INTRODUCTION
Prescriber's knowledge about the pharmacodynamic and pharmacokinetics aspects of medicines and their interaction with normal aging physiology is critical in the management of asthma. The knowledge is needed to minimize and even avoid the potentially adverse effects of seizures and side effects associated with the anti-asthmatics drug [1,2]. It is well known and obvious that adverse reactions to drugs can occur with any class of drug as the patient consumes any drugs or the various disease conditions. According to the World Health Organization, the adverse drug reactions (ADRs) can be defined as 'a response to a drug that is noxious and unintended and occurs at doses normally used in human or the prophylaxis, diagnosis and treatment of disease, or modification of physiological function [3-5]. The female gender age and multiple medications and the physiological state of renal and liver function, breastfeeding, pregnancy, and alcohol intake are considered as important risk factors of ADRs [6]. ADRs are considered as one of the most important leading cause of mortality in many countries. Adverse drug effects not only accounts for significant morbidity and mortality but can also lead to increase in the length of hospital stay and health-care cost. The overall rate of adverse effects is estimated to be 6.5%, and 28% of these, ADRs are preventable. One of the meta-analyses found an adverse effect rate of 6.7% among hospitalized patients [7,8].

METHODS
Study type
This study was based on those patients who experienced on adverse reaction to medicine use and visited the outpatient department and ultimately reported to clinical pharmacist for drug information center.
1163 patients, 48 were given with salbutamol; dose varied from 4 mg/day up to 8 mg/day. Of them, a total of 12 patients were reported one or more adverse effects after use of this drug; among them, there were 33.3% incidence of seizures, 10.5% incidence of tremor, 17.6% of anorexia, and 5.2% incidence of nausea, 15.7% of anxiety, 5.2% of gastric, and 5.2% of headache. A total of 15 patients were given with beclomethasone in our study group; dose varied from 600 to 800 mg/day. Among them, 33.3% of patients had symptoms of seizures (tremor, palpitation, vertigo, and dizziness) and 2 (16.6%) patients were complained about palpitation after the use of beclomethasone. Hence, a total of 130 patients were complained about adverse event due to beclomethasone use. A total of 24 patients were given salmeterol combination with salbutamol for controlling work-related asthma. Among them, 28.5% patients were tremor and anorexia. One of them had complained about angioedema. It was occur in the dose of 2 mg/day. The patients were given with combinations they are beclomethasone + salbutamol for 15 patients, salmeterol + fluticasone 20 patients, and here beclomethasone + salbutamol caused bronchospasm ADRs in 7 (46.6%). Patient’s seizures, totally 252 patients were reported about ADR, when using beclomethasone + salbutamol total 15 patients were reported adverse effects and using salmeterol + fluticasone total 20 patients were reported in Table 1.

The present study was analyzed the statistical parameter by GraphPad Prism online calculator and observed the drug-induced ADRs such as palpitation, paradoxical bronchospasm, sweating, anorexia, and seizure were reported in Table 2.

**DISCUSSION**

The present study has reported the incidence and attempted to profile suspected ADRs due to anti-asthmatic drug in the asthmatic OPD setting in the informed consent. Bronchospasm is the most common adverse events reported in most of the drug utilization studies, but our studies aim for the common adverse events due to oral anti-asthmatic drugs only [9]. Hence, it has tremor as the most common ADR, not seizures. In a study conducted in Italy, 148,289 ADR reports have been collected, of these, 3416 (2.3%) were due to antiasthmatic agents. The most reported serious ADRs were severe seizures (about 50% of serious ADR report) mainly caused by beclomethasone and salbutamol [10]. Regarding fluticasone and bronchodilators, gastrointestinal system was the most frequently affected site. Anorexia and tremor were the most common adverse effect reported by patients to doctors followed by salmeterol. Beclomethasone alone or its combination with salbutamol caused a few incidences of seizures; all of them were occurred if beclomethasone was used with dose of 2 mg/day or more. Salbutamol-induced tremor occurred only if it was used more than 10 mg/day. Incidence of tremor was also common with the use of salmeterol, as expected from its mechanism of action and salmeterol combination produced more frequent incidents of tremor [11-14]. The study has found a few cases of pedal angioedema with montelukast use, in dose of 10 mg. Higher than 10 mg dose for leukotriene antagonist was not used. The patients who reported angioedema, their dose for montelukast was reduced to 7.5 mg/day, which did not, produced pedal angioedema to any of the subjects. In our study, out of 11 adverse effects, 77% were reported by male and 23% were reported by female patients. There were no serious events recorded, may be due to insulin was kept out of the measurement, which is the most common agent to cause fatal seizures. Most of the adverse events were managed by reducing the dose of the drug, and in some cases by stopping the drug such beclomethasone if patients had prolonged palpitation [15]. Adverse effects can perhaps also be reduced using less medication and with adequate knowledge of drug interactions. An anti-asthmatic drug ADR database built upon the basis of such studies conducted across multiple centers, though active collaboration of pulmonologist and pharmacologist can be a worthy long-term goal in the Indian context [1,6,17].

**CONCLUSION**

ADRs due to oral anti-asthmatic drug are a very frequent problem. Although they are not likely to be life-threatening, they can cause various types of

| S. no | Total number of patients (1163) | Beclomethasone (130) | Salmeterol+fluticasone (20) | Montelukast (15) |
|-------|--------------------------------|----------------------|-----------------------------|------------------|
| 1     | 40 (33.7)                      | 23 (17.98)           | 22 (16.92)                  |                  |
| 2     | 1 (0.83)                       |                      | 1 (7.69)                    |                  |
| 3     | 2 (1.69)                       |                      | 2 (1.69)                    |                  |
| 4     | 1 (0.83)                       |                      | 1 (0.76)                    |                  |
| 5     | 5 (4.33)                       |                      | 5 (3.83)                    |                  |
| 6     | 2 (1.69)                       |                      | 2 (1.69)                    |                  |
| 7     | 1 (0.83)                       |                      | 1 (0.76)                    |                  |
| 8     | 1 (0.83)                       |                      | 1 (0.76)                    |                  |
| 9     | 8 (6.83)                       |                      | 1 (0.76)                    |                  |
| 10    | 1 (0.83)                       |                      | 1 (0.76)                    |                  |
| 11    | 1 (0.83)                       |                      | 1 (0.76)                    |                  |
| 12    | 1 (0.83)                       |                      | 1 (0.76)                    |                  |
| 13    | 15 (12.5)                      |                      | 15 (12.5)                   |                  |

**Table 1**: ADR observed in work-induced asthmatic patients

| ADR | Beclomethasone+salbutamol (15) | Salmeterol+fluticasone (20) |
|-----|-------------------------------|-----------------------------|
| Seizure | 2 (13.3) | 1 (6.66) |
| Palpitation | 1 (4.16) | - |
| Angina | 1 (4.16) | - |
| Nausea | 1 (4.16) | - |
| Headache | 1 (4.16) | - |
| Anorexia | 1 (4.16) | - |
| Dizziness | 1 (4.16) | - |

**Table 2**: ADR observed in work-induced asthmatic patients
discomforts in many patients. Few large multicenter studies on this matter need to be done to build a strong anti-asthmatic drug-ADR database.

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Table 2: Statistical analysis of observed ADR in anti-asthmatic agents

| Observed ADR | Mean  | SD    | SEM   | Confidence interval (95%) | p value |
|--------------|-------|-------|-------|---------------------------|---------|
| Seizures     | 15.75 | 17.25 | 8.63  | -1174.70–1119.80          | 0.0001***|
| Tremor       | 5.20  | 9.98  | 4.47  | -1170.20–1145.40          | 0.001** |
| Palpitation  | 7.20  | 11.21 | 5.01  | -1169.72–1141.98          | 0.0001**|
| Anorexia     | 4.20  | 7.26  | 3.25  | -1167.81–1149.79          | 0.001** |
| Bronchospasm | 13.17 | 7.81  | 3.19  | -1158.03–1141.64          | 0.0001***|

ADR: Adverse drug reaction, SD: Standard deviation, SEM: Standard error of the mean