

Lian-Sheng Ma,

Founder and Chief Executive Officer

Baishideng Publishing Group Inc

June 18th 2021.

Re: Manuscript 64838 Kidney transplant from donors with hepatitis B: a challenging treatment option.

Dear Chief Executive Officer, Chief Editor and Reviewers

Thank you for your e mail Date June 4th 2021 for the decision that the above manuscript is preliminary acceptable for publication after appropriate revision. We would like to express our deepest appreciation to the thoughtful and constructive comments toward the improvement of the manuscript. The point-by-point revision are described in this reply letter. The revised manuscript is upload with this resubmission.

Science Editor: Reviewer Comment

Comment 1. The criteria for recipients of a kidney transplant from a donor with HBV infection should be mentioned

Response to 1

1.1 This is shown in section 6 of the main text: RISK BENEFIT OF TRANSPLANTATION AND PROPOSE CRITERIA FOR HBsAg (+) DONOR UTILIZATION. Page 16 line 16-26.

“ Utilized kidneys from HBsAg (+) donors not only direct benefits to the potential recipients, but also the national society. However, the criteria for utilization of kidneys from donors with HBsAg positivity has not been well described. We would like to describe our proposed criteria to define three groups of potential recipients. The first group is patients with urgent need to receive kidney transplantation. Urgent condition included patients with exhausted vascular access for hemodialysis, patients with ongoing uremia despite adequate dialysis prescription, and patients who cannot remain in the dialysis treatment (hemodialysis or CAPD) due to any reason. The second group is the recipients with positive HBsAg [6, 30, 46]. The third group is patients being registered as active waiting list who have waiting time longer than the median time to receive a kidney in each national society”

1.2 The highlight is this comment is shown in the abstract line 14-16.

“A summary of reported long-term outcomes after kidney transplantation and proposed criteria to utilize kidneys from this group of donors was also defined and discussed.”.

Comment 2. The necessity of vaccinating kidney transplant recipients from HBV-infected donors, the importance of HBIG and antiviral therapy, and the need for close follow-up after transplantation should be noted.

Response to 2: This is described in section 6 of the main text: RISK BENEFIT OF TRANSPLANTATION AND PROPOSE CRITERIA FOR HBsAg (+) DONOR UTILIZATION, page 17 line 14-27 and page 18 line 1-2.

“Due to the risk of infection transmission before undergoing KT, recipients should be fully informed and consent must be obtained from each individual. In addition, all potential recipients should be vaccinated that aim to achieve anti-HBs at least > 10 mIU/mL. The potential recipients should not have HCV coinfection nor other cause of chronic liver disease which may worsen after KT. All recipients of HBsAg (+) donors should receive anti-viral medication, especially in the situation when the result of HBV DNA cannot be obtained before actual transplantation. HBIG may be considered for recipients with non-protective anti HBsAb level and/or in the situation of

unknown HBV DNAemia of the donor. A protocol for close surveillance of viral reactivation and liver disease must be implemented. For HBsAg (+) recipient candidates, they must be treated with NA and evaluated by a specialist in liver disease. Untreated patients result in a higher mortality rate, with liver-related complications [19] The American Association for the Study of Liver Diseases (AASDL) recommends further evaluation of HBV DNA, ALT and to undergo staging with biopsy or elastography to determine whether advanced fibrosis or cirrhosis is present in order to assess the need for simultaneous liver kidney transplantation [22, 72]."

Comment 3.

3.1 The cost of care for a patient on the waiting list should be compared with transplantation costs.

3.2 The new criteria for emergency cases where HBV-infected donors may be used should be addressed, and it should be noted that, if possible, the waiting list may be an option for awaiting an HBV-free donor.

Response 3.1: This is shown in section 6 of the main text: RISK BENEFIT OF TRANSPLANTATION AND PROPOSE CRITERIA FOR HBsAg (+) DONOR UTILIZATION, page 16 line 6-15.

" It has long been shown and recently confirmed that kidney transplants promoted both longer life expectancy and better quality of life at a lower cost relative to staying on dialysis treatment.[74, 75] In order to gain comparable survival benefit to kidney transplant, an intensive home hemodialysis has to be attained which would be a much higher effort than an in-center standard hemodialysis and this option is not feasible in some countries.[76] A recent economic study using data from USRDS showed that kidney transplants using standard donors were a cost saving procedure compared to remaining on dialysis. The same study also showed that kidney transplant using high risk donors were cost-effective. [77] All of the above studies have highlighted the benefit of expanding the donor pool by using kidneys from donors with HBsAg positivity."

Response 3.2: This is shown in section 6 of the main text: RISK BENEFIT OF TRANSPLANTATION AND PROPOSE CRITERIA FOR HBsAg (+) DONOR UTILIZATION, page 16 line 19-27 and page 17 line 1-3.

“The first group is patients with urgent need to receive kidney transplantation. Urgent condition included patients with exhausted vascular access for hemodialysis, patients with ongoing uremia despite adequate dialysis prescription, and patients who cannot remain in the dialysis treatment (hemodialysis or CAPD) due to any reason. The second group is the recipients with positive HBsAg [6, 30, 46]. The third group is patients being registered as active waiting list who have waiting time longer than the median time to receive a kidney in each national society. The potential recipients should be discussed about the willingness to receive a kidney from donors with HBsAg positivity. They may choose not to take this opportunity and continue to wait for HBsAg negative donors”. Examples of the use of kidneys with increased risk of blood borne viral infection has been previously described. [78]

Editorial office comment:

Comment 1. Language evaluation: B (Minor language polishing) A language editing certificate issued is not presented

Response 1. This revised manuscript has received language editing by a native English speaker and specialist in English for the healthcare community of our faculty. A certificate of language editing is uploaded with this resubmission.

Comment 2. The “Author Contributions” section is missing.

Response 2. This is described in the title page line 18-20.

Comment 3. The authors provide original pictures. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor

Response 3. The figures are prepared in PowerPoint format already.

Comment 4. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references.

Response 4. This is already done.

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

Response 5. This is described in main text page 21 line 24-27 and page 22 line 1-5.

“Within this era of several newer antiviral medications, the presence of positive HBsAg in potential organ donors should not preclude the use of kidney organs. Several additional steps and experienced transplant teams are specifically required to prepare waiting list candidates who are willing to receive a kidney from such donors. These steps should be regularly assessed for each individual during his or her registration as active waiting list to receive kidney transplantation from deceased donors. However, the criteria that we have described in this review, can also be applied to patients who are planning to receive living (related) kidney transplantation as well”.

We believe that this revision will result in improved scientific merit of the manuscript. This topic is formerly believed to be a difficult issue. The publication of this mini-review will result in a re-appraisal of several challenging steps of kidney transplant from donors with HBV. This will definitely benefit the readers of World Journal of Hepatology.

The authors have no conflicts of interest to disclose. All authors have agreed to the manuscript conclusion.

The reviewer’s comments are greatly appreciated. I strongly hope that the revisions being made will be satisfied by both the reviewers, chief editor, and the chief executive officer.

I am looking forward to hearing from you with my best personal wishes.

Yours Sincerely,

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