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A STUDY ON CLINICAL PATTERN OF ADVERSE DRUG REACTIONS TO THE DRUGS USED FOR HYPERTENSION AND ASSESMENT OF MEDICATION KNOWLEDGE IN SUCH PATIENTS.

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Conflicts of Interest: Nil

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ABSTRACT

The aim of the present study was to monitor adverse drug reactions associated with antihypertensive drugs. due to its high prevalence, Hypertension is a major health problem throughout the world and very less studies has been aimed at assessing the patient's knowledge and awareness about hypertension and adherence to antihypertensive medication among hypertensive patients .Hypertension is a major health problem and risk factor for stroke, coronary heart diseases and antihypertensive treatment is used to reduce renal and cardiovascular diseases by lowering blood pressure. Occurrence of adverse reactions among hypertensive patients could prevent or delay patients from achieving desired therapeutic goals. The study was conducted by one to one patient interview using a questionnaire-based medication knowledge form, Adverse Drug Reaction Monitoring Form drafted according to the World Health Organisation Monitoring Guidelines. A total of 86 adverse drug reactions were observed in 127 hypertensive patients during the 6 month study. In this study the ADRs were found probable (51.16%), possible (32.56%), unclassifiable (11.63%) and unlikely (4.65%) by using WHO causality assessment scale. By using Naranjo algorithm scale it was found that ADRs were possible in 77.91% and probable in 22.09% of cases. This study also found that amlodipine was responsible for most of the ADRs and among the entire ADRs reported headache was the commonest followed by dizziness, pedal oedema, fatigue, abdominal pain, dry cough, breathlessness, bradycardia, muscle cramps, sedation, diarrhoea and irritation all over thebody. After counseling by clinical pharmacist medication knowledge was found to be increased.

Keywords: Adverse drug reaction, medication knowledge, hypertension

INTRODUCTION

Hypertension is defined as systolic blood pressure of ≥ 140 mm Hg and diastolic blood pressure of ≥ 90 mm Hg, though the risk appears to increase even with blood pressure above 120/80 mm Hg. Hypertension or high blood pressure is a major public health problem due to increased morbidity, mortality It is an iceberg condition and the prevalence of hypertension has been considered as an increasing "silent killer" problem. Reasons for this growing trend is due to the unhealthy lifestyle practices, lack of awareness, distorted public health system, physicians not following the standard guidelines in treating hypertension and non-compliance to hypertension therapy. Keeping the blood pressure at an optimum level helps to prevent cardiovascular complications like stroke, myocardial infarction (MI), renal failure and mortality; this has been confirmed in epidemiological and interventional studies.[(1,2)]In developed countries, diastolic pressure is more than 90 mm Hg in about 25% adults; this prevalence is almost same in developing countries. where it is seen in 10% to 20% adults. Hypertension accounts for 20-50% of all deaths.Hypertension is present in all populations and it steadily increases during the first two decades of life. With advancing age, the prevalence of hypertension also increases.Systolic blood pressure is higher for adult males than females, but in older individuals, the age related rate rise is steeper for females. A middle aged or elderly individual has 90% chance of developing hypertension in his or her lifetime. Both genetic and environmental factors play a major role to produce regional and racial changes in blood pressure and prevalence of hypertension.In India the prevalence of hypertension was 35 in males and 36 in females per 1000 in rural population and 60 in males and 70 in females per 1000 in the urban population[(3,4,5)].

Classification[6,7,8] *:*

A. Essential or primary hypertension:

A patient is said to have essential hypertension when no particular cause of hypertension can be found.

B. Secondary hypertension:

A patient is said to have secondary hypertension when a particular cause of hypertension can be found.

Risk factors:

Risk factors of hypertension include age, gender, hereditary factors, race, overweight, increased salt and saturated fat intake, decreased intake of dietary fiber, alcohol consumption, sedentary lifestyle, high socio- economic status and environmental stress.

Clinical features:

Most hypertensive patients will not have any specific symptoms. Headache is the commonest symptom seen in patients with severehypertension; other symptoms include palpitations, dizziness, impotence and easy fatigability.

Treatment:

Lifestyle interventions:

Lifestyle changes help in prevention and treatment of hypertension**.** Hence, they are advised for individuals with prehypertension and for hypertensive individuals as an addition to drugs.

Lifestyle changes to manage hypertension[15] *:*

- Reduction of Weight with body mass index (BMI) < 25 kg/m^2
- Salt restricted diet < 6 g of NaCl/day
- Follow DASH (Dietary Approaches to Stop Hypertension) diet plan.

Diet should include vegetables, fruits and products with reduced amount of fat.

- Reduction of alcohol consumption
- Regular physical activity

Pharmacotherapy[15] *:*

Drug therapy is recommended for individuals with blood pressure ≥140/90 mmHg. Choice of antihypertensive agents and their combinations should depend on age, severity of hypertension, cardiovascular risk factors, comorbid conditions, cost, side effects and frequency of dosing. The antihypertensive drugs include α-blockers, β-blockers, CCBs (calcium channel blockers), diuretics, ACE inhibitors (Angiotensin converting enzyme inhibitors), ARBs (Angiotensin receptor blockers) etc.; these are either used as monotherapy or as combination therapy.

Antihypertensive drugs:

Lowering of blood pressure by antihypertensive drugs helps to prevent blood vessel damage and to reduce morbidity and mortality. Antihypertensive drugs acts by interfering normal arterial pressure regulation. Knowledge of mechanisms of antihypertensive drugs helps to predict their efficacy and toxicity resulting in rational use of these drugs.[16]

Classification of antihypertensive drugs[17] *:*

Diuretics:

- Thiazides and related agents: Hydrochlorothiazide, chlorthalidone, chlorothiazide, indapamide, methylclothiazide and metolazone.
- Loop diuretics: Furosemide, torsemide, bumetanide, and ethacrynic acid.
- K^+ sparing diuretics: Spironolactone, amiloride and triamterene.

Sympatholytic drugs:

- β-blockers: Metoprolol, betaxolol, nadolol, bisoprolol, esmolol, timolol, nebivolol, penbutolol, atenolol, pindolol and propranolol.
- α-blockers: Prazosin, terazosin, doxazosin, phenoxybenzamine and phentolamine.
- Mixed α and β receptor blockers: Labetalol and carvedilol.
- Centrally acting adrenergic agents: Methyldopa, clonidine, guanabenz and guanfacine.
- Adrenergic neuron blocking agents: Guanadrel and reserpine.

Current status of Pharmacovigilance in India[20-25] *:*

In the world, India stands fourth among producers of pharmaceuticals. It is rising as one of the clinical trial hub in the world. Our country introduces many new drugs and hence there is a need for an energetic pharmacovigilance system in the country to guard the people from the possible harm that may be caused by some of these new drugs. Evidently conscious about the extent of the task, the Central

Drugs Standard Control Organization (CDSCO) has started a well planned and highly participative National Pharmacovigilance Program. It is mainly based on the recommendations made in the WHO document titled "Safety Monitoring of Medicinal Products Guidelines for Setting up and Running a Pharmacovigilance Centre". Pharmacovigilance has not come up well in India and the subject is in its early stage. The rate of pharmacovigilance in India is less than 1% when compared with the world rate of 5%. This is because of lack of knowledge about the subject and also deficiency in training. Now a days in India, pharmacovigilance situation has been progressing step by step than what it was in the past.

Antihypertensive drugs are more prone for development of adverse drug reactions (ADRs); this decreases the available treatment options and also reduces the compliance of the patients; this in turn hinders blood pressure control.Hypertension is a disorder that requires long term therapy; this predisposes to ADRs. As many studies do not include pregnant ladies, the elderly and patients with many diseases, the study population may not be the real world where drug has to be used eventually; hence, safety monitoring has to be done to get information regarding ADRs to have a better treatment module and to prevent morbidity and mortality due to ADRs. Currently, ADR monitoring in India is in its infancy stage.

Many new antihypertensive drugs are now available, which alter quality of life of the patient in a better way. Thus a regular scrutinization is needed by systematic audit that gives feedback to doctors, which will help to prescribe drugs rationally and to avoid ADRs.

Adverse Drug Reactions: Classification, Mechanism And Interactions

The World Health Organization (WHO) defines a drug/medicine such as "any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient." As per WHO following are the definitions for adverse event/ adverse experience (AE) and adverse drug reaction (ADR).

Adverse Event (Or Adverse Experience)

"Any unwanted medical occurrence that may induce during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment."

Adverse Drug Reaction (ADR)

A response to a drug which may be noxious and unintended, and which occurs at doses generally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

ICH (International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use) guideline of Clinical Safety Data Management (E2A guidelines) further describes the definition of adverse drug reactions (ADR) during the pre-approval (before marketing of the pharmaceutical product) phase.

Classification of ADR[24]

Pharmacological Classification

Type A (Augmented): commonest type (up to 80%) of ADR which is predictable by the pharmacological mechanisms, e.g., , hypoglycaemia caused by insulins ororal hypoglycaemics, or hypotension bybeta-blockers, NSAID induced gastric ulcers. These type of adverse drug reactions are dose dependent henceforth severity increases with dose. Such ADRs are preventable in most part by slow introduction of low dosages. Sometimes regarded as Type I ADRs.

Type B (Bizzare): ADR is not expected from the known pharmacological mechanisms e.g. aplastic anaemia hepatitis caused by halothane caused by chloramphenicol, neuroleptic malignant syndrome caused by some anaesthetics and antipsychotics. Such ADRs are unrelated to dose. (Type 2 ADRs.)

Type C (Continuous drug use): ADR occurs due to continuous drug use. Such type of ADR may be irreversible, unexpected, unpredictable, e.g dementia by anticholinergic medications.

Type D (Delayed): ADR is characterized by the delayed occurrence even after the cessation of treatment, e.g., ophthalmopathy after chloroquine, or pulmonary/peritoneal fibrosis by methyserzide, corneal opacities after thioridazine

Type E (End of dose): ADR is usually characterized by withdrawal reactions. Such ADRs occur typically with the depressant drugs, e.g., seizures on alcohol or benzodiazepines.

Medication knowledge[26,27]**:**

Medication knowledge is the information that patients possess about the medications which he or she is taking. It includes information about the name of the drug, indication for uses, dose, dosage regimen, adverse effects, precautions to be taken during treatment, contraindications and storage

conditions. Patient educational status and awareness affects medication knowledge. The specialized skills of clinical pharmacists have proved to be beneficial for improving treatment outcomes. Because of their skills in identifying drug interactions, their excellent position of direct contacts and trust by patients, pharmacist can thus help patients remove evident adherence barriers and incorporate interventions into the care of their patients.

Objective: **This study was aimed to characterize the adverse reactions experienced in antihypertensive patients and to assess their causality, severity, and preventability . To assess the patient's medication knowledge related to antihypertensive drugs and the impact of clinical pharmacist mediated counseling on their medication knowledge.**

Methods:

The study was observational, prospective and follow up study.This study was conducted at sms hospital Hospital, ,Jaipur, Rajasthan.127 patients were recruited from OPD of department of medicine, at sms hospital Hospital ,Jaipur, Rajasthan. **Inclusion Criteria** Patients whose informed consent received, Patients with history of hypertension,Patients whose blood pressure are uncontrolled despite the use of medication,Patients who are experiencing adverse effects due to antihypertensive drugs,Patients of age above 18 years and either sex,Patients taking one or more antihypertensive medications at least for 1 month,Willingness to participate.

Exclusion Criteria Patients on treatment for hypertension for more than one year.Pregnant and lactating motherPatients who did not completely fill out questionnaire.Patients did not consent to participate.

The study duration was done for a period of 6 months.

Ethical considerations: Ethical approval was obtained from the Ethics and Research Committee of the Hospital, and informed consent was obtained from each patient verbally. The quality of the data and its confidentiality were ensured by keeping the patients' identity coded with their initials only. The data were fully anonymized and aggregated. Any information about any patient was kept strictly confidential and not shared with unauthorized individuals. The patient's right to confidentiality, information and privacy were respected.

Study procedure:. Patients of either sex diagnosed with hypertension visiting at Out Patient Department of sms hospital,Jaipur after satisfying the inclusion and exclusion criteria, explained in detail about the study and informed written consent was obtained from each patient before recruiting them in to the study. Details of prescribed antihypertensive drug or drugs like brand name or generic name,dose, route of administration, , diagnosis, laboratory results ,any adverse drug reactions,any other medications were recorded in case report form. Also noted down the information of patient demographic details such as age, gender, weight, height, BMI, education, occupation, family history, past medical history, personal habits of smoking and alcohol,and contact details. A Medication Knowledge Assessment Questionnaire consisted of 5 questions to assess the knowledge of patient regarding the Medications.

Casuality assessment of ADRs

Casuality assessment of ADRs reported in patients prescribed with antihypertensive drugs by using WHO-UMC causality assessment scale and Naranjo scale.

i. WHO-UMC system for causality assessment:

Certain:

- Event or laboratory test abnormality, with plausible time relationship to drug intake
- Cannot be explained by disease or other drugs
- Response to withdrawal plausible
- Event definitive pharmacologically or phenomenologically
- Rechallenge satisfactory, if necessary

Probable/ Likely:

- Event or laboratory test abnormality, with reasonable time relationship to drug intake
- Unlikely to be attributed to disease or other drugs
- Response to withdrawal clinically reasonable
- Rechallenge not required **Possible:**
- Event or laboratory test abnormality, with reasonable time relationship to drug intake
- Could also be explained by disease or other drugs
- Information on drug withdrawal may be lacking or unclear

Unlikely:

- Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable
- Disease or other drugs provide plausible

explanations

Conditional/ Unclassified:

- Event or laboratory test abnormality
- More data for proper assessment needed, or
- Additional data under examination

Unassessable/ Unclassifiable:

- Report suggesting an adverse reaction
- Cannot be judged because information is insufficient or contradictory
- Data cannot be supplemented or verified

ii. Naranjo Causality Scale:

a. Are there previous conclusive reports on this reaction?

Yes (+1), No (0), Do not know or not done (0)

b. Did the adverse event appear after the suspected drug was given?

Yes (+2), No (-1), Do not know or not done (0)

c. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?

Yes (+1), No (0), Do not know or not done (0)

d. Did the adverse reaction appear when the drug was readministered?

Yes (+2), No (-1), Do not know or not done (0)

e. Are there alternative causes that could have caused the reaction?

Yes (-1), No (+2), Do not know or not done (0)

f. Did the reaction reappear when a placebo was given?

Yes (-1), No (+1), Do not know or not done (0)

g. Was the drug detected in any body fluid in toxic concentrations?

Yes (+1), No (0), Do not know or not done (0)

h. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?

Yes (+1), No (0), Do not know or not done (0)

i. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?

Yes (+1), No (0), Do not know or not done (0)

Scoring> 9 = definite ADR

5-8 = probable ADR

1-4 = possible ADR

0 = Doubtful ADR

Results *The present observational study of Total of 127 prescriptions and 86 ADRs were reported and analyzed. In this study it was noted that in all prescriptions lifestyle modifications were recommended for all patients with hypertension irrespective of antihypertensive drug therapy. In all the prescriptions recorded, the route of administration of antihypertensive drugs was oral.*

Age distribution of patients studied:In the current study out of 127 patients, 65 patients (51.18%) belonged to age group of 61-70 years. There were 34 patients (26.77%) in age group of 51-60 years, 16 patients (12.6%) in age group of 71-80 years, 10 patients (7.87%) in age group of 41-50 years and 2 patients (1.58%) in age group of 81-90 years as shown in Table 1.

Gender distribution of patients studied:In the current study out of 127 patients, 32 (25.2%) were male and 95 (74.8%) were female as shown in Table 1.

Body mass index of patients studied: Calculation of body mass index showed that out of 127 patients, 73 (57.48%) were of normal weight, 44 (34.65%) were overweight and 10 (7.87%) were underweight as shown in Table 1.

Socioeconomic status of patients studied:Socioeconomic status of the patients studied were grouped as per their monthly per capita income according to modified Prasad classification 2013.Out of 127 patients, 67 (52.76%) belonged to class III. Number of patients in other classes were 34 (26.77%) in class IV, 11 (8.66%) in class II, 8 (6.3%) in class V and 7 (5.51%) in class I as shown in Table 2.

Number of patients receiving monotherapy of antihypertensive drugs:In present study 96 (75.59%) patients had received single drug for the treatment of hypertension. Amlodipine was the most commonly used drug which was prescribed for 84 (87.5%) patients. Other drugs prescribed as monotherapy were ramipril for 3 (3.14%) patients, nifedipine for 2 (2.08%) patients, telmisartan for 2 (2.08%) patients, metoprolol for 2 (2.08%) patients, losartan for 1 (1.04%) patient, nebivolol for 1 (1.04%) patient and furosemide for 1 (1.04%) patient as shown in Figure 3.

Number of patients receiving two drug combination therapy of antihypertensive drugs:

Out of 127 patients two drugs were prescribed for 22 (17.32%) patients. Amlodipine + atenolol was most commonly prescribed two drug combination which was prescribed for 6 patients (27.26%). Other two drug combinations prescribed were amlodipine + furosemide for 5 patients (22.72%), telmisartan + hydrochlorothiazide for 3 patients (13.63%), amlodipine + ramipril for 2 patients (9.09%), enalapril + hydrochlorothiazide for 1 patient (4.55%), amlodipine + losartan for 1 patient (4.55%), telmisartan + amlodipine for 1 patient (4.55%), losartan + hydrochlorothiazide for 1 patient (4.55%), carvedilol + ramipril for 1 patient (4.55%) and amlodipine + nebivolol for 1 patient (4.55%) as shown in Figure 4.

Number of patients receiving three drug therapy of antihypertensive drugs:

Out of 127 prescriptions three drugs were prescribed for 7 (5.51%) patients. In that losartan + hydrochlorothiazide + amlodipine was the most commonly prescribed three drug combination prescribed for 3 patients (42.84%). Other three drug combinations prescribed were ramipril + amlodipine + atenolol for 1 patient (14.29%), amlodipine + atenolol + furosemide for 1 patient (14.29%), bisoprolol + ramipril + furosemide for 1 patient (14.29%) and telmisartan + amlodipine + hydrochlorothiazide for 1 patient (14.29%) as shown in Figure 5.

Number of patients receiving four drug therapy of antihypertensive drugs:

The four drug combinations were the least prescribed. Four drugs were prescribed only for 2 (1.58%) patients. Telmisartan + hydrochlorothiazide + amlodipine + atenolol and telmisartan + hydrochlorothiazide + amlodipine + metoprolol were the two four drug combinations prescribed for 2 patients as shown in Figure 6.

Adverse drug reactions recorded: In present study it has been observed that 86 ADRs developed for different types of antihypertensive drugs during the period of six months .

Gender distribution of patients developing ADRs to antihypertensive drugs:Among 86 patients who showed ADRs to antihypertensive drugs, 55 (63.95%) were female and 31 (36.05%) were male as shown in Figure 7.

Age distribution of patients developing ADRs to antihypertensive drugs:ADRs to antihypertensive drugs were observed most commonly in age group of 61–70 years (n = 40, 46.51%). Other age groups affected were 51– 60 years (n = 24, 27.91%), 71–80 years (n = 13, 15.12%) and 41–50 years (n= 9, 10.46%) as shown in Figure 8.

ADRs shown on treatment with different classes of antihypertensive drugs: CCBs were found to be the commonest therapeutic class of antihypertensive drugs associated with ADRs (n = 54, 62.79%). Other groups associated with ADRs were ARBs (n = 11, 12.79%), β-blockers (n = 10, 11.63%), ACE inhibitors (n = 6, 6.98%) and diuretics (n = 5, 5.81%) as shown in Figure 10. Among individual drugs amlodipine was found to be the commonest drug associated with ADRs (n = 41).

ADRs to antihypertensive drugs affecting various systems: In present study ADRs to

antihypertensive drugs associated with central nervous system (n = 37, 43.03%) were found to be the most frequent [headache, dizziness, sedation and giddiness]. Other systems associated with ADRs were musculo-skeletal system (n = 25, 29.07%) [pedal edema, fatigue and muscle cramp], respiratory system (n = 11, 12.79%) [dry cough and breathlessness], gastrointestinal system (n = 8, 9.3%) [abdominal pain and diarrhoea], cardiovascular system (n = 4, 4.65%) [bradycardia] and skin (n = 1, 1.16%) [irritation all over the body] as shown in Figure 11.

WHO causality assessment scale: According to WHO causality assessment scale most of the ADRs were "probable" 44 (51.16%), followed by "possible" 28 (32.56%), unclassifiable 10 (11.63%) and unlikely 4 (4.65%) as shown in Figure 12.

Naranjo scale: According to Naranjo scale 67 (77.91%) ADRs were "Possible", 19 (22.09%) were "Probable" and none were "Definite" as shown in Figure 13.

Table 1: Demographic profile of the patients studied

1.	**Age in years**		**Number of patients**
	i.	41 - 50	**10**
	ii.	51 - 60	**34**
	iii.	61 - 70	**65**
	iv.	71 - 80	**16**
	v.	81 - 90	**2**
2.	**Sex**		
	i.	**Male**	**95**
	ii.	Female	**32**
3.	**Body mass index** in Kg/m^2		
	i.	Normal weight (18.5 – 24.9)	**73**
	ii.	Overweight (25 – 29.9)	**44**
	iii.	**Underweight (<18.5)**	**10**

Table 2: Socioeconomic status and comorbid conditions of the patients studied

1.	Socioeconomic status **(Prasad classification)**		Number of patients
	i.	Class I	**7**
	ii.	Class II	**11**
	iii.	Class III	**67**
	iv.	Class IV	**34**
	v.	**Class V**	**8**

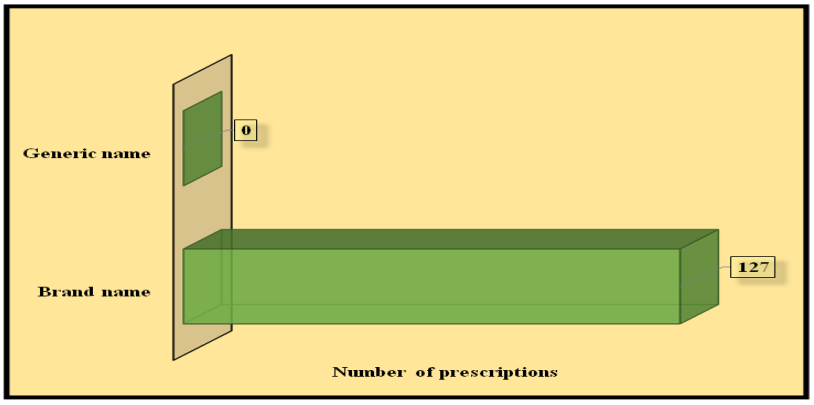

Figure 1: Bar diagram showing the number of prescriptions of antihypertensive drugs by generic and brand names

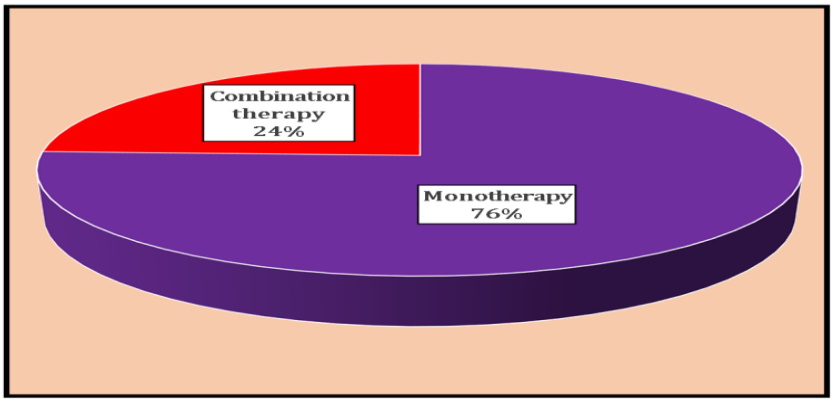

Figure 2: Pie diagram showing the percentage of prescriptions of antihypertensive drugs as monotherapy and combination therapy

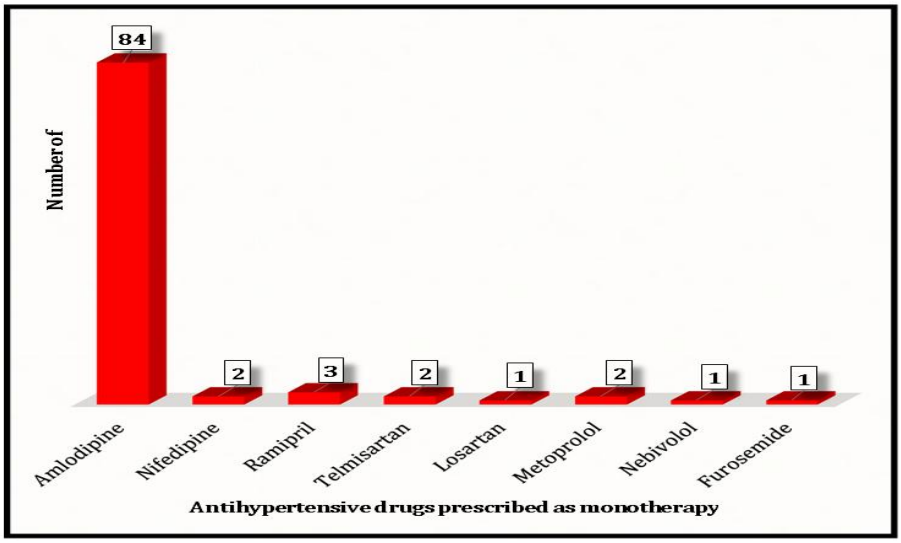

Figure 3: Bar diagram showing the number of prescriptions of antihypertensive drugs as monotherapy

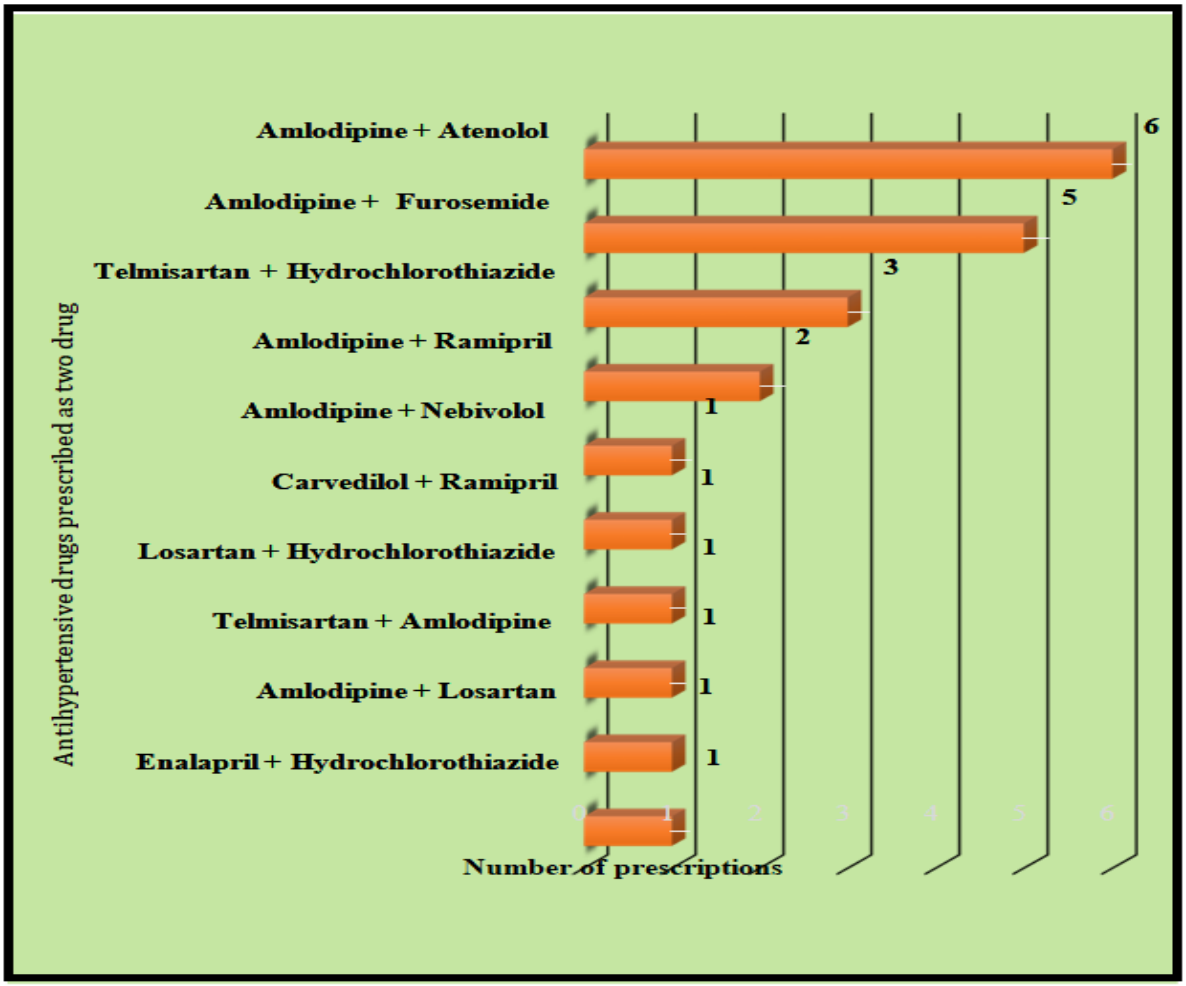

Figure 4: Bar diagram showing the number of prescriptions of antihypertensive drugs as two drug combination therapy

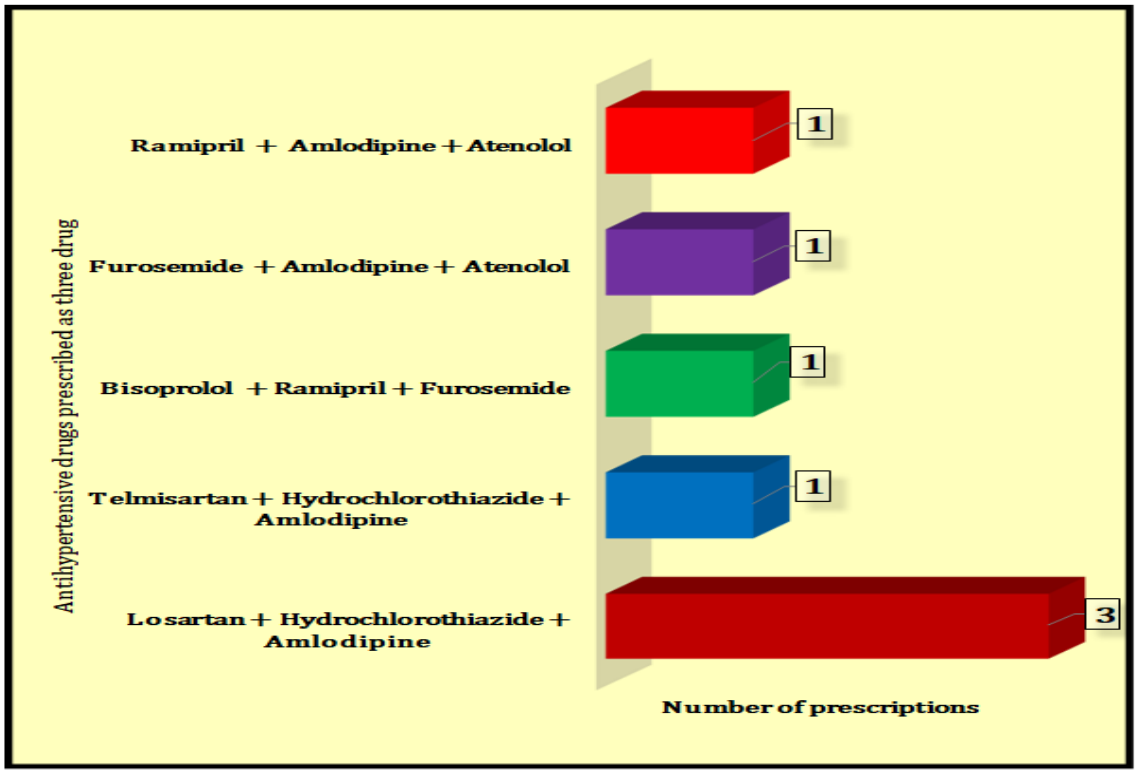

Figure 5: Bar diagram showing the number of prescriptions of antihypertensive drugs as three drug combination therapy

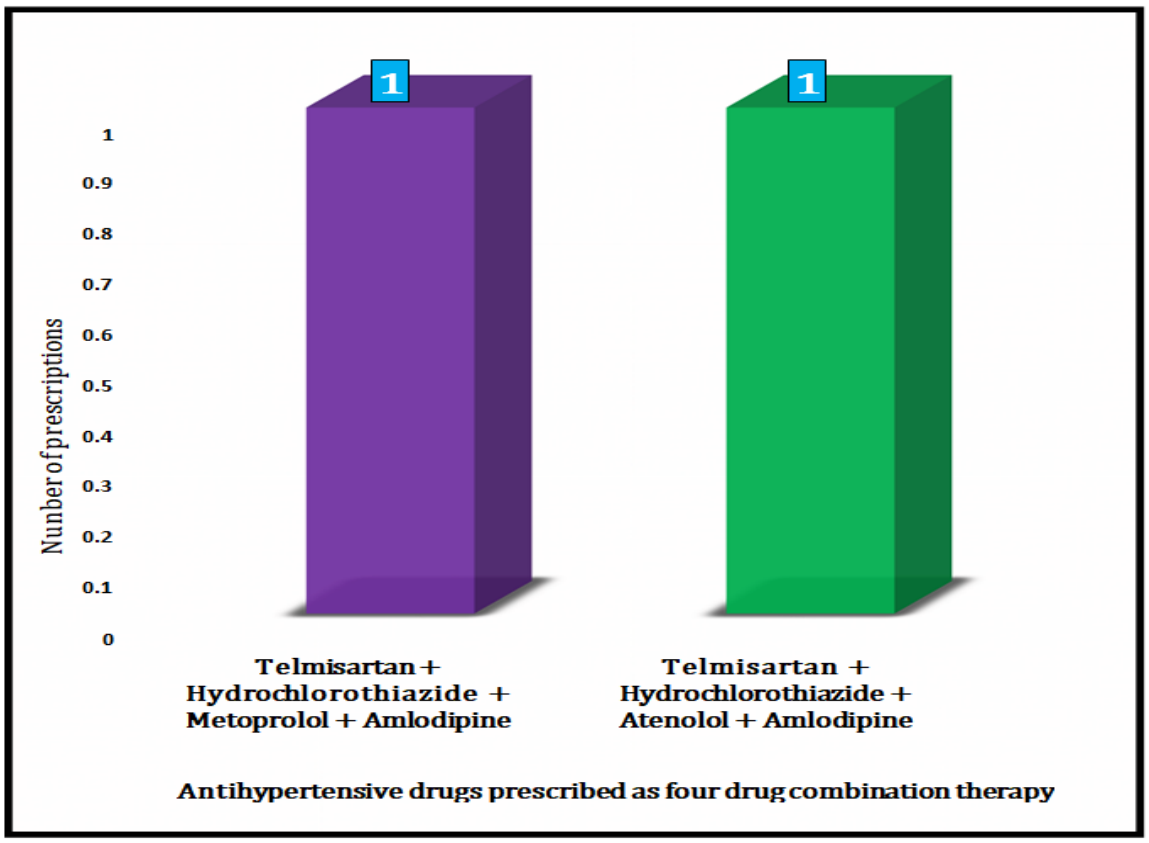

Figure 6: Bar diagram showing number of prescriptions of antihypertensive drugs as four drug combination therapy

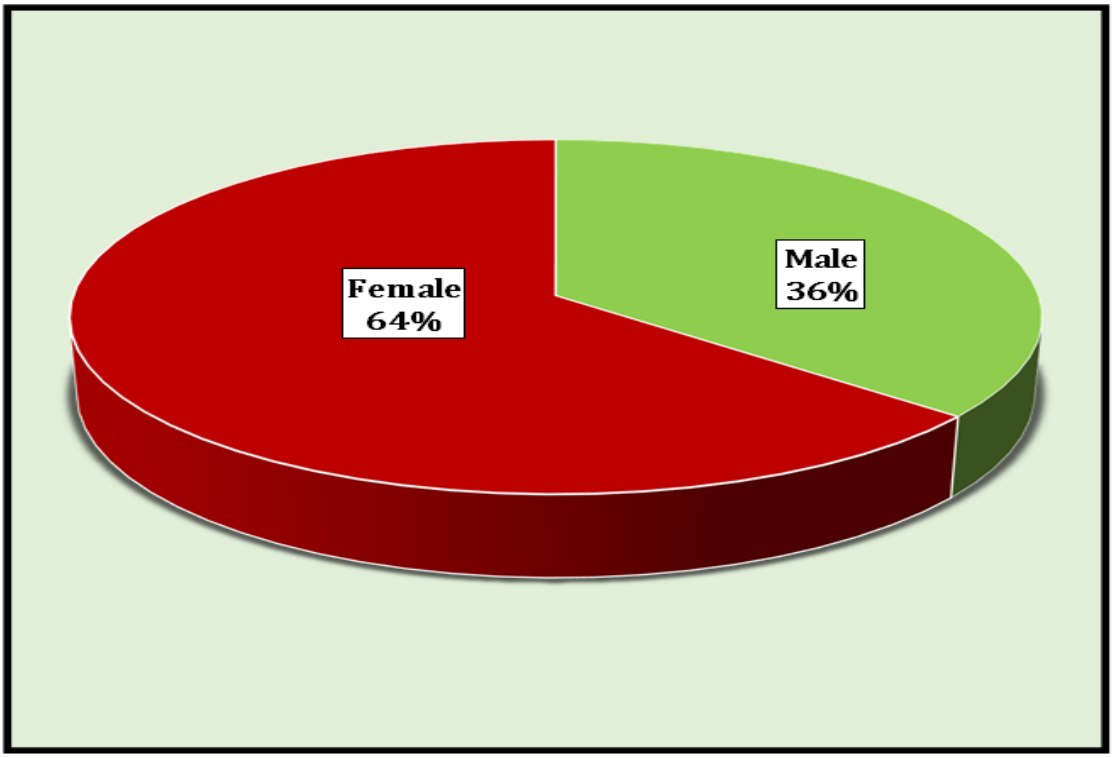

Figure 7: Pie diagram showing the percentage of males and females who experienced ADRs due to use of antihypertensive drugs

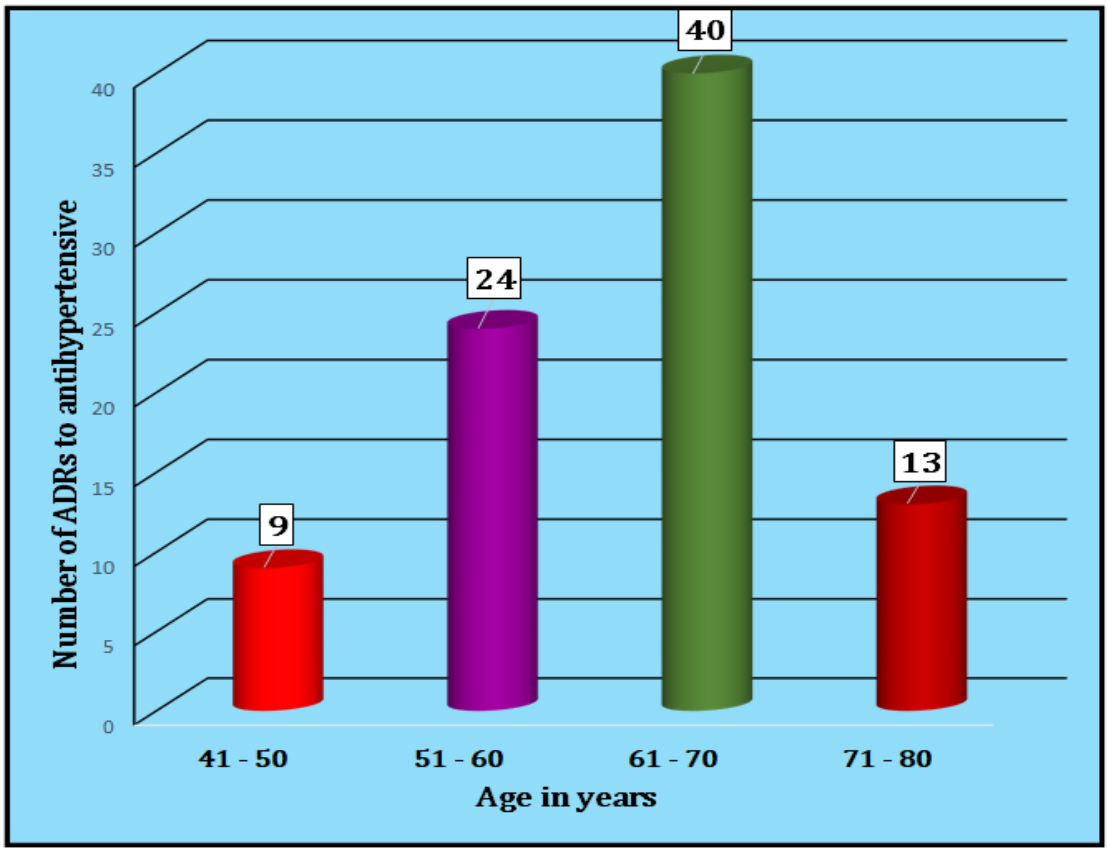

Figure 8: Bar diagram showing the age wise distribution of patients who experienced ADRs due to use of antihypertensive drugs

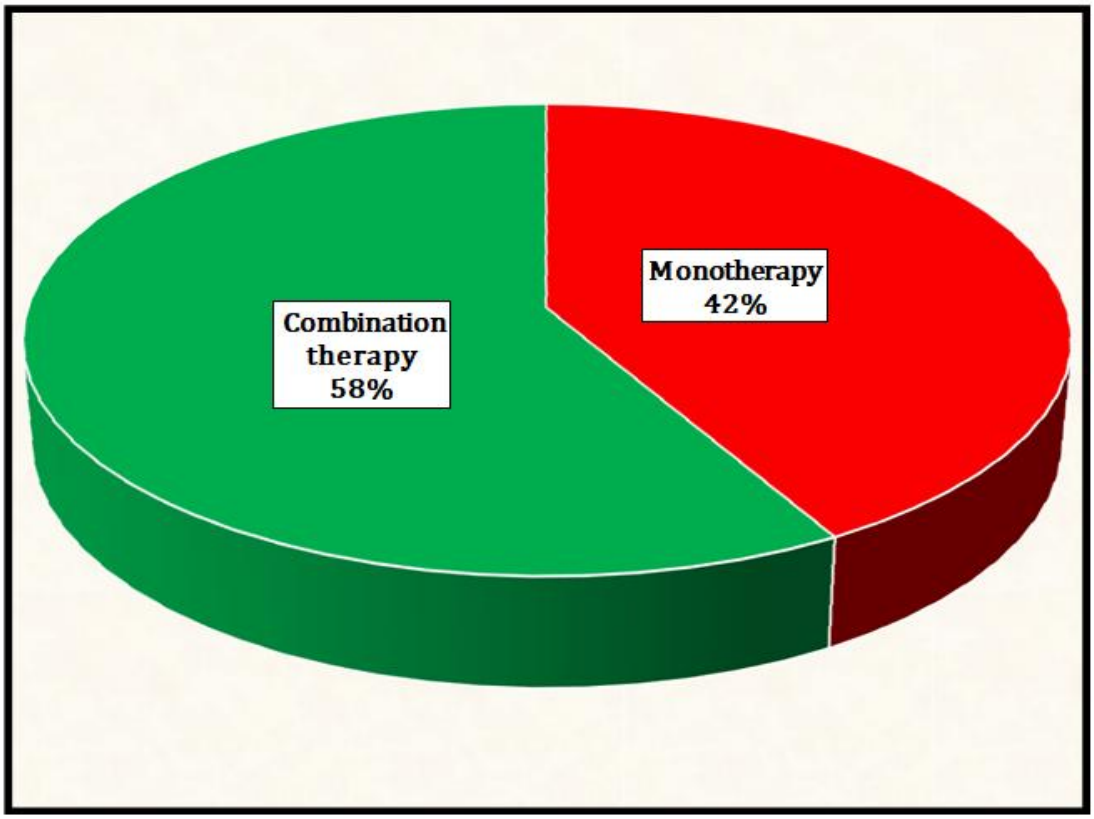

Figure 9: Pie diagram showing the percentage of ADRs experienced in patients who received monotherapy and combination therapy of antihypertensive drugs

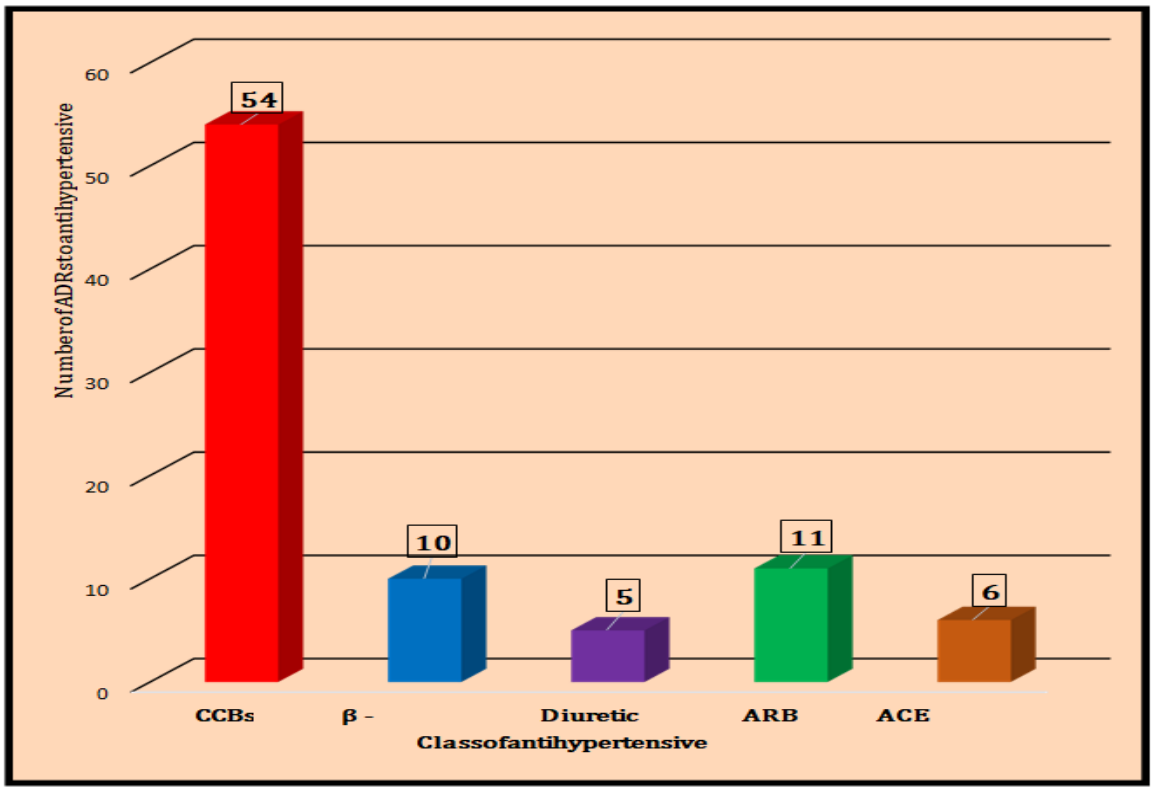

Figure 10: Bar diagram showing the number of ADRs experienced with different classes of antihypertensive drugs

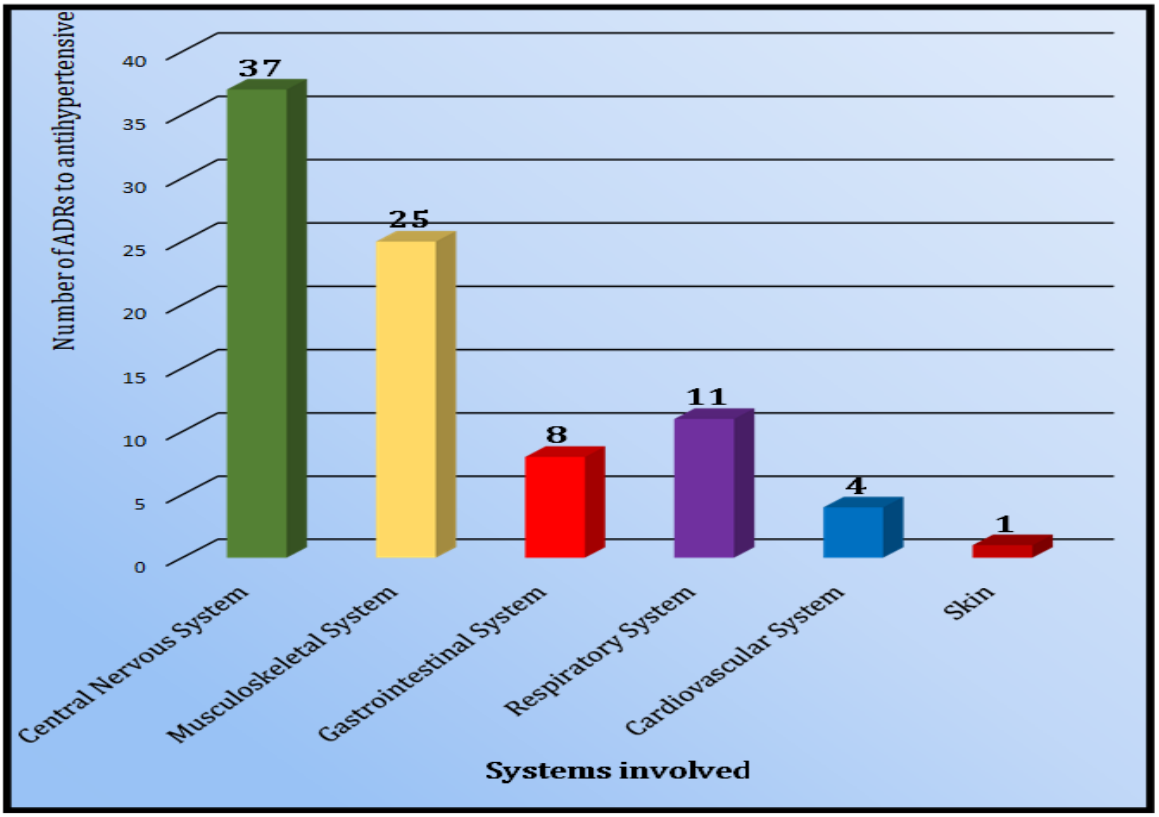

Figure 11: Bar diagram showing system-wise distribution of ADRs to antihypertensive drugs

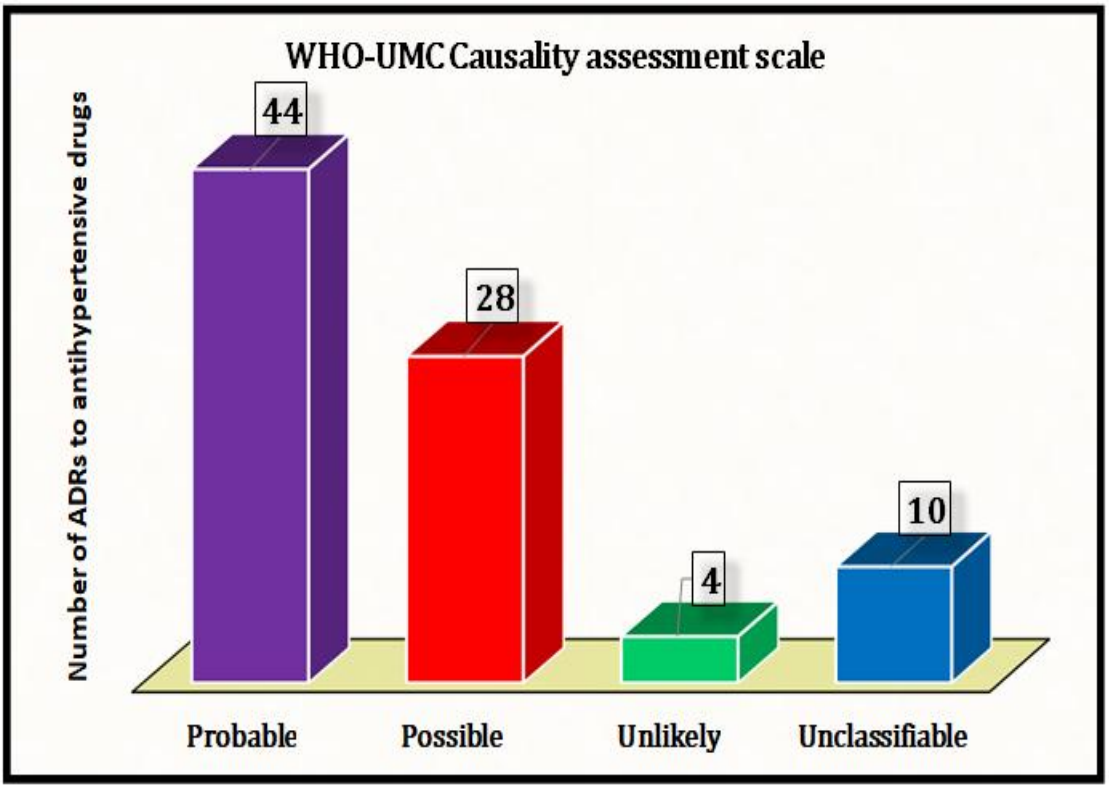

Figure 12: Bar diagram showing the causality assessment of ADRs due to antihypertensive drugs by WHO-UMC Causality assessment scale

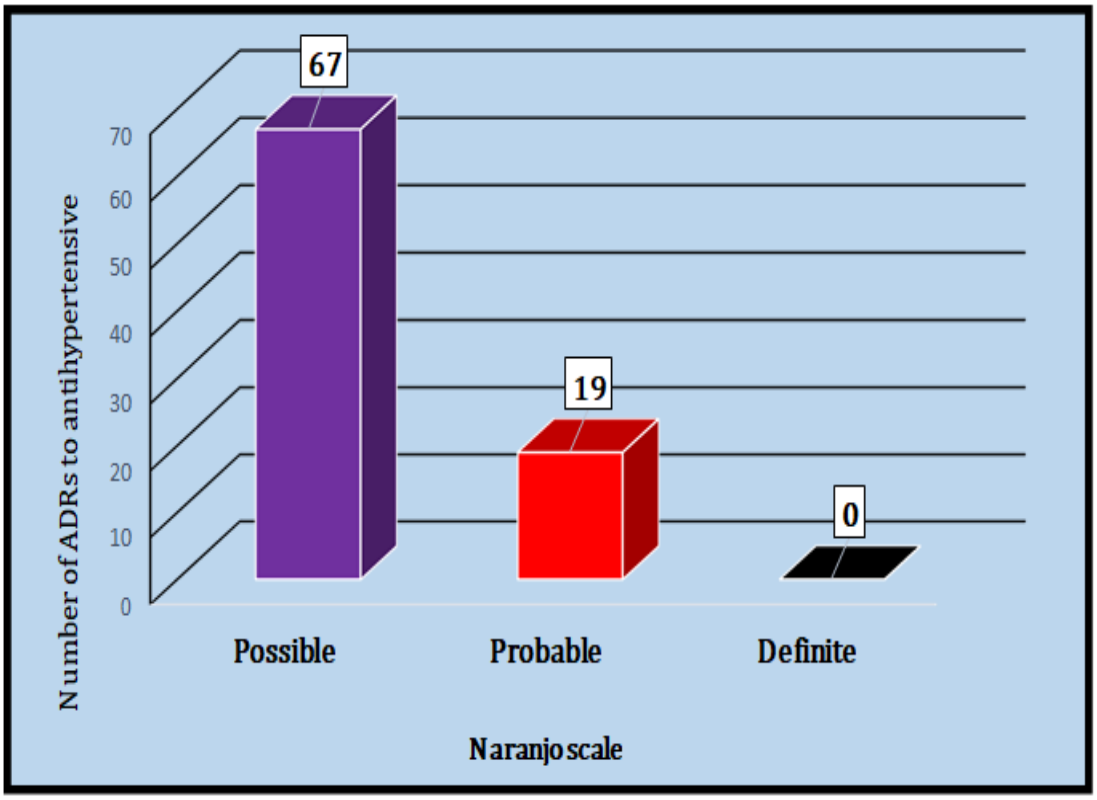

Figure 13: Bar diagram showing the causality assessment of ADRs due to antihypertensive drugs by Naranjo scale

Certain

- Event or laboratory test abnormality, with plausible time relationship to drug intake
- Cannot be explained by disease or other drugs
- Response to withdrawal plausible
- Event definitive pharmacologically or phenomenologically
- Rechallenge satisfactory, if necessary **Probable/ Likely**
- Event or laboratory test abnormality, with reasonable time relationship to drug intake
- Unlikely to be attributed to disease or other drugs
- Response to withdrawal clinically reasonable
- Rechallenge not required **Possible**
- Event or laboratory test abnormality, with reasonable time relationship to drug intake
- Could also be explained by disease or other drugs
- Information on drug withdrawal may be lacking or unclear

Unlikely

- Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable
- Disease or other drugs provide plausible explanations

Conditional/ Unclassified

- Event or laboratory test abnormality
- More data for proper assessment needed, or
- Additional data under examination **Unassessable/ Unclassifiable**
- Report suggesting an adverse reaction
- Cannot be judged because information is insufficient or contradictory
- Data cannot be supplemented or verified

WHO :World Health Organization
UMC :Uppsala Monitoring Centre

Naranjo algorithm or adverse drug reaction probability scale[26] - The total score calculated from this table defines the category as: Possible (total score 1–4), Probable (total score 5–8), Definite (total score >9)

S.No.	Questionnaires	Yes	No	Do not know
1.	Are there previous conclusive reports on this reaction?	**1**	**0**	0
2.	Did adverse drug reaction (ADR) appear after the suspected drug was administered?	**2**	**-1**	0
3.	Did ADR improve when the drug was discontinued or a specific antagonist was administered?	**1**	**0**	0
4.	Did the adverse reaction appear when the drug was readministered?	**2**	**-1**	0
5.	Are there any alternative causes (other than the drug) that could have caused the reaction?	**-1**	**2**	0
6.	Did the reaction reappear when placebo was given?	**-1**	**1**	0
7.	Was the drug detected in the blood (or other fluids) in concentration known to be toxic?	**1**	**0**	0
8.	Was the ADR more severe when dose was increased or less severe when dose was decreased?	**1**	**0**	0
9.	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	**1**	**0**	0
10.	**Was the adverse event confirmed by any objective evidence?**	1	0	0

Comparison of the Mean Medication Knowledge Score of Patients

Mean medication knowledge score was assessed at baseline, first follow up and second follow up. It was observed that there was significant improvement in the mean medication knowledge score of the patients at each follow ups ($p < 0.001$). Mean score increased from 29.66 at baseline to 49.82 at first follow up and 64.60 at second follow up.

Table 3: Comparison of the mean medication knowledge score of patients at baseline and first follow up

ean baseline score ± SE	first follow up score ± SE	ference of means	p- value
29.66 ± 2.085	**49.82 ± 1.900**	**20.16**	**<0.001**

Table 4: Comparison of the mean medication knowledge score of patients at first follow up and second follow up

ean first follow up score ± SE	econd follow up score ± SE	ference of means	p- value
49.82 ± 1.900	**64.60 ± 1.850**	**14.79**	**<0.001**

Table 5: Comparison of the mean medication knowledge score of patients at baseline and second follow up

ean baseline score ± SE	econd follow up score ± SE	ference of means	p- value
29.66 ± 2.085	**64.60 ± 1.850**	**34.94**	**<0.001**

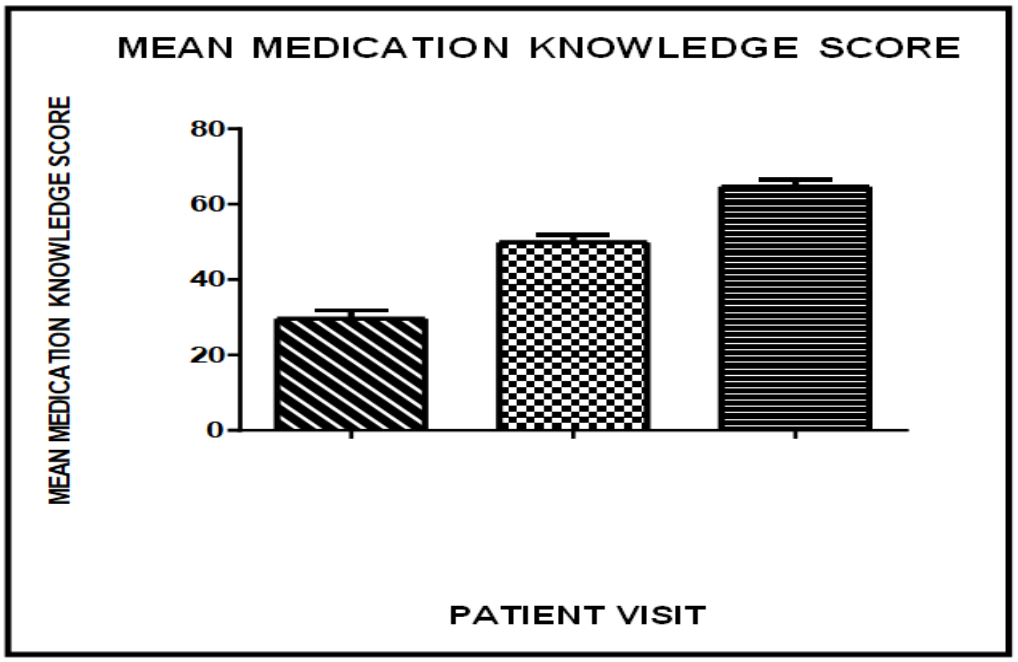

Figure 14: Overall comparison of mean Medication Knowledge Score (0-100)

Results show that there is consistent improvement in the medication knowledge of the patients at every visit. After applying 'ANOVA' test for repeated measures analysis, it is found that the difference in means is highly significant. This shows that there is definite positive impact of patient counselling and patient information leaflets on the medication knowledge of patients.,. The results of our study show that there is poor medication knowledge in the patients at baseline. After counselling, there is significant improvement in the medication knowledge of the patients. There is direct correlation of Medication Knowledge with Medication Adherence in the patients.

Conclusion:

In this study the ADRs were found probable (51.16%), possible (32.56%), unclassifiable (11.63%) and unlikely (4.65%) by using WHO causality assessment scale. By using Naranjo algorithm scale it was found that ADRs were possible in 77.91% and probable in 22.09% of cases. This study also found that amlodipine was responsible for most of the ADRs and among all the ADRs reported headache was the commonest followed by dizziness, pedal oedema, fatigue, abdominal pain, dry cough, breathlessness, bradycardia, muscle cramps, sedation, diarrhoea and irritation all over the body. The study was conducted for a period of 6 months. The data was collected using a case record form. The study included patients of all age group. The results of this study reveal that there is Significant improvement in the medication knowledge in patients after counselling by the pharmacist.If counselled appropriately, pharmacist can bring about major change in the adherence related attitude of the patients. There is definite relationship between the medication related knowledge and medication adherence. Hence improving the medication knowledge can lead to greater awareness and hence better medication adherence. The results at baseline showed that there was less knowledge and awareness to treatment in patients regarding their medications. As the drug therapy is mainstay of hypertension it is very much essential to educate patients regarding their medications to improve their knowledge about the medications. Factors like age, gender, family history affect the knowledge of the patients regarding their medications.Pharmacist's efforts can contribute to the optimization of disease management for the patients thereby helping them to improve their medication adherence and hence in long term quality of life.

Bibliography

1. Halemani SS, Narendranth S, Somashekhar HS, Reshma SR, Sagar JK, Ramachandra K. Prescriptive pattern of antihypertensives in tertiary care hospital using DU-90%. Int J Pharm Res Dev 2012;4(1):107-13.
2. Kalamdani AR, Bhandare B, Hemamalini MB, Krishna MV. A prospective study of

prescribing pattern of antihypertensive drugs in tertiary care hospital, Bangalore. J Evol Med Dent Sci 2014;2(52):10339-44.
3. Mohd AH, Mateti UV, Konuru V, Parmar MY, Kunduru BR. A study on prescribing patterns of antihypertensives in geriatric patients. Perspect Clin Res 2012;3(4):139-42.
4. Joshi M, Rao BS, Khan GM. Study of drug use in essential hypertension and their compliance. Kathmandu Univ J Sci Eng Technol 2006;2(1):1-13.
5. Lee PKF, Li RKL, Chan JCN, Chang S, Lee SC, Tomlinson B, Critchley JAJH. A prescription survey in a hospital hypertension outpatient clinic. Br J Clin Pharmacol 1997;44(6):577–82.
6. Al-Windi A. Detection and treatment of hypertension in general health-care practice: a patient-based study. J Hum Hypertens 2005;19(10):775-86.
7. Rimoy GH, Justin-Temu M, Nilay C. Prescribing patterns and cost of antihypertensive drugs in private hospitals in Dar es Salaam, Tanzania. East Cent Afr J Pharm Sci 2008;11(3):69-73.
8. Khurshid F, Aqil M, Alam MS, Kapur P, Pillai KK. Antihypertensive medication prescribing patterns in a university teaching hospital in South Delhi. Int J Pharm Sci Res 2012;3(7):2057-63.
9. Kumar VR, Ram VR, Prasad BG, Mohanta GP, Manna PK. A study of adverse drug reactions due to antihypertensive drugs in a tertiary care teaching hospital. Int J Pharm Life Sci 2011;2(5):767-72.
10. Khurshid F, Aqil M, Alam MS, Kapur P, Pillai KK. Monitoring of adverse drug reactions associated with antihypertensive medicines at a university teaching hospital in New Delhi. DARU J Pharm Sci 2012;20(1):1-6.
11. Ahmad SR. Adverse drug event monitoring at the food and drug administration. J Gen Intern Med 2003;18(1):57-60.
12. Park K. Park's Textbook of Preventive and Social Medicine. 22nd ed. Jabalpur: Banarsidas Bhanot; 2013. p. 344-8.
13. Esunge PM. From blood pressure to hypertension: the history of research. J R Soc Med 1991;84(10):621.
14. Newby DE, Grubb NR, Bradbury A. Vascular disease. Walker BR, Colledge NR, Ralston SH, Penman ID editors. Davidson's Principles and Practice of Medicine. 22nd ed. Edinburgh: Churchill Livingstone; 2014. p. 607-13.
15. Kotchen TA. Hypertensive Vascular Disease. Longo DL, Fauci A, Kasper D, Hauser S, Jameson JJ, Loscalzo J editors. Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw-Hill; 2011. p. 4139-65.
16. Benowitz NL. Antihypertensive Agents. Katzung BG, Masters SB, Trevor AJ editors. Basic and Clinical Pharmacology. 12th ed. New York: McGraw-Hill; 2012. p. 169-92.
17. Michel T, Hoffman BB. Treatment of Myocardial Ischemia and Hypertension. Brunton L, Chabner BA, Knollman B editors. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12th ed. New York: McGraw-Hill; 2011. p. 765-85.
18. Tripathi KD. Essentials of Medical Pharmacology. 7th ed. New Delhi: Jaypee; 2013. p. 558-74.
19. Patel A, Giles D, Thomas V, Gurubasavarajaswamy PM, Patel R. Pharmacovigilance: a review. Int J Pharm Biol Arch 2011;2(6):1569-74.
20. Rohilla A, Singh N, Kumar V, Sharma MK, Dahiya A, Kushnoor A. Pharmacovigilance: needs and objectives. J Adv Pharm Edu Res 2012;2(4):201-5.
21. Zaki SA. Adverse drug reaction and causality assessment scales. Lung India 2011;28(2):152-3.
22. Raut AL, Patel P, Patel C, Pawar A. Preventability, predictability and seriousness of adverse drug reactions amongst medicine inpatients in a teaching hospital: a prospective observational study. Int J Pharm Chem Sci 2012;1(3):1293-9.
23. Srinivasan R, Ramya G. Adverse drug reaction-causality assessment. Int J Res Pharm Chem 2011;1(3):606-12.
24. Augustine L, Prasanth NV, Dev KTS, Jasmin S, Kappekkat Y, Shinu C, Thayyil A. A study conducted on prescribing pattern and cost of anti-hypertensive drugs in a tertiary level hospital in South Malabar region of Kerala. Der Pharma Chemica 2010;2(6):332-41.

25. Beg MA, Dutta S, Varma A, Kant R, Bawa S, Anjoom M. Study on drug prescribing pattern in hypertensive patients in a tertiary care teaching hospital at Dehradun, Uttarakhand. Int J Med Sci Public Health 2014;3(8):1-5.
26. Kardas P, Lewek P, Matyjaszczyk M. Determinants of patient adherence: a review of systematic reviews. Front Pharmacol. 2013;4:91.
27. Shin S, Song H, Oh S-K, Choi KE, Kim H, Jang S. Effect of antihypertensive medication adherence on hospitalization for cardiovascular disease and
28. Tandon VR, Sharma S, Mahajan S, Mahajan A, Khajuria V, Mahajan V, Prakash C. Antihypertensive drug prescription patterns, rationality, and adherence to Joint National Committee-7 hypertension treatment guidelines among Indian postmenopausal women. J Mid-life Health 2014;5(2):78-83.
29. McAlister FA, Campbell NR, Duong-Hua M, Chen Z, Tu K. Antihypertensive medication prescribing in 27,822 elderly Canadians with diabetes over the past decade. Diabetes Care 2006;29(4):836-41.
30. Liu P, Wang J. Antihypertensive medication prescription patterns and time trends for newly-diagnosed uncomplicated hypertension patients in Taiwan. BMC Health Serv Res 2008;8:1-11.
31. Yoon EY, Cohn L, Rocchini A, Kershaw D, Freed G, Ascione F, Clark S. Antihypertensive prescribing patterns for adolescents with primary hypertension. Pediatr 2012;129(1):1-8.
32. Gupta SK, Nayak RP. The pattern of antihypertensive medication use among elderly patients in a tertiary care teaching hospital in South India. Trop J Med Res 2014;17(2):81-5.
33. Sakthi RS, Thomas S, Sivakumar KK, Karhikeyan J, Kumar NS. Assessment of antihypertensive prescribing pattern and patient counseling in an urban population. Der Pharmacia Lettre 2010;2(4):156-63.
34. Kehinde AG, Ismail AS. Assessment of antihypertensives utilization in a private teaching hospital in Nigeria. Int J Pharm Pharm Sci 2012;4(5):480-3.
35. Sultana S, Hamid K, Islam KMS, Roy S, Saha MR, Zulfiker AHM et al. Assessment of prescription pattern of hypertensive patient's prescription: A prescription survey study from various hospitals of Bangladesh. Eur J Sci Res 2010;40(4):500-5.
36. Clement YN, Ali S, Harripaulsingh S, Lacaille K, Mohammed O, Mohammed S et al. Drug prescribing for hypertension at primary healthcare facilities in Trinidad. West Indian Med J 2012;61(1):43-8.
37. Janaki RT, Narendra.SH. Drug prescription pattern of antihypertensive drugs in a tertiary hospital. J Pharm Biomed Sci 2009;9(9):1-5.
38. Baig MR, Yuit WS, Ramani M, Jin PC, Asma M, Tahir MK. Drug utilization pattern and co-morbidtities among hypertensive patients in sub-urban hospital, Malaysia. Rev Global Med Healthcare Res 2011;2(2):139-46.
39. Hooli TV, Santoshkumar J, Manjunath S, Vinodkumar CS. Drug utilization study of antihypertensives in obstetric practice in a tertiary care hospital. Int J Appl Biol Pharm Technol 2010;1(3):1006-10.
40. Azarisman SMS, Aszrin A, Sahimi M, Ngow HA, Marzuki AO, Jamalludin AR, Sapari S, Maskon O. Evaluation of antihypertensive drug utilisation and cost in Hospital Tengku Ampuan Afzan, Kuantan. Int Med J 2009;8(2):29-36.
41. Arief M, Harika B, Satyanarayana B, Pasha SW, Paladugu ND, Pasha SI, Poloju D, Pokkula S. Evaluation of prescribing pattern of antihypertensive drugs in a tertiary care hospital. Acta Chim Pharm Indica 2013;3(2):172-81.
42. Ghori SAU, Baig MMA, Ilyaz M, Areif M, Tabassum N. Evaluation of prescribing pattern of antihypertensives against the clinical condition. J Pharm Biol Sci 2014;9(2):133-40.
43. Xavier D, Mathew N, Pradeep J, Pais P. Pattern of drug use in hypertension in a tertiary hospital: A cross sectional study in the in-patient wards. Indian J Pharmacol 2001;33(6):456-7.
44. Majumder AAS. Patterns of antihypertensive drug utilization among the cardiologists of Bangladesh in initiating hypertension treatment. Cardiovasc J 2012;4(2):114-9.
45. Pittrow D, Kirch W, Bramlage P, Lehnert H, Hofler M, Unger T, Sharma AM, Wittchen HU. Patterns of antihypertensive

drug utilization in primary care. Eur J Clin Pharmacol 2004;60(2):135–42.

46. Wong MC, Jiang JY, Lam AT, Fung H, Griffiths S, Mercer SW. Patterns of antihypertensive prescribing, discontinuation and switching among a Hong Kong Chinese population from over one million prescriptions. J Hum Hypertens 2008;22(10):714-6.
47. Sweileh W. Pharmacotherapeutic Analysis and prescription pattern of antihypertensive drugs dispensed at community pharmacies in Palestine. An-Najah Univ J Res 2003;17(2):168-81.
48. Sagar JK, Narendranath S, Somashekar HS, Reshma SR, Halemani SS, Adake P. Prescribing pattern of antihypertensives in individuals with hypertension alone and with coexisting diabetes mellitus - a comparative study. Int J Cur Biomed Phar Res 2012;2(2):300- 3.
49. Pai PG, Shenoy J, Sanji N. Prescribing patterns of antihypertensive drugs in a South Indian tertiary care hospital. Drug Invention Today 2011;3(4):38-40.
50. Kale A, Maniyar YA. Prescribing patterns of antihypertensive drugs in a tertiary care hospital. Sch Acad J Pharm 2013;2(5):416-8.
51. Tiwari H, Kumar A, Kulkarni SK. Prescription monitoring of antihypertensive drug utilisation at the Panjab university health centre in India. Singapore Med J 2004;45(3):117-20.
52. Maduram A, Harikrishna. Prescription pattern of antihypertensive drugs in Shri Sathya Sai medical college & research institute. Int J Basic Med Sci 2013;4(2):68-72.
53. Janagan T, Kavitha R, Sridevi SA, Veerendra V. Prescription pattern of antihypertensive drugs used in hypertensive patients with associated type 2 diabetes mellitus in a tertiary care hospital. Int J Pharm Res Rev 2014;3(1):1-5.
54. Dhanaraj E, Raval A, Yadav R, Bhansali A, Tiwari P. Prescription pattern of antihypertensive agents in T2DM patients visiting tertiary care centre in North India. Int J Hypertens 2012:520915.
55. Al-Drabah E, Irshaid Y, Yasein N, Zmeili S. Prescription pattern of antihypertensive drugs in family practice clinics at Jordan University Hospital. Med Sci 2012;2(1):469- 88.
56. Bajaj JK, Sood M, Singh SJ, Jerath P. Prescription patterns of antihypertensive drugs and adherence to JNC VII guidelines in a tertiary care hospital in North India. Int J Med Clin Res 2012;3(2):118-20.
57. Pavani V, Cidda M, Krishna TR, Parmar MY, Nalini M. Study of prescribing patterns of antihypertensive drugs. Int J Pharm Bio Sci 2012;2(2):317-27.
58. Shah J, Khakhkhar T, Bhirud S, Shah RB, Date S. Study of utilization pattern of antihypertensive drugs in hypertensive diabetic patients with or without reduced renal function at tertiary care teaching hospital. Int J Med Sci Public Health 2013;2:167-72.
59. Sindhu PR, Reddy MS. Study of prescriptive patterns of antihypertensive drugs in South India. Int J Adv Res Technol 2013;2(6):295-311.
60. Sandozi T, Emani VK. Survey of prescription pattern of antihypertensive drugs in hypertensives and hypertension associated diabetics. Int J Pharm Biosci 2010;1(4):23- 6.
61. Bhardwaj A, Alam N, Dabas V, Tiwari R, Sharma S. To evaluate the drug utilization pattern in patients using antihypertensive drug therapy. Asian J Biochem Pharm Res 2012;2(1):425-33.
62. John LJ, Devi P, Guido S. Utilization of antihypertensive medications among the critically ill patients. Res J Pharm Biol Chem Sci 2012;3(3):650-4.
63. Fretheim A, Oxman AD. International variation in prescribing antihypertensive drugs: its extent and possible explanations. BMC Health Serv Res 2005;5(1):21.
64. Hussain A, Aqil M, Alam MS, Khan MR, Kapur P, Pillai KK. A pharmacovigilance study of antihypertensive medicines at a South delhi hospital. Indian J Pharm Sci 2009;71(3):338-41.
65. Joshi VD, Dahake AP, Suthar AP. Adverse effects associated with the use of antihypertensive drugs: An overview. Int J Pharm Tech Res 2010;2(1):10-3.
66. Kale S, Patil A, Mandlecha RH. Compliance and adverse drug effects of antihypertensives in rural India. J Clin Diagn Res 2011;5(4):775-9.

67. Upadhayai JB, Kumar NA, Mukhija RD, Mukum M, Lalit M, Singh KK. Cutaneous reactions due to antihypertensive drugs. Indian J Dermatol 2006;51(3):189-91.
68. Minto-Leon D, Reyes-Morales, Galvan-Plata ME, Ponce-Monter H, Palma-Aguirre JA, Amato D, Figueras A. Drug treatment of hypertension: Compliance and adverse reactions in a cohort of hypertensive patients in a primary care setting. Rev Invest Clin 2007;59(1):8-14.
69. Rende P, Paletta L, Gallelli G, Raffaele G, Natale V, Brissa N, Costa C, Gratteri S, Giofre C, Gallelli L. Retrospective evaluation of adverse drug reactions induced by antihypertensive treatment. J Pharmacol Pharmacother 2013;4(1):47-50.
70. Suhas D, Bhosle D, Atre K. Review on pharmacovigilance study of telmisartan in hypertension patients. Asian J Pharm Clin Res 2013;6(3):17-20.
71. Alomar MJ, Strauch CC. A prospective evaluation of antihypertensive medications safety and efficacy in United Arab Emirates private hospitals. Am J Pharmacol Toxicol 2010;5(2):89-94.
72. Ibn YS, Tata F, Abdulganiyu G, Jamilu M, Tom MG. Evaluation of the relative incidence of adverse effects leading to treatment discontinuation of recommended antihypertensive drugs. Int Res J Pharm 2013;4(6):58-61.
73. Basak SC, Ravi K, Manavalan R, Sahoo K. A study of adverse drug reaction to antihypertensive drugs perceived by patients in a rural hospital. Indian J Pharm Sci 2004;66(6):814-7.
74. Dudala SR, Arlappa N. An updated Prasad's socio economic status classification for 2013. Int J Res Dev Health 2013;1(2):26-8.
75. Etuk E, Isezuo SA, Chika A, Akuche J, Ali M. Prescription pattern of antihypertensive drugs in a tertiary health institution in Nigeria. Ann Afr Med 2008;7(3):128-32.
76. Kousalya K, Chirumamilla S, Manjunath S, Ramalakshmi S, Saranya P, Chamundeeswari D. Prescribing trend of antihypertensive drugs in hypertensive and diabetic hypertensive patients. Asian J Pharm Clin Res 2012;5(4):22-3.
77. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL et al. The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. J Am Med Assoc 2003;289(19):2560-72.
78. Hypertension: Clinical management of primary hypertension in adults- NICE guideline: Aug 2011. [Internet]. 2012 [cited 2012 Sep 20]. Available from: http://www.nice.org.uk/nicemedia/live/13561/56008/56008.pdf.
79. Quick JD, Hogerzeil HV, Velasquez G, Rago L. Twenty-five years of essential medicines. Bull World Health Organ 2002;80(11):913-4.