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Original Article

Potential Food Interactions of Antibiotics and Risk of Antimicrobial Resistance: A Database Research Study

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ABSTRACT

Objectives: The present study describes about the Antibiotic-Food Interactions (AFI) and development of Antimicrobial resistance (AMR). **Materials and Methods:** The Micromedex medication database was used to find and identify potential antibiotic interactions. Micromedex is a trustworthy drug database that used to research medications, interactions, diseases, and dose estimations. **Results:** As a result, a total of 68 AFIs were obtained, including major, moderate, and Minor AFIs among them. AMR-causing interactions were found in 34 of the 68 AFIs (50%). Only 3 (4.41%) of these 34 (50%) interactions were minor, whereas the remaining 31 (45.58%) were moderate. Only moderate and minor interactions were expected to induce AMR evolution; no major interactions were found to be unrelated to AMR development. **Conclusion:** Antimicrobial resistance is an important public health concern throughout the world. A pharmacist is a healthcare expert who analyzes a prescription for possible medication interactions and eliminates them in order to improve the patient's prognosis.

Keywords: Antimicrobial resistance, Drug-food interactions, Antibiotics, Clinical pharmacist.

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INTRODUCTION

Drugs taken at the same time can interact and affect the pharmacokinetics and pharmacodynamics of the medicine. Drug-Food Interactions (DFIs) have the same clinical significance as Drug-Drug Interactions (DDIs). When a drug is taken with food, the absorption, distribution, metabolism, excretion, and pharmacological impact of the medication are all affected. DFIs can result in therapeutic failure, major life-threatening side effects, or ADRs, and a patient's hospital stay being extended. The DFI may influence the drug's effectiveness and concentration available to be reduced or increased in some cases. It can result in treatment failure and drug toxicity.[1-3]

The antibiotics are the focus of this database study. Antibiotics, also known as antimicrobial medications, are secondary metabolites produced by bacteria, and synthetic or semi-synthesized compounds can suppress bacterial growth and survival, allowing the immune system the upper hand. As a reason, these medications can be used to treat infectious diseases.[4,5] As a consequence, when antibiotics are used concurrently, there is a risk of developing Antimicrobial Resistance (AMR). It's possible that the reason for prescription numerous antibiotics. Actually, these medications are to improve therapeutic efficacy and patient outcomes. Antibiotic interactions, on the other side, can be both synergistic and antagonistic, leading to the development of AMR.[6,7] In the same way, AMR might arise as a result of Antibiotic-Food Interactions (AFIs). The AFIs can cause changes in the antibiotic's pharmacokinetics and pharmacodynamics, which can lead to the development of AMR. The objective of this study is to predict the AMR through the AFIs by using the Micromedex database, the results are analyzed and documented for the future use to council the patients about the possibilities of AMR with food.

MATERIALS AND METHODS

IBM Micromedex 20.0 database was used to identify the AFIs. Micromedex is an evidence-based drug information database that contains information on drugs, drug interactions, patient care comments, IV compatibility, dose calculations, drug comparisons, and disease information.

Antibiotics Search Strategy

A Micromedex database keyword search revealed the entire number of antibiotics available in databases. When you type in the name of an antibiotic in a keyword search, we will get about 200 results. Some antibiotics in the above list were not found in the Micromedex database which includes sulfadoxine, sulfamethopyrazine, sulfasalazine, mafenide, co-trimoxazole, pefloxacin, prulifloxacin, ceftazolin, ceftamet pivoxil, cefpirome, ceftobiprole, faropenem, sisomicin, framycetin, tedizolid, fusidic acid, colistin, methenamine, phenazopyridine, and isoniazid.

Procedure for Drug Interactions

The technique for getting medication interactions for the available antibiotics in the database, as well as the findings of interactions, is depicted in Figure 1. Select the drug interaction option after logging into the database, and then enter the 200 antibiotic drugs one by one using the database's choices. By giving the name of the antibiotic and transferring it into the drug to check, you can find the necessary antibiotic in the matching antibiotic medications. Once entered all of the antibiotics, click the submit button. It lists all of the antibiotic interactions and allows the user to switch to alternative interactions options as needed (drug, food, ethanol, lab, pregnancy, and lactation).

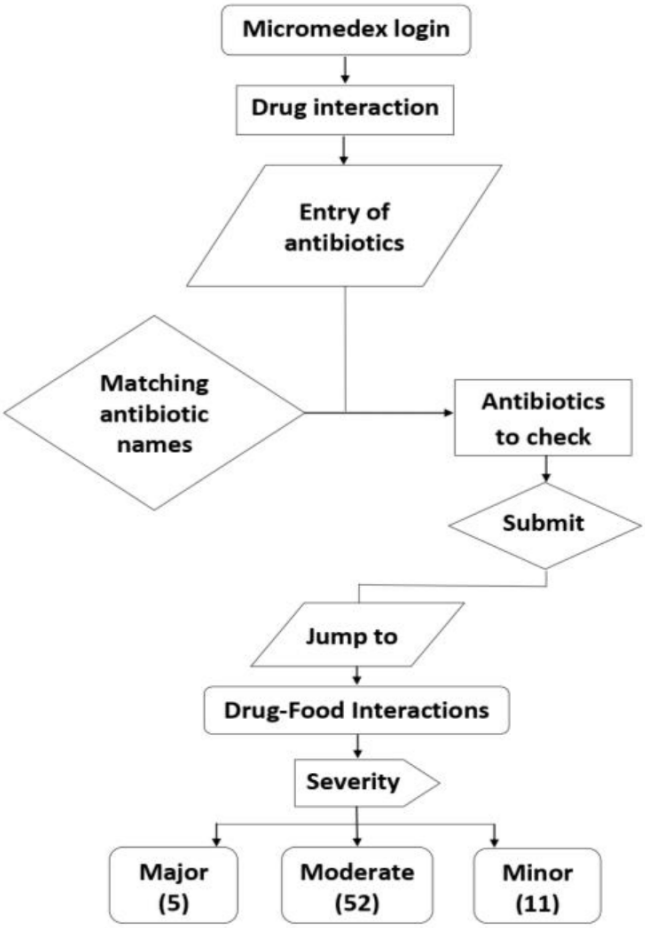

Figure 1: The procedure for determining DFIs and their outcomes.

Drug Interaction Analysis

After receiving all the antibiotic medication interactions, the information was double-checked to see if there were any antibiotics that had been missed. During the drug's entry into the system, no antibiotics were missed, according to the analysis.

RESULTS

A total of 68 AFIs were obtained as a result, in those AFIs some was major, moderate and minor. Among the 68 AFIs 34 (50%) were identified as AMR causing interactions. In these 34 (50%) interactions, only 3 (4.41%) were minor interactions and the remaining 31 (45.58%) were as moderate interactions. There were no major interactions, which were not relating to AMR development; only moderate and minor interactions were predicted as to cause the AMR evolution. The all predicted AFIs were displayed in the Table 1. As a result of the concomitant use of antibiotics with food or dairy products, the concentration of antibiotics was decreased/ altered, and the antibiotic's efficiency was reduced. Penicillins, macrolides, cephalosporins, fluoroquinolones, and tetracyclins were the most involved antibiotics in AFIs. The prediction of AMR was done based on the spectrum of activity antibiotics. The AMR prediction information was given the Table 2.

DISCUSSION

Antibiotics proved effective in treating bacterial infections. Unfortunately, antibiotics have been misused for the past 50 years, and experts have recommended combination therapy to improve patient outcomes.[8] Oral administration of medications is the most commonly prescribed dosage form by clinicians, and these dosage forms may be contributing to the emergence of AMR. When an antibiotic is taken with food, it causes an interaction that affects the patient's Absorption, Distribution, Metabolism and Excretion (ADME) and therapeutic action.[1-3]

Finally, the efficiency of antibiotics will be reduced, and their concentration will be reduced. This was the rationale for predicting the AMR. That information was given in Table 1. Penicillins, macrolides, fluoroquinolones, cephalosporins, and tetracyclines were the most commonly involved classes in AFIs. The antibiotic efficacy and peak concentration of antibiotics were both reduced in all AFIs. In similar, and the repeated use of these drugs with foods surely can cause AMR development. AFIs can contribute to the emergence of AMR in patients and treatment failure as a result of these processes predicting that. The spectrum of activity of antibiotics was used to predict resistant microbes. The spectrum, which were illustrates how antibiotics affect microorganisms. The antibiotic either may be Narrow-spectrum, broad-spectrum, or extended-spectrum if involved in AFIs chances to get AMR. Even while antibiotics are effective at killing or inhibiting the growth of bacteria, misuse or improper use can lead to AMR.[9-11]

In Indian marketing, enoxacin was banned drug. Thus enoxacin was not available in the market. Although the risk of AMR was estimated, antibiotic and food interaction was available in the database. Loracarbef was a carbacephem antibiotic sometimes grouped together with the second-generation cephalosporin antibiotics and that was banned in the year 2006. As a reason, there was no information provided about loracarbef.[12,13]

To combat AMR, the consumer or patient required education and awareness. Health professionals will play a vital role in solving this important global health issue. The pharmacist must educate and counsel patients on the use of antibiotics, and the patient will be free of such outcomes and other consequences as a result. Because the pharmacist is a healthcare practitioner, they must aware of possible and actual DDIs as well as drug-food interactions. Before discharging a patient, pharmacists analyze the prescription and examine the drug chart for any drug-related issues, DDIs, and AFIs. Not only the assessment of the prescription, but it's also important to educate and counsel the patient about medications, diseases, and lifestyle changes. The clinical pharmacy is a professional service that is widely available in all nations and will be beneficial in this regard. To ensure the rational use of drugs, clinical pharmacists will attend to ward rounds and review every prescription for drug, dose, duration, frequency, and dosage forms. Thus, the clinical pharmacist will act as a link between the patient and the physician, leading to improved pharmaceutical care for the patient.[3,14,15]

One of the advantages of this database research is the ability to predict AMR using antibiotics and interactions. The databases offered documentation for interactions, but the risk must be further assessed using AMR databases, which validates AMR by microorganisms against antibiotics; this is the study limitation. This study suggests that if the AMR database is employed in this study, it will be able to confirm antimicrobial resistance predictions.

CONCLUSION

Antimicrobial resistance is a major public health concern around the world. The pharmacist is a healthcare expert who examines a prescription for possible medication interactions and eliminates them in order to improve the patient's prognosis.

Table 1: Interactions between antibiotics and food indicating a risk of antimicrobial resistance.

S. No	Drug involved in drug-food interaction		Severity	Summary	Documentation
	Drug	Food			
1	Ampicillin	Food	Moderate	Concurrent use of ampicillin and food may results in decreased ampicillin concentration	Good
2	Ampicillin sodium			Decreased concentration	Good
3	Ampicillin sodium + Sulbactam sodium			Decreased concentration	Good
4	Benzoyl peroxide + erythromycin			Altered concentrations.	Good
5	Cefaclor			Decreased concentration	Good
6	Enoxacin			Decreased effectiveness	Fair
7	Erythromycin			Altered concentrations	Good
8	Erythromycin estolate			Altered concentrations	Good
9	Erythromycin ethylsuccinate			Altered concentrations	Good
10	Erythromycin ethylsuccinate + sulfisoxazole acetyl			Altered erythromycin concentrations	Good
11	Erythromycin gluceptate			Altered concentrations	Good
12	Erythromycin lactobionate			Altered concentrations	Good
13	Erythromycin stearate			Altered concentrations	Good
14	Lincomycin hydrochloride			Decreased exposure	Good
15	Demeclocycline hydrochloride			Decreased levels	Good
16	Norfloxacin		Minor	Reduced effectiveness	Fair
17	Nafcillin sodium			Decreased concentrations	Fair
18	Penicillin G benzathine			Decreased peak concentrations	Good
19	Penicillin G procaine			Decreased peak concentrations	Good
20	Penicillin G potassium			Decreased peak concentrations	Good
21	Penicillin G potassium/sodium chloride			Decreased peak concentrations	Good
22	Penicillin G sodium			Decreased peak concentrations	Good
23	Oxacillin sodium			Decreased concentration	Fair
24	Loracarbef			Prolonged time to peak concentration	Good
25	Ciprofloxacin			Decreased concentrations	Good
26	Ciprofloxacin hydrochloride		Moderate	Decreased concentrations	Good
27	Ciprofloxacin lactate			Decreased concentrations	Good
28	Democlocycline hydrochloride			Decreased absorption and efficacy	Fair
29	Gemifloxacin mesylate	Dairy Foods		Decreased concentrations	Fair
30	Minocycline hydrochloride			Decreased concentrations	Good
31	Norfloxacin			Reduced mean peak plasma concentration.	Good
32	Oxytetracycline hydrochloride			Decreased effectiveness	Good
33	Oxytetracycline hydrochloride+polymyxin B sulfate			Decreased effectiveness	Good
34	Tetracycline hydrochloride			Decreased concentrations.	Good

Table 2: Antibiotics and the risk of antimicrobial resistance.

Family/Antibiotic	Risk of resistant microorganism	
	Gram Positive	Gram Negative
Ampicillin	*Listeria monocytogenes*	*Escherichia coli* Proteus species *Salmonella typhi* Shigella *Haemophilus influenzae* *Helicobacter pylori* *Pseudomonas aeruginosa* Klebsiella
Cefaclor	*Streptococcus pneumonia* *Streptococcus pyogenes*	*Haemophilus influenzae* *Escherichia coli* *M catarrhalis* Proteus species Klebsiella
Loracarbef	Marketing end on 2006	
Enoxacin	*Staphylococcus epidermis*	*Neisseria gonorrhoeae* *Escherichia coli* Klebsiella Proteus species *Pseudomonas aeruginosa*
Erythromycin	*Streptococcus pyogenes* *Streptococcus pneumonia* *Clostridium perfringens* *Corynebacterium -diphtheriae* *Listeria monocytogenes*	*Neisseria gonorrhoeae* Mycoplasma *Legionella pneumophila* *Chlamydia trachomatis* *Bordetella pertusis*
Lincomycin	*Penicillin resistant* staphylococci	*Bacteroides fragilis*
Tetracyclines: e.g: Demeclocycline Minocycline Oxytetracycline Tetracycline	*Bacillus anthracis*	Rickettsiae species Chlamydiae species *Brucella abortus* *Mycoplasma* *Leptospira*
Semisynthetic penicillins: e.g: Nafcillin Oxacillin	*Staphylococci species*	-
Penicillin G	*Streptococcus species,* *Bacillus anthracis* *Corynebacterium diphtheriae,*	*Neisseria gonorrhoeae* *Neisseria meningitidis* *Treponema* species Leptospira
Fluoroquinolones: e.g: Ciprofloxacin Gemifloxacin Norfloxacin	*Bacillus anthracis* *Staphylococcus aureus* *Mycobacterium Tuberculosis* *Streptococcus species* *Enterococcus species* *Mycobacterium avium*	*Escherichia coli* Klebsiella Proteus species *Salmonella typhi* Shigella *Haemophilus influenzae* *Pseudomonas aeruginosa* *Legionella pneumophila* *H. ducreyi* *Vibrio cholera* *Neisseria gonorrhoeae* *Neisseria meningitidis* Mycoplasma

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

DFIs: Drug-Food Interactions; **DDIs:** Drug-Drug Interactions; **ADRs:** Adverse Drug Reactions; **AMR:** Antimicrobial Resistance; **AFIs:** Antibiotic-Food Interactions; **ADME**: Absorption, Distribution, Metabolism, Excretion.

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