Reviewer's report

Title: Dynamics of Enterococcus faecium Clones Colonizing Hospitalized Patients: data from a prospective observational study

Version: 1 Date: 25 October 2011

Reviewer: Rama Narayana Deepak

Reviewer's report:

Major Compulsory Revisions:

1) State the aims of the study in very clear detail upfront. The study is not at all clear about what it purports to study. In Background (p5), "analyze the genetic diversity of E. faecium clones..." is not quite precise because only ARE were typed. The introduction to the study needs to be far more focussed.

2) Use a validated method (as recommended by an authoritative guideline like EUCAST or CLSI) to perform susceptibility testing on all isolates (not just invasive isolates). Enterococcosel agar with ampicillin is fine for screening, but it need to be followed up by a proper susceptibility test. Quote the breakpoints that are being used (presumably greater than or equal to 16 mg/L for resistance, but this needs to be clearly stated with a reference to back it up).

3) Numerous apparent errors and inconsistencies in the figures and calculations need to be addressed. Examples:

a) p9: "From a total of 184...25 were hospitalized...Sixteen patients (55%)". Why 55%? 16 patients out of 25 patients = 64%. I think you were taking the patients as the numerator but the hospitalizations (29) as the denominator, which is clearly unsound.

This is a recurring issue in the manuscript - confusion between "patients" and "hospitalizations". Please be more consistent and clear in your meaning.

b) Again, on p9. "Overall 354 RS from 80 patients..." How did you arrive at this? There were 33 included patients from group 1a, 25 from group 2 and 22 from group 3. But remember that group 3 also included 3 patients from group 1a, so this should be subtracted away, otherwise you're double-counting. So the total no. of patients should be (33 + 25 + 22 - 3) = 77.

c) Relating to a) above, on p11, "During three (7%) of hospitalizations..." - the entire paragraph is very confusing because it's not clear whether you're using patients or hospitalization episodes as your base of calculation. Clarify your meaning.

d) p11: Pertaining to group 2, "In only 3 patients (4 hospitalizations) no ARE were detected. This is inconsistent with Table 2 which shows: 2 patients with only ASE, and 2 patients with no E. faecium. 2 + 2 = 4, so why does your text mention
"3 patients"?

e) p12: a plethora of minor numerical inconsistencies between text and tables. Listing them:

"median of 21 days" in text, whereas table 4 says 20.

"most often polymicrobial (66%)" in text, table 4 says 67%.

"occurred early (median of 4 hospitalization days)." in text, table 4 says 3.

Please ensure your figures are internally consistent, at the least.

4) How exactly were ASE to ARE and ARE to ASE replacements identified in the study? More should be done to explain this. In any event, taking Table 2 at face value, in group 1a, there are seven ARE to ASE replacement events, in contrast to only one ASE to ARE event. This fairly interesting finding was left uncommented upon. However, for e.g. on p13, it's stated that "In hematological...ASE carriage was rapidly replaced by ARE, mainly MT159." which seems to be the opposite message from that given by the table. There may not actually be an inconsistency here, but there is certainly insufficient clarity as to how this conclusion was arrived at (and why the table seems to say something else).

5) Insufficient data on antibiotic consumption at an individual patient level greatly weakens the study. Since these patients were all admitted at least partially during the follow-up, extensive data on antibiotic consumption could have been collected from the medical record and analysed in correlation with the risk of ARE acquisition. Even though I appreciate that this would be an extensive undertaking, it should be done before resubmission.

6) On p14, these lines: "We used the SID...Therefore, we calculated the SID only..." seem to be a non sequitur. If (as you argued) the no. of isolates were too small to adopt the SID index, how does calculating the SID for a shorter timeframe mitigate the issue?

7) Another possible non sequitur (or poor clarity) in the next paragraph on p14: "During follow-up, 55% of patients...low sensitivity of the RS...". If more than half the patients carried more than 1 clone, how does this reflect low sensitivity of the culture method?

8) p16: "most ASE infections were polymicrobial cholangitis (83%)" should be rephrased to "most invasive ASE infections...". Please account for the fact that Table 4 states that 83% of invasive ASE infections manifested as hepatobiliary disease (which is presumably what you were referring to as cholangitis), yet, only 67% were polymicrobial. Clearly 83% could *not* have been "polymicrobial cholangitis".

9) Table 1: In group 1b, in the section under "Rectal swabs", why are there 3 median swabs per hospitalization, with an IQR given? Aren't these outpatients (hence precluding hospitalization)?
Minor Essential Revisions:

1) Justify this part: "If growth was documented only in a single swab, colonization time was defined as three days." Is there published precedent for this? If this is an arbitrary choice, please state this.

2) Various grammatical and typing errors:
   a) e.g. "2-3 months (sic) intervals" - "month" or "monthly" is better
   b) duplication of a line, viz. on page 12: "All 22 isolates.. None of the 22 invasive..."
   c) p16: patients misspelled as "pateints" (sic).
   d) Certain parts can be rephrased: ".including 6 not previously identified..." to ".including 6 previously unidentified...".
   e) Another example on page 7: "Randomly five..." to "Five colonies...were picked at random."
   f) One more instance on page 9: "43 hospitalizations. Among these...admitted from home." can be altered to: "hospitalizations, of which 41...were admissions from home."
   g) Another instance, p 10: "...and in 21 (84%)...this was an ARE was detected..." - the "this was" is unnecessary and ungrammatical.
   h) A final example of poor phrasing in Legend to Fig. 1: "Numbers of swabs and are shown..."

Please ask a native speaker/writer of English to edit the manuscript before resubmission.

3) p10: "The highest amount of patients". Amount should be replaced by proportion or percentage. The following line: "A minority of patients had one E. faecium clone" should be rephrased to "A minority of patients had one ARE clone" for precision.

4) p16: "associated with an immunosuppressed status...". This is vague, so please clarify what you're referring to here. if you meant "haematology patients", it's better to just state this for greater precision.

Discretionary Revisions:

1) Justify the use of 60mg/L aztreonam in Enterococcosel agar. Why is this gram-negative inhibitor necessary when you're subculturing from presumably isolated colonies on blood agar plates?

2) p12: "sensitive to vancomycin". Perhaps "susceptible" is a better substitute.
Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.