Incidence of Adverse Drug Reactions in a South Indian Tertiary Care Hospital

Authors
Yella Dinesh, MK. Misbahuddin, Syed Akheel Ahmed
Pharm-D, Bhaskar Pharmacy College, Yenkapally Village, Moinabad, Hyderabad, Telangana, India

Abstract
The World Health Organization defines an adverse drug reaction (ADR) as “a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.” The fact that drugs might have effects on humans other than the ones intended has been known for many years. During the six month study period, a total 232 patients visited the tertiary care hospital and Celestee skin and hair Clinic. Highest number of patients were from the age group of 21-30 i.e. 33.81%. Majority of the ADRs were from the drug class antibiotics 24 (25.35%). According to Naranjo’s causality assessment scale, out of 71 ADRs the dechallenge was done in all cases, out of which 45 cases (63.3%) were probable and 14 cases (19.7%) were possible where as remaining 12 cases (16.9%) were in unlikely category. We also assessed the severity by using Hartwig and Siegel severity assessment scale; it shows that highest number of cases i.e., 42 (59.15%) fall into moderate type and 10 cases (14.08%) were mild type whereas 19 cases (26.76%) fall into severe ADRs.

Keywords: Adverse drug reactions, Pharmacovigilance.

1. Introduction
Definition: (WHO, 1972)
The World Health Organisation defines an adverse drug reaction (ADR) as “a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.” The first remarkable adverse drug reaction (ADR) reported in Japan was anaphylactic shock caused by penicillin. The malformation of limbs, etc. caused by thalidomide was a global problem, and thalidomide was withdrawn from the market. The clinical presentation of cutaneous drug reactions is highly variable, ranging from benign reactions such as exanthematous or maculopapular eruption to severe and potentially life-threatening reactions such as Stevens-Johnson Syndrome.

2. Methodology
The study has been carried out in both outpatient and inpatient departments of Bhaskar General Hospital and Celestee Skin, Laser and Hair Clinic, Hyderabad. The design used for the study is Prospective Observational Study which was carried out for 4 months from November 2017 to Jan 2018.

2.1 Study setting
The study was conducted on patients those who are experiencing Adverse Drug Reactions to medicine
used during their hospital stay or visiting the outpatients department of Dermatology and General Medicine

**Study Criteria**

**Inclusion Criteria**
- Study includes adults, pediatric and geriatric patients.
- Subjects who are under multi drug therapy.
- Subjects under long term treatment.
- Subjects detected with ADRs

**Exclusion Criteria**
- Expectation of surgery
- Pregnant Women’s
- Lactating mothers.

**Study population**
The patients who were coming to the dermatology and general medicine departments of Bhaskar General Hospital and Celestee Skin, Laser and Hair Clinic Hyderabad during November 2017 to January 2018 were enrolled in the study.

**2.2 Data collection**
The data was collected on regular basis with direct patient interaction at inpatient and outpatient wards of Dermatology and General Medicine departments. It includes patient’s demographic details, medical history, medication history, social history and present medications which are the main sources to find out the possibility of adverse drug reactions.

**2.3 Analysis of ADRs**
The reported CADRs can be analyzed by considering the following methods:
Causality assessment of the ADRs based on the scores of the Naranjo’s probability scale: Probability is assigned via a score termed definite, probable, possible or doubtful. Values obtained from this algorithm are sometimes used in peer reviews to verify the validity of author's conclusions regarding adverse drug reactions. Severity assessment of ADRs analyzed by using the Modified Hartwig’s and Siegel Severity assessment scale this can be classified into Mild, Moderate and Severe.

**3. Results**
The study was conducted for four months during which a total 232 patients visited the Dermatology and General Medicine departments. The demographic details are as follows:

**Table-1: Gender wise distribution of ADRs**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>109</td>
<td>123</td>
</tr>
<tr>
<td>ADR cases</td>
<td>32</td>
<td>39</td>
</tr>
</tbody>
</table>

In a total of 232 patients, the ADR patients were 71. And among those reported 71 cases, 32 were male with 45.07% incidence and 39 were female with 54.92% incidence.

**Table-2: Gender wise Incidence of ADRs**

<table>
<thead>
<tr>
<th>Gender</th>
<th>No.of ADRs</th>
<th>Incidence%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>32</td>
<td>45.07</td>
</tr>
<tr>
<td>Females</td>
<td>39</td>
<td>54.92</td>
</tr>
</tbody>
</table>

Among the reported 71 ADRs, the incidence of females is 45.07% which is relatively 9% higher than males where the incidence is 45.07.
Based on age, the age-group of 21-30 had relatively highest number of ADRs i.e., 24 cases (33.8%) followed by the age group 31-40 with 19 cases (26.76%). The age groups 11-20 and 41-50 had same number of ADRs with 07 cases (9.85%) each. Similarly the age groups 51-60 and 61-70 shared same number of cases that is 02 (2.81%) ADRs each.

Table 3: Age-wise distribution of ADRs

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of ADRs</th>
<th>Incidence%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>10</td>
<td>14.08</td>
</tr>
<tr>
<td>11-20</td>
<td>07</td>
<td>9.85</td>
</tr>
<tr>
<td>21-30</td>
<td>24</td>
<td>33.8</td>
</tr>
<tr>
<td>31-40</td>
<td>19</td>
<td>26.76</td>
</tr>
<tr>
<td>41-50</td>
<td>07</td>
<td>9.85</td>
</tr>
<tr>
<td>51-60</td>
<td>02</td>
<td>2.81</td>
</tr>
<tr>
<td>61-70</td>
<td>02</td>
<td>2.81</td>
</tr>
</tbody>
</table>

In the causality assessment using the scale, there were 45 cases with 63.3% incidence that were found to be probable type, 14 cases with 19.7% incidence that were possible type and 12 cases with 16.9% incidence that were unlikely type. There were zero (0) cases that came under definite category.

Table 5: Distribution of Naronjo Causality Assessment Scale

<table>
<thead>
<tr>
<th>Causality</th>
<th>No. of ADRs</th>
<th>Incidence%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Probable</td>
<td>45</td>
<td>63.3</td>
</tr>
<tr>
<td>Possible</td>
<td>14</td>
<td>19.7</td>
</tr>
<tr>
<td>Unlikely</td>
<td>12</td>
<td>16.9</td>
</tr>
</tbody>
</table>

Table 4: Age-wise distribution of ADRs among gender

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Incidence</th>
<th>Females</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>4</td>
<td>12.5</td>
<td>6</td>
<td>15.3</td>
</tr>
<tr>
<td>11-20</td>
<td>4</td>
<td>12.5</td>
<td>3</td>
<td>7.6</td>
</tr>
<tr>
<td>21-30</td>
<td>9</td>
<td>28.1</td>
<td>15</td>
<td>38.4</td>
</tr>
<tr>
<td>31-40</td>
<td>9</td>
<td>28.1</td>
<td>10</td>
<td>25.6</td>
</tr>
<tr>
<td>41-50</td>
<td>3</td>
<td>9.3</td>
<td>4</td>
<td>10.2</td>
</tr>
<tr>
<td>51-60</td>
<td>1</td>
<td>3.1</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>61-70</td>
<td>2</td>
<td>6.2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Distribution of cases based on gender among different age groups is seen in the table. There were 04 male cases each in the age groups 0-10 and 11-20 with 12.5% incidence whereas there were 06 (15.3%) and 03 (7.6%) female cases respectively.
On categorizing the drug based on their severity most of them fell under Moderate category with 42 cases and 59.15% incidence followed by the category Severe with 19 cases and 26.76% incidence and the least were under Mild category with 10 cases and 14.08% incidence.

4. Discussion
The study was aimed at assessing the incidence of ADRs in the population of age group from 1-70 years. Out of 232 patients 71 cases were suspected with the ADRs in the Dermatology and General medicine departments. Of the total cases 32 ADRs were males and 39 ADRs were females. Highest number of patients were from the age group of 21-30 i.e. 24ADRs with 33.8% incidence followed by 31-40 i.e. 19 ADRs with 26.76% incidence, which is in accordance with the Sharma et al. study that also reported similar observations. (Sharma et al., 2001). According to Naranjo’s causality assessment scale, of the total ADRs the dechallenge was done in all cases, and was found out that most of them were Probable cases with 45 ADRs at 63.3% incidence, whereas Possible cases were 14 ADRs at 19.7% incidence followed by Unlikely cases with 12 ADRs at 16.9% incidence. The severity assessment of cases was also done using Hartwig and Siegel severity assessment scale; which shows that highest number of cases i.e., 42(59.15%) fall into moderate type, 19 cases(26.76%) were Severe type and 10 (14.08%) cases were mild type.

5. Conclusion
In our study we screened a number of subjects attending Dermatology and General Medicine departments. The findings of which were as follows A total of 232 patients were screened of which 71 patients were found with ADRs, among which females were reported with more ADRs than males. The number of ADRs reported in the age group of 21-30 were more prominent than other age groups. Causality assessment was performed using Naranjo’s Causality Assessment scale through which it is concluded that more number of ADRs reported were of probable type followed by Possible and Unlikely types. The Severity Assessment was performed using Hertwig & Seigel Severity Assessment scale where most of them were of Moderate category followed by Severe and Mild types.

5.1 Drug Therapies that could be used in case of ADRs
Corticosteroids (applied topically, taken orally, or given intravenously), such as Prednisone, hydrocortisone.
Antihistamines, Antipruritic treatments (to relieve itching)
Surgical removal of dead tissue debris may be necessary in cases of severe reactions.

Nutrition
Vitamin C helps skin heal. Some studies suggest that vitamin C can lower histamine levels (which cause hives). Lower dose if diarrhea develops.
B-complex with extra B12 aids in skin health. Vitamin B12 injections help reduce the severity of hives, but it is not clear whether taking B12 orally has the same effect. Vitamin B5 or Pantothenic acid helps heal wounds.
Vitamin E and zinc help skin heal. Both are also sometimes applied topically.
Bromelain, an enzyme derived from pineapple, reduces inflammation.
Omega-3 fatty acids, such as those found in fish oil, help maintain skin health and may have anti-inflammatory properties. If you take blood-thinning
medication, talk to your doctor before taking omega-3 fatty acids.
Rutin or quercetin may improve skin health.

Acknowledgement
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