II ESTUDIO ESPAÑOL DE COLONIZACIONES / INFECCIONES POR *ACINETOBACTER BAUMANNII.* EPIDEMIOLOGIA CLINICA Y MOLECULAR. Estudio GEIH-REIPI-Ab 2010.

GRUPO DE ESTUDIO DE INFECCION HOSPITALARIA (GEIH).

SOCIEDAD ESPAÑOLA DE ENFERMEDADES INFECCIOSAS Y MICROBIOLOGIA CLINICA (SEIMC).

RED ESPAÑOLA DE INVESTIGACIÓN EN PATOLOGIA INFECCIOSA (REIPI), INSTITUTO DE SALUD CARLOS III

CENTROS COORDINADORES DEL ESTUDIO

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1. OBJETIVOS.

1.1. Epidemiología clínica:

A. Evolución de la incidencia de colonizaciones e infecciones por *Acinetobacter baumannii* en hospitales españoles en una década (2000 vs. 2010).

- Incidencia por tipos de hospital
- Comparación con los datos de 2010

B. Conocer la distribución de aislamientos (colonizaciones e infecciones) de *A. baumannii* por áreas del hospital:

- Areas médicas, quirúrgicas y de alto riesgo
- Comparación de los datos respecto a 2000.

C. Evaluar la repercusión clínica de la colonización / infección por *A. baumannii*:

- Características predisponentes de los pacientes
- Colonizaciones e infecciones por tipos de muestra
- Tipos de infección y gravedad
- Impacto del tratamiento empírico y dirigido en la mortalidad
- Estancia hospitalaria
- Mortalidad cruda y relacionada con la infección
- Impacto del tratamiento en la evolución de los pacientes con cepas resistentes a carbapenemas
- Comparación de los datos con respecto a 2000
- Factores asociados a determinadas características microbiológicas de las cepas (resistencia a carbapenemas, cepas clonales, etc)

2. METODOLOGIA.

2.1. Epidemiología clínica:

A. Duración del estudio: 2 meses (1 de Febrero a 31 de marzo de 2010).

B. Diseño: estudio prospectivo de cohortes. Cada paciente será seguido desde su inclusión hasta el alta (ó hasta 30 días desde su inclusión, si el ingreso se prolonga más de ese tiempo) o fallecimiento (si este ocurre durante el ingreso).

C. Criterios de inclusión:
- Todos los pacientes (adultos y niños) con infección o colonización nueva por *A. baumannii*. Es decir, se incluirán todos los casos nuevos en que se aisle en cualquier muestra clínica este microorganismo durante el período de estudio, independientemente de la significación clínica de las mismas.

D. Criterios de exclusión
- Pacientes detectados como colonizados por *A. baumannii* exclusivamente a través de muestras de vigilancia activa (frotis cutáneos, rectales, etc), cultivos de vigilancia periódicos (p.e., no se seleccionarán los aislamientos procedentes de cultivos de broncoaspirados que se hagan a todos los pacientes con ventilación mecánica un día de cada semana de forma rutinaria o similar).
- Pacientes con aislamiento de *A. baumannii* en los 2 meses de estudio que ya hubiera tenido un cultivo positivo para este microorganismo en el año previo.

E. De cada hospital se recogerán los datos necesarios para el cálculo de las incidencias y características de los centros (anexo I). Además, de cada paciente incluido se recogerán los datos según protocolo adjunto (anexo II), en el que se incluyen:
- Identificación del paciente (codificada).
- Area de hospitalización.
- Datos demográficos.
- Enfermedades subyacentes y clasificación.
- Factores de riesgo para infecciones nosocomiales (endógenos y exógenos).
- Duración de la hospitalización previa al aislamiento.
- Colonización o infección.
- En caso de infección:
  - Tipo de infección
  - Sepsis, sepsis grave ó shock séptico.
  - Tratamiento antimicrobiano
- Estancia hospitalaria tras el episodio:
- Pronóstico (al alta o a los 30 días):
  - Muerte y muerte relacionada

Medicine

Epidemiological and clinical impact of Acinetobacter baumannii colonization and infection: a reappraisal.

--Manuscript Draft--

Manuscript Number:	MD-13-112R1

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and the GEIH/GEMARA/REIPI-Ab2010 Group.

Medicine

Epidemiological and clinical impact of Acinetobacter baumannii colonization and infection: a reappraisal.

--Manuscript Draft--

Manuscript Number:	MD-13-112R1

- **Objetivo**:
  - Investigar los cambios ocurridos en la epidemiología clínica y molecular de *A. baumannii* entre 2000 y 2010.
- **Método:**
  - Dos estudios prospectivos de cohortes incluyendo todos los pacientes con infección o colonización por *A. baumannii* de nuevo diagnóstico.
  - Aislamientos solo en muestras clínicas, no en estudios de portadores.
  - Exclusión de los pacientes con aislamiento de *A. baumannii* en el año previo.
  - Seguimiento durante 30 días.

Medicine

Epidemiological and clinical impact of Acinetobacter baumannii colonization and infection: a reappraisal.

--Manuscript Draft--

Manuscript Number:	MD-13-112R1

- **Variables:**
  - Edad, sexo, tipo de adquisición, área de admisión, enfermedades crónicas y gravedad de las mismas por la clasificación de McCabe, procedimientos invasivos, uso de antibióticos en los dos meses previos, diagnóstico de colonización o de infección, tipo de infección según criterios de los CDC, tratamiento de la infección, días de estancia antes y después del diagnóstico y mortalidad cruda a los 30 días.
- **Análisis estadístico:**
  - Doble:
    - De todos los hospitales.
    - Solo de los que participaron en ambos estudios.
  - Densidad de incidencia x 1000 pacientes día.

Medicine

Epidemiological and clinical impact of Acinetobacter baumannii colonization and infection: a reappraisal.

--Manuscript Draft--

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	2000	2010
Período estudio	noviembre	febrero y marzo
Nº hospitales	27	38
Nº hospitales > 500 camas	21	23
Nª hospitales que repiten	22	22
Nº pacientes	183	246

Incidencia

Table 1. Incidence density rate of colonization/infection due to *A. baumannii* in the whole set of centers.

	Cases/1,000 patient-days	2000[1]	2010
Global	Pooled	0.39	0.23
	Median (range)	0.22 (0–1.17)	0.39 (0–3.78)
Medical services	Pooled	0.14	0.52
	Median (range)	0 (1–0.73)	0 (0–1.53)
Surgical services	Pooled	0.22	0.05
	Median (range)	0 (0–0.94)	0 (0–1.43)
Intensive care units	Pooled	4.35	1.23
	Median (range)	1.96 (0–13.2)	0 (0–58.09)

[1]These data have been published previously (reference 25).

All comparisons between 2000 and 2010, $p<0.001$.

- 41%

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Factores predisponentes

	Whole set of centers			Hospitals participating in both studies		
Variable	**2000 (n=183)**	**2010 (n=246)**	**P**	**2000 (n=154)**	**2010 (n=143)**	**P**
Female gender	54 (29.5)	85 (34.6)	0.2	46 (29.9)	48 (33.6)	0.5
Median age (IQR), years	63 (44–70)	63 (52–75)	0.1	62 (43–70)	65 (53–75)	0.005
Type of service of admission			<0.001			0.002
Medical service	30 (16.4)	76 (30.9)		24 (15.6)	37 (25.6)	
Surgical service	50 (27.3)	52 (21.1)		44 (28.6)	29 (20.3)	
Intensive care unit	103 (56.3)	108 (43.9)		86 (55.8)	69 (48.3)	
Not-admitted	0	10 (4.1)		0	8 (5.6)	
McCabe classification:			<0.001			<0.001
Non-fatal	142 (77.6)	121 (49.2)		121 (78.6)	67 (46.9)	
Ultimately fatal	37 (20.2)	106 (43.1)		32 (20.8)	64 (44.8)	
Rapidly fatal	4 (2.2)	19 (7.7)		1 (0.6)	12 (8.4)	
Non-nosocomial acquisition[1]	3 (1.6)	35 (14.2)	<0.001	3 (1.9)	18 (12.6)	<0.001

Factores predisponentes

	Whole set of centers			Hospitals participating in both studies		
Variable	**2000 (n=183)**	**2010 (n=246)**	**P**	**2000 (n=154)**	**2010 (n=143)**	**P**
Diabetes mellitus	30 (16.4)	55 (22.4)	0.1	26 (16.9)	30 (21.0)	0.3
Chronic pulmonary disease	27 (14.8)	35 (14.2)	0.8	21 (13.6)	18 (12.6)	0.7
Liver cirrhosis	8 (4.4)	18 (7.3)	0.2	7 (4.5)	10 (7)	0.3
Cancer	35 (19.1)	32 (13)	0.08	33 (21.4)	23 (16.1)	0.3
Hemodialysis	9 (4.9)	10 (4.1)	0.6	5 (3.2)	3 (2.1)	0.7
Organ transplant recipient	4 (2.2)	5 (2)	0.5	4 (2.6)	2 (1.4)	0.5
Central venous catheter	133 (72.7)	130 (52.8)	<0.001	106 (68.8)	81 (56.6)	0.03
Urinary catheter	143 (78.1)	146 (59.3)	<0.001	124 (80.5)	90 (62.9)	0.001
Mechanical ventilation	103 (56.3)	93 (37.8)	<0.001	86 (55.8)	55 (38.5)	0.003
Surgery	94 (51.4)	66 (26.8)	<0.001	83 (53.9)	45 (31.5)	<0.001
CSF drainage system	13 (7.1)	2 (0.8)	<0.001	10 (6.5)	0	0.002
Prior antibiotic use	147 (80.3)	205 (83.3)	0.4	122 (79.2)	116 (81.1)	0.6
Amoxicillin/clavulanate	39 (21.3)	46 (18.7)	0.5	38 (24.7)	30 (21)	0.4
Piperacillin/tazobactam	26 (14.2)	53 (21.5)	0.05	25 (16.2)	31 (21.7)	0.2
Cephalosporins	71 (38.8)	39 (15.9)	<0.001	59 (38.3)	20 (14)	<0.001
Carbapenems	30 (16.4)	71 (28.9)	0.003	26 (16.9)	39 (27.3)	0.03
Fluoroquinolones	30 (16.4)	66 (26.8)	0.01	29 (18.8)	35 (24.5)	0.2
Aminoglycosides	57 (31.1)	27 (11)	<0.001	48 (31.2)	12 (8.4)	<0.001

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Factores predisponentes independientes

	Whole set of centers		Hospitals participating in both studies	
Variable	OR (95%CI)	P	OR (95%CI)	P
Fatal underlying disease	3.64 (2.25–5.96)	<0.001	4.19 (2.33–7.54)	<0.001
Urinary catheter	0.52 (0.31–0.86)	0.01	0.46 (0.22–0.80)	0.009
Surgical procedure	0.40 (0.25–0.64)	<0.001	0.36 (0.20–0.64)	0.001
Piperacillin/tazobactam	2.45 (1.33–4.49)	0.004	2.12 (1.02–4.38)	0.04
Carbapenems	2.79 (1.56–4.99)	0.001	3.25 (1.53–6.92)	0.002
Cephalosporins	0.50 (0.29–0.86)	0.01	0.37 (0.18–0.73)	0.004
Aminoglycosides	0.36 (0.09–0.66)	0.001	0.26 (0.11–0.62)	0.002
Length of previous hospital stay	0.99 (0.98–1.00)	0.3	0.99 (0.98–1.01)	0.8
Non-ICU Ward	1.61 (0.97–2.66)	0.06	1.08 (0.58–2.01)	0.7

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Características clínicas

	Whole set of centers			Hospitals participating in both studies		
	2000 (n=102)	2010 (n=151)	P	2000 (n=85)	2010 (n=91)	P
Infection site:						
Pneumonia	38 (37.3)	58 (38.4)	0.8	31 (36.5)	29 (31.9)	0.5
Tracheobronchitis	16 (15.7)	15 (9.9)	0.1	10 (11.8)	10 (11)	0.8
Skin and skin structure	23 (22.5)	31 (20.5)	0.7	22 (25.9)	20 (22)	0.5
Urinary tract	10 (9.8)	15 (9.9)	0.9	9 (10.6)	7 (7.7)	0.5
Primary bacteremia	4 (3.9)	7 (4.6)	0.7	2 (3.5)	6 (6.6)	0.4
Catheter-related	5 (4.9)	3 (2)	0.1	5 (5.9)	3 (3.3)	0.4
Intra-abdominal	2 (2)	15 (9.9)	0.01	2 (2.4)	11 (12.1)	0.01
Meningitis/ventriculitis	4 (3.9)	0	0.02	2 (2.5)	0	0.2
Others	0	7 (4.6)	0.04	2 (2.3)	5 (5.4)	0.4
Definitive treatment:						
Carbapenems	46 (45)	35 (23.2)	<0.001	40 (47.1)	28 (30.8)	0.02
Colistin	15 (14.7)	76 (50.3)	<0.001	12 (14.1)	43 (47.3)	<0.001
Aminoglycosides	35 (34.3)	24 (15.9)	0.001	30 (35.3)	12 (13.2)	0.001
Sulbactam	0	5 (3.3)	0.08	0	5 (5.5)	0.06
Tigecycline*	-	31 (20.5)	-	-	14 (15.4)	-
Rifampin	0	8 (5.3)	0.02	0	6 (6.6)	0.02
Mortality	29 (28.4)	33 (21.9)	0.2	24 (28.2)	21 (23.1)	0.4
Median hospital stay after infection (IQR), days	22 (8–30)	21 (10–31)	0.2	23 (8–30)	21 (11–30)	0.1

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Factores predisponentes clones ST2, ST79 y esporádicos

	ST2 isolates (n=149)	ST79 isolates (n=26)	Sporadic isolates (n=46)
Predisposing factors			
Median age (IQR)	64 (48–73)	69 (59–72)	63 (44–71)
Female gender	46 (30.9)	9 (34.6)	11 (23.9)
Non-ICU admission	63 (42.3)[3]	17 (65.4)	30 (65.2)
Fatal underlying condition	66 (44.3)[1]	10 (38.5)	13 (28.3)
Central venous catheter	104 (69.8)[2]	11 (42.3)	21 (45.7)
Urinary catheter	117 (78.5)[4]	13 (50)	23 (50)
Mechanical ventilation	76 (51)[2]	9 (34.6)	14 (30.4)
Prior fluoroquinolones	40 (26.8)[2]	4 (15.4)	5 (10.9)
Prior cephalosporins	37 (24.8)	4 (15.4)[1]	16 (34.8)
Prior carbapenems	38 (25.5)	2 (7.7)[1]	11 (23.9)
Prior aminoglycosides	28 (18.8)	5 (19.2)	10 (21.7)

*Only patients with infection were considered. P values: [1]0.05–0.09; [2]0.04–0.01; [3]0.009–0.001; [4]<0.001. All others, ≥0.05.

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Factores predisponentes independientes para los clones ST2, ST79

	Adjusted OR (95% CI)	P
ST2:		
Central venous catheter	2.42 (10.3–5.68)	0.04
Prior fluoroquinolone use	4.27 (1.48–12.29)	0.007
Prior cephalosporin use	0.42 (0.19–0.93)	0.03
ICU admission	1.87 (0.79–4.41)	0.1
ST79:		
Prior cephalosporin use	0.30 (0.08–1.07)	0.06
Prior carbapenem use	0.22 (0.04–1.16)	0.07
ICU admission	1.24 (0.42–3.66)	0.6

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Características clínicas clones ST2, ST79 y esporádicos

	ST2 isolates (n=149)	ST79 isolates (n=26)	Sporadic isolates (n=46)
Clinical features and outcome			
Infection	86 (57.7)	16 (61.5)	31 (67.4)
Pneumonia*	31 (36)[2]	4 (25)	5 (16.1)
Tracheobronchitis*	6 (7)[3]	1 (6.3)	8 (25.8)
Skin and skin structures*	23 (26.7)	3 (18.8)	10 (32.3)
Urinary tract*	8 (9.3)	3 (18.8)	2 (6.5)
Others*	18 (20.9)	5 (31.2)	6 (19.3)
Sepsis criteria*	79 (91.9)[4]	13 (81.3)	20 (64.5)
Severe sepsis/septic shock	38 (44.2)[2]	4 (25)	7 (22.6)
Mortality*	26 (30.2)	1 (6.3)	6 (16.1)

ST: sequence types. IQR: interquartile range. ICU: Intensive care unit.

*Only patients with infection were considered. P values: [1]0.05–0.09; [2]0.04–0.01; [3]0.009–0.001; [4]<0.001. All others, ≥0.05.

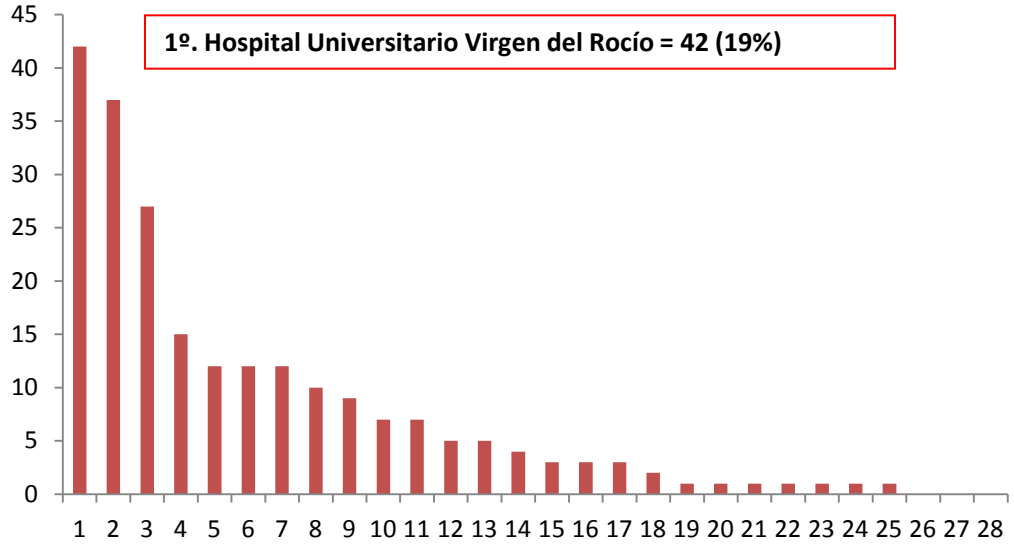
Conclusiones

"Some significant changes were noted in the epidemiology of *A. baumannii,* which is increasingly affecting patients admitted to conventional wards and is also the cause of non-nosocomial healthcare-associated infections. Epidemic clones seem to combine antimicrobial resistance and the ability to spread, while maintaining their clinical virulence".

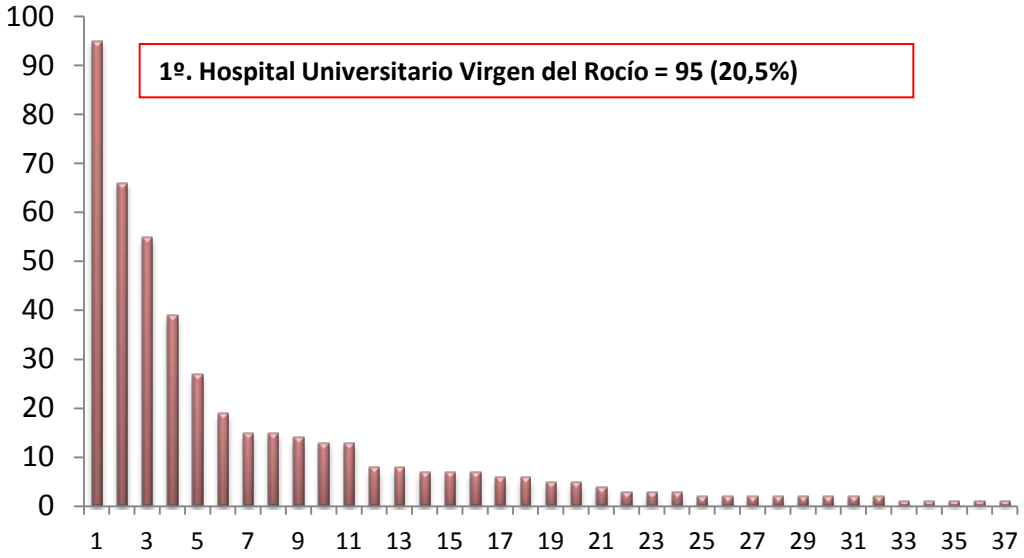
- La densidad de incidencia se ha reducido en un 41%

Incidencia nacional *A. baumannii*

2000



2010



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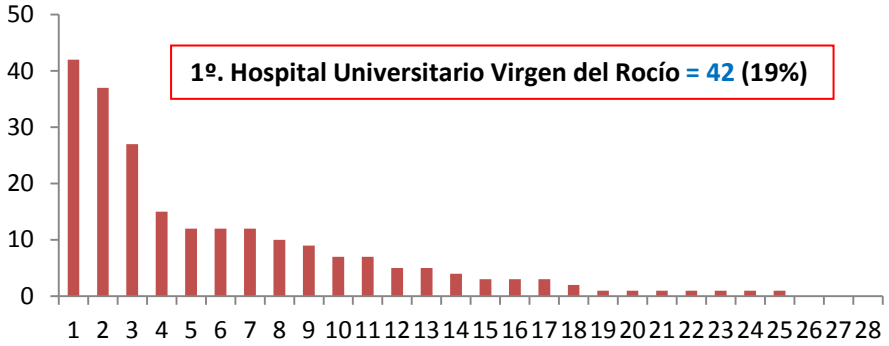
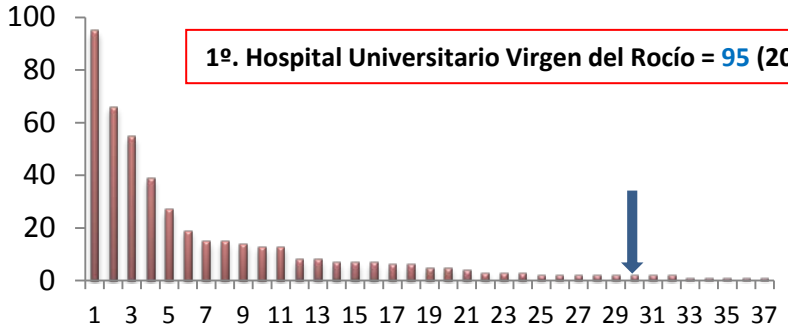
Incidencia nacional *A. baumannii*

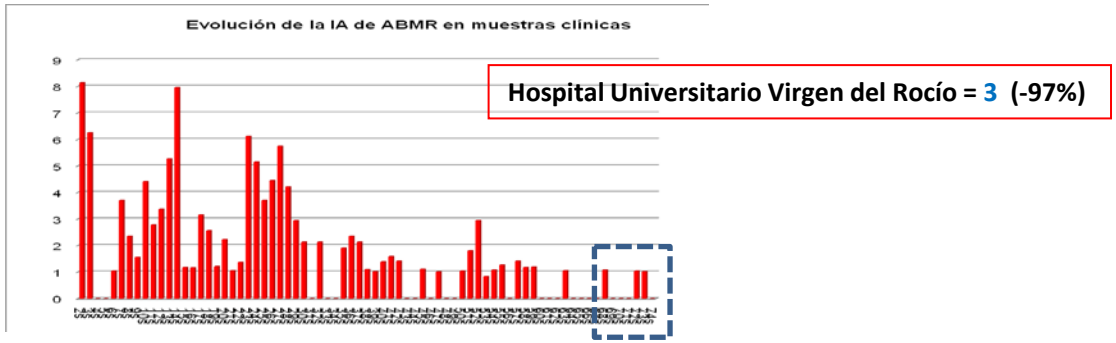
2000



2010



2014



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Monotherapy versus combination therapy for sepsis due to multidrug-resistant *Acinetobacter baumannii*: analysis of a multicentre prospective cohort.

Authors: Luis Eduardo López-Cortés[1], José Miguel Cisneros[1,2], Felipe Fernández-Cuenca[1], Germán Bou[3], María Tomás[3], José Garnacho-Montero[2,4], Alvaro Pascual[1,8], Luis Martínez-Martínez[5,6], Jordi Vila[7], Jerónimo Pachón[1,2,9], Jesús Rodríguez Baño[1,9], and the GEIH/REIPI-Ab2010 Group*.

Monotherapy versus combination therapy for sepsis due to multidrug-resistant *Acinetobacter baumannii*: analysis of a multicentre prospective cohort

- **Background:**
  - Treatment of multidrug-resistant *Acinetobacter baumannii* (MDRAB) infection presents a challenge because of the scarcity of available options.
  - Even though combination therapy (CT) is frequently used in clinical practice, data are needed to support its use instead of monotherapy (MT).
- **Methods:**
  - Prospective observational study was conducted in 28 hospitals.
  - Patients with sepsis caused by MDRA, defined according to strict criteria, and who received active antibiotic treatment (according to in vitro susceptibility testing) for at least 48 hours, were included.
  - The main outcome variable was all-cause 30-day mortality after initiation of targeted therapy.
  - Multivariate analysis, including a propensity score (PS for receiving CT, was performed by Cox regression.

Monotherapy versus combination therapy for sepsis due to multidrug-resistant *Acinetobacter baumannii*: analysis of a multicentre prospective cohort

- **Variables and definitions**
  - The main outcome variable was all-cause 30-day mortality after the initiation of targeted therapy.
  - As a secondary endpoint, all-cause 14-day mortality.
  - Therapy with a single antimicrobial agent active in vitro was considered to be MT,
  - Therapy with two or more active drugs was CT.
    - any bitherapy which included a carbapenem that was not active in vitro was considered as MT when the carbapenem MIC was ≥32 mg/L, and as CT when it was lower.
  - For patients whose targeted therapy changed during the course of treatment, we considered only the regimen that was used for at least 50% of the overall treatment duration (preferably the first one after receiving the microbiological data).

Factores predisponentes

Variable	All patients (n=101)	MT (n=68)	CT (n=33)	P value
Age in years, median (IQR)	60 (52-75)	60 (49-74)	61 (64-77)	0.41
Female gender	38 (37.6)	24 (35.3)	14 (42.4)	0.49
Comorbidities:				
Diabetes mellitus	20 (19.8)	11 (16.2)	9 (27.3)	0.19
Chronic pulmonary disease	14 (13.9)	8 (11.8)	6 (18.2)	0.38
Chronic liver disease	6 (5.9)	4 (5.9)	2 (6.1)	0.97
Malignancy	16 (15.8)	15 (22.1)	1 (3)	0.01
Dialysis treatment	3 (3)	1 (1.5)	2 (6.1)	0.20
Immunodeficiency	22 (21.8)	17 (25)	5 (15.2)	0.26
Age-weighted Charlson comorbidity index, median (IQR)	3 (2-6)	3 (2-7)	3 (2-6)	0.45
Pitt score, median (IQR)	4 (1-6)	4 (1-6)	4 (0-6)	0.68
Present ICU admission	63 (62.4)	43 (63.2)	20 (60.6)	0.80
Predisposing factors:				
Mechanical ventilation	49 (48.5)	32 (47.1)	17 (51.5)	0.67
Central venous catheter	72 (71.3)	49 (72.3)	23 (69.7)	0.81
Major surgery	33 (32.7)	23 (33.8)	10 (30.3)	0.72
Previous antibiotic treatment	87 (68.1)	57 (83.8)	30 (90.9)	0.33
Severe sepsis or septic shock	42 (41.6)	30 (44.1)	12 (36.4)	0.46
Hospital-acquired	91 (90.1)	62 (91.2)	29 (87.9)	0.60
Previous hospital stay, median (IQR)	12 (7-21)	12 (6-23)	11 (7-19)	0.47

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Características clínicas

Variable	All patients (n=101)	MT (n=68)	CT (n=33)	P value
Source of infection:				
Upper respiratory tract	10 (9.9)	7 (10.3)	3 (9.1)	0.85
Lower respiratory tract	51 (50.5)	33 (48.5)	18 (54.5)	0.57
Skin and soft tissue	13 (12.9)	8 (11.8)	4 (12.1)	0.96
Urinary tract	10 (9.9)	9 (13.2)	1 (3)	0.11
Intra-abdominal	8 (7.9)	6 (8.8)	2 (6.1)	0.63
Others*	18 (17.2)	11 (16.2)	7 (21.2)	0.54
Ventilator associated pneumonia	35 (34.7)	21 (30.9)	14 (42.4)	0.25
Polymicrobial infection	44 (43.6)	30 (44.1)	14 (42.4)	0.87
Bacteraemia	42 (41.6)	24 (35.3)	18 (54.5)	0.07
Susceptibility profile:				
MDR	101(100)	68 (100)	33 (100)	1.0
XDR	5 (4.9)	3 (4.4)	2 (6.0)	0.73
Carbapenem-resistant	64 (64)	44 (64.7)	20 (62.5)	0.83
Susceptible only to COL and TIG	21 (20.8)	17 (25)	4 (12.5)	0.14
Susceptible only to COL	5 (5)	3 (4.4)	2 (6.1)	0.72
Inadequate empirical treatment	53 (52.5)	35 (51.5)	18 (54.5)	0.77

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Table 2. Targeted antibiotic regimens used for the treatment of multidrug-resistant *A. baumannii*.

Targeted treatment	Number of patients (%)
Monotherapy	N=68
Colistin	46 (67.6)
Carbapenem	10 (14.7)
Tigecycline	5 (7.4)
Sulbactam	5 (7.4)
Tetracycline	2 (2.9)
Combination therapy	N=33
Colistin + tigecycline	9 (27.3)
Carbapenem + tigecycline	4 (12.1)
Colistin + carbapenem	3 (9.1)
Colistin + sulbactam	2 (6.1)
Colistin + aminoglycoside	2 (6.1)
Colistin + rifampin	2 (6.1)
Carbapenem + aminoglycoside	2 (6.1)
Tigecycline + rifampin	2 (6.1)
Tigecycline + aminoglycoside	1 (3)
Colistin + tigecycline + carbapenem + aminoglycoside	3 (9.1)
Colistin+ tigecycline + aminoglycoside	2 (6.1)
Tigecycline + carbapenem + rifampin	1 (3)

70%

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Table 3. Univariate analysis of variables associated with 30-day mortality.

Variable		Deaths/number exposed (percentage)	RR (95% CI)	P-value
Age-weighted Charslon comorbidity index	< 5 ≥ 5	9 (14.5) 15 (38.5)	Ref. 2.64 (1.29-5.46)	0.006
Type of infection	Urinary tract Upper respiratory tract Lower respiratory tract Skin and soft tissue Abdominal	0 4 (40) 14 (27.5) 3 (25) 2 (25)	Ref. 4 (0.53-29.80) 2.74 (0.40-18.57) 2.5 (0.30-20.45) 2.5 (0.27-22.86)	0.30 0.43 0.59 0.56
Bacteraemia	No Yes	13 (22) 11 (26.2)	Ref. 1.18 (0.59-2.39)	0.63
Type of infection according to mortality risk*	Low-risk High-risk	7 (19.4) 17 (26.2)	Ref. 1.34 (0.62-2.94)	0.45
Pitt score	< 3 ≥ 3	5 (11.6) 19 (32.8)	Ref. 2.81 (1.14-6.94)	0.01
Present ICU admission	No Yes	7 (18.4) 17 (27)	Ref. 1.46 (0.67-3.20)	0.33
Polymicrobial infection	No Yes	11 (19.3) 13 (29.5)	Ref. 1.53 (0.76-3.08)	0.23
XDR *A. baumannii*	No Yes	23 (24) 1 (20)	1.19 (0.20-7.17) Ref.	0.66
Empirical treatment	Inappropriate Appropriate	8 (15.1) 16 (33.3)	Ref. 2.20 (1.03-4.69)	0.03
Targeted treatment	Monotherapy Combination therapy	16 (23.5) 8 (24.2)	Ref. 1.03 (0.49-2.16)	0.94

*High-risk types of infection included pneumonia, intra-abdominal infection and any bacteraemic infection.

Tabla 4. Multivariate Cox regression models for the impact of combination therapy on 30-day mortality. The propensity score for combination treatment was included in the models.

	HR (95% CI)	P value
Model 1		
Combination treatment	1.35 (0.53 - 3.44)	0.53
Age-weighted Charslon comorbidity index (per unit)	1.19 (1.04 - 1.47)	0.09
Appropriate empirical treatment	0.55 (0.23 - 1.33)	0.19
Pitt score (per unit)	1.15 (1.02 - 1.29)	0.02
Model 2		
Combination treatment	1.26 (0.51 - 3.01)	0.62
High-risk source*	1.70 (0.58 - 4.97)	0.33
Appropriate empirical treatment	0.46 (0.18 - 1.21)	0.12
Pitt score (per unit)	1.20 (1.06 - 1.35)	0.004

*High-risk source: pneumonia, bacteraemia, intra-abdominal infection.

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Conclusion: Our data do not support that CT is associated with reduced mortality in MDRAB infections. More data for specific types of infection and combinations are needed.