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A PROSPECTIVE OBSERVATIONAL STUDY ON DRUG UTILISATION PATTERN IN CARDIOVASCULAR PATIENTS IN MULTISPECIALITY HOSPITAL

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ABSTRACT:
Cardiovascular disease is a group of disorders affects heart and blood vessels. The primary cause of heart attacks and strokes which are usually acute events is the blockage that prevents blood from flowing to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that can supply from heart or brain. Blood clots or haemorrhage from blood vessels can both results in strokes. This survey can explain about the detailed research and the factors involved that cause cardiovascular disease. Its drug utilization pattern from the patients and observe its binding energy of the given drugs. Thisobservational survey was taken from the multispecialty hospital in Chennai.

Keywords: Cardiovascular disease, Age grouping, Drugs involved, CADD, Docking softwares, Binding energy, Molecular structure.

INTRODUCTION:

PHARMACOVIGILANCE:

Pharmakon in Greek is meant as Medicinal substance: Vigilia in Latin is meant as monitoring. Pharmacovigilance is a branch of science that deals with the detection, assessment, understanding and prevention of adverse effects or any other drug related problem.

DRUG UTILISATION PATTERN:

Drug utilization studies provide the principles that are related to the prescribing, dispensing, administering and medication adherence and its related factors.

A drug consumption pattern study is a useful exploratory technique for assessing current trends in drug use and prescription appropriateness. It's a descriptive and analytical strategy for gathering, quantifying, interpreting, and evaluating prescribing patterns, as well as dispensing and conception, in order to improve present therapy and improve patient safety.[1]

POLYPHARMACYAND DRUG INTERACTION:

Multiple medicines are frequently necessary due to a variety of comorbidities, which can make it difficult to obtain proper treatment. As a result of polypharmacy, drug interactions might arise, confounding diagnosis and leading to various unwanted results. Diabetes, obesity, COPD, HTN, CAD, CVA, arrhythmia, OA, thyroid illness, hyperlipidaemia, renal dysfunction, and anaemia are all comorbidities associated with cardiovascular disorders. When a patient receives more than one drug, a drug-drug interaction (DDI) occurs, with the risks of it increasing with the number of drugs taken. A wide range of DDIs can cause toxicity, modify desirable therapeutic outcomes, or possibly result in a life-threatening disease. One of the risk factors for drug-drug interactions is polypharmacy, which is utilised to address the patient's comorbidities. Drug - drug interactions are a common cause of adverse drug reactions (ADRs) that end up in the hospital or emergency room. Drug interaction is exacerbated by polypharmacy, which leads to further difficulties.[2]

MAINMOTO OF DRUG USAGE REVIEW:

Drug Utilization Studies (DUS) in government clinical settings, a common healthcare option in developing nations like India, are critical to the country's development of an effective healthcare system. When drug consumption trends are studied across different regions/times, hypotheses about the causes and consequences of the variances can be generated. There is a scarcity of information on pharmacological trends for Indian outpatients with cardiovascular problems.[3]

The primary goal of drug use research is to help people utilise medications more rationally. The heart and circulatory system are mostly affected by cardiovascular disorders. It is a leading cause of morbidity and mortality in children. Cardiovascular disease progression is very high in India, and it is the main cause of death in those aged 25 to 69 years. In India, ischemic heart disease is the leading cause of death. Ischemic heart disease is expected to kill two and a half million Indians between now and 2020. Males are more afflicted than females. Coronary artery disease, angina, myocardial infarction, stroke, hypertensive heart disease, cardiomyopathy, endocarditis, congestive heart failure, and deep vein thrombosis are all examples of cardiovascular illness.According to a population-based study, atherosclerosis is the leading cause of cardiovascular disease. Antiplatelet medications, anticoagulants, anti-anginal pharmaceuticals, beta-blockers, angiotensin converting enzyme inhibitors, angiotensin receptor II blockers, calcium channel blockers, and diuretics are some of the treatments available. Aspirin, beta blockers, angiotensin converting enzyme inhibitors, and statins should be used in all cardiovascular disease patients, according to guidelines based on evidence from randomised controlled trials, as well as percutaneous coronary intervention or coronary bypass surgery as secondary prevention.[4]

Study Design:

Inclusion criteria-

- The prescription form of the outpatients.
- Case report of inpatient of cardiac department.

Exclusion criteria-

- Prescription report of Emergency cases.
- Prescription report of patients below 18 years of age.

Hospital based, pre-post interventional study was conducted at Cardiology department ward of ACS Medical Hospital, Chennai, Tamil Nadu, India from February 2022 to April 2022. Patients who met the inclusion criteria were included in the study.

METHODOLOGY:

Permission to carry out the study was obtained from the authority before commencement. Patients attending the hospital were approached by three trained research assistants, and asked whether they would participate in the survey. The research assistants collected the data

through a face-to-face pre-tested questionnaire. Data collection was conducted after explanation to each patient background, objectives, data protection, and privacy.
All participants, before answering signed an informed consent form explaining the study procedures and that they were free to leave out questions if they did not wish to answer. The participants were assured that all information was kept confidential, because no names were recorded. The participants did not receive any compensation for participating.
Data was collected by a means of a questionnaire composed of 20 questions developed in English language. The investigators provided aid to illiterate

e patients in explaining and filling the questionnaire. Patients were asked to answer 20 questions that assess their lifestyle, current medication use, any allergies caused by their current medication, their smoking/alcohol habit etc.
The patient's use of medication wasused to analyse data and generate tables and figures to explain the relationship between several variables of this study

SURVEY RESULTS:

According to this review, when compared on the basis of age, the age group between 51-60 years have been highly affected by cardiovascular disease. The major reason for the cause of CVD among this age group was found to be the increased stress and among the people who do not have enough of sleep of at least 7 hours.
When compared among the gender 59.03% of male are affected by cardiovascular disease while only 40.96% of women were affected. Among these women mostly affected women are found to be working women who have a stressful lifestyle.
The maximum number of (CVD) patients are male due to their improper lifestyle such as usage of tobacco and other harmful products while women do not use that. Men face a lot of stress due to work pressure and lack of sleep. Improper diet following and lack of exercise. Most of the patients with CV disease were found to obese, thus obesity is also a major cause for cardiovascular disease.
The commonly prescribed drugs were found to be, NSAIDs – Aspirin (63.83%), Angiotensin II receptor antagonist (31.52%), ACE inhibitors (30.12%), Beta blockers (22.89%), Proton pump inhibitors (15.6%), Calcium channel blockers (14.45%), HMG Co-A reductase inhibitors (13.26%), Antiplatelets (12.03%), DDP IV inhibitors (10.84%), Nitrates and sulphonyl urea (9/63%), 3 KAT inhibitors, Biguanides, Antibiotics (8.43%).
The statistical reports of the mentioned data, provides a basic drug utilisation pattern for further studies. This prospective study is performed to get an overview about the drug prescribing pattern in cardiovascular patients.
The resulting commonly prescribed drugs are then presented using Computer Aided drug design (CADD).

Computer aided drug design (CAAD):

Computer Aided Drug Design is a modem computational technique used in the drug discovery process to identify and develop a potential lead CADD includes computational chemistry, molecular modelling molecular design and rational drug design. It is being used to optimize identified leads.[5]
CADD approach can be utilized in 4 phases (screen small molecule library against the target using virtual screening (US) protocol to identify hits/leads, (i) investigate specificity of the selected hits from US using molecular docking in the active site of other known targets, id predicting ADMET properties of the selected hit using in silica techniques and the promising hits are called as lead and (iv) helps to optimize the leads by designing better molecules For synthesis and testing Based on the availability of the 2D structure of the target protein,

CADD techniques are grouped into either of two types structure based and ligand-based drug design (S800 and LBDD).[6]

CADD approach saves time it is fast and cost-effective in our current study, we have utilized these CADD techniques to design and analyse new chemical structures to the already existing drug rosiglitazone Thus, keeping in mind the toxicity of this compound, the physiochemical properties, toxicity studies and docking studies were performed for newly designed thiazolidinedione analogues, in order to bring compounds with increased efficacy and decreased toxicity.[7]

MOLECULAR DOCKING:

The structure-based drug designing (SBDD) methods which relies on the knowledge of three-dimensional structure of biological target, have a distinguished role in modem drug discovery process. Molecular docking is most common method used in structure-based drug designing use of its accurate prediction confining to the suitable binding sites.[8]

Molecular docking is the computational prediction of favoured orientation of a ligand to its target molecule when complexed with each other. By knowing the optimized conformation and orientation through molecular docking.

We can determine the binding affinity using scoring functions. The docking can be: (a) Rigid docking (b) Manualdocking and (c) Flexible docking, the most common method being the flexible ligand docking where in the ligand is free to move and the protein is kept stationary. Different software are available for docking namely: Glide, AutoDock , AutoDock vina, Gold, Pass prediction, Pyrx, Biovia etc. In our study, we've used the Pyrx software to predict the docking score.[9]

Pyrxis a docking software which predicts the ligand-protein binding score via high-throughput virtual screening. Unlike other methods for docking ligands to the rigid 3D structure of a known protein receptor, Pyrx provides a high degree of accuracy of the conformational, orientational and positional of the docked ligand.

STATISTICAL REPRESENTATION OF VARIOUS PARAMETERS

AGE FACTOR

AGE GROUP	NUMBER OF PATIENTS
31 – 40	4
41 – 50	7
51 – 60	32
61 – 70	31
71 – 80	9

TABLE 1: Age factor

GENDER	NUMBER OF PATIENTS
MALE	49
FEMALE	34

FIGURE 1: Various age group affected by CVD

Among 83 patients the people under age group 51-60 have been highly affected with the cardiovascular disease and patients in age group 31-40 has least affected. The number of people affected in various age groups are represented in the above graph. (Fig.2)

GENDER FACTOR

TABLE 2: Gender factor

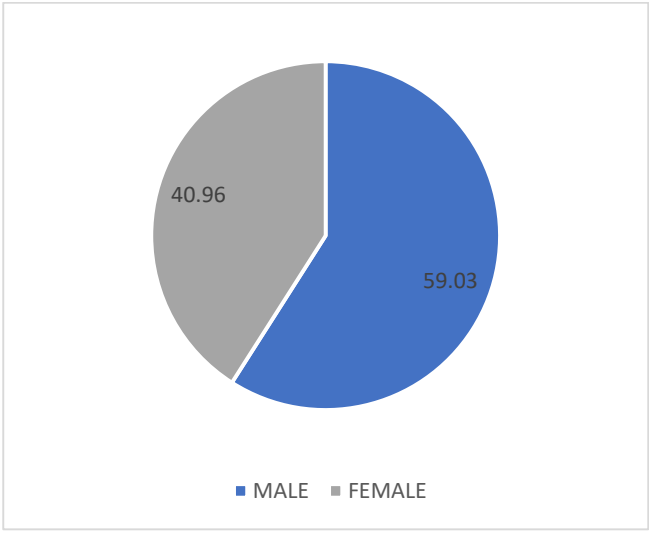


FIGURE 2: Various gender group affected by CVD

Among 83 patients, male have been highly affected when compared to females, this may be due to the differentiation in the stress between working hours for male and female. The graphical representation of this is mentioned in the above graph.

DIET FACTOR

DIET	NUMBER OF PATIENTS
VEGETARIAN	12
NON – VEGETARIAN	71

TABLE 3: Diet factor

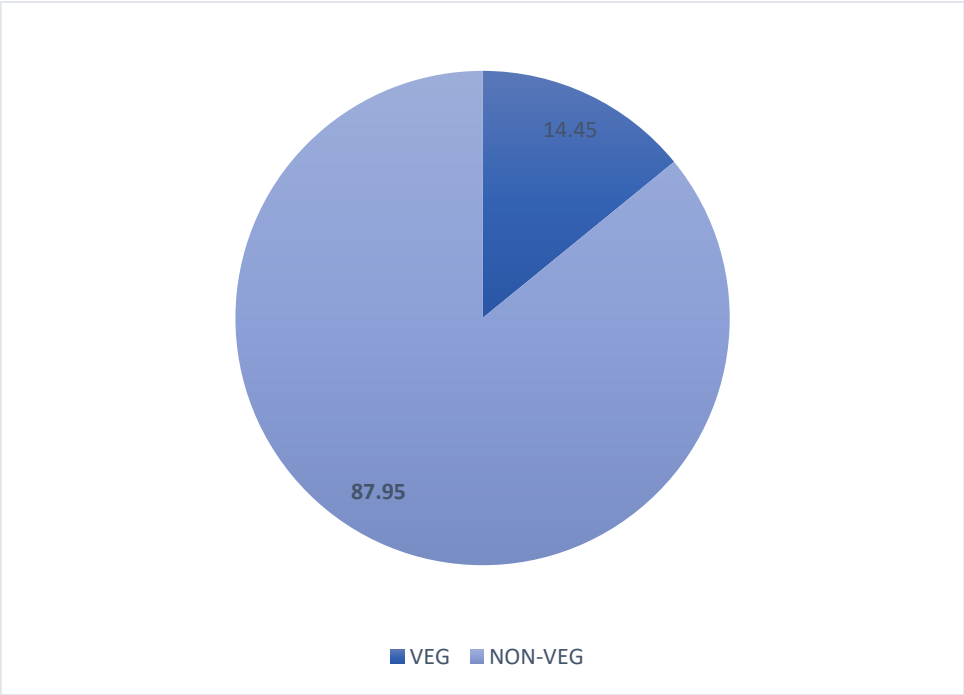


FIGURE 3: Dietary habits

Among 83 patients 71 are Non vegetarians and remaining 12 are vegetarians. The maximum number of CVD patients are found that they usually follow non veg diet. The graphical representation is mention in the above graph. (Fig.3)

WEIGHT FACTOR

WEIGHT (IN KG)	NUMBER OF PATIENTS
41 – 50	3
51 – 60	41
61 – 70	24
71 – 80	15

TABLE 4: Weight factor

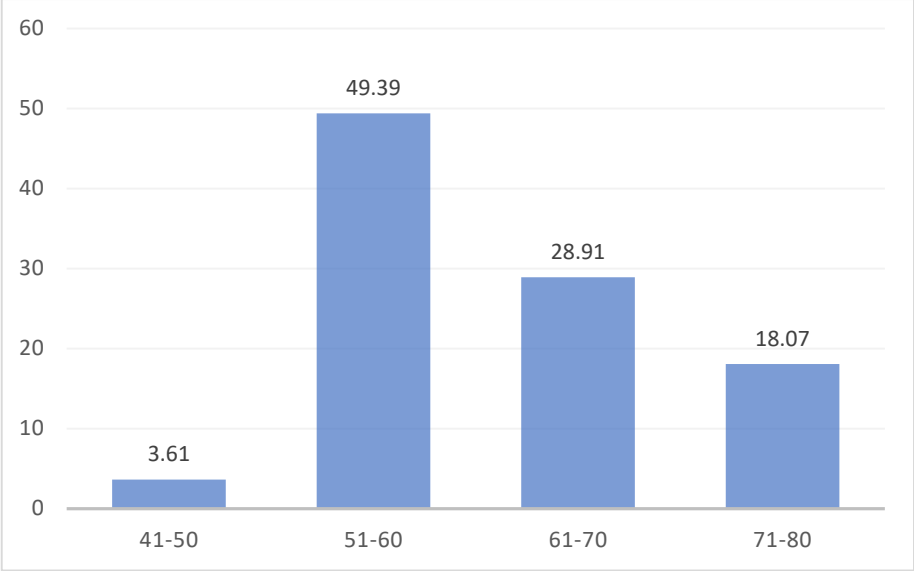


FIGURE 4: Various weight groups affected by CVD

Among 83 patients the maximum number of people affected by CVD are in the weight group of 51-60 kg and the least number of people affected fall in the weight group of 41-50 kg category. This data represents that the obese patients.(Fig.4)

SMOKING AND OTHER HABITS

HABIT	NUMBER OF PATIENTS
SMOKING ONLY	11
SMOKING AND ALCOHOL	19
NIL	53

TABLE 5: Smoking and other habits

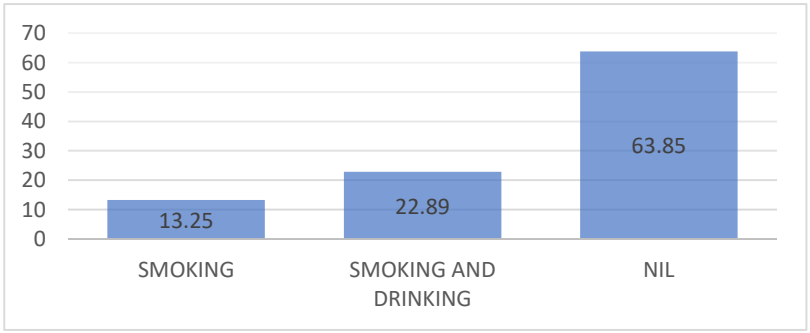


FIGURE 5: Smoking and other habits

Among 83 patients, 22.89% of people are drinkers and 13.25% of people are smokers. The above graph represents the statistical report of the number of people who use tobacco and other products. (Fig.5)

DRUGS PRESCRIBED:

The common drugs prescribed by the physician are as follows

COMMONLY PRESCRIBED DRUGS (1)

DRUGS PRESCRIBED	NUMBER OF PATIENTS
Calcium Channel Blockers	12
HMG Co-A reductase inhibitors	4
Beta Blockers	19
Nitrates	8
3 KAT inhibitors	7
Sulphonyl Urea	8

TABLE 6: Commonly prescribed drugs (1)

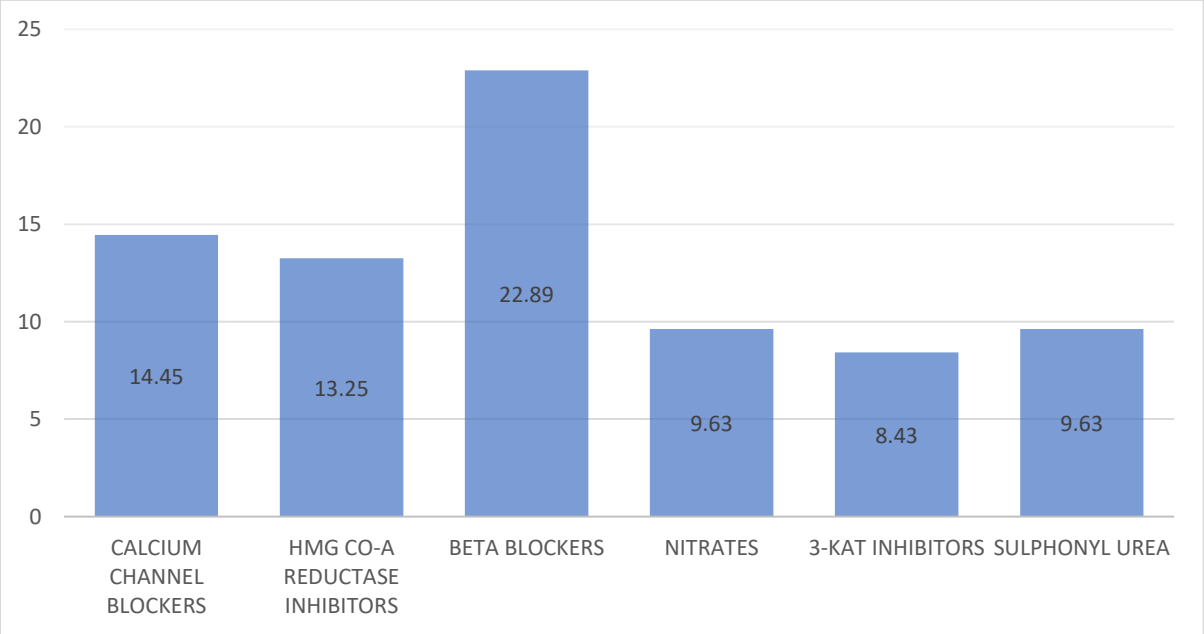


FIGURE 6: Commonly prescribed drugs(1)

Among the abovementioned drugs, Beta blockers are highly prescribed and 3 KAT inhibitors are the least prescribed when compared to other class of drugs present in the above table. The graphical representation of this data is mentioned above.

COMMONLY PRESCRIBED DRUGS (2)

DRUGS PRESCRIBED	NUMBER OF PATIENTS
DPP IV inhibitors	9
Antiplatelets	10
ACE inhibitors	25
NSAID	7
Biguanides	53

TABLE 7: Commonly prescribed drugs (2)

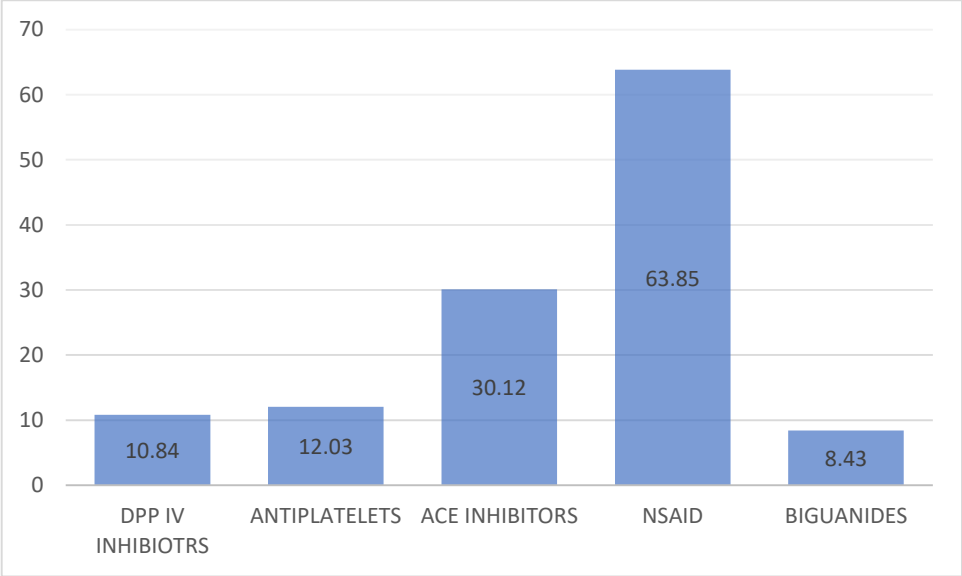


FIGURE 7: Commonly prescribed drugs (2)

Among the above mentioned drugs, NSAID are highly prescribed and biguanides is the least prescribed drug when compared to other class of drugs in the above table. The graphical representation of this data is mentioned above.

COMMONLY PRESCRIBED DRUGS (3)

DRUGS PRESCRIBED	NUMBER OF PATIENTS
Antibiotics	7
Proton Pump Inhibitors	13
Angiotensin II receptor antagonist	26
Diuretics	7
Nutritional Supplement	14

Others	23

TABLE 8: Commonly prescribed drugs (3)

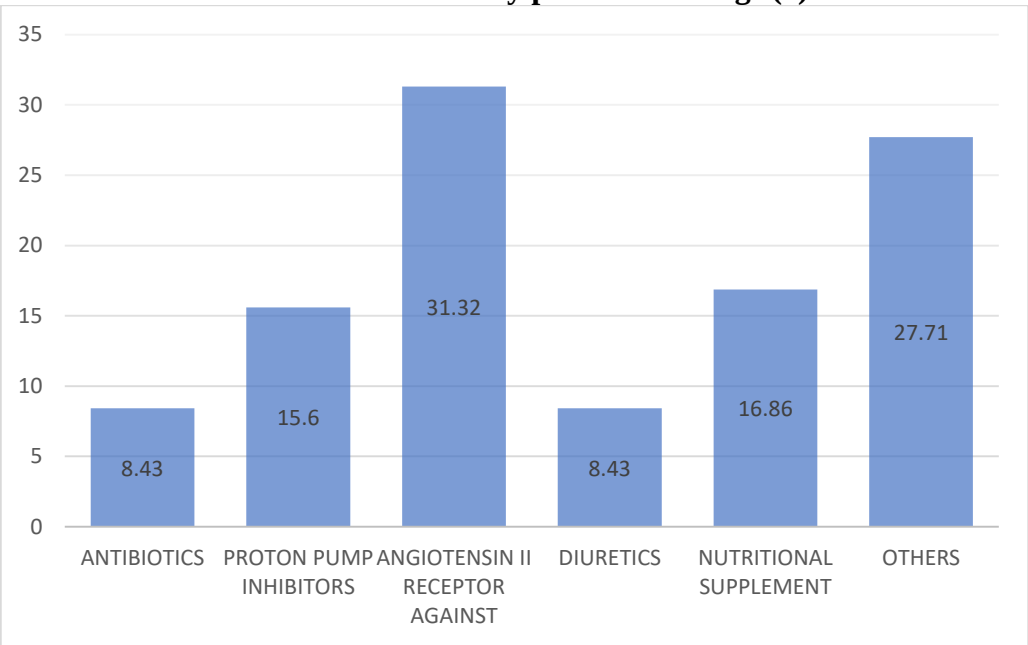


FIGURE 8: Commonly prescribed drugs (3)

Among the above mentioned drugs, angiotensin II receptor agonist are highly prescribed and antibiotics and diuretics are the least prescribed drugs when compared to other class of drugs in the above table. The graphical representation of this data is mentioned above. (Fig.8)

For these commonly prescribed drugs, Docking studies were performed to find the binding affinities for few drugs and to determine the 2D and 3D model structures for each drug. The most commonly prescribed drugs were found to be – Pantoprazole,Ramipril, Telmisartan, Phenytoin, Losartan, Amlodipine, Aspirin, Enalapril, Carvedilol,Metoprolol succinate, Metformin, Alprazolam.

DOCKING STUDY:

SOFTWARE AND HARDWARE-

The computer system with intel ® core ™ i5 9th Gen CPU processor having 4GB RAM and 500 GB hard disk with windows 10 as the operating system was used. All the computation studied were carried out in various softwares such as Schrodinger (2020-3)-Maestro, version 8.0 and discovery studio visualizer v21.1.0. online tools like swiss ADME, GUSAR and chemical database such as protein databank were used.

TARGET SELECTION-

The target are precise components evidently existing in cellular or molecular shape that are involved in the pathology of disease; they will be receptors, enzymes, nucleic acids, hormones, ion channels etc. The computational techniques mainly used, molecular docking by setting a digital molecular shape into a binding site of the biological micro molecules. In this case the three-dimensional (3D) crystal structure of Turkey beta 1 adrenergic receptor (PDB ID: 4AMJ) was obtained from the protein databank (www.rcsb.org/pdb) in pdb format.

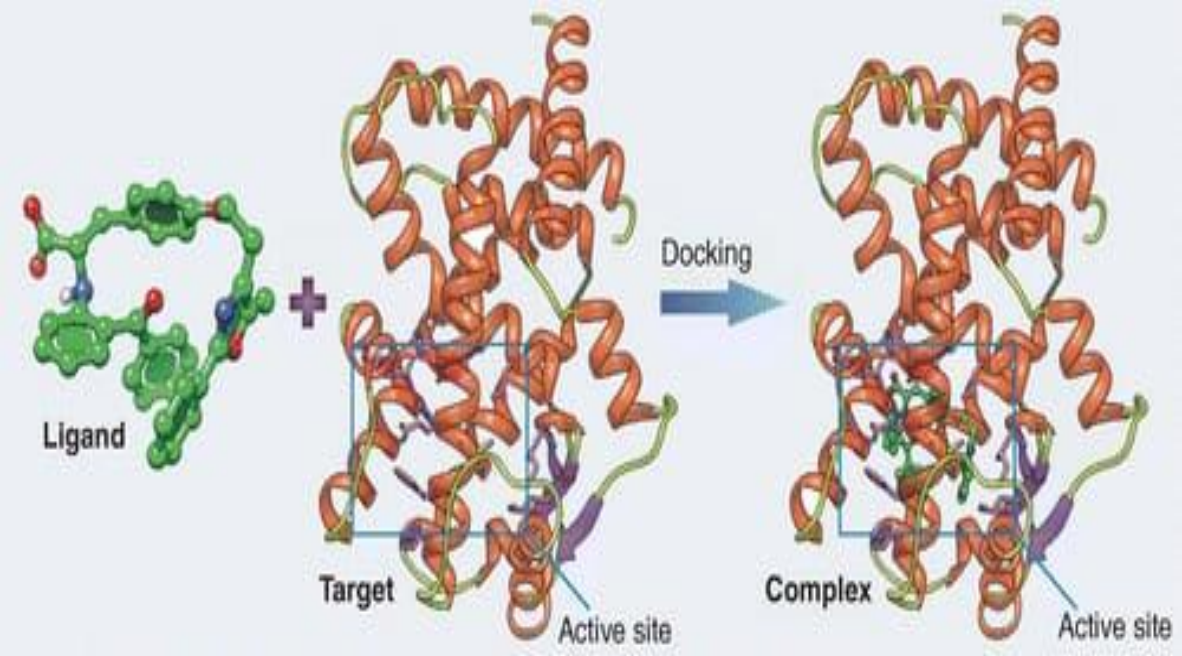


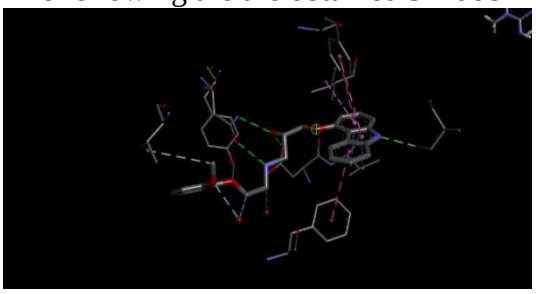
FIGURE 9: Molecular Docking

S.NO:	COMPOUND NAME	BINDING AFFINITY (kcl/mol)
1	Pantoprazole	-7.4
2	Ramipril	-7.7
3	Telmisartan	-9.0
4	Phenytoin	-7.4
5	Losartan	-8.2
6	Amlodipine	-6.2
7	Aspirin	-5.7
8	Enalapril	-7.4
9	Carvedilol	-7.1

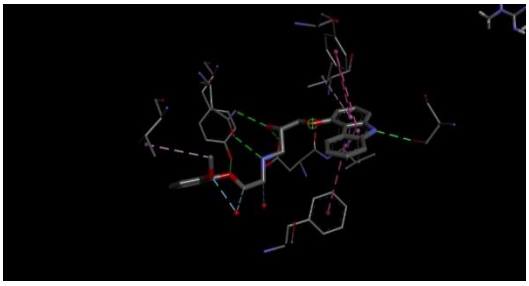
10	Metoprolol succinate	-6.1
11	Metformin	-4.8
12	Alprazolam	-7.6

TABLE 9: Molecular Docking Scores

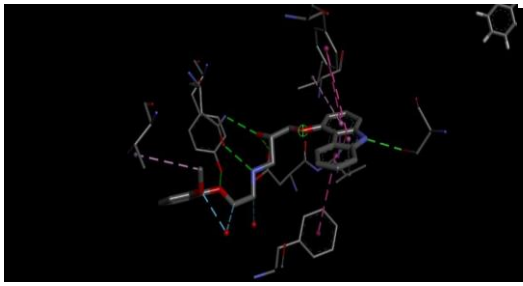
The following are the obtained 3D docking poses,



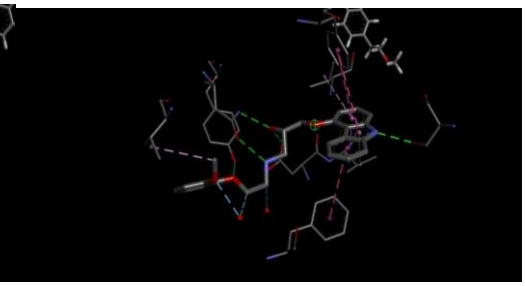
Alprazolam



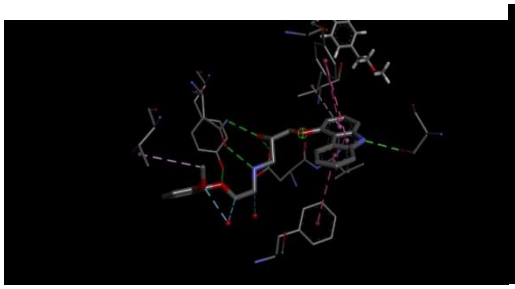
Metformin



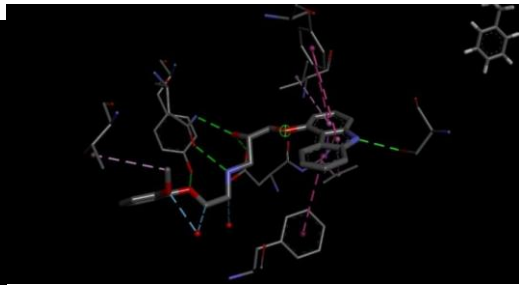
Aspirin



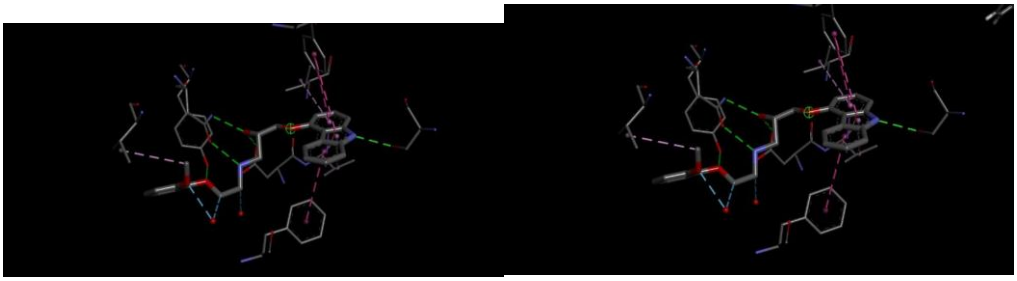
Metoprolol succinate



Amlodipine



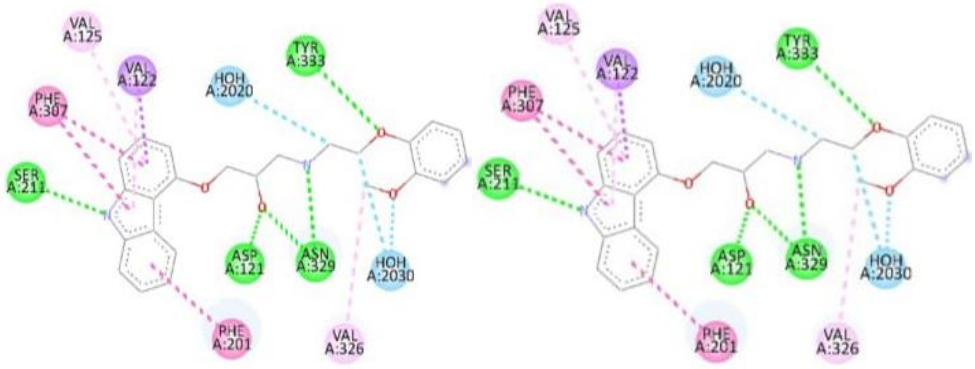
Ramipril



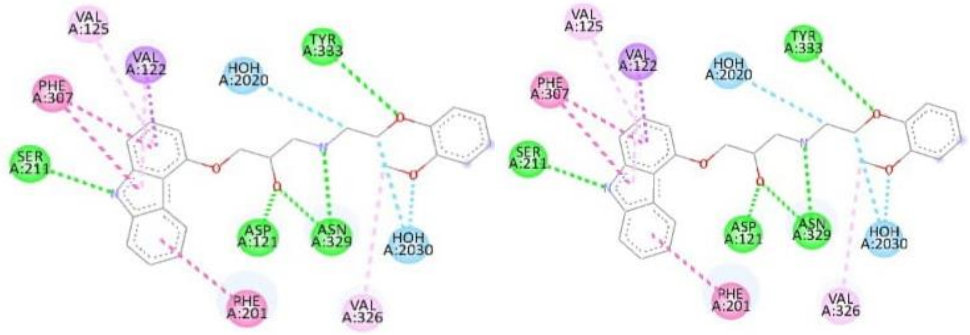
Losartan Phenytoin

FIGURE 10: 3 D Docking poses

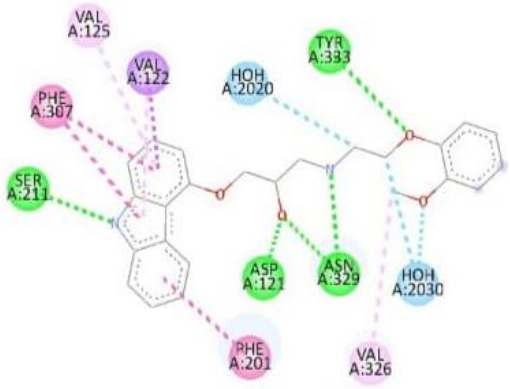
The following are the 2D docking poses,



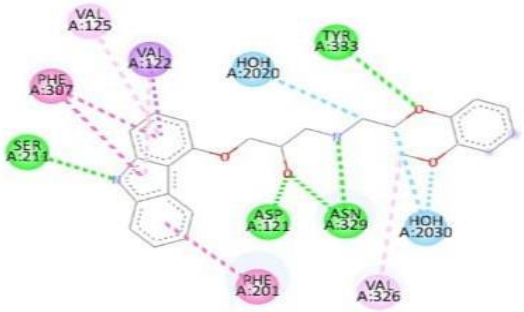
Alprazolam Metformin



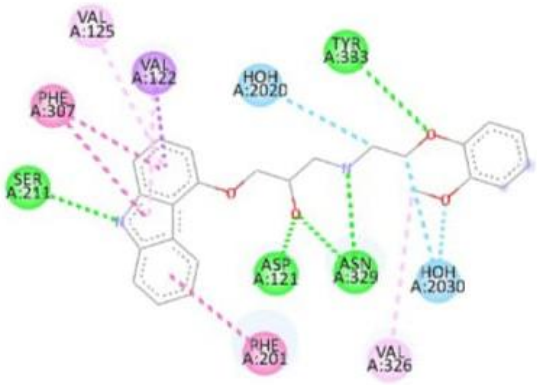
Aspirin Metoprolol succinate



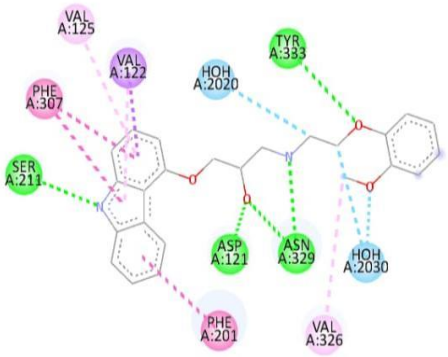
Amlodipine



Ramipril



Losartan



Phenytoin

FIGURE 11: 2D Docking poses

CONCLUSION:

This review has demonstrated the drug utilisation pattern in cardiovascular patients including both male and female above 18 years of age. The study was performed in a multispecialty Hospital, Chennai. The commonly prescribed drugs by the physicians were observed. The commonly prescribed drugs were found to be, Losartan, Enalapril, Phenytoin, Aspirin, Amlodipine, Metoprolol succinate, Metformin, Alprazolam, Carvedilol, Ramipril, Telmisartan, etc.

The drugs were designed and investigated for safety and efficacy for treating cardiovascular diseases. For this, we have performed molecular docking analysis (Pyrx). In conclusion, the compounds Telmisartan, Losartan, Ramipril and Alprazolam showed the maximum potency and binding affinity to the 4AMJ receptor.

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