Author's response to reviews

Title: Clinical presentation and predictors of outcome in patients with severe acute exacerbation of chronic obstructive pulmonary disease requiring admission to intensive care unit

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Author's response to reviews:

The manuscript has been once again revised as per the valuable suggestions of the Reviewer and the further revised manuscript is being submitted for re-consideration for publication. A point-wise reply to the Reviewer's comments is also being enclosed.

Version: 3 Date: 5 November 2006
Reviewer: Angshu Bhowmik
Reviewer's report:

General
Comment #1
Regarding comment 4d in the previous review, the authors have justified the inclusion of patients with past or treated pulmonary tuberculosis in the current study and I accept this argument. However, my query was about the inclusion of current or active pulmonary tuberculosis. This study purports to examine the predictors of outcome of severe AE-COPD. But by including active tuberculosis, the study is confounded as the predictors and features found may turn out to be those of tuberculosis (which is also often a fatal disease). Hence, we cannot be sure if the results are leading us to risk factors for mortality in AE-COPD or risk factors for mortality in tuberculosis. The fact that 5 of the 16 deaths were in patients with active tuberculosis leaves me wondering if the predictors of mortality would change if these patients were excluded from the analysis.

Reply
We would like to clarify to the Reviewer once again as to why we wish to include the patients with active tuberculosis in this study. None of the five patients with AE-COPD who had active pulmonary TB had any symptom or sign suggestive of active TB when they last presented to the out-patient department for follow-up prior to the ER visit with AE-COPD. Furthermore, they also did not have any past history of TB. Only at the time of the ER visit with AE-COPD was pulmonary TB diagnosed in them. Similar to bacterial and viral causes that are known to cause AE-COPD in the west, we consider pulmonary TB to be an infective aetiological cause of AE-COPD. We believe this information to be new and useful especially in areas where TB is highly endemic. These details have been incorporated in the further revised manuscript under the "Results" and "Discussion" sections.

Comment #2
Regarding comment 5a, the authors have not actually changed the first paragraph of the discussion as suggested but merely added 2 lines about the background of the study. The remainder of the paragraph largely remains an analysis of bidi smoking rather than a summary of the important findings and relevance of this paper.

Reply
We have once again attempted to redraft the first paragraph of the discussion as per the Reviewer's suggestion. The redrafted paragraph reads as follows: "Reliable epidemiological data regarding the burden of AE-COPD in the ER are lacking from India. Even less is known regarding the clinical presentation and outcome of AE-COPD in a predominantly bidi smoking population similar to the patients included in the present study. Observations from the present study indicate that patients with AE-COPD had one or more co-morbid conditions and metabolic abnormalities at presentation. Furthermore, high prevalence of past pulmonary TB was observed and active pulmonary TB was identified to be an important infective cause of AE-COPD.

Comment #3
In paragraph 2 of the discussion, the sentence "When patients present to the ER with severe AE-COPD, and "is in" (should be "and are found to have an") altered sensorium; in addition to type II respiratory failure and carbon dioxide narcosis, metabolic derangements such as dyselectrolytemia, uremia and hepatic function derangement could also contribute to the altered sensorium." is poorly constructed and should be revised.

Reply
As suggested, the sentence referred to by the Reviewer has been revised and it reads as follows: "Several causes can contribute to altered sensorium in patients with AE-COPD. These include, type II respiratory failure and carbon dioxide narcosis, metabolic abnormalities such as dyselectrolytemia, uremia and hepatic function derangement among others. As these can be corrected, an active attempt must be made to identify them when patients present to the ER with AE-COPD."

Comment #4
Comment 5b: The authors have included the information that all the patients with altered sensorium had dyselectrolytemia. However, dyselectrolytaemia is used for a range of metabolic abnormalities and I am not clear about how the relationship between specific abnormalities and altered sensorium was tested - the details of statistical tests, if any, have not been included. Table 4a still only includes hypoalbuminaemia, elevated transaminases and acidosis as the only predictors of poor outcome.

Reply
We would once again like to clarify to the Reviewer that our study provides evidence that many patients with AE-COPD also have metabolic abnormalities such as dyselectrolytemia (hyponatremia, hypokalemia), uremia, hepatic function derangement. These could have been due to the disease process per-se or due to the co-morbid conditions that co-existed. If the hospital setting where patients with AE-COPD are treated did not have the facilities for round-the-clock ABG analysis and serum biochemistry evaluation (which is by and large the situation in primary health centres, district hospitals and general hospitals in India), many of these otherwise correctable abnormalities would have been missed. These were specifically looked for in the present study. However, in the analysis for predictors of death, not all but only some of these factors (hypoalbuminaemia, elevated transaminases) emerged as significant predictors of mortality.

We presume, therefore, that if metabolic abnormalities such as hyponatremia and hypokalemia which did not emerge as predictors of mortality had remained undetected, they would have further contributed to the mortality. In light of this background we would like to retain the information about electrolyte abnormalities as it is written in the revised manuscript.