

## ASSESSMENT OF FIXED DOSE COMBINATIONS IN CARDIOVASCULAR DISEASES

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### ABSTRACT

**Aim:** The study aims at assessing fixed dose combinations in cardiovascular diseases. **Background:** Cardiovascular disease (CVD) includes hypertension, myocardial infarction, atherosclerosis, coronary artery disease and congestive heart failure. Fixed dose combinations (FDC) are the drugs with more than one drug in fixed ratio with valid therapeutic principles. **Methodology:** A number of effective therapies reduce the risk of morbidity and mortality in patients with a retrospective study conducted in a tertiary care hospital at Hyderabad for 8 months from November 2017 to June 2018. During this period a total of 150 prescriptions were collected and analysed. **Results:** The study is comprised of 57% males and 43% females with more than 50% of patients being obese. 2110 FDCs are prescribed and all of them were Branded products. The total No. of FDCs prescribed were 69.95% and 30.04% were of Repeated FDCs Drugs. The number of combinations were 56.66% of FDCs were Two drugs combination, 42% of FDCs were Three drugs combination, 1.34% of FDCs were More than three drugs. The margin of error of repetitive drugs is in between 0.53%-1.70%. 23% of cases were the highest comorbid percentage assessed for Hypertensive patients. 24% of cases are having a social background of consuming both alcohol and smokers. The highest number of FDCs prescribed were Antihyperlipidemic and Antiplatelet

**KEYWORDS:** FDC, hypertension, myocardial infarction, Branded, Repeated FDCs, retrospective study.

### INTRODUCTION

Fixed dose combinations are pills that combine two or more drug molecules with distinctive modes of pharmacological activities in a single dosing unit and optimize the treatment. We will depict the information sets assets, the cohort studied in these investigations, additionally the factual strategies utilized to examine the information. At that point, the results of the examinations performed which have inspected the endorsing uniformities and imbalances of FDCs for age, sex, financial hardship, comorbidities after to begin with determination of MI, angina, Pad and PAD/CHD, besides, will provide about these results in ensuing segments beneath each illness. Final chapters are in general discussion and outline of this thesis finding, examining the study's quality/ impediments and conclusion, separately.

### BACKGROUND

CVD is one of the foremost common causes of passing worldwide. Within India more than one in three passings (35%) are due to CVD, and around 198000 passings are inferable to CVD each year. Several hazard components can increment the probability of creating any CVD. These chance components are either modifiable, for case

hypertension or non-modifiable such as age. In expansion, once a individual creates CVD, alteration of risk components can decrease horribleness and mortality.

A number of successful treatments exist that decrease the chance of mortality in patients with CVD. These treatments are basically, but are not restricted to, pharmacotherapies. This proposition will look at a number of cardiovascular illnesses, to be specific coronary heart disease (CHD) which incorporates (myocardial infarction (MI) and angina), and peripheral arterial disease (Pad) and look at the pharmacoepidemiology of prove based medicate treatments for each of these illnesses.

### AIM AND OBJECTIVES

#### Aim

To monitor the assessment of prescribing practice of fixed dose combinations in cardiovascular diseases.

#### Objectives

To highlight the prescribing practice of fixed dose combinations in cardiovascular diseases of inpatient department.

To ensure our points of interest are:

- Is there rationalist in the prescription of FDCs,
- Is there any polypharmacy,
- Whether the doses are prescribed by generic name,
- Whether the prescribed drugs are from EDL (Essential Drug List)
- Whether the treatment improves quality of life of the patient

## Methodology

### Study Design

It is a retrospective study conducted in a tertiary care hospital at Hyderabad for 8 months from November 2017 to June 2018. During this period a total of 150 prescriptions were collected and analysed.

### Epidemiology of Study

The study includes all patients in cardiology department suffering from cardiovascular diseases who were electively selected by prescription for the assessment of fixed dose combinations during the study period.

### Inclusions and Exclusions Criteria

#### Inclusion Criteria

All selective prescriptions consist of fixed dose combinations drugs.

### Exclusions Criteria

All sampling prescriptions in which all patients who had coronary artery disease doesn't consist of prescribed of fixed dose combinations drugs are excluded.

### Sampling Technique

Convenient enrolment technique was employed in which all patients in cardiac department who were electively prescribed with fixed dose combinations drugs in Prime Hospital from November 2017 to June 2018 were enrolled.

### Data Processing and Analysis

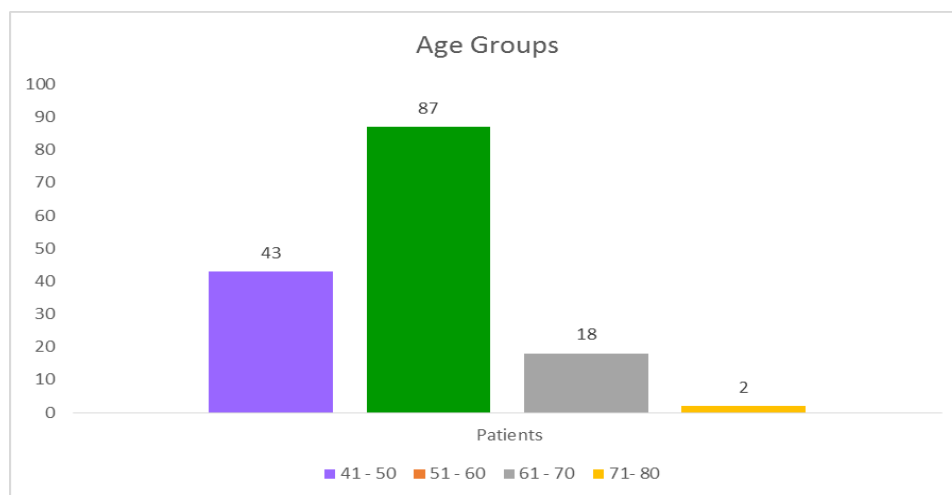
Data recorded on the case collecting sheets and was processed and checked for completeness and consistency using MS EXCEL program followed by data calculating and then data analysis using frequency tables and cross tabulation with respective statistical tests. After analysis of the data followed by interpretation, report was written and presented.

## RESULTS

Fixed dose combinations are pills that combine two or more drug molecules with different modes of pharmacological actions in a single dosing unit and optimize the treatment.

**Table 1: Demographic data of our studied Patients.**

Sl. no.	Demographics		Number of patients
1.	Age in years		
	i.	41 - 50	43
	ii.	51 - 60	87
	iii.	61 - 70	18
	iv.	71- 80	2
2.	Sex		
	i.	Male	86
	ii.	Female	64
3.	Body mass index in Kg/m2		
	i.	Underweight (<18.5)	21
	ii.	Normal weight (18.5 – 24.9)	53
	iii.	Overweight (25 – 29.9)	76



**Figure 1: Demographics of Age Groups.**

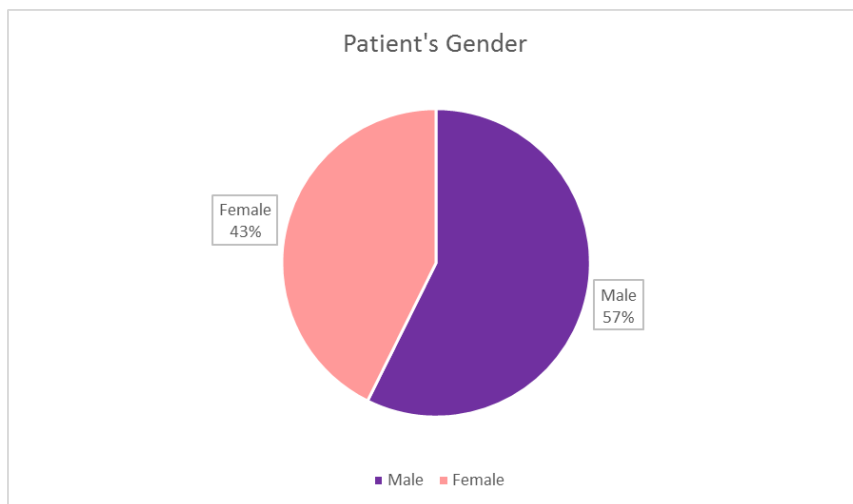


Figure 2: Demographics of Patient's Gender.

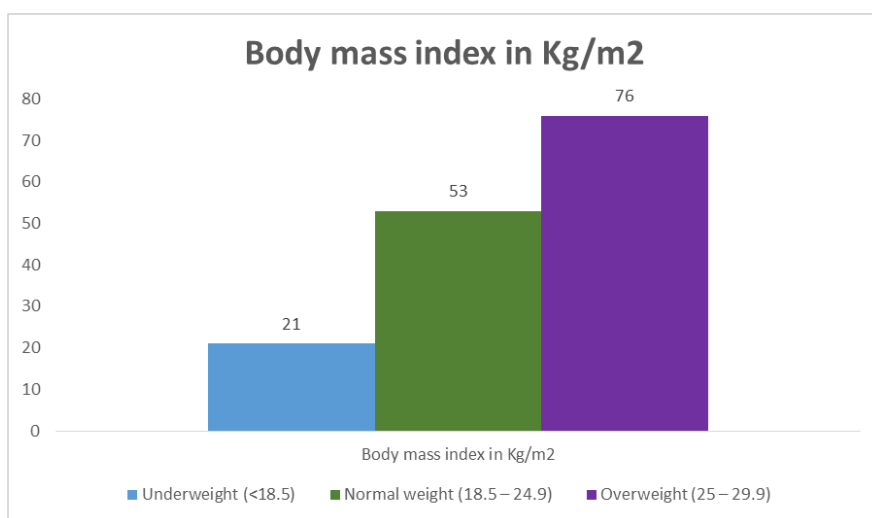


Figure 3: Demographics of Patient's Body mass index.

Table 2: Social History of Patients.

S. no	Social history	N	%
1	Smokers	25	29%
2	Alcoholic	14	16%
3	Both smoking & Alcohol consumption	20	24%
4	None	26	31%

Table 3: Fixed dose combination drugs prescribed in our study.

S. no	Fixed dose combinations	No. of Drugs	Prescription rate (%)
1	<b>Lipid lowering agents</b>	<b>217</b>	
	Rosuvastatin+ Clopidogrel + Aspirin	98	45.16%
	Atorvastatin + Clopidogrel + Aspirin	119	54.83%
2	<b>Anti-atherogenics</b>	<b>122</b>	
	Clopidogrel + Aspirin	52	42.85%
	Atorvastatin + Clopidogrel	70	57.14%
3	<b>Anti-Anginals</b>	<b>231</b>	
	Nitroglycerine + Isosorbide	84	36.36%
	isosorbide mononitrate and hydralazine	147	63.63%

<b>4</b>	<b>Beta blockers</b>	<b>217</b>	
	Metoprolol + Nifedipine	66	30.64%
	Hydrochlorothiazide and Metoprolol	150	69.35%
<b>5</b>	<b>Diuretics</b>	<b>238</b>	
	Ramipril+Telmisartan +Hydrochlorthiazide	94	39.70%
	Metoprolol + Hydrochlorthiazide	35	14.70%
	Spironolactone + Furosemide	108	45.58%
<b>6</b>	<b>ARBs</b>	<b>224</b>	
	Telmisartan +Amlodipine	129	57.81%
	Olmесartan +Hydrochlorthiazide	94	42.18%
<b>7</b>	<b>Miscellaneous</b>	<b>227</b>	
	Amlodipine + Atorvastatin,	77	33.84%
	Amlodipine + Valsartan	52	23.07%
	Atenolol + Amlodipine	98	43.07%

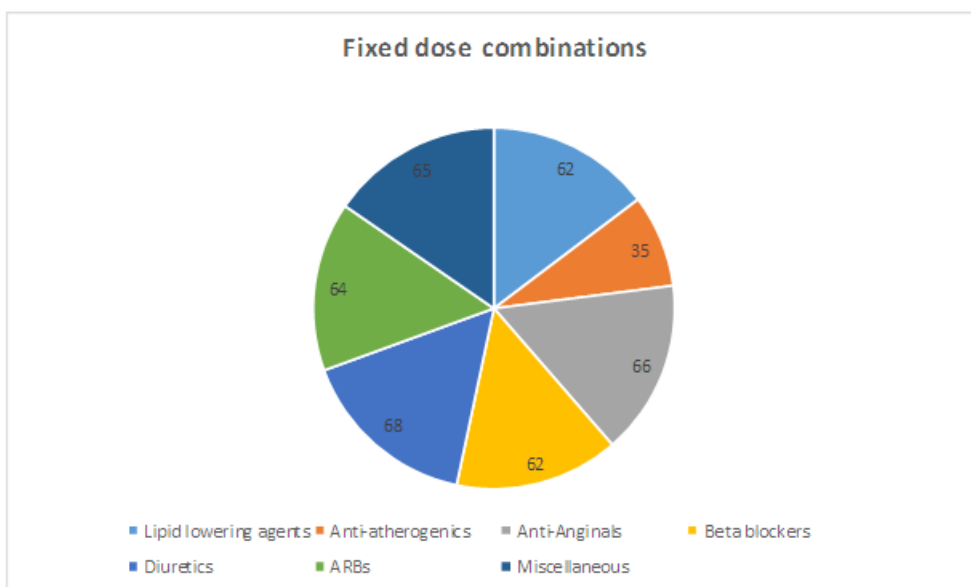


Figure.4 Fixed dose combination drugs prescribed in our study

Table 4: Grouping of prescriptions as per diseases and age.

CARDIOVASCULAR DISEASES	41 – 50 years of age	51 – 60 years of age	61 –70 years of age	71- 80 years of age	Percentages (%)
Hypertension	3	2	3	1	5.47% (9)
Ischaemic heart disease	7	14	11	2	23.04% (34)
Heart failure	3	15	13	1	21.55% (32)
Myocardial infarction	4	16	8	2	20.25% (30)
Stroke	1	3	4	-	5.60% (8)
Hyperlipedemic	5	14	5	2	17.05% (26)
Angina	2	4	5	-	7.58% (11)
<b>N=150</b>	<b>25</b>	<b>68</b>	<b>49</b>	<b>8</b>	<b>100% (150)</b>

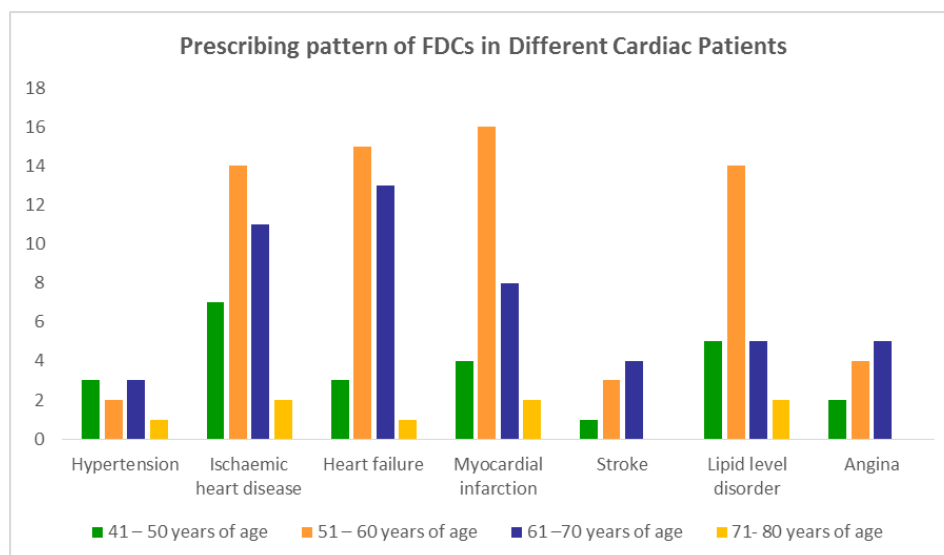


Figure 5: Prescribing pattern of FDCs in Different Cardiac Patients.

Table 5: Comorbidity conditions.

Comorbidity	No of Prescriptions	%
Hypertension + Ischemic Heart Disease	34	23%
Hypertension + Diabetes Mellitus	18	12%
Kidney disease	7	5%
Arrhythmias	6	4%
Respiratory Disease	6	4%
Anaemia	5	3%
GIT disorder	2	1%

Table 6: Drugs prescribed for Comorbid Conditions.

Class of Drug	No of Drugs	Prescription rate (%)
<b>Antidiabetic Drugs</b>		
Regular Insulin	15	10%
Metformin + Glyburide	9	6%
Glibenclamide + Metformin	4	3%
Glimepiride + Metformin	2	1%
<b>Antimicrobial agents</b>		
Amoxicillin+Clavulanic acid	39	26%
Ceftriaxone + Levofloxacin	18	12%
Cefotaxime + Sulbactam	15	10%
Ciprofloxacin + Tinidazole	12	8%
Metronidazole + Nalidixic Acid	4	3%
<b>Antiulcer/ antiemetic agents</b>		
Ranitidine + Domperidone	42	28%
Ondansetron + Omeprazole	18	12%
Pantoprazole + Naproxen	4	3%
<b>Bronchodilators</b>		
Theophylline + Salbutamol	31	21%
Salbutamol + Beclomethasone	4	3 %
Budesonide + Formoterol fumarate	18	12%
<b>Anti-arrhythmics</b>		
Amiodarone + Metoprolol	3	2%
Diltiazem + Amlodipine	2	1%
<b>Corticosteroids</b>		
Hydrocortisone + Neomycin Sulphate	12	8%
Dexamethasone + Ondansetron	10	7%
<b>Anticonvulsants</b>		

Phenytoin + Phenobarbitone	15	10%
Mannitol + Dibasic Calcium Phosphate	12	8%
Multi Vitamin + Antioxidant + Multi Mineral	43	29%
Cinnarizine + Dimenhydrinate	3	2%
<b>Anxiolytics</b>		
Clonazepam+ Escitalopram	6	4%
Diazepam+ Imipramine Hydrochloride	4	3%

Table 7: Single Dose Drugs Prescribed for Patients.

S. no.	Single dose drugs	No. of Drugs	Prescription rate (%)
<b>1</b>	<b>Lipid lowering agents</b>	<b>189</b>	
	Rosuvastatin	70	37.03 %
	Atorvastatin	42	22.22 %
	Simvastatin	77	40.74%
<b>2</b>	<b>Anti-atherogenics</b>	<b>108</b>	
	Clopidogrel	32	29.62 %
	Atorvastatin	56	51.85 %
	Warfarin	28	25.92%
<b>3</b>	<b>Anti-Anginals</b>	<b>94</b>	
	Nitroglycerine	24	25.92 %
	Isosorbide mononitrate	70	74.07 %
<b>4</b>	<b>Beta blockers</b>	<b>224</b>	
	Metoprolol	98	43.75 %
	Carvedilol	126	56.25 %
<b>5</b>	<b>Diuretics</b>	<b>154</b>	
	Indapamide	63	40.90 %
	Furosemide	35	22.72 %
	Spironolactone	56	36.36 %
<b>6</b>	<b>ARBs</b>	<b>129</b>	
	Telmisartan	59	45.94 %
	Olmесartan	70	54.05 %
<b>7</b>	<b>Miscellaneous</b>	<b>98</b>	
	Amlodipine	42	42.85 %
	Valsartan	56	57.14 %

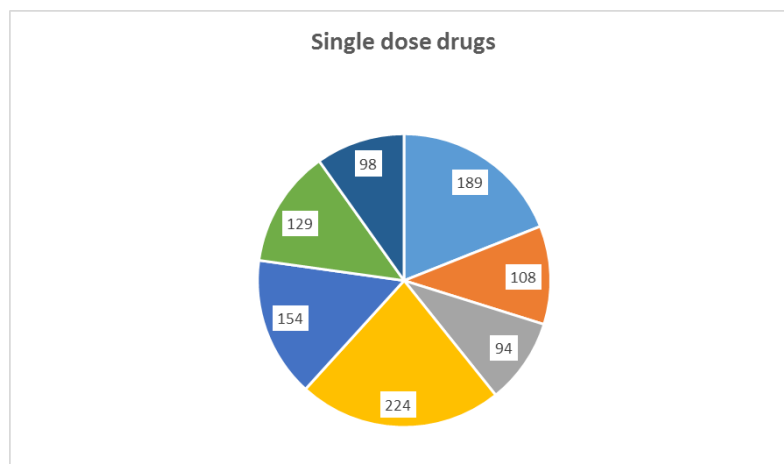
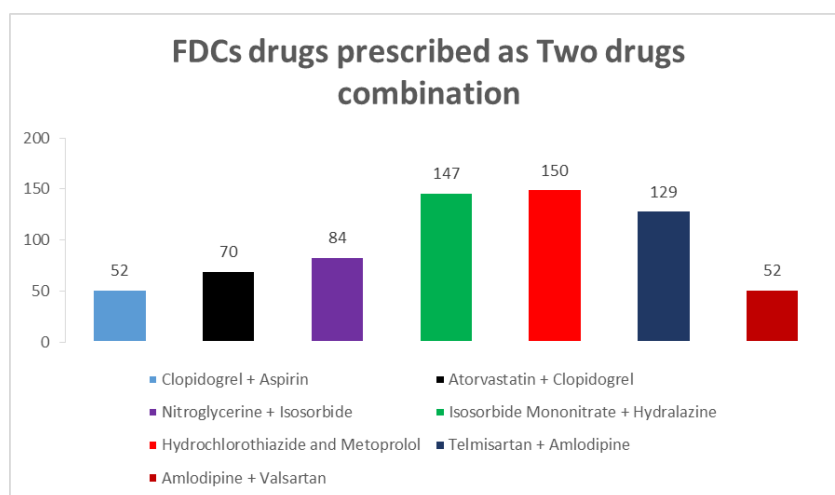


Figure 6: Single Dose Drugs Prescribed for Patients.

**Table 8: FDCs drugs prescribed as Two drug combination.**

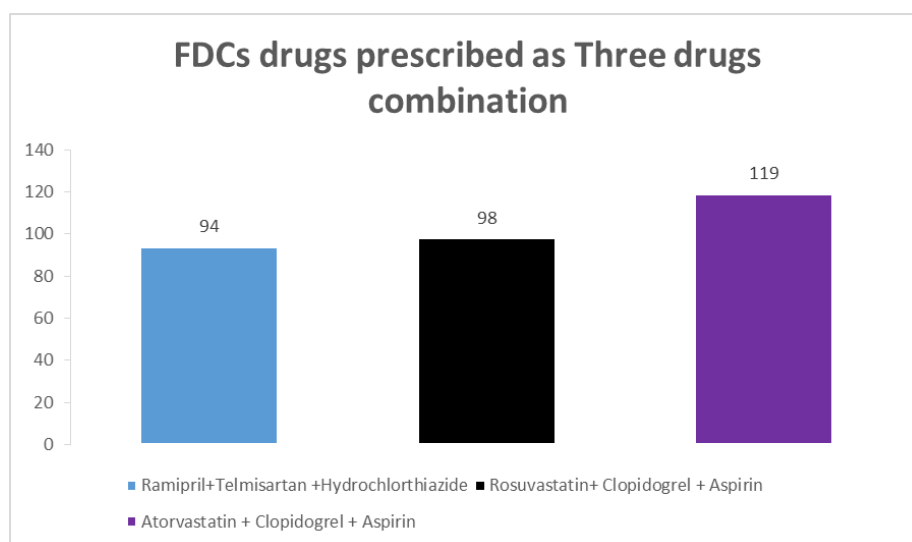
Two drug combination Prescribed	Number of Drugs
Clopidogrel + Aspirin	52
Atorvastatin + Clopidogrel	70
Nitroglycerine + Isosorbide	84
Isosorbide Mononitrate + Hydralazine	147
Hydrochlorothiazide and Metoprolol	150
Telmisartan + Amlodipine	129
Amlodipine + Valsartan	52



**Figure 7: FDCs drugs prescribed as Two drugs combination.**

**Table 9: FDCs drugs prescribed as Three drug combination.**

Three drug combination Prescribed	Number of prescriptions
Ramipril+Telmisartan +Hydrochlorthiazide	94
Rosuvastatin+ Clopidogrel + Aspirin	98
Atorvastatin + Clopidogrel + Aspirin	119



**Figure 8: FDCs drugs prescribed as Three drugs combination.**

The combinations of {Atorvastatin + Clopidogrel + Aspirin}, {Atorvastatin + Clopidogrel}, {Hydrochlorothiazide and Metoprolol}, {Ramipril + Telmisartan + Hydrochlorthiazide}, {Spironolactone + Furosemide}, {Telmisartan +Amlodipine}, {Amlodipine

+ Atorvastatin} were listed in Essential drug list (EDL 2018) which comprises of 54.13% of all prescribed drugs. The National List of Essential Medicines (NLEM) comprises of 21.46% and remaining 24.41% in (DCG) Drug Controller General list.

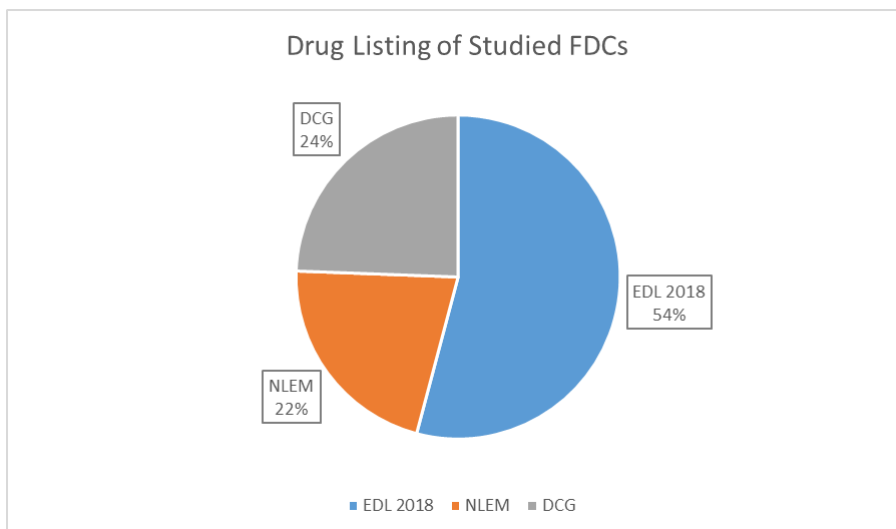


Figure 9: Drug Listing of Studied FDCs Prescribed for Patients.

Table 10: Single vs FDCs Drugs Prescribed.

S. no	Category of drugs	No. of Single dose Drugs	No. of FDCs dose Drugs
1	Lipid lowering agents	189 (18.97%)	217 (14.70%)
2	Anti-atherogenics	108 (10.84%)	231(15.65%)
3	Anti-Anginals	94 (9.43%)	238(16.12%)
4	Beta blockers	224 (22.48%)	227(15.37%)
5	Diuretics	154 (15.46%)	122(8.26%)
6	ARBs	129 (12.95%)	217(14.70%)
7	Miscellaneous	98 (9.83%)	224(15.17%)
	<b>Total</b>	<b>996</b>	<b>1476</b>
	<b>Percentage</b>	<b>40.29%</b>	<b>59.70%</b>

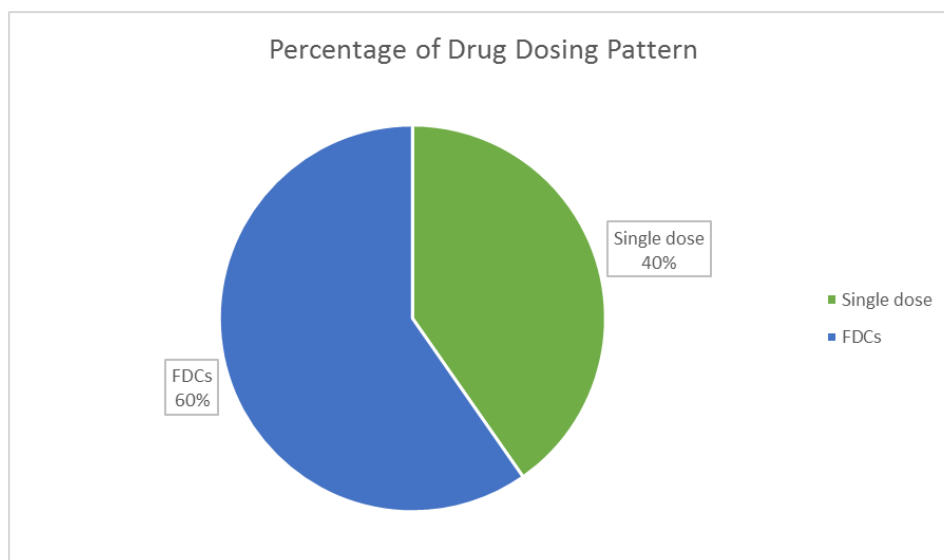
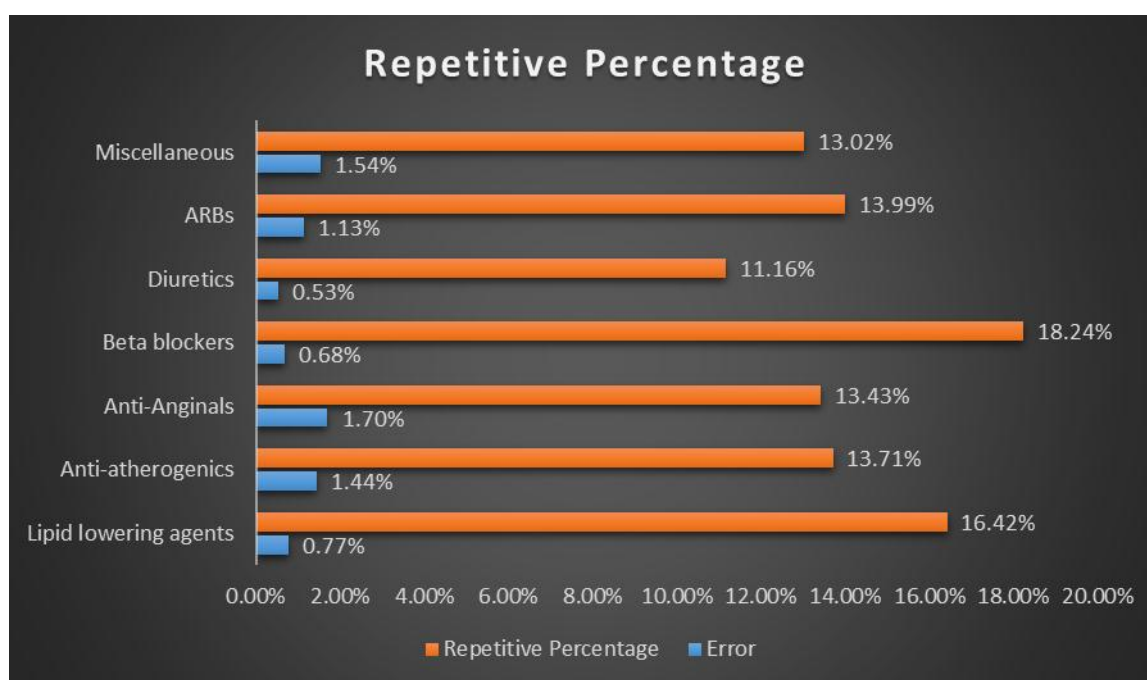


Figure 10: Percentage of Drug Dosing Pattern Prescribed for Patients.



**Table 11: Repetitive Percentage of Prescriptions.**

S. no	Category of drugs	Error	Repetitive Percentage
1	Lipid lowering agents	0.77%	16.42%
2	Anti-atherogenics	1.44%	13.71%
3	Anti-Anginals	1.70%	13.43%
4	Beta blockers	0.68%	18.24%
5	Diuretics	0.53%	11.16%
6	ARBs	1.13%	13.99%
7	Miscellaneous	1.54%	13.02%

**Figure 11: Repetitive Percentage Prescribed for Patients****CONCLUSION**

This study has indicated that some fixed dose combinations in cardiovascular diseases patients at Prime Hospital is mostly appropriate. Elective prescriptions were collected. There were additional single dosage drugs given for cardiovascular diseases patients comprising almost 30% of total drug prescribed to cardiovascular diseases patients. Among the FDCs repetitive drugs are prescribed for almost 40% of total FDCs. The outcome of my work is FDCs are of low cost with less adverse effects compared to single dosage form.

The study is comprised of 57% males and 43% females with more than 50% of patients being obese. 2110 FDCs are prescribed and all of them were Branded products. The total No. of FDCs prescribed were 69.95% and 30.04% were of Repeated FDCs Drugs.

The number of combinations were 56.66% of FDCs were Two drugs combination, 42% of FDCs were Three drugs combination, 1.34% of FDCs were More than three drugs. The margin of error of repetitive drugs is in between 0.53%-1.70%.

23% of cases were the highest comorbid percentage assessed for Hypertensive patients. 24% of cases are having a social background of consuming both alcohol and smokers. The highest number of FDCs prescribed were Antihyperlipidemic and Antiplatelet.

**Recommendations** Prime Hospital should establish FDC and Single Drug Dosing ratio profile guideline which should be open and accessible by every member of the clinical team. Medical checklist should be practiced effectively Frequent audit of prescriptions is needed to improve proper practices. Doctors should adhere to

FDCs guidelines for preventing or curbing adverse drug reactions.

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