

Reviewer 1#

**Comment :** The manuscript focus on Assessment of tumor markers CA19-9, CEA, CA 125, CA 242 for early diagnosis and predicting prognosis of gallbladder cancer, after checked the references in Pubmed, many researches focus on gallbladder cancer and CEA,or CA125, but no research on the 4 markers together.

**Comment 1:** Among the 4 markers which was most important with gallbladder cancer?

**Response:** All the four markers was important but in the present study CA 242 followed by CA 19-9 was most sensitive in the detection of GBC while CA125 was most specific in the diagnosis of GBC, however CA 242 and CA19-9 in combination was more specific and sensitive.

**Comment 2:** In discussion we can add in previous data which was the most relevant marker and in our study what is the interpretation.

**Response:** Added (please refer discussion section, page number 12)

**Comment 3:** Any maker was no relation with the survival looks strange? Can you analysis combined of 2 or 3 Or 4 markers expressions with the survival?

**Response:** We agree that the difference between mean survival with respect to normal and elevated levels of tumor markers was not significant in this study. These findings may be explained by the inclusion criteria, as in the present study, only early and suspicious cases of GBC were included. (Added as the limitation of this study, please refer page number 13)

We have tried to analyze the combination of 2 or 3 or 4 markers expression with the survival but there was no significant difference in any of the combinations may be due to small sample size.

**Comment 4:** The Figures need perfect.

**Response:** Revised. (Please refer Figure number 1, 2, and 3)

**Comment 5:** The English need much more polish.

**Response:** We have revised the draft to the best possible extent. Hope this is acceptable.

Reviewer 2#

**Comment 1:** The present study suggested that serum levels of tumor markers including CA19-9, CA125, CEA and CA242 were significantly associated with GBC. However, no significant association was observed between the presence of elevated levels of any marker and survival. This is an observational study, but the novelty may not be very high, because the role of each molecular indicator in the disease has been reported.

**Response:** We agree that we couldn't find any significant correlation between tumor markers and survival outcome as the limitation of this study was that we included only early and suspicious cases of GBC. The main aim of this study was to make early diagnosis of GBC on the basis of tumor markers which itself will lead to better survival outcome. Many researchers focus on gallbladder cancer and CEA, or CA125, but no research has been done on four markers together, especially from India.

**Comment 2:** Add DSS, DFI, PFS of patients.

**Response:** We have calculated the DFI from master chart and added in the result section. However, DSS and PFS are beyond the scope of this study. (Please refer result section, page number 11)

**Comment 3:** The language needs some correction.

**Response:** We have revised the draft to the best possible extent. Hope this is acceptable.

**Comment 4:** Limitations also require further discussion.

**Response:** Added (Please refer page number 13)

**Comment 5:** The discussion section should also be expanded to comprehensively evaluate current research progress.

**Response:** We have revised the section. (please refer page number 12)