Reviewer's report

**Title:** Cefditoren: Comparative efficacy with other antimicrobials and risk factors for resistance in clinical isolates causing UTIs in outpatients

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**Reviewer:** Spiros Miyakis

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The study by Hatzaki et al. reports the susceptibility results for ceftidoren, in comparison to several other antibiotics, tested on a big collection of UTI samples from a Greek multicentre surveillance network.

This is one of the largest cohorts reporting on this agent and the methodology is overall sound. The data presented are of potential interest to the readership.

Comments/suggestions for improvement are as follows:

1. Given the high rates of antimicrobial drug resistance in Greece, and that ceftidoren is a relatively new antibiotic, a comparison of its MICs in this study with those in the cohorts previously reported (refs 7-11) might be of interest.

2. P. 8 bottom to P. 9 top: I believe one of the most important findings of the study was the lack of association between resistance to ceftidoren and to first-line non-b lactam treatment options for community acquired UTIs (ie mecillinam, fosfomycin, aminoglycosides). But, I suspect that this might also be true for cefuroxime (since: A. the majority of cefuroxime-resistant strains -ie ESBL- were also likely resistant to ceftidoren, and B. The non-susceptibility rates between the two did not differ much). Was this tested? If true, it is worth mentioning, substituting for the first sentence of p. 9. Likewise, some of the statements throughout the manuscript (ie Abstract-Conclusions: ...representing an alternative... etc" and Conclusion p. 11: ...revealing its potential...antimicrobials") might need reconsideration in such a case, should they also apply for a 2nd generation cephalosporin.

3. In view of the above, perhaps a more detailed description of the susceptibility profiles of the ceftidoren-resistant strains (perhaps in a separate Table) might be informative.

4. p.5, 2.1 Demographic analysis, line 2: Can the authors provide more data on the random selection method?

5. The discussion does not address any weaknesses of the study. As such, I consider:

-the lack of clinical information in more than a third of patients (I realize that susceptibility results did not significantly differ between samples where data were available and the whole cohort, yet again some clinical data were associated with
ceftidoren non-susceptibility)
-the absence of outcome data (which attenuates the strength of the conclusions about its potential usefulness, view also of some available in vitro data, like those in ref 9 that the authors acknowledge)
-the absence of multi-variate analysis of factors for ceftidoren non-susceptibility

6. Have the authors any explanation on the co-resistance between ceftidoren and quinolones that was frequently observed?

7. Similarly, can the authors offer any interpretation for their findings on the risk factors for ceftidoren non-susceptibility? For example, fever might signify a pyelonephritis, which -along with history of UTIs- have been correctly classified by the authors as complicating factors (4.4 definitions p. 13). However, in page 10, authors advocate for the use of ceftidoren "in UTIs that...are not episodes of uncomplicated cystitis".

8. In the abstract is mentioned that Ceftidoren was tested via broth dilution MIC, whereas agar dilution is mentioned in the Methods section.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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'