Dear Editor,

Please find enclosed the edited manuscript in Word format (Manuscript number 4534 - World Journal of Hepatology.)

TITLE: Disease dependent qualitative and quantitative differences in the inflammatory response to ascites occurring in cirrhotics

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NAME OF JOURNAL: *World Journal of Hepatology*

ESPS Manuscript NO: 4534

The manuscript has been improved according to the suggestions of the reviewers.

General:

Abstract: Conclusion is now 26 words or less

Manuscript: References were adjusted ad described

Reviewer 1:

Introduction:

Reviewer: Why did we choose to assess these 12 cytokines, interlukins and growth factors?
Response: We added: Previous studies have reported that cytokine characteristics of the Th1 response are increased in decompensated cirrhosis especially with infection. IL-4 which is a major cytokine of the Th2 response was not significantly different between decompensated cirrhotic patients with infected or non-infected ascites. The current study was designed to confirm these findings and expanding it to study the role of growth factors in cirrhotics with non-infected ascites.

Reviewer: What end points were used to make the decision?
Response: Decompensated cirrhotic patients with infected or non-infected ascites.

Methodology:

Reviewer: How to group? These were added:
Response: Four distinct etiologic groups of cirrhotics were identified and the cytokine levels were compared between groups in an effort to examine the role of the etiologic factor responsible for cirrhosis in each subgroup.

Reviewer: Inclusion criteria?
Response: We added: Inclusion and exclusion criteria
Inclusion criteria: 1) cirrhosis documented by imaging (either an abnormal CT or US) or liver biopsy 2) ascites requiring a large volume paracentesis because of tense ascites and failure to control the ascites with diuretics (furosemide and spironolactone) 3) willingness to undergo a large volume paracentesis and sign an informed written consent documenting their participation and allowing for the additional studies required as a result of their participation.
Exclusion criteria: 1) no evidence for cirrhosis 2) no ascites or adequate ascites control with diuretics. 3) unwillingness to participate and sign an informed written consent.

Reviewer: The authors'analysis? You should add the label such as *p<0.05 in tables 2-6
Response: We agree with reviewer. We have mentioned in the text that our results did not reach statistical significance between the four etiologic groups ($p<0.05$) and we added the P value to our tables.

Reviewer: There are some mistakes in table 1(0.5/3→ 5/3) 0.2/2 →2/2)
Response: We apologize for a mistake in typing this table. The table was corrected. Thanks to the reviewer

Reviewer: The authors did not tell us what's the meaning of the positive/negative value for the plasma-ascitic fluid gradient. The authors did not describe the relative data from table 6 (now it is table 5 because we merged table 1 and 2)
Response: We added: The data shown in table 5 (it was # 6 in original manuscript) consisting of the serum-ascites gradient enables one to determine whether the primary source of the measured factor arose from the vascular space or the peritoneal cavity. Specifically, those with the positive value identify a primary vascular source of the measured factor while a negative value identifies these factors having their origin in the peritoneal cavity.

Discussion:

Reviewer: There is no emphasis on results and conclusion on findings. Which cytokines present a high vs. low risk for SBP

Response: We added: Factors likely to represent protective cytokines associated with a reduced risk for SBP include EGF, TNF-α, IL-1A, IL-8, and IL-10. Those are more likely to be associated with potential for SBP include: IL-1B, IL-4, MCP-1, and IFN-γ

Reviewer 2

Reviewer: What kind of patients with CA? HCC? Or others?
Response: The cancer patients consisted only of those with extra-hepatic neoplastic disease other than hepatomas.

Reviewer: Table 1:
There are some mistakes in table 1(0.5/3→ 5/3) 0.2/2 →2/2)
Response: We apologize for a mistake in typing this table. The table was corrected. Thanks to the reviewer

Reviewer: What is the meaning of CPS
Response: Child-Pugh Score (CPS). We apologize for the abbreviation without text. We corrected it to: Child-Turcotte-Pugh (CTP) score.

Reviewer: Better expression of data
Response: We added further explanation to the tables in the discussion section

Reviewer 3

Reviewer: The statistical values in table 2-6?
Response: None of these values were significant. The p Value was added to all tables. They did not reach statistical significance because of the range of values which is very broad and relatively small number in each of the four groups.

How often bacterial peritonitis occur in this study
Response: None. Infection was considered as part of the exclusion criteria

Reviewer: In general, PCT is related to bacterial infection. PCT level was higher in malignancy group than in other three groups. Malignancy group is unlikely to develop bacterial peritonitis.
Response: Yes, the reviewer is correct about the statement. But we have no explanation for why PCT values are increased in malignancy except to suggest because of their malignancies some occult subclinical infection may have existed in this subgroup.

Reviewer 4

Reviewer: Further clarification on patterns?
Response: To clarify the suggested role of cytokines in this study we added: Factors likely to represent protective cytokines associated with a reduced risk for SBP include EGF, TNF-α, IL-1A, IL-8, and IL-10. Those are more likely to be associated with potential for SBP include: IL-1B, IL-4, MCP-1, and IFN-γ.

Reviewer: The project needs to move on to an interventional study
Response: We agree with the author that our next project should involve an interventional study.

Reviewer: The introduction is very brief
Response: We expanded the introduction

References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,

Bashar Attar

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