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RESEARCH ARTICLE
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THE POTENTIAL DRUG-DRUG INTERACTIONS BETWEEN ANTIBIOTICS AND OTHER PRESCRIBED MEDICATIONS IN A TERTIARY CARE CENTRE

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Background: Antibiotics are among the most commonly prescribed drugs in clinical practice and are frequently co-prescribed with other medications various indications. This polypharmacy increases the risk of drug-drug interactions, which can lead to adverse drug events, treatment failure and increased healthcare costs. India being one of the top consumers of antibiotics, evaluating potential DDIs is crucial for optimizing patient safety.
Aims and Objectives: To assess the prevalence, severity, and clinical relevance of potential drug–drug interactions involving antimicrobial agents among adult patients in a tertiary care centre.
Methodology: A cross-sectional descriptive study was conducted at HIMS Teaching Hospital, Hassan. A total of 400 treatment charts and prescriptions of adult patients prescribed with antibiotics were reviewed. DDIs were identified using the Lexicomp and Medscape drug interaction databases and categorized by severity and analyzed with appropriate statistical tests.
Results: A total of 2,284 drugs were prescribed across 400 prescriptions, with an average of 5.71±1.62 drugs per patient and antibiotics accounted for 31.69% of prescriptions (31.69%). Lexicomp identified 68 potential DDIs, most of which were minor (Category C: 70.5%), followed by monitoring-required (D: 23.5%) and contraindicated (X: 16.1%) combinations. Medscape reported 142 potential DDIs: minor (69.95%), monitor closely (22.3%) and contraindicated (7.75%). No significant correlation was observed between the number of drugs per prescription and the number of DDIs. Ciprofloxacin, Doxycycline and Aminoglycosides were most frequently involved in interactions.
Conclusion: The study highlights the frequent occurrence of potential DDIs involving antibiotics, particularly fluoroquinolones and aminoglycosides. Lexicomp and Medscape databases showed

significant variability in DDI detection, emphasizing the need for clinicians to use reliable drug interaction tools during prescribing. Continued pharmacovigilance and antibiotic stewardship are essential to reduce DDI-related risks in hospitalized patients.

Keywords: Antibiotics, Drug-drug Interactions, Polypharmacy, Antibiotic resistance

Introduction

Antimicrobials, particularly antibiotics, have been a mainstay drugs of modern medicine for the last eight decades. India is considered to be one of the top users of antibiotics. High burden of infectious diseases could be one of the reasons for high antibiotic use in India.[1] Reports say that per capita antibiotic consumption in the retail sector in India has increased by around 22%, from 13.1 in 2012 to 16.0 DID (daily defined dose of antibiotics for 1000 people per day) 2016.[2]

Gastrointestinal infection, Lower and upper respiratory tract infections, Urinary tract infection, Skin and soft tissue infection, prophylactic need were the most common conditions necessitating the antibiotic use.[3,4] Anti-inflammatory drugs, proton pump inhibitors, bronchodilators, antitussive agents, corticosteroids, antihistaminics, antihypertensives and antidiabetics are prescribed along with antibiotics for treatment of a disease. Although prescribed drugs significantly improve the range of health outcomes, there is occurrence of drug-drug interactions (DDI).[5]

DDI is defined as a clinically meaningful alteration in the effect of one drug due to coadministration of another. It may result from pharmacokinetic interactions, pharmacodynamic interactions, pharmaceutical incompatibility, a combination of these mechanisms, or other unknown mechanisms. DDIs are a leading cause of preventable adverse drug events (ADEs), accounting for 17% of all preventable ADEs in hospitalized patients. Approximately 1% of hospitalized patients experience an ADE due to DDI.[6] DDIs can lead to treatment failure, increased morbidity and mortality,] and higher healthcare costs.[7,8] Polypharmacy, having multiple prescribers, and advanced age are defined risk factors for the occurrence of DDIs, highlighting the need for careful medication management to prevent these interactions.[9,10]

Around 6.5% of hospital admissions are thought to be related to adverse drug reactions(ADRs), with DDIs accounting for 16.6% of the ADRs. Potential DDIs with antimicrobials were 26.4% of all interaction.[11] Antibiotics being commonly prescribed drugs consisting of many subgroups have various DDIs accounting to various reactions. Studies have reported on DDIs with antibiotics and medicines such as calcium channel blockers, digoxin, diuretics and sulphonylureas.[12] Thus DDIs become an important factor in prescribing decisions, especially in patients on other medications for chronic illness.

Thus our study aims to assess the prevalence and clinical relevance of potential drug–drug interactions (pDDIs) involving antimicrobial agents among hospitalized adult patients.

Objectives:

1. To identify and classify pDDIs with antimicrobials using Medscape and Lexicomp® databases.
2. To evaluate the severity of identified pDDIs based on standard categorization criteria.
3. To examine association of pDDIs with the polypharmacy

Methodology:

Its a cross-sectional descriptive observational study conducted at Hassan Institute of Medical Sciences (HIMS), a tertiary care teaching hospital in Hassan, Karnataka. We assessed the prevalence and clinical significance of potential drug–drug interactions (pDDIs) involving antimicrobial agents among hospitalized and patients attending out patient department. Ethical clearance for the study was obtained from the Institutional Ethics Committee (IEC) of HIMS, and the research was conducted in accordance with the principles of the Declaration of Helsinki (2013) and the Good Clinical Practice (GCP) guidelines. The study methodology and reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist to ensure transparency, reproducibility and methodological rigor.

The sample size was determined based on a previously reported prevalence of pDDIs with antibiotics is 26.4%, as documented by Kuscu et al[11], using the formula $n=4p(1-p)/d^2$, where p is the prevalence and d is the margin of error (5%). A total of 400 prescriptions were included to enhance statistical reliability and accommodate potential exclusions. The patients aged 18 years and above, who were prescribed at least one antimicrobial agent along with other concurrent medications were included in the study. Exclusion criteria comprised pregnant and lactating women, prescriptions containing antitubercular, antipsychotic or antiretroviral drugs and incomplete or illegible prescriptions.

Data were collected from inpatient prescription charts, case records, and pharmacy records in the month of November 2024. The patient demographics, diagnoses and details of all prescribed medications were documented. The prescribed drugs were evaluated for potential DDIs using the Medscape Drug Interaction Checker and Lexicomp® (Wolters Kluwer) databases.

Interactions were categorized based on severity: Medscape classified them as contraindicated, monitor closely or minor. While, Lexicomp categorized them into C (monitor therapy), D (consider therapy modification), and X (avoid combination). Discrepancies between the two databases if noted and addressed through clinical judgment guided by standard pharmacotherapeutic protocols. Drug names were coded using the WHO Anatomical Therapeutic Chemical (ATC) classification system and special attention was given to interactions involving high-alert medications, as defined by the Institute for Safe Medication Practices (ISMP).

Data were entered into Microsoft Excel and analyzed using descriptive statistics. Continuous data were expressed as mean ± standard deviation and categorical data was represented in proportions. Associations between categorical variables were evaluated using the Chi-square or Fisher's exact test, with a p-value <0.05 considered statistically significant. Serious interactions identified during the study were immediately communicated to the treating physicians as per institutional guidelines.

Results:

A total of 400 treatment charts prescribed with antibiotics were reviewed. A total of around 2284 drugs, averaging to 5.71±1.62 drugs were prescribed per patient. Among them 724 antibiotics were prescribed accounting for 31.69% of prescribed medications with the average of 1.81antibiotics per prescription. Fig1 depicts the prescription pattern of antibiotics with Ceftriaxone (195 cases), Amoxicillin (147), Ciprofloxacin (92), Doxycycline (79), Metronidazole (59) being the most commonly prescribed antibiotics.

Fig 2 shows the common causes that required antibiotic prescription which includes Upper Respiratory Tract Infection, Lower respiratory tract infection, Urinary Tract Infection, Acute Febrile Illness, Surgical Prophylaxis, Acute Gastroenteritis, Skin and Soft Tissue Infection and others

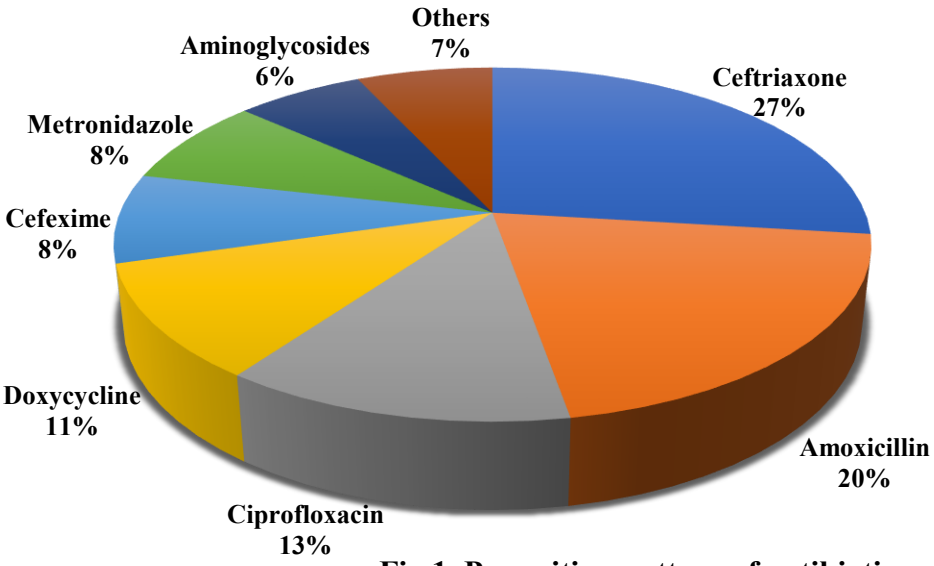

Fig 1. Prescrition pattern of antibiotics

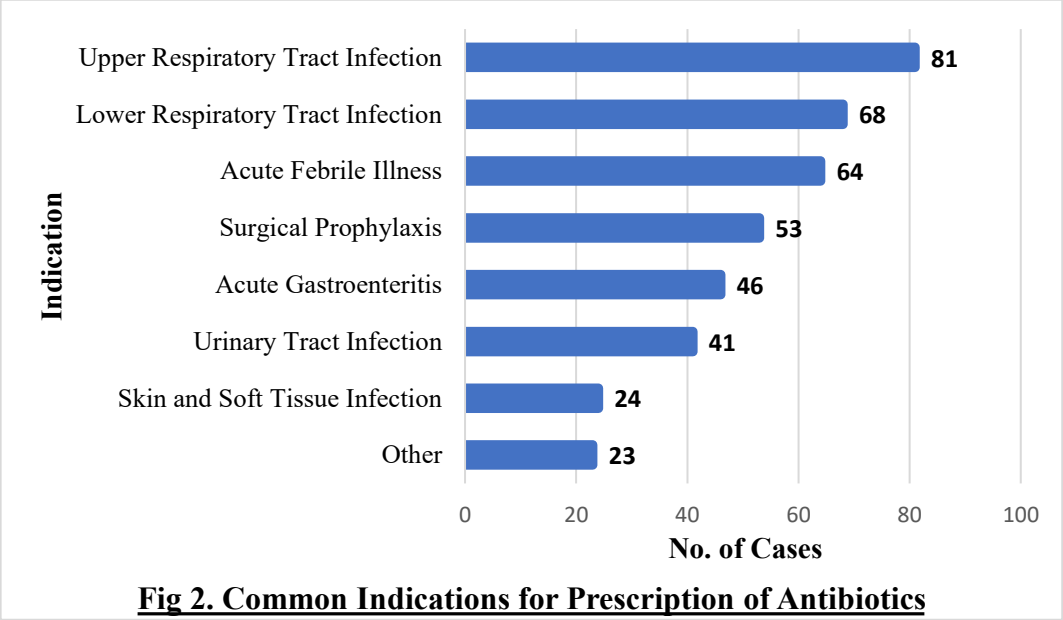

Fig 2. Common Indications for Prescription of Antibiotics

As shown in Table 1, According to the Lexicomp database 68 potential DDIs with antibiotics were noted accounting for 0.17 DDIs per prescription. Among them 48 were of category C(minor), 16 were in category D (monitoring required), 11 belonged to category X (combination to be avoided). On the basis of evaluation by Medscape database 142 potential DDIs were noted averaging to 0.36 DDIs per prescription. Out of them 11 belonged to combination contraindicated. 33 and 98 were Monitor Closely and Minor interactions category respectively.

Table 1. Severity of DDIs according to Lexicomp & Lexicomp

	Lexicomp		Medscape		P value
Combination Contraindicated	11	16.18%	11	7.75%	0.92
Monitor Closely	16	23.52%	33	22.30%	0.012
Minor Interactions	41	60.30%	98	69.95%	<0.001

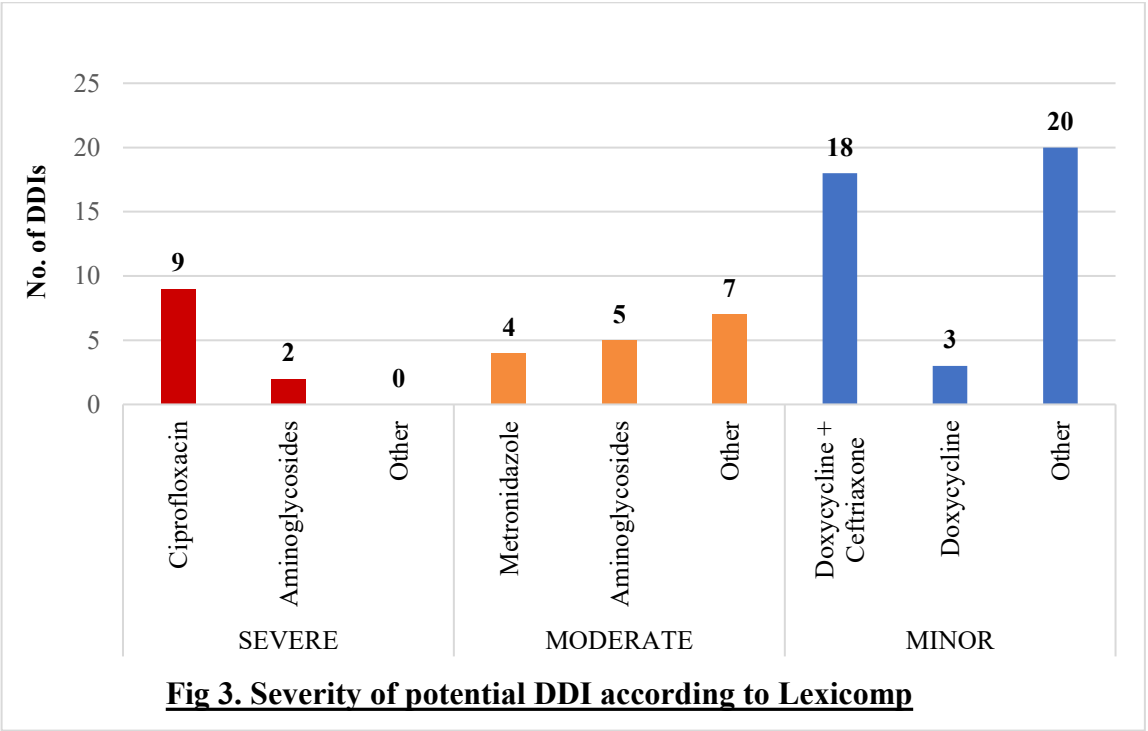

Fig 3. Severity of potential DDI according to Lexicomp

There was no statistically significant difference among the number of severe potential DDIs where the combination is contraindicated in both the database. A statistically significant difference between the two databases were noted in number of potential DDIs requiring close monitoring and minor interactions ($p<0.05$). No significant correlation was observed between the number of drugs prescribed and number of DDIs in both databases($p>0.05$). The antibiotics with more number of Potential DDIs were Ciprofloxacin, Aminoglycosides, Doxycycline, Ceftriaxone and Metronidazole (Fig 3,4).

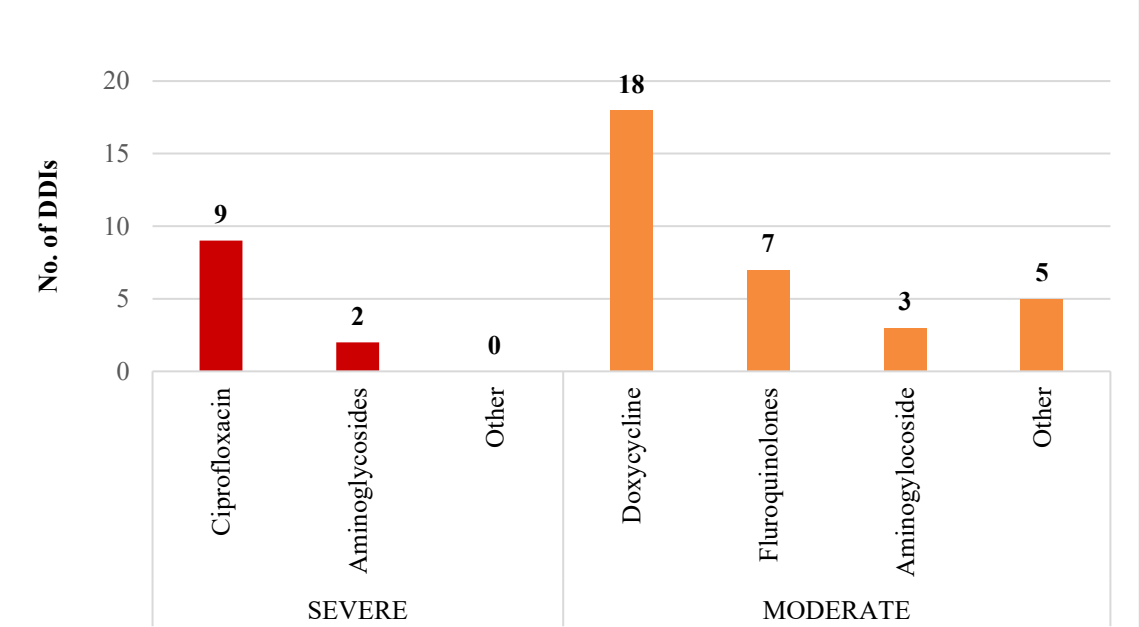

Fig 4. Severity of potential DDI according to Medscape

Discussion:

The present study provides insight into the prevalence and severity of potential drug-drug interactions (PDDIs) involving antibiotics in a tertiary care teaching hospital setting. Out of 400 prescriptions reviewed, an average of 5.71 drugs per patient were prescribed, with antibiotics comprising 31.69% of the total medications. These findings highlight the widespread and frequent use of antibiotics in clinical practice, corroborating earlier reports of high antibiotic consumption.

In the present study, respiratory tract infections , acute febrile illness, gastroenteritis and surgical prophylaxis were among the most common indications, which were similar to study by **Bhattacharjee et al**[16] and **Bade et al**[17]. Another notable comparison was with study by **Bhattacharjee et al** empirical therapy in 48.96% of prescriptions, indicating a high rate of antibiotics being used without culture-confirmed infection. While empirical use wasn't explicitly quantified in our study, the limited diversity in antibiotic choice strongly suggests a similar empiric trend. A study by **Radkowski et al**[18]. observed a high incidence of pDDIs with anatibiotics, especially Fluoroquinolones, Tetracyclines and Macrolides, which aligns with our results identifying Ciprofloxacin and Doxycycline among the top antibiotics involved in DDIs.

In our study, we utilized both Lexicomp and Medscape databases to evaluate pDDIs, considering previous evaluations of DDI databases by **Shakeel et al,**[19] shown that Lexicomp had performance score of 0.54, while Medscape had 0.52 demonstrating accuracy and reliability in detecting clinically relevant interactions. We identified total of 68 and 142 DDIs in Lexicomp and Medscape respectively, with a significant difference in classification of severity. The findings **Kshethi et al**.[20] also support our observations , although Medscape yielded a higher number of total interactions (possibly due to broader inclusion criteria), Lexicomp offered more focused and likely more clinically relevant alerts. This underscores the importance of combining multiple interaction checkers in clinical decision-

making to enhance both sensitivity and specificity in detecting DDIs, especially when prescribing complex regimens.

Earlier studies by **Dookeram et al**[21] and **Corsonello et al**[22] indicated that polypharmacy is a major risk factor for DDIs. This was not in accordance with our results. The discrepancy could be due to the relatively uniform prescribing practices in the study setting or possibly due to the exclusion of prescriptions involving complex regimens such as antiretroviral, anti-tubercular and antipsychotic drugs.

Conclusion:

The study demonstrated a notable prevalence of pDDIs involving antimicrobial agents among hospitalized adult patients. While both Medscape and Lexicomp® identified a comparable number of severe and moderate interactions, Medscape reported a higher proportion of minor interactions. This discrepancy highlights the variability between drug interaction databases and underscores the importance of utilizing multiple reliable tools to ensure a comprehensive assessment of potential interactions.

Clinically, this finding is significant as it influences the prioritization of alerts and decision-making in real-time settings. Overreporting of minor interactions may lead to alert fatigue, potentially causing clinicians to overlook critical warnings. At the same time, underreporting may result in missed opportunities for intervention. These insights emphasize the need for careful interpretation of DDI classifications, guided by clinical judgment and context.

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