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ORIGINAL ARTICLE

Perceived differences between intensivists and infectious diseases consultants facing antimicrobial resistance: a global cross-sectional survey

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Abstract

To identify differences in perception on multi-drug-resistant (MDR) organisms and their management at intensive care units (ICU). A cross-sectional survey was conducted. A proposal addressing a pathogen priority list (PPL) for ICU, arising from the TOTEM study, was compared with a sample of global experts in infections in critically ill patients. The survey was responded by 129 experts. Globally, ESBL Enterobacteriaceae, followed by carbapenem-resistant *Acinetobacter baumannii* and carbapenem-resistant Klebsiella *pneumoniae*, were the main concerns. Some differences in opinion were identified between 63 (49%) ICU physicians (ICU/anesthesiology) and 43 (33%) infectious disease consultants (ID physicians/microbiologists). The pathogens most concerning in the ICU for intensivists were ESBL Enterobacteriaceae (38%) versus carbapenem-resistant *A. baumannii* (48.3%) for ID consultants, ($p < 0.05$). Increasing number of ID consultants over intensivists (26% vs 14%) reported difficulty in choosing initial therapy for carbapenem-resistant *A. baumannii.* For intensivists, the urgent measures to limit development of antibiotic resistance were headed by cohort measures (26.3%) versus increasing nurse/patient ratio (32.5%) for ID consultants, ($p < 0.05$). Regarding effectiveness to prevent MDR development and spread, education programs (42.4%) were the priority for intensivists versus external consultation (35.7%) for ID consultants. Finally, both groups agreed that carbapenem resistance was the most pressing concern (> 70%) regarding emerging resistance. Differences in priorities regarding organisms, infection control practices, and educational priorities were visualized between ID/clinical microbiologists and ICU/anesthesiologists. Multidisciplinary collaboration is required to achieve best care for ICU patients with severe infections.

Keywords Multidrug-resistant bacteria · Infection control · Colonization · Prevention · Antimicrobials · Intensive care · Sepsis

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Introduction

The World Health Organization (WHO) proposed a global priority pathogen list (PPL) of multidrug-resistant (MDR) bacteria [1]. However, critically ill patients are particularly susceptible to infections arising from MDR bacteria [2], and a critical care specific list of PPL has been recently reported in TOTEM study [3]. The scope was to identify the most important resistant bacteria for intensive care units (ICU) and their challenges. In this cross-sectional survey, we assessed whether these perceptions were validated by a global sample of professionals with expertise in severe infections. The secondary objective was to prioritize the list to focus efforts proportionately according to perceived clinical need. The hypothesis was that differences in perception on MDR organisms and their management occur and might be associated with the primary training background and geographic differences.

Methods

A steering committee (Appendix 2) with experience of identification, prevention, and treatment of MDR bacteria in critically ill patients developed and refined the study protocol and selection of pathogens. Mycobacteria, rickettsia, viruses, and parasites were excluded. MDR bacteria was defined as non-susceptibility to at least one agent in ≥ 3 antimicrobial categories [4]. The study group was represented by intensivists, anesthesiologists, clinical microbiologists, and infectious disease (ID) consultants with experience in ICU settings (Table S1, supplemental material). Pediatric and neonatal intensive care units (ICUs) were excluded.

The survey was performed using an electronic platform (SurveyMonkey®) and was distributed by invitation from members of the Steering Committee in February 2018. The survey was an online questionnaire requiring no patient-specific data, and thus, the need for research ethics committee approval and informed consent were waived. The study protocol and questionnaire were published elsewhere [5].

Statistical analysis

Analysis by Chi-square test (or Fisher's exact test when appropriate) was performed to evaluate potential associations. A two-tailed *P* value less than 0.05 was considered statistically significant.

Results

The cross-sectional survey was completed by 129 respondents. The overall representation from within and outside Europe was 54% and 46% while the ICU practitioners (intensivists and anesthesiologists) constituted for 58% and 42%, respectively. Distribution according to regions, respondents, and IC characteristics are listed in Tables S1 and S2 (supplemental material).

Globally, extended spectrum beta-lactamase (ESBL) Enterobacteriaceae, followed by carbapenem-resistant (CR) *Acinetobacter baumannii* and CR *Klebsiella pneumoniae* were the main concerns. The mortality rankings of the organisms, therapy concerns, and opinion on measures to prevent emergence and spread of MDR are detailed in Table 1. Some differences in opinion were identified between 63 (49%) ICU physicians (ICU/anesthesiology) and 43 (33%) infectious disease consultants (ID physicians/microbiologists) (Table 1). The pathogens most concerning in the ICU for intensivists were ESBL Enterobacteriaceae (38%) versus CR *A. baumannii* (48.3%) for ID consultants, ($p < 0.05$). Increasing number of ID consultants over intensivists (26% vs 14%) reported difficulty in choosing initial therapy for CR *A. baumannii*. For intensivists, the urgent measures to limit development of antibiotic resistance were headed by cohort measures (26.3%) versus increasing nurse/patient ratio (32.5%) for ID consultants ($p < 0.05$). Regarding effectiveness to prevent MDR development and spread, education programs (42.4%) were the priority for intensivists versus external consultation (35.7%) for ID consultants. Finally, both groups agreed that carbapenem resistance was the most pressing concern regarding emerging resistance (72.9% versus 77.5%, $p > 0.20$). All these results are detailed in Table 1.

Global top five organism by site and differences between geographic regions ranks according most common sites involving MDR pathogens in ICUs are shown in Table 2. The details of practiced preventive measures to limit the MDR organisms are reported in Tables S1 and S2, supplemental section.

Discussion

Our findings emphasize the global concern regarding Gram-negative bacteria, although Gram-positive organisms dominated concern regarding community-acquired pneumonia and CSSI. Differences between intensivists and ID/clinical microbiologists and regional differences in priority pathogens and strategies are important observations.

Carbapenem-resistant organisms were indisputably perceived as highest threat for mortality, treatability, and cost. In addition, the results support the difficulty faced in managing MDR *P. aeruginosa* infections in ICUs [6]. Mortality by CR organisms is contributed particularly by the non-availability of effective drugs rather than increased virulence [7–9]. Adequacy of antimicrobial therapy, but not pathogen resistance pattern, impacted attributable mortality thus indicating the grim situation arising from the failing antibiotic pipeline [10]. The increased risk of mortality was strongly evident

Table 1 Characteristics of the answers to TOTEM items and differences between primary specialty ICU staff versus ID consultants

Study variables	All 129	ICU[a] 63 (49%)	ID[b] 43 (33%)	*P* value*
Main concern in your ICU				
Extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBL).	42 (32.6)	24 (38.1)	8 (18.3)	*0.003*
Carbapenem-resistant *Acinetobacter baumannii*.	38 (29.5)	10 (15.9)	21 (48.3)	*0.001*
Carbapenemase expressing *Klebsiella pneumoniae* (KPC).	32 (24.8)	18 (28.6)	11 (25.6)	0.956
Carbapenem-resistant *Pseudomonas aeruginosa*.	12 (9.3)	8 (12.7)	2 (9.7)	0.762
Oxacillin/methicillin-resistant *Staphylococcus aureus* (MRSA).	2 (1.6)	2 (3.2)	–	–
Urgent measures to limit development of antibiotic resistance				
Increase nurse/HCP ratio	26 (20.1)	9 (16.1)	12 (32.5)	0.116
De-escalation therapies	25 (19.3)	13 (21.3)	7 (16.3)	*0.044*
ID consultation	24 (18.6)	11 (18.3)	9 (23.7)	*0.012*
Cohort measures	22 (17)	15 (26.3)	5 (12.8)	0.184
Formulary restriction	20 (15.5)	9 (15)	7 (16.3)	0.704
Effective measures to prevent MDR development and spread				
Education programs	42 (32.5)	24 (42.4)	12 (30.8)	0.261
Antibiotic de-escalation	28 (21.7)	14 (24.1)	6 (15.8)	0.089
ID consultation	24 (18.6)	8 (13.8)	15 (35.7)	*0.001*
Formulary restriction	19 (14.7)	9 (15.3)	6 (14.6)	0.778
Cycling of antibiotics	6 (4.6)	3 (5.6)	1 (2.4)	0.101
Concern for emerging resistance to antibiotics				
Carbapenem	84 (65.1)	43 (72.4)	31 (77.5)	0.609
Beta Lactam inhibitors	13 (10)	7 (11.9)	1 (2.4)	0.165
Quinolones	10 (7.7)	6 (10.2)	3 (7.7)	0.693
3rd and 4th generation cephalosporins	9 (6.9)	1 (1.7)	3 (7.7)	*0.024*
Glycopeptides	6 (4.6)	3 (5.1)	(4.7)	0.264
Difficulty for adequate initial treatment				
Multidrug-resistant *Pseudomonas aeruginosa*	31 (24)	16 (32)	14 (36.8)	0.797
Carbapenemase expressing *Klebsiella pneumoniae* (KPC)	25 (19.3)	9 (18.4)	10 (11.5)	0,335
Carbapenem-resistant *Acinetobacter baumannii*	22 (17)	7 (14.3)	11 (26.2)	0,082
Oxacillin/methicillin-resistant *Staphylococcus aureus* (MRSA).	12 (9.3)	4 (7.8)	3 (7.7)	0.890
Vancomycin-resistant Enterococci (VRE)	6 (4.6)	4 (7.8)	1 (2.6)	0.850
Carbapenem-resistant Pseudomonas aeruginosa	6 (4.6)	4 (7.8)	1 (2.6)	0.753
Extended-spectrum beta-lactamase *Klebsiella pneumoniae*	5 (3.8)	2 (4.2)	–	0.257
Extended-spectrum beta-lactamase *Escherichia coli*	5 (3.8)	3 (6)	1 (2,6)	*0.042*
TMP/SMX-resistant *Stenotrophomonas maltophilia*	5 (3.8)	4 (7.8)	1 (2.6)	0.712
Extended-spectrum beta-lactamase *Serratia* spp	1 (0.8)	1 (2.1)	–	0.836

[a] Anesthesia or intensive care

[b] Infectious disease/internal medicine or clinical microbiology, * Significant <0.05

in Asia [11] with variations in carbapenemase production across different regions [12]. Currently, the biggest gap exists in the investigational pipeline for compounds active against CR *A. baumannii*. Our findings suggest that this organism is of major concern, despite it being conventionally considered low virulence [13].

Importantly, issues contributing to misuse of existing antibiotics need serious attention. Lack of suitable rapid diagnostics and non-availability in a timely manner is a major impediment in appropriately using antibiotics [14, 15]. Our survey reinforces the differential prevalence of MDR bacteria by site of infection and the importance of recording this when undertaking surveillance programs.

WHO reports estimate that approximately 30% of ICU patients are affected by at healthcare-associated infections [16]. Several reports suggest the lack of surveillance data having a

Table 2 Rank of the most commonly reported pathogens in 2017 in participating ICUs according to specific infection sites

Infections and associated pathogens	*N* (%)	Overall rank	Africa	Europe	Asia	America
Community acquired pneumonia						
Macrolide-resistant *Streptococcus pneumoniae*	45 (34.9)	1	1	1	1	4
3rd generation cephalosporin-resistant Enterobacteriaceae	22 (17)	2	3	3	2	1
Quinolones-resistant *Pseudomonas aeruginosa*	21 (16.3)	3	4	2	3	2
Oxacillin/methicillin-resistant *Staphylococcus aureus* (MRSA)	15 (11.6)	4	5	5	4	3
3rd generation cephalosporin-resistant *Streptococcus pneumoniae*	11 (8.5)	5	2	4	5	5
Hospital-acquired pneumonia/ventilator-associated pneumonia						
Carbapenem-resistant *Acinetobacter baumannii*	42 (32.5)	1	3	1	1	1
Multidrug-resistant *Pseudomonas aeruginosa*	22 (17)	2	4	4	2	4
Carbapenem-resistant *Klebsiella pneumonia*	21 (16.3)	3	1	2	3	2
Carbapenem-resistant *Pseudomonas aeruginosa*	17 (13.2)	4	2	3	4	3
Oxacillin/methicillin-resistant *Staphylococcus aureus* (MRSA)	16 (12.4)	5	5	5	5	5
Intra-abdominal infection						
Multidrug-resistant *Escherichia coli*	58 (44.9)	1	1	1	1	1
Vancomycin-resistant Enterococci	17 (13.2)	2	5	5	5	4
Carbapenem-resistant *Klebsiella pneumoniae*	15 (11.6)	3	2	3	2	3
Multidrug-resistant *Pseudomonas aeruginosa*	13 (10)	4	4	2	3	2
Carbapenem-resistant *Acinetobacter baumannii*	12 (9.3)	5	3	4	4	5
Skin and soft tissue infections						
Oxacillin/methicillin-resistant *Staphylococcus aureus* (MRSA)	72 (55.8)	1	1	1	1	1
Multidrug-resistant *Escherichia coli*	17 (13.2)	2	2	3	2	2
Multidrug-resistant *Pseudomonas aeruginosa*	16 (12.4)	3	3	2	3	3
Carbapenem-resistant *Klebsiella pneumoniae*	8 (6.2)	4	4	4	4	4
Vancomycin-resistant Enterococci	4 (3.1)	5	5	5	5	5
Catheter-associated bacteremia						
Oxacillin/methicillin-resistant *Staphylococcus aureus* (MRSA)	48 (37.2)	1	1	1	1	1
Multidrug-resistant *Escherichia coli*	28 (21.7)	2	2	2	4	2
Carbapenem-resistant *Klebsiella pneumoniae*	22 (17)	3	3	4	2	3
Multidrug-resistant Pseudomonas aeruginosa	12 (9.3)	4	4	3	3	4
Vancomycin-resistant Enterococci	4 (3.1)	5	5	5	5	5

negative influence on the implementation of preventive measures [17–21]. Two world-wide ICU infection prevalence studies in a span of 10 years have demonstrated 20% increase in prevalence [22, 23]. Accompanying this rise in infections is a parallel increase in antimicrobial resistance rates, thus changing the status from MDR to extreme drug resistance (XDR).

We identified apparent differences in resistant organism prevalence by site of infection and geographic location. MRSA was increasingly common in CSSIs and device-related BSIs. Among Asian participants, CR *K. pneumoniae* was the second most commonly reported cause of device-related BSIs. Macrolide-resistant

S. pneumoniae was perceived with lower priority in America, perhaps because the predominant mechanism of resistance is different from other regions. Similarly, CR *K. pneumoniae* was perceived as more important in Africa. Regional priorities for different infectious sites were reported to be similar among participants with minimal variations. Interestingly, few participants in the survey felt that adequate initial treatment for CR *P. aeruginosa* was difficult, although this organism featured in the top four priority organisms in the preceding MCDA analysis [3]. This difference might be due to the perception of availability of colistin and aminoglycosides for therapy, despite recent evidence suggesting that the efficacy of these choices is similar to inappropriate therapy in clinical practice [6].

Overall, the current opinion from the survey highlights the dominant burden of Gram-negative bacterial infections over the Gram-positive infection in critical care settings. Although rates of MRSA bacteremia are declining in Europe, the occurrence of SSIs and other serious infections by MRSA are still high [24]. USA reports the opposite trend that is observed in Europe [25]. Our results reflect these trends, likely due to higher representation of European colleagues.

Our results bring attention to the variations in opinions of intensive care and ID physicians about issues such as occurrence, management, and containment of MDR infections in ICUs that might have implications on patient care. However, there was an overall consensus on components of antimicrobial stewardship (AMS) and infection prevention measures for confronting MDR infections. Interestingly, intensivists did not consider ID consultation as a priority measure to reduce antimicrobial resistance. The difference in perception might probably arise due to the non-availability of ID round the clock and their focus on the overall patient status rather than the antibiotic resistance and selection pressures. Moreover, the difficulty in differentiating colonization and true infection also contributes to differences in perceptions towards management of MDR organisms which could not be assessed in the current survey.

There are several limitations to this study. Although survey respondents came from across the globe, they represent only a small fraction of clinicians and units care for critically ill patients and universal coverage of nations was not achieved. National representation did not correlate with relative population size, and we could not assess regional variation in MDR bacteria at a national or regional level. Neither were we able to examine differences between patient types (for instance cardiac, burns, or neuro-trauma) and our findings are restricted to adult populations. Although our survey was largely focused on health-care-acquired infections, community-acquired MDR organisms in pneumonia were enquired about although not community-acquired infections at other sites.

Conclusions

The pathogens most concerning in the ICU for intensivists were ESBL Enterobacteriaceae versus CR *A. baumannii* for ID consultants. Differences in priorities regarding organisms, infection control practices, and educational priorities were visualized between ID/clinical microbiologists and ICU/anesthesiologists. Overall, both agree on concerns on resistant Gram-negative organisms. Need of team working is required to address best care for ICU subjects with severe infections.

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Compliance with ethical standards

Conflicts of interest Dr. Rello served in the speaker's bureau or consultant for Pfizer, Anchoagen, ROCHE. The remaining authors have no conflicts of interest to declare.

Ethical approval/informed consent Not required.

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Appendix 2- Steering Committee members

Jordi Rello, Spain (Chair); Joana Alves, Portugal; Leonel Lagunes, Mexico; Nieves Larrosa, Spain; Mervyn Mer, South Africa; Emine Alp, Turkey; Zhongheng Zhang, China.

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