Original Article

Prevalence of Varicella Zoster Virus Infection in Renal Transplant Recipients; A Single Centre Study

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ABSTRACT

Objective: Varicella zoster virus (VZV)-related disease, particularly herpes zoster, is important infective viral complication of renal transplantation due to long-term immunuo suppression. In our study we examined the clinical presentation, prevalence and outcome of herpes zoster virus in post renal transplant patients.

Study Design: Retrospective / cross-sectional study

Place and Duration of Study: This study was conducted at the Institute of Kidney Diseases Peshawar (both as in-patient and out-patient department) from August, 2010 to July, 2018.

Materials and Methods: A cross-sectional retrospective study design was followed in this research in which medical record files of all the patients who underwent renal transplant at Institute of Kidney Diseases (IKD) Peshawar were reviewed.

Results: n=8 subjects (3.33%) developed herpes zoster during a follow-up of 8 years post-transplant. Mean time to the development of VZV infection was 2.27 years (ranging from 06 month to 4.16 years).All patients in cohort had presented with single dermatomal distribution of lesions, none of the patients developed disseminated disease or post herpetic neuralgia.

Conclusion: VZV is a common complication after renal transplantation, but in our study the prevalence was very low i.e. 3.3%. Prompt diagnosis and treatment prevent the complication of VZV and visceral disease. Pre transplant active immunization for VZV negative patients should be done to prevent VZV infection.

Key Words: Renal Transplantation, Varicella zoster virus infection, Mycophenolate Mofoetil

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INTRODUCTION

Varicella-zoster virus (VZV) is a double-stranded DNA virus member of the herpes virus family. VZV also has the ability to establish lifelong latency in cranial nerve or dorsal nerve root ganglion after primary infection and persist in the infected host for life.[1]

VZV is the second most common viral infection in solid organ transplant (SOT) recipients (after cytomegalovirus), with a prevalence of about 29%.[1, 2]While, zoster occurs in approximately 11% of SOT recipients within four years of transplant due to long term immunosuppressive therapy.[2,3,4] An increased incidence of zoster were reported among SOT receipts used MycophenolateMofoetil.[5,6] Herpes zoster classically occurs in the first 6 months after transplantation in SOT recipients; however it can manifest clinically longer after transplant. VZV infection in adult renal transplant recipient results from reactivation rather than primary infection with severe sequel occurs.[6,7]Reactivation disease (herpes zoster or shingles) occurs with an annual incidence of 1.5-3.0 cases/1000 in general population and is clearly age related with incidence rising to 10cases/1000 in subjects over 65years of age.[8] The incidence in SOT recipient is 10-100 folds higher than general population ranging from 1-12%.[9, 10]

The most common clinical manifestation of varicella zoster virus reactivation is cutaneous HZ, involving usually less than two adjacent dermatome, however atypical clinical findings, disseminated disease, visceral involvement and lethal outcome has been described.[11]In addition 20-40% of transplant patients will acquire post-herpetic neuralgia as a secondary complication, considerably greater than the rate in immunocompetent population.[12]

After the primary episode, VZV remains dormant in cranial nerves and dorsal root ganglia and potentially can revive up to decades later as zoster (shingles).[13,14] Zoster is more commonly observed in older age recipients and those individuals having decreased cell mediated immunity.[8-14]

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MATERIALS AND METHODS

A cross-sectional retrospective study design was followed in this research in which medical record files of all the patients who underwent renal transplant between August 1st, 2010 and July 31st, 2018, at Institute of Kidney Diseases (IKD) Peshawar were reviewed. Demographic, clinical and laboratory information of the patients were gathered from the medical files including age, gender, dialysis duration, duration of transplantation, type of donor, immunosuppression protocol, episodes of allograft rejection, pre-transplant VZV status, distribution of VZ, complications, treatment given and outcome of treatment.

All the renal transplant recipients had received antiviral prophylaxis according to their documented cytomegalovirus (CMV) status, while all the transplant recipients received induction with interlukin-2 receptor (IL-2R) antagonist (Basiliximab).

Maintenance immunosuppression constituted of triple regimen selecting either a Calcineurin inhibitor (Tacrolimus or Cyclosporine), or anti-proliferative drug (Mycophenolate sodium MPA, or Everolimus (mTORi) with oral prednisolone**.**

RESULTS

Medical record of 250 patients was reviewed during the study period. Those patients who were lost to follow up after 3 months were excluded. Finally 240 patients were considered for further study with mean age of 34.408 ± 8.306 year, and were further followed for a period of 39.51 ±10.37 months. The characteristics of these patients are shown in Table 1.

Table No.1: Characteristics of renal transplant patients (n=240).

Characteristics		*n* (%)
Age at transplantation	Less than 40 years	174 (72.5)
	More than 40 years	66 (27.5)
Gender	Male	182 (75.8)
	Female	58 (24.2)
Follow-up time (months) mean	39.516 ± 10.371	
Deaths at last follow up	No	240 (100)
	Yes	0 (0)
Rejection	No	216 (90)
	Yes	24 (10)
Pre-transplant Varicella Zoster Disease	No	218 (90.8)
	Yes	22 (9.2)
Post-transplant Varicella Zoster Disease	None	232 (96.7)
	Single Dermatome	8 (3.33%)

Majority of the patients, about 75.8% (n=182), were male, and 27.5% (n=66) of the patients were above age of forty year at the time of transplantation. About 9.2% (n=22) patients had pre-transplant Varicella zoster virus disease. Almost 10% (n=24) patients had an episode of either acute or chronic rejections during the follow up period.

All patient received maintenance immunosuppression during the follow up period, 62.9% (n=151) received Cyclosporine and Mycophenolate Mofoetil (CSA + MMF), while rest received either Tacrolimus and Mycophenolate (TAC + MMF) or Cyclosporine and Everolimus (CSA + EVERO). The frequencies of immune suppression used in patient are shown in figure 1.Out of these n=240 renal transplant patients, 3.33% (n=8) patients showed post-transplant Varicella zoster virus infection. And all had only single dermatomal involvement. There were no recurrence and none of the patient had disseminated disease. No death has been reported as a result of VZV infection. All of the affected patients were treated with oral antiviral acyclovir as outpatient and all recovered completely**.**

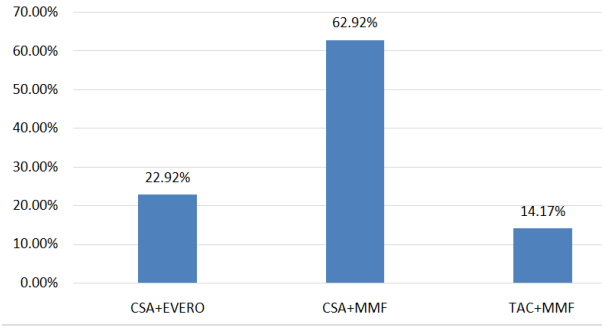

Figure No.1: Frequency of Maintenance Immuno-suppression

DISCUSSION

VZV is the 2nd most common viral infection in post renal transplant patients after cytomegalovirus (CMV). A variety of complications of VZV has been noted in different studies worldwide with unfavorable outcomes.[6] The prevalence of VZV in our study was 3.33% which is lower than in comparison to other studies which have reported higher prevalence of VZV.[2,3,9,15,16] Our study findings revealed that VZV infection were higher in male while other study showed VZV predominance in female.[17] All the patients who developed VZV infection had a history of the VZV infection before renal transplant and none of them received vaccination for VZV.

The prevalence and severity of the VZV infection is related to the intensity of the immunosuppression including induction, maintenance and anti-rejection therapy.[15,18,19]

Although MMF inclusion to the transplant treatment protocols has improved the graft survival but on other hand it has increased the prevalence of different viruses like VZV or CMV.[2 ,20] All our patients with VZV were

on MMF based regime with induction therapy with Basliximab and had received anti-rejection therapy. All the patients were found to involve only single dermatome. There was no case of disseminated disease; additionally no case of post-herpetic neuralgia was reported in our study. All the cases were managed with oral administration of acyclovir 800mg thrice daily for ten days with reduction of MMF dose with complete recovery and no relapse was observed.

The limitation of our study is being retrospective, single center study and also low sample size. No pre-transplant VZV serology status records were present in our study. But despite all these above limitation our study is the real first to study the prevalence, risk factors, complications, treatment and outcome of VZV infection in post renal transplant patients in Pakistan.

CONCLUSION

VZV infection is frequent viral infection in post renal transplant patients in our center after CMV infection. Intense immunosuppression (induction, maintenance and anti-rejection) is a risk factor for VZV infection despite use of universal viral prophylaxis.

Recommendations: VZV serology should be done before renal transplant and all seronegative patients should be vaccinated before transplantation. This will decrease the prevalence of VZV infection in our renal transplant recipients. Prompt treatment with acyclovir and reduction of MMF dose is cost effective treatment for VZV infection in renal transplant patients.

Author's Contribution:

Concept & Design of Study:	Syed Munib
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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