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Research Article

Retrospective Drug Utilization Review: Potential Drug-Drug Interactions in General Medicine ward of a Tertiary Care Hospital

Dr. Samhitha Chetty[1]*, Chetan A[2], Meghana K[2], Abdul Bazith H[2]

[1]Assistant Professor, Department of Pharmacy Practice, [2] B. Pharmacy, K.K. College of Pharmacy, 1/161, Sankaralinganar Road, Gerugambakkam, Chennai-600128.

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ABSTRACT

Our study was aimed to identify and evaluate the frequency, severity, mechanism and common pairs of Drug-Drug Interactions (DDIs) in prescriptions. The objective was to categorize the drug-drug interactions in prescriptions based on the mechanism involved, to determine the severity of drug-drug interactions in prescriptions, to determine the relationship between number of drugs in the prescription and its potential for drug-drug interactions and to determine the potential drug-drug Interactions with different diagnosis. The data was collected retrospectively and recorded in a data collection form from prescriptions provided in the cases at the Department of General Medicine, Vijaya Group of Hospitals, Vadapalani, Chennai. The study was conducted for a period of 6 months from January to June 2019. Among 150 prescriptions analyzed, a total of 298 drug-drug interactions were found. Majority of drug-drug interactions were of major severity. When analyzed the major mechanism of drug-drug interactions was pharmacodynamic interaction. Under pharmacokinetic drug-drug interactions, interaction through absorption were predominant than other. Our study was conducted in order to determine, analyze the potential drug-drug interactions in general medicine ward of a hospital.

Keywords: Potential Drug-Drug interactions, Pharmacodynamic Interaction, Pharmacokinetic Interactions, Drug Prescription

INTRODUCTION

The Pharmacy benefit management companies came about due to the need for a point-of-service system to adjudicate pharmacy claims in the 1980s. Over the years other value-added programs such as Drug Usage Review (DUR), generic substitution and step-care protocols have been added to improve quality of medical care and control health care costs. According to the 2006 Novartis Pharmacy Benefit Report, [1] services such as DUR and generic substitution are now used by over 90% of the managed care organizations surveyed. The use of generic substitution and DUR is now the most frequently reported quality and cost control measure. Specifically, the use of DUR increased over the period for preferred provider organizations (2003–2004, 60.9%–70.4%) and health maintenance organizations (2003–2004, 68.4%–

Address for Correspondence: Dr. Samhitha Chetty, Assistant Professor, Department of Pharmacy Practice, K.K. College of Pharmacy, 1/161, Sankaralinganar Road, Gerugambakkam, Chennai-600128;
E-mail: chettysamhitha24@gmail.com

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74.4%). It has long been recognized that drugs are not frequently used to their full potential, nor according to usually accepted criteria [2,3] since the majority of the prescriptions are written by physicians, their prescribing habits are important when considering the inappropriateness of drug use. [4] The goals of DUR were explained as the encouragement of optimal drug use and the provision of high-quality drug therapy as cost-effectively as possible. Pharmacists are frequently called upon to assess medication prescribed by physicians and provide the important service of DUR. [2] The outcomes of these assessments often lead to improvements in cost-effective prescribing and better utilization of limited resources. [4] Although DUR is a part of the vast majority of managed care quality assurance programs, the benefit of such program has conflicting results reported in the literature. DUR is a quality assurance approach for the facility per se, and it involves the setting of criteria and standards, an assessment phase using a set of screening criteria, and a follow-up correctional phase with the prescriber. It comprises all aspects of drug treatment from the time a patient presents to a prescriber to the final outcome of the therapy. [5] Claims-based analysis using computerized, retrospective drug utilization review (DUR) offers a powerful tool to better understand the incidence of potential DDIs as well as other types of potential medication errors. [7] Despite the popularity of such programs in both the private and public health care sectors, very little data are available on the detection of potential DDIs. [8] Sharing these data would not only assist in determining which co-prescribed drug pairs to target for intervention but also would assist in developing and tracking the success of DUR intervention programs. Retrospective DUR system uses programmed criteria, before and after pharmacist assessment. It is our hope that detailing the data on case findings of potential DDIs at various steps in the detection process will assist others in determining how to develop and optimize such DUR programs. A pharmacy benefit management (PBM) company use a computerized, retrospective DUR program to monitor and intervene in cases of potentially serious DDIs. This DUR program was established in 1999 and continues as an ongoing program within the PBM. [9] As Schulman et al. euphemistically noted the literature on the benefit of DUR is "underdeveloped," echoing the findings of Soumerai and Lipton, who found that computer-based DUR programs have been "implemented without satisfactory evidence of efficacy and safety". [7] Even so, DUR programs rapidly expanded into general use after 1990, when the Omnibus Budget Reconciliation Act (OBRA '90) mandated states to provide such reviews for ambulatory Medicaid patients. [10,11]

MATERIALS AND METHODS:

Materials: This was a retrospective observational study involving prescription pattern and common drug-drug interactions occurring in prescriptions obtained from cases at Vijaya Group of Hospitals, Department of General Medicine, Vadapalani, Chennai for a period of 6 months.

Study Site: The study was conducted in the Department of General Medicine, Vijaya Group of Hospitals, Vadapalani, Chennai.

Study Period: The study was conducted for a period of 6 months from January 2019 to June 2019.

Study Design: This study was a Retrospective observational study.

Study Population: A total of 150 prescriptions were collected in the study.

Study Criteria

Inclusion criteria:

1. Patients who are of either gender and of age > 18 years and < 70 Years.
2. All inpatients of Medical ward and Medical unit.
3. All patients' prescriptions having 4 or more drugs per prescription.

Exclusion criteria:

1. Patients < 18 years and > 70 years
2. Pregnant and lactating women
3. Outpatients

Study Procedure: The data was collected using a data collection form and entered into Microsoft Excel and stratified.

Source Data: The data were collected from case sheets and laboratory reports.

Data Collection Form

Data was recorded in preformed pro-forma with the following consideration

1. Patient Demographic Details
2. Presenting Complaints
3. Personal & Occupational History
4. Past Medical & Medication History
5. Family & Social History
6. General And Systemic Examination
7. Investigations Performed
8. Drug Chart
   - Drug
   - Dose
   - Dosage
   - Route of admin

Statistical Analysis

The data collected was processed and entered into Microsoft Excel Sheet. Descriptive statistical procedure and evaluation was done to analyse the results.

RESULTS

Gender-wise distributions of patients

Table 1: Gender wise distribution of patients

S.No	Gender	N (%) (n=150)
1	**Male**	**89 (59.33%)**
2	Female	61 (40.66%)

Among the 150 patients evaluated for our study, majority of patients were Male, 89 (59.33%) and least were Female, 61 (40.66%) as shown in Table 1.

Age Wise Distribution of Patients

Table 2: Age wise distribution of patients

S.No	Age In Years	No. of Patients (n=150)	Percentage (%)
1	18-20	3	2
2	21-30	27	18
3	31-40	18	12
4	41-50	20	13.3
5	51-60	36	24
6	**61-70**	**46**	**30.6**

Out of 150 patients, 46 (30.66%) patients were in the age group of 61-70, 36 (24%) patients were in the age group of 51-60, 20 (13.3%) patients were in the age group of 41-50, 18 (12%) patients were in the age group of 31-40, 27 (18%) patients were in the age group of 21-30 and 3 (2%) patients were in the age group of 18-20. The Mean age of the study population was 49.3 ± 2.828 years old as shown in the Table 2.

Length of stay of study population

Table 3: Length of hospitalization

S.No	Length of Stay (Days)	No. of Patients (n=150)	Percentage (%)
1	**1-5**	**85**	**56.6**
2	6-10	54	36
3	More than 10	11	7.33

Out of 150 patients, 85 (56.6%) patients were hospitalized for less than 5 days, 54 (36%) patients were hospitalized for 6-10 days and 11 (7.33%) patients were hospitalized for more than 10 days. The Mean length of stay of study population is 5.49 ± 1.41 as shown in Table 3.

Diagnosis of patients

Table 4: Diagnosis of patients

S.No	Disorders	Percentage (%)
1	**Cardiac**	**17.3**
2	Respiratory	16.6
3	Endocrine	14.6
4	Digestive system	12.6
5	Neurology	12
6	Renal	6
7	Hepatic	4
8	Haematological	2.66
9	Musculoskeletal & Connective Tissue	2.66
10	Others	11.3

Among 150 patient under study project, majority of the patients were diagnosed with Cardiac Disorders, 26 (17.3%) patients followed by Respiratory disorders 25 (16.6%) patients, Endocrine disorder 22 (14.6%) patients, Digestive disorders 19 (12.67%) patients, and the least patients were diagnosed with Haematological disorders 4 (2.66%) as shown in Table 4.

Details of medicaments in prescriptions

Table 5: Details of medicaments in prescriptions

Total number of prescriptions	150
Total number of drugs prescribed	1390
Average number of drugs prescribed	9.26

A total of 210 prescriptions were collected of which 150 prescriptions were analysed. Total numbers of drugs prescribed were 1390 and average number of drugs prescribed per prescription was 9.26 as shown in Table 5.

Number of medications prescribed

Table 6: Number of medicaments prescribed

Sl. No	No. of Drugs	No. of Patients (n=150)	Percentage (%)
1	3	4	2.66
2	4	7	4.66
3	5	17	11.33
4	6	9	6
5	**7**	**22**	**14.6**
6	8	21	14
7	9	16	10.66

8	10	9	6
9	11	16	10.66
10	12	12	8
11	13	10	6
12	14	4	2.66
13	15	3	2

A total of 1390 medications were prescribed to the 150 patients enrolled in the study. The highest numbers of drugs prescribed per prescription were 15 medications in 3 (2%) patients followed by 14 drugs in 4 (2.66%) patients, 13 drugs in 10 (6%) patients, 12 drugs in 12 (8%) patients. The least number of drugs prescribed per prescription was 3 drugs in 4 (2.66%) patients as shown in the Table 6.

Drug Interactions

Table 7: Drug Interactions

1	Total prescriptions	150
2	Total medications	1390
3	Total number of Drug-Drug Interactions	298
4	Average Drug-Drug Interactions	2.7

Among the 1390 medications analysed in 150 prescriptions, a total of 298 drug interactions were found. Among the 150 patients, 110 (73.33%) patients had pDDI and 40 (26.66%) patients had no pDDI. The average pDDI was 2.70 ± 1.878 as shown in Table 7.

Mechanism of drug-drug interactions

Table 8: Mechanism of drug-drug interactions

S.No	Mechanism Of Action	No. of Interactions (n=298)	Percentage (%)
1	Pharmacokinetic	103	34.56
2	**Pharmacodynamic**	**195**	**65.43**

A total of 298 potential Drug – Drug interactions were identified in our study populations, out of which Pharmacokinetic pDDI were 103(34.56%) and Pharmacodynamic pDDI were 95(65.43%) as shown in Table 8.

Table 9: Categorization of drug-drug Interactions based on mechanism

Mechanism	No. of Interactions (N=298)	Percentage (%)	P Value
Pharmacokinetic drug-drug interactions	103	34.56	-
Absorption	***31***	***10.4***	***<0.05 ****
Distribution	23	7.7	-
Metabolism	30	10.06	-
Excretion	3	1	-
Pharmacodynamic drug-drug interactions	195	65.4	-

***P<0.05: Significant ns: Not significant**

The study prescriptions comprised 34.56% of pharmacokinetic pDDIs, 65.4% of Pharmacodynamic pDDIs. Statistical analysis showed a significant difference within the different pharmacokinetic DDI, where pDDIs due to absorption occur most often (10.4%) followed by metabolism (10.06%) then distribution (7.7%) and the least due to excretion (1%) as shown in Table 9.

Severity of potential drug–drug interaction

Table 10: Severity of potential drug-drug interaction

S.No	Severity	Percentage (%)
1	**Major**	**48.99**
2	Moderate	39.93
3	Minor	11.07

Table 11: Distribution of patients with PDDI

S.No	Severity	Percentage of Patients (%)
1	**Major**	**52.66**
2	Moderate	46
3	Minor	15.3

COMMON DRUG–DRUG INTERACTION

Table 12: COMMON DRUG-DRUG INTERACTIONS

S.No	Drug 1	Drug 2	Severity	Frequency of Interaction (%)
1	**Budesonide**	**Levofloxacin**	**Major**	**7 (4.66)**
2	**Ondansetron**	**Tramadol**	**Major**	**7 (4.66)**
3	Levothyroxine	Pantoprazole	Moderate	6 (4)
4	Atorvastatin	Clopidogrel	Moderate	4 (3.33)
5	Aspirin	Ranitidine Hcl	Minor	2 (1.33)

Among the 1390 medications analysed in 150 prescriptions, a total of 298 drug interactions were found. The most common major interacting drug pairs was Budesonide + Levofloxacin 7 (4.66%) and least minor interacting drug pair was Aspirin + Ranitidine Hcl 2(1.33%) as shown in the Table 12.

DISCUSSION

Drug-Drug interactions in patients receiving multidrug therapy are of wide concern. Such interactions are an important cause for adverse drug reactions and may lead to increased risk of hospitalization and higher health care cost. Drug-Drug interaction (DDI) has received a great deal of recent attention from the regulatory, scientific and health care communities worldwide. Prescribing appropriate drug(s) is the requirement of rational use of drugs. [12] Drug interactions and their consistent adverse effects are the major reasons of hospital admission and mortalities. Outcomes resulting from the drugs account approximately 10-20% of admissions to the hospital furthermore 1% hospital admissions result from DDIs. [13] Among all pDDIs encountered, only few results in ADRs. [14] Nevertheless, ADRs associated with DDIs can be of high clinical importance, [15,16] justifying close monitoring of medications for pDDIs. Factors such as increasing number of medications per prescriptions, drugs additionally given in case of certain co-morbid conditions contribute to increased risk of pDDIs. This study was conducted in order to identify and evaluate the frequency, severity, mechanism and common pairs of drug-drug interaction in prescription. Among the 150 patients take into the study, majority of the patients were male (59.33%) and were more predominant than the female patients. This trend was similar to that found in another report. [17] The mean age of the study population was 49.3±3 years. This finding was lesser than that of another report 68.4 years old [18] and most of the patients were in age group of 61 – 70 (30.66%). Although the length of stay of hospitalization of a patients does not affect directly the increased risk of pDDI, but as the length of hospitalization increases the chances of the patients getting nosocomial infections may increase thereby adding a greater number of drugs to the prescription followed by increased risk of a pDDI. In our study majority of the patients (56.6%) were hospitalized for less than 5 days and only 7.33% patients were hospitalized for more than 10 days. The mean length of stay of study population was 5.49±1.4 days. The length of hospitalization in another report was found to be greater 13 days. [18] Most of the patients in our study were diagnosed with cardiac disorders (17.3%) followed by respiratory disorder (16.6%), endocrine disorders (14.6%) and digestive disorders (12.6%). This result is similar to the finding obtained from another study where patients were most diagnosed with cardiac disorders. [19] In our study the total numbers of drugs prescribed were 1390 and average number of drugs prescribed per prescription was 9.26. This finding was different from another study reported in the literature, were average number of drugs per prescription was 4.4 ± 1.48. Our study found that the highest number of drugs prescribed per prescription was 15 in 3 patients followed by 14 in 4 and the least number of drugs was prescribed for 3 patients. Among the 1390 medications, a total of 298 drug interactions were found and potential drug – drug interaction was found in 70% of the study population. This result obtained was found to be greater than another study reported in the literature, were 58% of study population encountered potential drug-drug interaction. In the present study total number of potential drug – drug interactions was 298. Out of which 49% were major, 40% were moderate and 11% were minor interactions. There was a greater number of major DDIs than moderate or minor interactions. This finding was found to be

contraindicated from another published study report, were 2% were major, 76% were moderate and 22% were minor interactions. [17] In our study about 65.43% of drug interactions were caused by pharmacodynamic mechanism and 34.56% of interactions were at pharmacokinetic level. The Pharmacodynamic drug interactions were more common than Pharmacokinetic drug interactions. This finding was similar to the study reported in the literature. [17] In our study, frequently occurring pair of drug –drug interactions were **Budesonide – Levofloxacin, (7-M), Levothyroxine – Pantoprazole, (6-MO), Aspirin – Ranitidine Hcl (2-MI)**. It is known that in the combination of Budesonide and Levofloxacin, Levofloxacin has bactericidal property which inhibits the anti-inflammatory property of Budesonide. It is also known that Pantoprazole suppresses the gastric acid secretion, which might be expected to inhibit the absorption of Levothyroxine. Moreover, the combination of Aspirin and Ranitidine caused less inhibition of platelet aggregation and prolongation of platelet function analyser. When Aspirin concurrently administered with Ranitidine, it does not delay the healing of duodenal ulcer.

CONCLUSION

Drug- Drug interactions pose a significant risk to hospital admissions or hospital visits. This study was conducted in order to determine, analyse the potential drug-drug interactions in other general medicine ward of a hospital. Among 150 prescriptions analysed for the study, a total of 298 drug-drug interactions were found. Majority of drug-drug interactions were of major severity. When analysed the major mechanism of drug-drug interactions was pharmacodynamic interaction and under pharmacokinetic drug-drug interactions, interactions through absorption were predominant than the other. Even though our study didn't assess clinical outcomes such as changes in drug therapy, or changes in patient outcomes, the data on the potential DDI provide a baseline data to all health care professionals as a reference for intervention and outcome management when the drug with potential drug-drug interactions is being prescribed.

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