Gram-negative Bloodstream Infections (GNBSI): information for action

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INTRODUCTION

In 2016, the UK government announced an ambition to reduce healthcare-associated GNBSI by 50% by 2021. NHS Improvement (NHSI) mandated the reporting from April 2017 of *Klebsiella* species, and *Pseudomonas aeruginosa* BSI cases (in addition to *E. coli*) to Public Health England (PHE). Guidance on the definition of healthcare associated GNBSI was issued by PHE and NHSI in July 2017[1] (**Figure 1**).

Public Health England

NHS Improvement

Guidance on the definition of healthcare associated Gram-negative bloodstream infections

July 2017

Gram-negative bloodstream infections (BSIs) are a healthcare safety issue. From April 2017, there is an NHS ambition to halve the numbers of healthcare associated Gram-negative BSIs by 2021.

Figure 1 shows the terminology the NHS will use to categorise healthcare associated Gram-negative BSIs according to where they are detected (community or hospital), and their relationship to healthcare (healthcare vs non-healthcare associated). The relative proportions of Gram-negative BSIs in each category are also shown for the top three Gram-negative BSI causative organisms, *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Klebsiella* species (*Klebsiella* spp.) for 2016/17.

Figure 1. Definitions of different categories of bloodstream infections

Figure 1: Guidance on the definition of different categories of Gram-negative bloodstream infections[1].

According to this guidance, **a healthcare associated GNBSI was defined as** a case in a patient who had:
- received healthcare in either the community or the hospital in the previous 28 days, including but not limited to:
  - indwelling vascular access devices (insertion, *in situ*, or removal)
  - urinary catheterisation (insertion, *in situ* with or without manipulation, or removal)
  - other devices (insertion, *in situ* with or without manipulation, or removal)
  - invasive procedures (eg endoscopic retrograde cholangio-pancreatography, prostate biopsy, surgery including, but not restricted to, gastrointestinal tract surgery)
  - neutropenia (<500/microL at time of bacteraemia)
  - antimicrobial therapy, and/or
- had an intervention up to 12 months earlier that remained operational during the previous 28 day period eg urinary catheter, and/or
- onset at least 48 hours after admission, and/or
- onset within 28 days of discharge, and/or
- been receiving nursing home care

Opportunities to intervene "should not be lost":

> **"The presence of a healthcare associated risk factor is enough to assume that the GNBSI is healthcare associated."[1]**

AIM

We reviewed the epidemiology of the first six months of cases detected at the Royal Free Hospital (RFH), a London teaching hospital, to inform infection control actions.

METHODS

Individual patient hospital and summary care records were reviewed. GNBSI were categorised above. Antibiotic sensitivity results were obtained from the laboratory information system. Chi-squared tests were performed using Open-Epi version 3.01 (www.openepi.com).

RESULTS

From April to September 2017, 163 GNBSI were detected, 110 (67%) *E. coli*, 31 (19%) *Klebsiella* species and 22 (14%) *P. aeruginosa*. 88 (54%) cases occurred in males. Females predominated in age groups up to age 50, above which males predominated (**Figure 2**).

Figure 2: Gram negative blood stream infections by age group and sex (N=163)
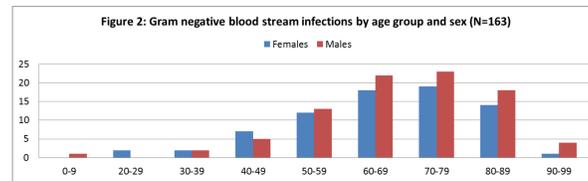
39 cases (24%) were community onset, non-healthcare associated (CO-non-HCA); 124 (76%) HCA; and 57 (35%) Hospital onset (HO). 67 (41% of total) were community onset, healthcare-associated (COHCA) versus 30% for England[1] (p<0.001), of which 28 (17% of total) and 39 (24% of total) were associated with community and hospital care, respectively. Comparison with proportions for England are shown in **Table 1**.

Category	Name	England 2016/17 (%)[1]	RFH Apr-Sep 2017 (%)	P-value
A+B+C	All infections	53920 (100)	163 (100)	
A	HO	15687 (29)	57 (35)	
B+C	CO	38233 (71)	106 (65)	
B	COHCA	16351 (30)	67 (41)	<0.001
C	CO-non-HCA	21882 (41)	39 (24)	
A+B	HCA	32038 (59)	124 (76)	<0.001

Table 1: Categories of GNBSI at Royal Free Hospital (RFH) compared to England[1]. HO=hospital onset, CO=community onset, HCA=healthcare associated. See **Figure 1** for definitions of categories.

There were differences in the focus of infection for *E. coli*, *Klebsiella* species, and *P. aeruginosa*. The most common sources were, respectively: hepatobiliary 29(26%), 12(39%), 2(9%); lower urinary tract (UT) 28(25%), 7(23%), 7(32%); upper UT 30(27%), 4(13%), 3(14%); and gastrointestinal or intra-abdominal excluding hepatobiliary 12(11%), 3(10%), 0(0%) (**Figure 3**). A primary focus in the UT was significantly less common in *Klebsiella* species cases (11, 35%) than *E. coli* (58, 53%)(p=0.048).



Figure 3: Primary focus of bacteraemia
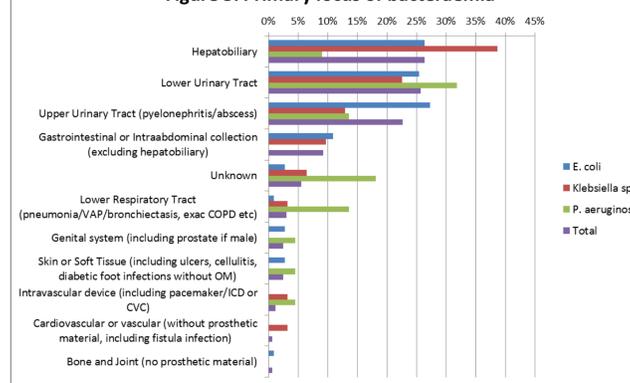
The most common HCA risk factors were antimicrobial therapy (42%), urinary catheter (UC) (28%), UC manipulation (20%), surgery (20%), and a vascular device (20%). Risk factors differed by organism (**Figure 4**).

Figure 4: Risk factors for Gram negative bloodstream infections
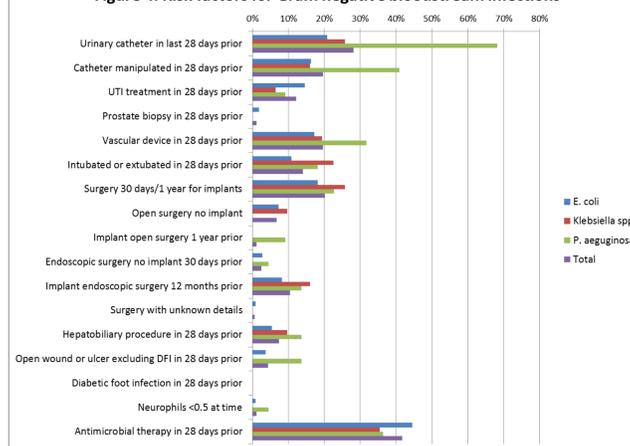
RESULTS

Compared to non-HCA cases, HCA cases were more likely to be non-*E. coli* (*Klebsiella* species plus *P. aeruginosa*) (p=0.012) (**Figure 5**), and less likely to have a focus in the upper UT (19% versus 33%, p=0.041).

Figure 5: GNBSI healthcare association, by organism (N=163)
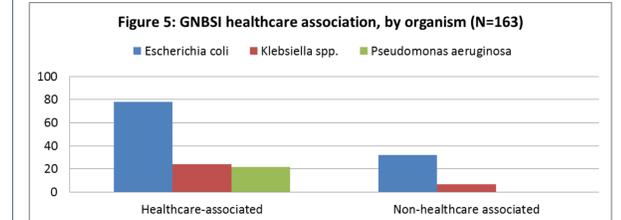
For *E. coli* plus *Klebsiella* species cases with susceptibility results (N=135), compared to cases arising on day <2 of admission (non-HO), cases arising on day >=2 (HO) were more likely to be non-susceptible to piperacillin-tazobactam (18% versus 6%, p=0.031) and temocillin (25% versus 7%, p=0.005) (**Figure 6**).

Figure 6: *E. coli* plus *Klebsiella* species BSI antibiotic non-susceptibility and ESBL positivity by hospital onset (N-135)
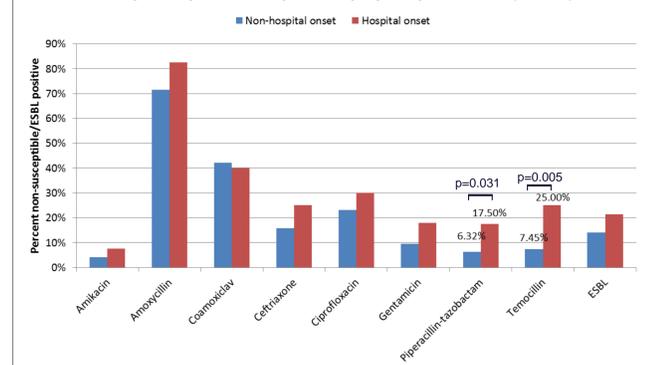
DISCUSSION

1. High proportion of HCA and COHCA cases. This may be the result of patient case mix factors, and/or the more inclusive definitions used in our data compared to a recent study of *E. coli* BSI in England[2] which formed the basis for the guidance[1]. Compared to this study[2], our *E. coli* cases were more likely to have a hepatobiliary focus (26% versus 16%, p=0.003) which may reflect our large tertiary hepatopancreatobiliary surgery service. 81% of these cases were HCA compared to 76% of the total.

2. Causative organism varied by primary focus and risk factors. *Klebsiella* species predominated in hepatobiliary infections while *P. aeruginosa* predominated in lower respiratory tract infections and lower UT infections and when a urinary catheter was present or had been manipulated in the previous 28 days. These findings should be considered when managing individual cases and when updating prophylactic and empiric antimicrobial guidelines.

3. Organisms varied by healthcare onset status and susceptibilities varied by hospital onset status. *Klebsiella* species and *P. aeruginosa* were more prevalent in HCA cases and antimicrobial resistance was higher in HO cases. These findings should be considered when managing cases and updating guidelines.

Further analysis of associated mortality, and preventable and avoidable factors, related to infection control, antimicrobial stewardship and patient pathways will enable the development of interventions to reduce the burden of infections in our organisation.

REFERENCES

1. Guidance on the definition of healthcare associated Gram-negative bloodstream Infections, Public Health England, © NHS Improvement, June 2017 Publication code: IG 33/17
2. Abernethy J, *et al.* Epidemiology of Escherichia coli bacteraemia in England: results of an enhanced sentinel surveillance programme. Journal of Hospital Infection 2017; 95:365-375.