>E. faecalis</i>	>32	1	2	>32	16
4	F / 2Y	2017	<i>E. gallinarum</i>	>32	3	>32	>32	>256
5	F / 14Y	2017	<i>E. faecalis</i>	>32	1.5	4	>32	16
6	M / 3m	2018	<i>E. faecium</i>	>32	6	>32	>32	>256
7	M / 6m	2018	<i>E. faecalis</i>	1.5	0.25	0.75	1	3
8	M / 6Y	2020	<i>E. avium</i>	>32	8	>32	>32	>256
9	F / 9Y	2020	<i>E. faecalis</i>	16	2	4	>32	12
Overall R (%)				7 (77.8)	2 (22.2)	5 (55.6)	8 (88.9)	5 (55.6)

* ASPR strains which were initially determined by MicroScan, were retested by Etest (1 strain failed to recover, therefore Etest was not performed)

- Pink shaded columns are discordant results of the Etest compared to MicroScan MIC results
- Emerald colored lines are the ASPR strains confirmed by Etest

- Annual distribution showed *E. faecium* becoming more dominant in the recent years (2019-2020)
- Among the MicroScan-detected ASPR strains, 3 of 9 (22.2%) strains showed discordant results with Etest
→ A total of **6 ASPR strains by Etest**
- 3 of 6 (50%) ASPR strains** proved to be **susceptible to imipenem and piperacillin**
- All 6 (100%) strains** were **resistant to meropenem**

Summary & Conclusions

- During March 2014 through September 2020 at AMC Children's Center, a total of 205 nonduplicates of Enterococcal strains' prevalence and AST was analyzed
- E. faecalis* (47.3%), *E. faecium* (41.5%) were the predominant strains
- 10 of 205 (4.9%) enterococcal strains were ASPR strains by MicroScan**
- 6 of 10 MicroScan confirmed ASPR strains were confirmed as ASPR by Etest**
- 3 of 6 (50%) ASPR strains by Etest was resistant to imipenem and piperacillin and all were resistant to meropenem**
- Antimicrobial susceptibility patterns of ASPR strains suggest that **susceptibility results of ampicillin may not always agree with that of imipenem or piperacillin** and that **meropenem has a high chance of resistance**
- Further studies on resistance pattern and clinical correlation regarding this newly emerging ASPR enterococcal strains is in progress

References

- European Committee on Antimicrobial Susceptibility Testing (EUCAST) Clinical Breakpoint Tables v. 12.0, valid from 2022-01-01
- Clinical and Laboratory Standards Institute (CLSI) M100: Performance Standards for Antimicrobial Susceptibility Testing, 31st Edition, 2021
- Conceição et al., 2012. *E. faecalis* Resistant to Penicillin, J. of Clin. Microbiol. 50:3729-3731