***Original Research Article***

# ADVERSE DRUG REACTION REPORTING SYSTEM AT DIFFERENT HOSPITALS OF LAHORE, PAKISTAN - AN EVALUATION AND PATIENT OUTCOME ANALYSIS

**Ghulam Mustafa[1], Saeed-ur-Rasheed[1], Muhammad Tahir Aziz[2]**

1 Department of Pharmacy, University of Sargodha, Sargodha, Pakistan
2 Department of Pharmacy, Shaukat Khanum Memorial Cancer Hospital, Lahore, Pakistan

## ABSTRACT

Adverse drugs reactions (ADRs) are known to be a major cause of morbidity and mortality. However, only a very little proportion is reported. ADRs contribute to the incidence of adverse events, resulting in increased health care costs. An increase in the number and quality of reports by improving ADR reporting system in hospitals, highlight the importance of ADR including general awareness could improve patient outcome and save healthcare costs. Ministry of Health has done some work but still major requirements are needed to run a proper ADR program. The first part of this project was to review the ADR reporting system in Pakistan hospitals, to determine the factors contributing to the ADR reporting rate and benchmark with developed countries. Data were collected by self-administered questionnaire. The response rate was 83.3%. 24 (80%) hospitals have no proper ADR system; five (16.7%) hospitals are targeting few of the drugs for ADR reporting while only one (3.3%) hospital has a proper ADR policy including online reporting system as well. Only seven (23.3%) hospitals have a policy of ADR reporting which is running under Pharmacy Department. The next part of the project was a survey of 84doctors and 52 Pharmacist selected from Lahore city, Pakistan to evaluate their involvement, understanding and reasons for reporting ADRs. A self-administered questionnaire was used to collect the data. Response rate obtained for the doctors was (39.3% n=33) and (67.3% n=35) for hospital pharmacists. Thirty three (39.3%) doctors and thirty four (65.4%) pharmacists knew how to report ADR within the hospital while 9 (10.7%) doctors and 13 (25%) Pharmacists knew about the ADR reporting to MOH. Factors that would encourage respondents to report ADRs included seriousness of reaction (75.8%), unusual reaction (63.6%), reaction to a new product (66.6%) and confidence in the diagnosis of ADR (31.5%). Similarly, the discouraging factors are uncertain association (65.7%), awareness (57.6%), and concern about legal liability (51.4%). It is observed that awareness of ADRs program need special attention with some concrete steps should be taken for the improvement of ADRs system in Pakistan. Continuous medical education, training and integration of ADR reporting into the clinical activities would definitely improve the patient outcome.

***Keywords*:** Adverse Drug Reaction, ADR Reporting System, Patient Outcome Analysis

***Corresponding author:*** **Dr. Muhammad Tahir Aziz** B.Pharm., M.Phil., Ph.D., Department of Pharmacy, Shaukat Khanum Memorial Cancer Hospital, Lahore, Pakistan. Email: C.: +92 321 488 7801; Email: tahir@skm.org.pk

## INTRODUCTION

An adverse drug reaction is any unintended response to a drug, which includes prescription, non–prescription, biological, and herbal drug products. Drug abuse, drug interactions, and overdoses are also monitored using the reporting system. A possible link between a drug and an adverse reaction is sufficient to file a report.

The concept of ADR reporting system is still in its infancy in Pakistan. This study is aimed at investigating ADR reporting system and to suggest possible ways of improving the method of reporting. By using questionnaire, the knowledge and attitude of doctors & pharmacists have been evaluated in different public and private hospitals of Lahore. The questionnaire sought the demographics of doctors & pharmacies, their knowledge and attitude to ADR reporting. Provision is also made for suggestions on the possible ways to improve ADR reporting. Doctors & pharmacies have not reported ADRs either due to lack of education and training on ADR reporting & because of lack of tradition. But now they should be encouraged to a large role in reporting ADRs.

The public health importance of adverse drug reactions in the hospitals cannot be ignored. It has long been a principle of practice of medicines, “Premium non-nicer” first of all be sure you do know harm. In 1955 addressing the American Medical Association, it was argued that one of the great hazards in the use of potent drugs is their inherent toxicity e.g. digitalis because its actual ingredients continue to be implicated in many adverse drug reactions. Most people get far more benefits from medicine than harm. Some patients experience undesirable effects by using medicines. These effects are so severe to required hospital treatment and a few will die e.g. (NSAIDS) cause 12,000 admissions per year due to GI bleeding and causing about 2000 deaths. They kill (one) 1 in 1200 people who use them for 2 months or more. From 39 various American Studies, the rate of serious ADR was calculated as 6.7% and the rate of fatal ADR was 0.3%, making ADR a serious health issue (1).

ADR reporting is the cornerstone of drug safety after the release of a drug into the market. It has been shown over the years that ADR reporting has provided early warning in drug safety.

In Pakistan there are no proper diagnostic ways to identify ADRs, so chances of ADRs incidences are greater in hospital out-patient departments. The studies of ADRs system are very rare. Irrational prescribing is common. Internationally a lot of work has been done in this sector. In Pakistan actually the environmental and so many other problems are different therefore the results are different.

It is a formal or informal process whereby verbal or written accounts of health care related adverse events are shared with others either internally within an organization or externally with other interested parties. The purpose of a reporting system is often to provide a medium for sharing lessons learned and opportunities for improvement, and to prevent recurrence of similar incidents in future. It is a reporting system whereby accounts of health care related adverse events are compelled by law, policy, or by any other formal means. A reporting system whereby verbal or written accounts of health care related adverse events are shared without the inclusion of any identifiable details of the patient or care providers involved. The information contained in anonymous reporting systems is often less complete than information contained in confidential reporting systems.

## METHODOLOGY

Prospective observational study was conducted to investigate the current ADR Reporting System at Different hospitals of Lahore and compare it with the ADR system in the developed countries. Information relevant to the study was accessed by circulating Questionnaire to the respondents after obtaining ethical clearance from the Hospital. Survey method involving Doctors, Pharmacists of different hospitals of Lahore was carried out

**Inclusion Criteria:** All specialized and tertiary care hospitals in public and private sectors in Lahore were included in the study.

**Exclusion Criteria:**The Hospitals where the health care professionals (Doctors, Pharmacists) were not willing to participate in the study and the ones who were on leave were excluded from the study.The hospitals where the Administration was reluctant to provide information about the ADR System were also excluded from the study.

**Sample Size:** A total of 84 Doctors and 52 Pharmacists from 30 different hospitals in Lahore participated in the study.

**Sampling technique:**A Random Sampling technique was applied to collect the sample.

**Sampling Procedure:**The relevant data or the related information was collected from all the health care professionals through one-to-one interview.

**Study Tool:**The initial draft of the Questionnaires was made by utilizing different ADR systems of developed countries, Literature evaluation, published research articles. In addition, this draft circulated to different health care professionals of different hospitals of Lahore and then finalized after necessary changes keeping in view the objectives of the study. Different questionnaires were designed to collect the required information. One of the questionnaires was developed to gather the general hospital information including ADR systems. Other two questionnaires were specific for Doctors and Pharmacists.

**Pre Testing:** Pre Testing is critical for identifying problems for both respondents and interviewers. No matter how experienced you are in developing questionnaire or how “routine” the survey might he considered, it is always important to pre-test your instrument before it is printed and fielded. Give the questionnaire to a small group of health care professionals, who preferably know little or nothing about the research itself. Ask them to read the questionnaire to see if they, too, can clearly understand what is required and whether the flow makes sense to them. After Pre-Testing, some changes were made on the basis of responses. There was some question that didn’t work. I have excluded these questions and modified some questions in such a manner that might work next time. Order of some questions was also changed to make it logical and systematic.

**Field Experience & Data Collection:**After pre-testing, the next step was data collection. The data collection lasted for four months. Considering the behavior of the health care professionals and response from the Hospital Administration, some hospitals were excluded from the study. Initially, difficulties were faced in collecting the data, but it was assured that the study is meant for academic purpose only and all information will be kept confidential. However, the staff of some hospitals was very cooperative.

**Statistical Analysis:**Statistical Analysis was conducted by using the statistical package – SPSS (statistical package for social sciences), Version 11.5.This analysis was carried out in two steps:

1) Descriptive Analysis
2) Inferential Analysis

Arithmetic Mean (Average) was calculated for quantitative variables, while for qualitative variables, frequencies and percentages were measured. Histogram was obtained for quantitative variables, while Pie chart and Bar chart were used to express the graphical picture of qualitative variables.

Pearson's Chi-Square test was used to measure the associations between different Variables in this study. For 2x2 Contingency table, where observed frequency less than 5, Fisher's Exact test was used to measure the associations between different variables.

## RESULTS AND DISCUSSION

Twenty-two (73.3%) hospitals were acute care / general, while twenty (66.7%) hospitals were teaching. Fifteen (50.0%) hospitals have more than or equal to 500 beds and in four (13.3%) hospitals, there were less than 100 beds. eleven (36.7%) hospitals have between 1000-15000 no of admissions and six (20.0%) hospitals show 45000 – 60000 admissions. In fifteen (50.0%) hospitals there are 0-150 doctors and eleven (36.7%) hospitals have between 150-300 doctors and one (3.3%) hospital has 750-900 doctors.

Only seven (23.3%) hospitals have ADR reporting policy while in ten (33.3%) hospitals the pharmacy department has an ADR reporting policy. In few hospitals, certain reasons have been described for the absence of an ADR reporting policy e.g; no clinical set-up in the hospital, lack of interest and absence of separate pharmacy department in the hospital. Majority of hospitals have no ADR reporting policy. In five (16.7%) hospitals, all drugs are targeted for ADR reporting. While in one (3.3%) hospitals, only few drugs and MOH listed drugs are targeted for ADR reporting.

Out of 33 doctors, six (18.2%) doctors and out of 35 pharmacists, three (8.6%) pharmacists suggest that "doctors" should do documentation of ADR. Similarly seven (21.2%) doctors and ten (28.6%) pharmacists suggest "pharmacists" to do documentation of ADR.

One (3.3%) hospital respond to drug assays, microbiology and biochemistry tests for screening of suspected ADRs. No hospital shows response regarding use of triggers to identify possible ADRs. Five (16.7%) hospitals respond to "doctors", while three (10.0%) hospitals respond to "pharmacists" and two (6.7%) hospitals consider both "doctors & pharmacists" as the concerned personnel involved in ADR reporting. In ten (33.3%) hospitals, pharmacy department is involved in ADR reporting. One (3.3%) hospital responds to formulary alteration, information bulletins and regular reporting to MOH to prevent ADRs. One (3.3%) hospital shows that patient is informed through e-mail or verbally. Four (13.3%) hospitals respond to add information on the discharge slip. Eleven (36.7%) hospitals respond to "No", regarding any reward / fee for reporting ADRs in hospitals.

Patient reporting ADR can be a good solution and can help to improve the ADR reporting program. Six countries provided information on patient reporting system while summary data was obtained from four countries. Possible new ADRs were identified by patient report that had not previously been reported, by health professionals. The quality of patients reports appeared to be similar to that of health professional reports. Some evidences showed that patients reported an

ADR when they came to know that their health professional had not listened to their concerns properly. In the beginning, patient reports might be time consuming to be processed. All evidences indicated that patients reporting of suspected ADRs had potential benefits than drawbacks(2).

Thirty three (39.3%) doctors and 35 (67.3%) pharmacists gave response in this study. Thirty three (39.3%) of doctors and thirty four (65.4%) of pharmacists know how to report ADRs within the hospital. While nine (10.7%) of doctors and thirteen (25%) of pharmacists know about ADR reporting to MOH. In this project, 136 health care professional participated. Among 84 doctors, sixty two (73.8%) were males and twenty two (26.2%) were females. Similarly among 52 pharmacists, twenty two (42.3%) were males and thirty (57.7%) were females. Thirty Nine (46.7%) doctors have registration period from 7-10 years followed by sixty four (76.2%) doctors with the registration duration under 7 years. Similarly thirty five (67.3%) pharmacists have registration duration under 7 years followed by ten (19.2%) pharmacists between 7-10 years. The working experience of seventy four (88.1%) doctors is below 7 years and five (6.0%) have between 7-10 years. In the same way, forty eight (92.3%) pharmacists have working experience under 7 years and three (5.8%) above 10 years and one (1.9%) between 7-10 years.

Thirty three (39.9%) doctors have knowledge about ADR reporting within the hospital while nine (10.7%) know how to report ADR to MOH. Similarly thirty four (65.4%) pharmacists have awareness about ADR reporting within the hospital and thirteen (25.0%) know report ADRs to MOH. The average awareness about ADRs is 50.9% and 49.1% for doctors and pharmacists respectively.

The involvement of pharmacists in ADR reporting pharmacists actual contributions were evaluated by using an international questionnaire based survey among countries participating in the WHO drug monitoring program in September 2002 (3). The respondents showed their assessment for quality and significance of contributions out of 68 participating countries, 41 responded by returning the questionnaire. In the countries having more experience and with greater number of pharmacists ADR reports, the appreciation is high whereas the countries that received fewer reports from pharmacists gave lower scores to their contribution. The improvement in the international adverse drug reaction reporting system was possible by the specific contribution of pharmacists.

The factors that discourage respondents from reporting ADR are uncertain association (60.6%), awareness (57.6%), report forms not readily available (57.6%), Concern about legal liability (51.4%). From hypothetical ADR questions, the respondents liked to report thrombocytopenia with heparin (48.5%), duodenal ulcer with Diclofenac (45.4%), Neutropenia with ACE-Inhibitors (42.9%). The average awareness in doctors is 32.5% and in pharmacists 30.4%.

Doctors were Shows un-awareness about ADR of “Headache with venlafaxine” (87.9%) and information about weight loss with venlafaxine (81.8%). Similarly pharmacists show more unawareness regarding the following factors i.e.; Constipation with Montelukast (82.9%), headache with venlafaxine (91.4%). The average unawareness in doctors is (67.5%) which is less than pharmacists (69.6%).

In Pakistan, people consume drugs at a large scale. In the market, counterfeit and substandard drugs are available. These drugs belonged to alternative systems of medicine like Unani, Homeopathy and the drugs which have been banned in developed countries. These factors indicate that a comprehensive ADR reporting system should be established in Pakistan. One of

the examples of three German departments of clinical pharmacology Jena, Dresden, Rostock, served as pharmacovigilancecenters in collaboration with pharmaco-epidemiology Research Group of the University of Munich improved the spontaneous substantial reporting system (4). It is possible to remove harmful drugs from the market by using a proper ADR system.

In Pakistan, the concept of ADR reporting system is in the very early stages as compared to rest of the world. We are facing the problem of poor post marketing surveillance. Therefore, Ministry of Health (MOH) should initiate the National Pharmacovigilance Program and under this program various peripheral, regional and zonal pharmacovigilancecentres should be established. Pharmacovigilance is the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects of medicines. It is an important and integral part of clinical research. Developed countries have done major advancement in this field. In Pakistan not much has been achieved, so there is an immense need to understand and implement pharmacovigilance.

Pakistan should join World Health Organization (WHO) adverse drug reaction monitoring program based in Uppsala, Sweden (5). This program is meant to detect, evaluate, to study ADR and to inform prescribing physicians. There must be a central drugs standard control body that would launch NPP under the influence of Directorate General of Health Services, Ministry of Health. The basic purpose of this program is to analyze and achieve ADR data for making regulatory decisions regarding drugs marketed in Pakistan. The physicians, pharmacists and nurses can complete prescribed ADR form and report to the nearest Peripheral Pharmacovigilance Centre. Then the report may be forward to the regional center. It can make analysis and then submit to zonal center where the data will be statistically analyzed and send to the global Pharmacovigilance database managed by WHO Uppsala Monitoring Centre in Sweden. The National Pharmacovigilance Advisory Committee (Constituted by MOH) will review the final report based on analyzed data.

Majority of People in Pakistan visit Government hospitals to get health care facilities which can be helpful to generate good ADR data. Initially a culture of ADR reporting has to be created among clinicians, pharmacists and junior doctors. Further Government has to make it mandatory for health care providers to report ADRs. Lack of awareness, education and training and time are potent reasons for showing no interest in reporting ADRs. So education and training programs will have to carry out for health care professionals to produce the habit of ADR reporting. There should be strong collaboration between clinical departments and department of pharmacology. For postgraduate students, ADR monitoring programs should be taught during training. Even the undergraduate students and interns should be given lectures on ADR reporting. Pharmacovigilance programs can be provided to all nurses and other allied health staff. All Government hospitals as well as medical colleges should adopt this strategy to generate a real ADR database for the people of Pakistan. Even a computer based on-line reporting system could be launched as utilized by many developed countries.

## REFERENCES:

1. Jason Lazarou, MSc; Bruce H. et al, Incidence of adverse drug reactions in hospitalized patents Vol. 279 No. 15, April 15, 1998. The Journal of the American Medical Association.

2. A Blenkinsopp, P Wikie, M Wang, and P ARoutledge, et al, Patient reporting of suspected adverse drug reactions: a review of published literature and international experience. Br J ClinPharmacol. 2007 February; 63(2):148-156.

3. Kees van Grootheest, MD, Sten Olsson, MSc, Pharm, Mary Couper, MD, Lolkje de jong van den Berg, PhD, PharmD, et al, Pharmacist, role in reporting adverse drug reactions in an international perspective. Pharmacoepidemiology and Drug Safety Volume 13 issue 7, pages 457 – 464 Published Online: 15 Sep 2003.

4. Hippious M, Humaid B, Sicker T, Hoffmann A, Gottler M, Hasford J, et al, Adverse drug reaction monitoring – digitoxin over dosage in the elderly. In J ClinPharmacolTher 2001; 39: 336-43.

5. Wester K, Jonsson A, Spigset O, Hagg S, et al, Spontaneously reported fatal suspected adverse drug reactions: a 10-year survey from Sweden. Pharmacopidemiol Drug Saf. 2007 Feb; 16(2): 173-80.