Reviewer's report

Title: The effect of trauma and alcohol on the relationship between level of cytokines and depression among patients entering psychiatric treatment

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Reviewer: Pablo Barrio

Reviewer's report:
In this manuscript, the authors conduct a study to investigate how alcohol use and trauma might influence the relationship between depression and cytokine levels. After completing the analysis, authors suggest trauma might have some influence on particular cytokine levels in depression patients, while finding no evidence of alcohol use affecting the immune response in this population.

Overall, I think the manuscript is well written and deals with an interesting and important subject. However, I have some concerns regarding its methodology, especially statistical analysis, that make it unacceptable for publication in its current form.

Basically, my main concern is that, as authors themselves acknowledge, it looks like there are many potential confounding variables and using univariate tests as the manuscript does in its current form does not provide an accurate and reliable methodology for dealing with such "dangers", which in fact increase the risk of type I error (also type II, but type I is far more important, see limitations section). Although authors try to address this limitation by stratifying analysis and selecting some patients to be compared with controls, there is definitely better ways to handle this at the statistical level. I suggest authors perform regression analysis taking into account confounding variables available in their dataset, such as age, gender, (weight, if measured, ), level of depression, AUDIT score, and so on. Actually if one looks at similar, previous literature, this kind of analysis is rather the norm. Also worth mentioning, in its current form, the analysis of data runs into a multiple comparison situation, where at least a Bonferroni correction or similar method should be used, again to provide a reliable "prevention" of type I error. Maybe authors could construct a regression model for each of the cytokines investigated,
and see what the results are. I think that would provide a much more reliable estimate of the putative influences of trauma and AUDIT on cytokine levels.

Given the previous comment, it is not possible to comment on the discussion, since regression analysis might change the results and therefore a new discussion should be elaborated.

Other minor comments that I would make are:

- minor language corrections needed (for example abstract section, methods: "the study was a cross-sectional assessment of patients at admission to a (not the) specialized psychiatric center in Norway)

-In line 37, it is not clear to me whether authors mean that il-6, 10, 17A and ifn-Y were measured in all patients but in none of them detectable values were found? Isn't that a little bit surprising?

-authors talk about speramsn correlation coefficient used in the methods section, but it is never mentioned again in the results section.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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.

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