

## Assessment of Potential Drug Interactions in Asthma Patients at a Tertiary Care Hospital in Tamilnadu

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### Abstracts:

**Objective:** The aim of the study was to assess the potential drug interactions in asthma patients at a tertiary care hospital

**Methods:** The Prospective observational study was carried out over a period of 10 months from July-2018-April 2019, in the respiratory department of a tertiary care hospital. The Institutional ethics committee approval was obtained for the study. 229 patients aged between 17-70 years were randomly selected from among patients diagnosed with asthma. The patient data was collected from the case sheets of the hospitalized patients and all the necessary relevant data was collected from the case notes such as treatment charts, and laboratory data reports were entered in the predesigned proforma. According to our study drug interactions were classified on their severity basis and risk of potential drug-drug interactions was estimated by using computerized drug-drug data based system such as drugs.com, medscape, upto date and Micromedex ® software (2.7) **Results:** A total of 229 Patient prescriptions were analyzed. These prescriptions contained a total of 916 drugs. A total of 516 Drug drug interactions (DDIs) were identified. Most of the DDIs were pharmacokinetic drug interactions (47%) followed by pharmacodynamic mechanisms (22%). The study findings showed that the prescriptions for respiratory disease conditions had the greatest number of drug interactions on an average. Severity assessment showed that majority of the DDIs were moderate (75.38%) Major (4.45%) followed by Minor (20.15%). The study results showed that as the number of drugs increases in a prescription, the number of DDIs also increases.

**Keywords:** Drug drug Interactions, Micromedex, Polypharmacy, Patient safety

**Introduction:** Asthma is a global health problem that imposes a substantial burden on patients, their families, and communities<sup>[1]</sup>. It affects an estimated 300 million individuals worldwide. Asthma affects all age groups, with increasing prevalence in many developing countries<sup>[2]</sup>. Drugs have beneficial therapeutic effects but they can also produce undesirable side effects. Drug-drug interactions (DDIs) are one such undesirable or a beneficial consequence of using two or more drugs simultaneously. DDI is a specific type of adverse event (AE) that occurs when there is an alteration in the effectiveness or toxicity of one drug due to presence of co administration of a another drug. This interaction leads to reduced, null or increased drug response.<sup>[3, 4]</sup> The effect of a drug-drug interaction might be apparent as decline in therapeutic effect of a drug, increased occurrence of ADRs and compromised treatment outcomes<sup>[5, 6]</sup>. Advanced age, poly-pharmacy and multiple prescribers have been identified as risk factors for occurrence of potential drug interactions<sup>[7]</sup>. DDIs are more likely to happen in the elderly because they tend to use multiple medications and have altered

pharmacokinetics<sup>[8,9]</sup>. When two or more drugs are administered, the activity of one or both the drugs may be altered, resulting in the formation of a new compound, before the administration of drug in the body is pharmaceutical interaction. The pharmacological effect of the drug is altered during its absorption, distribution, and metabolism or elimination process. This is known as pharmacokinetic interaction. The synergism and antagonism effects among drugs occurring at the site of action are called pharmacodynamic interactions<sup>[10,11]</sup>. A potential drug-drug interaction is an event that is likely to develop if pharmacists do not make any appropriate intervention. Physicians are not averse to the use of multiple medications to manage complicated diseases. This could result in the proverbial double-trouble of drug-drug interactions which are side effects and difficulties in compliance. Such effects can be severe, moderate or of a mild type. and there is also a chance for that effect is not associated with either drug.<sup>[12]</sup>

## **MATERIALS AND METHODS**

### **Study design and ethical considerations**

The study design was a prospective Observational study conducted in the outpatient department of a tertiary care hospital in Erode, after obtaining the approval of the institutional ethics committee

### **Study population**

The study included a total of 229 asthma patients who had undergone treatment

### **Study period**

Study was carried over a period of 10 months

### **Study criteria**

#### **Inclusion criteria**

Patients diagnosed with asthma and are currently on anti-asthmatic medications were included in the study.

#### **Exclusion criteria**

Asthmatic patients who suffered from other diseases such as hypertension, diabetes, heart problems, bronchitis, chronic obstructive pulmonary disease (COPD), peptic ulcer, diabetes mellitus or any other co-morbidities were excluded.

### **Data collection and Report**

The patient data was collected from the case sheets of the hospitalized patients and all the necessary relevant data was collected from the case notes such as treatment charts, and laboratory data reports were entered in the predesigned proforma. According to our study drug interactions were classified on their severity basis and risk of potential drug –drug interactions by using drugs.com, medscape, upto date and Micromedex software

### **Results:**

Of the selected 229 patients, 145 (63.31%) were males and 84 (36.68%) were females. Most of the patients i.e., 179 of them belong to the age group 41-70 years. (78.16%). The Length of stay of these patients was more than 8 days. Of the total 516 DDI<sub>s</sub> encountered in our study 389(75.38%) fall under the category of moderate drug interaction. Major drug interactions were found to be 23 (4.45%) and those of minor category were determined to be 104(20.15%). These DDI<sub>s</sub> were found to occur when the prescriptions contain more than 4-5 drugs. The most common drug which manifested drug drug interactions is Budesonide+Levofloxacin

Moderate Drug interaction. The gender ratio in our study showed that the Males were more prone to asthma as compared to females

**Patient distribution based on Age and Gender Table: 1**

Gender	No of the Patients	% of the Patients (n=229)
Male	145	63.31%
Female	84	36.68%
Total	229	100%

**Asthma Patient distribution based on Age Group Table: 2**

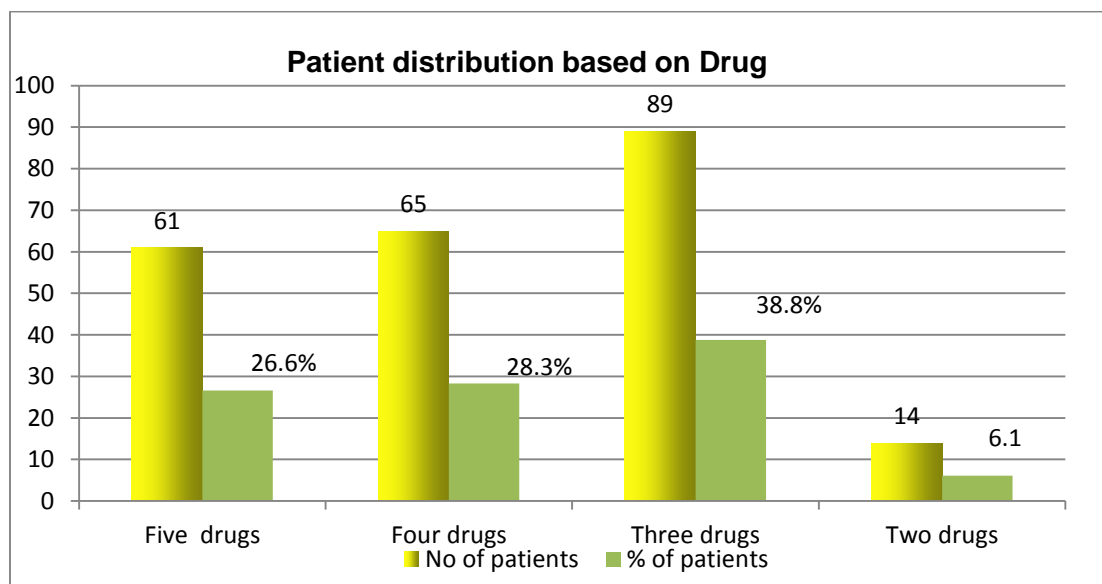
Age of years	No of the Patients	% of the Patients (n=229)
17-30	22	9.60
31-40	29	12.6
41-50	69	30.1
51-60	57	24.8
61-70	52	22.7
Total	229	100

**Most commonly prescribed Anti-asthmatic drugs: Table: 3**

Anti-asthmatic drugs	No of prescriptions	% of patients(n=229)
Methyl xanthine	122	53.2
corticosteroids	47	20.5
Anti-histamines	37	16.1
short acting $\beta_2$ agonist	13	5.6
Leukotriene antagonist	6	2.6
anticholinergics	4	1.7

**Patient distribution based on Drug therapy regimen Table: 4**

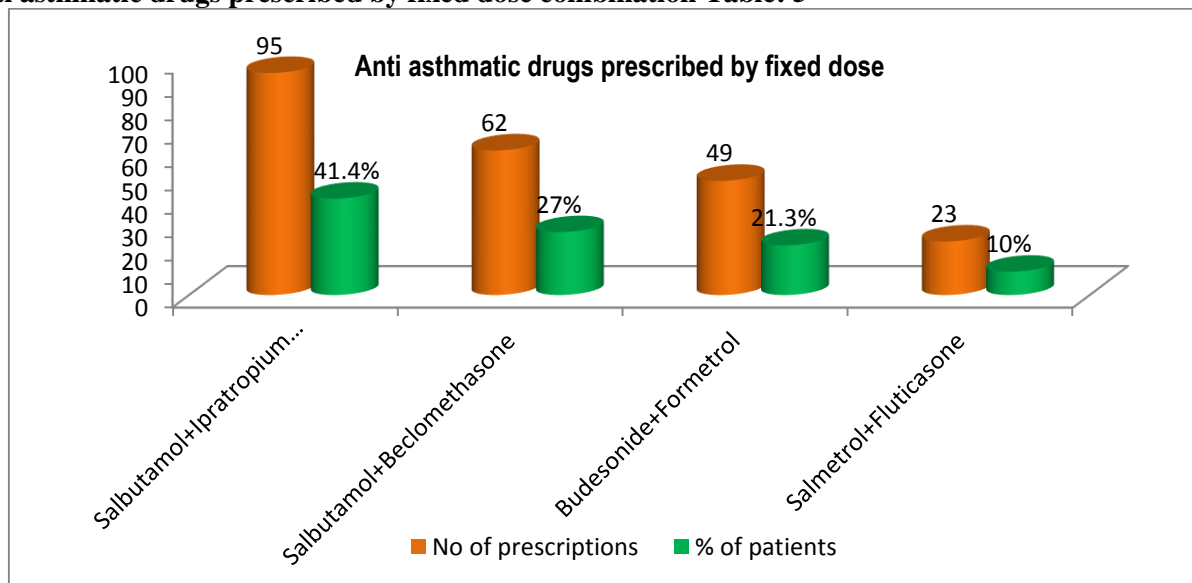
Out of 229 patients, majority of them 61(26.6%) received multiple drug therapy (>4 drugs) followed by 4 drugs 65(28.3%), 3 drug 89 (38.8%) and 2 drug 14(6.1%) (Table::4).



**Patient distribution based on fixed dose combinations.**

Majority of the patients were prescribed with Salbutamol+Ipratropium bromide 95 (41.48%), followed by Salbutamol+Beclomethasone 62(27.07%), Budesonide+Formetrol 49 (21.39%) and Salmeterol+Fluticasone 23 (10.04%)

**Anti asthmatic drugs prescribed by fixed dose combination Table: 5**



**Patient distribution based on Adjuvant therapy.**

Our study showed that 98 (42.7. %) received antibiotics, 39 (17.0%), received antacids. multi-vitamins were prescribed for 56 (24.4%) of the patients. And while 36 (15.7%) were prescribed NSAIDS as adjuvant therapy. the antibiotics that were prescribed as tabulated below levofloxacin 14(41.48%) were prescribed mostly followed by, ofloxacin13 (28.38%), amoxicillin 11(19.65%) and azithromycin18 (10.91%) which are highly effective against respiratory infections. Among antacids, pantoprazole17 (43.13%), omeprazole7 (37.25%) and ranitidine13 (19.60%) were prescribed. Paracetamol12 (74.04%) ibuprofen9 (14.81%) and diclofenac3 (11.11%) were given for pain management.

**Drugs prescribing to asthma patients with adjuvant therapy Table: 6**

Adjuvant therapy drugs	No of Patients	% of patients
Antibiotics	98	42.7
Antacids	39	17.0
Multivitamins	56	24.4
NSAIDS	36	15.7

**Drug Interaction based on severity Table: 7**

Category	Number of potential drug interaction DDI=516
Major	23(4.45%)
Moderate	389 (75.38%)
Minor	104 (20.15%)

**Effect of Potential Drug-drug interaction combinations in asthma patients: Table: 8**

Interacting drugs	Severity	Interactive Effects	Type	No of Patients%(n=229)
Levofloxacin+Theophylline	Major	Results in theophylline toxicity(nausea, vomiting, palpitation, tremor)	PD	12(2.32%)
				11(2.13%)

Azithromycin+Levofloxacin	Major	Results in increased risk of QT interval prolongation	PD	
Budesonide+Levofloxacin	Moderate	Results in increased risk of tendon rupture	PK	195(37.7%)
Azithromycin+Theophylline	Moderate	Results in increased serum theophylline concentrations	PD	96(18.60)
Budesonide+ Ofloxacin	Moderate	Results in increased risk of tendon rupture	PK	98(18.9)
Theophylline+Ranitidine	Minor	Results increase risk of theophylline toxicity	PK	104(20.15)

**Discussion:**

Out of 229 prescriptions in our study contained a total of 916 medications. The prescriptions contained any were between two to five medicines each. Patients received therapy at an average of 4-5 drugs per prescription. The common route of drug administration was by the oral route i.e., 98 patient (116). Parenteral medication were administered to 59 patients. The remaining 72 patient received (135) medication by other routes. Table 3 Methyl xanthines were the most frequently prescribed group of anti-asthmatic drugs (122 patients) followed by corticosteroids (47 patients), antihistamines (37 patients), short acting  $\beta_2$  agonist (13 patients), leukotriene receptor antagonist (6 patients) and anticholinergics (4 patients). Our study showed Methyl xanthenes were the most prescribed (86.27%) probably because of their lower cost. A similar conclusion has been drawn by Arumugam et al and Kumar et al. <sup>12,13</sup> The study analysis suggests that symptomatic relief agents were more prescribed than asthma controlling agents. In our study some patients were also prescribed with fixed dose combinations. Among them Salbutamol with ipratropium bromide was the most frequently prescribed combination (52.49%) These results are in contrast to the study of Adil Hameed et al in which Salbutamol with Beclomethasone (90%) was the most frequently prescribed drug.<sup>14</sup>

Our study also showed that antibiotics, multivitamins, antacids and NSAID's were prescribed as adjuvant therapy. Among the antibiotics, Levofloxacin (41.48%) were prescribed commonly followed by, Ofloxacin (28.38%), Amoxicillin (19.65%) and Azithromycin (10.91%) which are highly effective against respiratory infections. This fact is in contrast to the studies of T Rajathilagam et al in which amoxicillin was the most prescribed antibiotic. The present study reveals that the equal numbers of Minor and moderate drug interactions occur were found. This is in contrast to the studies of R. D. Shimpi et al who did not report any serious drug interactions. Major interactions were noted Levofloxacin+Theophylline, and Azithromycin+Levofloxacin combination. Moderate interactions were noted with Budesonide+Levofloxacin, Azithromycin+Theophylline, Budesonide+Ofloxacin. Combinations. Either prescribing an alternative drug or adjusting the dose of prescribed medicine can resolve the effects of drug interactions.

**Conclusion:**

Our study helped in understanding about the most prone age groups, disease conditions, and the common mechanisms that can cause DDIs in asthma patient prescriptions. Drug – drug interactions were observed more in asthma patients with polypharmacy and length of stay in hospital for more than 8 days. Hence the clinical pharmacist can play an important role in identifying and resolving drug-drug interaction through absolute pharmaceutical care practices. This may help in improving the safe and effective use of drugs in our hospital

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