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## "Safety of Cyclosporine in Patients with Different Organ Transplants" Case Reports:

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#### **ABSTRACT:**

This Research paper deals with the Case Studies of the various patients with their organ transplantations treated mainly with "Cyclosporine" used as an "Immuniosupressant drug". The case reports of different patients presented in this research paper are studied and analysed through MedDRA PTC app. In this study we have made use of "Pharmacovigilance studies" and their official software as well. For the screening of the patient's data. Through this Case Studies we come to know the safety of the cyclosporine used as an immunosuppression in the patients with organ transplants, successfully treated with cyclosporine in all the patients. By this Study we come to know that Cyclosporine can be used as organ transplant rejection in various patients with organ transplantation as this medicament has both safety and efficacy. This study is Retrospectively completed by which we could analyse the patient's safety data, from year 2010 to 2023. Through which we could analyse the safety ratio.

**KEYWORDS**: Cyclosporine, Case Study, MedDRA PTC, Analysis.

#### 1. INTRODUCTION:

"Cyclosporine" was discovered by Jean Borel and his colleagues the 1970s. Borel was a researcher at Sandoz who isolated the compound from Tolypocladium inflatum. Cyclosporine was revealed in 1969, Sandoz biologist Dr. Hans Peter Frey discovered cyclosporine in a soil sample. In 1970, Borel and his colleagues isolated cyclosporine. In 1973, a pure form of cyclosporine was synthesized.



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#### **CHEMICAL STRUCTURE:**

Figure No 1 Cyclosporine A

#### **MOLECULAR FORMULA:**

#### C62H111N11O12

#### **BIOCHEMICAL PROPERTY:**

1) Molecular Formula: C<sub>62</sub>H<sub>111</sub>N<sub>11</sub>O<sub>12</sub>

2) Molecular Weight: ~1202.6 g/mol

3) **Solubility**: Poorly soluble in water; soluble in organic solvents like ethanol, methanol, and chloroform.

4) Lipophilicity: High (Log P ~2.92)

5) **Metabolism**: Extensively metabolized in the liver by cytochrome P450 enzymes, primarily CYP3A4 and CYP3A5.

#### **DRUG INTERACTIONS:**

Cyclosporine is metabolized by the CYP3A4 enzyme. Consuming grapefruit or grapefruit juice can inhibit this enzyme, leading to increased cyclosporine levels in the blood and a higher risk of side effects.

#### **SPECIAL CASE SCENARIOS:**

According to the rules of EMA, there are certain situations where any possible side effects from medicines need to be reported quickly. These include:

- 1) Use during Pregnancy or Breastfeeding: If someone has a reaction to a medicine while they are pregnant or breastfeeding, it should be reported right away.
- 2) Use in children or older Adults: If a child or elderly person has a bad reaction to a medicine, it's important to report it, since these age groups may react differently.



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- 3) Overdose, Misuse, or Mistakes: If someone takes too much medicine, uses it in the wrong way, takes it for a reason it's not meant for, or takes it by accident (even if they don't get sick from it), this still needs to be reported.
- 4) Medicine Doesn't Work (Lack of Effect): If a medicine doesn't work especially in serious or life-threatening conditions—it should be reported within 15 days.
- 5) Quality Issues or Fake Medicines: If a side effect seems to be caused by a bad-quality or fake medicine, it should be reported immediately to keep others safe.

#### **MONITORING:**

Regular monitoring of cyclosporine A blood concentrations, kidney function, blood pressure, and blood sugar levels is essential to ensure therapeutic efficacy and minimize toxicity. In summary, cyclosporine A is a vital immunosuppressant with significant benefits in managing autoimmune diseases and preventing organ transplant rejection.

Pharmacovigilance: Pharmacovigilance encompasses all aspects of medicine-related issues, including their identification, evaluation, understanding, and prevention. This process ensures the safety and efficacy of pharmaceutical items by continuously monitoring them throughout their lives.

#### **CASES PRESENTATION:**

#### **CASE STUDY NO 1:**

An individual with a 56-year-old male patient record who had a liver transplant is the subject of the first case study. Heparin, Acarbose, Tacrolimus, and methylprednisolone were all part of his drug history. Cytotoxicity was one of the adverse effects observed in the patient. Total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and  $\gamma$ -glutamyl transferase ( $\gamma$ -GTP) all improved in the patient's blood levels to 1.7 mg dl, 49 UL, 141 IUL, and 47 IUL, respectively. Histopathological analysis of the patient's biopsy sample showed enlarged liver cells, polynuclear cells, and necrosis in various spots. On the other hand, by POD 60, the levels of ALP,  $\gamma$ -GTP, and total bilirubin had risen to 454 UL, 170 IUL, and 10 mg dL, respectively. There was no endotheliosis of the portal vein, no bile duct damage, and most of the portal triads revealed no cellular infiltration; the patient underwent abdominal computed tomography and ultrasonography at that time. As soon as it was diagnosed, the doctors stopped the patient from using cyclosporine, which corrected his issues and improved his health significantly. This was because the cyclosporine dosage was causing hepatotoxicity. The patient's condition improved after stopping cyclosporine, suggesting that it may be causing hepatotoxicity.

#### **CASE STUDY NO 2:**

A 24-year-old man with a history of psoriasis and ulcerative colitis is the subject of this study. He has a history of using amoxicillin and prednisone. Diarrhea and a decrease in body weight were among symptoms experienced by the patient. The patient's ulcerative colitis had been effectively managed for two years with a consistent dosage of 125 mg of cyclosporine taken twice daily. He



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expressed a desire to transition to a biologic drug in the future. Results from the patient's laboratory tests showed significant hypokalaemia cells/mL and pancytopenia (haemoglobin 7g/dL, white blood cell 3,100 cells/mL, and platelet 125,000 cells/mL). The suspected causes of diarrhoea, enteropathy-causing Escherichia coli and norovirus, were confirmed by stool analysis. After finishing a seven-day treatment of ciprofloxacin, the patient was readmitted to the hospital for potassium repletion. He underwent a colonoscopy evaluation due to concerns about CMV infection as a possible cause of his diarrhoea. The results revealed several hemorrhagic and ulcerated nodules throughout the colon and terminal ileum. Histologic analysis revealed that the lymph node had been replaced by Vaso formative spindle cells, just like the colon biopsy, and the patients' thoracic, abdominal, and pelvic computed tomography had shown diffuse lymphadenopathy. A peritonsillar and axillary lymph node biopsy had also been taken. Rituximab and pegylated liposomal doxorubicin 20 mg/m2 were among the medications that the patient was prescribed. The use of cyclosporine and emtricitabine to treat Kaposi sarcoma was quickly halted. The patient was discharged from the hospital shortly after he began to feel better from his illness following the termination of the cyclosporine dosage. With his health, the patient saw an improvement.

#### **CASE STUDY NO 3:**

This case study details the medical history of a 31-year-old male patient who has had visual difficulties in the past. Cyclosporine and mycophenolate were his medications in the past. Headache, hypertension, dysfunction, and urine retention were among the side effects the patient experienced. The patient's reports of the widespread tonic-colonic seizure led to their referral to the emergency room. Other tests, including those for the patient's neurological system, came back normal, although the patient did have cervical lymphadenopathy and an axillary fever of 39 degrees Celsius. Despite the patient undergoing pathological testing, the computed tomography (CT) and electroencephalography scans did not reveal any abnormalities. Additionally, the patient had magnetic resonance imaging (MRI) tests, which showed alterations in grey matter and a bilateral hyperintense patch of white matter in the supratentorial and infratentorial domains. Shortly after the patient's doctors lowered the cyclosporine dose, they found that the patient was suffering from cyclosporine neurotoxicity. The patient's condition rapidly improved upon tapering off the cyclosporine, and he was eventually allowed to leave the hospital after a few days. Patients experiencing neurotoxicity may benefit from reducing their cyclosporine dosage, since the patient reported an improvement after doing so.

#### **CASE STUDY NO 4:**

This case study details the experiences of a 56-year-old woman with a history of uncontrolled bullous pemphigoid confirmed by biopsy. The patient has previously used cyclosporine and other medications. Pain, redness, swelling, a burning feeling, trembling, and anxiety were among the side effects experienced by the patient. After seven weeks, the patient went to the hospital to complain about how the redness, swelling, and discomfort in her left hand had greatly deteriorated, and how the right hand had begun to become involved. There was noticeable redness and swelling in the right hand, particularly in the second proximal phalanx. When exposed to heat or sunlight,



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the patient's pain—which she characterized as "burning similar to a sunburn"—became much worse, according to her complaints. The patient reported less discomfort when he or she ran cold water over their hands, and this improvement was further aided by exposing the hands to freezing temperatures. The patient's skin condition improved shortly after the physicians reduced the cyclosporine dosage following a diagnosis of erythromelalgia. Reducing the patient's Cyclosporine dosage improved her erythromelalgia symptoms.

#### **CASE STUDY NO 5:**

This article details the case of a 44-year-old woman who had aplastic anemia and a history of using cyclosporine and heparin. Headache, nausea, vomiting, seizures, subarachnoid haemorrhage, and intracranial pressure were some of the unpleasant effects that the patient experienced. The patient's tongue was in the middle, and the patient had a gag reflex as well. The patient's Cyclosporine dosage was promptly changed with Testosterone Undecanoate after computed CT revealed sinus thrombosis in the superior sagittal sinus area and the patient's cerebral arteries were found to be normal. The patient did not experience any more thrombosis after 30 days. The content of her haemoglobin, however, dropped to 55 g/L. The haematology experts and neurologists recommended resuming cyclosporine A and warfarin administration simultaneously. Due to the patient's cerebral venous sinus thrombosis, the dosage of cyclosporine was decreased. Upon reducing the dosage of cyclosporine, the patient's health began to improve. Reducing the patient's Cyclosporine dosage improved their symptoms, suggesting that the patient had cerebral venous sinus thrombosis.

#### **TABLES**:

#### **Tables of Screened Case Study Reports:**

Table No 1

S.no	Age	Sex	Medical History	Past Drugs	Suspect Drug	Dose	Adminis tration	Indicat ion	Co- suspect	Conco mitant Medica tion	Preferred Term	HLT	HLGT	soc	Additional ADR	Impact to Suspect Drug	Treatment Medication	ADR Status	Caus ality
1	56	М	Liver Transpla nt	Acarbo se, Tacroli mus, methyl prednis olone, heparin	CsA	-	-	Liver Transpl antation	-	Mycop henolat e mofetil	Hepatotoxi city	Hepa tocel lular dama ge and hepat itis NEC	Hepati c and hepato biliary disorde rs	Hepa tobili ary disor ders	-	D	Tacrolimus	R	s
2	24	М	Ulcerativ e colitis and psoriasis	amoxici llim, prednis one	CsA	125 mg BID/ D	Orally	Ulcerati ve colitis	-	ciproflo xacin, doxoru bicin	Kaposi's sarcoma	Kapo si's sarco mas	Soft tissue sarcom as	Neop lasm s beni gn, mali gnan t and unsp ecifi ed (incl cysts and poly ps)	-	D	rituximab	R	s
3	31	М	Vision problems	Cyclos porine and mycoph enolate	CsA	5mg/ kg/D	Orally	Kidney Transpl antation	Mycop henolat e Mofetil	-	Neurotoxi city	Nerv ous syste m disor ders NEC	Neurol ogical disorde rs NEC	Nerv ous syste m disor ders	Headache, Urinary retention, Hypertensi on	R&D	-	R	S
4	56	F	uncontrol led biopsy- proven bullous pemphig oid.	cyclosp orine	CsA	100g m/D	Orally	Bullous pemphi goid	-	-	Erythrome lalgia	Skin vaso moto r cond ition s	Skin vascula r abnorm alities	Skin and subc utane ous tissu e disor	Injection site joint redness, Swelling, pain, Burning sensation, Tremor,	R&D	-	R	s



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Table No 2

5	44	F	Aplastic anemia	cyclosp orin, heparin	CsA	150 mg BID	Orally	Cerebra 1 venous simus thromb	Testost erone Undeca noate	Warfari n	Cerebral thrombosis	Cent ral nerv ous syste m haem orrha ges and cereb rovas cular accid ents	Central nervou s system vascula r disorde rs	Nerv ous syste m disor ders	Headache, Nausea, Vomiting, Atonic seizures, Suberachno id haemorrhag e	R&D	-	R	s
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#### **MATERIAL AND METHODS: -**

The present research study would be carried out by screening of case reports patients from various research journals which are freely available on search engines.

Sr NO	Name of Journal	Sr NO	Name of Journal
1	Nippon Medical School	54	Interactive Cardio Vascular and Thoracic Surgery
2	AGC case reports journal	55	The Tohoku Journal of Experimental Medicine
3	Open Access Emergency Medicine	56	Pulmonary Circulation
4	Open access case report	57	Metabolism
5	Clinical Case Report Medicine	58	Department of Nephrology, Dialysis, and transplantation
6	Drug Safety case Report Springer	59	PediatricRheumatalogy
7	Frontiers in Pharmacology	60	Modern Rheumatology
8	Psychiatry and Clinical Psychopharmacology	61	International Wound Journal
9	Nephrology Forum	62	Transplant Infectious
10	Case reports in dentistry	63	International Journal of Surgery Case Reports
11	Nature Reviews Nephrology	64	Annals of Medicine and Surgery
12	American Journal of Transplantation	65	Ocular Immunology and Inflammation
13	Frontiers in Neurology	66	Allergy, Asthma & Clinical Immunology
14	Enilepsy & Behavior Case Reports	67	B Freyne - Transplantation Proceedings
15	BMJ Case Reports	68	Case Reports in Rheumatology
16	American Journal of Kidney Diseases	69	Heliyon
17	Wiley InterScience	70	Medical Mycology Case Reports
18	BMC neurology	71	Hematology
19	Journal of Infection and Chemotherapy	72	European Heart Journal-Case Reports
20	Clinical, Cosmetic and Investigational Dermatology	73	Nephrology
21	Journal of Oncology Pharmacy Practice	74	International Journal of Dermatology and Venereology
22	Journal Renal Failure	75	The oncologist
23	Prontiers in Pediatrics	76	Science Progress
24	World Allergy Organization Journal	77	Renal Failure
25	BMC gastroenterology	78	Journal of Surgical Case Reports
26	Indian Journal of Dermatology, Venereology and Leprology	79	SAGE Open Medical Case Reports
27	Austrilian journal of Dermatology	80	Frontiers in Medicine
28	Dermatologic Therapy	81	The American Journal of Case Reports
29	International Medical Case Reports Journal	82	Case Reports in Neurology
30	Americal Academy of Dermatology	83	The Egyptian Rheumatologist
31	American Journal of Health-System Pharmacy	84	Journal of Nepal Paediatric Society
32	JMIR dermatology	85	Journal of Asthma and Allergy
33	The Cureus journal of Medical Science	86	Case Reports in Hematology
34	BMC psychiatry	87	Clinical, Cosmetic and Investigational Dermatology
35	Clinical Toxicology	88	Open Access Emergency Medicine
36	Case reports in dermatological medicine	89	Journal of Pharmacy Practice
37	Frontiers in Immunology	90	Oxford Medical Case Reports
38	American Journal of Transplantation	90	Journal of Vascular Surgery Cases, Innovations and Technique
39	BMC Musculoskeletal Disorders	92	Sase Journal Author Gateway
40	JAAD Case Reports	93	
41		94	Drug Safety-Case Reports
	The Journal of pediatrics		Kidney International Reports
42	Oxford Medical Case Reports	95	Oxford Academic
43	JAMA Dermatol	96	European Journal of Hospital Pharmacy
44	BMC gastroenterology	97 98	Journal of the American Academy of Dermatology
	Journal of Dermatological Treatment		European Heart Journal-Case Reports
46	American Journal of Ophthalmology	99	Japanese journal of ophthalmology
47	Medicine	100	Mycoses
48	BMC Oral Health	101	MedPharmRes
49	World Journal of Clinical Cases	102	Case Reports in Gastroenterology
50	Journal of medical case reports	103	Biologics: Targets and Therapy
51	Clinical Rheumatology	104	Epilepsy & behavior case reports
52	Transplantation Proceedings	105	Journal of Psoriasis and Psoriatic Arthritis
53	Dermatology and Therapy		

#### MedDRA: -

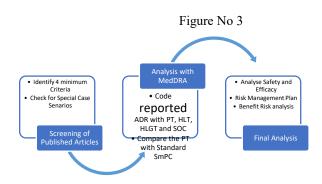
In this retrospective research study, the MedDRA dictionary software would be used, which is a well-organized software of medical terms that is developed and maintained by a government group called the ICH MedDRA Management Committee. The MedDRA software is mainly used in Pharmacovigilance sector to code the ADRs. There are different codes of ADRs such as PT, HLT, HLGT and SOC which are coded according to the patient's reported ADRs. The usage of MedDRA Dictionary.



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#### **METHODS:**

#### **Process Flow Chart**



# Identification of 04 Minimum Criteria and Special Case Scenarios as per Pharmacovigilance Guidelines: -

In this present retrospective study, we would be extracting four minimum criteria which are as follows:

- 1. Identifiable Patient: -Means patient recognizable factors like his/her Age, Sex, Gender or by Medical Condition.
- 2. Identifiable Drug: Means the medicine or medicinal product.
- **3. Identifiable ADR**: -Means which can recognise that the medication is causing harmful effects to the patient or body.
- **4. Identifiable Reporter**: -Means the person or source of information from whom we can confirm the disease disorder like Doctors or Healthcare workers.

#### **ANALYSIS: -**

In the present study, we have collected the data of 5 patients from the overall data of 200 patients case reports in which patients have who undergone organ transplantation or has rheumatoid arthritis, psoriasis, plaque psoriasis, amyotrophic lateral sclerosis, nephrotic syndrome was treated with Cyclosporine. The cyclosporine is a potent immunosuppressive agent that in animals prolongs survival of allogeneic transplants involving skin, kidney, liver, heart, pancreas, bone marrow, small intestine, and lung. Cyclosporine has been demonstrated to suppress some humoral immunity and to a greater extent, cell mediated immune reactions such as allograft rejection. The effectiveness of cyclosporine results from specific and reversible inhibition of immunocompetent lymphocytes in the G0- and G1-phase of the cell cycle. T-lymphocytes are preferentially inhibited. The helper cell is the main target, although the T-suppressor cell may also be suppressed. Cyclosporine also inhibits lymphokine production and release including interleukin-2. In the present research study, we have extracted 5 patients case report out of 200 patients case reports where adverse reactions were analysed with use of MedDRA dictionary and checked the preferred term and checked further classifications like high level term, high level group term and system organ class. Post analysis the adverse drug reaction preferred terms were compared with monograph of standard drug like Neoral



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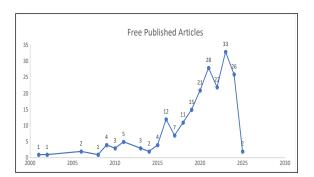
and Gengraf, it was understood that the reported adverse drug reactions of 5 patients extracted from 200 patient case reports in this present research study were well know adverse drug reactions which were summarised for standard drugs from phase 1 to phase IV clinical trials.

#### **RESULT AND DISCUSSION: -**

In this Research paper we have analysed 5 patient safety reports from the overall data of 200 patients which are freely available on various search engines. With the help of MedDRA dictionary the adverse drug reaction term reported in literature articles are analysed and extracted Preferred Term, High Level Group Term and System Organ Class for reported Adverse Drug Reaction. This analysis would further help us to determine the safety of compound when compared to (SmPC) of Cyclosporine, which is freely available in various search engines like Gengraf (SangStat) and Neural.

#### Patient Safety Awareness Trend Table and Graphical Representation: -

Table No 4



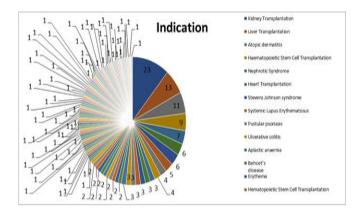
ADR Reported Indications Graphical Representation of Indication Pie Chart of ADR: - Table No  $5\,$ 

ADR Reported Indications	Count	ADR Reported Indications	Count	ADR Reported Indications	Count
Kidney Transplantation	23	Abdominal Aortic Aneurysm	1	Juvenile Dermatomyositis	1
Liver Transplantation	13	Acne fulminans	1	Juvenile Idiopathic Arthritis	1
Atopic dermatitis	11	Alopecia	1	Lichenoid Dermatitis	1
Haematopoietic Stem Cell Transplantation	9	Aplastic Anaemia	1	Liver/Kidney transplantation	1
Nephrotic Syndrome	7	Bone marrow transplantation	1	Medullary aplasia	1
Heart Transplantation	6	Bullous pemphigoid	1	Membranoproliferative Glomerulonephritis	1
Stevens Johnson syndrome	6	Central Cord Syndrome	1	Multicentric Castleman's disease	1
Systemic Lupus Erythematosus	5	Cerebral venous sinus thrombosis	1	Myasthenia gravis	1
Pustular psoriasis	4	Chronic Mild Leukopenia	1	Myelodysplastic syndrome	1
Ulcerative colitis	4	Chronic glomerulonephritis	1	Necrobiosis Lipoidica Diabeticorum	1
Aplastic anaemia	3	Chronic Urticaria	1	Nephrotoxicity	1
Behcet'sdisease	3	Crohn's Disease	1	Neurotoxicity	1
Venous sinus thrombosis	1	Cutaneous lesions	1	Neutropenia	1
Erythema	3	Cytopenia	1	Neutrophilic dermatosis	1

Figure No 3



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#### **Table of Reported Adverse Drug Reaction:**

Table No 6

Reported Adverse Drug Reaction	Count	Reported Adverse Drug Reaction	Count	Reported Adverse Drug Reaction	Count
Extrapyramidal disorder	15	Bronchopulmonary aspergillosis	1	Rash follicular	1
Neurotoxicity	7	Pyoderma gangrenosum	1	Aortic aneurysm	1
Pyoderma gangrenosum	4	Involuntary movement of extremities, walking disorder	1	Renal failure	1
Toxic epidermal necrolysis	4	Pulmonary nodule	1	Plaque Psoriasis	1
Thrombocytopenia	3	Kaposi's sarcoma	1	Renal failure acute, Overdose	1
Dermatomyositis	3	Helicobacter pylori infection	1	Chest discomfort	1
Interstitial lung disease	3	Kawasaki's disease	1	Convulsion	1
Alopecia	3	Pruritus allergic	1	Atopic Dermatitis Exacerbation	1
Pustular psoriasis	3	Keratitis	1	Renin-angiotensin system inhibition	1

#### **Table of ADR of Reported SOC: -** Table No 7

Row Labels	System Organ Class (SOC) of ADR Reported
Skin and subcutaneous tissue disorders	63
Nervous system disorders	39
Blood and lymphatic system disorders	15
Epidermal and dermal conditions	12
Immune system disorders	11
Renal and urinary disorders	9
Gastrointestinal disorders	8
General disorders and administration site conditions	7
Cardiac disorders	6
Vascular disorders	5
Infections and infestations	5
Musculoskeletal and connective tissue disorders	5
Respiratory, thoracic and mediastinal disorders	4
Psychiatric disorders	4
Eye disorders	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2
Injury, poisoning and procedural complications	2



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**Table of ADR Reported HLT: -** Table No 8

	High		High		High
Row Labels	Level Term (HLT) of Reported ADR	Row Labels	Level Term (HLT) of Reported ADR	Row Labels	Level Term (HLT) of Reported ADR
Dyskinesias and movement disorders NEC	17	Peripheral neuropathies NEC	2	Kaposi's sarcomas	1
Psoriatic conditions	12	Purpura and related conditions	2	Leukaemia's acute NEC	1
Dermatitis and eczema	11	Pustular conditions	2	Leukaemia's chronic lymphocytic	1
Nervous system disorders NEC	9	Renal vascular and ischaemic conditions	2	Lymphomas unspecified NEC	1
Erythema's	8	Rheumatoid arthritis and associated conditions	2	Mixed acid-base disorders	1
Bullous conditions	6	Skin and subcutaneous conditions NEC	2	Muscular autoimmune disorders	1
Gingival disorders NEC	6	Skin vasomotor conditions	2	Mycoplasma infections	1
Skin and subcutaneous tissue ulcerations	6	Therapeutic and nontherapeutic responses	2	Nasal disorders NEC	1

#### Table of Reported ADR'S of HLGT: - Table No 9

Row Labels	HLGT	Row Labels	HLGT
Epidermal and dermal conditions	50	Changes in physical activity	2
Movement disorders (incl parkinsonism)	17	General system disorders NEC	2
Neurological disorders NEC	11	Leukaemia's	2
Skin and subcutaneous tissue disorders NEC	9	Joint disorders	2
Skin appendage conditions	8	Encephalopathies	1
Immune disorders NEC	8	Gastrointestinal stenosis and obstruction	1
Dental and gingival conditions	7	Angioedema and urticaria	1
Renal disorders (excel nephropathies)	5	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	1
Anaemias nonhemolytic and marrow depression	5	Seizures (incl subtypes)	1
Nephropathies	5	Ancillary infectious topics	1
Embolism and thrombosis	4	Soft tissue sarcomas	1
Peripheral neuropathies	4	Haemolyses and related conditions	1
Skin vascular abnormalities	4	Upper respiratory tract disorders (excel infections)	1
Therapeutic and nontherapeutic effects (excel toxicity)	4	Coronary artery disorders	1

#### 2. DISCUSSION: -

Cyclosporine is a drug used as an Immuniosupressant for the different organ Transplants, in this study we have analysed the case reports of the patients who have undergone different organ transplants and with different disease disorders. Cyclosporine works primarily by inhibiting T-cell activation. It does this by binding to cyclophilin, forming a complex that inhibits calcineurin, a phosphatase crucial for T-cell signaling. This inhibition prevents the dephosphorylation and nuclear translocation of Nuclear Factor of Activated T-cells, a transcription factor needed for the production of interleukin-2 (IL-2) and other cytokines. Since IL-2 is a key growth factor for T-cells, reduced production leads to decreased T-cell proliferation and dampened immune responses. By which it is used as Immuniosupressant as an organ transplant rejection to the patients. Through this study we could analyse that the cyclosporine can be used



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for the organ transplantation which is been studied by different authors in different journals according to the references which are attached in the reference section below/

#### 3. CONCLUSION:

This research paper talks all about the entire case studies of the patients who have undergone different organ transplants and had disease disorders which have been successfully treated with the Immuniosupressant drug Cyclosporine assured by the correct analysis of the patients, hence by this analysis of the patients case studies we can say that the Cyclosporine drug can be used further to as an Immuniosupressant drug in Organ Transplant rejection due to its safety and efficacy.

#### 4. AKNOWLEDGEMENT: -

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