

Geniřlemiř Spektrumlu ve İndüklenebilir
Beta Laktamaz Salgılayan Gram Olumsuz
Bakteri İnfeksiyonları; Epidemiyoloji,
Patogenez ve Tanısı

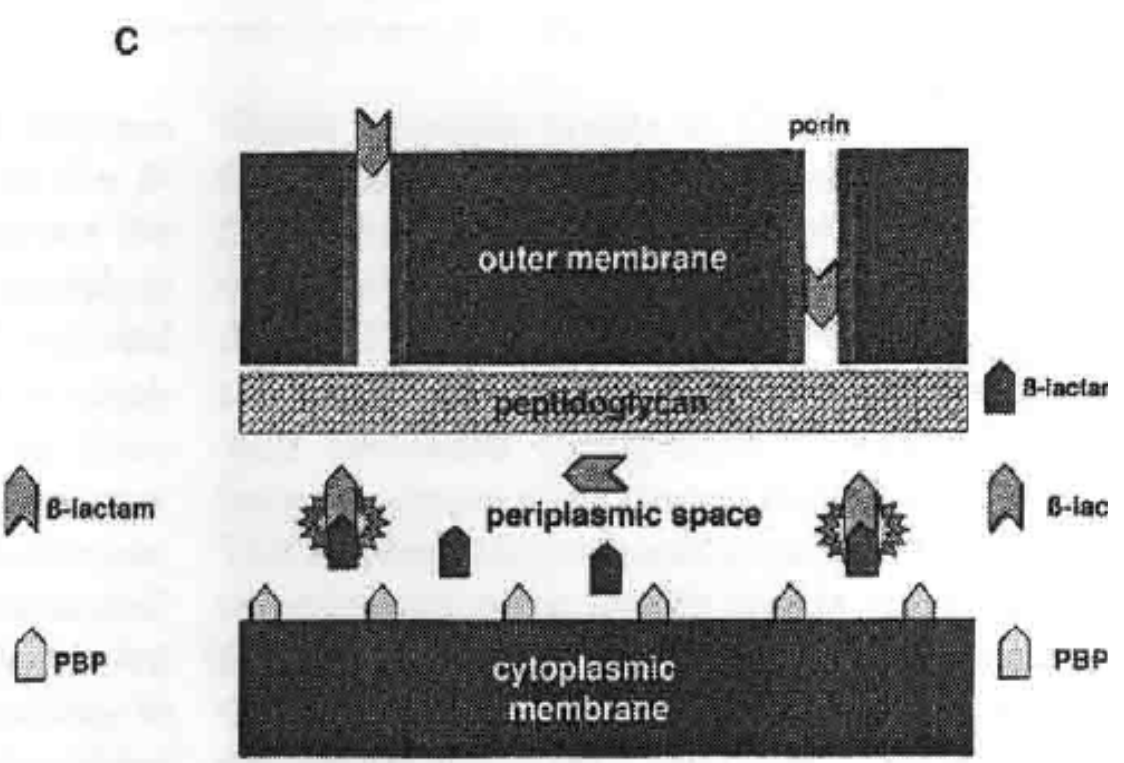
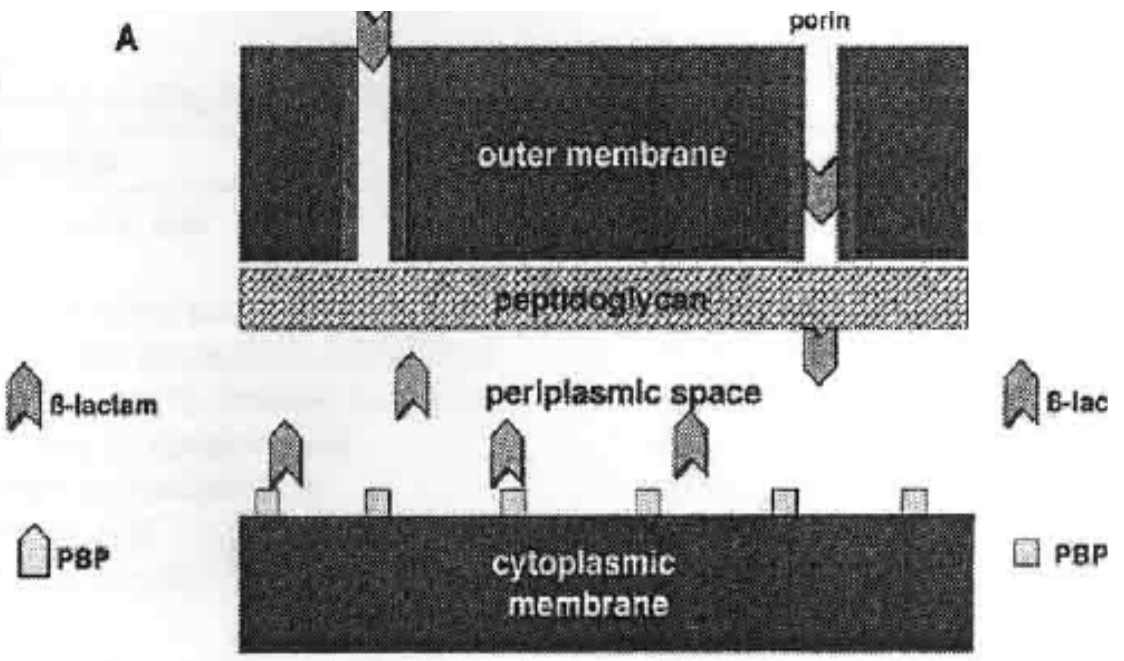
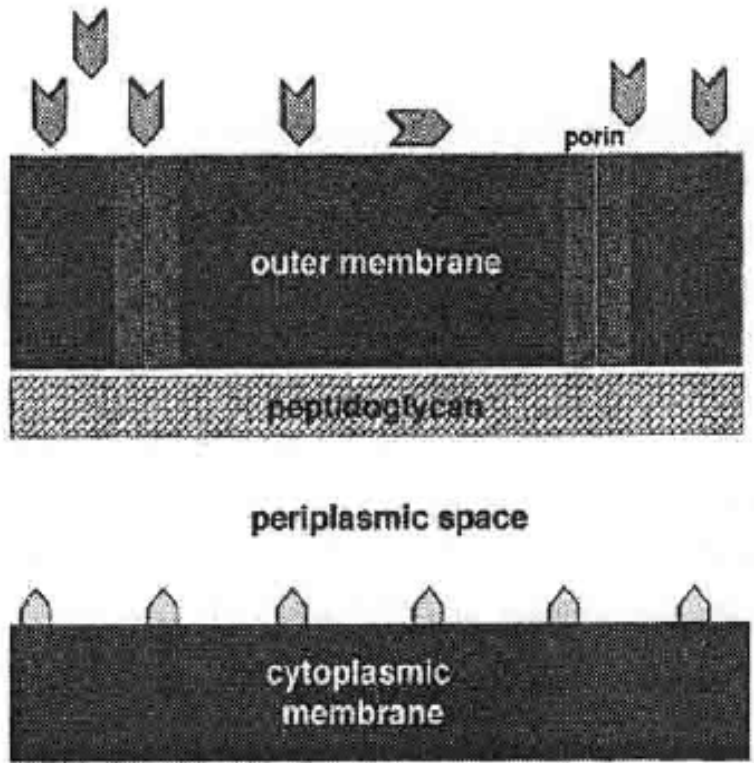
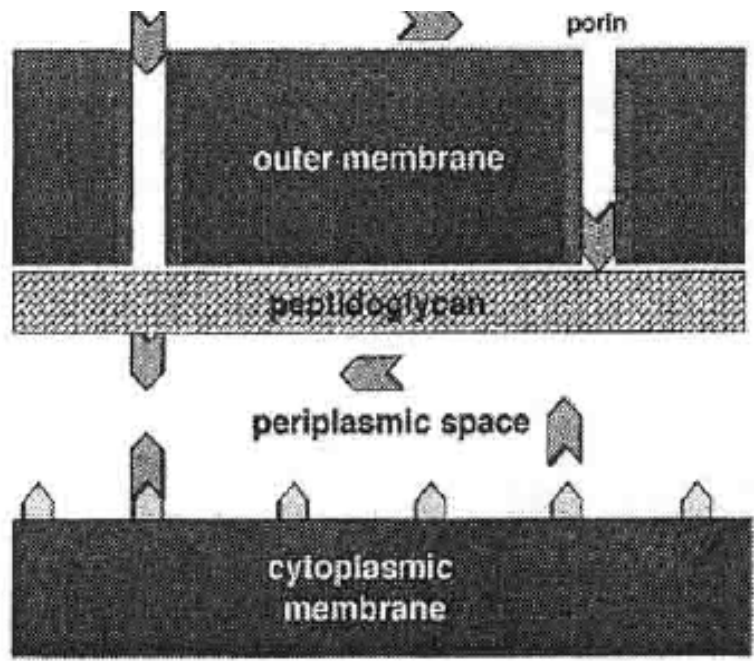
Dr. Oral Öncül

GATA Haydarpařa Eđitim Hastanesi

Enfeksiyon Hst. Kl. Mik. Srv.

Beta Laktam Antibiyotikler İçin Direnç Mekanizmaları

- Hücre içindeki B.laktam antibiyotiğin konsantrasyon azalması
 - Porin kaybı
 - Pompa sistemi
- Hedef bölgesindeki PBP değişimi
 - Mevcut PBP değişimi
 - Dışarıdan yeni PBP alımı
- B.laktam antibiyotiğin parçalanması
 - Beta-laktamaz üretiminin artışı
 - Mevcut Beta-laktamaz yapısında mutasyon gelişimi
 - Farklı spektrumda yeni Beta-laktamazların alınması



GSBL Evrimi

TEM-1 (1965)



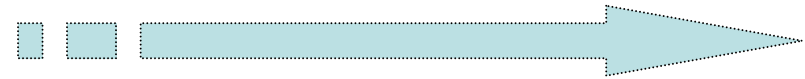
1 aminoasit Penisilin ve I.kuşak SS

TEM-2 (1970)



2 aminoasit

CTX-M (1987)



Geniş spektrumlu beta-laktam

Sınıf	Aktif Bölge	Örnek
A	Serin	Tüm plazmid kökenli enzimler, <i>Klebsiella</i> sp. <i>Proteus</i> sp. PER-1
B	Çinko	<i>S.maltophilia</i> (Kromozomal) <i>P.aeruginosa</i> (IMP-1)
C	Serin	Kromozomal Amp-C
D	Serin	OXA Enzimleri

Ambler RP, 1980

E.Coli ve K.pneumoniae'da Beta-Laktamazlar

Jacoby GA, et al. N Engl J Med, 2005; 352: 380-91

Beta-Laktamaz	Örnek	Antibiyotikler	Klavulanata yanıt	Sınıf
Geniş spektrumlu	TEM-1, TEM-2, SHV-1 OXA	Penisilinler, SS (dar spektrum) Oksasilin..	+++	A D
GSBL	TEM, SHV CTX-M OXA Diğer (BES-1, VEB-1..)	Pen, Monobaktam, SS.. Sefepim	++++ ++++ + ++++	A D A
Amp C	ACC-1, ACT-1, CFE-1, CMY..	GSBL + sefamisinler	0	C
Karbapenemaz	IMP, VIM, GIM-1, SPM-1(MBL) KPC-1, 2, 3 OXA-23, 24, 25..	GSBL + sefamisinler + karbapenem	0 +++ +	B A D

GSBL'nin Güncel Boyutu

- TEM ve SHV grubundan fonksiyonel 2be elemanları
- TEM ve SHV mutantları (CTX-M ve VEB türleri)
- TEM ve SHV mutantları, sınırlı GSBL aktivitesi (TEM-12)
- OXA Beta-Laktamazlar ve mutant AmpC tipi (2be dışında)

GSLB Varlığını Düşündüren Laboratuvar İpuçları

- Etkili antibiyotiklerde saptanan sürpriz duyarlılık azalması
- İnokulum etkisi (5×10^7) ile MIK değerinde 100-500 kat artış
- Çoklu ilaç direnç bulguları (Gentamisin, TMP/SMX)
- Çeşitli antibiyotik zon çapı ve MIK değerlerinde artış
 - Aztreonam ve III.kuşak SS $\geq 2 \mu\text{g/ml}$
 - Seftazidim inhibisyon zon çapı $\leq 22 \text{ mm}$
 - Aztroenam ve sefotaksim $\leq 27 \text{ mm}$
 - Seftriakson inhibisyon zon çapı $\leq 25 \text{ mm}$

GSBL İçin Tarama Testi Olarak Önerilen İnhibisyon Zon Çapları ve MIK Değerleri

Antibiyotik	İnhibisyon Zonu (mm)	MIK (mg/L)
Sefotaksim	≤ 27	≥ 2
Seftriakson	≤ 25	≥ 2
Seftazidim	≤ 22	≥ 2
Sefpodoksim	≤ 17	≥ 8
Aztroenam	≤ 27	≥ 2

GSBL Doğrulama Testleri

- Kombine Disk Yöntemi
 - Sefotaksim (30 μg)
 - Seftazidim (30 μg) } + klavul.asid
(10 μg)
- Çift Disk Sinerji Yöntemi
- E Test Yöntemi
- Mikrodilüsyon Yöntemi
- Üç boyutlu Test
- Ticari kitleler
- Moleküler yöntemler

Kombine Disk Yöntemi

Kombine Disk Yöntemi, GSBL Doğrulama Testi



Sefotaksim (30 μ g)

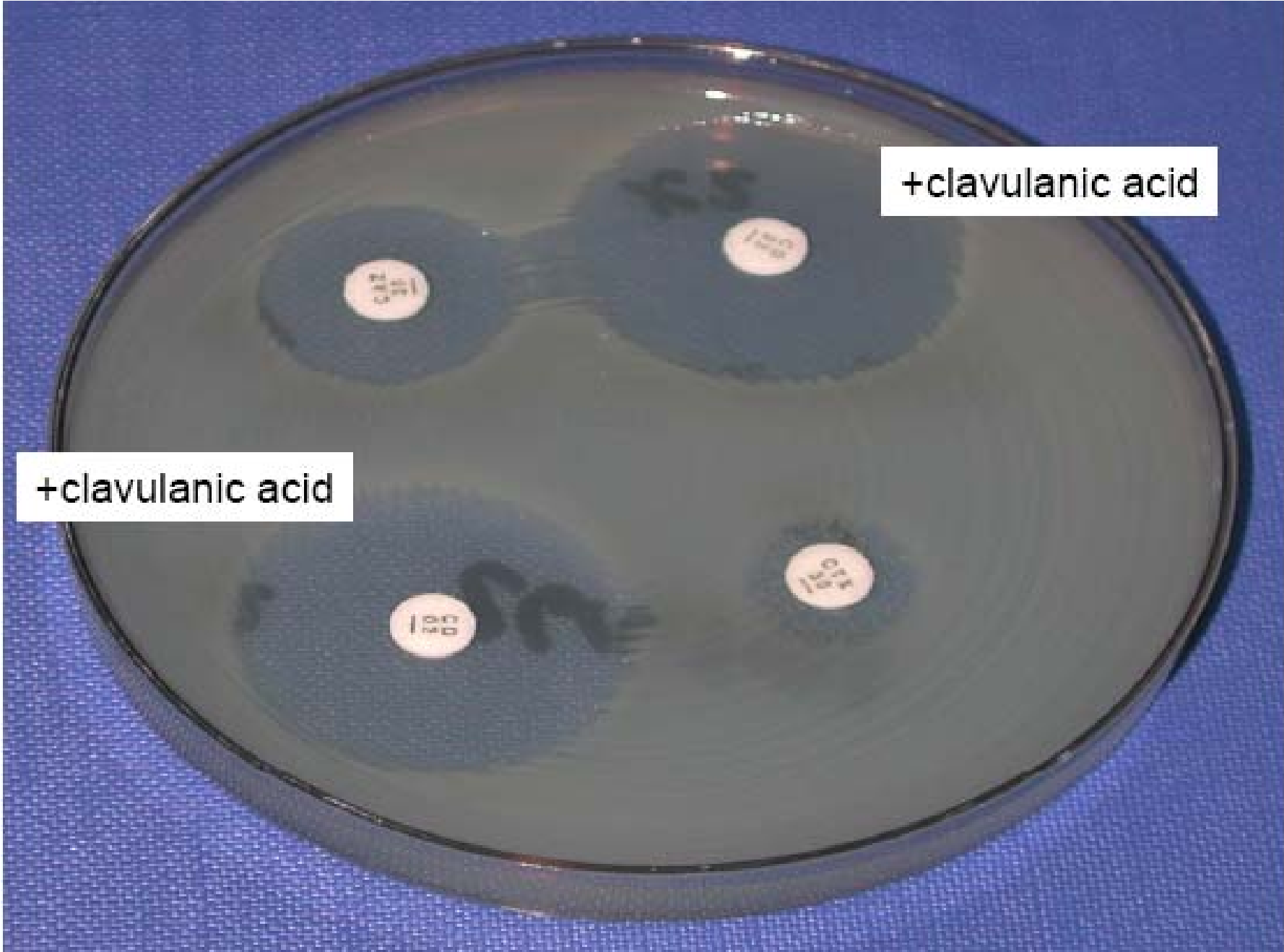
Sefotaksim + klavulonik asid (10 μ g)



≥ 5 mm

Seftazidim (30 μ g)

Seftazidim + klavulonik asid (10 μ g)



+clavulanic acid

+clavulanic acid

Çift Disk Sinerji Yöntemi

- AMC (20/10 mg)
- CAZ
- CRO
- CTX
- ATM
- POD
- İnhibisyon zon genişlemesi

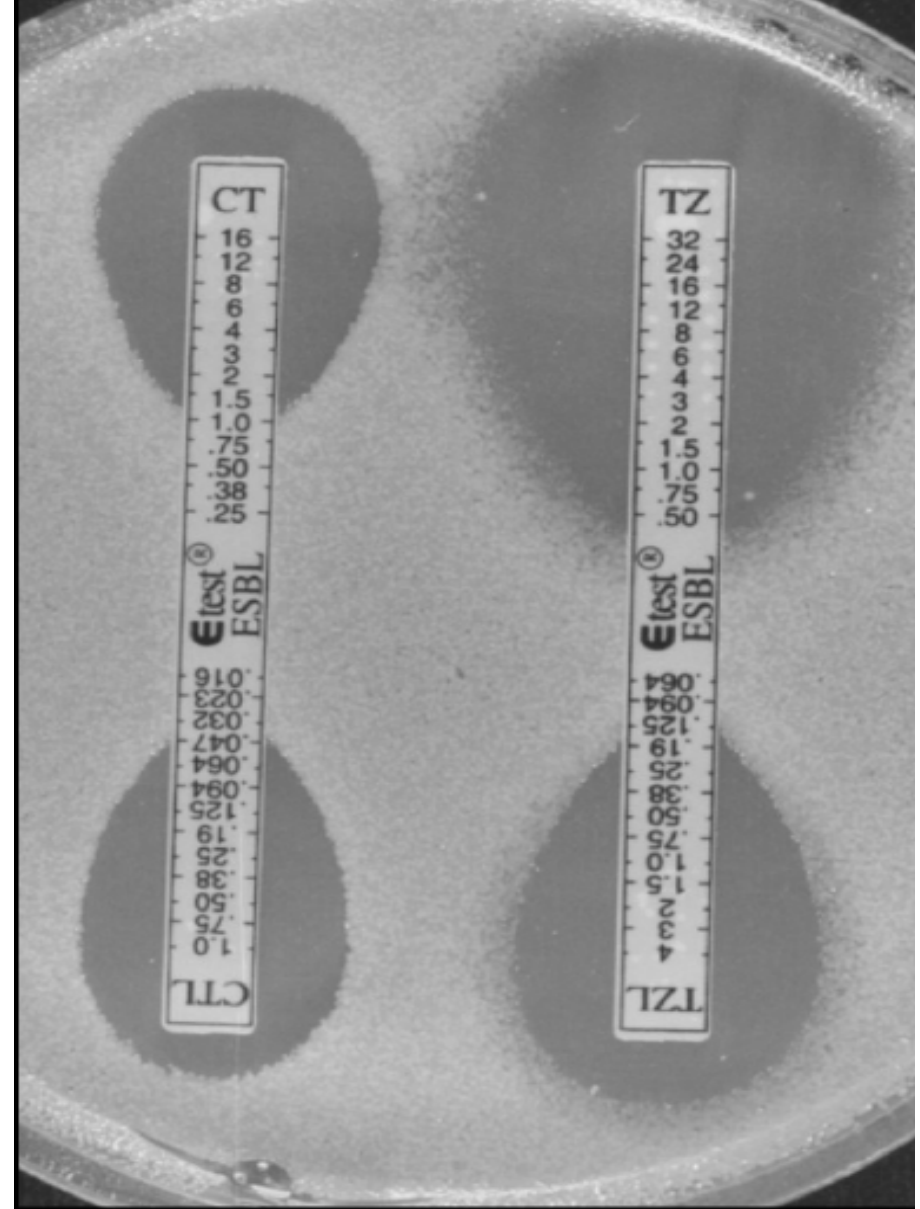


Çift Disk Diffüzyon Testi



E Test Yöntemi

- Seftazidim
- Seftazidim klavulonat
- Sefotaksim
- Sefotaksim klavulonat
- $MIK \geq 8$ kat artış

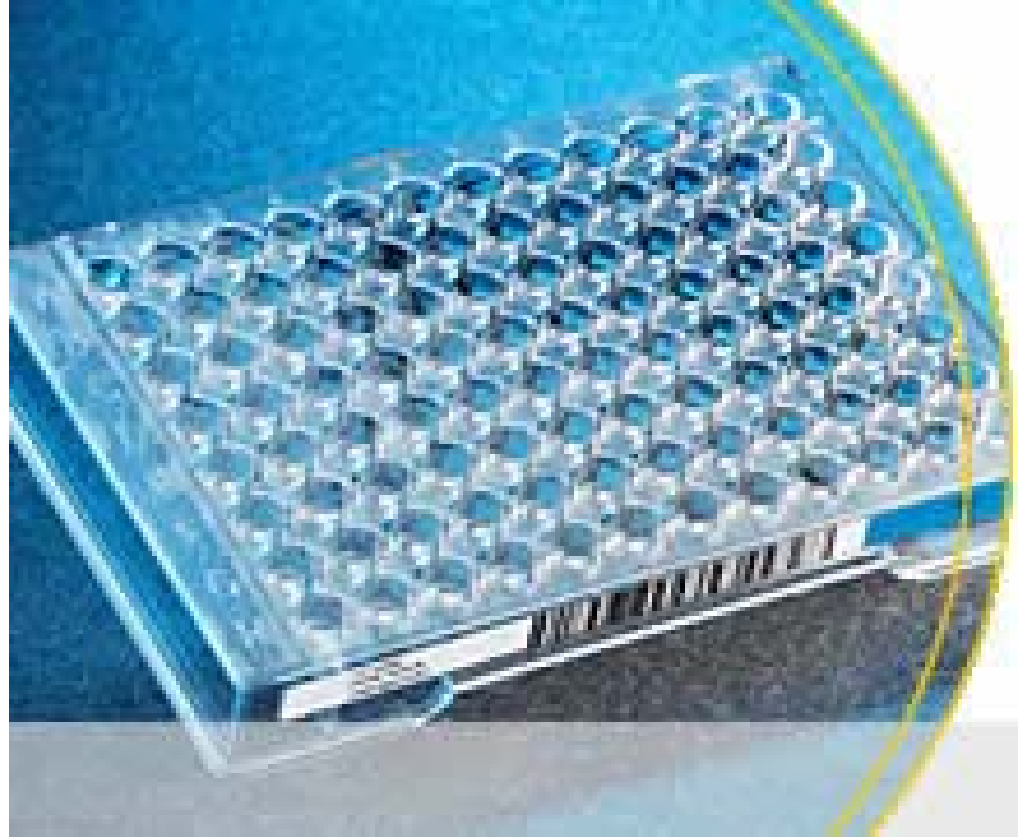


K. pneumoniae
TZ/TZLpozitif, CT/CTL hayalet zon
ESBL pozitif



Mikrodilüsyon Yöntemi

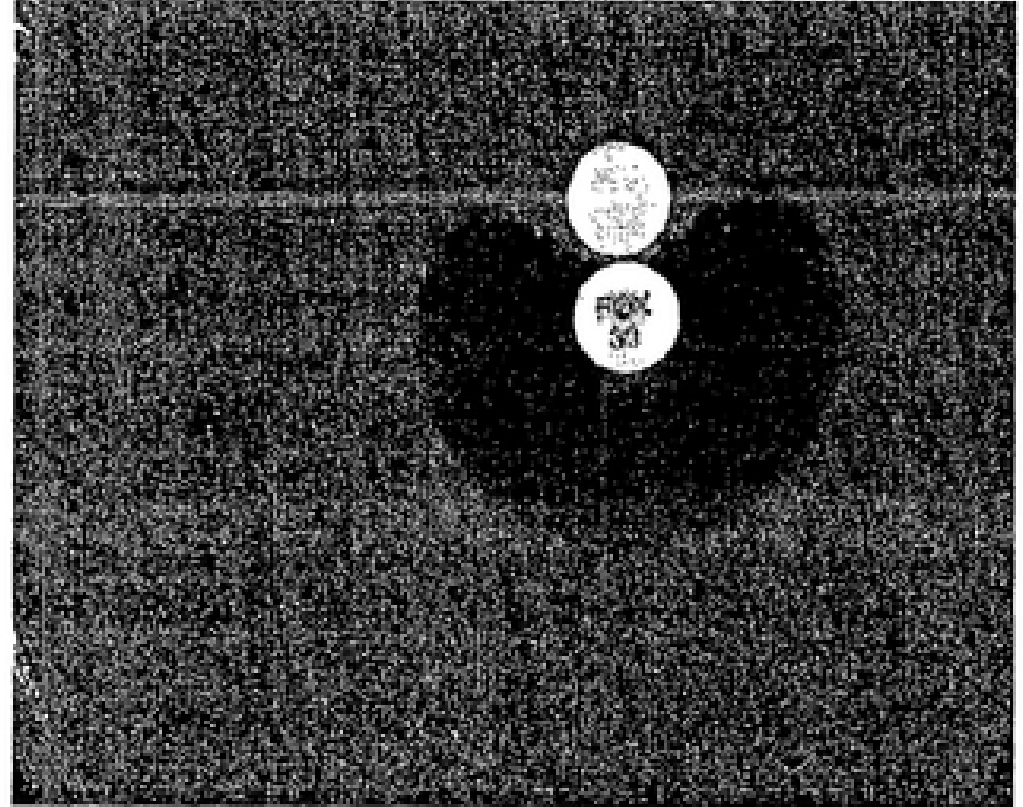
- Seftazidim
- Sefotaksim
- Klavulonik asit
- $MIK \geq 3 \log_2 (8)$ kat artış



Üç Boyutlu Test

Fig. 1

- Besiyerinde yarık
- Yarık içi sıvı besiyeri
- Diskler 3 mm mesafe
- İnhibisyon zon bozulması



GSBL Tanımlanmasında Karşılaşılan Sorunlar

- İnokulum yoğunluđuna bađlı sorunlar
- Bakteri türüne bađlı sorunlar
 - *Proteus mirabilis* (40 mm)
 - *Enterobacter cloacae* (20 mm)
- Besiyeri kalınlıđına bađlı sorunlar
- Disk aralıklarından kaynaklanan sorunlar
- Antibiyotik türlerinden kaynaklanan sorunlar
- Isı, pH ve diđer kimyasallar..

GSBL Tanımlanmasında Sorunlar

Queenan AM, et al. J Clin Microbiol, 2004: 269-75

Düşük inokulum etkisine bağlı sorunlar

- TEM-1 salgılayan suşlar 10^5 - 10^6 cfu/ml
- GSBL için Y. Negatif sonuç (CTX-M 10, TEM-3, 10, 28..)

• Yüksek inokulum etkisine bağlı sorunlar

- MIK değerlerinde yaklaşık 4 kat artış (TEM-28, 43, SHV-5, 18, K-1..)

GSBL Salgılayan Suşların Klinik Önemi

- Geniş spektrumlu SS ve Aztroenam direnci
- Beta laktam dışı çoklu antibakteriyel direnç
- Hastane ortamında daha yaygın
- Toplum kökenli suşlarda artış
- Yetersiz raporlanma ve uygunsuz antibiyotik
- Hastane kökenli salgın riski
- Mortalite, morbidite ve yatış süresine olumsuz etki
- Maliyet artırıcı etki..

GSBL Riski

- Geniř spektrumlu antibiyotik kullanımı
- Uzun süreli hastanede yatıř
- İnvaziv giriřimler
- Parenteral beslenme
- Altta yatan ciddi hastalıklar
- Uygunsuz cerrahi proflaksi
- Cerrahi giriřim
- Dekübitis ülserleri
- Hastane florası (GSBL varlığı)
- Fekal taşıyıcılık

The Relationship between Antimicrobial Resistance and Patient Outcomes: Mortality, Length of Hospital Stay, and Health Care Costs

Sara E. Cosgrove

Division of Infectious Diseases, The Johns Hopkins Medical Institutions, Baltimore, Maryland

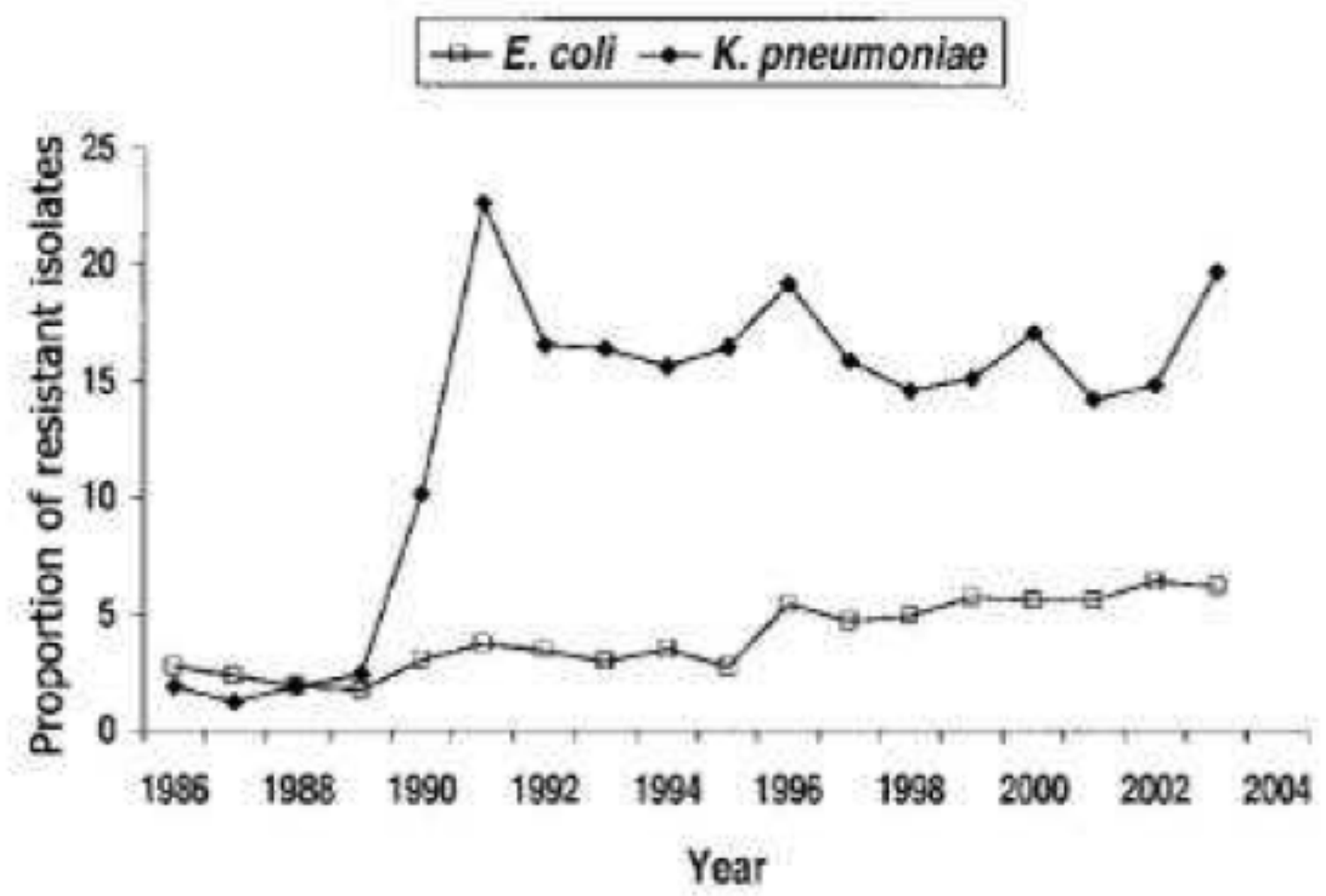
There is an association between the development of antimicrobial resistance in *Staphylococcus aureus*, enterococci, and gram-negative bacilli and increases in mortality, morbidity, length of hospitalization, and cost of health care. For many patients, inadequate or delayed therapy and severe underlying disease are primarily

Table 4. Outcomes for patients with emergence of third-generation cephalosporin-resistant *Enterobacter* species, according to multivariate analysis [33].

Outcome	Patients with emergence of resistance	Patients without emergence of resistance	Value attributable to emergence of resistance	RR	P
Death, ^a % of patients	26	13	...	5.02	.01
LOS, ^b days	30	19	9	1.47 ^c	<.001
Hospital charges, ^d \$US	79,323	40,406	29,379	1.51 ^c	<.001

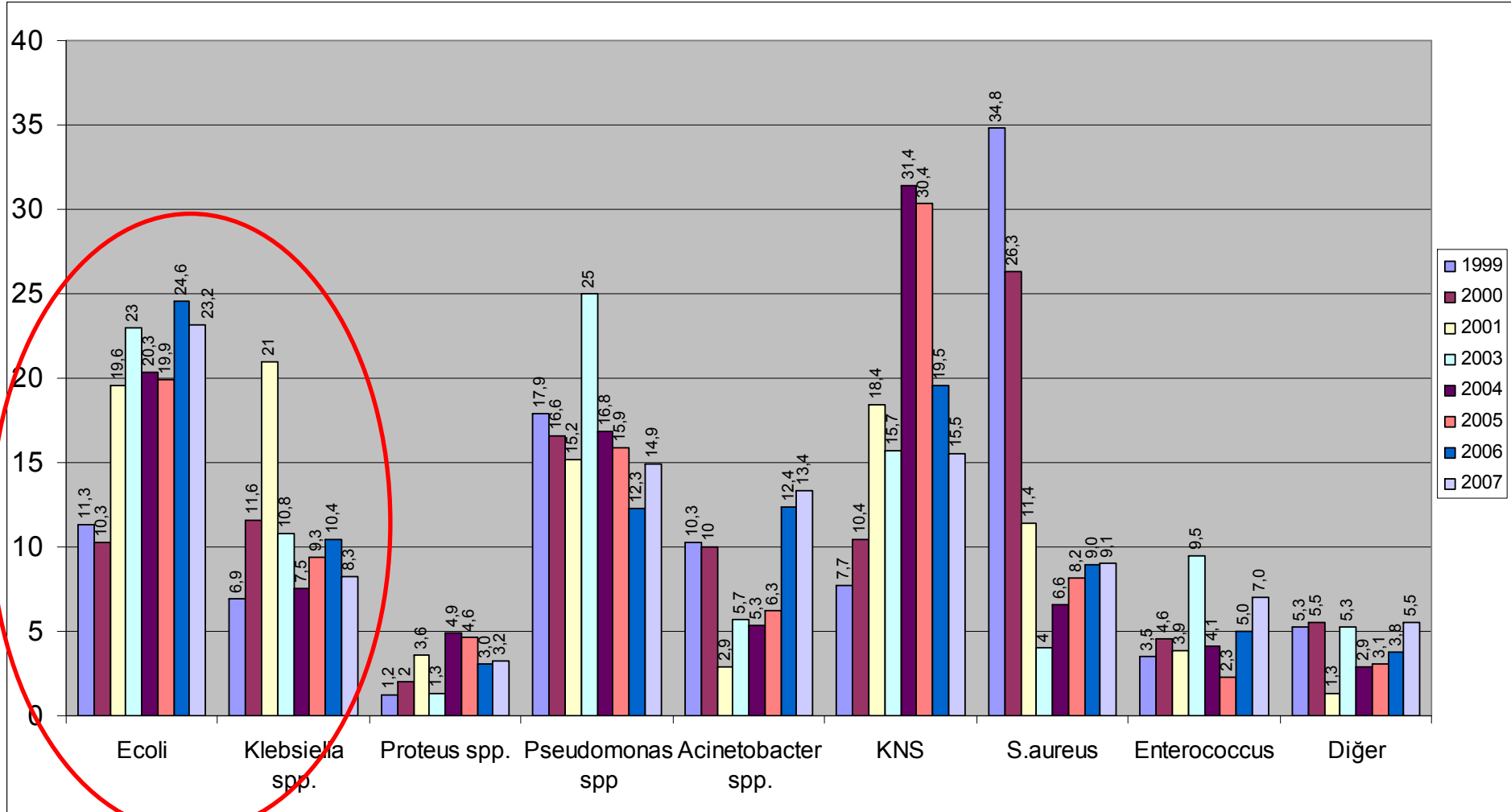
NOTE. LOS, length of hospital stay; RR, relative risk.

GSBL Salgılayan E.coli ve Klebsiella Suşları

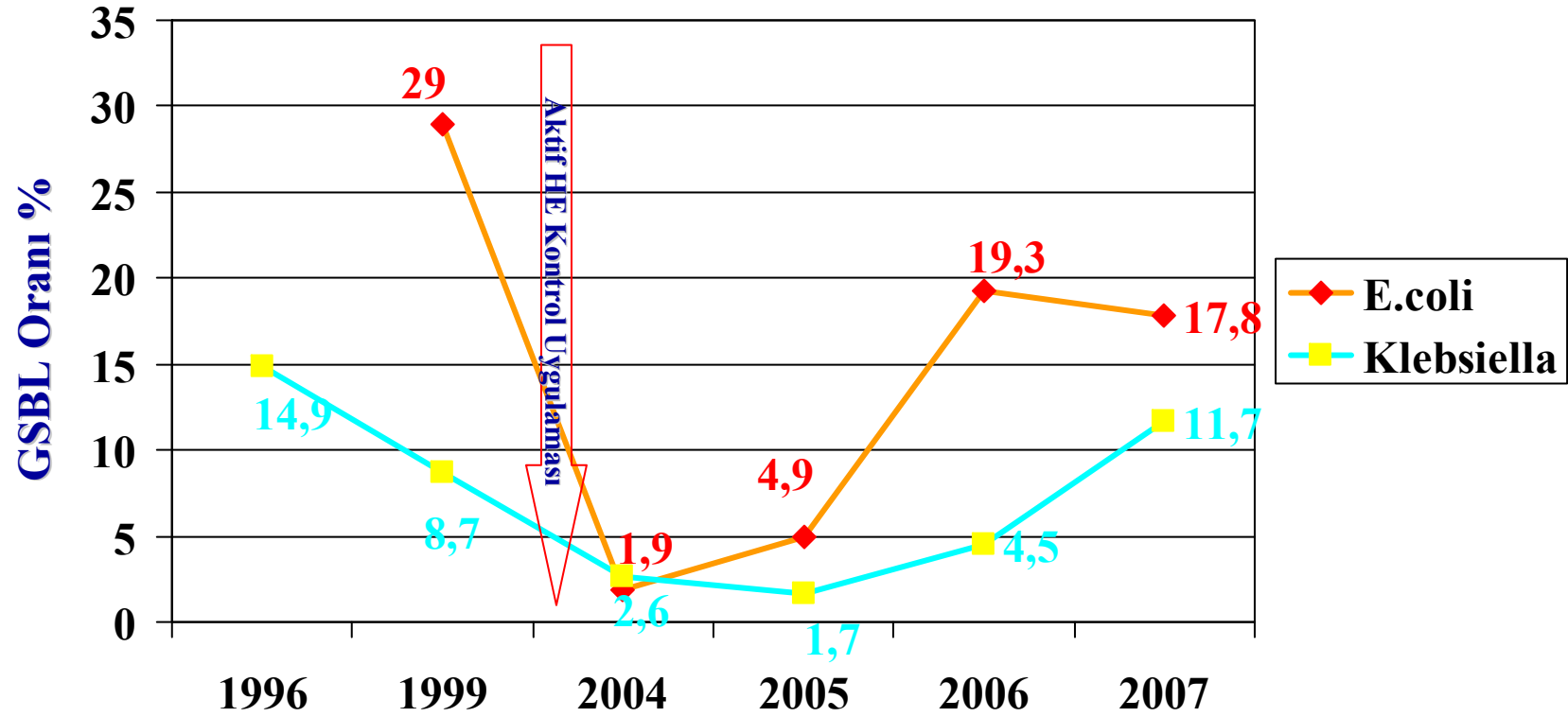


NNIS, 1986-2003. Clin Infect Dis, 2005; 41: 848

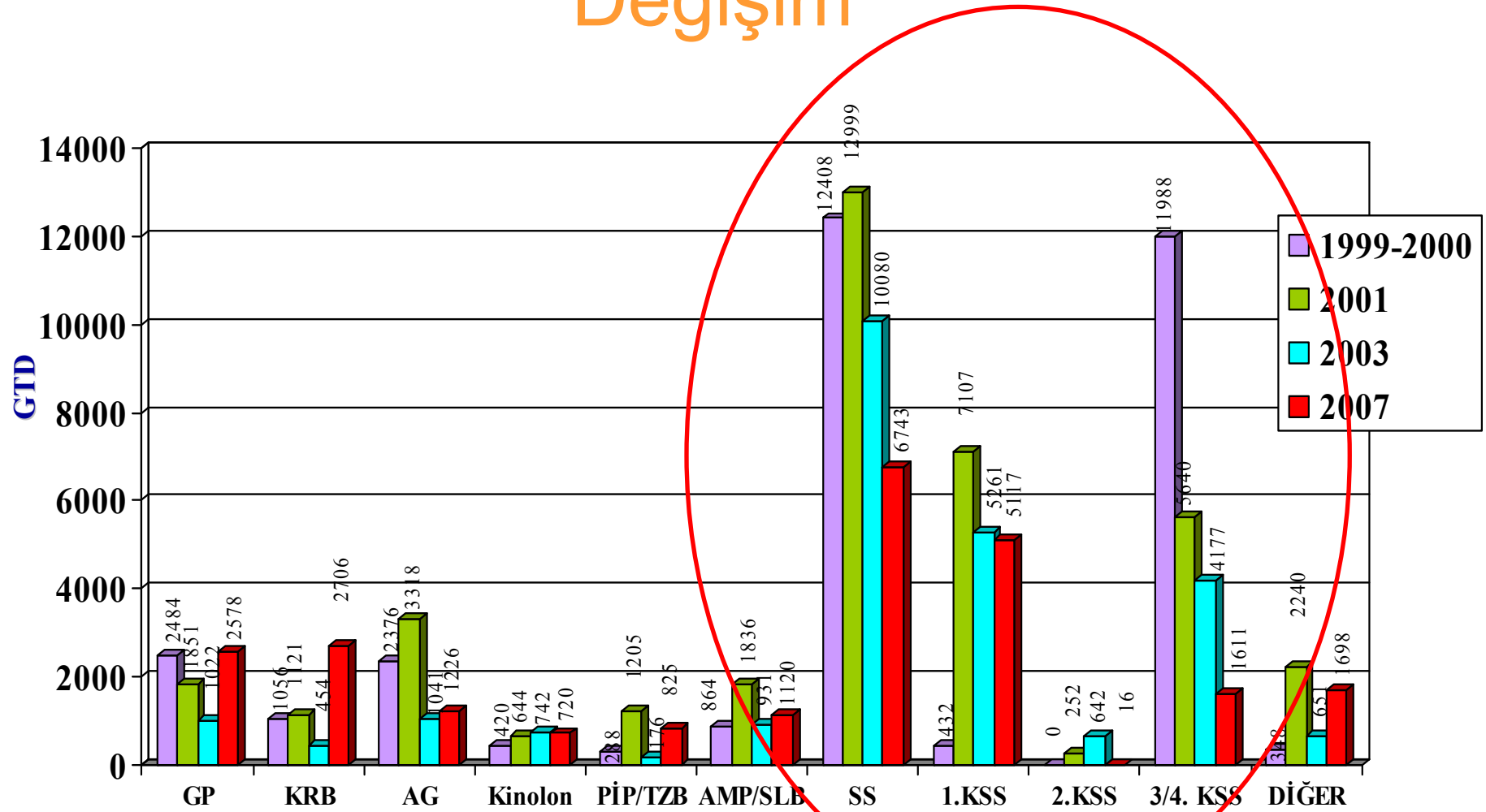
Hastane Enfeksiyonlarında Etken Dağılımı



GATA H.Paşa GSBL Oranları



Antibiyotik Kullanım Oranlarındaki Değişim



Sefalosporin Kullanımında Kısıtlama ile GSBL Kontrolü

Yıl	Arařtırmacı	Antibiyotik	Kısıtlama oranı (%)	Kullanılan antibiyotik	GSBL Kontrolü
1993	Meyer	Seftazidim	73	IMP	+
1996	Rice	Seftazidim	50	PIP/TAZ	+
1998	Pena	3.Kuřak SS	83	PIP/TAZ	+
1998	Rahal	Tüm SS	80	IMP	+
1999	Landman	Seftazidim	89	SAM, PIP/TAZ	+
2000	Patterson	Seftazidim	71	PIP/TAZ	+

New York Hastanesi

K. pneumoniae (TEM-26) Salgını

Uygulama

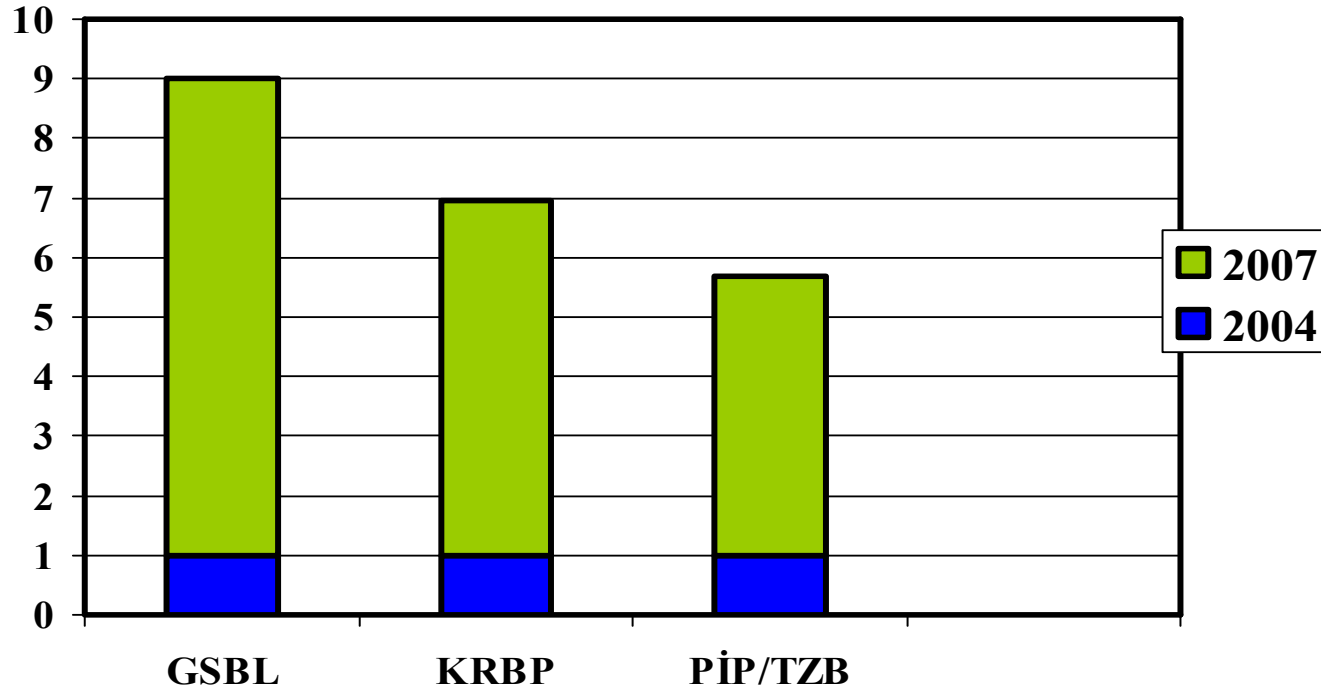
- Seftazidim kullanımının kontrol altına alınması
- İnfeksiyon kontrol önlemleri
- Dirençli suşların tedavisinde imipenem

Sonuçlar

- K. pneumoniae insidansında azalma
- YBÜ'de polimiksin B ve sulbaktam dışında tüm antibiyotiklere karşı da dirence sahip olan imipeneme dirençli A. baumannii salgını

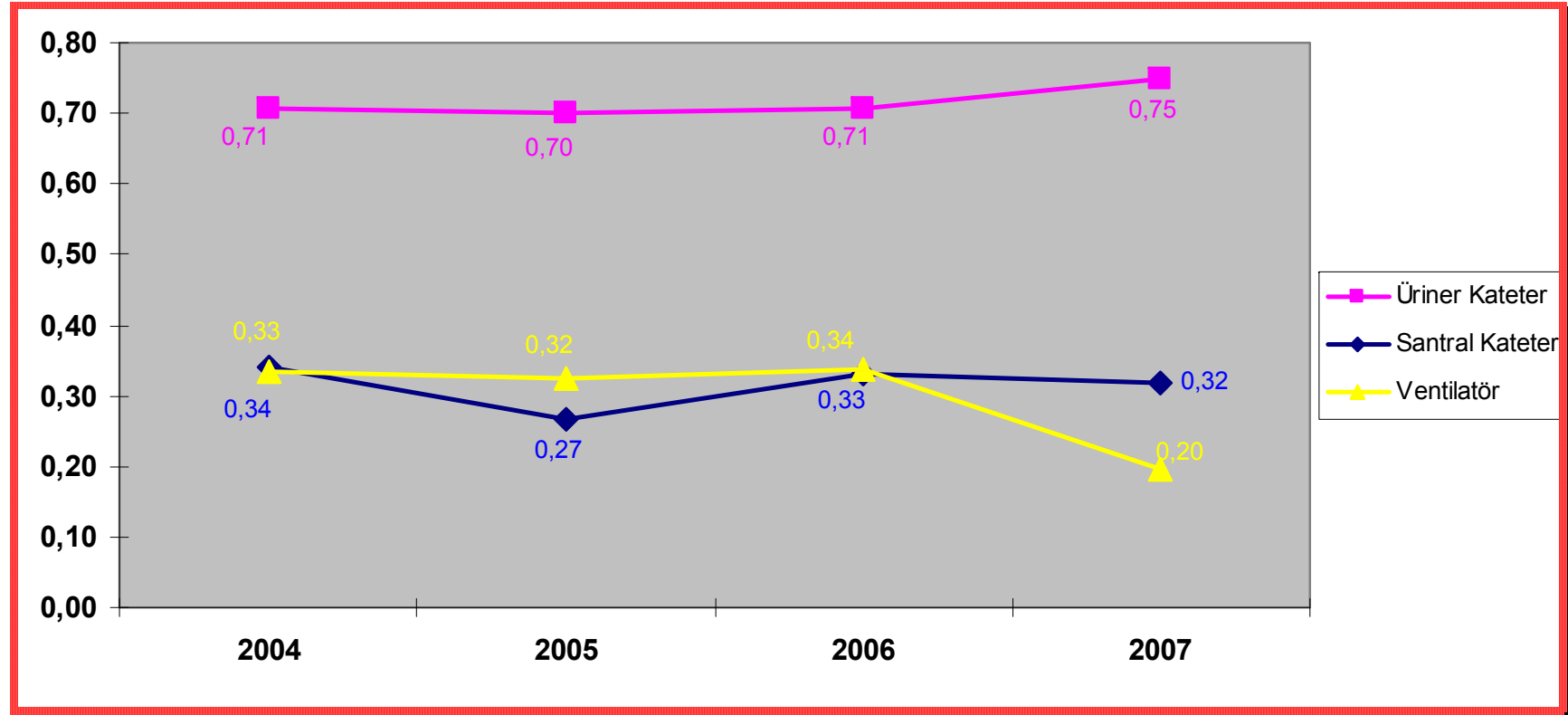
Go ES et al. Lancet 1994;344:1329-1332
Meyer KS et al. Ann Intern Med 1993;119:353-358
Urban C et al. Antimicrob Agents Chemother 1994;38:392-395

Karbapenem-PIP/TZB Kullanımında Artış

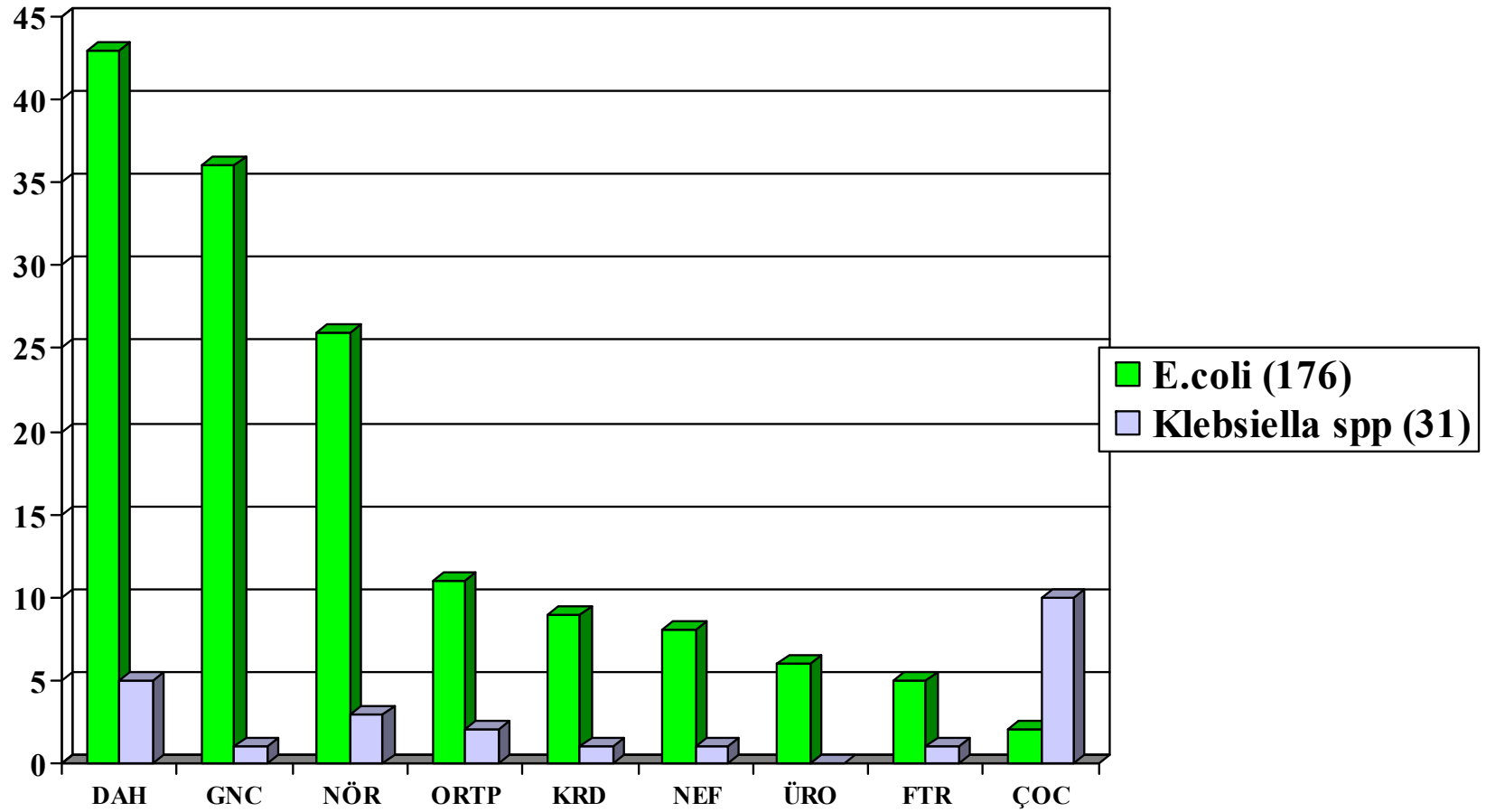


GSBL oranlarında 8 kat artış
Karbapenem kullanımında 6 kat artış

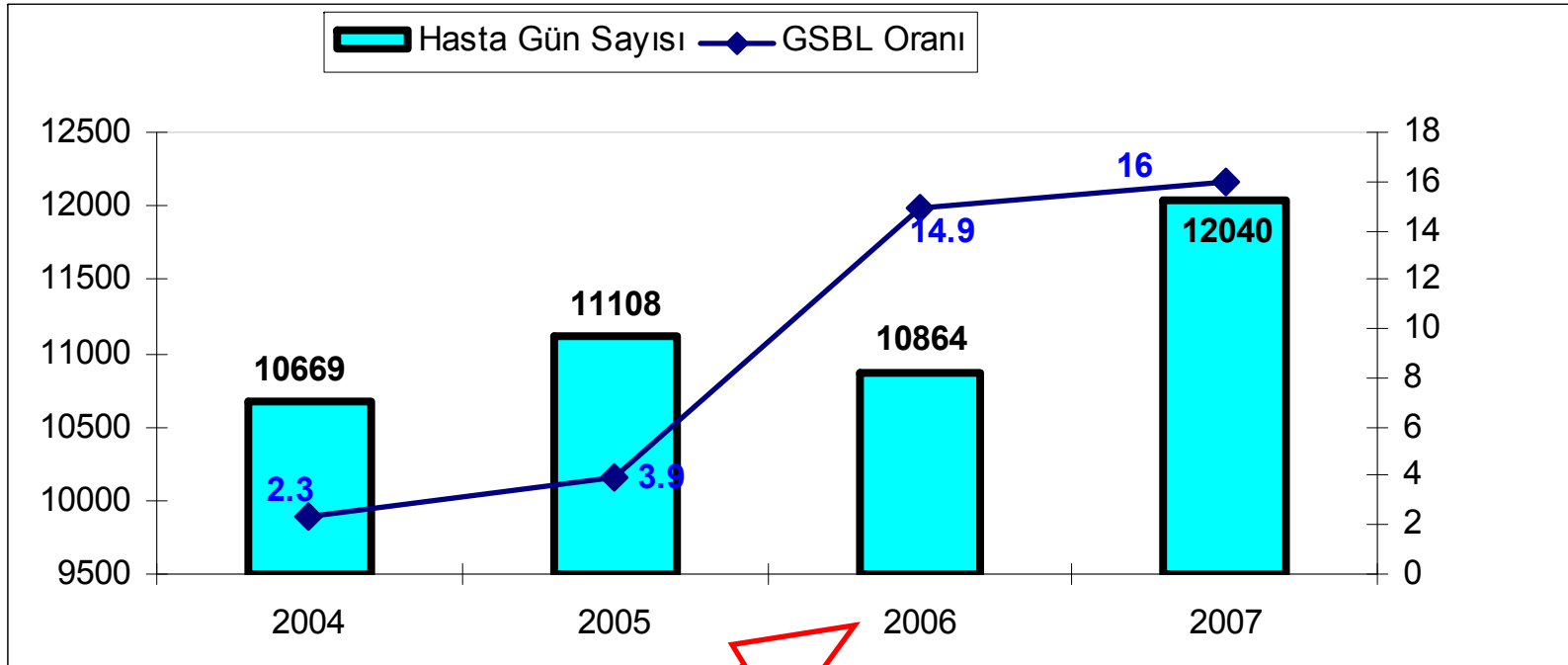
Aygıt Kullanım Oranlarında Artış?



GSBL (+) Suşlar Servislere Göre Dağılımı

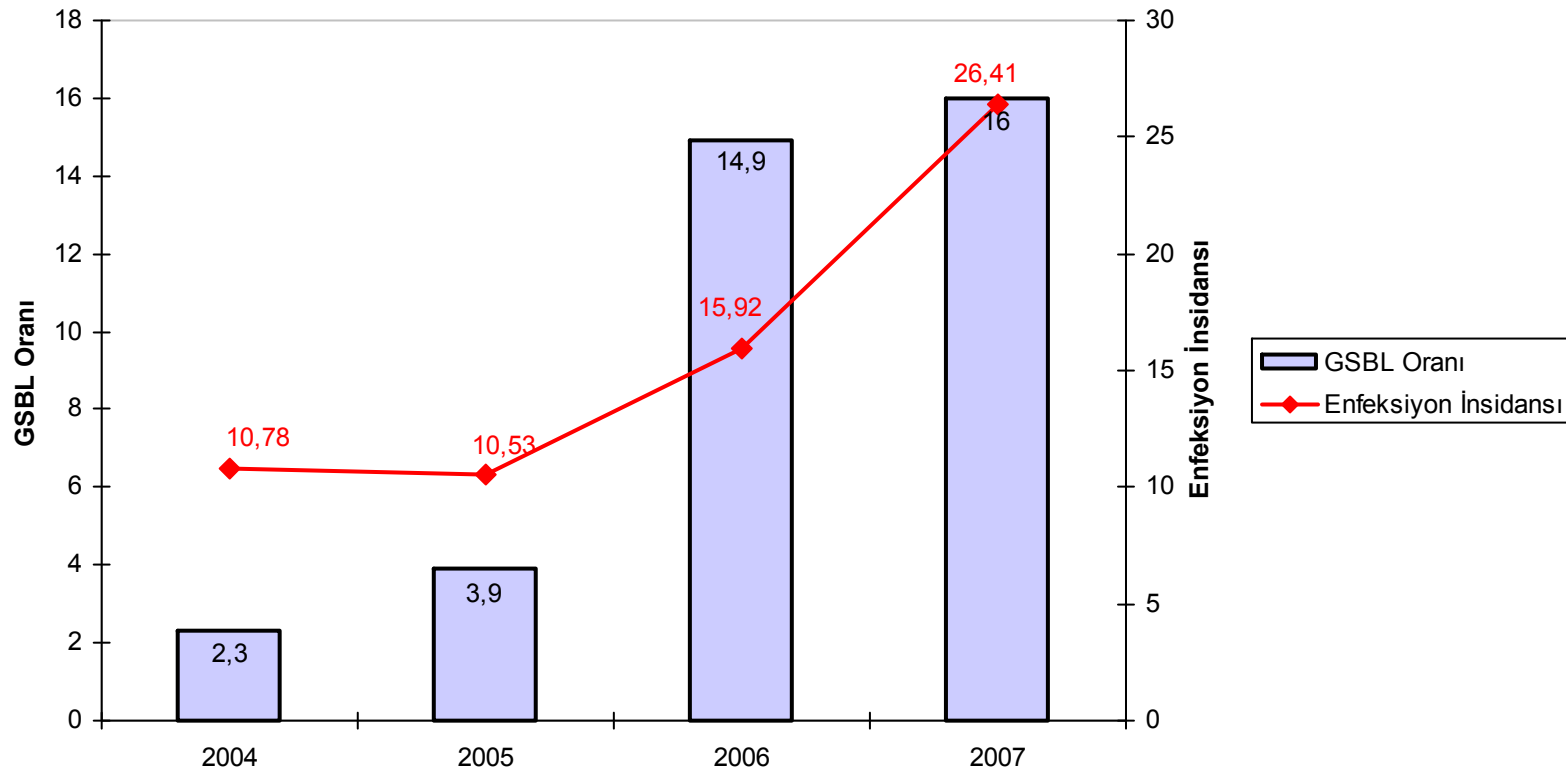


Hasta Yatış Gününde Artış?

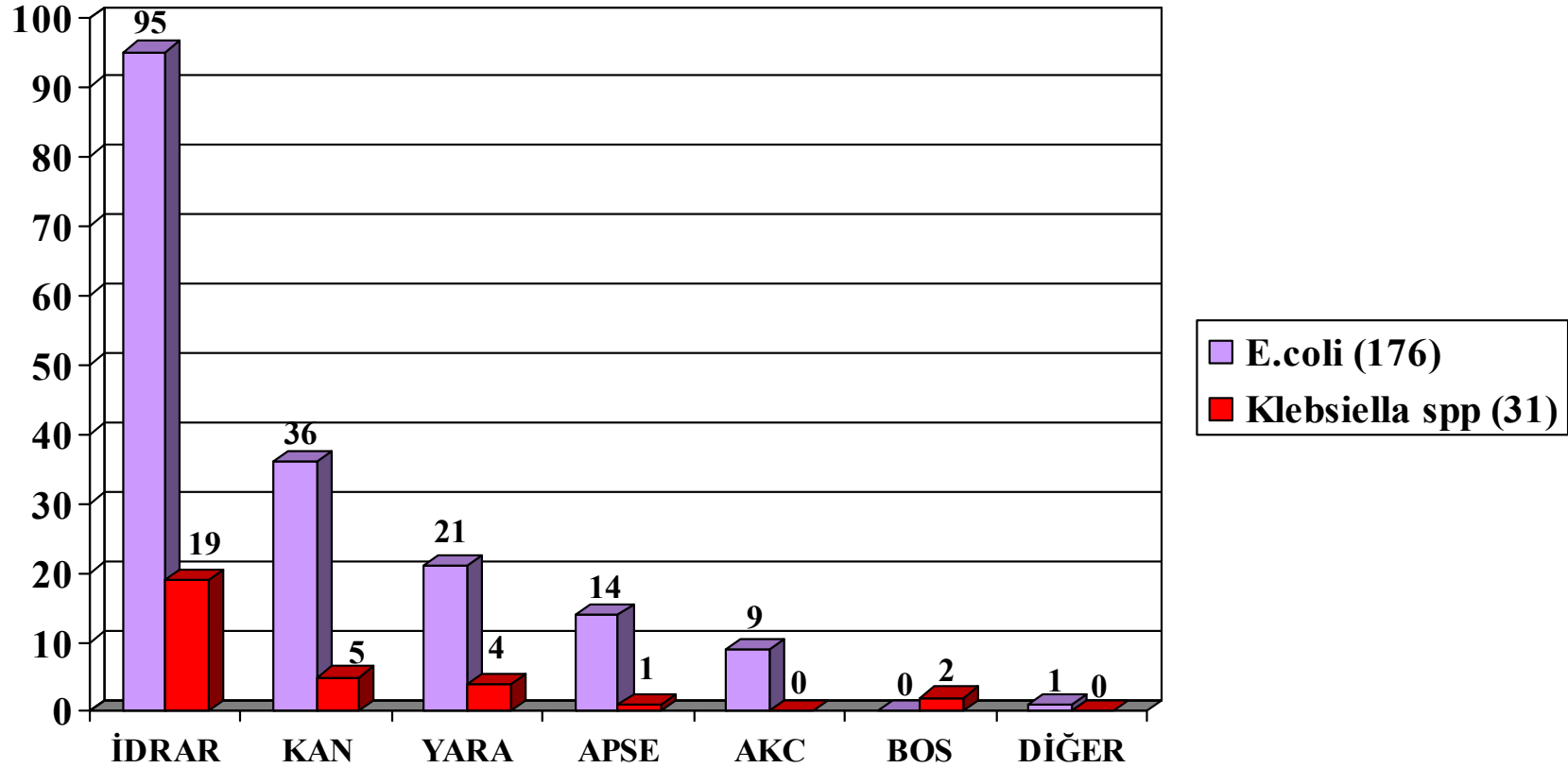


Taşınma

Hastane Enfeksiyon İnsidans Dansitesinde Artış

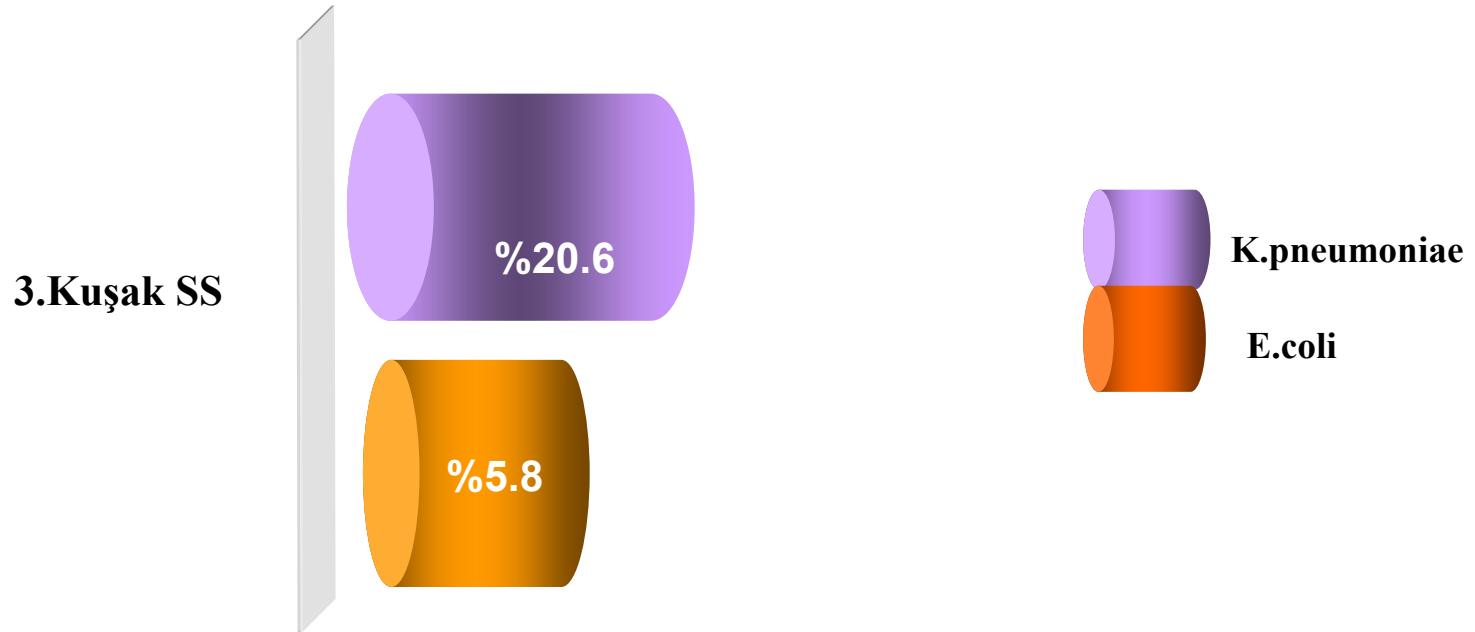
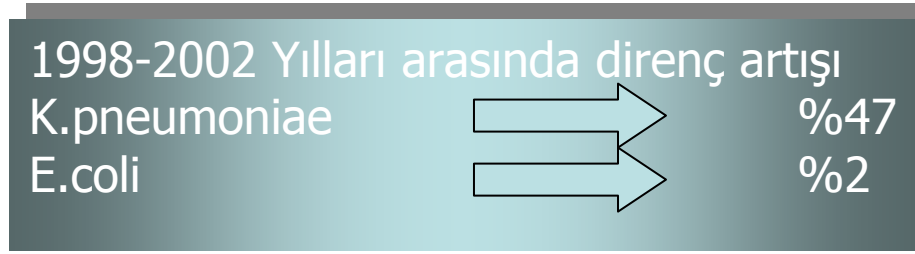


GSBL (+) Suşlar İzole Edildiği Klinik Örnekler





GSBL Artışı (NNIS)

- NNIS Report, Am J Infect Control, 2004; 32: 470-85



GSBL Düzeyleri (SENTRY 1997-2000)

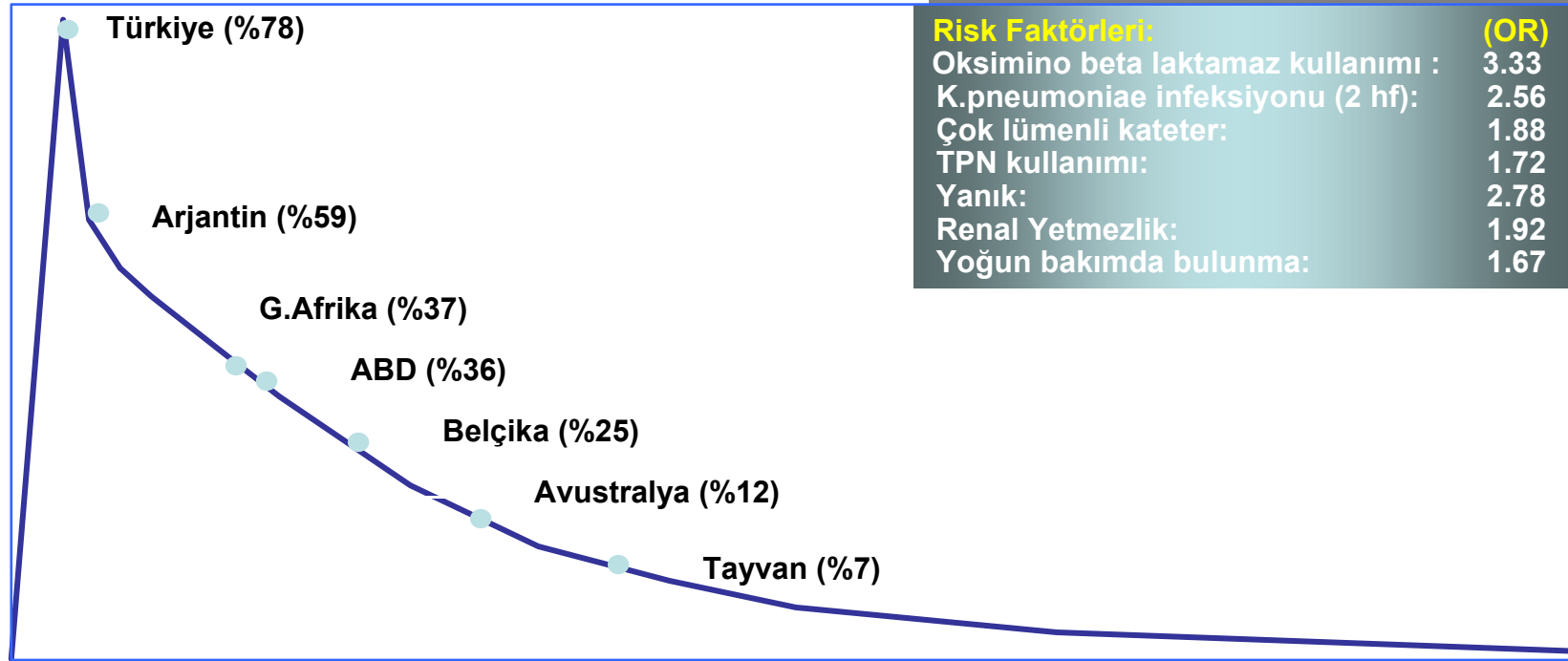
Gales A.C, et al. Diagn Microbiol Infect Dis, 2002; 44: 301-11

- Latin Amerika Akciğer infeksiyon etkenleri
- *K.pneumoniae*  %44
- *E.coli*  %29

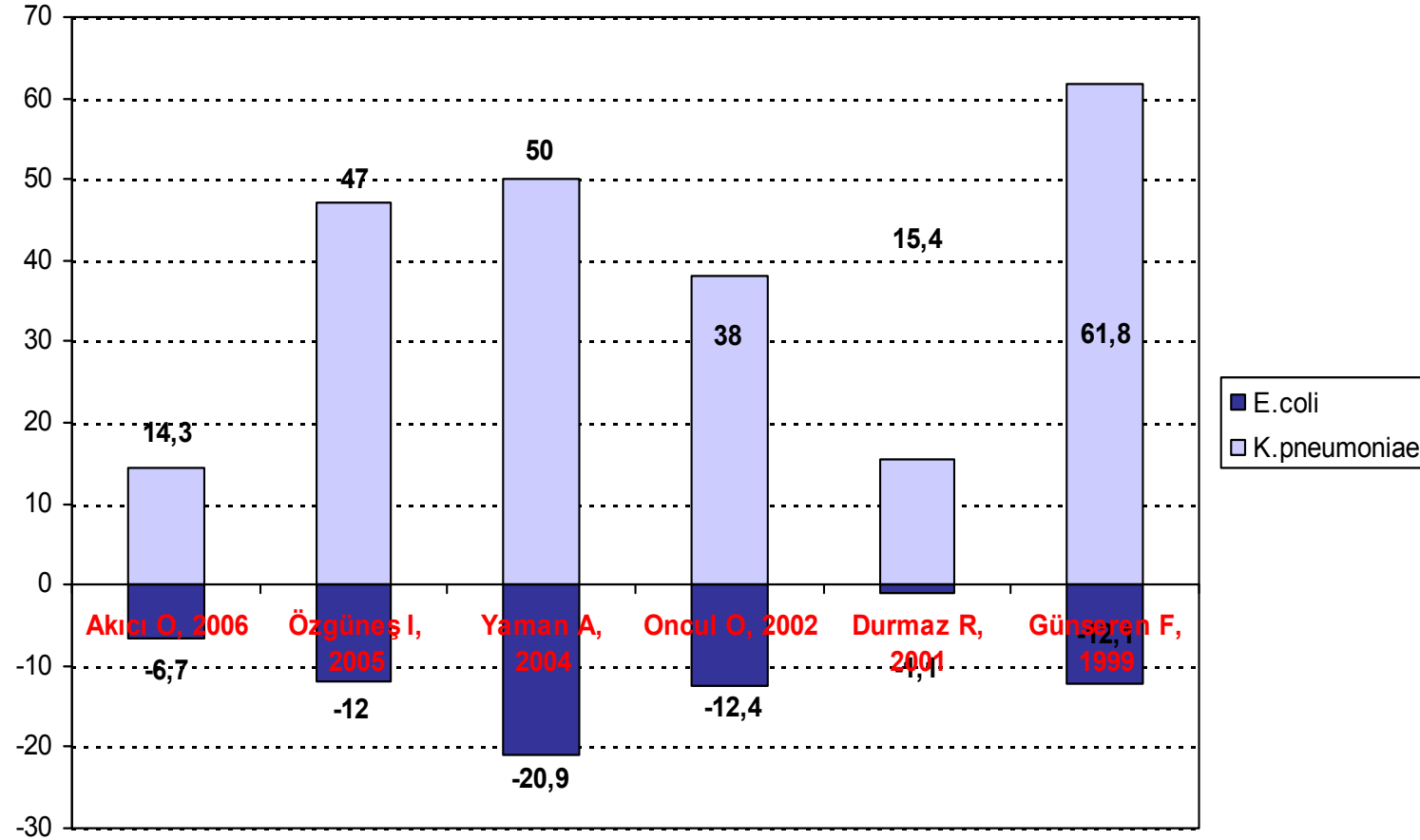
GSBL Salgılayan E.coli / K.pneumoniae

Suşları-Türkiye ve Diğer Ülkeler

GSBL (+) E.coli ve K.pneumoniae izolatları diğer ülkelere oranla Türkiye'de daha fazla görülüyor



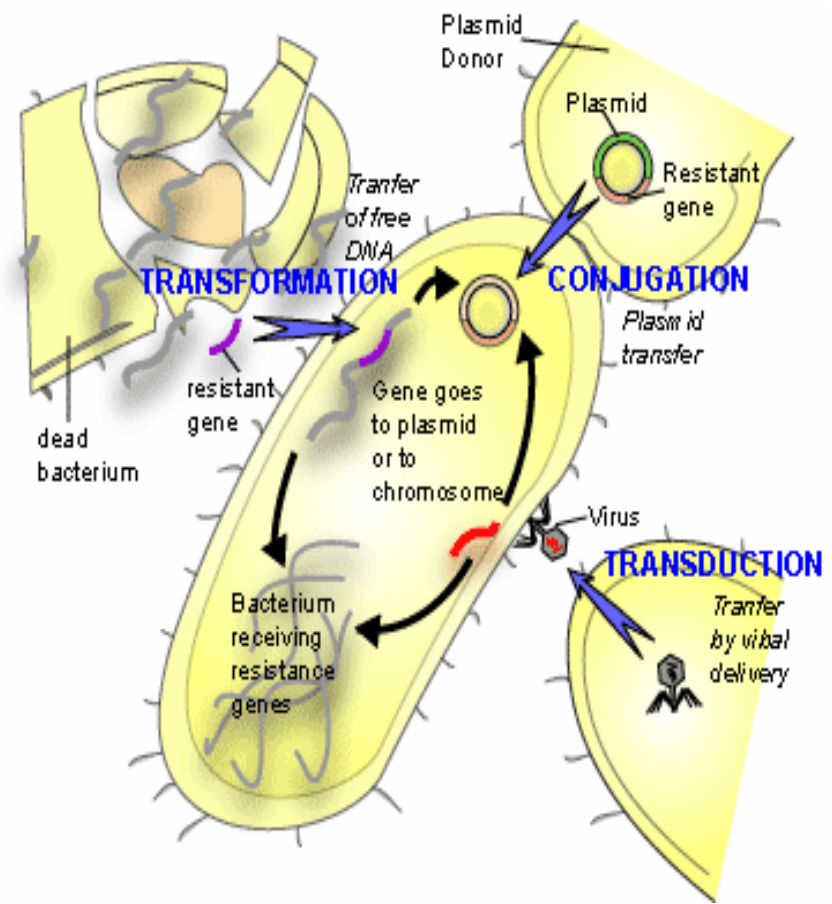
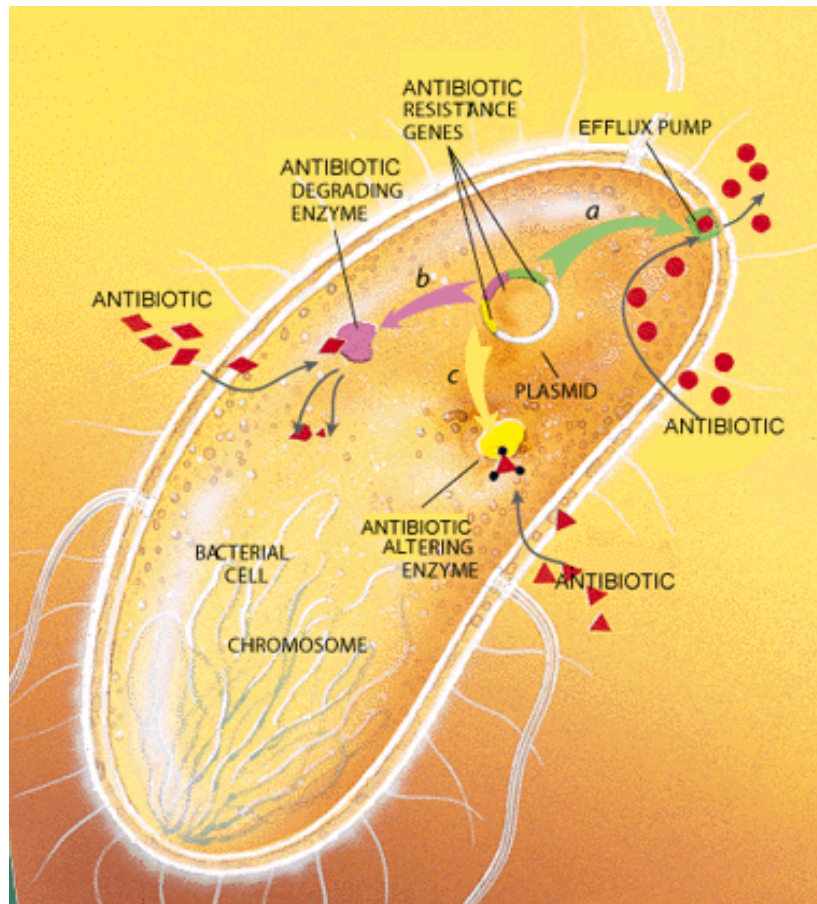
GSBL Salgılayan E.coli / K.pneumoniae Suşları-Türkiye



GSBL Oluşturan *E.coli* ve *K.pneumoniae* Suşları (Türkiye 2002-2005)

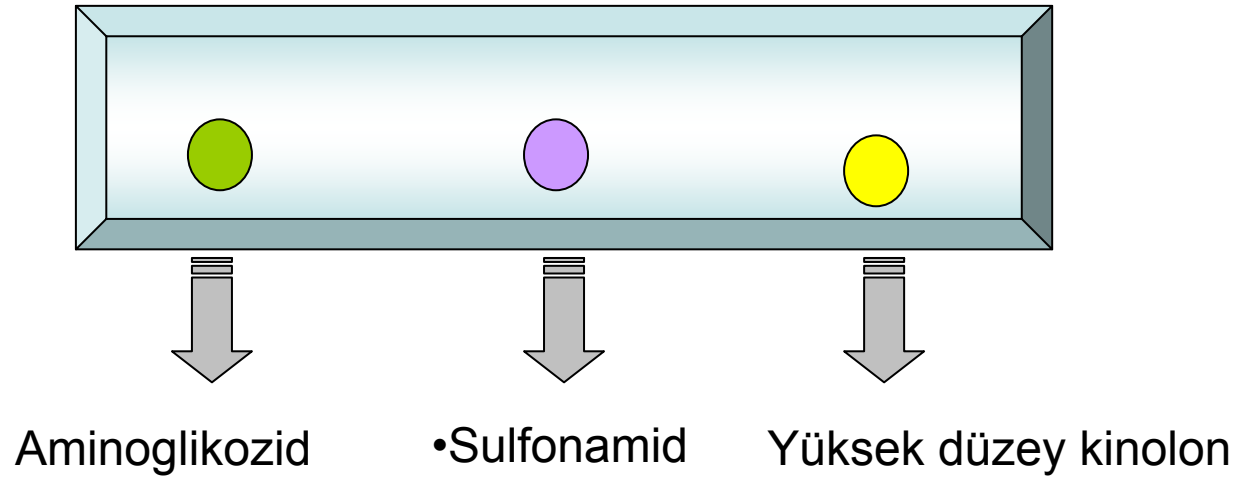
- Kandemir Ö ve ark. XIII. KLİMİK Kongresi, Antalya- 2007

Bakteriler	GSBL Direnci (%)	Direnç Aralığı (%)
<i>E. coli</i>	24.5	5-63
<i>K.pneumoniae</i>	37.8	7.6-72.2



GSBL ve Diğer Antibiyotik Dirençleri

Paterson DL, Am J Med, 2006; 119: 20-8

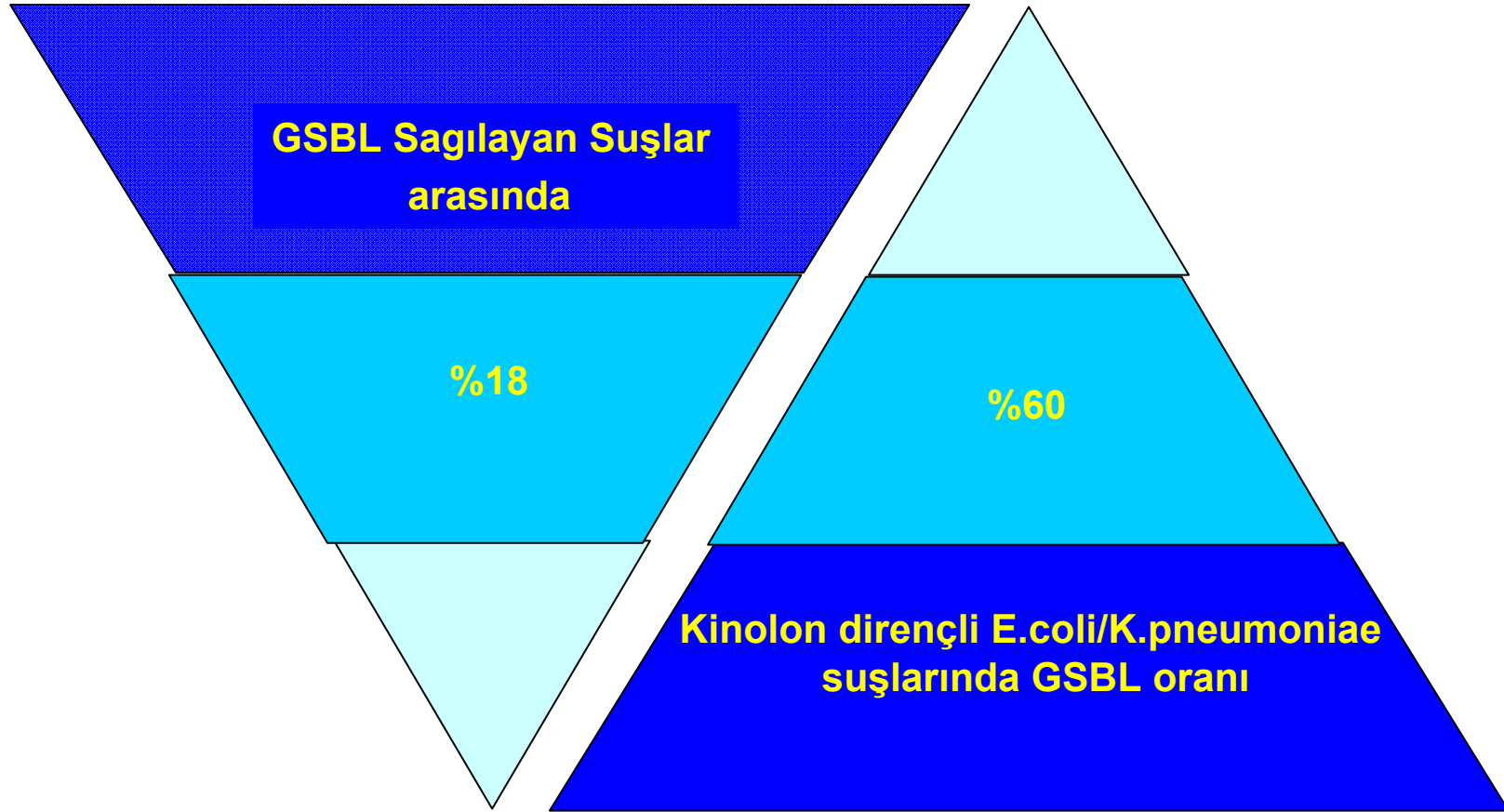


GSBL (+) E.coli/K.pneumoniae İnfeksiyonlarında Tedavi

- Kinolonlar
 - Paterson DL, et al. Clin Infect Dis, 2004; 39: 31-7
- TMP-SMX
- Aminoglikozidler
 - Paterson DL, Am J Med, 2006; 119: 20-8
- Sefepim
 - Zanetti G, et al. Antimicrob Agents Chemother, 2003; 47: 3442-7
- Beta laktam/Beta laktamaz
 - Martinez-Martinez L, et al. Antimicrob Agents Chemother. 1996; 40: 342-8

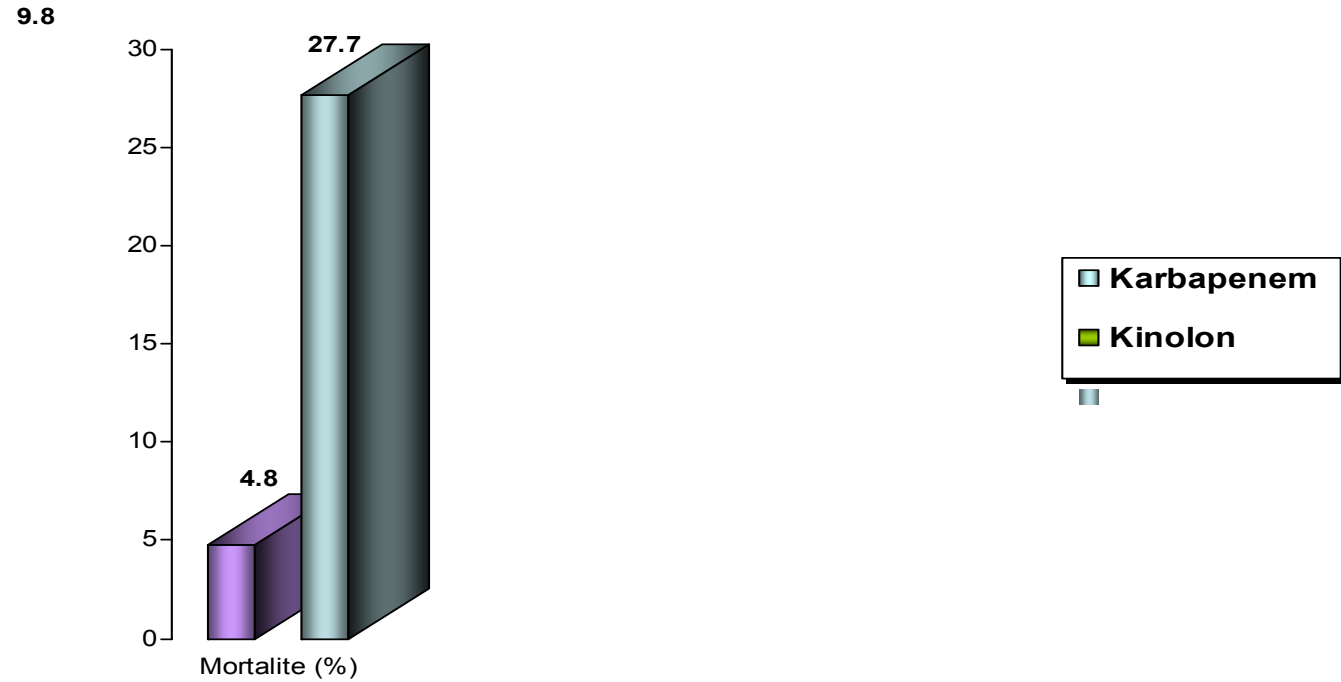
GSBL (+) E.coli/K.pneumoniae İnfeksiyonlarında Kinolon Direnci

7 Ülke ve 12 hastane kaynaklı çalışma



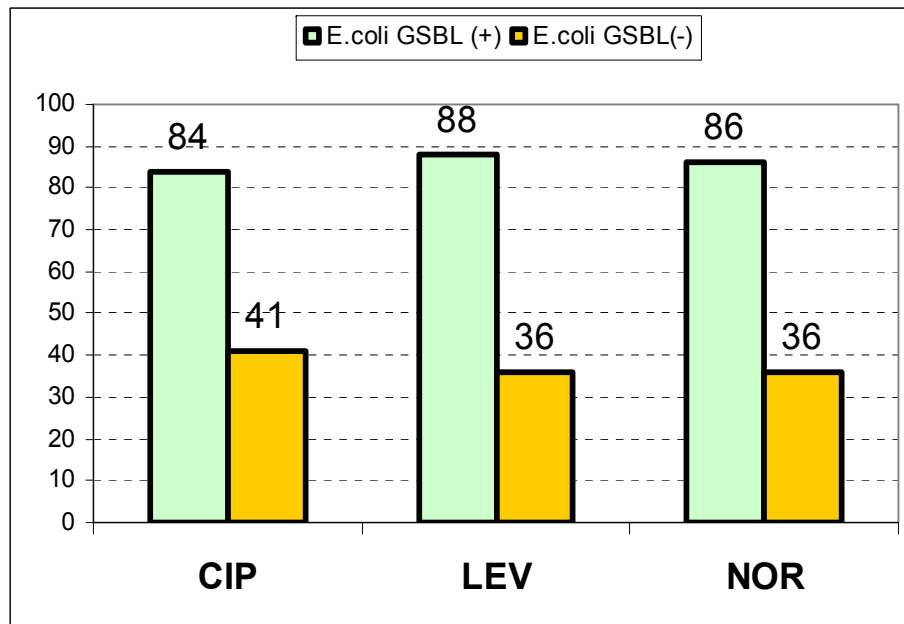
GSBL (+) *E.coli*/*K.pneumoniae* İnfeksiyonlarında Tedavi Yanıtları: KİNOLON

Paterson DL, et al. Clin Infect Dis, 2004; 39: 31-7



- GSBL (+) *K.pneumoniae* infeksiyonu: 14 günlük mortalite oranları:
 - Karbapenem (2/42)
 - Kinolon ya da beta laktam (8/29)

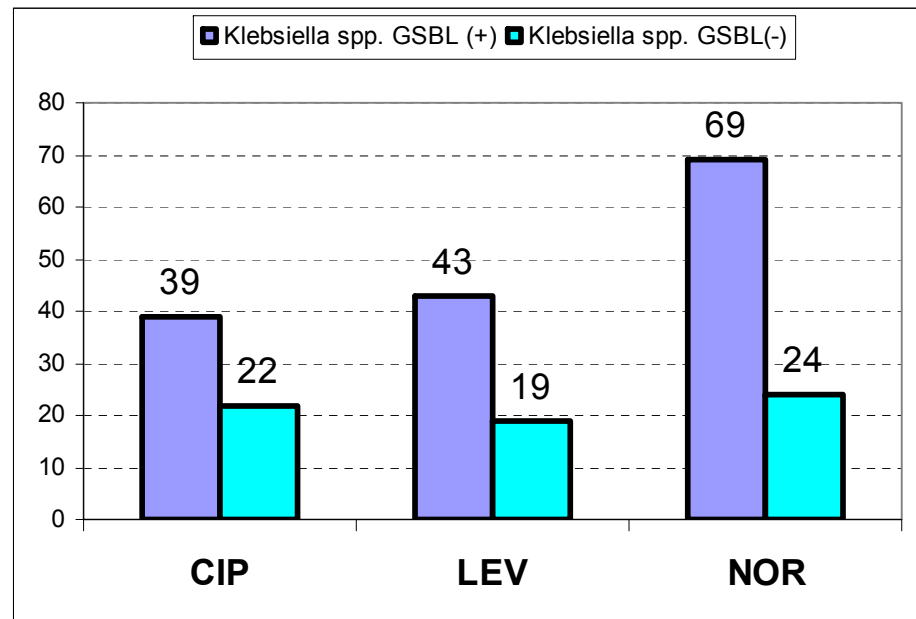
Kinolon Direncide Artış



$p < 0,0001$

$p < 0,0001$

$p < 0,0001$



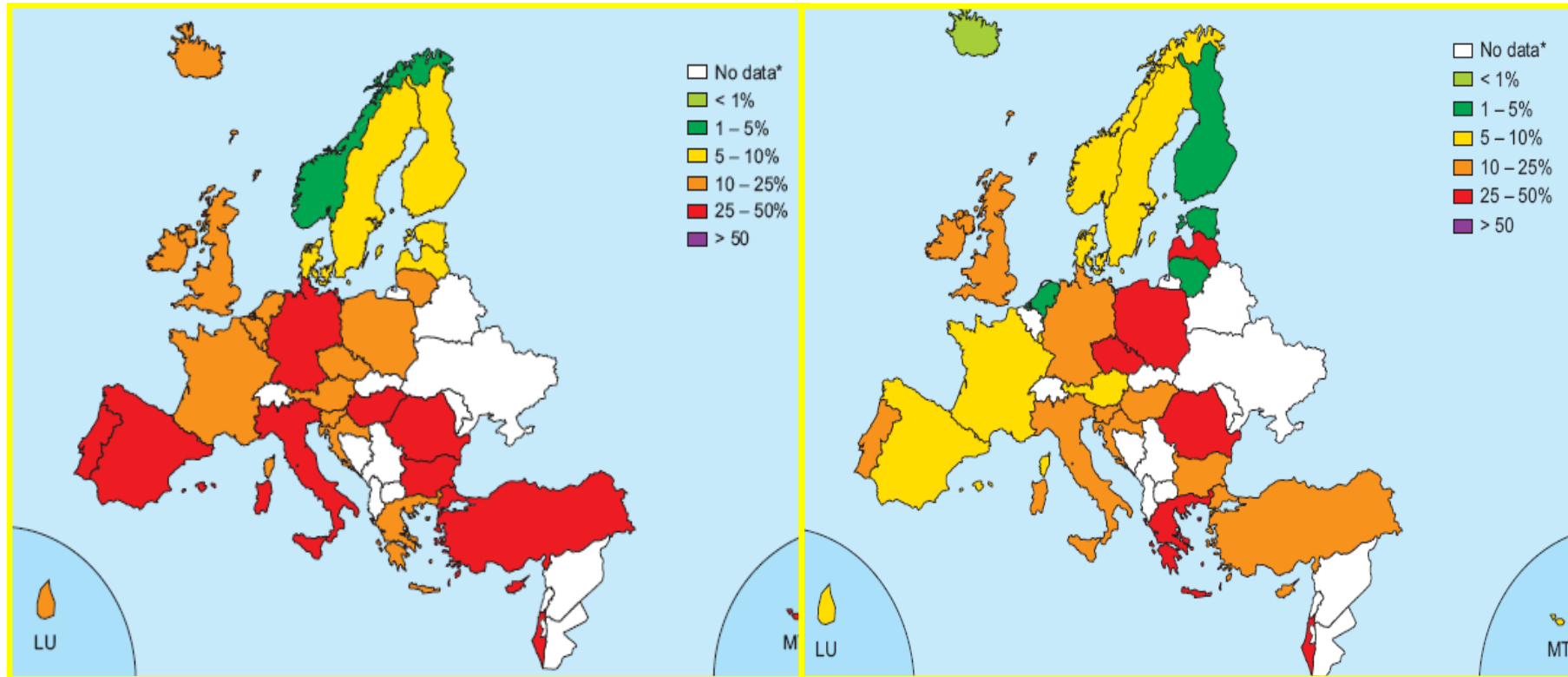
$p = 0,0447$

$p = 0,2651$

$p = 0,0006$

E.coli/K.pneumoniae Kinolon Direnci

EARs 2006



E.coli Kinolon Direnci

K. pneumoniae Kinolon Direnci

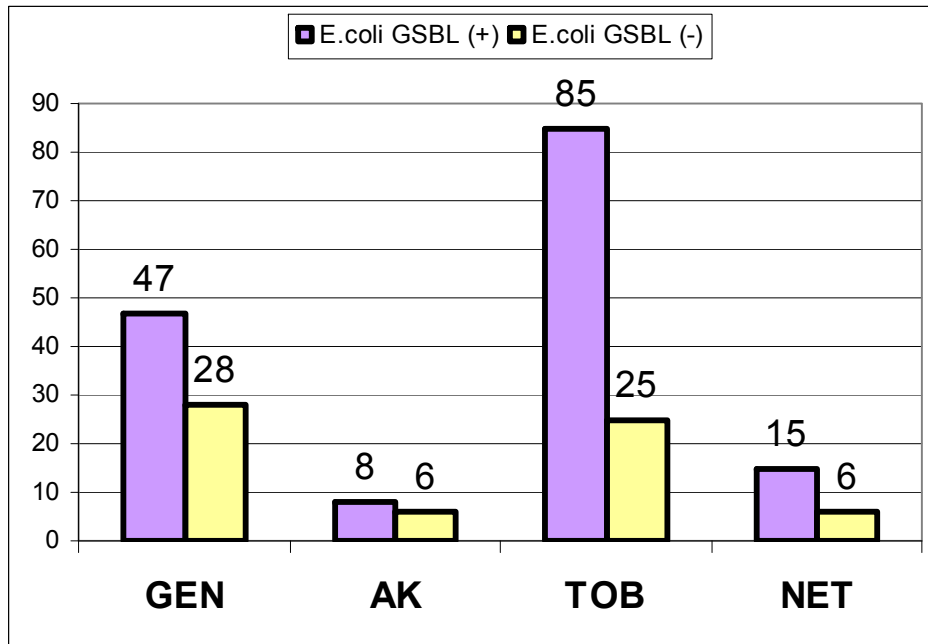
GSBL (+) *E.coli*/*K.pneumoniae* İnfeksiyonlarında Tedavi Yanıtları: SEFEPİM

İmipenem tedavisi alanların %100'ü, Sefepim tedavisi alanların %69'unda tedavi yanıtı alındı



Zanetti G, et al. Antimicrob Agents Chemother, 2003; 47: 3442-7

Aminoglikozid Direncinde Artış

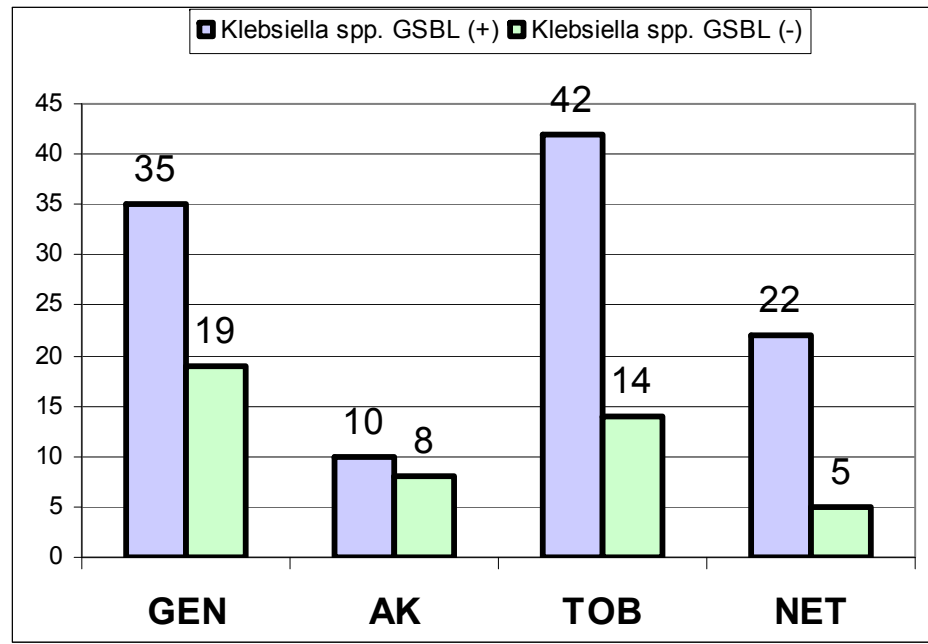


$p < 0,0001$

$p = 0,3379$

$p < 0,0001$

$P = 0,0004$



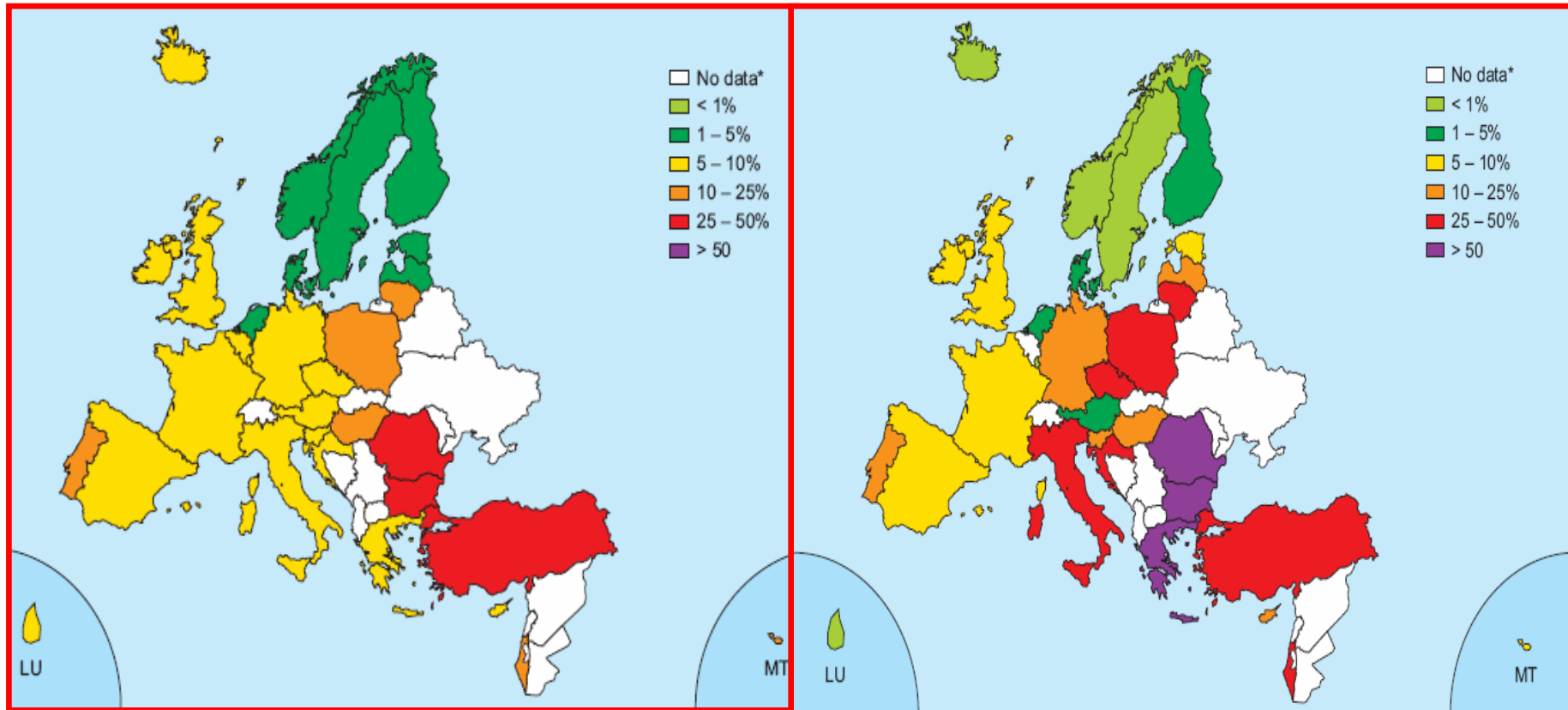
$p < 0,0447$

$p < 0,8947$

$p < 0,0013$

$p < 0,0046$

E.coli/K.pneumoniae AG Direnci EARS 2006



E.coli Aminoglikozid Direnci

K.pneumoniae Aminoglikozid Direnci

GSBL (+) Suşlarla Gelişen İnfeksiyonların Tedavi Yanıtları

Paterson DL, et al. J Clin Microbiol, 2001; 39: 2206-12

MIK ($\mu\text{g/mL}$)	Hasta, % (sayı)	
	SS Tedavi başarısızlığı	14 gün içinde bakteremi ile ölüm
8	100 (6/6)	33 (2/6)
4	67 (2/3)	0 (0/3)
2	33 (1/3)	0 (0/3)
≤ 1	27 (3/11)	18 (2/11)
Toplam	54 (15/28)	

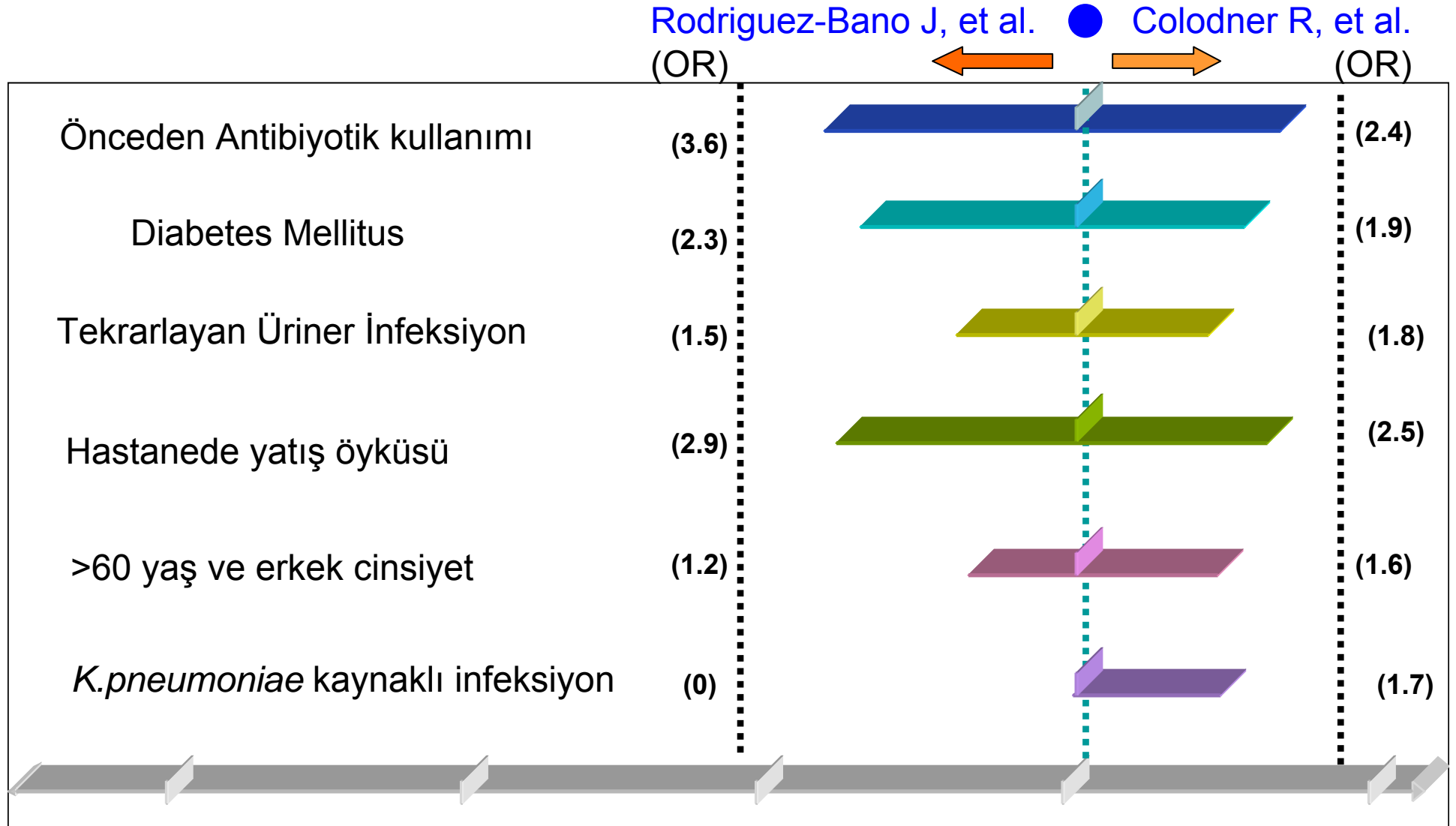
Toplum Kökenli GSBL Salgılayan *E.coli* / *K.pneumoniae* Suşları

- Sık üriner infeksiyon geçiren yaşlı bayan hastalar
- 65 yaş üstü prostat infeksiyonlu yaşlı erkekler
- CTX-M beta-laktamaz salgılayan *E.coli*
- Çoklu antibiyotik direnci fazla
 - Siprofloksasin
 - TMP / SMX
 - Gentamisin
 - Seftriakson
- Rodriguez Bano, JCM 2004

Toplum Kökenli GSBL Salgılayan *E.coli* / *K.pneumoniae* Suşları

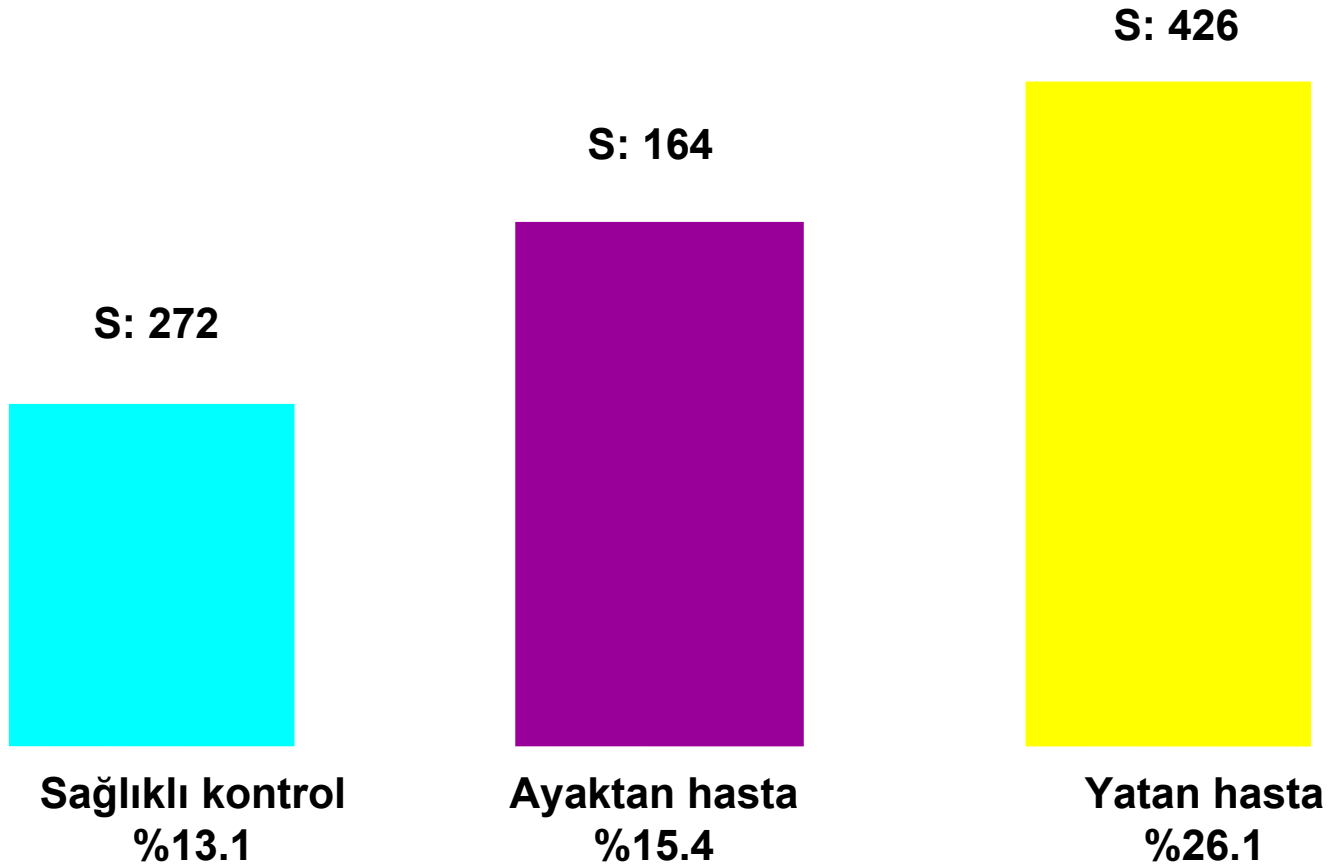
- Toplum kökenli *E.coli* suşlarında GSBL varlığı
 - İspanya
 - Rodriguez B, JCM 2004
 - İsrail
 - Pitout, CID 2004
 - İngiltere
 - Munday, JAC 2004
 - Kanada'dan bildirildi
 - Woodbord, JAC 2004

Toplum Kökenli GSBL Gelişiminde Risk Faktörleri



- Colodner R, et al. Eur J Clin Microiol Infect Dis. 2004; 23: 163-
- Rodriguez-Bano J, et al. J Clin Microbiol. 2004; 42: 1089-94

GSBL Üreten E.coli ve K.pneumonia suşlarının Fekal Taşıyıcılığı



GSBL ve Amp-C Dirençleri

	GSBL	Amp-C
• 3.Kuşak SS'e etkisi	+++	+++
• Sefoksitine etkisi	-	+++
• İmipeneme etkisi	-	-
• Klavulonata etkisi	-	+++
• Klebsiella'da bulunma	+++	+
• Enterobacter'de bulunma	+	+++

Kromozomal AmpC Beta-laktamazlar

- *Escherichia coli* ◆
- *Shigella* ◆
- *Enterobacter spp.* ●
- *C.freundii* ●
- *M.morganii* ●
- *Providencia spp.* ●
- *Serratia spp.* ●

İndüklenebilir AmpC ● Düşük düzeyde ◆

Plazmid Kaynaklı Amp C

- Çoğunlukla *Klebsiella*, *E.coli*, *Salmonella* ve *Proteus*..
- Biyokimyasal özellikler kromozomal AmpC ile aynı
- Epidemiyolojik olarak tehlike potansiyeli daha fazla
- GSBL ile mozaik direnç yapı oluşumu
- Penisilin, SS, monobaktam hidrolizi
- OMP geçirgenlik azalması ile karbapenem direnci

Rodriguez Bano, JCM 2004

Plazmid Kaynaklı AmpC Türleri

- MIR
- CMY (11)
- DHA (2)
- MOX (2)
- FOX (5)
- BIL
- LAT (4)
- ACC
- ACT...

K.pneumoniae Suşlarında Çoklu Antibiyotik Direnci

- ACT-1 a (Dış Membran protein kaybı) + Amp-C Beta-Laktamaz (Plazmid)
 - Patricia A, et al. *Antimicrob Agents Chemother*, 1997; 41: 561-9
- VIM-1 (MBL) aktiviteli IMP-dirençli *K.pneumoniae* suşu
 - Giaokoupi P, et al. *Journal Clin Microbiol*, 2003; 41: 3893-6
- Kmr-A geni (Çoklu direnç pompa sistemi)
 - Ogawa W, et al. *Biol Pharm Bull*, 2006; 29: 550-3
- VIM-1, SHV-5 (MBL) aktiviteli IMP-dirençli 8 *K.pneumoniae* salgını (Fransa)
 - Kassis-Chikhani N, et al. *JAC*, 2006; 57: 142-5

Imipenem Resistance in *Klebsiella pneumoniae* Is Associated with the Combination of ACT-1, a Plasmid-Mediated AmpC β -Lactamase, and the Loss of an Outer Membrane Protein

PATRICIA A. BRADFORD,^{1*} CARL URBAN,^{2,3} NORIEL MARIANO,² STEVEN J. PROJAN,¹
JAMES J. RAHAL,^{2,4} AND KAREN BUSH^{1†}

Wyeth-Ayerst Research, Pearl River, New York¹; The New York Hospital Medical Center of Queens, Flushing, New York²; and Departments of Microbiology³ and Medicine,⁴ Cornell University Medical College, New York, New York

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Six *Escherichia coli* and 12 *Klebsiella pneumoniae* isolates from a single hospital expressed a common β -lactamase with a pI of approximately 9.0 and were resistant to cefoxitin and cefotetan (MIC ranges, 64 to >128 and 16 to >128 μ g/ml, respectively). Seventeen of the 18 strains produced multiple β -lactamases. Most significantly, three *K. pneumoniae* strains were also resistant to imipenem (MICs, 8 to 32 μ g/ml). Spectrophotometric β -lactamase assays with purified enzyme indicated hydrolysis of cephamycins, in addition to cephaloridine and benzylpenicillin. The gene encoding the pI 9.0 β -lactamase (designated ACT-1 for AmpC type) was cloned and sequenced, which revealed an *ampC*-type β -lactamase gene that originated from *Enterobacter cloacae* and that had 86% sequence homology to the P99 β -lactamase and 94% homology to the partial sequence of MIR-1. Southern blotting revealed that the gene encoding ACT-1 was on a large plasmid in some of the *K. pneumoniae* strains as well as on the chromosomes of all of the strains, suggesting that the gene is located on an easily mobilized element. Outer membrane protein profiles of the *K. pneumoniae* strains revealed that the three imipenem-resistant strains were lacking a major outer membrane protein of approximately 42 kDa which was present in the imipenem-susceptible strains. ACT-1 is the first plasmid-mediated AmpC-type β -lactamase derived from *Enterobacter* which has been completely sequenced. This work demonstrates that in addition to resistance to cephamycins, imipenem resistance can occur in *K. pneumoniae* when a high level of the ACT-1 β -lactamase is produced in combination with the loss of a major outer membrane protein.

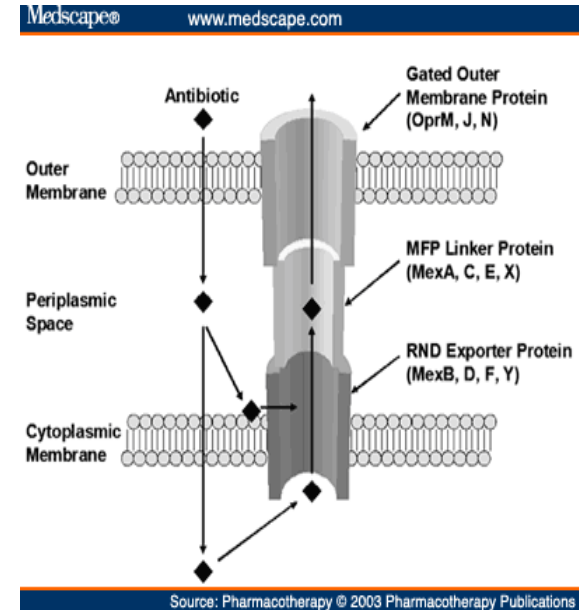


GSBL (+) E.coli/K.pneumoniae İnfeksiyonlarında Karbapenem Direnci

10 New York Hastanesi'nde izole edilen 96 izolatin %80'inde KPC enzim üreten *K.pneumoniae* izole edildi. Bu suşlar tek genotipik kaynaklıydı

- Dış membran porin kaybı (KPC-1, 2, 3)
- Sınıf B beta-laktamaz (MBL)

Bratu S, et al. J Antimicrobi Chemother, 2005; 56: 128-32



Detection and Prevalence of Active Drug Efflux Mechanism in Various Multidrug-Resistant *Klebsiella pneumoniae* Strains from Turkey

Ufuk Over Hasdemir,^{1,2} Jacqueline Chevalier,² Patrice Nordmann,³ and Jean-Marie Pagès^{2*}

Department of Microbiology, School of Medicine, Marmara University, Istanbul, Turkey,¹ and Enveloppe Bactérienne, Perméabilité et Antibiotiques, EA 2197, IFR48, Faculté de Médecine, Université de la Méditerranée, Marseille,² and Service de Bactériologie-Virologie, Hôpital de Bicêtre, Faculté de Médecine Paris Sud, Université Paris XI, Le Kremlin-Bicêtre,³ France

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The prevalence of active drug efflux pump and porin alterations was investigated in Turkish nosocomial strains of *Klebsiella pneumoniae* exhibiting a multidrug-resistant phenotype. MICs of various antibiotics, including quinolones, chloramphenicol, tetracycline, and β -lactams, for those strains were determined either with or without the efflux pump inhibitor phenylalanine arginine β -naphthylamide (PA β N). Thirty-nine percent of the strains exhibited a PA β N-modulated resistance for quinolones, chloramphenicol, and tetracycline. In these strains, a significant increase of chloramphenicol accumulation was gained in the presence of the efflux pump inhibitor PA β N or with the energy uncoupler carbonyl cyanide *m*-chlorophenylhydrazone. Moreover, high-level expression of the membrane fusion protein AcrA, which was immunodetected in most of those isolates, suggests that the AcrAB/TolC efflux machinery contributed to their antibiotic resistance. Studies of *K. pneumoniae* porins indicated that the majority of the strains, including extended-spectrum β -lactamase producers and efflux-positive ones, presented an alteration in their sorbitol-sensitive porin (OmpK35) expression. This is the first report showing the prominent role of active drug efflux in the antibiotic resistance of nosocomial *K. pneumoniae* strains from Turkey.

Characterization of a Large Outbreak by CTX-M-1-Producing *Klebsiella pneumoniae* and Mechanisms Leading to In Vivo Carbapenem Resistance Development

Ana Mena,¹ Virginia Plasencia,¹ Laura García,² Olga Hidalgo,³ José Ignacio Ayestarán,⁴
Sebastián Alberti,² Nuria Borrell,¹ José L. Pérez,¹ and Antonio Oliver^{1*}

*Servicio de Microbiología, Hospital Son Dureta and Instituto Universitario de Investigación en Ciencias de la Salud,¹ Área de
Microbiología and Instituto Universitario de Investigación en Ciencias de la Salud, Universidad de las Islas Baleares,²
Servicio de Medicina Preventiva, Hospital Son Dureta,³ and Servicio de Medicina Intensiva,
Hospital Son Dureta,⁴ Palma de Mallorca, Spain*

İspanya’da Karbapeneme dirençli CTX-M kökenli ilk *K.pneumoniae* suşu saptandı

2002-2005 yılları arasında

51 çoklu antibiyotik dirençli *K.pneumoniae*

2 suş karbapenem dirençli (MIK=8-32 mg/L) (Omp-K36)

Characterization of carbapenem-non-susceptible *Escherichia coli* isolates from a university hospital in Taiwan

Yi-Fang Liu^{1†}, Jing-Jou Yan^{2†}, Wen-Chien Ko³, Shu-Huei Tsai² and Jiunn-Jong Wu^{1,4*}

¹*Institute of Basic Medical Sciences, College of Medicine, National Cheng-Kung University, Tainan, Taiwan;*
²*Department of Pathology, College of Medicine, National Cheng-Kung University, Tainan, Taiwan;* ³*Department of Internal Medicine, College of Medicine, National Cheng-Kung University, Tainan, Taiwan;* ⁴*Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng-Kung University, Tainan, Taiwan*

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Objectives: To investigate characteristics of nine carbapenem-non-susceptible (CP-NS) *Escherichia coli* isolates collected between 1999 and 2005 at a Taiwanese university hospital.

Methods: Genetic relatedness was analysed by PFGE. β -Lactamases were characterized by PCR and isoelectric focusing. Outer membrane proteins and transcripts were investigated by SDS-PAGE and northern blotting. Cloning experiments were performed to investigate the role of membrane permeability in carbapenem non-susceptibility.

Results: The nine CP-NS isolates were found to produce the CMY-2 AmpC enzyme ($n = 8$), the CTX-M-14-type extended-spectrum β -lactamase (ESBL) ($n = 1$), the SHV-12 ESBL ($n = 1$) and the IMP-8-type metallo- β -lactamase ($n = 1$) alone or in combination. All CP-NS isolates revealed a decrease in the transcription and protein expression of *ompC*, and susceptibility to carbapenems was restored in one isolate by introducing the cloned *ompC* gene. PFGE revealed genetic diversity among the nine isolates. All patients with the CP-NS isolates had been treated with carbapenems (six patients) and/or extended-spectrum cephalosporins (five patients) before isolation.

Conclusions: Our study suggests that the decreased susceptibility to carbapenems in *E. coli* in the hospital might arise by the stepwise accumulations of multiple drug-resistance determinants in different clones.

Keywords: outer membrane proteins, *ompC*, β -lactamases

Carbapenem-non-susceptible *E. coli* in Taiwan

Table 1. Results of β -lactamase characterization and susceptibility testing

Isolate	PFGE type	β -Lactamase(s)	MIC (mg/L) ^a										<i>ompC</i> genotype
			GEN	AMK	CAZ	CTX	FEP	ATM	CIP	IPM	MEM	ETP	
784/99	I	TEM-1, CMY-2	256	8	256	>256	4	128	8	8	4	64	truncate form, EU372016
2272/02	NT ^c	CMY-2	64	2	256	256	4	128	0.5	8	1	32	truncate form, EU372007
464/03	II	TEM-1, CMY-2	256	16	>256	>256	>256	256	256	128	16	256	truncate form, EU372015
474-2/04	III	TEM-1, SHV-12, IMP-8	256	16	>256	>256	256	128	8	128	8	64	full length, EU372014
430/04	IV	TEM-1, CMY-2	256	16	>256	>256	32	>256	256	128	16	256	truncate form, EU372008
2881/04	V	TEM-1, CMY-2	256	4	>256	>256	32	128	256	32	8	128	truncate form, EU372009
983/05	VI	TEM-1, CMY-2, CTX-M-14	256	256	256	>256	32	128	>256	4	8	64	full length, EU372011
773-2/05	VII	TEM-1, CMY-2	256	0.5	>256	>256	32	256	1	128	16	256	full length ^d , EU372010
2837-1/05	VIII-1	TEM-1, CMY-2	256	4	>256	>256	32	256	>256	64	16	256	truncate form, EU372013
2837-2/05	VIII-2	TEM-1, CMY-2	256	1	>256	256	1	128	>256	0.5	0.25	8	full length, EU372012
2837-1/05 + <i>ompC</i> ^e			256	2	64	128	4	256	>256	0.5	0.25	4	
2837-1/05 + <i>ompF</i> ^f			64	2	>256	>256	16	128	>32	64	8	256	
2837-2/05 + <i>ompC</i> ^g			48	2	>256	256	3	128	>32	0.38	0.094	2	
2837-2/05 + <i>ompF</i> ^h			32	1.5	>256	>256	3	256	>32	0.38	0.19	16	

GSBL (+) E.coli/K.pneumoniae İnfeksiyonlarında GelineN Nokta..

- Toplum kökenli GSBL kökenlerinde artış
- Çoklu antibiyotik direnç gelişimi
- Yüksek mortalite, morbidite ve maliyet
- Tedavi seçeneklerinin azalması
- Salmonella, *Shigella spp.*, *V.cholerae* için kaynak
- Hemen her hastane için ciddi tehdit..

Korunma

- İdari önlemler..
- Eğitim
- El yıkama
- Sürveyansın sürdürülmesi
- Çevresel dekontaminasyon
- Akılcı antibiyotik kullanımı
- İzolasyon
- Bilgi işlem merkezi ile koordinasyon
- Enfeksiyon kontrol önlemleri

Nasıl Tedavi Edelim ?

- Üriner infeksiyonların uygun tedavisi
 - Nitrofrontain
 - Fosfomisin
- Temas izolasyonları
- GSBL taşıyıcılarının erken belirlenmesi
- İnfeksiyon Kontrol Önlemleri

- Teşekkürler..