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# **Assessment of Corticosteroid Use in Tertiary Care Hospital**

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#### **ABSTRACT:**

Corticosteroids - synthetic analogues of natural adrenal cortex hormones, are widely used to treat various conditions. However, their long-term use can lead to risks. To assess the use of Corticosteroids in order to understand their benefits and risks, a prospective, observational study was conducted which analyzed corticosteroid use among 56 patients, 3.5% being infants, 8.9% being children, adults and older adults comprising 44.6% and 42.8% respectively, among which there were 20 males (36%) and 36 females (64%). A total of 92 corticosteroids were prescribed: 42 (45.6%) Dexamethasone, 9 (9.7%) Hydrocortisone, 12 (13%) Prednisolone, 27 (29.3%) Budesonide, 1 (1%) Beclomethasone, and 1 (1%) Fluticasone. Administration routes included oral (15, 16.3%), intravenous (48, 52.1%), and inhalation (29, 31.5%). The most common conditions treated included bronchitis (19.6%), pneumonia (17.8%), and COPD (14.2%). Adverse drug reactions (ADRs) occurred in 23 patients (41%), with common ADRs being hyperglycemia (29%), post-injection flare (32.2%), and hoarseness (16.1%), followed by osteoporosis, and least being hypertension, Cushing's syndrome, facial puffiness, electrolyte imbalance, GI disturbances. Dexamethasone was associated with ADRs in 13 patients (56.5%), and Budesonide in 8 (34.7%), Prednisolone in 3 (4.3%), Hydrocortisone, Beclomethasone, Fluticasone in 1 patient each. Interactions were observed in 42 patients (75%), mainly between corticosteroids and other drugs (57.3%), 1.4% with food, 41.1% with co-morbidities. Minor interactions occurred in 38 patients (55.8%) and moderate in 30 (44.1%). Significant associations (p < 0.05) were found between short-term use and hyperglycemia and hoarseness. This underscores the need for vigilant monitoring of side effects during therapy.

Keywords: Corticosteroids, Adverse Drug Reactions, Drug-Interactions, Indications.

#### **INTRODUCTION:**

Corticosteroids commonly referred to as Steroids, are anti-inflammatory and immunosuppressive drugs prescribed for a wide range of conditions. They are synthetic analogues of the natural steroid hormones produced by the adrenal cortex. They are involved in carbohydrate, fat and protein metabolism, and have anti-inflammatory, immunosuppressive, anti-proliferative and vasoconstrictive effects. These highly efficacious drugs are mostly used for the treatment of various autoimmune, respiratory and dermatological conditions. However, these may show harmful effects when used for a longer duration of time. The dose of Corticosteroids that is prescribed, dispensed and administered must be carefully considered, as too little



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steroid can show poor response whereas excess use can increase the risk of adverse reactions. For this, rational use is necessary to minimize both systemic and cutaneous side effects. As per the information available on the Central Drugs Standard Control Organization (CDSCO) website, it's off label use is more commonly practiced in India. This will increase the adverse effects and can lead to dependence on these medications. So, urgent steps are required to eliminate the root of this problem at the earliest.

They may be used individually or in combination with other drugs and are prescribed in both short and long courses depending on the condition being treated and the response of the patient. The adverse effects from short-course use include electrolyte abnormalities, hypertension, hyperglycaemia, hematologic, immunologic and neuropsychologic effects. Long-course use of Corticosteroids may lead to side effects such as osteoporosis, aseptic joint necrosis, adrenal insufficiency, gastrointestinal, hepatic, and ophthalmologic effects, hyperlipidaemia, growth suppression, and possible congenital malformations. Many of the side effects are reversible if the medication is stopped, while others may be permanent.

In order to limit systemic toxicity, novel steroids with limited oral bioavailability such as the second generation glucocorticosteroid i.e., Budesonide have been developed as an alternative to Classic Corticosteroids. In case of COVID-19, the early control of initial immune-mediated lung injury is helpful. Corticosteroids do not directly inhibit virus replication, their main role is inhibiting inflammation and suppressing the immune response.

Drug interactions with systemic Corticosteroid therapies are ubiquitous and have pharmacodynamic and pharmacokinetic foundations. Many are related to similar adverse reaction profiles with concomitant therapies, whereas pharmacokinetic interactions are often based on cytochrome P450 3A4 isoenzyme interactions. Corticosteroids are metabolic substrates for cytochrome 3A4, so any agents that inhibit or induce 3A4 activity will either increase or decrease Corticosteroid activity.

Ex: ACE Inhibitors, Amphotericin B, anti-diabetic agents, anti-hypertensives, Carbamazepine, Cobicistat, Ritonavir, Oestrogens, Grapefruit juice, inhaled Beta 2 agonists, Ketoconazole, Itraconazole, NSAIDs, Phenobarbital, Rifampin, vaccines, Warfarin, Cyclosporin.

Properties that may minimize these drug-drug interactions include- less systemic exposure as measured by glucocorticosteroid relative receptor binding affinity, which can translate to decreased nasal passage and lung receptor binding and decreased potency, lower systemic oral bioavailability, higher plasma protein binding, which results in a lower fraction of unbound drug and prevents diffusion of the drug into the tissue, a shorter elimination half-life, which is determined by the volume of distribution and clearance of the drug, and lower lipophilicity, which translates to lower distribution and binding of the drug to the tissue.

Rational use of Corticosteroids can minimize the systemic and cutaneous side effects associated with these drugs. In order to derive the optimum benefits with least adverse effects, various factors such as nature of the disease, age of the patient, site affected and the pharmacology of the Corticosteroids like potency, frequency of use and the vehicle have to be taken into consideration while prescribing.

Clinical pharmacist involvement in patient care helps in planning the therapy, prevention and early detection of adverse drug reactions and will directly promote better patient compliance and drug safety. Disease-specific dosing guidelines provide guidance on maximum daily doses in patients treated with Corticosteroids. It is important to determine methods of improving adherence to ADR prevention guidelines via health system and health policy research.



#### MATERIALS AND METHODS:

#### **Research Design:**

A prospective and observational study was conducted on the in-patients across different wards of CSI Holdsworth Memorial (Mission) Hospital to study the use of Corticosteroids, including their indications, dosage, route and duration of therapy, as well as to document any associated complications.

#### **Study Site:**

This study was conducted on the in-patients of the different wards (male ward, female ward, special ward and ICU) of CSI Holdsworth Memorial (Mission) Hospital, located in Mysuru, Karnataka, India.

#### **Study Period:**

This study was conducted over a period of 6 months from March 2023 to August 2023.

#### **Study Approval:**

This study has been approved by the Institutional Ethics Committee of Farooqia College of Pharmacy, Mysore.

#### **Study Materials:**

Patient data collection form was designed which included patient demographics (name, age, gender), current diagnosis, medical history, medications, prescribing dose, route of administration, frequency, duration of therapy, lab data, clinical notes. ADRs and drug-interactions with Corticosteroids were documented in suitably designed ADRs and drug interaction documentation forms.

#### Source of Data:

**Patient Case Sheets**: In-patient data relevant to the study like the patient's disease and their management was collected from the patient case notes and treatment chart was reviewed.

**Patient Treatment Charts:** In-patient data relevant to the study was collected. Interviewed the patient or patients' care taker(s) to know more about the patients' condition. During this study period we interacted with other healthcare workers and patients to obtain accurate data which was necessary for our research work and evaluation.

#### **Study Criteria:**

In-patients of different wards like male ward, female ward, special ward and ICU receiving Corticosteroids were followed from the day of admission to the day of discharge. On day one patient's details like demographics, reason for admission, past medication history, personal history, social and family history, allergy history, comorbid conditions, prognosis and diagnosis was collected and documented. Patient treatment chart review, progress reports and other lab investigations was followed on the subsequent days up to the day of discharge. Patient data was reviewed on a daily basis. All the ADRs, drug interactions and the conditions in which Corticosteroids were prescribed along with their doses, route and duration was documented.

#### **Study Analysis:**

All the required data was collected and the same was documented in a suitably designed data collection form, ADR documentation form, drug-interaction documentation form. Biostatistician was consulted for the sample size calculation. The data was entered in Google form and in Microsoft Excel Sheet for easy analysis of data. Fischers exact test was used to calculate the p-value.

#### **RESULTS:**

#### **Details of age distribution of patients:**

A total of 56 patients who were prescribed Corticosteroids were selected from various wards including the



male ward, female ward, special ward and ICU. Age categories were divided into neonates (birth to 1 month), infants (1month to 1 year), children (1 year to 12 years), adolescents (13 years to 17 years), adults (18 years or older), older adults (65 years or older). Specifically, among the 56 patients, 2 (3.5%) were infants, 5 (8.9%) were children, 25 (44.6%) were adults and 24 (42.8%) were older adults.

| Table 1. Details of age distribution of patients. (in 50) |                  |            |  |
|---|------------------|------------|--|
| Age Groups  | Frequency (n=56) | Percentage |  |
| Neonates (birth-1 month)                                  | -                | -          |  |
| Infants (1 month-1 year)                                  | 2                | 3.5%       |  |
| Children (1-12 years)                                     | 5                | 8.9%       |  |
| Adolescents (13-17 years)                                 | -                | -          |  |
| Adults (18 years or older)                                | 25               | 44.6%      |  |
| Older adults (65 years or older)                          | 24               | 42.8%      |  |

#### Table 1: Details of age distribution of patients. (n=56)

#### Details of gender distribution of patients:

Among the 56 patients who were prescribed with Corticosteroids, 20 (36%) were males, 36 (64%) were females.

| Gender | Frequency (n=56) | Percentage |
|--------|------------------|------------|
| Male   | 20               | 36%        |
| Female | 36               | 64%        |

#### Table 2: Details of gender distribution of patients. (n=56)

#### Details of patient distribution among wards:

The distribution of patients prescribed with Corticosteroids varied, with the maximum number i.e., 22 patients each (39.2%) coming from female ward and special ward, while the minimum number i.e., 4 patients (7.1%) was from ICU. Remaining 8 (14.2%) patients were from the male ward.

| Unit         | Frequency (n=56) | Percentage |
|--------------|------------------|------------|
| Male Ward    | 8                | 14.2%      |
| Female Ward  | 22               | 39.2%      |
| Special Ward | 22               | 39.2%      |
| ICU          | 4                | 7.1%       |

Table 3: Details of patient distribution among wards. (n=56)

#### **Details of the Corticosteroids prescribed:**

A total of 92 Corticosteroids were prescribed to 56 patients among which 42 (45.6%) were Dexamethasone, 9 (9.7%) were Hydrocortisone, 12 (13%) were Prednisolone, 27 (29.3%) were Budesonide, 1 (1%) Beclomethasone and 1 (1%) Fluticasone.



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| Table 4: Details of the Corticosteroids prescribed. (II-50) |                  |            |  |
|---|------------------|------------|--|
| Corticosteroids   | Frequency (n=56) | Percentage |  |
| Dexamethasone   | 42               | 45.6%      |  |
| Hydrocortisone  | 9                | 9.7%       |  |
| Prednisolone  | 12               | 13%        |  |
| Budesonide  | 27               | 29.3%      |  |
| Beclomethasone  | 1                | 1%         |  |
| Fluticasone   | 1                | 1%         |  |

#### Table 4: Details of the Corticosteroids prescribed. (n=56)

#### Details of the different routes of Corticosteroid administration:

Among the 92 Corticosteroids prescribed, the route of administration varied, with 15 (16.3%) given orally, 48 (52.1%) administered intravenously, 29 (31.5%) through inhalation and none administered intramuscularly or topically.

| Table 5: Details of the different routes of Corticosteroid administration | l. |
|---|----|
|---|----|

| Route of Administration | Frequency | Percentage |
|-------------------------|-----------|------------|
| Oral                    | 15        | 16.3%      |
| Intravenous             | 48        | 52.1%      |
| Intramuscular/Topical   | -         | -          |
| Inhalation              | 29        | 31.5%      |

#### Details of different indications for which Corticosteroids were prescribed:

Corticosteroid use was indicated for various medical conditions, with 8 (14.2%) patients receiving it for COPD (Chronic Obstructive Lung Disease), 5 (8.9%) for asthma, 11 (19.6%) for bronchitis, 2 (3.5%) for spondylosis, 10 (17.8%) for pneumonia, 2 (3.5%) for poisoning, 2 (3.5%) for respiratory distress, and 1 (1.7%) each for cellulitis, septic shock, SLE (Systemic Lupus Erythematosus), hyperreactive airway disease, gastritis, pulmonary oedema, myeloradiculopathy, intracranial lesion, otitis media, encephalitis, wheezing, arthritis, tracheitis, thrombocytopenic purpura, interstitial lung disease and pregnancy-induced thrombocytopenia.

| Indication                            | No. of patients (n=56) | Percentage |
|---------------------------------------|------------------------|------------|
| Chronic Obstructive Pulmonary Disease | 8                      | 14.2%      |
| Asthma                                | 5                      | 8.9%       |
| Bronchitis                            | 11                     | 19.6%      |
| Spondylosis                           | 2                      | 3.5%       |
| Pneumonia                             | 10                     | 17.8%      |
| Poisoning                             | 2                      | 3.5%       |
| Respiratory distress                  | 2                      | 3.5%       |
| Cellulitis                            | 1                      | 1.7%       |
| Septic shock                          | 1                      | 1.7%       |
| Systemic Lupus Erythematosus          | 1                      | 1.7%       |

#### Table 6: Details of different indications for which Corticosteroids were prescribed. (n=56)



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| Hyperreactive airway disease       | 1 | 1.7% |
|------------------------------------|---|------|
| Gastritis                          | 1 | 1.7% |
| Pulmonary oedema                   | 1 | 1.7% |
| Myeloradiculopathy                 | 1 | 1.7% |
| Intracranial lesion                | 1 | 1.7% |
| Otitis media                       | 1 | 1.7% |
| Encephalitis                       | 1 | 1.7% |
| Wheezing                           | 1 | 1.7% |
| Arthritis                          | 1 | 1.7% |
| Tracheitis                         | 1 | 1.7% |
| Thrombocytopenic purpura           | 1 | 1.7% |
| Interstitial lung disease          | 1 | 1.7% |
| Pregnancy-induced thrombocytopenia | 1 | 1.7% |

#### Details of distribution of patients based on Adverse Drug Reactions:

23 (41%) experienced adverse drug reactions to Corticosteroids, while the remaining 33 (58.9%) did not experience any such reactions.

| ADRs | No. of patients (n=56) | Percentage |
|------|------------------------|------------|
| Yes  | 23                     | 41%        |
| No   | 33                     | 58.9%      |

#### Table 7: Details of distribution of patients based on Adverse Drug Reactions. (n=56)

#### Details of distribution based on different Adverse Drug Reactions:

Among the 23 patients who experienced ADRs, 31 adverse drug reactions were observed. Notably, 9 (29%) ADRs were found to be hyperglycaemia, 10 (32.2%) were post-injection flare, 5 (16.1%) were hoarseness, 2 (6.4%) were osteoporosis. Singular cases i.e., 3.2% each included hypertension, Cushing's syndrome, facial puffiness, electrolyte imbalance and gastrointestinal disturbances.

#### Table 8: Details of distribution based on different Adverse Drug Reactions.

| Adverse Drug Reaction         | No. of patients | Percentage |
|-------------------------------|-----------------|------------|
| Hyperglycaemia                | 9               | 29%        |
| Post-injection flare          | 10              | 32.2%      |
| Hoarseness                    | 5               | 16.1%      |
| Osteoporosis                  | 2               | 6.4%       |
| Hypertension                  | 1               | 3.2%       |
| Cushing's syndrome            | 1               | 3.2%       |
| Facial puffiness              | 1               | 3.2%       |
| Electrolyte imbalance         | 1               | 3.2%       |
| Gastrointestinal disturbances | 1               | 3.2%       |



#### **Details of the type of adverse drug reaction: Systemic effect v/s local effect:**

Among the 31 adverse drug reactions, it was observed that 15 (48.3%) were local effects, while 16 (51.6%) of them were systemic effects.

| Type of effect  | Frequency | Percentage |
|-----------------|-----------|------------|
| Systemic effect | 16        | 51.6%      |
| Local effect    | 15        | 48.3%      |

#### Table 9: Details of the type of adverse drug reaction: Systemic effect v/s local effect.

#### Details of the duration of adverse drug reactions:

A total of 31 adverse drug reactions were found in the 23 patients, with 27 (87%) being short-term and 4 (12.9%) being long term reactions.

| Tuble 10. Detuils of the unfution of unverse unug reactions. |           |            |  |
|--|-----------|------------|--|
| Duration of effect   | Frequency | Percentage |  |
| Short-term effect  | 27        | 87%        |  |
| Long-term effect   | 4         | 12.9%      |  |

#### Table 10: Details of the duration of adverse drug reactions.

#### Details of the suspected Corticosteroids that caused ADRs:

Out of 23 ADRs observed, Dexamethasone was associated with adverse reactions in 13 (56.5%) patients, while Budesonide caused adverse reactions in 8 (34.7%) patients, followed by Prednisolone in 3 (13%) patients. Hydrocortisone, Beclomethasone and Fluticasone each led to adverse reactions in 1 (4.3%) patient.

| Suspected medication | No. of patients | Percentage |
|----------------------|-----------------|------------|
| Dexamethasone        | 13              | 56.5%      |
| Budesonide           | 8               | 34.7%      |
| Hydrocortisone       | 1               | 4.3%       |
| Prednisolone         | 3               | 13.0%      |
| Beclomethasone       | 1               | 4.3%       |
| Fluticasone          | 1               | 4.3%       |

 Table 11: Details of the suspected Corticosteroids that caused ADRs.

#### Details of distribution based on duration of Corticosteroid use:

Among the 23 patients who showed adverse drug reactions, 21 (91.3%) patients experienced it after short-term use of Corticosteroids, while 6 (26%) patients after long-term use.

| Duration of useNo. of patientsPercentage |    |       |  |  |
|--|----|-------|--|--|
| Short-term use                           | 21 | 91.3% |  |  |
| Long-term use                            | 6  | 26%   |  |  |

#### Table 12: Details of distribution based on the duration of use.



#### Details of the Corticosteroid-interactions in the patients:

It was observed that 42 (75%) patients experienced Corticosteroid interactions, while the remaining 14 (25%) did not.

| Corticosteroid interactions No. of patients (n=56) Percentage |    |     |  |  |  |
|---|----|-----|--|--|--|
| Yes   | 42 | 75% |  |  |  |
| No  | 14 | 25% |  |  |  |

 Table 13: Details of the Corticosteroid-interactions in the patients. (n=56)

#### Comprehensive analysis of Corticosteroid interactions:

It was observed that interactions related to Corticosteroids were prevalent in our patient population in which 39 (57.3%) interactions were between Corticosteroids and other drugs, 1 (1.4%) was between Corticosteroids and food, 28 (41.1%) were between Corticosteroids and underlying medical conditions.

| Interactions              | Frequency (n=56) | Percentage |  |
|---------------------------|------------------|------------|--|
| Drug-drug interactions    | 39               | 57.3%      |  |
| Drug-food interactions    | 1                | 1.4%       |  |
| Drug-disease interactions | 28               | 41.1%      |  |

 Table 14: Comprehensive analysis of Corticosteroid-interactions. (n=56)

#### Details of severity-based Corticosteroid-interaction analysis:

It was observed that 38 (55.8%) patients encountered minor interactions, 30 (44.1%) exhibited moderate interactions, and there were no instances of severe interactions documented.

| Table 15: Details of severity-based Corticosteroid-interaction ana | lysis. |
|--|--------|
|--|--------|

| Severity | No. of patients | Percentage |  |
|----------|-----------------|------------|--|
| Minor    | 38              | 55.8%      |  |
| Moderate | 30              | 44.1%      |  |
| Severe   | -               | -          |  |

#### List of Corticosteroid-interactions found in our study: Table 16: List of Corticosteroid-drug interactions.

| Sl.<br>No. | Drugs involved in the interaction   | <b>Complications of interaction</b>          |  |
|------------|---|--|--|
| 1          | Dexamethasone + Pantoprazole         Decreases the level/effect of Pantoprazol      |  |  |
| 2          | Dexamethasone + Montelukast   | Decreases the level/effect of Montelukast    |  |
| 3          | Dexamethasone + Hydrocortisone         Decreases the level/effect of Hydrocortisone |  |  |
| 4          | Prednisolone + Levofloxacin Pharmacological synergism                               |  |  |
| 5          | Dexamethasone + Ondansetron   | Decreases the level/effect of Ondansetron    |  |
| 6          | Dexamethasone + Furosemide  | Pharmacodynamic synergism                    |  |
| 7          | Budesonide + Hydrocortisone   | Decreases the level/effect of Hydrocortisone |  |



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| 8  | Hydrocortisone + Metronidazole       | Metronidazole will increase the level/effect of                    |  |  |
|----|--------------------------------------|--|--|--|
|    |                                      | Hydrocortisone   |  |  |
| 9  | Hydrocortisone + Clopidogrel         | Increases the level/effect of Clopidogrel                          |  |  |
| 10 | Hydrocortisone + Montelukast         | Decreases the level/effect of Montelukast                          |  |  |
| 11 | Dexamethasone + Enoxaparin           | Decreases the anticoagulant effects of                             |  |  |
|    |                                      | Enoxaparin, risk of bleeding                                       |  |  |
| 12 | Dexamethasone + Glimepiride          | Decreases the effect of Glimepiride by                             |  |  |
|    |                                      | pharmacodynamic antagonism   |  |  |
| 13 | Dexamethasone + Metformin            | Decreases the effect of Metformin by                               |  |  |
|    |                                      | pharmacodynamic antagonism   |  |  |
| 14 | Dexamethasone + Heparin              | Decreases the anticoagulant effects of Heparin,                    |  |  |
|    |                                      | risk of bleeding   |  |  |
| 15 | Budesonide + Pantoprazole            | Pantoprazole decreases the effects of Budesonide                   |  |  |
| 16 | Budesonide + Montelukast             | Decreases the level/effect of Montelukast                          |  |  |
| 17 | Budesonide + Dexamethasone           | Decreases the level/effect of Dexamethasone                        |  |  |
| 18 | Prednisolone + Furosemide            | Pharmacodynamic synergism  |  |  |
| 19 | Dexamethasone + Aspirin              | Pharmacodynamic synergism  |  |  |
| 20 | Prednisolone + Heparin               | Decreases the anticoagulant effects of Heparin,                    |  |  |
|    |                                      | risk of bleeding   |  |  |
| 21 | Dexamethasone + Calcium gluconate    | Decreases the level of Calcium gluconate by increasing elimination |  |  |
|    |                                      |  |  |  |
| 22 | Dexamethasone + Phenytoin            | Phenytoin will decrease the level/effect of                        |  |  |
|    |                                      | Dexamethasone  |  |  |
| 23 | Dexamethasone + Amlodipine           | Decreases the level/effect of Amlodipine                           |  |  |
| 24 | Dexamethasone + Torsemide            | Pharmacodynamic synergism  |  |  |
| 25 | Dexamethasone + Diclofenac           | Pharmacodynamic synergism  |  |  |
| 26 | Prednisolone + Glimepiride           | Decreases the effects of Glimepiride by                            |  |  |
|    |                                      | pharmacodynamic antagonism   |  |  |
| 27 | Prednisolone + Metformin             | Decreases the effects of Metformin by                              |  |  |
|    |                                      | pharmacodynamic antagonism   |  |  |
| 28 | Hydrocortisone + Fluconazole         | Fluconazole will increase the level/ effect of                     |  |  |
|    |                                      | Hydrocortisone   |  |  |
| 29 | Hydrocortisone + Theophylline        | Decreases the level/effects of Theophylline                        |  |  |
| 30 | Dexamethasone + Vildagliptin         | Decreases the level/effects of Vildagliptin by                     |  |  |
|    |                                      | pharmacodynamic antagonism   |  |  |
| 31 | Hydrocortisone + Atorvastatin        | Decreases the level/effects of Atorvastatin                        |  |  |
| 32 | Dexamethasone + Hydrochlorothiazide  | Pharmacodynamic synergism  |  |  |
| 33 | Prednisolone + Insulin regular human | Pharmacodynamic antagonism   |  |  |
| 34 | Prednisolone + Hydrochlorothiazide   | Pharmacodynamic synergism  |  |  |
| 35 | Prednisolone + Repaglinide           | Pharmacodynamic antagonism   |  |  |
| 36 | Dexamethasone + Sildenafil           | Decreases the level/effects of Sildenafil                          |  |  |



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| 37 | Dexamethasone + Nifedipine  | Nifedipine will increase the level/effects of |  |  |
|----|-----------------------------|---|--|--|
|    |                             | Dexamethasone                                 |  |  |
| 38 | Prednisolone + Levofloxacin | Pharmacological synergism                     |  |  |
| 39 | Dexamethasone + Sitagliptin | Decreases the effects of Sitagliptin by       |  |  |
|    |                             | pharmacodynamic antagonism                    |  |  |

#### List of Corticosteroid-food interaction found in our study:

#### Table 17: List of Corticosteroid-food interactions.

| SI. | Drug and food involved in the    | Complications of the interaction              |
|-----|----------------------------------|---|
| No. | interaction                      |   |
| 1   | Dexamethasone + Grapefruit juice | Grapefruit will increase the level/effects of |
|     |                                  | Dexamethasone                                 |

#### List of Corticosteroid-disease interactions found in our study:

| SI.<br>No. | Drug and disease involved in the interaction | n Complications of the interaction               |  |  |  |
|------------|--|--|--|--|--|
| 1          | Dexamethasone + Type 2 DM                    | Causes hyperglycaemia                            |  |  |  |
| 2          | Dexamethasone + Hypertension                 | Causes fluid retention, increases blood pressure |  |  |  |
| 3          | Prednisolone + Type 2 DM                     | Causes hyperglycaemia                            |  |  |  |
| 4          | Prednisolone + Hypertension                  | Causes fluid retention, increases blood pressure |  |  |  |
| 5          | Budesonide + Type 2 DM                       | Causes hyperglycaemia                            |  |  |  |
| 6          | Hydrocortisone + Type 2 DM                   | Causes hyperglycaemia                            |  |  |  |
| 7          | Hydrocortisone + Hypertension                | Causes fluid retention, increases blood pressure |  |  |  |
| 8          | Budesonide + Hypertension                    | Causes fluid retention, increases blood pressure |  |  |  |
| 9          | Fluticasone + Type 2 DM                      | Causes hyperglycaemia                            |  |  |  |

Table 18: List of Corticosteroid-disease interactions.

Note: DM – Diabetes Mellitus

#### Association between duration of Corticosteroid use and adverse drug reactions:

Number of patients who experienced hyperglycaemia after short-term use of Corticosteroids were 8 (88.9%), hoarseness was 4 (80%). The p-value for association between Short-term use of Corticosteroids and hyperglycaemia was <0.001 and hoarseness was found to be 0.041, both of which is lesser 0.05 which means that the association between short-term use and hyperglycaemia and hoarseness is significant.

#### Table 19: Association between Short-term use of Corticosteroid and adverse drug reactions.

| Adverse Drug Reactions |     | Short-term use |           | Test Statistics | P-value  |
|------------------------|-----|----------------|-----------|-----------------|----------|
|                        |     | Yes            | No        | Value           | I -value |
| Hyperglycaemia         | Yes | 8 (88.9%)      | 1 (11.1%) | 14.449#         | < 0.001  |



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|                          | No  | 11 (23.4%) | 36 (76.6%) |        |       |
|--------------------------|-----|------------|------------|--------|-------|
| Post-injection flare     | Yes | 10 (100%)  | 0 (0%)     |        |       |
|                          | No  | 9 (19.6%)  | 37 (80.4%) |        |       |
| Hoarseness               | Yes | 4 (80%)    | 1 (20%)    | 5.198# | 0.041 |
|                          | No  | 15 (29.4%) | 36 (70.6%) |        |       |
| Hypertension             | Yes | 1 (100%)   | 0 (0)      |        |       |
|                          | No  | 18 (32.7%) | 37 (67.3%) |        |       |
| Osteoporosis             | Yes | 0 (0%)     | 2 (100%)   |        |       |
|                          | No  | 19 (35.2%) | 35 (64.8%) |        |       |
| Cushing's syndrome       | Yes | 0 (0%)     | 1 (100%)   |        |       |
|                          | No  | 19 (34.5%) | 36 (65.5%) |        |       |
| Facial puffiness         | Yes | 0 (0%)     | 1 (100%)   |        |       |
|                          | No  | 19 (34.5%) | 36 (65.5%) |        |       |
| Electrolyte disturbances | Yes | 1 (100%)   | 0 (0%)     |        |       |
|                          | No  | 18 (32.7%) | 37 (67.3%) |        |       |
| GI disturbances          | Yes | 1 (100%)   | 0 (0%)     |        |       |
|                          | No  | 18 (32.7%) | 37 (67.3%) |        |       |

Note: GI- gastro-intestinal

#### Table 20: Association between Long-term use of Corticosteroid and adverse drug reactions.

| Adverse Drug Reactions |     | Long-term use |            | Test Statistics | P-value |
|------------------------|-----|---------------|------------|-----------------|---------|
|                        |     | Yes           | No         | Value           | r-value |
| Hyperglycaemia         | Yes | 2 (22.2%)     | 7 (77.8%)  | 2.331#          | 0.178   |
|                        | No  | 3 (6.4%)      | 44 (93.6%) |                 |         |
| Post-injection flare   | Yes | 0 (0%)        | 10 (100%)  |                 |         |
|                        | No  | 5 (10.9%)     | 41 (89.1%) |                 |         |
| Hoarseness             | Yes | 1 (20%)       | 4 (80%)    | 0.828#          | 0.385   |
|                        | No  | 4 (7.8%)      | 47 (92.2%) |                 |         |
| Hypertension           | Yes | 0 (0%)        | 1 (100%)   |                 |         |
|                        | No  | 5 (9.1%)      | 50 (90.9%) |                 |         |
| Osteoporosis           | Yes | 2 (100%)      | 0 (0%)     |                 |         |
|                        | No  | 3 (5.6%)      | 51 (94.4%) | -               |         |
| Cushing's syndrome     | Yes | 1(100%)       | 0 (0%)     |                 |         |
|                        | No  | 4 (7.3%)      | 51 (92.7%) | -               |         |
| Facial puffiness       | Yes | 1 (100%)      | 0 (0%)     |                 |         |
|                        | No  | 4 (7.3%)      | 51 (92.7%) |                 |         |
| Electrolyte            | Yes | 0 (0%)        | 1 (100%)   |                 |         |
| disturbances           | No  | 5 (9.1%)      | 50 (90.9%) | ]               |         |
| GI disturbances        | Yes | 0 (0%)        | 1 (100%)   |                 |         |
|                        | No  | 5 (9.1%)      | 50 (90.9%) | ]               |         |

**Note:** GI- gastro-intestinal



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#### **DISCUSSION:**

The utilization of Corticosteroid in a diverse patient population within a Tertiary Care Hospital was assessed. It was found that 56 patients were prescribed with Corticosteroids, among which 44.6% fell within the adult category (18 years or older), 42.8% of the patients belonged to the older adult group (65 years or older), 8.9% of the patients were children (1 to 12 years) and 3.5% of them were infants (1 month to 1 year). There were 20 (36%) males, while the majority, comprising 36 (64%) were females which is in contrast to the study conducted by Madhurilatha Thadanki et.al [24]. It was observed that the highest number of patients, accounting for 39.2% of the total sample, were from the female ward and the special ward, ICU had the lowest representation, with only 7.1% of the patients, 14.2% of the patients were from the male ward.

A total of 92 Corticosteroid administrations were documented among 56 patients. Dexamethasone was the most common, making up 45.6% of the administered Corticosteroids. Hydrocortisone, Prednisolone, and Budesonide constituted 9.7%, 13%, and 29.3%, respectively. Beclomethasone and Fluticasone each accounted for 1%. This contrasts with the study conducted by Arjan Aryal et.al [2], where Clobetasol was the most commonly prescribed, followed by Dexamethasone. Notably, 52.1% of the Corticosteroids were administered intravenously, 31.5% through inhalation, 16.3% were administered orally. No other routes were used. These medications were indicated for a diverse range of medical conditions. The most common conditions for Corticosteroid prescription were bronchitis (19.6%), followed by pneumonia (17.8%), Chronic Obstructive Pulmonary Disease (COPD) (14.2%), and asthma (8.9%). Spondylosis, poisoning, respiratory distress accounting for 3.5% each. Other conditions, such as cellulitis, septic shock, systemic hyperreactive airway disease, lupus ervthematosus (SLE), gastritis, pulmonary oedema. myeloradiculopathy, intracranial lesion, otitis media, encephalitis, wheezing, arthritis, tracheitis, thrombocytopenic purpura, interstitial lung disease and pregnancy-induced thrombocytopenia each represented smaller percentages of the cases, i.e., 1.7%. These findings were in contrast to study conducted by Madhurilatha Thadanki et.al [24], where the most common indication was skeletal system disorders.

It is noteworthy that 41% of the total patients experienced adverse drug reactions, in contrast to study conducted by Madhurilatha Thadanki et.al [24], where no adverse drug reactions were found. On the other hand, the majority of patients, comprising 58.9% of the patients, did not experience any adverse drug reactions. A total of 31 distinct adverse reactions were documented, with hyperglycaemia being the most prevalent, affecting 29% of the patients. Post-injection flare was also a common reaction, observed in 32.2% of cases. Additionally, 16.1% of patients reported hoarseness, while 6.4% developed osteoporosis. Singular cases of hypertension, Cushing's syndrome, facial puffiness, electrolyte imbalance, and gastrointestinal disturbances each accounted for 3.2% of the observed adverse reactions. These ADRs were categorized into two types: local effects and systemic effects. Local effects accounted for 48.3% of the reactions, 51.6% of the observed reactions were systemic. Out of these, 87% of them were short-term effects, while the remaining 12.9% were long-term effects.

Dexamethasone was the Corticosteroid most frequently linked to ADRs, affecting 56.5% of the patients in our study. Budesonide followed closely, causing adverse reactions in 34.7% of patients, Prednisolone in 13.0% of cases. Hydrocortisone, Beclomethasone, and Fluticasone each led to adverse reactions in 4.3% of patients, demonstrating a relatively lower incidence compared to the other Corticosteroids. It was found that, 26% of the patients who suffered ADRs had used Corticosteroids for a long-term duration, while a significant majority, comprising 91.3% of the patients, had been on Corticosteroid therapy for short-term.



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In a total of 56 patients, 75% of the participants' prescriptions had interactions with Corticosteroids, while the remaining 25% did not show any interactions. Among the 75%, 57.3% of cases exhibited interactions between Corticosteroids and other medications, 1.4% of interactions between Corticosteroids and food, and 41.1% of interactions between Corticosteroids and underlying medical conditions. Shifting our focus towards the severity of interactions, 55.8% of the patients encountered minor interactions attributed to Corticosteroid utilization, 44.1% of patients exhibited moderate interactions. Remarkably, our study did not document any instances of severe interactions associated with Corticosteroid-therapy which was in contrast to study conducted by Madhurilatha Thadanki et.al [24], where severe Corticosteroid interactions (11.47%) were found, followed by moderate and then minor interactions.

The p-value for association between Short-term use of Corticosteroids and hyperglycaemia was <0.001 and hoarseness was found to be 0.041, both of which is lesser than 0.05 which means that the association between short-term use and hyperglycaemia and hoarseness is significant.

The study sample consisted of 56 patients which was a limitation, as the relatively small sample size may limit the generalizability of the findings to a broader population. Due to time constraint, causality assessment could not be done and measures to reduce the instances of adverse effects could not be studied. Dose optimization can be studied which involves lowest effective dose to minimize adverse events. The efficacy and safety of different formulations of Corticosteroids can be compared. Cost-effectiveness of Corticosteroids can be analysed. Assessment of the impact of patient education programs on adherence to Corticosteroid regimens, as well as patient understanding of potential adverse events can be done. Assessment of the impact of Corticosteroid use on the quality of life of the patients can be conducted. Measures/strategies to prevent and manage the adverse events associated with Corticosteroids can be studied. Comparison between the impact of adherence and non-adherence to Corticosteroids can be studied. Impact of Corticosteroid use on co-morbidities or underlying conditions can be studied. Comparison between the effect of Anti-histamines and Corticosteroids in allergic conditions can be studied. Effects of dose tapering of Corticosteroids can be studied.

#### **CONCLUSION:**

In conclusion, the study provides valuable insights into the multifaceted realm of Corticosteroid use, revealing a broad demographic spectrum, encompassing patients across various age groups and a higher prevalence among females. Dexamethasone was found to be the favoured choice, and intravenous administration was the dominant route. From respiratory diseases such as COPD and asthma to inflammatory and infectious conditions, Corticosteroids find utility in a wide array of health issues. Patients experienced hyperglycaemia, post-injection flare, and hoarseness ranking among the most

frequently occurring ADRs.

Intriguingly, a range of drug interactions were identified, with the majority involving interactions between Corticosteroids and other drugs. While the overall nature of these interactions tends to be minor or moderate. The association between duration of Corticosteroid use and hyperglycaemia and hoarseness was found to be significant. The results showed that there is a need for vigilant monitoring and active management of potential side effects when employing Corticosteroid therapy.



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