Analysis of the historical evolution of antimicrobial resistance in the main bacteraemia-causing organisms at MFT

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BACKGROUND

Illness associated with bacteraemia ranges from self-limiting infection to life threatening sepsis that requires rapid and aggressive antimicrobial treatment. The selection of the appropriate antimicrobial treatment is complicated by the increase in antibiotic resistance worldwide (reviewed in ref. 1) and by the time-consuming identification of the pathogen and its resistances via blood cultures (2). Thus, analysis of local trends in antibiotic resistance in bacteraemia aids prescribing and infection control policy making (3).

Sepsis is a systemic, deleterious host response to infection that can lead to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation). Severe sepsis and septic shock are major healthcare problems, affecting millions of individuals around the world each year (reviewed in ref. 4) and are among the main causes of death regarding hospitalised patients (5). In severe sepsis, early administration of appropriate broad-spectrum antibiotics led to reduced mortality, emphasising that prompt and adequate antimicrobial therapy is the cornerstone in sepsis treatment (5, 6).

HYPOTHESIS

The objective of this study was to identify local trends in antibiotic resistance to aid prescribing and infection control policy-making.

This is of particular importance regarding sepsis of unknown source, since blood cultures can take longer to grow and reveal antibiotic sensitivities than the time available for sepsis patients to react to appropriate therapy, emphasising the need to get the best treatment as soon as possible at first try and, therefore, the need for historical data.

Our rationale is that knowledge of which antibiotics are more likely to work given the historical evolution of resistance for the key bacteraemia-causing species in this Trust will greatly improve the outcomes of present-day patients.

METHODS

We reviewed trust wide bacteraemia and antimicrobial sensitivity data between 2013 and 2017, broken down regarding organism/organism type , including carbapenemase-producing enterobacteriaceae (CPE) as Manchester has been reported as an area with high prevalence of healthcare-associated infections caused by these pathogens; main organisms were selected (7, 8).

The MicroGuide™ app was used to obtain current antimicrobial recommendations for this Trust. Antimicrobials examined: co-amoxiclav, amikacin, amoxicillin, azithromycin, ceftazidime, ciprofloxacin, co-trimoxazole, cefotaxime, cefuroxime, ertapenem, cefepime, cefoxitin, gentamicin, meropenem, temocillin, tigecycline, tobramycin, trimethoprim, piperacillin+tazobactam.

We considered as contaminants all *Micrococcus* spp. and, if not line- or device-associated, coagulase-negative staphylococci, propionibacteria, *Bacillus* spp. and diphtherioids. Duplicates were discarded to avoid over-representation of the same case (same patient from the same location growing the same organism within 14 days).

Data analysis was performed with the appropriate SQL queries.

RESULTS

E. coli is the most common organism in significant positive blood cultures

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Organism	2013 No.	2013 %	2014 No.	2014 %	2015 No.	2015 %	2016 No.	2016 %	2017 No.	2017 %
Escherichia coli	*220*	26.4	*236*	22.3	*253*	24.6	*273*	27.3	*248*	24.9
Staphylococcus aureus	*81*	9.7	*101*	9.5	*102*	9.9	*101*	10.1	*120*	12.1
MRSA	*6*	0.7	*3*	0.3	*5*	0.5	*12*	1.2	*6*	0.6
Klebsiella spp.	*62*	7.5	*88*	8.3	*64*	6.2	*71*	7.1	*47*	4.7
Streptococcus pneumoniae	*29*	3.5	*28*	2.6	*27*	2.6	*31*	3.1	*28*	2.8
Enterococcus spp.	*59*	7.1	*85*	8.0	*66*	6.4	*52*	5.2	*51*	5.1
VRE	*14*	1.7	*19*	1.8	*10*	1.0	*15*	1.5	*7*	0.7
Pseudomonas spp.	*18*	2.2	*62*	5.8	*21*	2.0	*27*	2.7	*33*	3.3
Other streptococci	*94*	11.3	*98*	9.2	*124*	12.0	*101*	10.1	*119*	12.0
Coagulase-negative staph.	*98*	11.8	*120*	11.3	*133*	12.9	*94*	9.4	*135*	13.6
Proteus spp.	*10*	1.2	*22*	2.1	*25*	2.4	*14*	1.4	*25*	2.5
Enterobacter spp.	*14*	1.7	*26*	2.5	*15*	1.5	*19*	1.9	*30*	3.0
Serratia spp.	*7*	0.8	*10*	0.9	*13*	1.3	*7*	0.7	*12*	1.2
Anaerobes	*15*	1.8	*23*	2.2	*23*	2.2	*25*	2.5	*13*	1.3
Others	*72*	8.7	*93*	8.8	*95*	9.2	*104*	10.4	*75*	7.5
Fungi	*33*	4.0	*46*	4.3	*54*	5.2	*53*	5.3	*46*	4.6
Total	*832*	100	*1060*	100	*1030*	100	*999*	100	*995*	100
Contaminants										
Coagulase-negative staph.	*311*	75.3	*300*	80.6	*306*	82.9	*318*	81.1	*355*	84.1
Diphtheroids	*54*	13.1	*28*	7.5	*23*	6.2	*18*	4.6	*17*	4.0
Propionibacteria	*23*	5.6	*18*	4.8	*23*	6.2	*29*	7.4	*27*	6.4
Micrococcus spp.	*22*	5.3	*22*	5.9	*10*	2.7	*22*	5.6	*14*	3.3
Bacillus spp.	*3*	0.7	*4*	1.1	*7*	1.9	*5*	1.3	*9*	2.1
Total	413	100	372	100	369	100	392	100	*422*	100

B

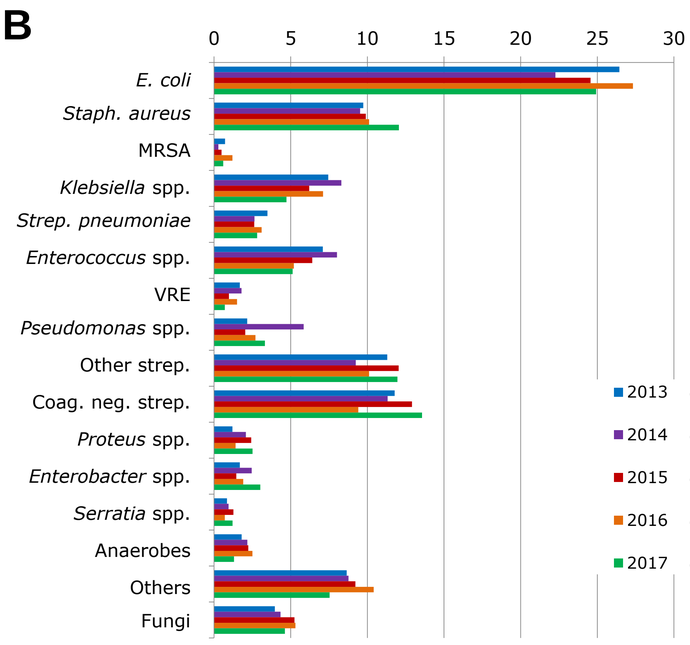

Fig. 1. The main species responsible for bacteraemia remained globally unaltered throughout the years analysed, with *Escherichia coli* being the main contributor (22.3-27.3% of total significant isolates between 2013-2017). (A) Absolute numbers and percentages are indicated and contaminants are included below. (B) Bar chart with percentage data from Fig. 1A.

Urinary tract infection (UTI) is the main source of *E. coli* bacteraemias

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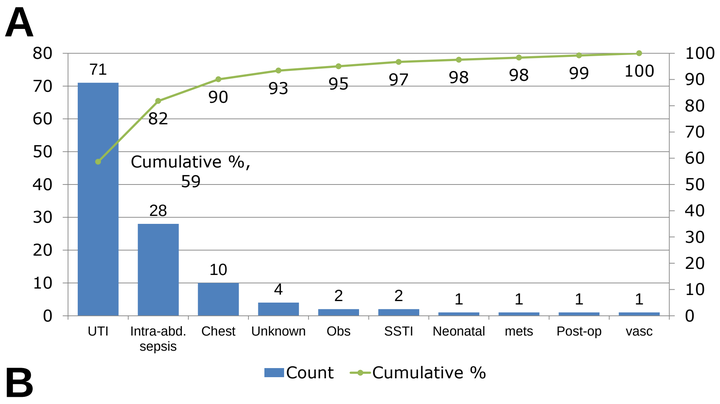

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Year	Positive Enterococcal BCs	Enterococcal BCs	BC&U*	Enterococcal BCs %	BC&U % relative to enterococcal BCs	BC&U % relative to positive BCs
2017	824	45	1	5.5%	2.2%	0.1%
2016	850	45	3	5.3%	6.7%	0.4%
2015	844	53	1	6.3%	1.9%	0.1%
2014	854	74	1	8.7%	1.4%	0.1%

Fig. 2. (A) Pareto chart with sources of *E. coli* bacteraemia in 2017; Biliary is grouped with intra-abdominal sepsis; community-acquired pneumonia with 'chest'; post-partum with 'obstetrics'. Mets, metastatic cancer; SSTI, skin and soft tissue infection. (B) The role of enterococci in urosepsis appears negligible. Enterococci in significant blood cultures vs urines, without duplicates. *Count of patients with an enterococcal blood culture and urine sample within a day of collection of the former.

Rise in carbapenemase-producing and ESBL/AmpC Gram-negatives

	2015 Total	2015 CPE N	2015 CPE %	2015 ESBL/AmpC N	2015 ESBL/AmpC %	2016 Total	2016 CPE N	2016 CPE %	2016 ESBL/AmpC N	2016 ESBL/AmpC %	2017 Total	2017 CPE N	2017 CPE %	2017 ESBL/AmpC N	2017 ESBL/AmpC %
Escherichia coli	*232*	1	0.4%	27	11.6%	*267*		0.0%	24	9.0%	*231*	4	1.7%	32	13.9%
Klebsiella spp.	*54*	2	3.7%	1	1.9%	*59*	3	5.1%	4	6.8%	*43*	4	9.3%	3	7.0%
Enterobacter spp.	*13*		0.0%	1	7.7%	*16*		0.0%	3	18.8%	*17*		0.0%	4	23.5%
Pseudomonas spp.	*13*		0.0%		0.0%	*19*		0.0%	0	0.0%	*27*		0.0%		0.0%
Proteus spp.	*19*		0.0%		0.0%	*14*		0.0%	0	0.0%	*20*		0.0%	1	5.0%
Serratia spp.	*9*	1	11.1%	2	22.2%	*6*		0.0%	0	0.0%	*9*		0.0%		0.0%
Citrobacter spp.	*3*		0.0%		0.0%	*4*		0.0%	0	0.0%	*5*		0.0%	1	20.0%
Morganella spp.	*6*		0.0%		0.0%	*1*		0.0%	0	0.0%	*2*		0.0%	1	50.0%
Providencia spp.	*1*	1	100.0%		0.0%	*0*		-		-	*0*		-		-
Salmonella spp.	*2*		0.0%		0.0%	*7*		0.0%	0	0.0%	*1*		0.0%		0.0%
Acinetobacter spp.	*6*		0.0%		0.0%	*3*	1	33.3%	0	0.0%	*1*		0.0%		0.0%
Total	358	5	1.4%	31	8.7%	396	4	1.0%	31	7.8%	356	8	2.2%	42	11.8%

Fig. 3. Carbapenemase-producing Gram-negatives showed an increase of 60.1% between 2015 and 2017 whereas ESBL/AmpC increased 36.2% in the same time period.

With *E. coli*, addition of gentamicin can be beneficial

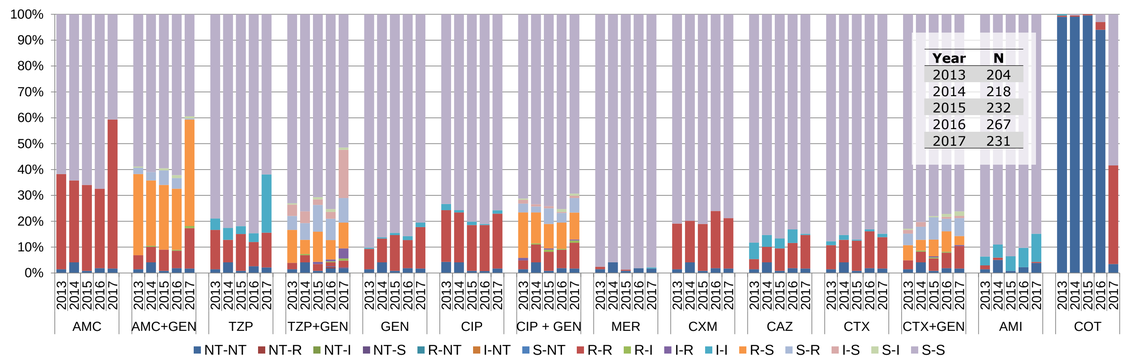

Fig. 4. For *E. coli*, resistance to antimicrobials was mainly found to be stable or exhibit a slight increase. Combining gentamicin with other antibiotics is still beneficial in initial empirical treatment. The spike in AMC resistance in *E. coli* and other Gram-negatives was largely due to changes in sensitivity testing based on EUCAST recommendations. NT, non-tested; R, resistant; I, intermediate; S, sensitive.

CONCLUSIONS

Our results provide clinicians with reassurance that current antimicrobial recommendations for empiric treatment of sepsis at our Trust are evidence-based and appropriate in the majority of cases. They support the continued inclusion of aminoglycosides for additional empiric cover in the acute management of septic patients at our hospital.

Performing periodic studies of the aetiology of bacteraemia as well as assessing antimicrobial resistance levels and the resistance mechanisms present in blood culture isolates is crucial. However, changes in laboratory practice must always be taken into account when interpreting resistance data in the clinical context.

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