Reviewer's report

Title: 'Sepsis-related anemia' is absent at hospital presentation; a retrospective cohort analysis.

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Reviewer: Angela Lipshutz

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In this retrospective cohort study of ICU patients, Jansma, et al. determine the hemoglobin concentration during the acute phase of sepsis, prior to medical intervention, and compare this value to non-sepsis controls. They find that prior to intervention, the hemoglobin concentration does not differ between the two groups. In a secondary analysis, they compare the hemoglobin concentration between the two groups at ICU admission (after resuscitation in the ED), and find that, even after controlling for the amount of fluid administered, sepsis patients have a lower hemoglobin concentration. Although this finding is interesting, I believe the manuscript requires significant revision prior to publication. Please see my comments below.

Major Compulsory Revisions:

- The authors have several interesting findings in this paper: (1) the hemoglobin concentrations between sepsis and control group do not differ and ED admission and (2) the hemoglobin drop between ED and ICU admission was larger for sepsis patients even after controlling for intravenous fluid administration. (It goes without saying that hemodilution may cause a larger drop in Hgb in septic patients who are fluid resuscitated in the ED, but it is interesting that even when controlling for IVF, the difference persists). I recommend making these two messages more clear in your manuscript. Elaborate on how this paper adds to the literature on this topic.

- Please describe further the “database” you used (Materials and Methods, page 6). What database? How is the data collected? Prospective? Retrospective? Was it collected for another study?

- What severity of illness score was used? (I assume APACHE II since it is mentioned in the results. This should be detailed in the Methods section.)

- You state you collected data on the “existence of co-morbidities.” Please elaborate—what co-morbidities? (Is it only the co-morbidities listed in Table 3? What about CAD? CHF? CKD? Hematologic disorders?)

- Please describe further what is meant by the subgroup of patients who were “directly transferred from the ED to the ICU.” These patients received no treatment in the ED?

- It would be interesting to know what percent of patients in each group were brought in by ambulance. These patients may have received fluids in the field,
such that the Hgb in the ED is not really “prior to medical intervention.”

- Please describe further your multivariate regression. Include a table with multivariate regression results, as well as the results of a goodness of fit test.

- You state that there were 2500 nonelective ICU admissions during your study period, but only 616 patients are included in your study. Why were the other ~1900 patients excluded?

- You state in your results that “except for age and APACHE – II score, there were no significant differences…” I would argue that age and APACHE II score are two major factors and would reword this sentence to reflect that. (ie: “Patients in the S group were older and sicker than patients in the C group.”)

- Creatinine and urea was higher in the S group, which could be a marker of chronic renal disease but could also be an indicator of critical illness and organ failure (S patients were older/sicker, and organ failure was an indicator for inclusion in that group). Do you have the ability to compare to baseline creatinine to see if the elevation is acute or chronic? Can you look at urine output during the ED course?

- LDH and bili were also higher in the S group. Do you have data from peripheral smear to suggest hemolysis? LFTs?

- A much larger group of C patients were directly admitted to the ICU than S patients, which could affect your results. This should be discussed in the discussion section.

- Second sentence of “Secondary outcomes” on page 8 is confusing, since the sentence before it is discussing the direct admits. (But the second sentence must be referring to the patient NOT directly admitted since it is comparing ED to ICU Hgb.)

- In your discussion, you state that the “clear correlation with intravenous fluid administration…point[s] towards an iatrogenic component…” However, you also find that IVF alone doesn't explain the difference. You should state this here and elaborate on potential reasons for that.

- Page 10 “we confirmed the absence of hemolysis.” How? You state previously that LDH and bili were higher and may be due to hemolysis.

Minor Essential Revisions:

- This is a well written paper but would benefit from editing by a native English speaker.

- You should mention fluid administration as one mechanism of anemia in sepsis both in your abstract and your introduction.

- Please include p values (do not say “ns”)

- Page 11 “Forty-two patients could not be identified in one of both groups as a result of incomplete documentation..” Not sure what this means. Please clarify.

**Level of interest:** An article of limited interest
Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare I have no competing interest.