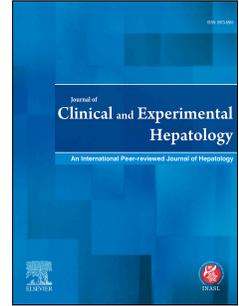


# Journal Pre-proof

Practice of Immunosuppression in Liver Transplant Programs in India: Results of a Survey

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**Title: Practice of Immunosuppression in Liver Transplant Programs in India: Results of a Survey**

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**Key words-** Immunosuppression practices, Immunosuppression in Liver transplant

### **Abbreviations**

Calcineurin inhibitors, CNIs; Simultaneous liver kidney transplant, SLKT

### **Introduction**

Introduction of newer immunosuppressive drugs was one of the biggest changes that improved the outcome of solid organ transplants. Immunosuppression management is crucial for graft survival in any organ transplant program. With newer drugs like tacrolimus, rate of graft rejection and graft loss has decreased markedly but challenges of long-term effects of immunosuppression remains.<sup>1</sup> Selection of patients who are likely to achieve clinical tolerance and gradual withdrawal of immunosuppression in these patients is another emerging area of interest. Liver transplant centres in India have variable immunosuppression practices due to lack of uniform clinical practice guidelines. <sup>2,3</sup> We conducted this online survey to study the different immunosuppression protocols being followed across various liver transplant centre in India. This survey will help in formulation of standard recommendations on immunosuppression in liver transplant for Indian population.

### **Methods**

We conducted this survey between 10<sup>th</sup> November to 10 December 2021. This was an online survey conducted virtually and a google form questionnaire was emailed to the participants. A follow-up reminder email was sent after 15 days of initial mail. Responses were collected and analysed. Study participants included transplant hepatologists and liver transplant surgeons who are working currently at various liver transplant centres in India. Responses were invited from transplant centre all over India. Centres performing routine deceased and or living donor

transplantation were included in this survey. Online google form was sent to 50 centres and response was received from 17 centres.

Survey included the questions regarding immunosuppression at various stages of post liver transplant period. The results of this survey were then discussed and endorsed in the transplant hepatology course December 2021 entitled “Immunosuppression in Liver Transplantation.

### ***Results***

Total seventeen responses were received that represented seventeen liver transplant centres throughout India including both high volume and low volume centres. Results of survey are as follows.

#### *1. Intraoperative methylprednisolone dose*

Most common dose of intravenous Methylprednisolone being used is 500 mg (43.8%) followed by 10 mg/kg (31.2%) and 1000 mg (25%).

#### *2. Tapering of IV Methylprednisolone dose*

Most common practice was to taper IV methylprednisolone over a week (68.7%) while 18.8% participants said that they usually taper it over the period of 5 days and switch over to oral prednisolone. According to 12.5% participants IV steroid tapering depends on liver function tests. (Figure 1)

#### *3. Use of Basiliximab in induction regime in patients with renal dysfunction*

Use of Basiliximab in early postoperative period can help delaying introduction of (calcineurin inhibitors) CNIs and so preserving the renal function. In this survey 56.3% participant said that they regularly use Basiliximab as a part of induction regime in patients with renal dysfunction.

#### *4. Oral steroid pulse regime*

Intravenous Methylprednisolone 500 mg for three days was the most common (62.5%) dose of steroid pulse being used by survey participants while 37.5 % people used 1 gram IV methylprednisolone for 3 days.

#### *5. Choice of CNIs*

Tacrolimus has been the CNIs of choice because of lesser risk of rejection and improved overall outcome. Cyclosporin is used only in limited number of patients. For most of the participants (87.5%) tacrolimus induced neurotoxicity was the only indication for using cyclosporin. Small number of participants (6.25%) said that they use it in patients transplanted for primary biliary cholangitis while similar number of participants said that they never use cyclosporin.

#### *6. Use of Everolimus in early liver transplant period*

Use of everolimus in place of CNIs has the benefit of decreasing the risk of renal dysfunction in high-risk patients. However, in early post-transplant period everolimus use can lead to delayed wound healing, surgical site incisional hernia and hepatic artery thrombosis. In our survey 81.3 % participants said that they would avoid using the everolimus in early post-transplant period. In patients with renal dysfunction 68.8% participants follow the practice to start everolimus after 4 weeks while 31.3% start everolimus after 2 weeks. For the patients who underwent liver transplant for HCC, 93.8% participants said that they use everolimus routinely.

#### *7. Use of Azathioprine in post-liver transplant period*

Azathioprine is not used commonly as immunosuppressive agent in liver transplant recipients. Pretransplant diagnosis of autoimmune hepatitis, concomitant inflammatory bowel disease and paediatric liver transplant recipients were the only indications found in this survey for which Azathioprine use can be considered.

#### *8. Once a day Tacrolimus in clinical practice*

Once a day Tacrolimus preparation has been shown to improve the compliance although experience has been limited. Surprisingly in this survey 81.3% participants said that they routinely use once a day preparation of tacrolimus.

#### *9. Stopping of oral steroid in post-liver transplant period*

Three month was the most common (75%) time period after transplant when oral steroids are stopped with gradual tapering. While 12.5% participants each said that they stop oral steroids usually at the end of 1 months and 2 months in their clinical practice. (Figure 2)

#### *10. Immunosuppression in simultaneous liver and kidney transplant (SLKT)*

Most common response (93.75%) from the participants was that they use similar immunosuppression in combined liver kidney transplant as in isolated liver transplant however,

6.25% participants said that in SLKT they will use lower doses than isolated kidney but higher than isolated liver transplant.

#### *11. Optimal time to stop mycophenolate*

Most common time to stop Mycophenolate was at the end of 2 year after liver transplant as told by 43.8 % participants while 37.5% people said that they usually stop mycophenolate at the end of 1 year. Remaining participants said that timing to stop Mycophenolate depends on other factors also like presence of chronic kidney disease and metabolic syndrome in which case they prefer to decrease the dose of CNIs while continuing Mycophenolate for longer time.

#### **Conclusion**

It is one of the first survey conducted among the liver transplant surgeons and physicians at various centres across India. Although brief in nature our survey covered important aspects of immunosuppression management in liver transplant recipients. Survey highlighted the variable practices and immunosuppression protocols being followed across India. There is a need for formulation of evidence based clinical practice guidelines on immunosuppression management in liver transplant recipients. We also propose the formation of clinical task force involving persons from various transplant centre to create these practice guidelines.

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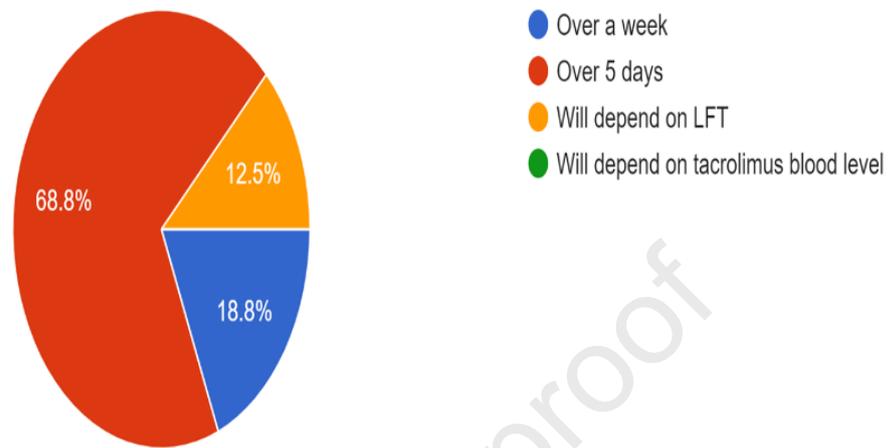


Figure 1. Tapering of IV Methylprednisolone in early postoperative period

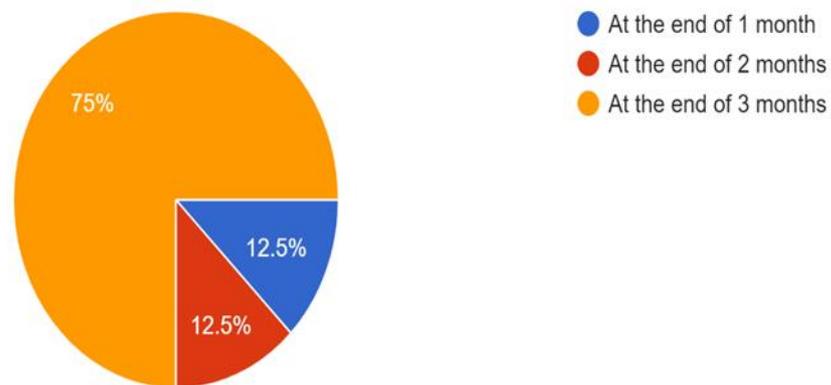


Figure 2. Time to stop oral steroids in post-transplant period.

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