

## **Successful Treatment of Hepatitis C in Renal Transplant Recipient. A Case Report from Pakistan**

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### **Abstract**

The treatment of hepatitis C is a therapeutic challenge in renal transplant recipients. Interferon based regimens are relatively contraindicated due to their side effects and high risk of graft failure. With the availability of direct antivirals the situation has changed now and sustained virological response (SVR) >90% had been achieved in patients with normal kidney function. There is limited data available on the safety of these agents in renal transplant recipients. Here we report a case of a kidney transplant recipient with Hepatitis C genotype 3 infections successfully treated with Sofosbuvir and Daclatasvir based regimen. This is the first reported case from Pakistan.

### **Key-words**

hepatitis C, Sofosbuvir , renal transplant

### **Introduction**

Chronic hepatitis C is the one of the commonest causes of chronic liver disease around the globe with approximately 170 million people affected worldwide<sup>1</sup> and in Pakistan the estimated sero-prevalence of hepatitis C ranged from 2.3 % to 28.6%.<sup>2</sup> It is also observed that the prevalence of hepatitis C in patients with end stage renal disease (ESRD) exceeds that in the general population and the reason being the greater exposure to blood products and breach in the standard precaution in haemodialysis units.<sup>3,4</sup> Multiple studies have shown that HCV infection is associated with increased mortality and adverse clinical outcomes in patient with ESRD<sup>5</sup> and renal transplant in patients with HCV infected ESRD patients is associated with improved survival.<sup>6</sup> Before the availability of direct acting antivirals, the treatment of hepatitis C was hampered by the toxicity of interferon and ribavirin in these patients and it was considered a therapeutic challenge. Now with the significant progress made in the development of direct acting antivirals, the clinical scenario has changed and many patients with ESRD and kidney transplant recipient are now candidates for the treatment. There is a paucity of data regarding safety of Sofosbuvir based regimens in post renal transplant patients but a few centers have tried them with excellent outcomes. Here we report a case of Hepatitis C genotype 3 infected renal transplant recipients successfully treated with Sofosbuvir and Daclastivir for 12 weeks.

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### **Case History**

A 56 year old male, known to have diabetes and hypertension, presented to us in clinic as a candidate for renal transplantation in December 2016. He was suffering from end stage renal disease, and was on maintenance hemodialysis, twice weekly for the prior 2 years. He was also taking fixed dose insulin for his diabetes, and was on Amlodipine 10 mg /day for hypertension. On further evaluation it was found that he was hepatitis C reactive and he had received treatment for hepatitis C in November 2015 with pegylated interferon and Sofosbuvir 400 mg once a day for 6 months and achieved end of treatment response. The HCV RNA quantitative and qualitative were ordered and it was found that he had hepatitis C genotype 3 infection and his viral load was 367,000 copies /ml . He had no signs of liver decompensation and his liver function tests showed bilirubin (total) 0.68, bilirubin (direct) 0.45, bilirubin indirect (indirect) 0.23, Gamma GT 450, SGPT(ALT) 30 U/L and alkaline phosphatase 387. The patient's Metavir score (for fibrosis) was F3. He was Hepatitis B surface antigen negative, HIV nonreactive and CMV Ig G positive. The patient had a renal transplant in March 2017 and received a kidney from his son. His son was seropositive for CMV. After 4 weeks post-transplant the patient was started on direct acting antivirals i.e. Sofosbuvir 400 mg once and a day and Daclatasvir 60 mg once day. The patient was also given cyclosporine 150 mg twice day and Mycophenolate mofetil 720 mg twice a day as immunosuppressant. Two month after transplant the patient's CMV PCR was checked and it showed rising trends and he was started on oral Valganciclovir 900 mg once a day. The patient continued Valganciclovir with Sofosbuvir and Daclatasvir and no adverse effects were noted during course of treatment except mild mucositis which was unrelated to hepatitis C therapy. His CMV PCR after 2 weeks of therapy with Valganciclovir was negative. His HCV PCR after 12 weeks of therapy came out negative. At 6 months follow up the repeat HCV PCR was negative and sustained viral response was achieved.

### **Discussion**

Treating chronic hepatitis C in renal transplant recipients was challenging before the availability of direct acting antivirals. The treatment with Pegylated interferon and Ribavirin was difficult in kidney transplant recipients due to toxicity of the regimen and risk of graft rejection in this population.<sup>7</sup> We observed that the direct acting antivirals Sofosbuvir and Daclatasvir were tolerated by our patient very well with no adverse effects. We decided to treat him post renal transplantation because of the availability of data on the safety of these regimens

in both renal and liver transplant recipients and achieving sustained virological response comparable to that in general population. Sofosbuvir is eliminated by kidneys however no dose adjustment is required if creatinine clearance is >30ml/min that is why we opted to start this treatment post-transplant when his creatinine clearance improved and patient's kidney function was normalized. Kamar N et al, in his case series of 25 hepatitis C reactive renal transplant recipients described the success of Sofosbuvir based regimen. All the patients in this case series were viral load negative at the end of 12 weeks therapy and all had sustained virological response as well.<sup>8</sup> Lin MV et al in their retrospective analysis of 24 kidney transplant recipients who received Sofosbuvir based direct acting antivirals for hepatitis C mentioned SVR rates of 91%.<sup>9</sup> Sofosbuvir and Daclatasvir are considered safe with immunosuppressants and appear not to alter the pharmacokinetic profile of tacrolimus and cyclosporine.<sup>10</sup> In our patient, no interaction was seen between immunosuppressants and antiviral therapy and no dose adjustment was required throughout the therapy because of drug drug interaction. We reported this case to share our success story of achieving virological response rapidly in patient who had many co morbidities and was on immunosuppressant as well. We started therapy in the early post-transplant period when patient is on high dose of immunosuppressants, large clinical studies are needed to determine the appropriate time to initiate the therapy and the effect of early therapy on the graft outcomes.

## Conclusion

Direct acting antivirals are effective and safe in treating hepatitis

## C post renal transplantation

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