

## ORIGINAL ARTICLE

# Presence of Affirmable Drug Affiliated Interactions in Medical Patients in Medical OPD of Pakistani Hospital

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## ABSTRACT

Drug-drug interactions (DDIs), are preventable medical related hazards having grave life menacing and unfavorable consequences

**Purpose:** To find the clinical adverse effects and interaction frequency witnessed in prescriptions of a medical OPD

**Study Design:** Comparative study

**Methodology:** A sample of 546 patients who were being prescribed at least two drugs simultaneously was assessed using a drug interaction program

**Statistical analysis:** SPSS v.20.0 was used to analyze the data to present results as proportions

**Results:** The 546 patients (72.8% male having mean age of 58.3±14.7 years. Out of these 186 (4.7%), 2595 (65.6%) and 773 (19.5%) were severe, moderate and mild interactions respectively

**Conclusions:** We concluded that large percentage of patients were detected having one or more potential drug-drug interactions

**Keywords:** Adverse Drug Interaction, Drug-Related Problems, Drug-Drug Interaction and Pharmaco-epidemiology.

## INTRODUCTION

There are many health hazards in medical field related with drugs given to patients. Drug-drug interactions (DDIs), are one of these preventable issues that have grave life menacing and unfavorable consequences.<sup>1,2</sup> Adverse drug reactions usually result in severe morbidity or mortality. According to one estimate, ADRs cause 05% admissions in healthcare settings with almost 0.25-25% are due to DDIs.<sup>3-6</sup> This high proportion of admissions can be reduced by taking correct preventive measures for DDIs that ultimately result in avoiding undesirable situations.<sup>7</sup>

Hospital admitted patients face a lot of DDIs of variable strengths.<sup>7-9</sup> Various studies showed that DDIs have been the main reasons for hospitalization and change of class of drugs when data was collected globally.<sup>10-14</sup> As Pakistan is a developing country and there is lack of research culture so there is a lack of data regarding DDIs among Pakistani population. Similarly, literature review showed that there was almost 28-83% prevalence of DDIs faced by OPDs patients among developed countries globally.<sup>15-18</sup> However, these studies had number of limitations that include working setups, planning, DDIs screening tool and drug prescribing pattern.

There are various number of reasons that results in drug drug interactions among outpatients. In our clinical setups, health workers face different challenges like over-crowded government hospitals with patients, faulty past medication histories with many ailments concurrently, poor drug compliance by patients, adverse therapeutic outcomes and ADR reporting.<sup>19-21</sup>

## OBJECTIVE

To find the clinical adverse effects and interaction frequency witnessed in prescriptions of a medical OPD.

## METHODOLOGY

All 546 patients who visited the medical OPD of DHQ hospital Jhelum, Punjab, Pakistan in June 2021, were enrolled in this study. This hospital is 258 bedded institution that provides modern diagnostic facilities to the surrounding population. Exclusion criteria was to not include patients who were being prescribed less than two drugs. Demographic information like age, sex, weight etc. Along with their principal diagnoses (according to ICD-11 classification) were collected. Anatomical therapeutic chemical (ATC) classification for drugs was employed. It provided information on potential clinical consequences (ADRs) following ethical review board approval.

**Statistical Analysis:** Data was analyzed by SPSSv.20. The results of this study were expressed in proportions, mean ± SD or in terms of medians within their corresponding ranges.

## RESULTS

Studied population comprised of 546 patients, amongst them 398 were males and 148 were females. The mean age± SD was 58.3±14.7 years. Also 38.4% of the total sample that equals to 210 patients consisted of age 65 years or above as shown in table-1.

A total of 3317 drugs were prescribed to 546 patients that lead to a median of 6 drugs per patient having range of 3 to 11. A median of 7 versus 5 drugs; (p<0.01) was found significantly higher in elderly (≥65 years) patients as compared in younger or lesser than 65 years of age. Amongst all drugs prescribed, 28% were for alimentary tract and metabolic dysfunctions, 19% prescribed for respiratory problems, 18% were for the treatment of cardiovascular diseases, 15% pertained to nervous system, 7% were prescribed for blood and blood forming organs,

while the rest of 13% drugs were prescribed for the treatment of other organ systems as shown in table-2.

Table-1: General Parameters Of Study Subjects (n=546)

Parameters	Categories	Percentage (%)
Age (years)	Mean age ± SD	58.3 ±14.7
	<65	61.6
	≥65	38.4
Gender	Males	72.8
	Females	27.2
Drugs Prescribed	median (range)	6 (3 – 11)
Main diagnoses according to ICD 11	Respiratory diseases	25.8
	Cardiovascular diseases	25.0
	Mental and behavioral disorders	17.6
	Endocrine, nutritional and metabolic diseases	13.7
	Musculoskeletal and connective tissue diseases	6.3
	Others	11.6

Table-2: Prescription Of Different Drug Classes

Therapeutic class	Frequency with Percentage
Drugs for acid related disorders	333 (60.9)
Drugs for obstructive airway diseases	182 (33.2)
Agents acting on the renin-angiotensin system	150 (27.2)
Antithrombotic agents	135 (24.7)
Lipid modifying agents, psychoanaleptics	122 (22.2)
Vitamins	120 (21.9)
Drugs used in diabetes	117 (21.4)
Psycholeptics	108 (19.7)
Diuretics, antiepileptics	105 (19.2)

Out of the total 546 patients, 522 patients proved to have possible drug-drug combinations. The median number i.e. 5.5 is the DDI in patients having possible interactions in range of 1 to 15. Ten potentially interacting drug combinations leads to more than 20% of the 3954 potential DDIs as shown in table-3.

Table-3: Most Common Interacting Drug Combinations

Theophylline + Salmeterol	Hypokalemia, cardiovascular toxicity	Moderate	140 (2.3)
Theophylline + Albuterol	Hypokalemia, cardiovascular toxicity	Moderate	135 (2.2)
Aspirin + Omeprazole	Decreased concentration and efficacy of aspirin	Minor	129 (2.1)

Theophylline + Omeprazole	Increased theophylline concentration and toxicity	Moderate	120 (2.0)
Furosemide + Aspirin	Loss of natriuretic and diuretic response of furosemide	Minor	107 (1.7)
Aspirin + Losartan	Decreased anti hypertensive effect, deterioration of renal function	Moderate	102 (1.7)
Aspirin + Nitroglycerin	Increased anti hypertensive effect of nitroglycerin	Minor	102 (1.7)
Omeprazole + Atorvastatin	Increased concentration of atorvastatin	Moderate	99 (1.6)
Albuterol + Fluticasone	Hypokalemia	Minor	86 (1.4)
Albuterol+ Salmeterol	Increased risk of cardiovascular side effects	Moderate	86 (1.4)

Top five most common DDIs associated with potentially severe clinical consequences were listed in table-4.

Table-4: Interacting drug combinations with potential major severity

Potential DDIs	Adverse effect	Documentation	Onset
Potassium sparing diuretics + ACE inhibitor	Hyperkalaemia	Good	Delayed
Omeprazole + Clopidogrel	Reduced cardioprotection	Good	Delayed
SSRIs + TCAs	Serotonin syndrome, TCA toxicity	Good	Rapid
Methotrexate + Omeprazole	Increased methotrexate concentration	Fair	Delayed
Ciprofloxacin + Theophylline	Increased theophylline concentration and toxicity	Good	Delayed

## DISCUSSION

This study revealed that clinical adversity due to possible and prudent drug-drug interactions and the frequency of the drugs prescribed in out-patient department. The percentage of aged people (having age 65 or above) in our study is 38.4 considering a total of 546 patients. In contrast to a recent study that revealed 29.4% aged people (age 65 or above).<sup>22</sup> The possible reason behind may be lesser health awareness, poor economic and balanced diet availability to the senior citizens in our country.

The predominance of DDIs in our findings show (95.8%) that seems quite higher in comparison with the related previous studies conducted in other nations i.e. (27.9 to 83.4%).<sup>15-18</sup> The possible reason behind may be over-burdened healthcare personnel due to patient

overload in hospitals, severe lacking of patient's follow up monitoring system. Furthermore, there is not proper inductance as well as pharmacist utilization in healthcare settings. The government's lack of interest is another big issue that can aggravate the situation. Our study reveals minor to moderate intensity of main types of interactions.

The implications drawn from our study recommend appropriate follow up procedure to be adopted to avoid any possible adverse effect as a result of administration of multiple drugs simultaneously by patients. Surveillance and observational procedures used for scrutinizing each and every patient's DDIs will be irksome, tedious, and sometimes futile. also it produces more burden upon healthcare practitioners. Furthermore, DDIs of minor intensities are of no clinical value. Every medical aid provider cannot differentiate DDIs from ADRs, and therefore, cannot take appropriate remedy or restorative therapy accordingly.

If clinicians are being made well aware about the DDIs encountered, the occurrence of undesirable outcomes can be minimized. Therefore, there must be clinical guidelines properly formulated and implemented in healthcare settings especially important for the visiting patients' health safety.

The most frequently interactions of drugs noticed in our study are: Theophylline plus salbutamol, theophylline plus albuterol, aspirin plus omeprazole, theophylline plus omeprazole, furosemide plus aspirin, aspirin plus losartan, aspirin plus nitroglycerin, omeprazole plus atorvastatin, albuterol plus fluticasone, and albuterol plus salmeterol. Our findings are different than previous studies performed due to different interactions screening process, and different drug prescriptions. The possible reason behind may be the availability of various healthcare settings in the close vicinities, lack of patient awareness, or non provision of patients' follow up plan. Only OPD patients were being analyzed in the study. The results might be different if other specialities were being considered. Thus multi-speciality studies are recommended. Also only one drug interaction screening program (Micromedex Drug-Reax®) is used to analyze DDIs. However, other scores can also be utilized and there exists differences among different programs.

**Limitation:** Our study had several limitations like financial constraints, time restrictions and fewer resources.

## CONCLUSION

We concluded that predominance of DDIs in our findings showed a very huge percentage of patients. This may be due to the overburdening of patients over the healthcare practitioners as well as hospital's limited facilities. Lack of appropriate patients' follow up monitoring system. Scarcity of DDIs detection system also adds up to adversity of situation.

**Author's Contribution:** HAB&MZA: Conceptualized the study, analyzed the data, and formulated the initial draft.

AS&FI: Contributed to the histomorphological evaluation.

ZS: Contributed to the analysis of data and proofread the draft.

SA: Contributed to data collection.

TL: Contributed to the proofreading the manuscript for intellectual content.

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