To
The Editor in chief
World Journal of Gastrointestinal Pathophysiology

Subject : Revisions as advised by peer reviewers

At the outset, let me express my sincere gratitude for the reviewer comments and the critique of the manuscript that I had submitted the details of which are given below :

Manuscript NO.: 33159

Column: Observational Study

Title: Endoscopic Therapy for Biliary strictures complicating Living Donor Liver Transplantation (LDLT): Factors predicting better outcome

Authors: Harshavardhan Rao B, Hasim Ahamed, Suprabha P, Sudhindran S and Rama P Venu.

I have studied the comments from the reviewers (**Reviewer code:** 03660289, 03548095 and 02570566) and made the necessary changes as follows :

1. Reviewer code 03660289 :

- ***Role of surgery for the treatment of this condition in India :***
  Our protocol added in methods : Surgical repair was undertaken only when both endoscopic and transhepatic approaches failed to cross the stricture, the so called "defiant strictures". Unlike BDS in deceased donors, those occurring in LDLT are surgically formidable to correct, since the length of donor duct (proximal to anastomosis) tends to be very short. BDS following LDLT therfore tend to extend intrahepatically and defining an appropriate donor duct for anastomosis can be a very formidable task surgically particularly in Type 4 strictures.
  Our results : Surgical repair was performed only for one patient in this cohort, who remain well following surgery. In one other patient, who developed secondary biliary cirrhosis, retransplantation was required.
  Added in discussion : Surgery(Hepaticojejunostomy and retransplantation) is only reserved for patients who do not respond to endotherapy with maximal stent therapy (More than 15 months).
  In general, the role of surgery in the Indian context is limited due to limited experience and medical costs. Innovative endoscopic therapies and techniques and more aggressive protocols have been shown to be effective thus minimizing the need for surgery in most cases.
- ***Treatment of 'defiant' bile duct strictures:***
  'Defiant' bile duct strictures are a sub group of patients whose understanding is evolving especially in the setting of LDLT. Use of

covered SEMS, cholangioscopy to traverse the strictures, Rendezvous procedure with a percutaneous biliary access, novel dilatation balloons and longer duration and aggressive stent therapy may be helpful in most patients with difficult BDS post LDLT. **(Added in discussion)**

- ***Multicentric or monocentric? :***
  Monocentric (**Added in methods)**
- ***Time interval of study ?***
  January 2012 till November 2015 (**Added in methods)**

- ***Definition of biliary stricture :***
  Added to methods - Patients who had at least two of the three following features were included in the study.
  1. Symptoms of cholestasis like Jaundice, pruritus and/or cholangitis in conjunction with elevated Serum bilirubin and/or Serum Gamma glutamyl transferase(GGT) to more than twice the upper limit of normal.
  2. Magnetic resonance cholangiopancreatography (MRCP) showing a narrowing with proximal duct dilatation.
  3. ERC Cholangiogram showing significant narrowing at the anastomotic site with/without ductal dilatation.

2. Reviewer code : 03548095

- References – Older than 2015
  References have been expanded to include articles from 2016 and 2017. The new references are as follows :
  - **Aparicio DPDS**, Otoch JP, Montero EFDS, Khan MA, Artifon ELDA. Endoscopic approach for management of biliary strictures in liver transplant recipients:A systematic review and meta-analysis. United European Gastroenterology journal 2016;0(0):1-19.
  - **Shin M**, Joh JW. Advances in endoscopic management of biliary complications after living donor liver transplantation: Comprehensive review of the literature. World J Gastroenterol 2016 July 21;22(27):6173-6191. [PMID:27468208 PMCID:PMC4945977 https://doi.org/10.3748/wjg.v22.i27.6173]
  - **Koh PS**, Chan SC. Adult-to-adult living donor liver transplantation: Operative techniques to optimize the recipient's outcome. J Nat Sci Biol Med 2017;8(1):4–10. PMID:28250667 PMCID:PMC5320821 https://doi.org/10.4103/0976-9668.198356]
  - **Lee DW**, Jo HH, Abdullah J, Kahaleh M. Endoscopic Management of Anastomotic Strictures after Liver Transplantation. Clin Endosc 2016;49:457-461. [PMID:27744664 PMCID:PMC5066406 https://doi.org/10.5946/ce.2016.130] (among others)
- ***Numbering of references*** : **Has been edited**
- ***Rephrase discussion :*** **Discussion has been rephrased**

3. Reviewer code : 02570566

- No changes suggested.

Editor's comments in the edited draft and actions are as follows :

- Name of author and institution details have been edited as per requirement.
- Format has been changed to .doc
- Signed separate pdf files of all statements are provided
- Correspondence address is updated to the complete postal address along with the phone number
- Abstract 'background' section has been changed to Aim and complies with the requirements
- All references have been written as a superscript within square brackets as mentioned.
- PubMed citation numbers and DOI citation are mentioned for all references
- Comments for each subsection has been added at the end of the manuscript
- In addition, we have provided an audio core tip and a report that describes the entire scientific research process

All changes have been highlighted in the edited manuscript which is submitted with this letter. I hope the iterations made are complete and fulfil the requisite rules and norms of the journal. Please consider this edited manuscript as re-submission for publication in your journal.

Thanks and regards

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Professor and Head

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