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# A CASE STUDY ON PHARMACOVIGILANCE AND PRESCRIBING TREND OF ANTIHYPERTENSIVE THERAPY IN GOVERNMENT HOSPITAL OF HYDERABAD, PAKISTAN

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## ABSTRACT

The purpose of this study was to evaluate the adverse drug reactions (ADRs) and prescribing trend of antihypertensive therapy in outpatient department of a government hospital setting. According to WHO 2012 fact sheet, one of the dominant causes of death in the world is hypertension; each year 7.1 million people die due to high blood pressure. ADRs are one of the major frequent problems and also one of the leading causes of mortality and morbidity in health care facilities all over the world. A descriptive observational study was conducted by collecting the patient's feedback on predesigned questionnaire per WHO monitoring guidelines. The data was evaluated by using authentic references of WHO probability scale and Lexi-comp. The observed results showed that out of 160 patients, 58.12%, 41.88% were male and female respectively. A total of 30 (18.75%) ADRs were reported whose high percentages were seen in male i.e 22.58% as compared to female 13.43%.The most prescribing therapy for management of hypertensive patients were ARBs (39.38%), while diuretics were the least prescribed (5.62%) therapy, while ADRs were seen mostly in users of beta blockers (21.42%) and Calcium channel blockers (21.05%). Among the drugs of different classes of antihypertensive, mostly dry cough

(15%) due to Telmisartan and 15.38% cough cases due to losartan were seen, while hypotension (10.71%) was seen due to beta blockers. Pedal edema (14.28%) was the most common ADR due to amlodipine and 20% in nifedipine. The present work will be helpful for healthcare professionals in rationale selection of drug therapy for management of hypertension and approaches to decrease the ADRs due to antihypertensive therapy. Pharmacovigilance is an opportunity for pharmacist to provide best patient care in Pakistan.

**Keywords: Pharmacovigilance, Adverse Drug Reactions, Hypertension, Antihypertensive Therapy and Pakistan**

## INTRODUCTION

The utmost important area during the therapy of a patient is pharmacovigilance and is ignored still in our society by healthcare professionals. In numerous studies, considering adverse drug reactions (ADRs) during the therapy helps to curb from drug induced illness and death **[1]**.

According to World Health Organization, Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem **[2]**. With this ADR was defined since last 30 years as, 'an appreciably unpleasant reaction harmful or, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product' **[3]**. According to Lazarous *et al.*, **[4]**, the dominating cause of death is between every fourth to Sixth due to overall serious ADRs in United States which contributed up to 6.7%. A Study conducted in India, in which 57 ADRs were detected and 63% were due to drug related on the basis of WHO scale which also notify the severe ADRs up to 12% and 49% were moderate **[5]**. One of the serious cause for hospital admissions were ADRs and accomplice 3.4% out of 9.8% of overall rate **[6]**. Another prospective study showed that the patients mostly experienced fatal ADRs which accounts 1.8% in 3.7% of hospitalized patients and 18.3% were associated with cardiovascular drugs **[7]**. Most common ADRS usually associated with antihypertensive drugs that may reduce the margin of treatment regimen and patient adherence mostly in younger ones, a major hurdle for controlling hypertension **[8]**. According to a general practice survey, those patients were on antihypertensive therapy revealed that the ADRs mostly due to the

users of Beta blockers and lowers the frequency in diuretic users **[9]**. While another study showed that the ADRs were experienced in those patients using ACE inhibitors were common cough, hypotension and hyperkalemia and mostly above ADRs were rectified when the drug stopped **[10]**. A study conducted in Urban areas of Pakistan and the outcomes of that study were, the most common class of antihypertensive medications that prescribed common in society were β-blockers (41.9%), angiotensin-converting enzyme (ACE) inhibitors (32.2%), and calcium channel blockers (7.1%). Thiazide diuretics were rarely prescribed (4.2%) by GPs **[11]**. Safety profile of all drugs is therefore required to be monitored on regular basis along with the review of therapeutic rationale in the guidance of add on information putting forward ADR monitoring activities mostly in Chronic ailments require more efficient monitoring such as hypertension, that is found to be asymptomatic disorder and its long term therapy may cause higher risk of ADRs.

## MATERIALS AND METHODS

The aim of this study was to monitor the ADRs and prescription writing trend of antihypertensive therapy in government hospital of Hyderabad, Pakistan. The descriptive observational study proposal was checked and approved by Scrutiny committee of Board of advanced studies and research (B.A.S.R), University of Sindh Jamshoro, Pakistan. The duration of the study was 3 months in which 160 patients were interviewed via purposive sampling after the written informed consent, in medicine and Cardiac outpatient department. The collected information were noted on approved designed questionnaire based on World health organization guidelines **[12]** and all drug related ADRs were further analyzed according to World health organization assessment scale **[13]** and drug information handbook by LEXICOMP **[14]**.

### Inclusion Criteria

Patients aged 18 years and above, with confirmed diagnosis of hypertension and taking at least one anti-hypertensive drug were included in this study regardless of gender.

### Exclusion Criteria

All mentally compromised or unconscious patients, febrile, Drug addicts, pregnancy/lactating women and patients unable to respond the verbal questions were excluded from this study.

### Statistical Analysis

Descriptive statistics and Microsoft office were used for analyzing and systematic arrangement of data. The collected data were

further analyzed through the software of statistical package SPSS; version 20.0.

**RESULTS**

A total of 160 hypertensive patients were interviewed [93 male (58.12%) and 67 female (41.88%] in a total duration of study. **Table 1** presents some characteristics of patients that mostly 36.87 % were aged between 39-48 years while only 5.62 % were between the aged of 18-28 years. The socio-economic status were also analyzed that a large proportion of patients (61.88%) were unemployed and only 38.12% were employed, Table-1 also shows that 73.75% patients respond positively with history of hypertension and 26.25% respond negatively, while maximum number of patients 38.12% were diagnosed hypertension between 3-5 years, 30.62% were diagnosed with more than 5 years, while only 8.75 % were diagnosed less than 1 year of hypertension. It was also noted that mostly combination therapies (73.125%) were prescribed as compared to monotherapy (26.875%) shows in **Table 2**.

A total of 30 (18.75%) adverse drug reactions were observed with high percentage in males 22.58% as compared to females 13.43%, while 77.42% of males and 86.57% of females patients did not experienced any ADR **(Table 3)**. The trend of therapy that mostly prescribed with occurrence of ADRs associated with different classes of antihypertensive were also noticed in our study, that mostly a high frequency of 63 (39.38%) patients were prescribed with Angiotensin receptor blockers (ARBs), 42 (26.25%) patients with beta blockers, 27 (16.88%) with Angiotensin converting enzyme inhibitors (ACE), 19 (11.87%) with calcium channel blockers and only 9 (5.62%) with diuretics. A high percentage of ADRS were reported with beta blockers 21.42% then Calcium channel blockers 21.02% and lastly only 11.11% with diuretics, while the percentages of ADRs not present were also given in **Table 4**.

In **Table 5**, 11 patients experienced ADRs related with ARBs viz, 6 patients (15%) were reported dry cough with Telmisartan, 2 (15.38%) patients of cough and 1 (7.69%) of patients experienced itching with losartan, 10% each headache and skin rash with olmesartan respectively. In Beta blockers maximum number of patients were on Atenolol with 7 numbers of ADRs were reported viz hypotension (10.71%), bradycardia (3.57%), headache (3.57%), and vertigo (7.14%) while 11 patients were on propanolol, 1 (9.09%) patient reported dizziness, and 3 patients were on metoprolol experienced 1 (33.33%) patient of G.I irritation. Among these a total of 5 ADRs

were experienced with maximum 15 % of patients on cough with ramipril and 14.28 % with enalapril. While 14.28% of patients experienced pedal edema and 7.14% xerostomia with Amlodipine. 20% of patients also experienced pedal edema with nifidipine. Among the diuretics only 11.11% patients feel pain in leg with hydrochlorothiazide. World health organization assessment of ADRs scale was also used in our study period (Table-6) divulged that 7 ADRs were assessed certainly that it was due to drugs and 12 were in category of probable to drugs, while 9 ADRs were found in the class of possible and 2 were classified in unlikely class of assessment scale of World Health Organization. It was also noted that those patients who experienced ADRs due to their antihypertensive therapy were not discussed their symptoms with health care providers (HCPs) and the percentage was 90% while only 10% of patients discussed their symptoms with HCPs.

**Table 1: Characteristics of Respondent**

| S. NO | CHARACTERISTICS | FREQUENCY | % (PERCENTAGE) |
|---|---|---|---|
| 1 | GENDER | | |
| | Male | 93 | 58.12 |
| | Female | 67 | 41.88 |
| 2 | AGE | | |
| | ≥18≤28 | 9 | 5.62 |
| | ≥29≤38 | 31 | 19.37 |
| | ≥39≤48 | 59 | 36.87 |
| | ≥49≤58 | 47 | 29.37 |
| | ≥59 | 14 | 8.75 |
| 3 | OCCUPATION | | |
| | Employed | 61 | 38.12 |
| | Unemployed | 99 | 61.88 |
| 4 | HISTORY OF HYPERTENSION | | |
| | Yes | 118 | 73.75 |
| | No | 42 | 26.25 |
| 5 | DURATION OF HYPERTENSION | | |
| | Less than 1 y | 14 | 8.75 |
| | 1-3 y | 36 | 22.5 |
| | 3-5 y | 61 | 38.12 |
| | More than 5 y | 49 | 30.62 |

**Table 2: Patients Therapy**

| S. NO | THERAPY | FREQUENCY | % (PERCENTAGE) |
|---|---|---|---|
| 1 | Monotherapy | 43 | 26.875 |
| 2 | Combination therapy | 117 | 73.125 |
| 3 | Total | 160 | 100 |

**Table 3: Number of ADRs Present in Respondents**

| S. NO | GENDER | TOTAL NO: OF PTS | ADRS PRESENT | % OF ADRS | ADRS NOT PRESENT | % OF ADRS NOT PRESENT |
|---|---|---|---|---|---|---|
| 1 | Male | 93 | 21 | 22.58% | 72 | 77.42% |
| 2 | Female | 67 | 9 | 13.43% | 58 | 86.57% |
| 3 | Total | 160 | 30 | 18.75% | 130 | 81.25% |

**Table 4: Trend of Prescribed Drugs with ADRs Report**

| S. NO | ANTIHYPERTENSIVE CLASS | NO: OF PATIENTS WITH % | ADRS PRESENT WITH % | ADRS ABSENT WITH % |
|---|---|---|---|---|
| 1 | Angiotensin receptor blockers | 63 (39.38%) | 11 (17.46%) | 52 (82.54%) |
| 2 | Beta Blockers | 42 (26.25%) | 9 (21.42%) | 33 (78.57%) |
| 3 | Angiotensin converting enzyme inhibitors | 27 (16.88%) | 5 (18.51%) | 22 (81.48%) |
| 4 | Calcium Channel Blockers | 19 (11.87%) | 4 (21.05%) | 15 (78.95%) |
| 5 | Diuretics | 9 (5.62%) | 1 (11.11%) | 8 (88.89%) |
| 6 | Total | 160 (100%) | 30 (18.75%) | 130 (81.25%) |

**Table 5: Class of Antihypertensive Therapy Associated with ADRs**

| S. NO | DRUGS | NO: OF PTS RECEIVING DRUGS | NO: OF PTS WITH ADRS | ADRS EXPERIENCED WITH % |
|---|---|---|---|---|
| 1 | Telmisartan | 40 | 6 | Dry cough=6 (15%) |
| 2 | Losartan | 13 | 3 | Cough=2 (15.38%)<br>Itching=1 (7.69%) |
| 3 | Olmesartan | 10 | 2 | Headache=1 (10%)<br>Skin rash=1 (10%) |
| 4 | Atenolol | 28 | 7 | Hypotension=3 (10.71%)<br>Bradycardia=1 (3.57%)<br>Headache=1 (3.57%)<br>Vertigo=2 (7.14%) |
| 5 | Propanolol | 11 | 1 | Dizziness=1 (9.09%) |
| 6 | Metoprolol | 3 | 1 | G.I Irritation=1 (33.33%) |
| 7 | Ramipril | 20 | 4 | Cough=3 (15%)<br>Hypotension=1 (5%) |
| 8 | Enalapiril | 7 | 1 | Cough=1 (14.28%) |
| 9 | Amlodipine | 14 | 3 | Xerostomia=1 (7.14%)<br>Pedal edema=2 (14.28%) |
| 10 | Nifidipine | 5 | 1 | Pedal edema=1 (20%) |
| 11 | Hydrochlorothiazide | 9 | 1 | Pain in legs=1 (11.11%) |

**Table 6: World Health Organization Probability Assessment Scale of ADRs**

| PROBABILITY SCALE | NO: OF ADRS |
|---|---|
| Certain | 7 |
| Probable | 12 |
| Possible | 9 |
| Unlikely | 2 |

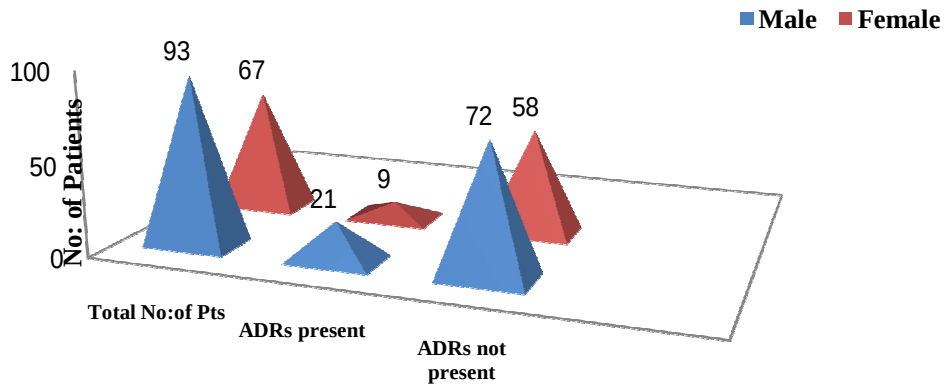


**Figure 1: Graphical Representation of Presence and Absence of ADRs with Respect to Male and Female**

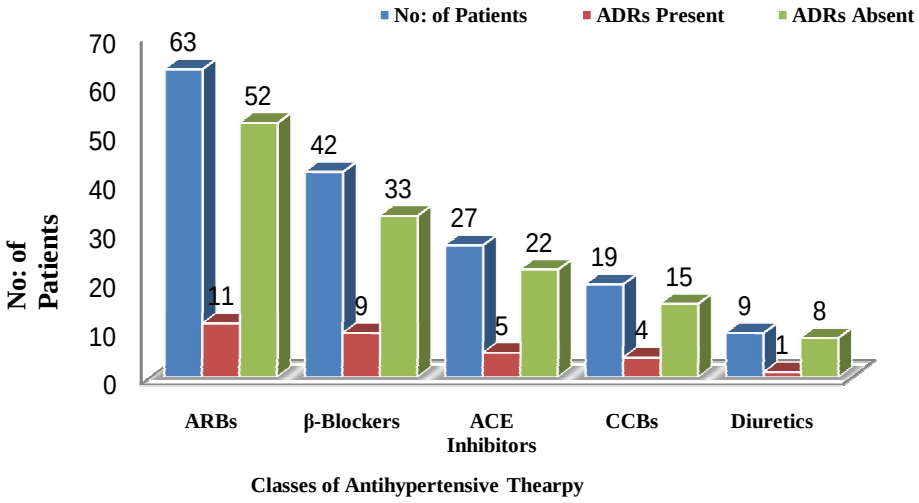


**Figure 2: Trend of Prescribed Drugs with ADRs Report**

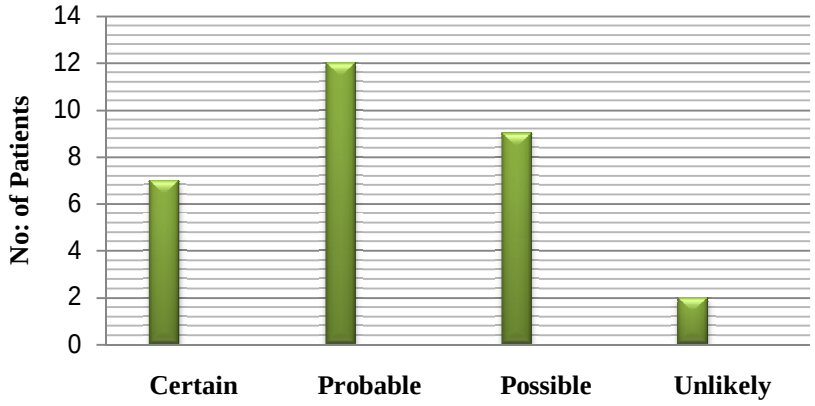


**Figure 3: World Health Organization Probability Assessment Scale of ADRs**

**DISCUSSION**

The demographic details in our study showed the population that male gender were dominant over female, then the probability of ADRs may enhanced in males as compared to females, so in our study male population had more prevalence of ADRs which was similar to that reported in other study **[15]**. While some previous studies reported that ADRs were more common in females as compared to males **[16, 17]**. Majority of ADRs were found in older patients i.e., aged between 39-48 years (n = 59) as compared to younger ones i.e., less than 28 years (n = 9). The reason behind that may be sedentary life style and socio-economic status such as unemployment and other household burdens, while another study which was conducted by Munir Pirmohamed *et. al*., 2004, in U.K. reported a maximum number of patients in the age group between 65-83 years **[18]**. With this our study shows that 22.5% of patients had hypertension for 1-3 years that nearly same to another study conducted in different area of Pakistan **[19]**. It was also found in this study that the most common class of antihypertensive therapy was prescribed to patients were angiotensin receptors blockers and a very few patients were prescribed with diuretics. Another finding of this study that mostly ADRs were reported in those patients using β-blockers (21.42%), and less ADRs reported using diuretic therapy and nearly same finding also reported by Olsen-et-al in Norway **[9]**. Hypotension was the most common adverse drug reaction that was reported due to beta blockers while dry cough and cough were common due to telmisartan and Losartan respectively. Results showed that the major complaints of the patients was cough that were on ramipril and enalapril but the study conducted in a teaching hospital had high percentage of cough due to ramipril and enalapril as compared to the results of this study **[10]**. It is recommended that only essential medicines should be prescribed in the management of hypertension. The common complaints with the usage of amlodipine were pedal oedema, and xerostomia. Oedema has been reported as the most common problem with amlodipine **[20]**. The patients who experienced any ADR were also reported to the HCPs for better understanding the therapy but here our study found that a very low number of patients (10%) were discussed their ADRs symptoms, so they may cause serious problem in future by continuing the therapy.

**CONCLUSION**

This study shows that the ADRs are persistently growing and widely spreading in our society, the major reasons behind it are;

improper patient counseling, irrational use of medication, lack of patient-prescribers communication. In order to curb this growing trend of ADRs, it is required to focus the above discussed facts and to keenly look ahead for their solution. It is also very important to implement and execute the new and apt public health policies in order to ensure rationale therapy for hypertensive patients. However it is also concluded that the coordination between HCPs and patients is very important to improve the quality of therapy and to prevent the future happenings of the ADRs. All the data shared in this study would be useful in establishing the further pharmacovigilance policies and the significant role of the pharmacist in the health care system in our society.

**Competing Interests**

The authors declare that they have no competing interests.

**Authors' Contributions**

All authors read and approved the final manuscript.

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