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An Observational Prospective on Cutaneous Adverse Drug Reaction – A Multicenter Study

Vinjavarapu L Anusha[1]*, Dr.B.Thangabalan [2], Avinash Goud K[1], Madhu B[1], Rupesh J[1], Jahnavi GVND[1], Ledia Devi[1], Sofiliya Devi[1], Diya[1]

[1]Sims college of pharmacy, Mangaldas nagar , Vijayawada Highway road , Guntur, India

[2]Principal of SIMS College of Pharmacy

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***Corresponding author:** Vinjavarapu. L. Anusha , Associate professor, Department of pharmacology, Sims college of pharmacy, Mangaldas nagar , Vijayawada Highway road , Guntur, India

ABSTRACT

This cutaneous reactions are one of the most common type of adverse drug reaction

The WHO defines an adverse Drug Reaction(ADRs) as any response to a drug which are noxious and unintended, and which occurs at a physiological function.

Cutaneous (CADRs) may vary from mildly discomforting to those that are life-threatening.

The patient to be hospitalization, systemic complications, mortality, and economic burden

INTRODUCTION

The WHO defines an Adverse Drug Reaction (ADRs) as any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of a physiological function. This definition excludes over dose , (accidental or intentional), drug abuse, and treatment failure and drug administration errors. It was also described ADRs to be the 4th 6th cause of death in US. A Swedish study has also implicated ADRs as 7th most common cause of death. ADRs are le 4th leading cause of death, ahead of Pulmonary disease, DM, AIDS C Pneumonia. Risk factors for ADRs include age, gender, concurrent illness, polypharmacy, narrow therapeutic

index drugs and genetics. Gender is one of the risk factors for development of ADR and women are more susceptible to ADRs than men possibly by an association of factors such as greater concentration of adipose tissue and hormonal determinants that can affect metabolism, leading to the development of ADR. Early recognition of these factors is important and ultimately leading to their prevention. ADRs may also result in diminished quality of life, increasing physician visits, hospitalizations, and even death. The World Health Organization (WHO) initiated a program for reporting all adverse reactions possessed by drugs. The Pharmacovigilance Program of India (PvPI) was started by the Government of India Although, India is participating in this program, its contribution to this database is relatively small. This problem is essentially due to the absence of a robust adverse drug reaction monitoring system and also the lack of awareness of reporting concepts among Indian health care professionals. .A suitably working pharmacovigilance system is important if medicines are to be used prudently.

Cutaneous reactions are one of the most common types of adverse drug reactions (ADRs). The disability such as blindness as a consequence of severe CADR could affect employment and quality of life. The commonly reported CADRs are maculopapular rash, fixed drug eruptions (FDEs), and urticaria. Majority of CADRs are diagnosed clinicallyThe Pharmacovigilance Programme of India was launched in 2010, and it operates through spontaneous reporting system to monitor ADRs. There are several advantages of this system in terms of being less cumbersome, generation of early safety signals about newer drugs, and identification of serious as well as rare ADRs. Prospective intensive monitoring can overcome these drawbacks and is also an important tool to identify the pattern and causative drugs of CADRs. The studies conducted in this field from India are scarce.

Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. According to WHO, Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem \ To safe guard the health of 1.27 billion people of India, the Central Drugs Standard Control Organisation (CDSCO), New Delhi has initiated a nation-wide, Pharmacovigilance programme of India (PVPI) which is coordinated by the Indian Pharmacopoeia Commission (IPC) located at Ghaziabad. The fundamental role of Clinical Pharmacist is to identify potential and actual drug related problems and prevent potential drug related problems. Glinical Pharmacists are encouraged to take responsibility in the development of Adverse Drug Reaction Monitoring and reporting programs. The role of Clinical Pharmacist in Monitoring and reporting ADRs is carried out as per the guidelines put forward by the American Society of Clinical Pharmacist (ASCp)

Features of ADR Monitoring and Reporting Program:

Features of ADR Monitoring and Reporting Program:According to ASCP, all Health professionals and other trained personnel should be educated on the importance and benefit of ADR reporting and encouraged to report any suspected ADR to the pharmacist.

All the Reports should have a high priority and be referred to the pharmacist for review. Pharmacist should simplify process

for reporting suspected ADRs by developing an ADR reporting form. The Program should be ongoing and the System should respect the confidentiality of the patient and facility. The ADR reporting should be promoted through an ongoing campaign.

Role of the Pharmacist:

The pharmacist's role is to promote the development, maintenance, of ongoing evaluation of a program to reduce the risk of ADRs through detecting, reporting and assessing any suspected ADR.

Pharmacist should investigate every suspected ADR for its nature, probability, severity and should develop risk reduction strategies as part of an on going program. He should also enlist the continued support of other health professionals in this program.

Detection

In the aspect of detection of ADRs identify triggers that signal an investigation by the pharmacist. Examples include emergency box usage, abrupt discontinuation of a drug,
multiple patients with similar unwanted symptoms on the same drug therapy, and the use of any drug used to treat a symptom rather than a disease, e.g., corticosteroids, epinephrine, antihistamines. Pharmacist should provide information to other health care professionals to better identify ADRs, e.g., list of common ADRs by therapeutic category.

Assessment

(Assessment of possible ADRs the pharmacist needs to review the reports of suspected ADRs and differentiate between obvious medication errors and suspected ADRs. He should use a validated algorithm to determine the probability that the event is drug related (remaining suspected ADR reports), Categorize severity and track ADRs for patterns and incidence.)

Reporting

Reporting of ADRs the pharmacist should provide feedback to physicians, nurses, residents, and family members about ADRs and Report ADRs in a systematic way that allows appropriate analysis and intervention. Causality assessment is the method through which the relationship between the drug and the suspected ADR is determined. There are two types of scales which are used widely in performing the assessment they are Naranjo's causality assessment scale and WHO probability assessment scale.

The study includes Drug safety monitoring of certain drugs like Antibiotics, Antipsychotics, Antiepileptics, NSAIDs and Antihypertensive

MostcommonCutaneous ADRs was:

Most common cutaneous adverse drug reactions were maculopapular rash, utricaria, steven johnson syndrome, pruritis, acneiform eruption, erythema multiforme, angioedema, tinea incognia, erthroderma, photosensitivity, contact dermatitis, hyperpigmentation, lichenoid eruption, vasculitis, purpura, erythematous skin lessions, drug induced hypersensitivity syndrome, acute generalised exanthematous pustulosis, oral ulcers.

Types ofCutaneousAdverseDrug Reactions:

1.1.1 Chemotherapy-Induced Acral Erythema:

Chemotherapy - Induced Acral Erythema is reddening, swelling, numbness and desquamation (skin sloughing or peeling) on palms of the hands and soles of the feet (and, occasionally, on the knees, elbows, and elsewhere) that can occur after chemotherapy in patients with cancer. (Acral erythema typically disappears within a few weeks

after discontinuation of the offending drug. The symptoms can occur anywhere between days to months after administration of the offending medication, depending on the dose and speed of administration. The patient first experiences tingling and/or numbness of the palms and soles that evolves into painful, symmetric, and well-demarcated swelling and red plaques. The cause of Palmar-plantar erythrodysesthesia (PPE) is unknown. In the case of PPE caused by PLD, the following mechanism has been demonstrated: sweat

deposits and spreads the drug on the skin surface; then the drug penetrates into the stratum corneum like an external agent; palms and soles have high density of sweat glands, and their stratum corneum is approximately 10 times thicker than the rest of the body, and becomes an efficient long-term reservoir for the penetrating PLD, which was deposited on the skin before.

Painful red swelling of the hands and feet in a patient receiving chemotherapy is usually enough to make the diagnosis. The problem can also arise in patients after bone marrow transplants, as the clinical and histologic features of PPE can be similar to cutaneous manifestations of acute (first 3 weeks) graft-versus- host disease, It

1.1.2 Urtricaria

Hives, also known as urticaria, is a kind of skin rash with red, raised, itchy bumps. They may also burn or sting. Often the patches of rash move around. Typically they last a few days and do not leave any long-lasting skin changes. Fewer than 5% of cases last for more than six weeks. The condition frequently recurs.) Welts (raised areas surrounded by a red base) from hives can appear anywhere on the surface of the skin. Whether the trigger is allergic or not, a complex release of inflammatory mediators, including histamine from cutaneous mast cells, results in fluid leakage from superficial blood vessels.

Welts may may be pinpoint in size, or several inches in diameter.

Angioedema is a related condition (also from allergic and non-allergic causes), though fluid leakage is from much deeper

blood vessels in the subcutaneous or submucosal layers.

Individual hives that are painful, last more than 24 hours, or leave a bruise as they heal are more likely to be a more serious condition called urticarial vasculitis. Hives can also be classified by the purported causative agent. Many different substances in the environment may cause hives, including medications, food and physical agents, In perhaps more than 50% of people with chronic hives of unknown cause, it is due to an autoimmune reaction.

Dermatographic urticaria (also known as dermatographism or "skin writing") is marked by the appearance of weals or welts on the skin as a result of scratching or firm stroking of the skin. it is one of the most common types of urticaria, in which the skin becomes raised and inflamed when stroked, scratched, rubbed, and sometimes even slapped.

The skin reaction usually becomes evident soon after the scratching, and disappears within 30 minutes. , antibiotic therapy, or emotional upset., Dermographism is diagnosed by taking a tongue blade and drawing it over the skin of the arm or back. The hives should develop within a few minutes.

The skin lesions of urticarial disease are caused by an inflammatory reaction in the skin, causing leakage of capillaries in the dermis, and resulting in an edema which persists until the interstitial fluid is absorbed into the surrounding cells)

Hives are caused by the release of histamine and other mediators of inflammation (cytokines) from cells in the skin. The cause of chronic hives can rarely be determined. In some cases regular extensive allergy testing over a long period of time is requested in hopes of getting new insight. The mainstay of therapy for both acute and chronic hives is education, avoiding triggers and using antihistamines, Chronic hives can be difficult to treat and lead to significant disability. People who experience hives with angioedema require emergency treatment as this is a life-threatening condition).

Aim: Monitor Cutaneous Adverse Drug Reactions (Adrs) In Patients

Objectives:

1. Identify The Nature And Characteristics Of Adrs
2. Assess The Severity Of Reported Adrs
3. Determine Causality Using The Who Causality Assessment Scale.

Scope Of The Study:

1. Focuses On Drug Safety (Pharmacovigilance) To Detect, Assess, And Prevent Side Effects

2. Aims To Improve Patient Safety By Understanding ADR Risks And Outcomes.

3. Encourages Active Reporting Of Adrs By Healthcare Professionals To Reduce Incidence Rates.

Literature Review:

Adrs Are Often Caused By Drugs Such As Anticonvulsants, Antibiotics, And Nsaids. Severe Cutaneous Adrs Include

Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), And Drug Reaction With Eosinophilia And Systemic Symptoms (DRESS).

Studies Emphasize The Importance Of Early Diagnosis, Monitoring, And Reporting To Prevent Morbidity And Mortality statistical Tools Were Used For Analyzing ADR Patterns, Severity, And Outcomes. SPSS Version 17 Was Used For Data Interpretation. Common Adrs Include Maculopapular Rashes, Fixed Drug Eruptions, And Erythema Multiforme. Severe Adrs Often Result In Hospitalization Or Life-Threatening Complicationsadrs Are Influenced By Drug Type, Gender, And Ethnicity.Recognition, Monitoring, And Reporting Are Critical To Managing ADR Risksantibiotics (E.G., Penicillin), Nsaids, And Anticonvulsants (E.G., Phenytoin).Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), And Fixed Drug Eruptions.ADR Incidence Shows Gender Variations, Often Affecting Women More Than Men. Age Group Analysis Highlights ADR Susceptibility In Younger And Middle-Age Patientsearly Recognition And Withdrawal Of Causative Drugs Are Life-Saving Measures. ADR Monitoring And Reporting Should Be Encouraged To Improve Drug Safety And Patient Outcomes.

Methodology

1. **Study Design:** Prospective Observational Study.

2. **Duration:** 6 Months (October 2019 To March 2020).

3. **Location:** Guntur, India (Adverse Drug Reaction Monitoring Centre, Government General Hospital).

4. **Sample Size:** 120 Patients

Early Identification Of Adverse Drug Reactions (Adrs) And Immediate Withdrawal Of The Causative Drug Can **Save Lives** And Prevent Severe Complications. Encourages Healthcare Professionals To Actively Monitor And Report Adrs. Emphasizes The Importance Of Pharmacovigilance In Improving Patient Safety proper ADR Reporting Reduces The **Burden Of Severe Reactions** Like Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), And Other Cutaneous Adverse Reactions.Enhances Rational Drug Prescribing Practices Among Physicians.ADR Monitoring Is Essential For Identifying Trends And Ensuring Safer Medication Use. Promotes Awareness And Training For Healthcare Workers To Recognize And Report Adrs Effectively, Ultimately Improving Patient Care And Outcomes.

Literature and review

We have done a literature review for one month and selected few literatures that helped us in the mady. The literatures we selected were-

1.Cristina Scavoneet.al. (2019) conducted a study on Severe Cutaneous Adverse Drug Reactions Asociated with Allopurinol, to describe the main characteristics of all ADRs associated with allopurinol, analyse the proportion of serious cutaneous ADRs of total ICSRs related to allopurinol and to compare the main features. Out of 56 ICSRs reporting serious cutaneous ADRs, 34% (n=19) referred to ADRs that were represented by cases of desquamative erythema, rash, skin swelling, and urticaria. The remaining 66(n=37)of serious cutaneous ADRS referred to cases of SCARS (DRESS syndrome (n=3,5.4%),SJS(n=8,14.3%) and TEN(n-26,46.4%). This study concluded that Serious cutaneous ADRs associated with allopurinol frequently required hospitalization or prolonged hospitalization, and almost half had an unfavourable outcome.

1.J. Borras-Blascoet.al., (2018) conducted a study on Adverse cutaneous reactions associated with the newest antiretroviral drugs in patients with human immunodeficiency virus infection. The aim of this study on adverse cutaneous reactions associated with the newest antiretroviral drugs in patients with HIV. Cutaneous adverse drug reaction associated with the newest antiretroviral drugs Protease inhibitors, Lopinavir/Ritonavir, Atazanavi, Amprenavir and Fosamprenavir, Tipranavir, Darunavir. Non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs) Efavirenz, Etravirine. Fusion inhibitors, E-g. Enfuvirtide, Abacavir. Nucleoside reverse transcriptase inhibitors (NRTIs) Tenofovir, Emtricitabine. Integrase inhibitors, E.g. Raltegravir. Inhibitors of the CCR5 chemokine receptor, E.g Maraviroc. This study concluded that the advance and development of new HIV drugs and treatment strategies increase the risk of unusual adverse drug reactions associated with HAART. It is important to recognize the safety profile of these new treatments. Skin toxicities are common complications of HIV infection, and this is a significant risk factor for adverse drug reactions. In HIV-infected patients, there is a high prevalence of severe bullous and hypersensitivity reactions induced by antiretroviral therapy.

2. **Qiancheng Deng et.al., (2017)** conducted a study on Severe cutaneous adverse drug reactions of Chinese inpatients a meta-analysis. The aim of this study on was to analyse epidemiology and characteristics of severe cutaneous adverse drug reactions of Chinese inpatients during the recent 15 years with meta-analysis. Twenty-five studies reported the gender of patients. There were 928 patients, comprising 495 men and 433 women. The proportion of men was 53.2% [12-56%, 95%CI (0.484 to 0.581), Twenty-one per cent of the patients had drug allergy history. Antibiotics (26.0%), sedative hypnotics and anticonvulsants (21.6%), and antipyretic analgesics (17.1%) were the most common causative drugs. The most frequent clinical subtype was Stevens-Johnson syndrome (50.1%),followed by toxic epidermal necrolysis (25.4),exfoliative dermatitis (21.0%) and drug-interaction hypersensitivity syndrome (1.6%) in addition to skin rashes, patients with sever cutaneous adverse drug retains suffered mostly from fever(73%), and blood routine abnormality (66.7%). This study concluded that this meta-analysis is the first to retrospectively analyses the epidemiology and characteristics of SCADRs among Chinese

inpatients affected that women. Nearly a quarter of the patients had a history of drug allergy. This pooled estimate revealed antibiotics, SHA, and AA was the most frequently drug associated with SCADRs. SJS was the most common clinical pattern, followed by TEN and ED.

1.Yoko Kano etal., (2017) conducted a study on Long-term outcome of patients with severe cutaneous adverse reactions. Visceral involvement associated with Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) and drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms (DIHS/DRESS) is well documented. However, little is known about the long-term outcomes of severe drug eruptions due to a lack of long-term follow-up. Long-term sequelae may arise in patients who survive the acute complications of severe drug reactions. This study concluded that the development of long-term sequelae after resolution of severe cutaneous adverse drug reactions may be overlooked because of an asymptomatic interval after resolution of the acute disease. The emergence of sequelae should be closely monitored following the resolution of SJS/TEN and DIHS/DRESS, especially autoimmune disease in DIHS/DRESS.

1.Fabrizio De Luca et.al., (2016) conducted a study on Tolerated drugs in subjects with severe cutaneous adverse reactions (SCARs) induced by anticonvulsants. The aim of this study was to describe a group of six patients with SCARS induced by anticonvulsant drugs and to report which alternative antiepileptic drugs and drugs of other classes were tolerated. This study concluded that anticonvulsants and benzodiazepines were well tolerated as alternative treatments in six patients with reactions to aromatic anti convulsants and that the risk of hypersensitivity reactions to other drug classes was not increased as compared to general population.

1. Emine Dibek Misirlioglul conducted a study on Severe Cutaneous Adverse Drug Reactions in Pediatric Patients, A Multicenter Study. The objective of this study was the evaluation of the clinical characteristics of patients with the diagnosis of SCARs. Fifty-eight patients with SCARs were included in this study. The median age of the patients was 8.2 years and 50% were males. Diagnosis was SJS/TEN in 60.4%, DRESS in 27.6%. In 93.1% of the patients, drugs were the cause of the reactions. Antibiotics ranked first among the drugs (51.7%) and antiepileptic drugs were the second (31%) most common. This study concluded that SCARs in children are not common but potentially serious. Early diagnosis and appropriate treatment of SCARs will reduce the incidence of morbidity and mortality.

1. Rohini Sharma conducted a study on a clinical study of severe cutaneous adverse drug reactions and role of corticosteroids in their management. The aim of this study the clinical and epidemiological aspects of severe cutaneous adverse drug reactions (SCADRS) at a referral centre of Jammu region, with special reference to the role of corticosteroids in the management. During the 6 months period, a total of 44 patients were included in the study. A total of 20 patients were of SJS, 16 patients were of DRESS, 3 patients were of TEN, 3 patients were of AGEP, and 2 patients were of SJS/TEN overlap. The most common class of drug implicated was antiepileptics, and out of it. phenytoin was the most common. There were 27 males and 17 females in the study. The youngest patient was 3 years old and the oldest being 65 years. The duration between drug intake and drug eruption ranged from 3 to 5 weeks. This study concluded that SCARDs are associated with multiple organ involvement. Early recognition and prompt withdrawal of causative drugs can be lifesaving. Moreover, in a country like India, systemic corticosteroids can play a major role if judiciously used.

1.Fatma Al Mulia conducted a prospective observational study on prospective monitoring of cutaneous adverse drug reactions in a secondary care hospital. The aim of the study was to monitor the incidence and nature of cutaneous adverse drug reactions (CADRs) in the dermatology outpatients and identify the causative drugs. This study concluded that cutaneous ADRs was found to be 2.6%. Majority (43.4%) of the cutaneous ADRs were caused by nonsteroidal anti- inflammatory drugs. Majority (56.5%) of the study population reported itching as the most common cutaneous ADR. Nonsteroidal anti-inflammatory drugs were the common causes of cutaneous ADRS in the study.

1.Dr. Reena Verma conducted a study on Cutaneous Adverse Drug Reactions-A Study of Clinical Patterns, Causality, Severity & Preventability. The aim of this study was CADRs for clinical patterns, risk factors, causality, severity &preventability. A total of 35cases of suspected cutaneous ADRs were recorded during the period of study, out of which I case was excluded because the offending drug was not identified as the patient was taking ayurvedic (alternative) medicine simultaneously. The remaining 34 cases were analysed. Out of 34 patients, 15 cases (44.11%) were males and 19cases (55.88%) were females. Maximum patients belonged to the age group of 21-30 (35.2%) followed by 31-40 (20.15%) and 41-50 (17.6%). The most common pattern of cutaneous ADR observed was maculopapular rash (29.4%) followed by fixed drug eruption (23.5%). This study concluded that there are variations in the results in comparison to other studies like female predominance, offending drugs like among antimicrobials fluoroquinolones were found to be commonly involved. Among analgesics, anti-inflammatory group diclofenac &aceclofenac were commonly responsible drugs. Causality assessment also resulted in high score of definite category

1. **Seema Qayoom MD** conducted a study on Adverse Cutaneous Drug Reactions - A Clinico-demographic Study in a Tertiary Care Teaching Hospital of the Kashmir Valley, India. The aim was to study the incidence and clinico-demographic profile on ACDRS to identify any potential risk factors and compare the results with other studies. A total of 75 ACDRS were included in the final analysis of giving an incidence of 0.16%. The mean age of patients developing ACDRs was 39.36± 16.77 years and in females was 39.47±15.31 years. The most frequently reported cutaneous reactions were with antimicrobials (57.33%) followed by NSAIDs (21.33%) and antiepileptic drugs (17.33%). Less common groups involved were steroids, antipsychotics and bisphosphonates (1.33% each). Fixed drug eruptions (FDEs) were the commonest (45.33%) followed by maculopapular (17.33%), photoallergic (8%), erythema multiforme (6.66%), Stevens-Johnson syndrome (5.33%). This study concluded that health care providers should realize the importance of reporting every drug reaction they face. The patterns of ACDRs are changing every year due to emergence of newer drugs. Physicians should have an adequate knowledge of ADRs, especially of newer drugs in order to minimize such events.

2. **Ratan J. Lihite** conducted a study on Cutaneous Adverse Drug Reactions in ADR Monitoring Centre of Tertiary Care Hospital, Guwahati. The aim of this study was conducted to assess the incidence, causality, severity and preventability of CADRs reported to ADR Monitoring Centre, department of pharmacology,

Gauhati Medical College & Hospital. Out of 1537, 108 patients have experienced CADRs in dermatology department of GMCH. Out of these, 42 patients were male and 66 were female patients. 146 CADRs were detected and reported to ADR monitoring centre of GMCH during the study period. This study concluded that incidence of CADRs occurrence was high in female patients. Acne was highly reported CADR and most of the reported CADRs were possible, definitely preventable and mild in nature.

3. **Sejal Thakkar** conducted a prospective study on Cutaneous adverse drug reactions in a tertiary care teaching hospital in India. The aim of this study was is to analyse the CADRs with reference to the incidence, its subgroup analysis, causative drugs, and other clinical characteristics in Indian. This study concluded that Ethnic characteristics should be considered while interpreting the incidence and pattern of CADRs. Age and gender do not affect the incidence of CADRs in our population. Data of this study confirm the earlier studies about the pattern of common CADRs and their incriminated drugs. Almost one-fourth of CADRs remained inaccessible about causative drugs. There is a need to sensitize the patients about hazards of self-medications.

4. **Siew-Eng choon** conducted a study on an epidemiological and clinical analysis of cutaneous adverse drug reactions seen in a tertiary hospital in Johor. The aim of this study to determine the prevalence, the clinical patterns of drug eruptions, and the common drugs implicated, particularly in severe cADR such as Stevens-Johnson Syndrome/Toxic epidermal necrolysis (SJS/TEN) and drug rash with eosinophilia and systemic symptoms (DRESS) in our population. A total of 362 CADR were seen among the 42,170 new patients, yielding an incidence rate of 0.86% (yearly cADR rate range: 0.55-1.28%). Indians had lower cADR rates compared to Malay and Chinese. The most common reaction pattern seen was maculopapular eruptions (153 cases, 42.3%) followed by SJS (88 cases, 24.3%), DRESS (34 cases, 9.4%), TEN (21 cases, 5.8%), fixed drug eruptions (17 cases, 4.7%) and acute generalized exanthematous pustulosis (15 cases, 4.1%). This study concluded that The low rate of cADR in our population together with the high proportion of SCAR is probably due to referral bias. Otherwise, the reaction patterns and drugs causing CADR in our population are similar to those seen in other countries. Carbamazepine, Allopurinol, and Cotrimoxazole were the three main causative drugs of SJS/TEN in our population.

5. **M. V. Noel** conducted a prospective study on Cutaneous adverse drug reactions in hospitalized patients in a tertiary care centre. The aim of this study was Many of the commonly used drugs can produce cutaneous ADRs. This study concluded that cutaneous ADRs ranging from mild maculopapular rash to serious SJS and TEN was observed. The incidence of life-threatening cutaneous ADRs like SJS and TEN was found to be higher Antiepileptics were implicated in the majority of the hospitalized cutaneous ADRs. Infrequently reported adverse reactions for newer drugs like Leflunomide, Cefotaxime and Azithromycin were also detected in the present study.

6. **Michael Bigby** conducted a study on rates of cutaneous reactions to drugs. The objective of this study to determine the validity, magnitude, precision and applicability of the data on the rates at which drugs cause adverse cutaneous reactions. Nine studies met the study criteria. Five of the study based on prospectively collected data on medical inpatients, 2 were retrospective studies on chart or computerized medical report and, 2 were based on spontaneous reports and consumption data. The morbilliform drug exanthem and urticaria were the most common cutaneous reactions to drugs. This study concluded that despite differences in this method of the studies reviewed and the time of execution, there is remarkable agreement in this result. Reaction rates are available for many commonly used drugs.

MATERIAL & METHODS

Methodology:

Study site

The study was conducted 'In and around Guntur-A Multicentred study.

Study design

A Prospective Observational study.

Study period

The study was carried out for a period of 6months from October 2019 to March 2020 (6months)

Study criteria

Inclusion Criteria:

a)Patients of either sex who developed an ADR,

b) Patients of all age group who developed ADR

Exclusion Criteria:

a) Patients who developed ADR due to blood transfusion or platelets transfusion.

b) Patients who developed ADR due to infusion fluids.

c) Patients who are not interested to participate in the study.

Sample size:

Based on n-master formula, it is determined as 120.

Source of data:

From Case sheets and other medical records,

PROCEDURE

After prior approval from authentic research authorities of the institution, study was carried by maintaining a strict confidentiality about patient details. At the Adverse drug reaction Monitoring Centre, at Guntur Medical College/Government General Hospital, Guntur, Adverse Drug Reactions were reported in Suspected Adverse Drug Reaction Reporting Forms (SADRRFs) by various departments of the hospital, over a period of six months. The data from these SADRRFs were evaluated in the study. Each SADRRF data includes age,

sex, adverse drug reaction, severity of the event, causative drugs with dosage, route, frequency, duration of administration, concomitant medications and relevant investigations.

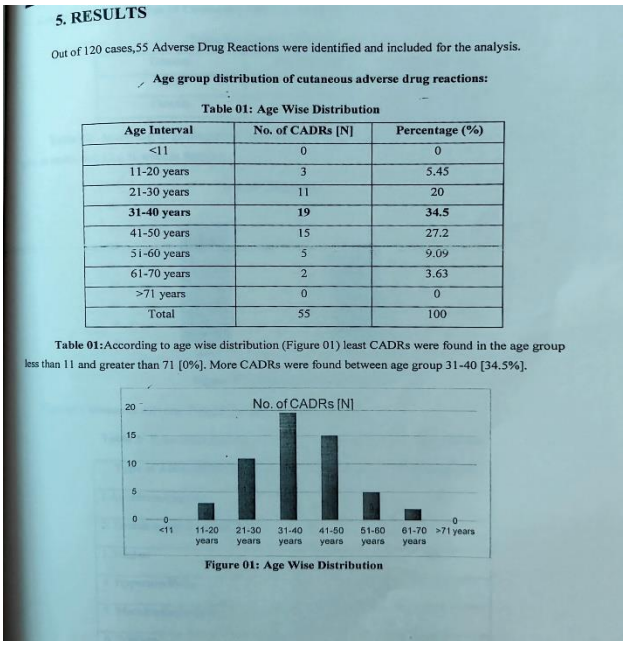
The seriousness of reactions was evaluated according to WHO criteria. ADRs were analysed for causality using WHO causality assessment scale. The collected data were recorded in Excel sheet using a structured format containing age group, gender, description of ADR, organ system involved, drugs, duration of reactions, outcome, causality, seriousness of ADRs. Finally, the data was analysed statistically.

Data collection and analysis:

Patient demographic details, Reason for admission, Medical history, Medication history, Medications prescribed, their dose & frequency of admission are collected from Patient medical records in a structured data collection forms.

The CADRs detected were analysed using appropriate tools, Software used: SPSS version 17.(P value <0.00 is considered significant since the CI is 00%).

RESULTS



5. RESULTS

Out of 120 cases,55 Adverse Drug Reactions were identified and included for the analysis.

Age group distribution of cutaneous adverse drug reactions:

Table 01: Age Wise Distribution

Age Interval	No. of CADRs [N]	Percentage (%)
<11	0	0
11-20 years	3	5.45
21-30 years	11	20
31-40 years	**19**	**34.5**
41-50 years	15	27.2
51-60 years	5	9.09
61-70 years	2	3.63
>71 years	0	0
Total	55	100

Table 01: According to age wise distribution (Figure 01) least CADRs were found in the age group less than 11 and greater than 71 [0%]. More CADRs were found between age group 31-40 [34.5%].

Figure 01: Age Wise Distribution

Gender wise distribution of Cutaneous Adverse Drug Reactions:

Table 02: Gender Wise Distribution

Gender	No. of CADRs	Percentage (%)
Male	33	60
Female	22	40

Table 02: According to gender wise distribution (table- 2), of all the CADRs found, 56.4 % were seen in males and 43.6 % were in females.

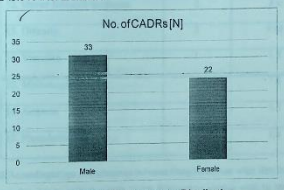


Figure 02: Gender wise Distribution

Type of Cutaneous Adverse Drug Reactions wise distribution:

Table 3: Type of Cutaneous Adverse Drug Reactions wise distribution

Type of ADR/ADR's Detected	No.of.CADRs	Percentage(%)
1.Acneform eruption	3	5.45
2. Stretch marks over abdomen	1	1.8
3. Rashes	10	18.1
4. Hypersensitivity	3	5.45
5. Maculopapular rash	4	7.2
6. Vitiligo	8	14.5
7.Swelling and blisters	4	7.2
8. Erythema nodosum	3	5.45
9. Hand and foot syndrome	3	5.45
10. Red spots	5	9
11. Peripheral eosinophilia	1	1.8
12. Steven Johnsons syndrome	2	3.6
13. Urticaria	3	5.45
14. Vasculitis	1	1.8
15. Methemoglobinemia	1	1.8
16. Alopecia	2	3.6
17. Photodermatitis	1	1.8

Table 03:Accordingtotype of Cutaneous Adverse Drug Reactions wise distribution, most common type of CADR was found to be as Rashes with 18.1% followed by vitiligo with 14.5%.

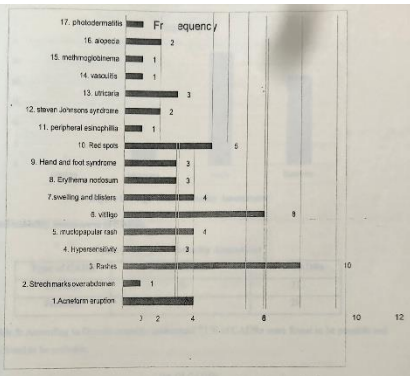


Figure 03: Type of Cutaneous Adverse Drug Reactions wise distribution

Identification of ADR's:

Table 4: Age Wise Causality Assessment

Age Group (years)	No.of.CADRs	Percentage (%)
Children (0 – 14)	0	0
Adolescent(15- 24)	5	9
Adults(25 – 40)	**28**	**50.9**
Geriatrics(41 – above)	22	40

Table 04: According to age wise causality assessment adults were found to be have more CADRs with 50.1% followed by geriatrics with 40%. Adolescent were less exposed to CADRs.

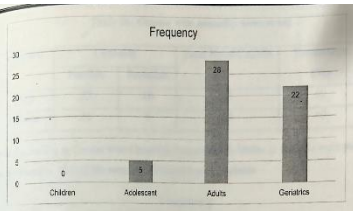


Figure 04: Age Wise Causality Assessment

Overall causality assessment of CADR:

Table 05: Overall Causality Assessment

Type of CADR	No.of CADR	% of CADRs
Possible	39	71
Probable	16	29

Table 5: According to Overall causality assessment 71 % of CADRs were found to be possible and 29 % were found to be probable.

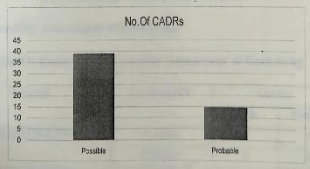


Figure05: Overall Causality Assessment of CADRs

Gender wise causality assessment of CADRs

Table 06: Gender wise causality assessment

Gender	Causality		Total No.of CADRs	Percentage (%)
	Possible	Probable		
Male	23	10	33	60
Female	16	6	22	40

Table 6: According to Gender wise Causality Assessment in Males 21 CADRs were possible and 10 were probable. In Females 18 CADRs were possible and 6 were probable.

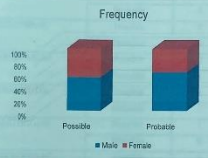


Figure 06: Gender wise causality assessment

Gender Wise Causality Assessment of Each drug:

Table 07: Gender Wise Causality Assessment of Each drug

DRUGS	CAUSALITY	Gender	
		Male	Female
TELITHROMYCIN	Possible	1	0
	Probable	0	0
ITRACONAZOLE	Possible	1	0
	Probable	0	0
IBUPROFEN+PARACETAMOL	Possible	0	2
	Probable	0	0
RITUXIMAB	Possible	0	1
	Probable	2	0

DISCUSSION

A Prospective observational study was conducted on Cutaneous adverse drug reactions at various hospitals in and around Guntur district for the period of 6 months October 2019 to March 2020 and a total 150 cases were included in our protocol by using 'n masters' formula. Also an inform consent form in bcal language were collected from patients and physicians during the course of the study.

Out of the total cases, 55 CADRs were detected and reported to the ADR monitoring center, Guntur using Suspected Adverse Drug Reaction Reporting Forms (SADRRFs). The data includes Age, Sex, ADR, Severity of the event, Dosage, Frequency, Route of administration.

The seriousness of the reactions wasanalysed by using WHO Causality Assessement scale. Causality assessment proved that Rashes were most common occurred CADR with 18.1% followed by Vitiligo with 14.5%, Red spots with 9%, Maculopapular rashes and Blisters with 7.2%, Acneform cruption, Hypersensitivity, Erythema nodosum, Hand and Foot syndrome and Utricaria with 5.45%, Allopecia and Steven Johnsons Syndrome with 3.6% and then Peripheral esinophillia, Vasculitis. Methmoglobinema and Photodermatitis with 1.8%.

Alopecia and Hypersensitivity by rituximab, rashes by ceftriaxone, papular lesions and erythema multiforme by allopurinol, hand and foot syndrome by capecitabine, vitiligo by ethambutol, peripheral eosinophilia by rifamycin, stevenjohnsons syndrome by rancyclovir, hypersensitivity by acylovir, maculopapular lesions by dapsone were the most probable CADRs identified in our study. Acne form eruption by telithromycin, cefperazone, dapsone, rashes by ibuprofen, tranexamic acid, rituximab. maculopapular lesions by ofloxacin. Vitiligo by ceftriaxone and aceclofenac. Erythema nodosum by diclofenac and allupurinol. Red spots by

lamotrigine. Rashes by levitracetam. Utricaria by piroxicam and ibuprofen. Phenytoin induced rashes by phenytoin were the most possible CADRs found in our study.

Out of the total CADRs found 71% were possible and 29% were probable and 56.3% were found in males and 43.6% were found in females. Adults and Males were experienced more CADRs compared to that of females and other age groups.

The causality assessment shown that more than half reported CADRs were possible and remaining were probable. Restricting to the framework of the study interventions were not made and rechallenge was not done due to Ethical reasons.

CONCLUSION

A successful CADR surveillance can have a positive impact on the medication use system to improve the quality of patient care and in reducing the occurrence of CADR. Pharmacist has a very important role in monitoring and reporting of CADR.

We perform our study for the monitoring and reporting of CADRs in various departments in various hospitals in and around Guntur for a period of 6 months Le., June 2019 to November 2019 and we detected 55 CADRs out of 150 cases. Among them males are more prone to CADRs compared to females, Adults are more effected compared to that of geriatrics and adolescents.

The study demographic data showed a moderately high incidence of CADRs in males. In our study adults showed high frequency of CADRs than geriatrics and adolescents. The commonly found CADRs in our study was Rashes, Vitiligo, Muclopapular Rash, Blisters, Utricaria, Acneform Eruption, Hypersensitivity, Erythema Nodosum, Hand & Foot Syndrome, Peripheral Esinophilla, Stevenjohnsons Syndrome, Vasculitis, Methmoglobinema and Phtotdermatitis.

This study helps the Indian Pharmacopoeia Commission (IPC) in detecting, monitoring and reducing the percentage of occurring CADRs thereby providing safety for the patient community. Further this study was continued for 6 months to submit annual report to the ADR monitoring Center, Guntur. So we could get more precise report for analyzing the CADRs.

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REFERENCES

1. Edwards IR, Aronson JK. Adverse drug reactions: Definitions, Diagnosis and Lancet, 2000;356:1255-1259.
2. Leape LL. Errors in medicine. Journal of American Medical Association, 1994-272:1851-1857.
3. Padmaja U. A Prospective Analysis of Adverse Drug Reactions in a South Indian Hospital. Online Journal of Health Allied Sciences. 2009;8(3):1.
4. WHO, Safety of medicines in public health programs: Pharmacovigilance an essential tool, WHO; 2006.
5. http://www.who.int/hiv/pub/pharmacovigilance/safety/en/
6. Sivanandypalanisamy, kottursgarulkumaran, alyalurajasekaran, a study on assessment, monitoring and reporting of adverse drug reactions in indian hospital, Asian Journal of Pharmaceutical and Clinical Research, 2011; 4(3):112-116.
7. Ascp guidelines on detecting and reporting adverse drug reactions in long-term care environments.
8. https://en.wikipedia.org/?title=Hand-foot_syndrome&redirect-no
9. https://en.wikipedia.org/wiki/Hives
10. https://en.wikipedia.org/wiki/Stevens%E2%80%93Johnson_syndrome
11. https://en.wikipedia.org/wiki/Drug_reaction_with_eosinophilia_and_systemic_symptoms
12. https://www.healthline.com/health/methemoglobinemia#symptoms
13. http://pennstatehershey.adam.com/content.aspx?productid=107&pid=33&gid=000155
14. https://www.mountsinai.org/health-library/condition/photodermatitis

15. https://www.medicalnewstoday.com/articles/70956.php

16. https://www.webmd.com/skin-problems-and-treatments/erythema-nodosum

17. https://emedicine.medscape.com/article/1081633-overview#a5

18. https://www.webmd.com/rheumatoid-arthritis/guide/vasculitis-treatment 1

19. https://www.mayoclinic.org/diseases-conditions/vasculitis/diagnosis-treatment/drc-20363485

20. htpp://www.whoumc.org/pdfs/causality.pdf.

21. Cristina Scavone, Cristina Di Mauro, et al. Severe Cutaneous Adverse Drug Reactions Associated with Allopurinol Drugs - Real World Outcomes 2019.

22. Borra's-Blasco J, et al. Adverse cutaneous reactions associated with the newest antiretroviral drugs in patients with human immunodeficiency virus infection Journal of Antimicrobial Chemotherapy, 2018;879-888.

23. Qiancheng Deng et al Severe cutaneous adverse drug reactions of Chinese inpatients a met analysis. An Bras Dermatol. 2017;92(3):345-349.

24. Yoko Kano et all.ong-term outcome of patients with severe cutaneous adverse reactions. Dermatological Sonica, 2017;211-216.

25. Fabrizio De Luca, et al. Tolerated drugs in subjects with severe cutaneous adverse reactions (SCARs) induced by anticonvulsants. Clin Mol Allergy. 2016.

26. Emine Dibek Misirlioglu et alSevere Cutaneous Adverse Drug Reactions in Paediatric Patients, A MulticenterStudy. The journal of allergy and clinical immunology: In practice 2016.

27. Rohini Sharma et alA clinical study of severe cutaneous adverse drug reactions and role of corticosteroids in their management. Indian Journal of Drugs in Dermatology, 10.4103/ijdd.ijdd 22-16 2016.

28. Fatma Al Mulla et al A prospective observational study on prospective monitoring of cutaneous adverse drug reactions in a secondary care hospital International Journal of Research in Dermatology 2015: 5(2):231-238.

29. Dr. Reena Verma et astudy on Cutaneous Adverse Drug Reactions-A Study of Clinical Patterns, Causality, Severity & Preventability FOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2014.

30. Seema Qayoom MD et alon Adverse Cutaneous Drug Reactions - A Clinico-demographic Study in a Tertiary Care Teaching Hospital of the Kashmir Valley, India. Archives of Iranian Medicine, 2015; 18(4): 228-233.

31. Ratan J. Lihite et alCutaneous Adverse Drug Reactions in ADR Monitoring Centre of Tertiary Care Hospital, Guwahati. Journal of Applied Pharmaceutical Science March, 2013.

32. Sejal Thakkar et alCutaneous adverse drug reactions in a tertiary care teaching hospital in India. Indian Journal of Dermatology 2012.

33. Siew-Eng choon et alepidemiological and clinical analysis of cutaneous adverse drug reactions seen in a tertiary hospital in Johor. Indian journal of Dermatology, venerology and leprology Jan 2011;78:734-739.

34. Noel MV, et alCutaneous adverse drug reactions in hospitalized patients in a tertiary care center.Indian

journal of Pharmacology feb 2002;36:292-295.

35. Michael Bigby.MD et al rates of cutaneous reactions to drugs. A cooperative effort of the Clinical Epidemiology Unit of the Istituto Dermopatico dell' Immacolata-Istituto di Ricovero e Cura a Carattere Scientifico (IDI-IRCCS) and the Archives of Dermatology. 2001.