Author’s response to reviews

Title: RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS IN BRONCHIECTASIS EXACERBATIONS

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Answer to reviewers BMC

Editor Comments:

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Reviewer reports:

Silvano Esposito (Reviewer 1): This is a good original paper investigating prospectively the possible risk factors for an MDR etiology in patients with exacerbation of chronic bronchitis and bronchiectasis.

The paper is well done, well designed and well written, but it would deserve some revision

Title: I would say ... in patients affected by exacerbations of chronic bronchitis and bronchiectasis

Answer: We have considered that suggestion, however we prefer to maintain only bronchiectasis in order to avoid misinterpretation with other patients with chronic bronchitis and/or COPD.

Patients and methods

Please specify which identification method was adopted and what susceptibility test was utilized as well.

If an automatic conventional test was utilized please note in the discussion its limits compared with newer molecular test citing the following paper

Answer: In the new version we have added the identification method used and the susceptibility tests. With regard to the comment about automated conventional tests we have added a sentence in discussion and the suggested reference below (Yeliz Çetinkol Y et al, reference 14)

In the same section you report that patients were investigated also for blood cultures, and bronchoalveolar lavage specimens but you don’t mention any result about that. It would be interesting to know the results of these investigation. Also for possible viral etiology no data is reported.

Answer: Blood cultures and BAL specimens were only required if indicated by the attending physicians. In the new version, we have added the number of samples obtained and we have also included the viral etiology.

The risk factors for MDR microorganisms have been investigated by several authors and they are well defined. I would add the following references.


Answer: Following the suggestion of the reviewer, the two prior references have been added in the discussion of the new version (references 22 and 25)

But none has investigated about the bronchiectasis and exacerbation on chronic bronchitis. The severity of respiratory dysfunction and the severity of bronchiectasis itself (you mentioned that a severity score was calculated) could play an important role also on the MRD etiology. This should be mentioned
Answer: We totally agree, the severity of bronchiectasis plays a very important role on MDR etiology. In fact, almost 80% of MDR exacerbations occurred in patients with higher punctuations in the well-validated specific bronchiectasis scores: FACED and BSI. However, in the multivariate analysis prior hospitalization was more decisive in prediction of MDR. It has been more extensively commented in the new version.

Sithembiso Velaphi (Reviewer 2):

Summary of the article from my understanding: This is a descriptive study with its objective being to determine risk factors associated with isolation of multi-drug resistant organisms (MDRO) in adults with non-cystic fibrosis bronchiectasis. A total of 233 patients were included in the study of which 159 had an organism isolated from the sputum or specimen sent. Of the 159 patients 32 grew multi-drug resistant organisms. Patients with multi-drug resistant organisms were more likely to require hospitalization. The risk factors associated with growing multi-drug resistant organisms were having renal disease, prior multi-drug resistant organism isolation and hospitalization previous year.

My Comments:

Abstract: Under results, the statement that MDRO were more frequent in hospitalized patients give impression that the specimens were taken in patients who were hospitalized already, yet it was not the case, rather those who had MDRO were more likely to require hospitalization. They must rephrase the sentence. They must put a p-value next to percentages comparing hospitalization rates. I suppose they meant Enterobactericeae when they used the word Enterobacteria- please recheck. They must include confidence intervals next to the Odds ratios.

Answer: The sentence has been rewritten in order to improve the information. Exacerbations caused by MDR microorganisms were more frequent in those with prior isolation of MDR, that is those with chronic colonization and/or infection (Table 1). Besides, during the current exacerbation, MDR microorganisms were more frequent isolated in patients that required hospitalization due to the exacerbation compared to those treated as outpatients. Those are our main results, and in the multivariate analysis we have also found that prior MDR was an
independent risk factor for MDR etiology during exacerbation. That circumstance is frequent in patients with chronic infection although it has not been studied in bronchiectasis until now.

We have added p-value as requested, we have used Enterobacteriaceae and we have included 95% Confidence Intervals to the odds ratio.

Methods: My understanding is that they included first exacerbations, suggesting that they included patients who never had bronchiectasis exacerbations before. They need to describe what they meant by first, because when they present the results they include patients with previous hospitalizations which is not clear whether the hospitalizations were related to bronchiectasis exacerbations or not. Because if they were then they cannot say the patient had first exacerbation. Therefore they need to describe what they meant by first or if first is what I understand they meant then should exclude patients with previous bronchiectasis exacerbations.

Answer: Bronchiectasis is a chronic disease and patients have been referred to our specific clinics in two tertiary care centers in different phases of the disease. We mean that we consider almost impossible to enroll patients in the first exacerbation in their natural course of their diseases. That circumstance is identical for all hospitals. In fact, in international registries for bronchiectasis in adults (EMBARC), it is allowed to enroll chronic patients not naïve and with prior hospitalizations as other colleagues in the world do. In our two clinics of bronchiectasis we assist patients from other hospitals, from primary care or other facilities, and in all cases after referral we confirm the bronchiectasis diagnosis, perform a diagnosis study according to Spanish guidelines and follow up patients. For this study, we have obtained approval from the ethics committee and then the signed consent of the patients; after that process we initiate the recruitment for exacerbations; that is why we have included the first exacerbation after obtaining the informed consent to recruit patients for this study. In the new version it has been more extensively explained.

Results: The authors state that there were 32 patients with MDRO which was 20.1% of 159 patients with microorganisms isolated, and but they also state that the 32 MDRO accounted for 20.1% of microorganisms isolated which is not correct as there were 241 microorganisms isolated according to Table 2 and therefore 32/241 is not 20.1% - they need to correct the statement in the first sentence under microbiological results. And number of MDRO listed is 31 not 32. They must state as to which other bacteria other than MRSA and Pseudomonas were MDR and which Enterobactericeae were MDR. What does the superscript 'a' in Table 2 next to MDR denote as it is not explained at the top or bottom of the Table?
Answer: In the new version, it has been corrected and better explained

The first sentence under the sub-heading Follow-up is difficult to understand- what are the numbers in parenthesis represent especially the numerators, as the totals 153 and 73 have not been explained or mentioned before.

In Table 4- they should include all the other variables that were included in the multivariate analysis even though they were not significant so that the readers can see what was included and what were the odds ratios or p-values.

Answer: In the new Table 4 we have included non-significant variables

In Figure 1- the last blocks must be changed to 'Required or Not Requiring Hospitalizations' because as they stand now, it appears as if the specimens were taken from patients who were in hospital and those who were outpatients which is not my understanding, as all patients were coming in with new exacerbations therefore could not have been hospitalized already.

Answer: In the new Figure 1 the blocks have been changed to “Required or not requiring hospitalization

Under discussion: In their conclusion to also relate to the main objectives of the study, regarding risk factors.

Answer: In the conclusion the independent risk factors have been specifically related.