GRAM NEGATIVE BACTERAEMIA RATES IN HAEMODIALYSIS

EC Murray[1], A Marek[2], PC Thomson[1], JE Coia[2]
1 Renal Unit, Western Infirmary, Dumbarton Road, Glasgow, G11 6NT
2 Medical Microbiology, New Lister Building, Glasgow Royal Infirmary, Glasgow, G31 2ER

INTRODUCTION

Rates of morbidity and mortality are significantly higher for patients on renal replacement therapy (RRT) than the general population (1). One-fifth of deaths on RRT are due to infection, the second-highest cause of mortality following cardiovascular disease (1). The proportion of BSIs caused by Gram negative pathogens is increasing (2), and while the rate of staphylococcal bacteraemia in the haemodialysis population is well described and closely monitored (3), less is known about the burden of Gram negative pathogens. In this study we characterise Gram negative bacteraemia in a contemporary period-prevalent haemodialysis population, detailing the identity of pathogens, sensitivity patterns, sources of infection, and clinical outcome.

METHODS

Setting: Observational data on Gram negative bacteraemia events in the haemodialysis (HD) population of NHS GGC and Forth Valley, collected July 2011 to April 2014.

Data collection: Data collected prospectively, obtained via interrogation of the Renal Unit electronic patient record. This database imports all microbiology results from any source. Cases confirmed by an independent search of the Microbiology database. Consecutive blood culture results >14 days apart were regarded as separate events. Mortality data collected over the study period and subsequent 3 months, maximum follow up therefore 36 months.

Microbiology: Cases were defined by positive growth on blood culture of a pathogenic organism.

Analysis: Event rates were expressed as per 1000 HD-exposed days.

RESULTS

Demographic data illustrated in Table 1. Over 544,377 HD days, 84 patients experienced 95 Gram negative BSI events (0.175 per 1000 HD days), which varied with dialysis modality: non-tunnelled central venous catheters (NTCVC) 4.77, arteriovenous grafts 0.24, tunnelled CVC 0.21, and arteriovenous fistulae 0.11/1000 HD days. The commonest sources of bacteraemia were CVCs (16.8%, n=16) and infected ulcers (14.7%, n=14), see Table 2.

The principal organisms are demonstrated in Figure 1. Table 3 demonstrates that 88% of Enterobacteriaceae were sensitive to gentamicin, and 100% to meropenem.

Three month patient mortality was 25.3% (n=24), Table 2. Ten patients (11.9%) had more than one Gram negative bacteraemia; of these, 9 patients (90.0%) were the same causative organism.

All patients with a NTCVC had it removed following Gram negative BSI; considering TCVCs, the vascular access outcome differed between BSIs due to CVC source compared to other sources of infection, P <0.001, see Figure 2.

DISCUSSION

ICU studies report rates of 0.178 to 1.13/1000 days, with mortality 48 to 60% (4). Our lower rates reflect a less acutely unwell population. Case mortality was however higher than death among prevalent RRT patients (8.7% per year), and that of the general population (1.16% per year) (1).

For Gram negative BSI, removal of CVCs is advised for severe sepsis, complications (e.g. endocarditis,) *P. aeruginosa*, or bacteraemia >72 hours on appropriate antibiotics. In our population, TCVC removal rates differed between BSI attributed to line sepsis versus other infection sources (Figure 2). The appropriateness of salvage versus removal of CVCs should be an area for future research.

Similar to the general population, *E. coli* and *Klebsiella spp.* are amongst the commonest organisms (5); resistance patterns were also comparable, despite the hospital and antimicrobial exposure associated with HD (Table 3). Renal unit policy of empirical vancomycin and gentamicin in suspected CVC-related BSI is supported by the results above, though apparent source and severity, healthcare exposure, and previous culture results should influence decision making.

CONCLUSIONS

CVCs and soft tissue ulcers remain significant risk factors for Gram negative bacteraemia; this highlights the importance of vascular access planning. Despite good levels of antibiotic sensitivity, mortality remains high, supporting aggressive treatment of such pathogens.

Table 1. Demographics	HD population n=1242, 544,377 HD days	Gram negative BSI group n=84 patients, n=95 BSIs
Median age at starting RRT, yrs (IQR)	60.8 (45.9 – 72.1)	61.2 (48.9 – 74.2)
Male	738 (59.4%)	53 (63.1%)
Female	504 (40.6%)	31 (36.9%)
Primary Renal Disease:		
Primary Glomerulonephritis	232 (18.7%)	16 (19.0%)
Interstitial Nephropathies	175 (14.1%)	16 (19.0%)
Multisystem Diseases	197 (15.9%)	19 (22.6%)
Diabetic Nephropathy	211 (17.0%)	21 (25.0%)
Unknown and Other	427 (34.4%)	12 (14.3%)
HD access, cross-sectional prevalence on the 1st July:		
% AVF 2011, 2012, 13 (Average)	68.3, 65.4, 61.0 (64.8)	61.3, 57.1, 49.4 (56.1)
% AVG 2011, 2012, 2013 (Average)	0.9, 1.8, 1.2 (1.3)	0.0, 5.4, 3.6 (2.9)
% TCVC 2011, 2012, 2013 (Average)	28.0, 31.1, 35.0 (31.5)	37.1, 30.4, 43.6 (37.0)
% NTCVC 2011, 2012, 2013 (Average)	2.8, 1.6, 2.8 (2.4)	1.6, 7.1, 3.6 (4.0)

Table 2. Source of BSI	AVF/G	NTCVC	TCVC	Total
CVC (firm diagnosis)	0 (0%)	2 (12.5%)	14 (35.9%)	16 (16.8%)
Unknown	8 (20.0%)	2 (12.5%)	6 (15.4%)	16 (16.8%)
Foot ulcer/soft tissue	9 (22.5%)	0 (0.0%)	5 (12.8%)	14 (14.7%)
Urinary	6 (15.0%)	3 (18.8%)	1 (2.6%)	10 (10.5%)
Biliary	7 (17.5%)	1 (6.25%)	1 (2.6%)	9 (9.5%)
Intra-abdominal	2 (5.0%)	4 (25%)	3 (7.7%)	9 (9.5%)
AVF/AVG	4 (10.0%)	0 (0.0%)	2 (5.1%)	6 (6.3%)
CVC (presumed)	1 (2.5%)	0 (0.0%)	5 (12.8%)	6 (6.3%)
Respiratory	0 (0%)	4 (25%)	1 (2.6%)	5 (5.3%)
Infected renal cyst	2 (5%)	0 (0.0%)	1 (2.6%)	3 (3.2%)
Calciphylaxis related	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
Total cases	**41 (43.2%)**	**16 (16.8%)**	**38 (40.0%)**	**95 (100%)**
Death within 3 months (% of BSI events)	13 (31.7%)	6 (37.5%)	5 (13.2%)	24 (25.3%)
Death during follow up (% of BSI events)	20 (48.8%)	6 (37.5%)	11 (29.0%)	37 (39.0%)

Table 3. Antibiotic sensitivities of 85 isolates of Enterobacteriaceae	Sensitive (n=84)	% of those tested sensitive	Resistant (n=84)	% of those tested resistant
Amikacin	77	93.9	0	0.0
Amoxicillin	14	17.9	64	82.1
Aztreonam	71	86.6	9	11.0
Ciprofloxacin	67	80.7	13	15.7
Co-amoxiclav	47	56.0	33	39.3
Gentamicin	74	88.1	9	10.7
Meropenem	83	100.0	0	0.0
Piperacillin-tazobactam	74	91.4	6	7.4

Figure 1. Gram negative organisms Isolated on culture

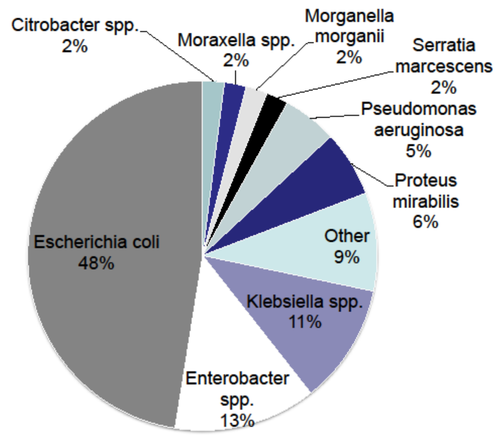
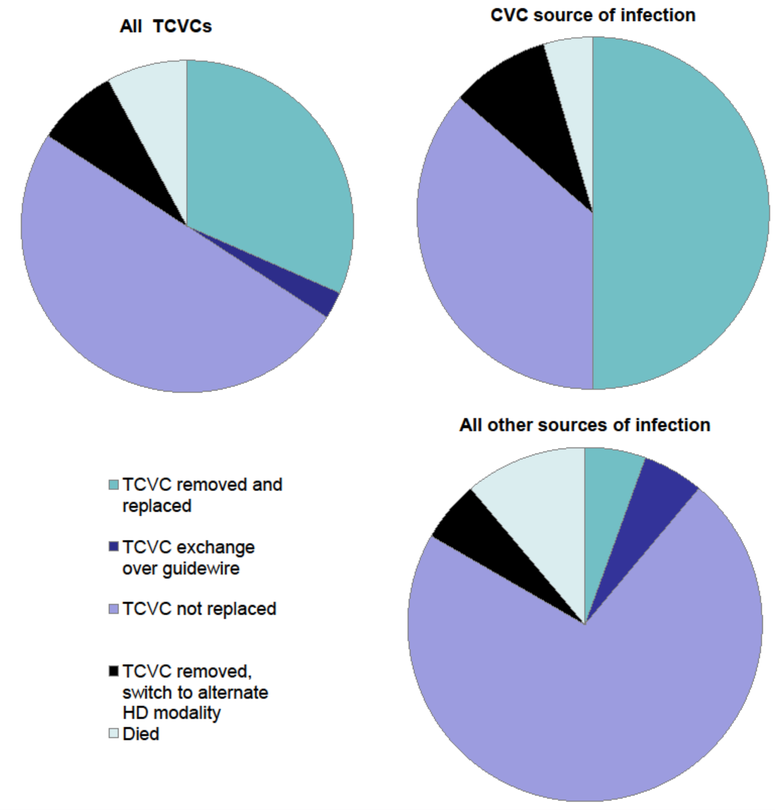


Figure 2. Outcomes of TCVCs following Gram negative bacteraemia, by source of infection



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