Pharmacovigilance study on the different drugs used for the management of eye disorders in Bangladesh


Abstract
At present, pharmacovigilance (PV) study is one of a key way to improve and ensure drug safety and health care sectors in the whole world including Bangladesh. Both primary and secondary data were collected for this study from two different hospitals in Dhaka and rural eye hospital in different district of Bangladesh. Results show that among 500 eye diseases patients, 20% patients were affected by cataracts, 10% are glaucoma, 5% are Blepharitis, 10% are Blindness, 5% are Presbyopia, 10% are Myopia, 10% are Allergic conjunctivitis, 5% are Dry eye, 15% are Blurry vision and others 10%. These results vary from rural to urban area in Bangladesh. The common drugs are used for the treatment of that patients are, Ciprofloxacin 0.3%, Optadim 0.1%, Prochlorperazine Maleate, Leflunomide 0.3%, Ascorbic acid + Copper + Lidex + Lutein + Zinc, Dexamethason 0.1%, Fexofenadine hydrochloride, Olopatadine 0.1%, Vitamin C, Hypromellose 0.5%, Loteprednol Etabonate, Olopatadine 0.2%, Dexamethasone 0.1% + Tobramycin 0.3%, Hypromellose 2%, Rupatadine, Multivitamin pediatric preparation, Polyelethylene glycol 0.4%, Flunarizine, Moxifloxacin 0.5%, Esomeprazole+ Naproksen, Polyelethylene glycol 0.3%, Fexofenadine Hydrochloride, Dexamethasone sodium phosphate, Fluomethalone 0.1%, Gentamycin 0.3%, Carbomer 0.3%, Multivitamin, Artificial tear, Rupatadine. Among these drugs there are some eye drops and some tablets and some capsules and multivitamins. In 500 ophthalmic patients there are some common adverse effects are obtain. The percentage of that adverse effect is, Allergy 15%, Dizziness 13%, Fatigue 10%, Nausea 8%, Diarrhea 13%, Blurred vision 7%, Itching eye 15%, Redness of eye 8%, Swelling of eye 17%, Dry eye 9%, Edema 5%, Headache 15%, GI disturbance 8%, Gastric pain 6%, Dry mouth 10%, Inflammation 20%, Back pain 6%, Dyspepsia 8%, Glaucoma 15%, Discomfort 20%.

Keywords: Pharmacovigilance, drugs, management and eye disorders

Introduction
Pharmacovigilance (PV), also known as Drug Safety Surveillance, is an important process that allows health regulatory authorities to continue to assess benefits and risks throughout the lifecycle of a medicine and potentially detect serious adverse effects and new drug safety signals that were not detected before marketing authorization (Maitra et al. 2014) [39]. WHO Program for International Drug Monitoring started the PV activity in 1961 along with 144 countries worldwide. In 2010, 134 countries of the world were part of WHO PV Program including Bangladesh during International Drug Monitoring in response of detection of thalidomide disaster (WHO 2015) [73]. In Bangladesh, Director General of Drug Administration (DGDA) is now actively participating in PV program across the world and formed a new adverse drug reaction (ADR) advisory committee comprising with 16 members and DGDA Chairman to monitor the hospitals as adverse drug reaction monitoring (ADRM) cell activity (Ahmed and Hossain, 2013) [1].

Eyes are the most important organs for vision. They detect light and convert it into electrochemical impulses in neurons. In higher organisms, the eye is a complex optical system which collects light from the surrounding environment, regulates its intensity through a diaphragm, focuses it through an adjustable assembly of lenses to form an image, converts this image into a set of electrical signals, and transmits these signals to the brain through complex neural pathways that connect the eye via the optic nerve to the visual cortex and other areas of the brain. Eyes with resolving power have come in ten fundamentally different forms, and 96% of animal species possess a complex optical system. (Land and Fernald, 1992) [133]. Image resolving eyes are present in mollusks, chordates and arthropods. (Frentiu et al. 2008) [126]. The simplest "eyes", such as those in microorganisms, do nothing but detect whether the surroundings are light or dark, which is sufficient for the entrainment of circadian rhythms.
From more complex eyes, retinal photosensitive ganglion cells send signals along the retinohypothalamic tract to the suprachiasmatic nuclei to effect circadian adjustment and to the pretectal area to control the pupillary light reflex. (Breitmeyer and Bruno, 2010) Many eye diseases have no early symptoms. They may be painless, and you may see no change in your vision until the disease has become quite advanced.

The single best way to protect your vision is through regular professional eye examinations. Of course, between examinations, if you notice a change in your vision – or you think your eye may be injured in any way – contact your eye care professional immediately.

The Pharmacovigilance study was on the basis of prescription and data collection from different sources, different people of different professions and different kind of areas for representing the average conception with some new ideas and information.

Methodology
Study Locations
The study was conducted in two different hospitals of Dhaka and rural eye hospital in different district of Bangladesh. The names of the hospitals include Dhaka Eye Hospital and Ispahan Islamia Eye Institute and Hospital. The protocol of this research has been approved by the administrative offices of both hospitals. These hospitals were chosen in terms of different factors such as availability of patients, affordability and accessibility of treatments for low income people, and modernized treatment facilities.

Data Collection
Both primary and secondary data were collected for this study. Primary data were collected through structured questionnaire survey, analysis of clinical histories and key informant interviews. On the other hand, secondary data were collected from a range of scientific and grey-literature and also from the information section of each hospital. Following methods were applied to collect both primary and secondary data:

Primary Data Collection
Structured Questionnaire Survey
A structured questionnaire survey was conducted among 500 eye patients in the study of the different eye hospitals in Dhaka and outside of Dhaka. In this questionnaire survey there are some basic questions write down and very easily done to asking patients.

Clinical History Analysis
Clinical histories were analyzed in detail for a range of information such as personal history, demographics, diagnosis, treatment, biophysical characteristics, prescription, ADR reaction of different eye diseases and other common ADRs and drugs used to manage the adverse effects were collected from the patient’s medical records.

Key Informant Interview
Fifteen semi-structured key informant interviews were performed with doctors, nurses, daycare managers related to eye disorder patients to collect information on study objectives. Study-related questions were asked during the key informant interviews to get to know the overall situation of eye disorder patients and adverse effects of drugs. In addition, several informal discussions were administered among the university faculty members to collect their views on Pharmacovigilance (PV).

Fig: Roadmap of data collection
**Secondary Data Collection**
Secondary data were collected though a range of literature around the world based on the study objectives and goal. Various scientific journal articles, technical reports and grey-literature were reviewed to support the study objectives and purposes. Additionally, different information on eye diseases and histories of Bangladesh were collected from the study hospitals to assess the existing eye patients and their historical background.

**Data Categorization and Analysis**
The data collected through structured questionnaire survey, clinical history analysis and interview were categorized based on type of eye diseases, adverse effects and agents used to manage the adverse effects. All data collected through structured questionnaire survey were analyzed by using Microsoft Excel and presented both graphical and tabular formats and discussed them accordingly.

**Results and Discussions**

**Demographic Information**

**Gender**
Figure 1 is showing the percentage of male and female respondents of eye disorder patients of both studies in hospitals. From the results of the survey and interviews, it has been reported that the males mainly affected by the eye diseases. However, the severities of such eye patients in females have been increased in recent decades. In Bangladesh, male are mainly working outside their houses due to the socio-cultural settings and lifestyles are very different than females. Now-a-days, females are also working for their livelihoods and, therefore, they are also exposed to various disease including eye diseases.

![Fig 1: Gender](image)

**Area of residence**
Most of the respondents came from rural areas (60%), whereas the rest of them (40%) were the residents of urban areas (Figure 2). It can be explained that the urban people may have less interests to get the treatment at the government hospitals and have high preference to get facilities from the private hospitals. Majority of respondents from urban areas were in the last stage of their eye disorder or required the palliative care unit for specialized care. On the other hand, most of the respondents from rural areas do not have ability to spend much for their treatment in private hospitals. Therefore, they had no other choices except the treatments by government hospitals.

![Fig 2: Area of residence](image)

**Age of the patients**
Among the respondents, 90% of their age ranged from 10-65 years who were suffered from eye diseases in different ratio. Below 15 years also suffered from eye diseases but their amount is not higher. The rest of the respondents (10%) include two age groups of 15-30 and 50-65. Which is shown in Figure 3.

![Fig 3: Age of the patients](image)

**Occupations of the patients**
Almost one third of the respondents were farmers (25%) by occupations. Other occupations include service-holders (20%), housewife (15%), labor (15%), business (10%), students (10%) and driving (5%). Rests of them were housewives and staying at home for taking care of children, houses and other domestic works. As the study was conducted in the governmental hospitals, most of the patients were found as poor people who came to seek the treatments. The study did not found any upper economic class patients in these hospitals for their treatment. It is represented in Figure 4.
Social class of patients
Figure 5 shows that majority of the patients (40%) are poor, 20% of patients are upper middle class, 15% are lower middle class and 25% are rich ophthalmic patients in this study.

Diseases state Information
In our country eye diseases are growing up rapidly. Some of the specific eye disorder such as, Dry eye syndrome, Presbyopia, Allergic conjunctivitis, Glaucoma, watery eyes, Night blindness, Blindness, Blepharitis, Myopia, Blurry vision and Cataracts. Most of them are suffered of cataracts. Especially older people are mainly suffered from cataracts. The percentage of different eye diseases is showing in this figure 6.

Treatment pattern
There are different types of eye disease so their treatment pattern also different. Commonly are prescribed drug and another is surgery or operation. In minor cases are mainly suggested prescribe drug, such as eye drop, orally tablet and capsule and etc. But major cases doctor are suggested surgery or operation. The ratio of surgery is 30% and prescribed drug is 70%.Mainly surgery is occurred in Cataracts patients (Figure 7).

Prescribed some common drugs for eye diseases
There are many drugs which are prescribed for eye diseases for prevention are given in Table 1.
Table 1: Prescribed drugs for eye diseases

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Dosage form</th>
<th>Number of prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin 0.3%</td>
<td>Eye drop</td>
<td>52</td>
</tr>
<tr>
<td>Optadin 0.1%</td>
<td>Eye drop</td>
<td>45</td>
</tr>
<tr>
<td>Prochlorperazine Maleate</td>
<td>Tablet</td>
<td>48</td>
</tr>
<tr>
<td>Lomefloxacin 0.3%</td>
<td>Eye drop</td>
<td>36</td>
</tr>
<tr>
<td>Ascorbic acid + Copper + Lutein + Vitamin E + Zinc</td>
<td>Capsule</td>
<td>85</td>
</tr>
<tr>
<td>Dexamethasone 0.1%</td>
<td>Eye drop</td>
<td>30</td>
</tr>
<tr>
<td>Fexofenadine hydrochloride</td>
<td>Tablet</td>
<td>35</td>
</tr>
<tr>
<td>Olopatadine 0.1%</td>
<td>Eye drop</td>
<td>45</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Tablet</td>
<td>60</td>
</tr>
<tr>
<td>Hypermellose 0.5%</td>
<td>Eye drop</td>
<td>35</td>
</tr>
<tr>
<td>Loteprednol Etabonate 0.5%</td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>Olopatadine 0.2%</td>
<td>Eye drop</td>
<td>65</td>
</tr>
<tr>
<td>Dexamethasone 0.1% + Tobramycin 0.3%</td>
<td>Eye drop</td>
<td>46</td>
</tr>
<tr>
<td>Hypermellose 2%</td>
<td>Eye gel</td>
<td>35</td>
</tr>
<tr>
<td>Rupatadine</td>
<td>Tablet</td>
<td>75</td>
</tr>
<tr>
<td>Multivitamin pediatric preparation</td>
<td>Eye drop</td>
<td>80</td>
</tr>
<tr>
<td>Polyethylene glycol 0.4%</td>
<td>Eye drops</td>
<td>40</td>
</tr>
<tr>
<td>Flunarizine</td>
<td>Capsule</td>
<td>32</td>
</tr>
<tr>
<td>Moxifloxacin 0.5%</td>
<td>Eye drop</td>
<td>58</td>
</tr>
<tr>
<td>Esomeprazole+ Naproxen</td>
<td>Tablet</td>
<td>32</td>
</tr>
<tr>
<td>Polyethylene glycol 0.3%</td>
<td>Eye drops</td>
<td>34</td>
</tr>
<tr>
<td>Fexofenadine Hydrochloride</td>
<td>Tablet</td>
<td>45</td>
</tr>
<tr>
<td>Dexamethasone sodium phosphate</td>
<td>Injection</td>
<td>51</td>
</tr>
<tr>
<td>Fluomethalone 0.1%</td>
<td>Eye drops</td>
<td>38</td>
</tr>
<tr>
<td>Gentamycin 0.3%</td>
<td>Eye drops</td>
<td>52</td>
</tr>
<tr>
<td>Carbomer 0.3%</td>
<td>Eye drops</td>
<td>38</td>
</tr>
<tr>
<td>Multivitamin</td>
<td>Tablet</td>
<td>80</td>
</tr>
<tr>
<td>Artificial tear</td>
<td>Gel</td>
<td>35</td>
</tr>
<tr>
<td>Rupatadine</td>
<td>Tablet</td>
<td>75</td>
</tr>
</tbody>
</table>

The percentage of common drugs use in different prescription
There are some same drugs are used in different prescription due to their therapeutic purpose. In 500 prescription of opthalmic patients some common drug are used (Figure 8).

![Fig 8: The percentage of common drugs](image-url)
Adverse Effects of prescribed Drugs

Adverse Effects
In medicine, an adverse effect is an undesired harmful effect resulting from a medication or other intervention such as surgery. An adverse effect may be termed a "side effect", when judged to be secondary to a main or therapeutic effect. If it results from an unsuitable or incorrect dosage or procedure, this is called a medical error and not a complication. Adverse effects are sometimes referred to as "iatrogenic" because they are generated by a physician/treatment. Some adverse effects occur only when starting, increasing or discontinuing a treatment.

The harmful outcome is usually indicated by some result such as morbidity, mortality, alteration in body weight, levels of enzymes, loss of function, or as a pathological change detected at the microscopic, macroscopic or physiological level. It may also be indicated by symptoms reported by a patient. Adverse effects may cause a reversible or irreversible change, including an increase or decrease in the susceptibility of the individual to other chemicals, foods, or procedures, such as drug interactions.

Some common adverse effects of collected prescribed drugs are

- Allergy
- Dizziness
- Fatigue
- Nausea
- Diarrhea
- Blurred vision
- Itching eye
- Redness of eye
- Swelling of eye
- Dry eye
- Edema
- Headache
- GI disturbance
- Gastric pain
- Dry mouth
- Inflammation
- Optic nerve damage
- Back pain
- Dyspepsia
- Corneal ulcer
- Glaucoma
- Discomfort
- Others

In 500 ophthalmic patients there are some common adverse effects occur. Table 2 and Figure 9 are showing the adverse effect of patients with percentage of total number of patients.

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Patients number</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy</td>
<td>75</td>
<td>15</td>
</tr>
<tr>
<td>Dizziness</td>
<td>60</td>
<td>12</td>
</tr>
<tr>
<td>Fatigue</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Nausea</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>65</td>
<td>13</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>35</td>
<td>7</td>
</tr>
<tr>
<td>Itching eye</td>
<td>75</td>
<td>15</td>
</tr>
<tr>
<td>Redness of eye</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Swelling of eye</td>
<td>85</td>
<td>17</td>
</tr>
<tr>
<td>Dry eye</td>
<td>45</td>
<td>9</td>
</tr>
<tr>
<td>Edema</td>
<td>25</td>
<td>5</td>
</tr>
<tr>
<td>Headache</td>
<td>45</td>
<td>15</td>
</tr>
<tr>
<td>GI disturbance</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Gastric pain</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Inflammation</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>Optic nerve damage</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Back pain</td>
<td>30</td>
<td>6</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Corneal ulcer</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>45</td>
<td>15</td>
</tr>
<tr>
<td>Discomfort</td>
<td>100</td>
<td>20</td>
</tr>
</tbody>
</table>

Fig 9: common adverse effects with percentage

Conclusions
Results show that among 500 eye diseases patients, 20% patients were affected by cataracts, glaucoma 10%, Blepharitis 5%, Blindness 10%, Presbyopia 5%, Myopia 10%, Allergic conjunctivitis 10%, Dry eye 5%, Blurry vision 15% and others 10%. This results vary from rural to urban area in Bangladesh. Both primary and secondary data were collected for this study from two different hospitals in Dhaka and rural eye hospital in different district of Bangladesh. The names of the hospitals include Dhaka Eye Hospital and IspahanIslamia.
Eye Institute and Hospital and the rural eye hospital name include Shahzadpur eye hospital, BNSB Base Eye Hospital, Sirajganj, Pabnaupazila eye hospital. The common drugs are used for the treatment of that patients are, Ciprofloxacin 0.3%, Optadin 0.1%, Prochlorperazine Maleate, Lemeofloxacin 0.3%, Asorbic acid + Copper + Lutein + Vitamin E + Zinc, Dexamethasone 0.1%, Fexofenadine hydrochloride, Olopatafide 0.1%, Vitamin C, Hypromellose 0.5%, Loteprednol Etabonate, Olopatadine 0.2%, Dexamethasone 0.1% + Tobramycin 0.3%, Hypromellose 2%, Rupatadine, Multivitamin pediatric preparation, Polyethylene glycol 0.4%, Flunarizine, Moxifloxacin 0.5%, Esomeprazole + Naproxen, Polyethylene glycol 0.3%, Fexofenadine Hydrochloride, Dexamethasone sodium phosphate, Fluromethalone 0.1%, Gentamycin 0.3%, Carbomer 0.3%, Multivitamin, Artificial tear, Rupatadine. In 500 ophthalmic patients there are some common adverse effects are obtain. The percentage of that adverse effect is, Allergy 15%, Dizziness 13%, Fatigue 10%, nausea 8%, Diarrhea 13%, Blurred vision 7%, Itching eye 15%, Redness of eye 8%, Swelling of eye 17%, Dry eye 9%, Edema 5%, Headache 15%, GI disturbance 8%, Gastric pain 6%, Dry mouth 10%, Inflammation 20%, Back pain 6%, Dyspepsia 8%, Glaucoma 15%, Discomfort 20%.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
MRIR, MA and MSI completed the main works of this study. MRIR, MA and MSI also carried out the conception and design of this study. MA and FF wrote the manuscript. MSI, MFMR and SP revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements
The authors are grateful to the people who gave facilities for working and also thankful to Department of pharmacy of Manarat International University and Southeast University. The authors are also grateful to School of Food Science and Technology, Chung-Ang University.

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