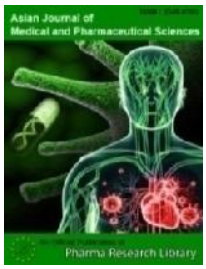
Asian Journal of Medical and Pharmaceutical Sciences

Journal Home Page: www.pharmaresearchlibrary.com/ajmps



R E S E A R C H A R T I C L E

Pharmacotherapeutic Management of Viral Infections in Post Renal Transplantation Recipients

[1]Kanthaiahgari Jamuna Rani, [2]Pilla Sree Surya Durga Devi*, [3]Palakunta Thejasree, [4]Boda Chaithanya Srinivas, [5]K. Umamaheswara Rao, [6]V. Siva Kumar

[1,3,4]Pharm-D [5th] year, Krishna Teja Pharmacy College, Tirupati.
[2]Patient Safety Pharmacovigilance Associate, PvPI, AMC-SVIMS, SPMC (W), Tirupati.
[5]Prof. & HOD Pharmacology, SVIMS, SPMC(W), Tirupati.
[6]Senior Professor, Department of Nephrology, SVIMS, Tirupati.

A B S T R A C T

This study mainly focuses on the post-transplant opportunistic viral infections and adverse drug reactions associated with Immunosuppressant therapy and Antiviral therapy. A retrospective study was carried out in the department of Nephrology for a period of six months. Apart from the viral infections, this study also aims to address the adverse drug reactions associated with the all the drugs involved in treatment plan which include immunosuppresants therapy and anti viral therapy. The data collected from patients medical records to analyse the nature and causative organism of viral infection, frequency of attack of viral infections and the treatment given as well as ADRs associated with given treatment. Out of 88 transplanted patients, 42 patients had viral infections. CMV infection (61.53%) shows higher incidence followed by HCV (9.61%), varicella zoster (9.61%), Herpes zoster (9.61%), BK(7.69%) and HBV(1.92%). 59.37% of population of CMV infection are treated with Tab. Valganciclovir. For varicella zoster and Herpes zoster parenteral acyclovir (60%) was given. 100% recovery was observed. 58 ADRs were observed in 88 patients. Prednisolone+Tacrolimus (25.86%) showed higher incidence of ADRs. New onset of diabetes after transplantation (NODAT) (25.86%) and urinary tract infections (18.9%) were most frequent ADRs. Except NODAT rests of all the ADRs are recovered in our study. Patients should be monitored throughout the post-transplant treatment period for opportunistic infections like viral infections. A proper monitoring of given treatment (Immunosuppressant therapy and anti-viral therapy) through the treatment period can reduce the incidence of preventable ADRs such that the term patient safety is the utmost priority can be justified.

Key words: Renal transplantation, viral infections, cytomegalo virus, Hepatitis C virus.

A R T I C L E I N F O

AUTHORD E T A I L S
Pilla Sree Surya Durga Devi
Patient Safety Pharmacovigilance Associate,
PvPI, AMC-SVIMS, SPMC(W), Tirupati.
Email ID: sreesuryadurgadevi@gmail.com
MS-ID: AJMPS4102

ARTICLE QR-CODE

A R T I C L E H I S T O R Y: Received 19 Aug 2019, **Accepted** 29 September 2019, **Available Online**19 December 2019

Citation: *Pilla Sree Surya Durga Devi.* Pharmacotherapeutic Management of Viral Infections in Post Renal Transplantation Recipients.*A. J. Med. Pharm, Sci.*, 2019, 7(2): 43-52.

C O N T E N T S

1. Introduction

End Stage Renal Disease [ESRD] is last stage of kidney disease, which is irreversible and requires immediate intervention with either dialysis or transplantation.(1) Renal transplantation offers a significant improvement in quality of life over hemodialysis in post renal transplanted patients. Multiple factors including pre-transplant Co morbidities, type of graft and degree of immunosuppression influence the survival of the transplanted patients. (2) For the success of transplantation it is essential to induce effective immunosuppression. Immunosuppressive protocols consist of triple therapy with Calcineurin inhibitors, an adjunctive agent and corticosteroids. Novel immunosuppressant drugs offer highest safety, less nephrotoxicity and minimal side effects (3). Report suggests that infections occur in 66.6% of renal transplant recipients and approximately 70% of severe Bacterial, Fungal and Viral infections occur within three months of transplantation. (4)(5)

Requirement of post-transplant immunosuppression to maintain allograft function predisposes transplant patients to a variety of viral infections. (6) Most of the viral infections cause significant mortality in renal transplanted patients. Most cases of reported organ transplantations have involved latent viruses such as CMV, HBV, HCV, Varicella zoster, Herpes zoster, BK polyoma virus and HIV. Previous studies demonstrated that incidence of CMV majorly seen in male's (39-41%) than female's (18-20%) after transplantation. (7)(8) To combat the viral infections, antiviral therapy include Acyclovir, Famciclovir, Ganciclovir, Valcyclovir and Foscarnet is often used in transplanted patients. (9)

2. Materials and Methods

A retrospective study was carried out in the department of Nephrology, Sri Venkateswara Institute of Medical sciences, Tirupati from August 2018 to January 2019. This study was approved by Institutional Ethical committee (Roc.No.AS/11/IEC/SVIMS/2017). Patients who underwent renal transplantation of both live related and deceased related recipient as well as patients who required maintenance immunosuppression and treatment with antiviral drugs for post-transplant opportunistic viral infections are considered for inclusion. Pediatric patients and pregnant women were excluded in this study. As per the inclusion, a total number of 88 patients were included in the study. The demographic details of the patient was collected by using predesigned data collection pro forma which includes demographic details, Induction therapy, date of transplantation, immunosuppressant therapy, diagnostic parameters, diagnosis of viral infection and antiviral therapy. In this study, the patient's medical records were used to analyse the nature and causative organism of viral infection, frequency of attack of viral infections and the treatment given as well as ADRs associated with given treatment. Adverse drug reactions associated with past medication, Induction therapy, immunosuppression therapy and antiviral therapy were collected and recorded on suspected drug reaction reporting form designed by Indian pharmacopoeia commission under Pharmacovigilance program of India. Causality of adverse drug reaction was assessed by using Naranjo scale and WHO-UMC scale (10,11). The severity and preventability of each reported adverse drug reaction was assessed using modified Hartwig and Seigel scale and modified Schumock and Thornton scale respectively(12,13). A descriptive analysis of the data was done using Microsoft Excel 2013 and results were expressed as numbers and percentage.

3. Results and Discussion

Out of 88 post kidney transplant patients, 4(4.54%) patients distributed in the 0- 20 age group, 60(68.18%) patients between 21-40 age group, 24(27.27%) patients between 4-60 age group and none of the patients were distributed in above 61 age group. 73(82.95%) out of 88 patients are male and rests of the 15(17.04%) patients are female. Majority of the native kidney disease patients 53(60.22%) are diagnosed with chronic glomerulonephritis (CGN) followed by 20(22.72%) patients with CKD of unknown type, 11(12.5%) patients with chronic interstitial nephritis (CIN) and 4(4.54%) patients with diabetic nephropathy respectively. 55(62.5%) of 88 patients had hypertension, 6(6.81%) patients had diabetes, 4(4.54%) patients had Tuberculosis and one patient had anemia as co morbidity. 20(22.72%) patients are free of comorbidities.

Amongst the 88 successful renal transplantations, out of 18 patients 8(9.09%) female and 10(11.36%) male patients received kidney from deceased donors. In rest of 70 live donor transplantation cases, 7(7.95%) are females and 63(71.59%) are males. Most of the donors including deceased and live donors fall under age group between 21-40 (49 live donors and 11 deceased donors), medium distribution from age group between 41-60 and few donors fall under 0-20 age group. Followed by native kidney disease according to type of graft chronic glomerulonephritis (CGN) is major cause for kidney transplantations in 42(47.72%) live donor kidney transplantation cases and in 11(12.5%) deceased donor kidney transplantation cases. CKD of unknown type stands second for kidney transplantations i.e., 17(19.31%) in live donor kidney transplantation cases and 3 in deceased donor kidney transplantation cases. Co morbidities are one of the

major causes for kidney transplantation, amongst the co-morbidities hypertension ranks first in 44(50%) out of 70 live donor kidney transplantation cases and 11(12.5%) out of 18 in deceased donor kidney transplantation cases. Diabetes stands second to Hypertension. No co-morbidity was observed in 16(18.18%) patients who received kidney from live donors and 4(4.45%) from deceased donor transplantation cases. Table-1 shows the demographic data of the patients who underwent renal transplantation are sorted in two groups; recipients with infections and recipients without infections. Induction therapy Basiliximab is majorly given than ATG (Anti thymocyte globulin) in this population. Table 2 represents age wise distribution of viral infections. Out of 88 transplanted patients, 42(47.72%) patients had viral infections and 46(52.12%) patients are free from viral infections. Patients under age group between 21-40 are more prone to viral infections, 41-60 age group stands second and age group between 0-20 are least affected by viral infections. Among these infections 6 patients had 2 episodes of infections and 1 patient had 3 episodes remaining patients (35) with single episode of viral infection. In our study, live donor kidney recipients (45 of 70) are much prone to viral infections than deceased donor kidney recipients (7 of 18) (Table-3). Cytomegalovirus infection (32, 61.53%) showed higher incidence followed by Hepatitis-C virus, Varicella zoster and Herpes zoster with similar incidence (5, 9.61%) (Table-4).

Some of the diagnostic parameters employed in this study for the diagnosis of viral infections, for CMV infections Quantitative CMV DNA PCR test was employed in 55.76% of population, followed by BK Quantitative DNA PCR test was performed in 5.76% of population, Varicella zoster and Herpes zoster infections was diagnosed based on clinical diagnosis in 19.22% of population and HCV, HBV are diagnosed by HCV RNA PCR test in 9.61% and HBsAg test in 1.92% of population (Table-5). Pharmacotherapy plays important role in treatment of viral infections. 59.37% of population of CMV infection are treated with Tab. Valganciclovir 41.63% of CMV infection population received Inj.Gancyclovir. For infections caused by Varicella zoster and Herpes zoster Oral Acyclovir (in 40% population) and Parentral Acyclovir (in 60% population) were given. Patients with BK virus infections are treated with Tab. Leflunomide only. HBV infections are treated with Lamivudine and HCV infections are treated with combination of several antiviral drugs. (Table-6). Recovery from viral infections is the outcome in 100% population.

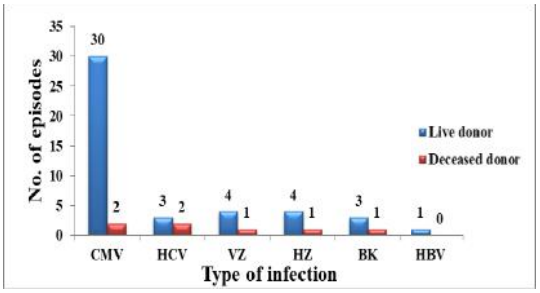


Fig 1: Distribution of viral infections related to allograft

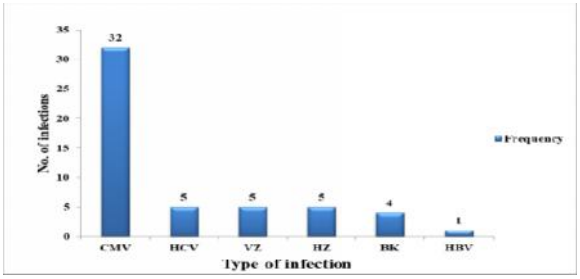


Fig 2: Frequency of viral infections

Out of 58 ADRs 15(25.86%) ADR's were due to Prednisolone +Tarolimus followed by Prednisolone+ Tacrolimus+ Mycophenolate mofetil (11, 18.96%)), and Tacrolimus (7, 12.0%) (Table-7). NODAT (15) is the most common ADR followed by UTI (11) (Table-8). Severity of reported ADR's was assessed by Modified Hartwig and Siegel scale, out of 58 ADR's, 47 ADR's were moderate, 9 ADR's were mild, and 2 ADR's were severe in nature. (Table-9). 32 of 58 ADRs lead to hospitalization of the patients. (Table-10). Causality assessment of ADR's by Naranjo and WHO scale suggested 37 ADR's were probable, 18 ADR's were possible and 3 ADR's were definite (Table-11). Preventability of ADR was assessed by Schumock and Thornton scale, 39 of 58 ADR's was probably preventable, 15 ADR's were not preventable and 4 ADR's were definitely preventable (Table-12).

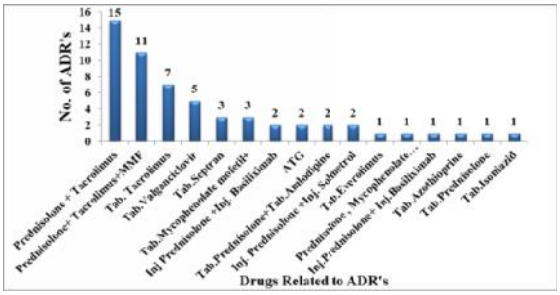


Fig 3: Contribution of drugs related to ADR's

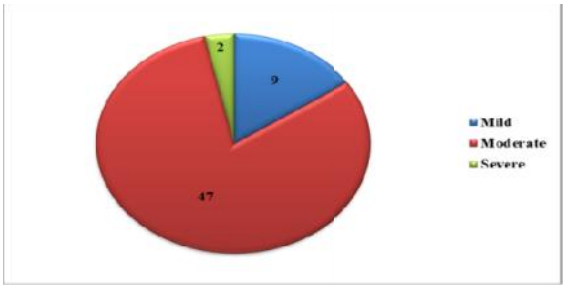


Fig 4: Severity of ADR's

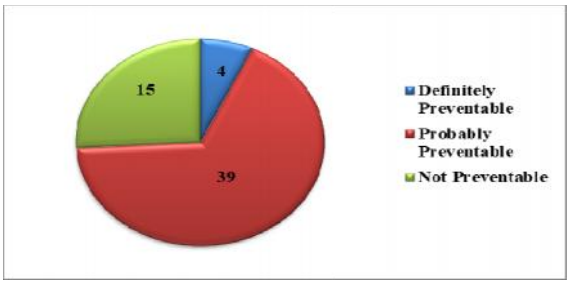


Fig 5: Preventability of ADR's

Table 1: Demographic data of patients who underwent renal transplantation

Variable	Recipients with infections	Recipients without infections
Mean age	35.3	33.6
Gender distribution	Males – 35 (83.33%) Females – 07 (16.6%)	Males – 38 (84.44%) Females – 08 (17.77%)
Native kidney disease	CGN – 29 (69.0%) CIN -05 (11.9%) Unknown type-06 (14.28%) Diabetic nephropathy -02 (4.76%)	CGN – 24 (53.33%) CIN – 06 (13.33%) Unknown type – 14 (31.11%) Diabetic nephropathy – 02 (4.44%)
Type of allograft	Live donor – 36 (85.71%) Deceased donor – 06 (14.28%)	Live donor – 34 (75.55%) Deceased donor – 12 (26.66%)
Donor wise distribution	Mother –17 (40.47%) Wife –12 (28.57%) Father – 01(2.38%) Brother – 01 (2.38%) Sister – 02 (4.76%) Brain death- 06 (14.28%) Unrelated –02 (4.76%) Son – 01 (2.38%)	Mother – 15 (33.33%) Wife – 05 (11.11%) Father – 05 (11.11%) Brother – 06 (13.33%) Sister – 02 (4.44%) Brain death –12 (26.66%) Unrelated – 01 (2.22%) Son – 0 (0%)
Induction therapy status	Basiliximab – 15 (35.71%) ATG - 02 (4.76%)	Basiliximab – 12 (26.66%) ATG – 0 (0%)

Table 2: Age wise distribution of viral infections

Age(years)	No. of patients with viral infections		No. of patients without viral infections	
	Male	Female	Male	Female
<20	01(2.38%)	0 (0%)	03 (6.52%)	0 (0%)
21-40	22(52.3%)	06(14.28%)	27 (58.69%)	06 (13.04%)
41-60	13(30.95%)	0(0%)	08 (17.39%)	02 (4.34%)
>60	0(0%)	0(0%)	0 (0%)	0 (0%)
Total	42(100%)		46 (100%)	

Table 3: Distribution of viral infections relating to type of allograft

Type of allograft	Viral infections					
	CMV	HCV	VZ	HZ	BK	HBV
Live donor	30 (57.6%)	3 (5.76%)	4 (7.6%)	4 (7.6%)	3 (5.76%)	1 (1.92%)
Deceased donor	2 (3.84%)	2 (3.84%)	1 (1.92%)	1 (1.92%)	1 (1.92%)	0 (0%)
Total	52(100%)					

Table 4: Frequency of viral infections

S. No	Viral Infections	Frequency
1.	Cytomegalovirus (CMV)	32 (61.53%)
2.	Hepatitis ‘C’ virus (HCV)	05 (9.61%)
3.	Varicella Zoster (VZ)	05 (9.61%)
4.	Herpes Zoster (HZ)	05 (9.61%)
5.	BK virus (BK)	04 (7.69%)
6.	Hepatitis ‘B’ virus (HBV)	01 (1.92%)
	Total	52 (100%)

Table 5: Diagnostic methods employed in infectious group

Viral infection	Diagnostic parameters (%)
Cytomegalo virus	IgG Positive – 2 (3.84%) IgM Positive – 01 (1.92%) DNA PCR Positive – 29 (55.76%)
BK virus	DNA PCR Positive – 03 (5.76%) Bone marrow PCR Positive – 01 (1.92)
Herpes zoster	Clinical diagnosis – 5 (9.61%)

Varicella zoster	Clinical diagnosis – 5 (9.61%)
Hepatitis ‘C’ virus	HCV RNA PCR Positive – 5 (9.61%)
Hepatitis ‘B’ virus	HBsAg Negative – 1 (1.92%)

Table 6: Pharmacotherapy of viral infections

Common viral Pathogens in renal Transplant recipients	No. of episodes	Percentage of total infections	Therapy	Average duration	Outcomes
Cytomegalovirus	32	61.5%	Tab.Valganciclovir 450mg OD (59.37%) Inj.Gancyclovir 175mg in 250ml NS IV (40.62%)	3 months	Recovered
Varicella Zoster	05	9.6%	Tab. Acyclovir 500mg OD (40%) Inj. Acyclovir 500mg OD (60%)	1 week	Recovered
Herpes Zoster	05	9.6%	Inj. Acyclovir 500mg OD (40%) Tab. Famciclovir 500mg OD (60%)	2 weeks	Recovered
Polyoma virus BK/JC	04	7.6%	Reduction in immunosuppression Tab.Leflunomide 10 mg OD (100%)	3 weeks	Recovered
Hepatitis ‘B’ virus	01	1.9%	Tab.Lamivudine 100mg OD (100%)	24 – 48 weeks	Recovered
Hepatitis ‘C’ virus	05	9.6%	Tab. Ribavirin 200mg OD (20%) Tab.Sofosobuvir 60mg OD (40%) Tab.Daclatasvir 400mg OD (20%) Interferon- alpha (20%)	24 – 48 weeks	Recovered

Table 7: Frequency of Adverse drug Reactions

Reaction	Frequency
NODAT	15 (25.86%)
UTI	11(18.9%)
Hyponatremia	5 (8.62%)
Leucopenia	4 (6.89%)
Pancytopenia	4 (6.89%)
Hypokalemia	3 (5.17%)
Hepatic dysfunction	2 (3.44%)
Proteinuria	2 (3.44%)
Bicytopenia	1(1.72%)
Hypotension	1 (1.72%)
Lower limb cellulitis	1 (1.72%)
Nausea	1 (1.72%)
Nausea and vomiting	1 (1.72%)
Optic Neuropathy	1 (1.72%)
Pancreatitis	1 (1.72%)
Seizure	1 (1.72%)
Tacrolimus toxicity	1 (1.72%)
Thrombophlebitis	1(1.72%)
Left central serous retinopathy	1(1.72%)
Total	58 (100 %)

Table 8: Severity of Adverse drug reactions

Reaction	Severity		
	Mild	**Moderate**	**Severe**
New onset of diabetes after transplantation		15	
Urinary tract infection	3	8	
Leucopenia		4	
Pancytopenia		4	
Hyponatremia	2	3	
Hypokalemia		2	
Proteinuria		2	
Thrombocytopenia	2		
Bicytopenia		1	
Hepatic dysfunction	1	1	
Hypotension		1	
Lower limb cellulitis		1	
Left central serous retinopathy			1
Nausea	1		
Nausea+ Vomiting		1	
Optic neuropathy			1
Pancreatitis		1	
Generalized Tonic Clonic seizures		1	
Tacrolimus toxicity		1	
Thrombophlebitis		1	
Total	9(15.51%)	47(81.03%)	2 (3.44%)

Table 9: Seriousness of Adverse drug reactions

Parameters	**No. of ADR's**
Death	0
Congenital anomaly	0
Life threatening	0
Hospitalization	32(55.17%)
Disability	0
Non- serious	26(44.82%)
Total	58 (100%)

Table 10: Causality Assessment of ADR's by Naranjo scale and WHO scale

Parameters	**No. of ADR's**	
	Naranjo scale	**WHO scale**
Definite / Certain	3 (5.17%)	0 (0%)
Probable / Likely	37 (63.79%)	23 (39.65%)
Possible	18 (31.03%)	35 (60.34%)
Doubtful / Unclassified	0 (0 %)	0 (0%)
Total	58 (100%)	

Table 11: Preventability Assessment by Modified Schumock and Thronton scale

Parameters	**No. of ADR's**
Definitely Preventable	04 (6.89%)
Probably Preventable	39 (67.24%)
Not Preventable	15 (25.86%)
Total	58(100%)

Discussion:

It is believed that renal transplantation prolongs the life span of patients with End stage renal disease. Immunosuppresants exacerbate the risk of post transplantation opportunistic infections such as fungal, bacterial, viral infections. Our study mainly focuses on viral infections, treatment options and their ADR risk in post transplantation patients. Cytomegalo virus (CMV) infection is the most common followed by Hepatitis 'C' virus (HCV), Hepatitis 'B' virus (HBV), Varicella zoster, Herpes zoster and BK polyoma virus infections are seen in patients after

transplantation. Prophylactic treatment for CMV must be initiated after transplantation else the CMV infection occurs within 1-3 months and if not treated it may leads to allograft dysfunction (or) acute graft rejections. Juthaporn cowan et al.,(14) documented that occurrence of viral infections are most common during first year post transplantation period, the same is observed in our study too.

In our study the mean age of Patients who had viral infections is 35.3 and 33.6 in non-infected population. It is closely matched to the findings of Boshra Hasanzamani et al., (6) study who reported that the age of Patients who had viral infections is 36.16 with that of 36.91 in non infected patients. Arun kumar et al.,(2) study population (77% are males and 22.2%) much similar to our study population (82.95% are males and 17.04%) in terms gender distribution.

The common indications for kidney transplantations in our study was CGN 60.2%, CKD of unknown type is 22.7%, CIN 12.5% and Diabetic nephropathy 4.5%. Indication for renal transplantation in our study is slightly matches with the Kevin Manuel et al as they too documented CGN (34%) and Diabetic nephropathy (23%) are the major causes for renal transplantation. However, Rajapurkar MM et al study report (Diabetic nephropathy is the major cause followed by CKD of unknown type) deviates from our study report. In our study, 80% are live donor renal transplantations and 20% are deceased donor renal transplantations. Fabienne Jennie et al,(16) documented that in their study 60% are deceased donors and 40% are live donors.

There were 88 renal allograft recipients in our study in them 42(47.72%) patients experienced 52 episodes of viral infections, 46(52.12%) patients never suffered from any infections. There was a prevalence of infection episodes between 3weeks to one year after transplantation. Incidence of CMV is high amongst the viral infections .There were 52 disease episodes CMV in 32 patients, it had a prevalence of 61.3%, HCV in 9.61%, HBV in 1.92% , BK in 7.69%, varicella zoster in 9.61% and Herpes zoster in 9.61% of population. Ram et al.,(17) had documented CMV in 21.89% , HCV in 7.67% and HBV in 9.46% in 46% of population. Kevin Manuel et al.,(7) documented prevalence of CMV in 21% , HCV in 2%, BK in 3% and HBV 4% in 30% of population and Arun kumar et al.,(2) documented CMV disease in 13.6% , HCV in 13.3% in 37.77% of population. These above studies doesn't documented incidence of varicella zoster and Herpes zoster in renal transplant recipients.

Patients underwent renal transplant encounters ADRs frequently as they will be on immunosuppressant therapy and antiviral therapy. In our study 65.5% of live donor renal transplantation Patients experienced the ADRs where as only 31.03% of deceased related donor renal transplanted patient experienced ADRs during the study period. In our study a total of 65.90% patients experienced ADR's during the study period, amongst the all drugs, Tab.Tacrolimus accounts for 24.5% of total ADR's, followed by Tab.Valganciclovir, which accounts for 17.2% of ADR's and rest of ADR's are due to immunosuppressant medications. Sharma love et al.,(18) also concluded that in their study incidence of ADR's are more in renal transplant recipients especially on patients with the Valganciclovir.
In our study the assessment of ADR's by Naranjo and WHO scale showed that 63.79% of ADR's are probable and 31.03% ADR's are possible. Followed by severity assessment our study results showed 81.03% of ADR's are moderate and 3.44% of ADR's are severe and preventability assessment showed 67.24% of ADR's are probably preventable and 25.86% of ADR's are not preventable. Our study findings similar to Lingala maneesha et al.,(19) documented that Naranjo and WHO scale showed 91.5% of ADR's are probable, severity assessment showed 5.9% of ADR's are moderate and 30% of ADR's are severe and preventability assessment showed 97.1% of ADR's are not preventable in their study and other studies conducted by Sharma love et al.,(18) documented that Naranjo and WHO scale assessment showed 55.95% are probable and 39.29% are possible, severity assessment showed 40.47% ADR's are moderate and preventability assessment showed 93.45% ADR's are not preventable in their study. Except New onset of diabetes after transplantation (NODAT), rests of all the ADRs are recovered in our study. The limitations of our study, it is a retrospective study, so follow up of patients and close monitoring of infections is not possible due to short period of time.

Table 12: Comparative assessment of viral infections

Parameters	Our study	Kevin Manuel et al	R. Ram et al	Arun kumar et al
Sample size	88	100	169	45
No. of patients with viral infections	52(59.09%)	30(30%)	46(27.21%)	17(37.77%)
CMV	61.53%	21%	21.89%	13.6%
HCV	9.61%	2%	7.67%	13.3%
VZ	9.61%	-	-	-
HZ	9.61%	-	-	-
BK	7.69%	3%	-	-
HBV	1.92%	4%	9.46%	11.1%

Table 13: Comparative assessment of ADR's

Study	Causality by Naranjo scale			Severity by Modified Hartwig and Seigel scale			Preventability by Modified Schumock and Thornton scale		
	Definite	**Probable**	**Possible**	**Mild**	**Moderate**	**Severe**	**Definitely preventable**	**Probably Preventable**	**Not preventable**
Lingala Maneesha et al.,[19]	0 (0%)	65 (91.5%)	6 (8.5%)	8 (11%)	42 (59%)	21 (30%)	0 (0%)	2 (2.9%)	69 (97.1%)
Sharma love et al.,[18]	4 (4.76%)	47 (55.95%)	33 (39.29%)	49 (58.33%)	34 (40.47)	01 (1.19%)	0 (0%)	4 (4.77%)	80 (95.23%)
Our study	3 (5.17%)	37 (63.79%)	18 (31.03%)	9 (15.51%)	47 (81.03%)	2 (3.44%)	4 (6.89%)	39 (67.24%)	15 (25.86%)

4. Conclusion

As believed immunosuppression is recommended even after transplantation, maintenance of immunosuppression is the major cause for opportunistic infections in renal transplantation patients. Poly pharmacy is the common practice to combat the severe complications after transplantation. Hence patients are at high risk to get experienced with Adverse Drug Reactions. Hence patients should be monitored throughout the post-transplant treatment period including Induction therapy, Immunosuppressive therapy and Antiviral therapy. A proper monitoring of treatment regimen can reduce the incidence of preventable ADRs such that highest level of patient safety can be achieved.

5. References

[1] Maaz Abbasi, Glenn Chertow, Yoshio Hall. End stage renal disease. Clinical Evidence Handbook 2010; 82(12):513.

[2] Arun Kumar, Chaturbhuj Agarwal, Ashok K.Hooda, Ashutosh Ojha, Mukesh Dhillon and K.V.S.Hari Kumar. Profile of infections in renal transplant recipients from India. J family med prim care 2016; 5(3):611-614.

[3] Sepideh Zununi vahed, Mohammadreza Ardalan, Nasser Samadi and Yadollah Omidi. Pharmacogenetics and drug-induced nephrotoxicity in renal transplant recipients. Bioimpacts2015; 5(1):45-54.

[4] Daniel L.Bohl, Matthew J.Koch, Daniel C.Brennan. Viral infections in renal transplantation: A clue to excessive immunosuppression. J Bras Nefrol; 29:186.

[5] Jad A.Khoury, Daniel C.Brennal. Infections complications in kidney transplant recipients: Review of Literature. Saudi J Kidney Dis Transplant 2005; 16(4):453-497.

[6] Ethem Unal, Ahmet Topcu, Muhammed Taha Demirpolat, Omer Faruk Ozkan.Viral Infections after Kidney Transplantation: An Updated Review. Int J Virol AIDS 2018;5(1):1-4.

[7] Boshra Hasanzamani, Maryam Hami, Vajihe Zolfaghari, Mahtab Torkamani, Mahin Ghorban Sabagh, Saiideh et al., The effect of cytomegalovirus infection on acute rejections in kidney transplanted patients. JRIP 2016; 5(2):85-86.

[8] Kevin Manuel, Marie Moses Ambroise, Renu G'Boy Varghese, Ilangovan veerapan, Georgi Abraham. Prevalence of cytomegalovirus and BK polyoma virus infection in post–renal transplant patients in a tertiary care centre in South India. J Nephropathol 2017; 6(4):380-388.

[9] Viral infection Treatment drugs. Available at: https://www.omicsonline.org/scholary/viralinfection-treatment-drugs-journals-articles-ppts-list.php

[10] Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA. Method for estimating the probability of adverse drug reactions. Clin PharmacolTher. 1981; 80:239-45.

[11] Guidance Document for spontaneous adverse drug reaction reporting. Available at: http://ipc.nic.in/writereaddata/mainlinkFile/File268.pdf

[12] Hartwig SC, Seigel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992; 49:2229-32.

[13] Schumock GT, Thronton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm.1992:27:538.

[14] Juthaporn Cowan, Alexandria Bennett, Nicholas Fergussion, Cheynne McLean, Ranjeeta Mallick, D.William Cameron et al., Incidence rate of post-kidney transplant infection: A retrospective cohort study examining infection rates at a large Canadian multicenter Tertiary-Care Facility. Canadian journal of kidney health & disease2018; 5:1-8.

[15] Mohan M Rajapurkar, George T John, Ashok L Kirpalani, Georgi Abraham, Sanjay K Agarwal, Alan F Almeida et al., What do we know about chronic kidney disease in India:First report of the Indian CKD registry. BMC Nephrology 2012; 13(10):2-8.

[16] Fabienne Jenni, Sebastian Riethmuller, Rudolf P.Wuthrich. Significance of urine diagnostic tests after renal transplantation. Kidney blood press Res 2013; 37:116-123.

[17] R.Ram, KV Dakshina Murty, N Prasad. Time table of infections after renal transplantation-South Indian Experience. Indian J Nephrol 2005; 15:S14-S21.

[18] Sharma Love, Kanodia Lalit, Singh Lokesh, Yadav Virendra, Thomas Binny, Hail Moza Al. A study of adverse drug events associated with the use of immunosuppressive agents in kidney transplanted patients. Int J Drug Dev & Res., 2012; 4(3): 283-291.

[19] Lingala Maneesha, Dr. Pilla S Surya Durga Devi, Pola Bogeswara Reddy, Tirupathi Devi Priya, Dr. K. Umamaheswara Rao, Dr. V. Siva kumar. Adverse drug reactions associated with immunosuppressive therapy in kidney transplantation patients as assessed using causality, Severity and preventability scales. Hosp. Pharmacy2018; 13(20):264-278.