ABSTRACT

Introduction: A drug–drug interaction is a pharmacological or clinical response to the administration of two or more drugs which is different from the response triggered by the individual use of these agents. The risk of drug–drug interactions with increases exponentially with number of drugs prescribed and is estimated of approximately 6% when 2 to 4 drugs are used, 50% when 5 drugs and nearly 100% when 8 drugs are prescribed. Drug interactions can occur both in vivo and in vitro. Drug interactions outside the body can occur when different drugs are mixed in an intravenous infusion. Poly therapy increases the complexity of the therapeutic management and there by the risk of clinically important drug–drug interactions which can both induce the development of adverse drug reaction or reduce the clinical efficacy. In general, a drug is a chemical substance meant for rectifying the altered physiological condition in the body. But currently drugs are becoming an important entity in the daily life of many individuals as the use of poly medication is increasing irrespective of rationality. Whatever it may be the cause for poly-medication, each and every drug encounters when they are concomitantly administered.

Methodology: A Prospective observational study was conducted in the general medicine department of Simhapuri Superspeciality Hospital, Nellore. Results: A total of 1436 drug–drug interactions were detected in 409 prescriptions. Of these, 688 were minor, followed by moderate 464 and 284 major interactions. Among these total drug interactions 1064 interactions were rectified by the physician and rest of the drug interactions were ignored.

Conclusion: Our study on drug–drug interactions helps in assessing the prevalence of potential drug–drug interactions and reducing their risk and adverse consequences also helps in focusing on the rational prescription of drugs.

KEYWORDS: Drug–drug interactions, Polymedication, polypharmacy, co-morbidities.

INTRODUCTION

A drug–drug interaction is a pharmacological or clinical response to the administration of two or more drugs which is different from the response triggered by the individual use of these agents.[1] Drug–drug interactions may produce favorable or undesirable or risky effects. The favorable effects are those whose intention is to treat concomitant disease, enhancing the efficacy reducing the dose, while the undesirable effects may reduce the drug efficacy and may produce superfluous, toxic and even life threatening effects in the body.

Drug therapy (DT) is growing more intricate, thus appropriate drug prescription becomes increasingly challenging. Drug interactions (DI) are one of the significant factors that modify the response to a drug. Drug–Drug Interactions (DDI) can result in anything from minor morbidities up to fatal consequences.[2]

Some studies have shown that drug–drug interactions may cause up to 3% of all hospital admissions. Approximately 37%-60% of patients admitted to hospital may have one or more potentially interacting drug combinations at admissions. Drug–drug interactions are a concern for patients and providers as poly-pharmacy is becoming more common in managing complex diseases or co-morbidities and the consequences can range from untoward effects to drug related morbidity and mortality.[3]
Drug interactions inside the body can be pharmacodynamic or kinetic in nature.

**Pharmacokinetic interactions**
Pharmacokinetic interactions are those that can affect the processes by which drugs are absorbed, distributed, metabolised and excreted.

**Pharmacodynamic interactions** are those where the effects of one drug are changed by the presence of another drug at its site of action. Pharmacodynamic interactions affect the physiological effect of drug involved. These interactions results in synergism [The interaction or co-operation of two or more substances or other agents to produce a combined effect greater than the sum of their separate effects]. Antagonism [active hostility or opposition] alteration of effect or an immune mediated Idiosyncracy [an abnormal physical reaction by an individual to a food or drug].

**RESULTS**
A Prospective observational study was conducted for 11 months, in the General Medicine Unit of Simhapuri Superspeciality Hospital, Nellore.

A total 552 patients were interviewed out of those 409 patients are recruited as per inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th>S.NO</th>
<th>TOTAL NO. OF PATIENTS</th>
<th>PATIENTS INCLUDED</th>
<th>PATIENTS EXCLUDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>552</td>
<td>409(74.9%)</td>
<td>143(25.1%)</td>
</tr>
</tbody>
</table>

**Table-1.**

![Figure-1](image1)

**Figure-1**

**Gender Wise Distribution**
In the total of 409 observed prescriptions males are 198 (48.4%) members and females are 211(51.5%).

**Table-2**

<table>
<thead>
<tr>
<th></th>
<th>TOTAL</th>
<th>MALES</th>
<th>FEMALES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>409</td>
<td>198(48.4%)</td>
<td>211(51.5%)</td>
</tr>
</tbody>
</table>

**Table-2**

![Figure-2](image2)

**Figure-2.**
The occurrence of interactions during this study period of 11 months was totally 1436 interactions in that we distributed in to gender wise.

Gender wise incidence of interactions

Severity of interactions in MALES

In the total of 409 prescriptions males were 198 (48.4%) in number in males total interactions were found to be 624 and the severity of interactions in males was as follows shown in table-3.

Table-3

<table>
<thead>
<tr>
<th></th>
<th>Minor</th>
<th>Moderate</th>
<th>Major</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALES</td>
<td>324[51.9%]</td>
<td>222[35.5%]</td>
<td>78[12.5%]</td>
</tr>
</tbody>
</table>

Figure-3

SEVERITY OF INTERACTIONS IN FEMALES

In the total of 409 prescriptions females were 211 (51.58%) in number in males total interactions were found to be 812 and the severity of interactions in females was as follows shown in table-4:

Table-4

<table>
<thead>
<tr>
<th></th>
<th>Minor</th>
<th>Moderate</th>
<th>Major</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEMALES</td>
<td>364[44.82%]</td>
<td>242[29.8%]</td>
<td>206[25.36%]</td>
</tr>
</tbody>
</table>

Figure-4
SEVERITY OF INTERACTIONS IN MALES AND FEMALES

The severity of interactions in males was found to be major 78 (12.5%), moderate 222 (35.57%), minor 324 [51.9%]. Whereas in females severity of interactions was observed as major 206 (25.36%), moderate 242 (29.80%) and minor 364 (44.82%).

Table-5

<table>
<thead>
<tr>
<th>S.NO</th>
<th>GENDER</th>
<th>MINOR</th>
<th>MODERATE</th>
<th>MAJOR</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MALE</td>
<td>324</td>
<td>222</td>
<td>78</td>
<td>624 (43.45%)</td>
</tr>
<tr>
<td>2</td>
<td>FEMALES</td>
<td>364</td>
<td>242</td>
<td>206</td>
<td>812 (56.54%)</td>
</tr>
</tbody>
</table>

SEVERITY OF INTERACTIONS IN MALES AND FEMALES

Interactions wise Distribution

The occurrence of interactions during this study period of 11 months was 1436 interactions in that minor 688 (47.91%), moderate 464 (32.31%), major 284 (19.77%).

Table-6

<table>
<thead>
<tr>
<th>S.NO</th>
<th>MINOR</th>
<th>MODERATE</th>
<th>MAJOR</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>688 (47.91%)</td>
<td>464 (32.31%)</td>
<td>284 (19.77%)</td>
<td>1436</td>
</tr>
</tbody>
</table>

SEVERITY OF INTERACTIONS

Figure-5

Figure-6.
MANAGEMENT
The results showed that when the number of drugs increased in a prescription, the number of DDIs also increased.

Table-7.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Management</th>
<th>Number of drug–drug interactions (1436)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dosage adjustment</td>
<td>390(27.15%)</td>
</tr>
<tr>
<td>2</td>
<td>No management required</td>
<td>266(18.52%)</td>
</tr>
<tr>
<td>3</td>
<td>Monitor for signs and symptoms</td>
<td>199(13.85%)</td>
</tr>
<tr>
<td>4</td>
<td>Monitor for drug levels</td>
<td>209(14.55%)</td>
</tr>
</tbody>
</table>

The drug interaction software showed that dosage adjustment was the most popular intervention following a DDI 266(18.52%) of 1436 interactions.

Most of the drug-drug interactions required no management 390(27.15%) out of 1436 interactions.

209 (14.55%) drug interactions have to be monitored for drug levels.

DISCUSSION
In Our study we found 1436 interactions in 409 patients among them males are 198 in number, i.e [48.4%] and females were 211 in number, i.e. [51.58%]. These findings were different from another study reported in the literature where the medications of the patients were of concern and Pharmacodynamic DDIs were dominant.[5]

The severity assessment of DDIs in our study showed that most of the interactions were minor 688 (47.91%) followed by moderate 464 (32.31%) and major 285 (19.77%) interactions.[4]

The most common management plan found in our study for most of the DDIs was dose adjustments, followed by no management required interactions, Dis to be monitored for symptoms and monitoring drug levels.

The significance of using electronic software has been reported in the literature.[32]

Of the total interactions 1436, 74% of drug interactions i.e.1064 drug interactions were accepted by the physician and prescriptions were rectified. Rest of the drug interactions were ignored by the physicians due to lack of alternative, busy schedule, superiority of physician.

The occurrence of adverse effects is more difficult to detect for newer drugs, where there is less clinical experience and fewer data, emphasizing the role for clinical interpretation.[33]

The result obtained in our study was based on the classification as minor, moderate or major according the interaction checkers that was used.

This review showed that there are different frequencies and types of DDIs and ADR, which are drug-related problems, associated with different classes of drugs. In daily care practice, the correct diagnosis of these problems requires skill and expertise of the multidisciplinary team, especially when older adults present themselves with nonspecific complaints and manifestations. To recognize and diagnose this undesirable outcome, goals should be set in the health care service, highlighting the role of the clinical pharmacist, who uses interventions for identification and minimization the drug-related problem (DRP), as demonstrated in studies.[8]

Statistical analysis was performed via Ms excel paired t test statistically significant for p value- 0.0181.

CONCLUSION
In general, a drug is a chemical substance intended for rectifying the altered physiological condition in the body. But currently drugs are becoming an important entity in the daily life of many individuals as the use of poly medication is increasing irrespective of rationality.

The increase in the poly medication may be due to many factors like multiple disease condition, increased age, patient complaints or due to the benefits of physician followed by the benefits of the pharmacy in the hospital.

Whatever it may be the cause for poly-medication, each and every drug encounters when they are concomitantly administered.

In our study we found 1436 drug interactions in the total of 409 prescriptions in the time period of 11 months. Of these total interactions 1064, 74% of drug interactions were accepted by the physician and the left behind 26% of interactions were ignored by the physician.

Our study on drug-drug interactions helps in assessing the prevalence of potential drug-drug interactions and reducing their risk and adverse consequences also helps in focusing on the rational prescription of drugs thereby minimizing the harmful drug-drug interactions as they are more in number when compared to beneficial interactions.
Our study also aids in minimizing the medication related problems in patients at risk and improving the role of clinical pharmacist in pharmaceutical care. This may also help in improving the safe and effective use of drugs in our hospital.

REFERENCES
Geriatric Patients in a Tertiary Care Hospital, 2018; 23: 489-497.