

Professor Subrata Ghosh,
Editor-in-Chief,
World Journal of Gastroenterology.

Subject: Revision and resubmission of **manuscript No.: 66727**, Case Control Study

Dear Professor Ghosh,

Thank you very much for considering our manuscript for publication in the reputed WJG. We greatly appreciate the reviewers for their valuable comments and suggestions. As per the suggestion of the worthy reviewers, we have performed the requisite editing and technical revision of the manuscript. Besides, please find the attached point-by-point response to reviewer's concerns according to journal guidelines. Looking forward to your positive decision on the manuscript.

Best Regards

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Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Abstract and Title significantly synchronize with the aim and methodology of the paper for evaluating the relevant biomarkers for early prognosis and diagnosis of pancreatic cancer. To the health community the paper has significant findings for the service of public health. The paper while clear in its objective and findings fails to represent the results and findings diagrammatically or through statistical charts and graphs analyzing the data from 50 patients. Authors of the paper themselves admitted their limitation to find the association of DPC-4 G>T and BRCA-2 6174 deletion mutations and hypermethylation of CpG islands in the promoter region of RASSF1A and hMLH1 gene towards the risk of PC. To validate these results in the Kashmiri population the future studies need comprehensive, cohort, and replicative studies with a large sample size.

Reply to specific comments: Thank you so much for your appreciation and positive comments of the current work which had significance for public health. As suggested by reviewer, we have performed the statistical analysis of results generated from patient data both diagrammatically as well as by statistical charts to better present the current findings by many ways. As admitted in the current study the limited number of pancreatic cancer samples, we are accumulating more pancreatic cancer samples in future study to analyse statistically significant association of various genetic predisposition mutations of DPC-4, BRCA-2, RASSF1A, hMLH1 and pancreatic cancer pathogenesis for improving diagnostics and prognosis of ethnic Kashmiri population.

LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

Reply: We have significantly improved the sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability grammar, of our manuscript by consulting all the authors of the manuscript who are native-English speakers and editors.

ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly. Now we list the abbreviations rules as follows.

(1) Title: Please spell out any abbreviation in the title. Abbreviations are not permitted.

Reply: As suggested we did not mention any abbreviation in the title

(2) Running title: Please shorten the running title to no more than 6 words. Abbreviations are permitted.

Reply: As per guidelines, we have edited the running title within the word limit of 6.

(3) Abstract: Abbreviations must be defined upon first appearance in the Abstract. Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*).

Reply: As per journal guidelines, we have defined the abbreviation upon first appearance in the abstract.

(4) Key words: Abbreviations must be defined upon first appearance in the Key words.

Reply: we have edited key words as per guidelines.

(5) Core tip: Abbreviations must be defined upon first appearance in the Core tip. Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

Reply: As per journal guidelines we have incorporated abbreviations after first appearance.

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text. Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

Reply: As per guidelines abbreviations have been defined upon first appearance in main text.

(7) Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights. Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

Reply: As per guidelines abbreviations have been defined upon first appearance in main text.

(8) Figures: Please verify the abbreviations used in figures and define them (separated by semicolons) at the end of the figure legend or table; for example, BMI: Body mass index; CT: Computed tomography.

Reply: we have defined all abbreviations separated by semicolons at the end of respective figure legends.

(9) Tables: Please verify the abbreviations used in tables and define them (separated by semicolons) at the end of the figure legend or table; for example, BMI: Body mass index; CT: Computed tomography.

Reply: we have defined all abbreviations separated by semicolons at the end of respective table legends

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific quality: The manuscript describes a case control study of the evaluation of biomarkers genetic mutations and epigenetic modifications in early diagnosis of ethnic Kashmiri patients with pancreatic cancer. The topic is within the scope of the WJG. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The authors evaluated the relevant biomarkers for early prognosis and diagnosis of pancreatic cancer. It has significant findings for the service of public health; (3) Format: There are 4 tables and 5 figures. (4) References: A total of 52 references are cited, including 9 references published in the last 3 years; (5) Self-cited references: There are no self-cited references; (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

Reply: Thank you so much for reading our manuscript keenly and appreciated our work to have public health significance. We also appreciate your efforts to raise some important queries to improve our manuscript for possible publications such as proper references cited in manuscript etc. We perform and incorporated *in-silico* network analysis in the manuscript at appropriate places to find out possible interaction of genes and their associated proteins with mutational analysis of the key regulatory genes involved in pancreatic cancer pathogenesis.

2 Language evaluation: Classification: Grade B. A language editing certificate issued by AJE was provided. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG.

5 Issues raised:

(1) The title is too long, and it should be no more than 18 words;

Reply: We have edited the title of the manuscript with less than 18 words

(2) The “Author Contributions” section is missing. Please provide the author contributions;

Reply: We have incorporated the Authors Contribution and have mentioned each authors contribution in current manuscript.

(3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Reply: As suggested by the reviewer, we have prepared and provided the original figures in powerpoint for easy editing.

(4) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Reply: As suggested by the reviewer, we provide all PMID and DOI numbers of all cited references in the manuscript.

(5) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text

Reply: We have incorporated the Article Highlights section at the end of the manuscript.

(6) The scientific quality can't meet the requirement of WJG. Recommendation: Transferring to the WJGO.

Reply: We have substantially revised the manuscript and addressed the concern of the science editor to meet the scientific standard of the WJG and hence would expect the manuscript to be considered for publication in the journal

(2) Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, please upload the primary version (PDF) of the Institutional Review Board's official approval in official language of the authors' country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Reply to company editor-in-chief: Thank you so much for the conditional acceptance of our manuscript for the publication. We have uploaded the scanned PDF version of the Institutional Review Board's in official language of the authors country to the system.