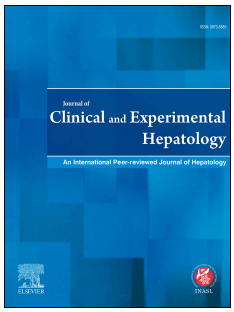
Journal Pre-proof



Practice of ABO incompatible living donor liver transplant in India: An initial experience based on a survey

Shekhar Singh Jadaun, Shaleen Agarwal, Shweta A. Singh, Subhash Gupta, Sanjiv Saigal

PII: S0973-6883(23)00065-8

DOI: https://doi.org/10.1016/j.jceh.2023.04.007

Reference: JCEH 1181

To appear in: *Journal of Clinical and Experimental Hepatology*

Received Date: 17 February 2023

Revised Date: 13 April 2023

Accepted Date: 21 April 2023

Please cite this article as: Jadaun SS, Agarwal S, Singh SA, Gupta S, Saigal S, Practice of ABO incompatible living donor liver transplant in India: An initial experience based on a survey, *Journal of Clinical and Experimental Hepatology*, https://doi.org/10.1016/j.jceh.2023.04.007.

Title: Practice of ABO incompatible living donor liver transplant in India: An initial experience based on a survey

Shekhar Singh Jadaun[1], Shaleen Agarwal[2], Shweta A Singh[3], Subhash Gupta[2], Sanjiv Saigal[1]

[1]Department of Gastroenterology and Hepatology, Centre for Liver and Biliary Sciences, Max Super Speciality Hospital, Saket, New Delhi, India

[2]Liver Transplant and Gastrointestinal Surgery, Centre for Liver and Biliary Sciences, Max Super Speciality Hospital, Saket, New Delhi, India

[3]Anesthesia & Critical Care, Centre for Liver and Biliary Sciences, Max Super Speciality Hospital, Saket, New Delhi, India

Author contribution

1. Shekhar Singh Jadaun**,** MD DM, Email*:* dr.shekhar@outlook.com; Draft writing
2. Shaleen Agarwal, MS, MCh, Email: agarwalshaleen@yahoo.com; draft writing
3. Dr. Shweta A. Singh, MD, Email*:* drshwetasingh29@gmail.com, draft writing
4. Subhash Gupta, MS, FRCSED, FRCS**,** Email: livertransplant@gmail.com; Revision
5. Sanjiv Saigal, MD DM, Email: sanjivsaigal@hotmail.com; Revision

Corresponding author:

Dr Sanjiv Saigal

MD DM MRCP CCST

Principal Director and Head

Hepatology and Liver Transplant Medicine

Centre for Liver and Biliary Sciences CLBS Max Super Speciality Hospital, Saket

New Delhi, India 110017

Email: sanjivsaigal@hotmail.com

Conflicts of interest: All authors declare no conflicts of interest.

Financial support- No grant or financial support was taken for this research.

Disclosure- None of the authors have any financial, professional or personal conflicts that are relevant to the manuscript.

Abbreviations- LDLT, Living donor liver transplant; ABOi, ABO incompatible; ABOc, ABO compatible;

Key words- Cirrhosis, ABO incompatible liver transplant, Living donor liver transplant

Introduction

With growing need of liver transplant, gap between the demand and availability of liver allograft is continuing to rise. Because of limited availability of cadaveric graft, living donor liver transplant (LDLT) has been the predominant form of liver transplant in India and other Asian countries. More than 90 % of liver transplants in India are LDLT while LDLT accounts for 76.5% of LT in Korea, 80% in Taiwan and more than 96% of all LT in Japan. [1, 2]. ABO incompatible (ABOi) LDLT is an important method to expand the donor pool in countries with scarcity of cadaveric donors.[3, 4] The protocol for ABOi LDLT is relatively well established in countries such as Japan, China, Korea and Taiwan. [5, 6] Encouraged with good outcomes, many centre in India have also started doing ABOi LDLT. However, there is marked variations in practices across various centres in India, and there is no established protocol as yet. [7]We conducted the first national course program on ABOi LDLT in India and did a google survey as part of this meeting to study the differences in these practices across various centres in India.

Methods

We conducted this survey between 1 January and 20 January 2023. This was an online survey conducted virtually and a Google form questionnaire was emailed to the participants. Subsequently follow up reminder email were also sent. Survey included questions covering the various aspects of ABOi LDLT management protocol involving pre- and post-transplant

period. All questions in survey were mandatory. Study participants included hepatologists and liver transplant surgeons working at various liver transplant centres in India. Participants in this included both high and low volume centres performing ABOi LDLT in India. Centres performing more than 100 liver transplants per year were defined as high volume while those conducting less than 100 transplant per year were considered low volume centres. Responses received from centres all over India were collected and analysed.

Results

Survey was sent to 60 participants and we received total 26 responses. 13 responders were from high volume centres while similar number of responses were received from low volume centres. Results of the survey are described below.

Pre transplant desensitization

Rituximab

Rituximab is the corner stone of desensitization protocol and is responsible for improving outcomes of ABOi LDLT. It usually given 3 weeks to few days before transplant surgery. Most of the participants (65.4%) in this survey said that they give Rituximab 2 weeks before transplant. About one forth participants (23.1%) used it 3 weeks before while 11.5% practice to give rituximab less 2 weeks before transplant surgery.

Pre-transplant ABO isoagglutinins removal

Removal of ABO antibodies before transplant is essential to decrease the risk of AMR and is done by plasmapheresis or immunoadsorption. Plasmapheresis was the preferred method for pre-transplant ABO antibodies removal used by 80.8% participants while immunoadsorption was preferred by 19.2% participants.

Pre-transplant ABO isoagglutinins target level

Preferred target titre of ABO antibodies before the surgery was 1:16 or less as told by 84.6% participants. 15.4 % participants answered that they prefer to keep the titres 1:64 or less before the surgery.

Pre transplant immunosuppression

Some centres follow the practice of starting immunosuppression (mostly Mycophenolate mofetil) before the surgery. In this survey 38.5% participants said that they use immunosuppression in pretransplant period in ABOi LDLT.

Post-transplant management

Biopsy for suspected graft rejection

Only 30.8% participant perform biopsy in all cases of suspected graft rejection while 69.2% participant said that biopsy for graft rejection is not mandatory and only performed when clinical diagnosis is in doubt after ruling out the vascular, biliary and infective cause of deranged liver biochemistry.

Treatment for antibody mediated rejection

Most preferred treatment (69.2%) for AMR in this survey was combination of steroid pulse and plasmapheresis. 26.9 % participant said that they preferred steroid pulse therapy alone while 3.9% participant used intravenous immunoglobulins (IVIG) as preferred treatment for AMR in ABOi LDLT.

Tacrolimus target trough level in early post-transplant period

Higher tacrolimus trough levels are targeted in ABOi LDLT as compared to ABO compatible LDLT. In this survey 65.4% participants said that they prefer to keep target trough levels between 8-10 ng/ml in early post operative period. 23.1% participants said that they keep tacrolimus trough level of 6-8 ng/ml while only 11.5 % participants practice the target level of 10-12 ng/ml.

CMV prophylaxis and antifungal prophylaxis in post-transplant period

Risk of infection is considered higher in ABOi incompatible transplant because of use of Rituximab, plasmapheresis and higher immunosuppression. In this survey 80 % participants said that they use prophylactic anti CMV therapy in post-transplant period in ABOi LDLT. Fluconazole was the preferred anti-fungal agent used by 68% participants while 32% used echinocandins for antifungal prophylaxis in post-transplant periods.

Post-transplant complications in ABOi

Most of the participants said that they experience higher rates of sepsis, rejection and biliary complications in ABOi LDLT as compared to ABOc liver transplant. 33% participants said that they experience same complications rates in ABOi and ABOc LDLT. There were no major differences in practices in high volume or low volume centres. Also, participants at low volume centres avoided ABOi liver transplants in ACLF patients.

In conclusion, it is the first survey conducted regarding the ABOi LDLT practices involving various centres across India. This survey covered important aspects of pre- and post-transplant management of ABOi liver transplant recipients. It highlighted the wide variations in the management protocols in ABOi LDLT across India like target trough levels of tacrolimus and incidence of post-transplant complications. There is some consensus on pretransplant desensitization method and target isoagglutinins levels. Most participants agreed on prophylactic anti CMV therapy in post-transplant period. Experience of most of the transplant centres in ABOi LDLT is still evolving in India. There is an imminent need for formulation of evidence based consensus guidelines on ABOi LDLT, relevant for Indian centres.

References

1. Goss MB, Rana A (2017) ABO-Incompatible Liver Transplantation: Is It a Viable Option With Modern Innovation?

2. Wen PH, Lu CL, Strong C, Lin YJ, Chen YL, Li CY, Tsai CC (2018) Demographic and Urbanization Disparities of Liver Transplantation in Taiwan. International Journal of Environmental Research and Public Health 2018, Vol 15, Page 177 15:177

3. Egawa H (2020) Challenge to ABO blood type barrier in living donor liver transplantation. Hepatobiliary & Pancreatic Diseases International 19:342–348

4. Egawa H, Ohdan H, Saito K (2023) Current Status of ABO-incompatible Liver Transplantation. Transplantation 107:313

5. Kawagishi N (2015) Current Aspects of ABO-Incompatible Liver Transplantation. International Journal of Surgery Research & Practice. https://doi.org/10.23937/2378-3397/1410033

6. Gan K, Li Z, Bao S, et al (2021) Clinical outcomes after ABO-incompatible liver transplantation: A systematic review and meta-analysis. Transpl Immunol. https://doi.org/10.1016/J.TRIM.2021.101476

7. Jadaun SS, Agarwal S, Gupta S, Saigal S (2023) Strategies for ABO Incompatible Liver Transplantation. J Clin Exp Hepatol. https://doi.org/10.1016/j.jceh.2022.12.008

Table 1. Showing cities and regions of survey responders

Cites	**Number of responders**
Delhi NCR	6
Hyderabad	5
Chennai	5
Bengaluru	3
Kochi	2
Bhuvneshwar	1
Mumbai	3
Ahmedabad	1

Figure 1. Pre transplant target level of ABO isoagglutinins titre before surgery at deferent centres

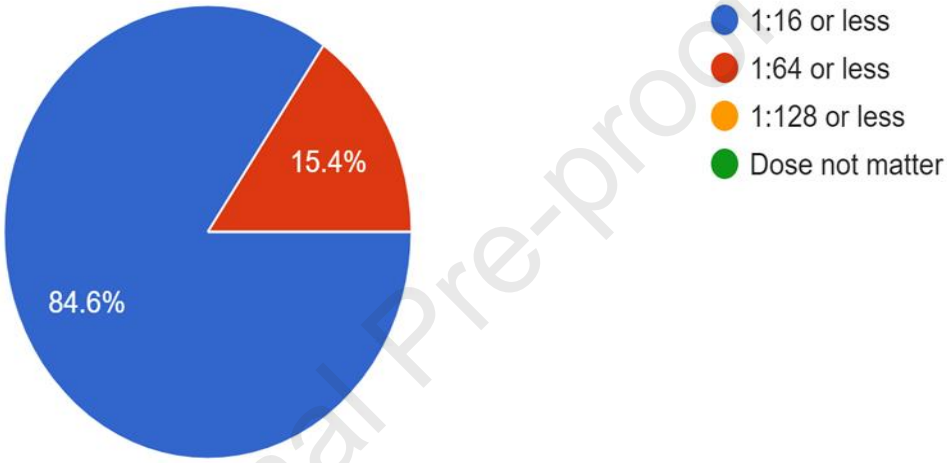


Figure 2. Timing of Rituximab before transplant