Answering reviewers

June 05, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 3457-review.doc).

Title: Predictors of *C. difficile* infection severity in patients hospitalised in medical intensive care

Author: Nagham Khanafer, Abdoulaye Touré, Cécile Chambrier, Martin Cour, Marie-Elisabeth Reverdy, Laurent Argaud, Philippe Vanhems

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 3457

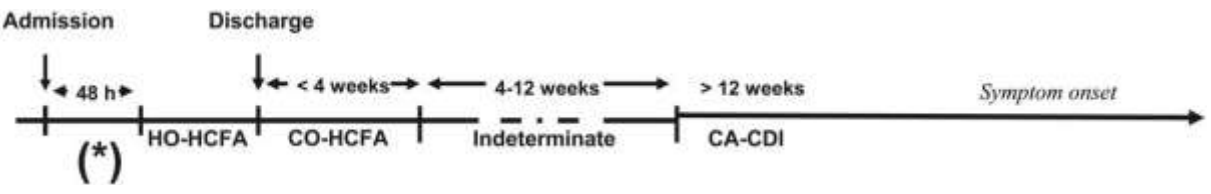
The manuscript has been improved according to the suggestions of reviewers. The format has been updated and references were corrected.

Response to "Reviewer 00420009"

1- Very well written. Risk factor assessment limited due to small sample size, but a tremendous time investment into the statistical analysis of this small sample makes the manuscript interesting. p 7 2nd paragraph and abstract - need clarification of case definition of a patient that was hospitalized 4-12 weeks prior to presentation. You have less than 4 weeks as hospital acquired and greater than 12 weeks as community acquired, what about those between 4-12 weeks?

Thank you for your comments.

We agree with your comment. According to French guidelines (Figure 1), a nosocomial CDI was assumed if diarrhoea onset took place more than 2 days after admission to hospital or if hospital admission occurred within 4 weeks of discharge and indeterminate or unknown if the patient had been discharged from a healthcare facility within the previous 4–12 weeks. Cases were defined as community-acquired if CDI signs presented in the absence of previous hospitalisation within the last 12 weeks in out- or in-patients within the first 48 h of admission. The definitions were corrected in page 7 and the abstract.



2- p 9 2nd paragraph - mortality is 12/40 for 52.5%, you wrote 55.5% p 10 final paragraph - clean up 3rd sentence where words run together

These typographical errors had been corrected.

Reviewed by 02457614

1- Good question to ask - do these factors hold true for sick medical patients? The same prognostic factors probably do. Some points: 1. this is a small numbered, single centre study and this should be acknowledged as a limitation with lack of generalisability.

We agree with this comment, our study has some limitations which need to be considered when interpreting the data. These limits were cited at the end of the discussion paragraph.

2- The description of the models is inadequate. were the final features added in and left in the model? or were some elimitated to test model fit? An additional table is needed: univariable OR and 95% Confidence intervals, and multivariable too.

Thank you for your comment. As you suggested, we added a table with the results of univariate and multivariate analyzes. Univariate analysis showed that Glasgow coma score, gender, diabetes mellitus, previous exposure to fluoroquinolones, PPI or Coamoxiclav, and C-reactive protein were statistically different between severe and non-severe patients. All potential risk factors significant at the 0.2 level in univariate analysis were entered into the model and goodness-of-fit was assessed by the Hosmer-Lemeshow test. Final multivariate analysis included male gender, C-reactive protein levels, and fluoquinolones which were independently associated with severe CDI.

3- there are too many unfocussed references, missing these key ones which should be inserted - a meta-analysis which covers most of this, and a relevant paper: Bhangu A, Nepogodiev D, Gupta A, Torrence A, Singh P. Systematic review and meta-analysis of outcomes following emergency surgery for Clostridium difficile colitis. Brit J Surg, 2012 Nov;99(11):1501-13. Bhangu S, Bhangu A, Nightingale P, Michael A. Mortality and risk stratification in patients with Clostridium difficile associated diarrhoea. Colorectal Disease, 2010. 12: 241-246.

We agree with the reviewer on the high quality of these two references. We added them in your suggestion.