Reviewer's report

Title: The Natural History of Anemia in Hospitalized Community-acquired Pneumonia

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Reviewer: Paula Peyrani

Reviewer's report:

This is a very interesting article trying to describe the natural history of anemia and CAP. However, I have major concerns with some sections of this manuscript. Please see my comments below.

1. MAJOR COMPULSORY REVISIONS

TITLE
Comment #1. The natural history of anemia in hospitalized CAP is difficult to be assessed.

Even though most of the patients had several hemoglobin assessments performed during hospitalization, the fact that prior medical history regarding hemoglobin values and values after discharge are not available makes very difficult to analyze the so called natural history. Instead it is more a descriptive evaluation of anemia status of hospitalized patients with CAP, on admission, during hospitalization, and at discharge. Given this scenario, I think that the association between anemia and mortality at 90 days becomes the relevant point and the title should be modified reflecting so. Examples would be “Association of Anemia with 90-day mortality in hospitalized patients with CAP” or already giving a hint about the results “Anemia is Associated with Increased 90-day mortality in hospitalized patients with CAP”.

ABSTRACT
Comment #2. Objective missing in the abstract.

Even though it can be inferred from the background paragraph, the objective of the study should be described and written in the abstract.

BACKGROUND
Comment #3. Natural history of anemia as primary objective is difficult to assess from available data.

In relationship with what it was already mentioned in comment #1, I would strongly suggest to modify the primary objective to the evaluation of the association of anemia with 90-day mortality and keep the descriptive section of hemoglobin as a secondary objective.

METHODS
Comment #4. Study outcomes not defined in M&M

The authors defined how anemia was classified and how mortality data was captured. It is not clear from this section if the analysis of variables independently associated with moderate to severe anemia was performed with hemoglobin values at any time during hospitalization (as stated for 90-day mortality) or at other time. Since different denominators are being used for the study outcomes, it may help if the paragraph of clinical definitions and outcome variables is divided in study definitions and study outcomes specifying for each study outcomes when it was assessed.

RESULTS

Comment #5. Anemia over time. Interpretation/discussion given in the results section.

Page 9. Second sentence to the last: “Over time, hemoglobin value converged…, due in part to the 176 subjects that received at least one blood transfusion”. Author’s interpretation of results should not be given in this section.

Comment #6. Variables independently associated with the development of moderate to severe anemia. Odd ratios should not be interpreted as relative risk/risk ratio.

The authors concluded that “white race and chronic respiratory disease were associated with lower odds of developing anemia”. Odds ratios should not be interpreted as relative risk or risk ratio when the outcome has a high prevalence such in this case where at least moderate anemia was found in 27% of patient during hospitalization and 16% at discharge. One solution could be to use a different statistical methodology to obtain risk ratio. Otherwise, I think this should be stated as a limitation of the study

DISCUSSION

Comment #7. Discussion about possible pathogenesis of results is not included.

The authors found that moderate to severe anemia is associated with increased 90-day mortality but they are not discussing why they think this association occurred. This may be the section to have some more detailed analysis/speculation regarding cytokines production in CAP and the link with anemia.

2. MINOR ESSENTIAL REVISIONS

RESULTS

Comment #8. Page 8. Study population and outcomes. Sentence starting: “After day 1, hemoglobin values… subjects that remained hospitalized each day” should read “… subjects who remained…”

Comment #9. Page 8. Study population and outcomes. Sentence starting: “Of the 1893 in…, 114 (6.0%) has positive…” should read “…114 (6.0%) had positive …”
Comment #10. Page 9. Anemia over time. Sentence stating: “Over time, hemoglobin values…, 176 (9.3%) subjects that received…” should read “…176 (9.3%) subjects who received …”

Comment #11. Page 9. Anemia over time. Sentence starting: “Of those that were transfused…” should read “…Of those who were transfused …”

Comment #12. Page 10. Anemia and its association with 90d mortality. Sentence starting: “This increased risk persisted… to subjects that survived…” should read “…to subjects who survived …”

DISCUSSION
Comment #13. Page 10. Anemia over time. Sentence starting: “Consequently, …depending on hemoglobin values for those that were not…” should read “…depending on hemoglobin values for those who were not …”

TABLES
Comment #14. Table 2. Page 23. Suggest to modify for each row title: “Anemia on …” to “Hemoglobin on….” No anemia is included as part of the results so technically this would not be Anemia.

3. DISCRETIONARY REVISIONS

DISCUSSION
Comment #15. Page 12. Last paragraph. Sentence starting: “In our study, the presence of moderate to severe anemia was independently associated with 90d mortality…” Suggest to add the word increased before 90d.

Comment #16. Page 13. Limitations. I would not consider as a limitation that outpatients were not included since it is stated in the title and M&M section that this were hospitalized patient with CAP.

Comment #17. Page 13. I think it is not appropriate to suspect that acute GI bleed was uncommon juts due to the reason of patients consenting to participate in the study. I would remove this explanation.

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