Reviewer's report

Title: Community-onset bloodstream infection with multidrug-resistant organisms: a matched case-control study

Version: 1 Date: 23 December 2013

Reviewer: Konstantinos Pontikis

Reviewer's report:

The study herein deals with the prevalence of MDR organisms causing community-onset bloodstream infections in the Emergency Department setting. It is a retrospective database review covering a 10 year period (2002-2011). The main finding is that MDR among Gram negatives (and especially E.coli) is rising, while the same is not true for gram positives (and especially S.aureus). A nested case-control study identified several plausible, but previously described, factors that confer to the prediction of MDR etiology.

This is a well-documented study on a clinically relevant subject. Nevertheless, certain methodological and interpretation points need to be addressed by the authors. In a few words significant shortcomings are the absence of MIC reporting and issues in interpretation of the data.

Major compulsory revisions

Data collection and definitions - i) prevalence and temporal trends of MDR organisms – 1st paragraph

1. The authors state that ‘For the majority of the study period susceptibility breakpoints were based on the BSAC guidelines. These were changed to the EUCAST guidelines from July of 2010. We observed no change in resistance patterns at the time of the change in breakpoints definitions’.

What is meant by ‘no change in resistance patterns’? Because confusion may be derived by the use of susceptibility breakpoints, MIC90 / MIC50 reporting is preferable.

Data collection and definitions – ii) risk factors associated with MDR COBSI – 2nd paragraph

2. The authors state that ‘Sources of BSI were divided into low risk sources including urinary, skin and soft-tissue, and catheter-related, and high risk sources including respiratory, intraabdominal, bone and joint, cardiovascular or unidentified’.

What does high and low risk imply? Why does bone and joint infection represent higher risk? Which are possible cardiovascular sources of BSI? (endocarditis, endarteritis, something else?)

Results, Temporal trend of MDR organisms causing COBSI, last paragraph
3. The authors state: ‘About 10% of Streptococcus pneumoniae blood culture isolates were non-susceptible to penicillin’.

Regarding S.pneumoniae, the description of a bacterial population (such as the 104 strains of pneumococcus in this study) by means of resistance thresholds is a source of confusion (for example EUCAST proposes different thresholds in different clinical settings: #0.064 for CNS infection, and #0.5 up to #2µg/ml for pneumonia). The use of MIC50 / MIC90 would bypass this interpretation obstacle.

Discussion, 1st paragraph

4. The authors state: ‘…. predominately affecting younger patients with a urinary source for their bloodstream infection,…’

The authors present not enough data to support this statement. On multivariate analysis, increasing age had a protective role (by a factor of 3% per year), but among factors examined, multi-drug resistance was predominately driven by previous contact with the healthcare system.

Furthermore, some data need to be presented to prove the primarily urinary source in younger patients with MDR COBSI.

Discussion, 1st paragraph

5. The authors state that the Friedman criteria were less predictive for MDR GNB than they were for MRSA.

The odds ratio regarding MRSA BSI was arithmetically superior the OR for MDR GNB, but the authors need to state whether this difference was statistically significant.

Discussion, 5th paragraph and Table 2

6. The authors suggest that the published risk factors may be too general for BSI and may lead to overuse of broad-spectrum antibiotics.

The authors need to acknowledge that one should rather prefer a sensitive predictor of MDR BSI in the ED setting, rather than a specific one. The cost of over-use of broad spectrum antimicrobials is rather minimal in the case of BSI, provided that a de-escalation strategy is adopted. Furthermore, disappointingly, no innovative risk factors for MDR COBSI were identified (or reported) that would increase the sensitivity of the Friedman et al criteria. (Factors that would identify MDR in the remaining 17.8% of case patients). Instead, the authors concluded to a list of well-known and epidemiologically closely inter-related risk factors for MDR infection.

Table 3

7. History of diabetes and surgery in the prior 30 days are reported as independent predictors of MDR GNB, while the p-value is >0.05.

Table 4

8. Unexpectedly, several well-established risk factors do not predict death. Apart
from inactive empiric therapy (which is commented in the text), severe sepsis/septic shock and ICU admission were not predictors of a fatal outcome. How would the authors comment on that? Is it possible that the control group was not representative enough, and 1:2 or 3 case-control study would be more appropriate?

Minor essential revisions:

Last paragraph in Methods, ii) risk factors and outcomes associated with MDR COBSI.
The reference [1] should be followed by the ‘comma’.

Results, Risk factors for COBSI due to MDR organisms, 1st paragraph
The sum of MDR GNB and MRSA does not equal 180.

Discretionary revisions

Title
1. The title is a little misleading since the vast majority of MDR infections were healthcare associated (community-onset kind of points to community-acquired)

Methods/ Data collection and definitions
2. The authors state that ‘Repeat cultures from an individual patient growing the same organism within 14 days, cultures reported as normal flora or probable contaminants (eg. coagulase-negative staphylococci from a single blood culture bottle)…. were excluded. Some clarifications are needed. How can an organism be identified in the previous 14 days, since the study population presents to the ED from the community? This exclusion criterion could also be a source of bias, since in patients with healthcare acquired bloodstream infections there is a greater probability of positive blood cultures in the 14-day period prior to their ED presentation. In other words, certain patients with healthcare acquisition and MDR etiology would thus be excluded.

2. It would be more acceptable if MDR was defined according to some official document or consensus report, than previous studies in the field (references 10 and 11)

3. The authors state that ‘Multi-resistant MRSA was defined as MRSA resistant to three or more of the following antibiotics…..’
The authors need to state whether this was an arbitrary definition or derives from some reference.

4. The authors state ‘The EMRSA-15-like strain was defined as….’
Some clarification needs to be given on EMRSA-15-like strain. The general public might not be familiar with the term.

Results, Temporal trend of MDR organisms causing COBSI, 2nd paragraph
5. The authors state: ‘In contrast the incidence of MDR Klebsiella spp (n=11) and other Enterobacteriaceae (n=20) did not show a significant increase over time.’ It seems as if the statistical power of the study is too small to reach any conclusions about Klebsiella and Enterobacteriaceae resistance rates over time.

Discussion, in general

6. The discussion is a little long in relation to the results presented.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests