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## Drug therapy and related adverse drug reactions in patient with arterial hypertension

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### Abstract

**Aim and Objective:** Analysis of pharmacotherapy and drug related problems in patient with arterial hypertension in Udaipur

**Background:** Arterial hypertension or high blood pressure is a chronic medical condition which is characterized by elevated blood pressure in the arteries and is an important risk factor for future development of cardiovascular disease. Also belongs to asymptomatic diseases because it usually does not cause symptoms for years until a vital organ is damaged. Moreover is a major cause of morbidity and mortality, due to its association with some other serious diseases like coronary heart disease, cerebrovascular disease, atherosclerosis, renal disease, dyslipidemia, diabetes, obesity and metabolic syndrome. Arterial hypertension for adults, who don't suffer from any other kind of diseases, is defined by an elevation of blood pressure to 140 / 90 mm Hg or to higher values.

**Methods:** 55 patient cases were collected regarding age, gender, pharmacotherapy, dosage scheme, strength and adverse drug reaction which were subjected to statistical analysis also.

**Results:** The present retrospective study was done with 55 patient cases. Hypertension most prevalently affects the male than female. Most common co-morbidities along with hypertension were dyslipidemia and coronary heart disease. Most frequently used antihypertensive drug groups was  $\beta$ -blockers and angiotensin II receptor blockers (alone or in combination with hydrochlorothiazide) along with antidyslipidemics as additive to antihypertensive therapy. Commonly noticed adverse drug reactions were bradycardia, fatigue, peripheral edema and dry cough, mainly due to  $\beta$ -blockers, amlodipine and angiotensin-converting-enzyme- inhibitors. Additionally increased levels of creatine phosphokinase and myalgia were observed mainly due to statins, as additive to antihypertensive therapy for management of co-morbidities, like dyslipidemia.

**Conclusion:** Data on 55 hypertensive patient cases was collected from dept. of Medicine. This study represents the distribution of this problem in population and the different adverse drug reactions on patients under study. This study can be used a model to treat patients with described problems. Further investigations it will be necessary in the future to produce more accurate and representative findings.

**Keywords:** Drug therapy, arterial hypertension

### Introduction

Hypertension is an established risk factor for stroke, ischemic heart disease (Lewington *et al.*, 2002) [1], and renal dysfunction (Huang *et al.*, 2014) [2]. The management and prevention of hypertension are important to the prevention of these diseases. Hypertension rarely occurs in isolation and insulin resistance (diabetes) and hyperlipidemia and in some cases chronic kidney disease are common accompanying medical conditions. Despite the number of available pharmacological groups for treatment of hypertension and accompanying conditions many times fails to achieve the goal due to drug related problems.

Drug related problems include medications errors and adverse drug reactions. Medication errors include mistakes that occurs in the process of prescribing, transcribing, dispensing or administering of a drug, whether adverse drug reactions according to World Health Organization (WHO) include any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis, therapy of disease or for the modification of physiological function.

Studies have shown that the persistence and adherence of antihypertensive medication that is observed in clinical trials often is not observed in clinical practice which shows lower level of adherence. In addition patients who were taking diuretics appeared less compliant

(adherent and persistent) comparing to patients who were using any other antihypertensive agents. Another factor that contributes to non adherence is polypharmacy (Johnson, 2008) [3]. In fact many hypertensive patients need multiple antihypertensive medications in order to achieve the blood pressure treatment goals. Multiple antihypertensive medications can be the reason of increasing adverse drug events and be the cause of poor patient's compliance.

Drug related problems to antihypertensive agents in hypertensive patients with diabetes type 2 also very common. However hypertensive patients with diabetes type 2 also had shown poor glycemic control, as well as suboptimal lipid control and suboptimal blood pressure control due to missing or contraindicated anti-platelet (not taking aspirin), lipid lowering, blood glucose lowering and blood control medications (Jong *et al.*, 2009) [4]. Moreover non-adherence was another factor which contributes to poor control and to significantly higher glycated hemoglobin (HbA<sub>1c</sub>). Also studies have shown that there is statistically association between DRPs and renal impairment, polypharmacy, cardiovascular disease, elderly status, and duration of hospital stay.

Drug related problems to antihypertensive agents in hypertensive patients with chronic kidney disease. Patients with CKD are considered as high risk population for experiencing ADEs due to aged-related structural and functional renal changes which causes alteration in drug pharmacokinetic and pharmacodynamic profile. In addition existence of co-morbidities including diabetes, hypertension and heart failure and multiple medication regimens increases the risk for potential medication errors, drug-drug interactions, and ADEs.

Present research study encompasses analysis of pharmacotherapy and adverse drug relations of 55 patients suffering mainly by arterial hypertension in India. For this purpose, data related to age, gender, diagnosis, pharmacotherapy, dosage scheme, strength, A.D.Rs collected and evaluated for the rate of utilization of particular drugs that are the most intently administered in hypertensive patients, their doses and the most frequently prescribed dosage schemes and analyzed statistically also and appear for potential drug related problems of these particular patients. In addition, discussion of therapy strategy and management of these particular patients regarding pharmacotherapy based evidence used in arterial hypertension were been also mentioned. On the basis of all data obtained a general conclusion was also drawn.

## Methods

### Data extraction

This is a retrospective study, to examine the pharmacotherapy and drug-related-problems in 55 hypertensive patients. The data was obtained from Dept of Medicine, PMCH Udaipur regarding age, gender, diagnosis, pharmacotherapy, dosage scheme, strength and adverse drug reactions for the selected patients and subjected to statistical analysis.

The data was collected between July 2019 to September 2019.

### Methodology – study population

Patients of age 40 and over were included in this study.

Inclusion criteria:

- Patients with arterial hypertension

- Patients who had during the last visit BP higher than 140/90 mmHg.

### Methodology – evaluation

All the data evaluated by incorporating to excel sheet and analyzed for the antihypertensive agents, as well as some additive agents like antidiyslipidemics. More specific, frequency of used active substances and pharmacological groups, as well as D.R.P to particular pharmacological groups was also preliminary examined.

Data were subjected to statistical analysis also.

### Result and Discussion

Raised blood pressure (BP) has emerged as the most important risk factor for global morbidity and mortality. The latest iteration of Global Burden of Diseases (GBD) study has reported that high systolic BP, poor dietary intake and tobacco use are most important risk factors for mortality as well as morbidity.

In India also, it has emerged as the most important risk factor for deaths and disability (Gupta *et al.*, 2018) [5]. According to reports from World Health Organization (WHO), GBD study (Farouzanfar *et al.*, 2017) [6], and Non-Communicable Disease Risk Factor Collaboration (NCDriSC) (NCD-RISC, 2017) [7] prevalence of hypertension is increasing globally and currently more than 1 billion people have hypertension (defined with standard criteria as systolic BP  $\geq$  140 and/or diastolic BP  $\geq$  90 mm Hg).

In the present work, 55 patient cases with diagnosis of arterial hypertension were incorporated that visited Dept. of Medicine, Pacific Medical College & Hospital, Udaipur. Gender wise distribution of hypertensive patients showed that prevalence of hypertension was higher in men than in female of aged 61 years and above. Several studies have shown that male older than 61 years consistently have higher levels of hypertension compared to women of the same age group (Everett and Zajacova, 2015) [8]. Observed gender differences in hypertension, which exist in human and animal populations, might be due to both biological and behavioral factors (Sandberg and Ji 2012) [9].

Accordingly, diabetes and hypertension are closely interlinked because of similar risk factors, such as endothelial dysfunction, vascular inflammation, arterial remodelling, atherosclerosis, dyslipidemia, and obesity. Results also suggested that dyslipidemia and C.H.D seems to be the most frequently coexisting diseases that accompany hypertension, accounting for 40% and 28% of the population respectively. These findings can be supported by the results of a study which have shown that hypertension, dyslipidemia, diabetes mellitus and obesity have been increased in alarming rates in India population, increasing the risk for C.H.D (Patrie *et al.*, 2018) [10].

Moreover the 89% of the total number of antihypertensive active substances was prescribed once daily and only 34% and 39% of the total population treated by monotherapy and dual therapy respectively and the rest by combination of three or more active substances (Figure 1 (A) and (B)). Concerning some other studies, have also showed that combination of two or more active substances in lower doses could be more effective comparing to monotherapy. In addition regimens that used once daily could be more effective by increasing patients' compliance (Thomas *et al.*, 2017; Gradman *et al.*, 2013) [11, 12].

In addition, the choices of drugs for treatment and management of arterial hypertension should be based on patient age, severity stage and existence co-morbidities, as well as should be in agreement with hypertension treatment guidelines. According to European society of hypertension in stage 1 hypertension, all first choice antihypertensive agents are appropriate for starting and maintenance of antihypertensive therapy, as monotherapy or in combination despite the age and gender. Also low dose diuretics are the best choice treatment on the beginning, in patients with uncomplicated hypertension stage 1. In case of stage 2 hypertension, combination of active substances should be preferred (Guerrero-García and Rubio-Guerra, 2018) [13].

In our retrospective study regarding the above results, the most favorable antihypertensive choices in case of monotherapy, appears to be BBs followed by ARBs. On the basis of findings obtained, most frequently drug formulations used were antihyperlipidemics, BBs, anticoagulant/antiplatelet and ARBs i.e. 75%, 63%, 45% and 39% of the population respectively (Figure 2 and 3). In addition to this, other drug formulations (Single as well as in combinations) were also given like ACEIs, CCBs, ARBs+CCBs, Thiazide Diuretics+ARBs/ACEIs, Loop Diuretics and some Other Agents like Digoxine, Amiodarone and Trimetazidine seems to be less effective and accounts for 14%, 18%, 18%, 12%, 11% and 15% (figures 9, 10) of the study population respectively (Figure 3 and 4).

In our study population, dyslipidemia and C.H.D are the most frequently co-morbidities along with hypertension, something that can explain also the high frequency usage of antidyplipidemics which is additive to antihypertensive therapy. According to Ariyanti and Besral (2019) [14] studied, combination of CCBs with statins especially of amlodipine with atorvastatin shows excellent efficacy and safety profiles for the treatment of hypertension and dyslipidemia.

In our study HCTZ which belongs to thiazide diuretics, was used only as a combination therapy, mainly with BBs, ACE is and ARBs. Combination of thiazides with newer antihypertensive agents is recommended by many guidelines in response to realization that most patients require multiple antihypertensive agents to reach B.P treatments goal. One explanation for that could be that one pill regimen can increase patient's compliance by decreasing A.D.Rs and also two active substances in lower doses in one pill are more effective in lowering the blood pressure comparing to monotherapy (Paudel *et al.*, 2017) [15].

Findings also suggested that ACE is having used much less effective as compared to ARBs. The main reason is some side effects, like dry cough or because couldn't be tolerated by the patients. It was observed that 65% of study population had an experience of one adverse drug reaction, 15% had an experience of two adverse drug reactions and only 16% had no experience of A.D.R (figure 4a).

A.D.Rs of particular drugs can influence compliance of antihypertensive agents, because they frequently decrease QoL, which is important by asymptomatic disease. Grassi *et al.* (2011) [16] reported that up to more than half of antihypertensive medication discontinuation can be attributed to adverse effects.

In more details 37% of the study population they experienced fatigue, dizziness, weakness, bradycardia mainly due to BBs, 24% they experienced peripheral edema

mainly due to amlodipine and 15% they suffered from dry cough due to ACEIs. Also 14% they showed myalgia and increased CPK levels due to statins which was an additive to antihypertensive therapy, and the rest of adverse drug reaction, each of them accounts 6% or less of the total study population (Figure 4 b and c).

Adverse effect significantly contributes to antihypertensive medication non-adherence in hypertensive patients. Patients should be counseled about adverse effects common to their antihypertensive medications and should be directly involved in the decision process. Studies with prospective study designs should be done in the future to help better understand the association between adverse effects and non-adherence.

Regarding study limitations, the obtained results are not representative of a whole population due to a small sample size used for the research. The results were gathered from just one health care professional, as a result, this does not correspond to a larger population. Moreover, the drug related problems commonly faced in India population and a means of dealing with them.

Furthermore knowledge of patient's beliefs about their disease and pharmacotherapy regarding price and effectiveness would be helpful in better management of patient adherence and would aid in better evaluation of the results.

As a result, in future studies, larger population size and the involvement of numerous health care professionals will be necessary to produce more accurate and representative findings.

It can be concluded that arterial hypertension is an important threat factor for cardiovascular diseases and also responsible for improved morbidity and mortality. So many pharmacological drugs are available for treatment; though, the preference depends on the patient's age, diagnosis, co-morbidities, suitable strength-dosage scheme and patient's permissibility. Additionally any appearance of adverse drug reactions (A.D.Rs) because of side effects of the drugs or due to bad manage and patients non compliance, it was treated chiefly by lessening the doses of the drugs, switching them to another active substances from the same pharmacological group or by adding more active substances from different pharmacological groups in lower dosages in order to achieve the B.P goals.

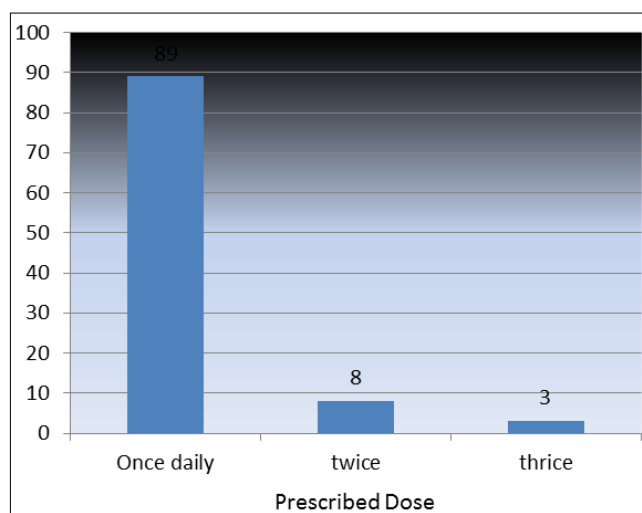
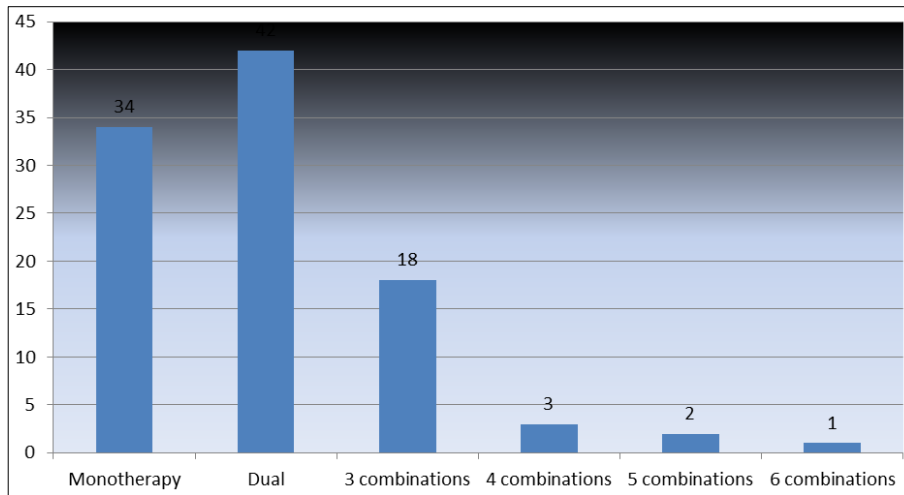
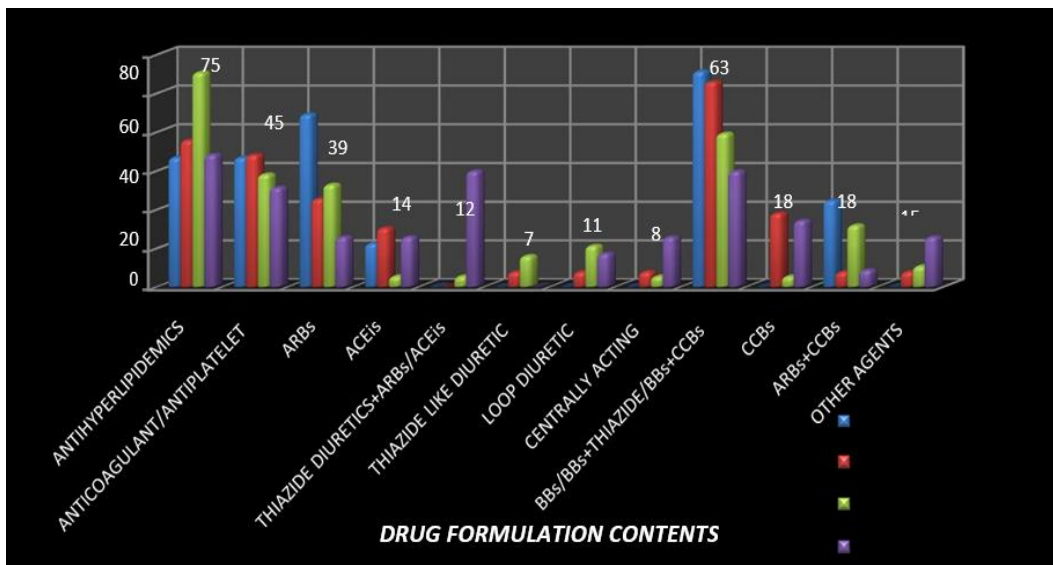


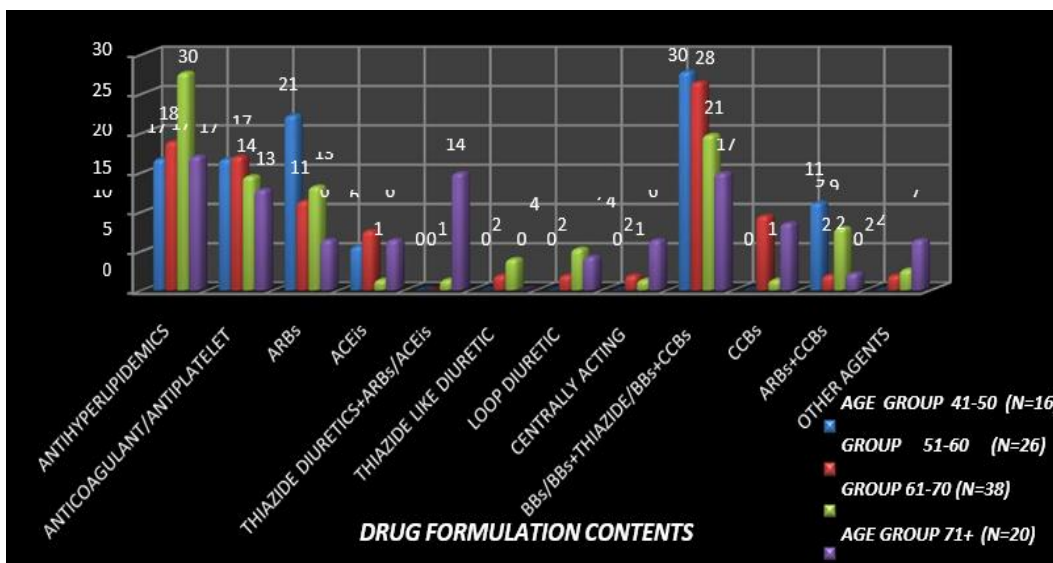
Fig 1(A): Percent frequency of dosage scheme, where 100% is the total number of antihypertensive active substances (N 30).



**Fig 1(B):** Total number of antihypertensive active substances per patient, where 100% is the total number of patients' population (N=55).



**Fig 2:** Percent frequency of different drug formulation contents use among patients' population, where 100% is the total number of patients' population (N=55).



**Fig 3:** Percent frequency of different drug formulation contents among patients' age group, where 100% is the total number of drug formulation contents per patient that have been used on each age group.

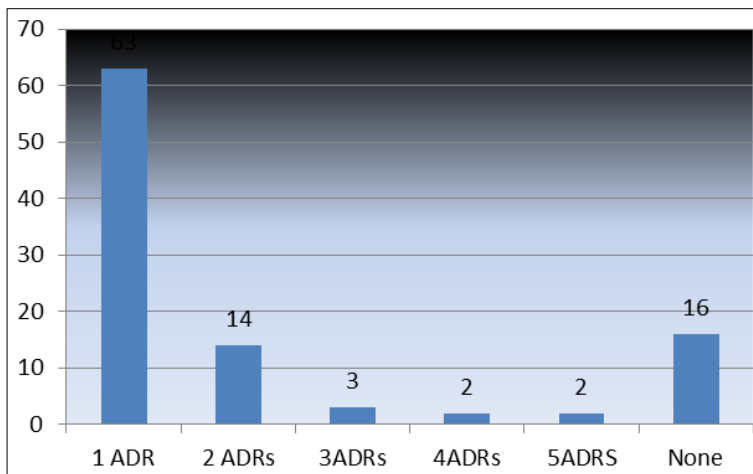


Fig 4(a): Numbers of A.D.R. per patient, where 100% is the total number of patient population (N=55).

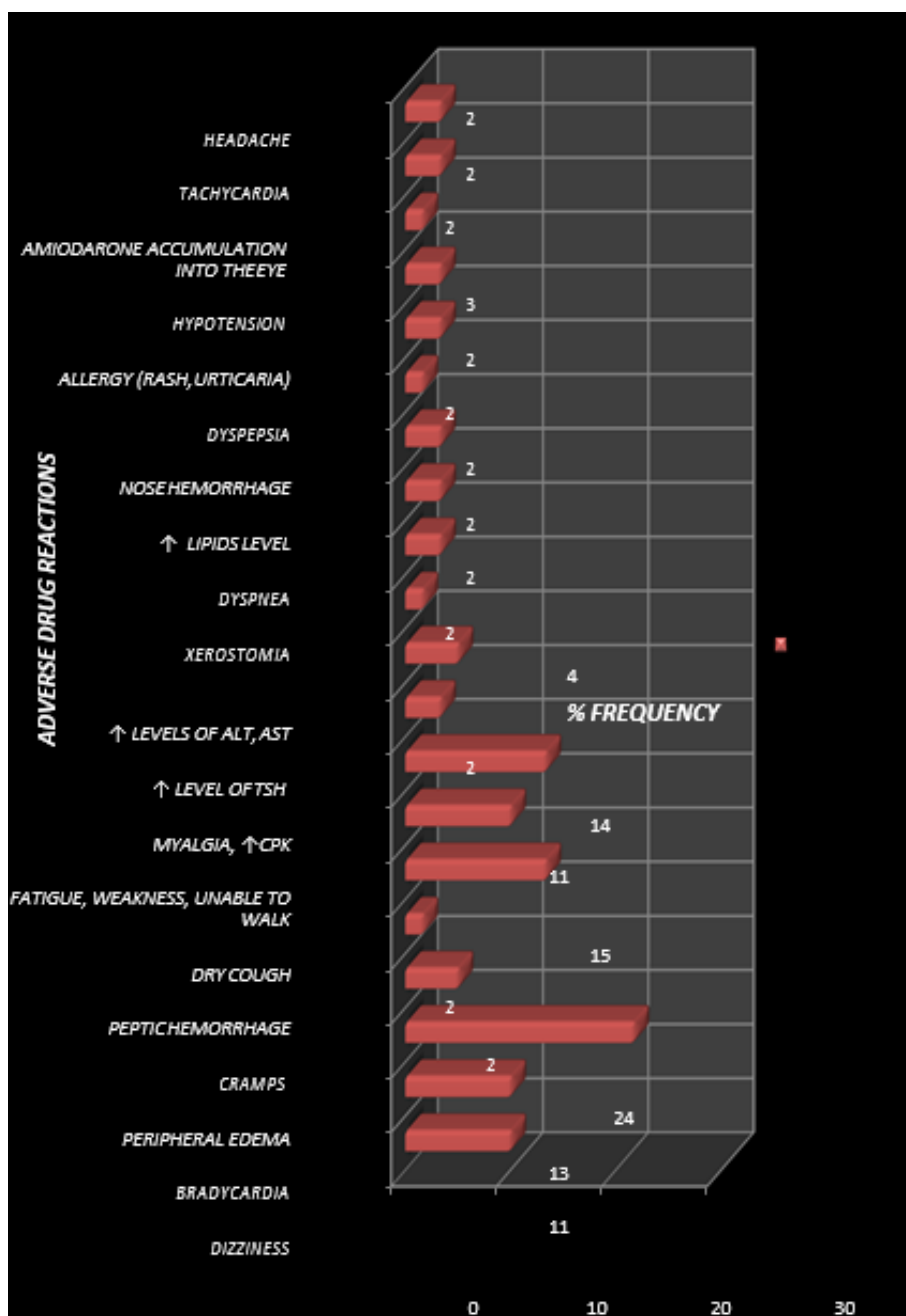
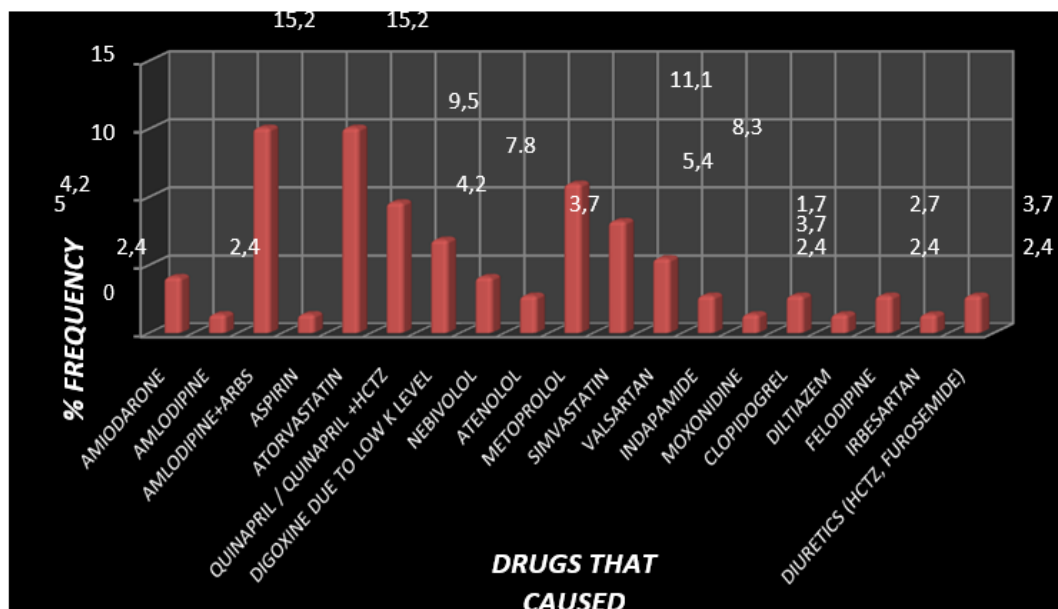


Fig 4(b): Percent frequency of adverse drug reactions among patients' population, where 100% is the total number of patients' population (N=55).





**Fig 4(C):** Percent frequency of A.D.R. per drug, where 100% is the total number of A.D.R. that was appeared for each drug (N=70).

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