Reviewer's report

Title: Vancomycin and daptomycin minimum inhibitory concentration distribution and occurrence of heteroresistance among methicillin-resistant Staphylococcus aureus blood isolates in Turkey

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Reviewer: Elizabeth L Alexander

Reviewer's report:

The above article by Sancak et al addresses an important question in both clinical microbiology and infectious diseases: what is the incidence of elevated vancomycin and daptomycin minimum inhibitory concentrations and glycopeptide heteroresistance among Staphylococcus aureus isolates. The methods are well-described and the manuscript (for the most part) well-written. Nonetheless, there are several concerns which the authors must address prior to acceptance.

Major Compulsory Revisions:
1. Results- paragraph 3, line 1. The statistical methods and program used to determine the correlation between vancomycin and daptomycin MICs need to be defined.

2. The authors utilize the MacroEtest protocol, which uses a higher inoculum density (2 McFarland versus 0.5) and more enriched media (brain heart agar) than the Etest-GRD strip protocol which is used by some of the referenced publications (3, 23). They discuss causes of discrepancy between reported prevalence rates of hVISAs in the literature, including differences in inoculum size, but then state "we followed the manufacturer's recommended method and used 100uL inoculum size and found low sensitivity, similar to results reported by some of the studies (3,10,23). This is a somewhat misleading statement as despite the same inoculum, the methodology was not the same as all referenced publications. This should be clarified as it speaks to the authors' point regarding the large amount of variation between reports of hVISA prevalence.

Minor Essential Revisions:
3. Results - paragraph 4, line 2, "Using the MET, 26/175 (14.9%) isolates met the criteria for hVISA. The MET identified only 14 of the hVISA strains (sensitivity, 58.3%), and there were 12 strains identified as hVISA unconfirmed by PAP-AUC (specificity, 92.1%)." These two sentences are unclear and, at first pass, appear to be contradictory. How did 26/175 strains "meet criteria" for hVISA by the MET, but the MET identified only 14 of the hVISA strains? What would be very helpful here is a 4 X 4 contingency table where columns are positive and negative by PAP-AUC and rows are positive and negative by MET for vancomycin heteroresistance. This would clarify the above statement and also generate positive and negative predictive values for the MET which would be useful,
particularly given the authors' comments regarding "reevaluation of currently recommended MET cutoff criteria." in the conclusions.

4. Discussion - paragraph 4, line 1, "... while the prevalence of hVISA was detected as 13.7% (24/175) among easily be clarified by a contingency table.

5. MIC50 and MIC90 should be defined for the non-microbiologist reader.

6. Background, line 2 "paralells with" should be changed to "paralells" or "tracks with"

7. Background line 8, "Turkish hospital still now" should be changed to "Turkish hospitals"

Discretionary Revisions:

8. Discussion, paragraph 1, last line: Besides, the emergence of VISA and hVISA has been associated

Emergence is a potentially confusing word choice - does the author mean the presence of intermediate/hetero-intermediate vancomycin resistance or the development/evolution of resistance over time in clonal isolate (e.g. as described by Sieradzki et al, JCM, 2003)? This could be reworded to clarify.

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

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