Reviewer’s report

Title: Clinical and Biochemical Factors to Predict Biochemical Adrenal Insufficiency in Hospitalized Patients with Indeterminate Cortisol Levels: a Retrospective Study

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Reviewer: Claudine Blum

Reviewer's report:

This is a small retrospective analysis on clinical and biochemical predictors of adrenal insufficiency in hospitalized patients. One very impressive result is that random cortisol in this cohort is a better predictor for adrenal insufficiency than 08h00 cortisol. What I am missing here is a potential bias through a smaller number of patients having a 08h00 cortisol than the random cortisol sample. If this is the case, I would expect this to be a limitation.

Apart from random cortisol level, a higher cholesterol, if I understood correctly, lower creatinine, and lower serum sodium were biochemical predictors of adrenal insufficiency.

A large subset of patients had a history of exogenous steroids including herbal remedies. Therefore, I invite the authors to discuss whether elevated cholesterol and a lower creatinine could be a side effect of previous steroid exposure - lower creatinine through steroid-induced sarcopenia. I would rather suggest these two biochemical indicators are a surrogate marker for previous steroid exposure. Hyponatremia, however, is a well-known concomitant phenomenon of adrenal insufficiency.

It would be interesting to know whether these three markers were similarly distributed between patients with and without previous exogenous steroid exposure. However, I understand that due to the small number of patients with adrenal insufficiency, the subgroups might be too small for comparison.

In the limitations section, I encourage the authors to highlight that due to the retrospective nature of the study, no conclusion can be drawn on cause or effect of the results.

As the authors aim to create a predictive model, I suggest giving cutoff values with probabilities. Crude numbers do not allow to calculate probability of adrenal insufficiency or individuals, as the crude values don't differ effectively between groups. Did you try cutoffs for developing a practical model?

Table 1: Lines with n (%) in the cell with indication of test shifted. Please adjust (separate lines for each item?)

In summary, this manuscript nicely describes clinical and biochemical predictors for adrenal insufficiency in a small cohort of hospitalized patients.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
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Acceptable

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