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A STUDY ON DRUG –DRUG INTERACTION INDUCED OUTCOMES IN ANTIBIOTIC COMBINATION THERAPY

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ABSTRACT
Intensive care unit patients are particularly at a risk of developing infections with multi-drug resistant organism, which are more prevalent in this environment. Appropriate and adequate antibiotic is essential in the treatment of these patients. Antimicrobial combination therapy is a rational option with potential benefits in the patients who are at the risk of developing infections with multi-drug resistant organism. However, some antibiotic combinations exhibit antagonistic interaction that hinders treatment efficacy. Therefore, screening antibiotic combinations in terms of their interaction types prior to treatment is crucial.From the 100 prescriptions, 468 DDIs were identified. Based on severity, major (100) shows higher; based on MOA, Pharmacodynamic interactions (283) were more and Different variables such as age, gender, no. of drugs per prescription, and hospital stay associated with DDIs. MDR Klebsiella pneumonia were found major cause of multi drug resistant infection in patient. Prevalence of hospital acquired infection in 100 patients was 24%.

KEY WORDS: Drug-Drug interactions, multidrug resistance, prevalence, antimicrobial combination therapy.

INTRODUCTION
Poly pharmacy is a growing problem now a day, which can increase the risk of potential drug interactions and result in a loss of effectiveness. This is particularly relevant to the anti-infective therapy, especially when infection is produced by resistant bacteria because therapeutic options are limited and introductions can cause treatment failure.[1]

WHO defines Drug-Drug interactions as the modification of response to one drug by another when they are administered simultaneously or in quick succession.[2] Stockley declares that a drug-drug interaction is said to occur when the effects of one drug is changed by the presence of another drug.[3] The drug whose activity is affected by such an interaction is called as an **Object drug** the agent which precipitate such an interaction is referred to as the **precipitant.** Drug interactions are one of the major therapeutic challenges to the treatment of patients, especially who are hospitalized. Drug-Drug interactions will affect the quality of life of the patients.[4]

Drug interaction may be a direct effect of one compound upon another, by modification of intestinal absorption, by affecting the transport of drug, by modification of a drugs action at its receptor site, by acceleration or retardation of the metabolism of a given drug or by affecting the rate of excretion. Each of these mechanisms will be discussed separately. By knowing structural activity relationships and the mechanism by which drug interact, one may predict possible problems with newly released agents. There are a number of modes of action, and even though much light has been thrown on the subject in recent years, quite often we still do not know exactly how they happen. [5]

Management of Drug-Drug Interactions
- Discontinue the drug causing the interaction, or the drug affected by the interaction.
- Alternatives might be to decrease the dose or change time of administration.
- All drugs in the active profile for appropriate indications are to be reviewed and target a lowest effective dose.
- Substitution of the suspected drug with another drug of similar efficacy but lower potential for interactions.
- Try to discontinue drugs rather than add new ones.
- Once an optimum drug profile is selected, observe the patient long enough for equilibration to be reached.
- Document and communicate to other health care professionals about the management of the drug

interaction to enhance continuity of care. Before starting any new prescription drug or over-the-counter drug, inform to physician or pharmacist before start the therapy.

- Make sure to read the patient information handout given at the pharmacy.
- Check the labels of the medications for any warnings and look for the "Drug Interaction Precaution." Read these warnings carefully.
- Make a list of all prescription medications and over-the-counter products, including drugs, vitamins, and supplements. Review this list with all health care providers and pharmacist.[6]

If possible, use one pharmacy for all your prescription medications and over-the counter products.

THE ROLE OF PHARMACIST IN MANAGING DRUG –DRUG INTERACTIONS

The pharmacist, along with the prescriber has a duty to ensure that the patients are aware of the risk of side effects. With their detailed knowledge of medicine, pharmacists have the ability to relate unexpected symptoms experienced by patients to possible adverse effects of their drug therapy. The practice in clinical pharmacy also ensures that drug interactions are minimized by avoiding drugs with potential side effects in susceptible patients. Thus, pharmacist has a major role to play in relation to prevention, detection, and reporting drug interactions. [7]

PREVENTION OF POTENTIAL DRUG-DRUG INTERACTIONS

- Establish appropriate drug choices.
- Regularly review the need for chronic drugs and discontinue unnecessary medications.
- Provide information on alcohol use.
- Document drug additions and discontinuations.
- When adding a new drug, screen for potential drug interactions.
- Try to avoid new prescription of a drug with a narrow therapeutic index when equally effective alternatives are available.
- Adjust dose and dosage interval.
- Document a complete up-to-date drug history, including over-the-counter medications, health supplements, alcohol and vitamins.
- Educate members of the health-care team on drug interactions.

MATERIALS AND METHODS

STUDY DESIGN

- Observational Cohort Study
- The study was a conducted over a period of six months with the approval of the hospital research and ethics committee. A total of 100 cases were selected randomly from MICU. The study was done by assessing the drug-drug interactions among the selected patients using the database LEXICOMP, MICROMEDEX, DRUGS.COM. The results obtained were analyzed to provide guidance regarding monitoring and therapeutic management of drug-drug interactions and were recorded and reported to the physician.

STUDY SETTING

Ernakulam Medical Centre Hospital.

STUDY DURATION

A 6-month duration study.

STUDY POPULATION

A minimum of 100 samples is required to conduct the study.

STUDY CRITERIA

Inclusion Criteria

- Patients admitted to MICU with antibiotics therapy are considered in this study.
- Patients with all multidrug resistance are included in this study.

Exclusion Criteria

- patients with age less than 18 years
- Patients taking concomitant herbal medications.

STUDY VARIABLES

- Age
- Gender
- Hospital stays

SOURCES OF DATA

- Patient case records which contain patient's demographics, laboratory investigations, other clinical reports, medication charts.
- MICROMEDEX, LEXICOMP software (drug interaction checker)

STUDY MATERIALS

- Data Collection Form
- Drug Interaction Reporting form
- LEXICOMP
- MICROMEDEX
- DRUGS.COM

STUDY PROCEDURE

PHASE 1:

Obtain the IEC approval for the study.
Detailed literature review.
Procure the scales/statistical tools/software.
Sample size was calculated.

PHASE 2

After obtaining permission from IEC, study begins with data collection. Randomly Selected 100 patients from various departments of the hospital during the study

period September to February according to the inclusion criteria. The medication records of the patients were checked and collected the details of medications along with patient demographics (age, sex, duration of hospital stay, social history, past medical and medication history, co-morbid conditions), laboratory investigations, radiological reports during the hospital stay. The collected information was entered in the data collection form. After that, detail of medications was entered in the Micromedex database and obtained the drug-drug interactions, its severity, scientific evidence, mechanism of action, the effect produced and its clinical management. The drug interactions were documented in the drug interaction form. Then we observed the patient in order to find out whether there is any clinically relevant drug interaction. Clinically relevant drug interactions were reported to the physician and made necessary management.

PHASE 3:-

Data collected were analyzed using Statistical Package for the Social Science(SPSS).

RESULTS AND DISCUSSION

Distribution According to Age group

Table 1: Categorization of study population according to age group

Age group	Frequency	Percent
<30years	16	16
31-40 years	11	11
41-50 years	14	14
51-60 years	20	20
>61 years	39	39
Total	100	100.0

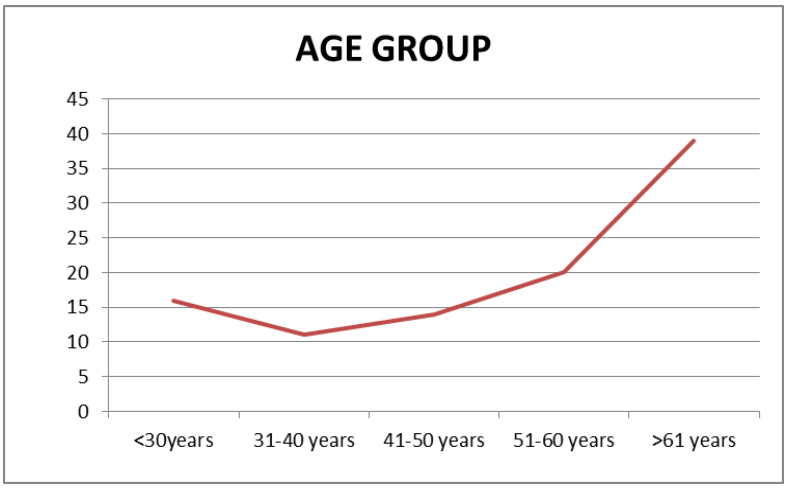

Figure 1: Percentage distribution of age among study population.

DISTRIBUTION OF GENDER

Table2 : Categorization of study population according to gender

Gender	Frequency	Percent
Male	58	58
Female	42	42
Total	100	100.0

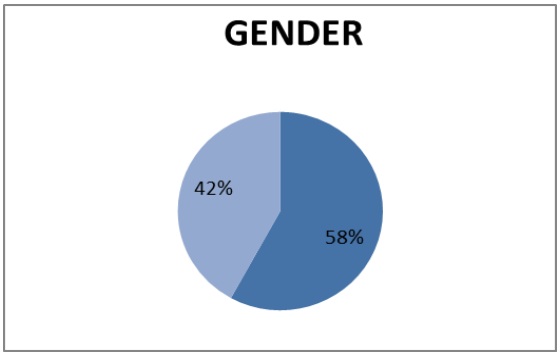

Figure 2: Percentage distribution of gender among study population.

Drug interaction based on Severity

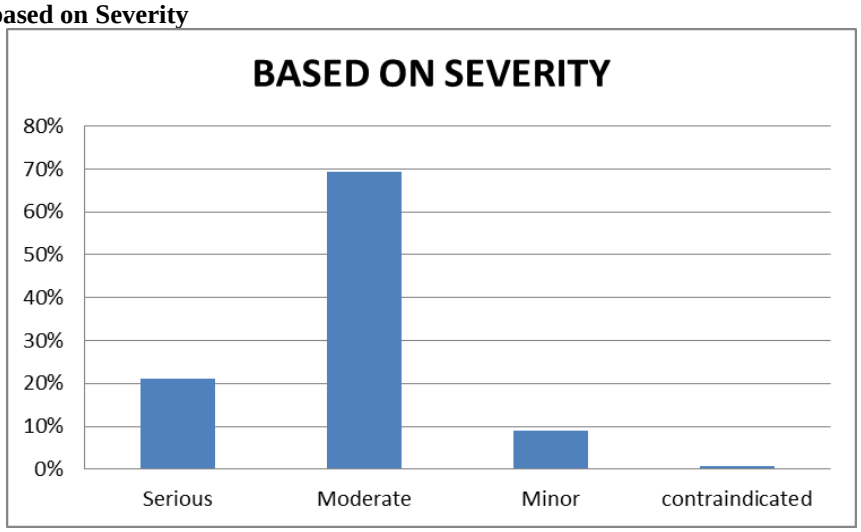

Figure 3: Percentage distribution based on severity among study population.

Based on severity the study categorizes the DDI as serious, moderate, minor, contraindicated. Percentage of serious DDI found in this study population was 21%. The moderate DDI was found to be 69.21%. About 8.92% were contributes minor DDI and the contraindicated were 0.64%. This is having a close resemblance with the study conducted by Binay Gupta et al.[8]

Drug interaction based on mechanism of action

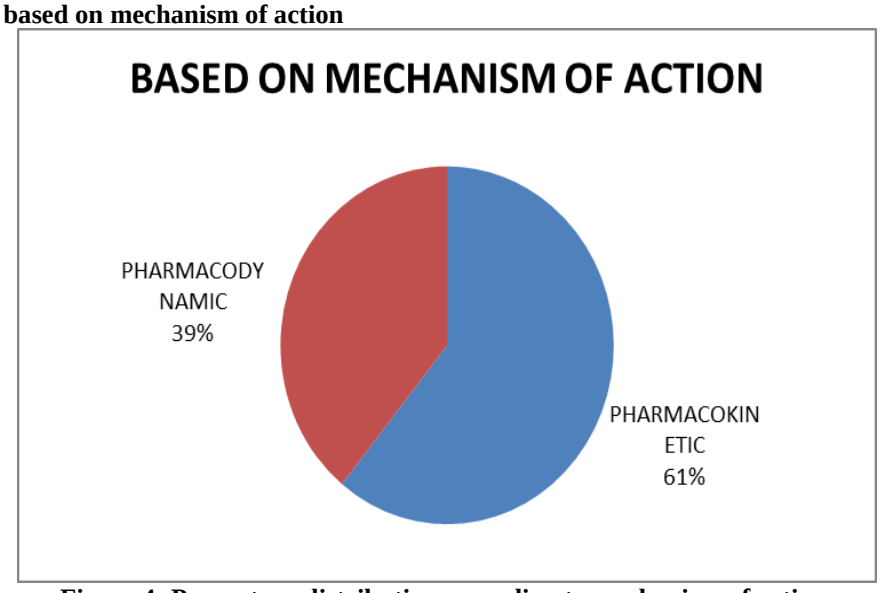

Figure 4: Percentage distribution according to mechanism of action.

Categorizing the interactions based on mechanism of action, pharmacodynamic interactions (39%) were found to be less followed by pharmacokinetic (61 %). The findings of the current study having a close resemblance with the study conducted by Tesfaye ZT, Nedi T.[9]

DISTRIBUTION ACCORDING TO HOSPITAL STAY

Table3: distribution according to hospital stay

NO: OF HOSPITAL STAY	FREEQUANCY	PERCENTAGE (%)
1-10	92	20.94
10-20	78	16.66
20-30	298	63.67
TOTAL	468	100

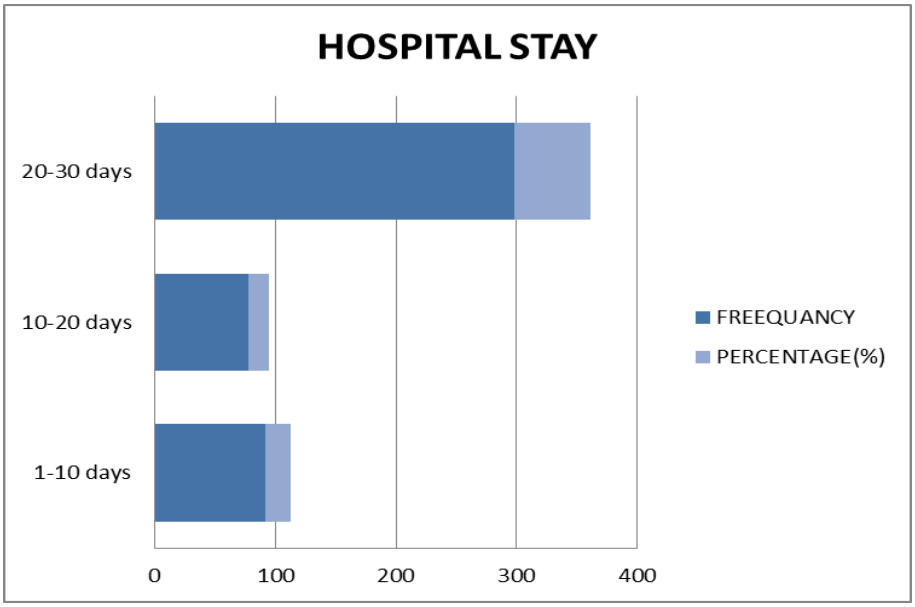

Figure 5: Percentage distribution according to hospital stay.

PREVALANCE OF DRUG-DRUG INTERACTIONS

Table4:-prevalance of drug –drug interaction		
DRUG-DRUG INTERACTIONS	**FREEQUANCY**	**PERCENATGE (%)**
PRESENT	92	92
ABSENT	8	8
TOTAL	100	100

Average Drug interactions per patient- 468/92 = 5.086

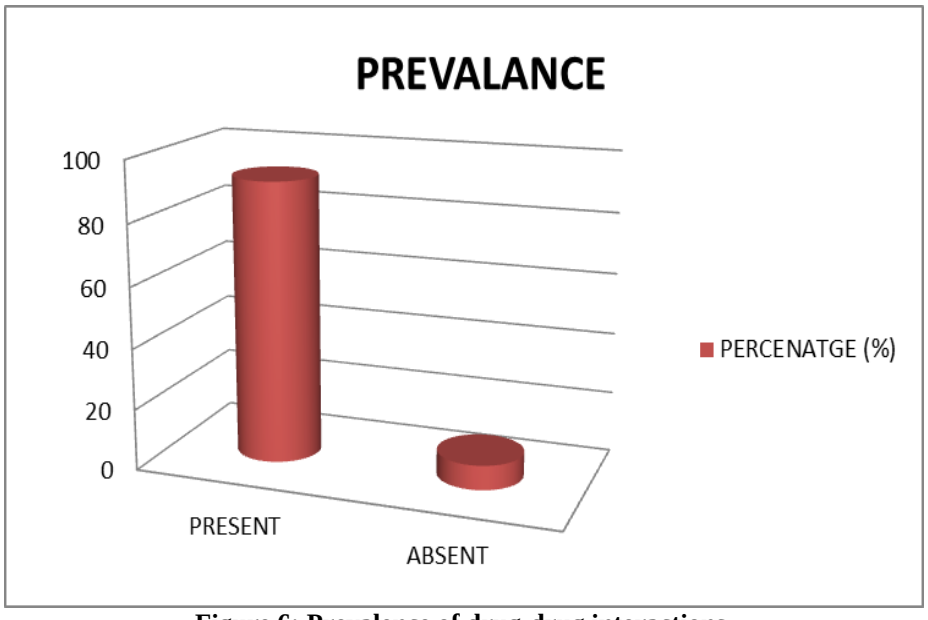

Figure 6: Prevalence of drug-drug interactions.

LIMITATIONS OF THE STUDY

The main limitations that we encountered in our study was the lack of availability of resources to confirm DDIs practically and. Also, we couldn't force the physicians to demand various test in patients to confirm DDIs. The period of study was 6 months, which limited the accuracy and sensitivity of our study.

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