

# A Cross-sectional Analysis of Potential Drug-Drug Interactions in Prescriptions at a Tertiary care Medical College of North India

Swagata Datta<sup>1</sup>, Sanjay Kumar Verma<sup>2</sup>, Neetu Gupta<sup>3\*</sup>, Akanksha Suman<sup>4</sup>, Parag Agrawal<sup>5</sup>

<sup>1</sup>Assistant Professor, Department of Pharmacology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, India

<sup>2</sup>Associate Professor, Department of Pharmacology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, India

<sup>4</sup>Professor, Department of Pharmacology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, India

<sup>5</sup>Assistant Professor, Department of Pharmacology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, India

**\*Address for Correspondence:** Dr. Neetu Gupta, Assistant Professor, Department of Pharmacology, Muzaffarnagar Medical College and Hospital, Muzaffarnagar, Uttar Pradesh, India

E-mail: [drneetu89@gmail.com](mailto:drneetu89@gmail.com)

Received: 16 Apr 2025/ Revised: 19 Jun 2025/ Accepted: 13 Aug 2025

## ABSTRACT

**Background:** Drug-drug interactions (DDIs) are a major apprehension in today's health care practice as the chances of adverse drug reactions increase, as well as cause therapeutic failure. Elderly patients with multiple-comorbidities are more prone to DDIs due to the use of multiple medications. The current study aimed to assess the types and severity of DDIs in a tertiary care hospital in North India.

**Methods:** A cross-sectional study was conducted in a tertiary care hospital for 15 days. A total of 342 prescriptions were analyzed for adverse DDIs using the online Medscape drug interaction checker of prescriptions. The DDIs were grouped into pharmacokinetic and pharmacodynamic interactions. The pharmacokinetic interactions were again categorized into absorption, distribution, metabolism and excretion. The DDIs were also classified into severe, moderate and minor based on their severity. The DDIs affecting numerous organ systems were also identified.

**Results:** Of these, 239 (69.88%) prescriptions showed 858 DDIs. Among the DDIs, 531 (62%) were pharmacokinetic interactions, 295 (34.3%) were pharmacodynamic interactions, and 32 (3.7%) were by an unknown mechanism. The severity of the DDIs showed 419 (48.8%) to be moderate, followed by 346 (40.3%) to be minor and 93 (10.9%) to be severe. The gastrointestinal system was the most frequently affected.

**Conclusion:** This study highlights the importance of adequate pharmacological knowledge, thorough medical history taking, and the careful consideration of concurrent medications.

**Key-words:** Adverse drug reactions; Absorption; Distribution; Drug-drug interactions; Excretion; Metabolism

## INTRODUCTION

Health care practice in today's world is mostly comprised of polypharmacy, especially among the elderly population, as they suffer from co-morbid conditions. The concomitant administration of numerous drugs can increase the danger of drug-drug interactions. This can lead to an increased risk of adverse drug reactions as

well as cause therapeutic failure, which escalates healthcare costs <sup>[1,2]</sup>.

Drug-drug interactions occur when two or more drugs interact, leading to an increase or decrease in the effect of one or both drugs. This includes other drug interactions as well as drugs with food and other substances <sup>[1]</sup>. A drug-drug interaction can affect the absorption, distribution, metabolism, and excretion (ADME) properties of another drug or modify its action, leading to either enhanced efficacy, reduced effectiveness, or increased toxicity <sup>[2,3]</sup>. In pharmacokinetic interaction, the plasma concentration of administered drugs can be increased or decreased depending on the type of interaction. Pharmacodynamic interaction involves the receptor effects of different

### How to cite this article

Datta S, Verma SK, Gupta N, Suman A, Agrawal P. A Cross-sectional Analysis of Potential Drug-Drug Interactions in Prescriptions at a Tertiary care Medical College of North India. SSR Inst Int J Life Sci., 2025; 11(5): 8286-8291.



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drugs, which can main to synergism or antagonism of drugs [4].

DDIs are responsible for 6-30% of all adverse drug reactions (ADRs), and 2.8% of ADR-related hospital admissions are due to DDIs [5]. In India, the prevalence of potential drug-drug interactions ranges from 8.3% to 63%. Worldwide, the prevalence of potential drug-drug interactions (pDDIs) ranges from 2.8-63% [6].

The drug-related factors contributing to pDDIs are polypharmacy, sequence of drug administration and drugs with a narrow therapeutic index. The patient-related factors include age, gender, co-morbid conditions, genetics and concurrent disease affecting drug metabolism and clearance [2]. The difficulties resulting from DDIs include nausea, vomiting, anorexia, diarrhoea, bleeding, arrhythmias, hypo-tension, CNS depression, seizures, electrolyte imbalance, hypoglycemia, myopathy, liver and renal failure [7,8].

Strategies to reduce DDIs include thorough patient history taking, standardized patient counseling and intervention, therapeutic drug monitoring, and avoiding poly-pharmacy and the unnecessary intake of over-the-counter drugs [5-7]. DDI studies that focus on the type and severity of pDDIs are very few. The present study intended to assess the severity and types of potential drug-drug interactions in a tertiary care setting in the Northern part of India.

## MATERIALS AND METHODS

**Research Design-** This observational cross-sectional study was conducted at the Department of Pharmacology, Muzaffarnagar Medical College, Uttar Pradesh, over 15 days, following ethical clearance from the institutional ethics committee. The OPD and IPD prescriptions from various clinical departments of Muzaffarnagar Medical College were collected. A total of 342 prescriptions were analyzed, and the study was conducted after obtaining informed consent from the patients. Prescriptions containing two or more medicines to participate were included in our study, and prescriptions from patients who were willing to participate. Prescriptions contained no or only one medication, and prescriptions of patients not willing to participate were excluded. A group of undergraduate medical students having their elective posting in the Department of Pharmacology was assigned to collect the prescriptions from various clinical departments. The DDIs

were gathered into pharmacokinetic and pharmacodynamic interactions. The pharmacokinetic interactions were again categorized into absorption, distribution, metabolism or excretion. Severe DDIs were those that caused life risk and required alternative medications, moderate DDIs were those that were harmful, treatment and close monitoring were needed, and minor DDIs were those that required no treatment or any change in medication. The drug interactions affecting various organ systems were also identified.

## Inclusion Criteria

- Prescriptions from OPD and IPD patients of Muzaffarnagar Medical College containing two or more medications.
- Patients willing to participate and who provided informed consent.

## Exclusion Criteria

- Prescriptions containing no medication or only a single drug.
- Patients not willing to participate in the study.

**Statistical Analysis-** Data were compiled and analysed using descriptive statistics. The frequency and percentage of DDIs were calculated. DDIs were classified as pharmacokinetic (absorption, distribution, metabolism, excretion) or pharmacodynamic, and further graded as severe, moderate, or minor based on clinical significance. Organ systems affected by DDIs were also identified. Results were presented in tables and charts to illustrate the distribution, severity, and patterns of interactions.

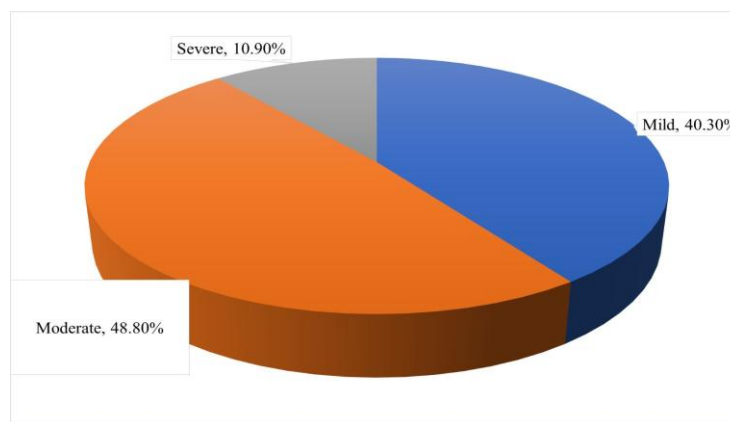
## RESULTS

Table 1 presents the distribution of drug-drug interactions based on their mechanisms. Among the 858 interactions, the majority were pharmacokinetic interactions, accounting for 531 cases (62%). Within pharmacokinetic interactions, the breakdown shows that 274 (51.6%) were related to excretion, 217 (40.9%) to metabolism, 34 (6.4%) to absorption, and 6 (1.13%) to distribution. Pharmacodynamic interactions contributed to 295 cases (34.3%), while 32 interactions (3.7%) had an unknown mechanism. This data highlights that pharmacokinetic interactions, particularly those involving excretion and metabolism, are the most common mechanisms in drug-drug interactions.

**Table 1:** Mechanisms based on Drug-Drug interactions

| Mode of action               | No. of interactions (n=858) | Percentage |
|------------------------------|-----------------------------|------------|
| Pharmacokinetic interactions | 531                         | 62         |
| Absorption                   | 34                          | 6.4        |
| Distribution                 | 6                           | 1.13       |
| Metabolism                   | 217                         | 40.9       |
| Excretion                    | 274                         | 51.6       |
| Pharmacodynamic interactions | 295                         | 34.3       |
| Unknown mechanism            | 32                          | 3.7        |

The severity of the DDIs showed 419 (48.8%) to be moderate, followed by 346 (40.3%) to be minor, and 93 (10.9%) to be severe (Fig. 1).

**Fig. 1:** Severity based on Drug-Drug interactions

The gastrointestinal system was the most frequently affected (n=247), followed by the renal system (n=220),

the Cardiovascular system (n=119) and the Central nervous system (n=105) (Fig. 2).

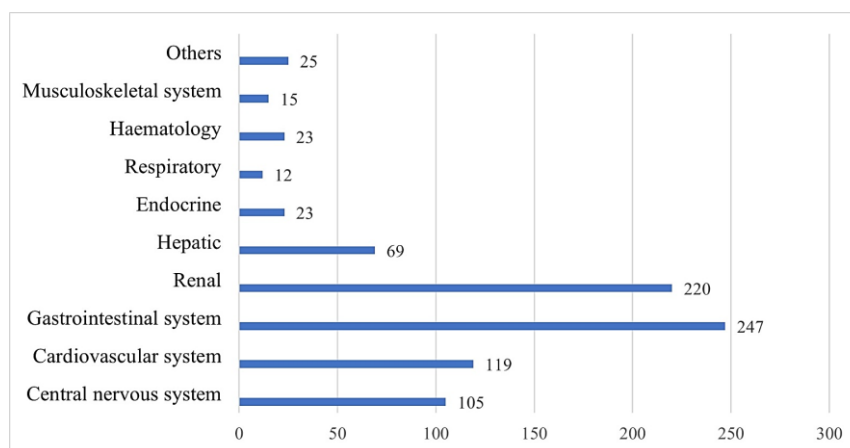
**Fig. 2:** Drug-Drug interactions based on organ system involvement

Table 2 shows the distribution of drug interactions among patients based on the number of drugs prescribed. Of the 239 patients, 89 were prescribed between 2-5 drugs, resulting in 198 drug interactions (23.08%), with an average of 2.22 interactions per patient. A larger group, 133 patients, had 6-10 drugs prescribed, leading to 568 drug interactions (66.20%)

and an average of 4.27 interactions. Finally, 17 patients with prescriptions of more than 10 drugs experienced 92 drug interactions (10.72%), with an average of 5.41 interactions. These findings suggest that the number of drug-drug interactions increases as the number of prescribed drugs rises.

**Table 2:** Number of drug interactions per patient

| Number of drugs | Number of patients<br>(n=239) | Number of drug<br>interactions (n=858) | Avg. DDIs per<br>prescription |
|-----------------|-------------------------------|--|-------------------------------|
| 2-5             | 89                            | 198 (23.08%)                           | 2.22                          |
| 6-10            | 133                           | 568 (66.20%)                           | 4.27                          |
| >10             | 17                            | 92 (10.72%)                            | 5.41                          |

## DISCUSSION

Drug-drug interactions (DDIs) significantly influence the pharmacokinetics and pharmacodynamics of concurrently administered medications [4]. These interactions can either enhance therapeutic efficacy when a synergistic effect occurs or lead to therapeutic failure if an antagonistic effect is present. DDIs are also known to exacerbate the frequency and severity of adverse drug events, especially when factors such as the patient's medical history, concurrent medications, and prescriptions for new conditions are not thoroughly evaluated [5]. In light of this, a study was designed to investigate the prevalence of drug-drug interactions in routine outpatient prescriptions at a medical college in North India [6,7].

In the present study, we collected a total of 342 prescriptions from IPDs and OPDs of the medical college as part of a 15-day elective program for students, and these were analyzed. They were observed for types of interaction as either pharmacodynamics or pharmacokinetics (ADME). Moreover, these DDIs were further analyzed as severe, moderate and minor interactions. These were also further analyzed to see the potential biological system (gastrointestinal, central nervous system, cardiovascular, renal, etc.) which were affected [7-10].

The total no. of DDIs observed in these 342 prescriptions was 858, which was better than in a study by Kulkarni *et al.*, where the incidence was 856 in 204 prescriptions [2]. When these DDIs were analyzed for mechanisms, it was observed that Pharmacodynamic interactions were 34.3%, Pharmacokinetic Interactions Were 62% (absorption-6.4%, distribution-1.13%, metabolism-40.9%, and excretion-51.6%), and the remaining 3.7% interactions were by unknown mechanisms [2,4]. Our results showed an increased number of pharmacokinetic interactions than pharmacodynamic interactions, which was similar to the study by Kulkarni *et al.*, where pharma

cokinetic interactions were 42% and pharmacodynamic interactions were 24% [2]. Our study findings were different to the study done by Patel *et al.* [4]. DDIs related to excretion were highest because many drugs hamper the excretion of other drugs due to the utilization of a common pathway for excretion, in most cases, being renal. Metabolism comes a close second in pharmacokinetic parameters because most of the drugs are either activated or deactivated by metabolizing enzymes in the liver or other parts of the body. Induction or inhibition of these metabolizing enzymes can both result in therapeutic failure as well as toxicity. Similarly, the polymorphism of these metabolizing enzymes, as well as their expression and suppression, can also be affected by co-administered drugs [9].

As these prescriptions were analyzed for severity, it was observed that out of the 858 interactions, severe interactions were 10.9%, moderate 48.8% and minor 40.3%. Our study results were consistent with the study completed by Bhagavathula *et al.*, where moderate interactions were more [10]. A study done by Dambro and Kallgren showed that severe, moderate, and minor interactions were 2%, 70%, and 28%, respectively [11]. Murtaza *et al.* studied that severe interactions were more common than minor and moderate interactions [12].

In our study, most of the DDIs were seen to affect the gastrointestinal system, followed by the renal, cardiovascular, and central nervous systems, and the least common were related to the respiratory system. The effect of several drugs causing favourable effects on the gastrointestinal system may alter the bioavailability of other drugs, leading to conditions of DDIs for the emergence. Change in gastric pH of other co-administered drugs may also influence the kinetics [13].

In our study, we categorized DDIs into prescriptions with 2-5 drugs, 6-10 drugs and greater than 10 drugs and corresponding DDIs observed were 23.08%, 66.20% and

10.72%, respectively. The average number of DDIs with the number of drugs per prescription was higher in those prescriptions where more than 10 drugs were prescribed, indicating polypharmacy. Among the geriatric population with multiple co-morbid conditions, polypharmacy is a commonly observed phenomenon. Polypharmacy increases the risk of DDIs, and its consequences may vary from a minor health hazard to fatality. Physicians should be cautious while prescribing medicines to avoid inappropriate polypharmacy and severe potential DDIs <sup>[14]</sup>.

Over-prescription or inappropriate prescription, to treat side-effects, misuse of medication, supplementary medicines prearranged, and poor doctor-patient relationships may increase the risk of DDIs. A complete plan by combining knowledge and skill to prescribe proper medicine with adjusted dose, if required, can reduce the occurrence of DDIs. In addition, an educational program on the rational use of drugs can encourage physicians to improve the quality of prescriptions <sup>[15]</sup>. Every study has its own set of limitations, ours being no different. The major limitation was that it was short-term, and the sample size was small.

## CONCLUSIONS

The study has concluded that the pharmacokinetic interactions, particularly those involving excretion and metabolism, are the predominant mechanisms behind drug-drug interactions (DDIs), accounting for 62% of all interactions. Additionally, the study highlights that the severity of DDIs is mostly moderate (48.8%), followed by minor (40.3%) and severe (10.9%) interactions. The gastrointestinal and renal systems were most commonly affected by these interactions. Furthermore, the number of DDIs increases with the number of drugs prescribed, with patients receiving more than 10 drugs experiencing the highest average number of interactions. This underscores the importance of careful monitoring and management of drug prescriptions, particularly for patients with polypharmacy. This study can pave the way for further studies of these kinds so that we can avoid avoidable DDIs or at least be vigilant for DDIs.

## CONTRIBUTION OF AUTHORS

**Research concept-** Dr. Swagata Datta, Dr. Parag Agrawal

**Research design-** Dr. Swagata Datta, Dr. Sanjay Kumar Verma, Dr. Neetu Gupta

**Supervision-** Dr. Akanksha Suman, Dr. Parag Agrawal

**Materials-** Dr. Neetu Gupta, Dr. Akanksha Suman

**Data collection-** Dr. Parag Agrawal

**Data analysis and interpretation-** Dr. Swagata Datta

**Literature search-** Dr. Neetu Gupta, Dr. Akanksha Suman

**Critical review-** Dr. Parag Agrawal, Dr. Swagata Datta

**Writing article-** Dr. Sanjay Kumar Verma, Dr. Neetu Gupta

**Article editing-** Dr. Swagata Datta, Dr. Sanjay Kumar Verma, Dr. Neetu Gupta

**Final approval-** Dr. Neetu Gupta, Dr. Sanjay Kumar Verma, Dr. Parag Agrawal

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