

Point-By-Point Response to Reviewer Comments

To
The Editors
World Journal of Hepatology

Dear Editors,

We would like to thank you for considering our manuscript for publication in the *World Journal of Hepatology*. We would also like to thank the reviewers for taking the time to review our manuscript and helping us improve the quality of our work. Please note that all the reviewer comments have been addressed in the re-submitted version of the manuscript and a point-by-point response has been provided for the reviewer comments. The manuscript has also been thoroughly revised again to ensure data accuracy and reporting. All authors agree to the resubmitted version of the manuscript and have no conflict of interest to report.

Please feel free to reach out to me at any time regarding this manuscript at dush.dahiya@gmail.com

Sincerely,
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Reviewer Comments

Reviewer #1

P1. Any abbreviation should be mentioned at first time in details then use the abbreviation afterwards.
eg. ESLD, LT, PSC, HRQOL

Author Response: We would like to thank you for taking the time to review our manuscript. We appreciate your effort, hard work, and enthusiasm in helping us improve the quality of our work. Please note that we have revised the manuscript according to your comments. We have added the full form for each abbreviation that is used for the first time in each section of the manuscript.

P2. Please add a short paragraph about the differences of PSC in pediatrics regarding incidence, clinical presentation and prognosis

Author Response: Thank you for raising this excellent point. We have added the comparison of pediatric PSC incidence, clinical presentation, and prognosis in the relevant sections as per your recommendation.

We have added the incidence of pediatric PSC in the 5th line of the first paragraph of the introduction section. "As compared to the adult population, the incidence and prevalence of PSC is lower in the pediatric population at 0.2 and 1.5 per 100,000 children."² We have added the comparison of the prognosis of PSC in children in the 7th line of the first paragraph and the 6th line of the second paragraph of the Clinical Presentation and Diagnosis of Primary Sclerosing Cholangitis section. "Disease progression may differ in children due to absence of other risk factors like alcohol abuse or polypharmacy that can lead to faster progression of the liver disease."³³ and "The dominant strictures are present in around 45% of adult patients at the diagnosis of PSC as compared to <5% in the pediatric population."³⁴ We have also added the diagnostic difference in children as compared to adults in the 3rd line of the second paragraph of the Clinical Presentation and Diagnosis of Primary Sclerosing Cholangitis. "ALP is not reliable in children as it can be elevated due to high bone turnover. So, gamma-glutamyl (GGT) transferase is more commonly used as a diagnostic marker in the pediatric population."³⁴

P3. Bacterial species would be written in italics.

Author Response: Thank you for pointing out this excellent point. We have written the bacterial species in italics.

P4. In the pathogenesis section, the word that is repeated twice

Author Response: Thank you for highlighting the repetition of that in the pathogenesis section in this sentence. We have restructured this sentence to remove the repeating word "that". It is modified in the 4th line of the Genetic and Environmental Factors in pathogenesis of Primary Sclerosing Cholangitis section. The restructured sentence is: "It is important to keep in mind that genetic findings can explain only less than 10% of the disease liability, while environmental factors could explain more than 50% of it."²¹

Reviewer #2

P1. Where is the list of abbreviations?

Author Response: We would like to express our sincerest gratitude and thank you for taking the time to review our manuscript. We appreciate your efforts and enthusiasm in helping us improve the quality of our work. Please note that we have revised the manuscript according to your comments. We have added the full form for each abbreviation that is used for the first time in each section of the manuscript. The list of abbreviations is as follows:

Abbreviations:

PSC: Primary Sclerosing Cholangitis
ESLD: End-Stage Liver Disease
LT: Liver Transplant
DDLT: Deceased Donor Liver Transplant
LDLT: Living Donor Liver transplant
IBD: Inflammatory Bowel Disease
MRCP: Magnetic Resonance Cholangiopancreatography
DAMPs: Danger-associated molecular patterns
PRRs: Pattern recognition receptors
ROS: reactive Oxygen Species
TIMPs: Tissue Inhibitors of Metalloproteinases
HLA: Human Leukocyte Antigen
ALP: Alkaline Phosphatase
UC: Ulcerative Colitis
ERCP: Endoscopic Retrograde Cholangiopancreatography
MELD: Model For End Stage Liver Disease
PREsTo: Primary Sclerosing Cholangitis RIsk Estimate Tool
UDCA: Ursodeoxycholic Acid
AASLD: American Association for the Study of Liver Disease
FXR: Farnesoid X Receptor
RCTs: Randomized controlled Trials
FISH: Fluorescence in situ Hybridization
CA 19-9: Cancer Antigen 19-9
UNOS: United Network of Organ Sharing
OPTN: Organ Procurement and Transportation in Network
INR: International Normalized Ratio
CCA: Cholangiocarcinoma
ACR: acute Cellular Rejection
AS: Anastomotic
NAS: Non anastomotic
HAT: Hepatic Artery Thrombosis
CMV: Cytomegalovirus
GF: Graft Failure
ReLT: Liver Re-transplant
HRQOL: Health-related Quality of Life
NFKB: Nuclear Factor Kappa B

P2. Abstract is good but needs some shortage.

Author Response: Thank you for suggesting this point. We have modified the language of the abstract and shortened it to 191 words from 218 words without impacting any important points and ensuring data accuracy.

P3. Introduction is good but needs some shortage

Author Response: We have modified the introduction to shorten it without impacting the important takeaway points from 506 to 396 words to convey the information more effectively.

P4. Discussion needs shortage. This article needs minor corrections regarding, scientific content, to be shorter.

Author Response: Thank you for this excellent suggestion. We have modified the language in different sections of the discussion to shorten the manuscript without affecting the information conveyed to our valued readers. We have modified the Genetic and Environmental factors in the pathogenesis of Primary Sclerosing Cholangitis section to shorten it without impacting the key takeaway points from 317 to 249 words to convey the information more effectively. We have modified the Staging, prognosis, and Management of Primary Sclerosing Cholangitis section to shorten it without impacting the key takeaway points from 742 to 684 words to convey the information more effectively. We have modified the Indications for Liver Transplant in Primary Sclerosing Cholangitis section to shorten it without impacting the key takeaway points from 277 words to 252 words to convey the information more effectively. We have modified the Indications for Ethical Considerations in Liver Transplant Candidates section to shorten it without impacting the key takeaway points from 334 words to 296 words to convey the information more effectively. We have modified the Future Aspects in Management of Primary Sclerosing Cholangitis section to shorten it without impacting the key takeaway points from 316 words to 281 words to convey the information more effectively.