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Prescription Pattern of Beta Blockers in Patients Diagnosed with Heart Failure

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Abstract
This study will be helpful to detect the dosage, frequency and duration of beta blockers which is prescribed for heart failure patients that is followed the guideline. The goal of the study was to describe the prescription pattern of beta blockers in patients diagnosed with heart failure. Hypothyroidism, hypertension, type 2 diabetes mellitus patients are very prone to get Heart failure. Beta blockers should be prescribed, respective with the symptoms that occurred specifically to a particular patient. This study helped to detect the parameters of prescribing beta blockers in different symptoms and co morbidities. A Total of 39 patients, among them It was observed that (46.05%) patients having heart failure were from age group 48-57, followed by (2.5%) of 78-87 age group, of which the males (58.96%) proportion where seems more than the females (41.04%). The prescription pattern for heart failure patients were found as 100% Beta adrenergic blockers, such as metoprolol-65%, bisoprolol-22%, Carvedilol-15% were given. It is evident that the beta blockers are mainly prescribed according to the symptoms, carvedilol exhibits a more pronounced BP lowering effect as a consequence of its α1- receptor blocking activities and thus causes more frequent dizziness and hypotension. In patients predisposed to symptomatic hypotension, metoprolol succinate may be the more desirable whereas in patients with uncontrolled hypertension, carvedilol may be preferred. A selective β1-blocker such as metoprolol succinate is a reasonable option for patients with reactive airway disease.

Keywords: Heart Failure, Beta Adrenergic Blockers, hypertension, dyspnea, fatigue.

1. Introduction

According to the World Health Organization (WHO), poor nations, where monitoring and evaluation of drug consumption are in their infancy, are responsible for the incorrect prescription of more than half of all medications worldwide. Ineffective and risky treatments, the escalation or protracted treatment of the patient's illness, and inflated expenditures are all consequences of improper prescribing procedures [1]. The Heart Failure Society of America (HFSA) and the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) define Heart Failure (HF) as a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or blood ejection, leading to the cardinal manifestations of dyspnea, fatigue, and fluid retention [2]. According to NYHA guideline heart failure is classified:

- **Stage A:** High risk of heart failure without structural disease of heart, it is happened because of

Hypertension, Type 2 diabetes mellitus, Obesity, Cardio myopathy.
Drug of choice for this category is ACE Inhibitors, ARBs and Statins.

- **Stage B:** It is a structural disease of heart, it occurs because of previous history of Myocardial Infarction, left ventricular heart failure with reduced ejection fraction, left ventricular hypertrophy. Drug of choice for this category is ACE Inhibitors, ARBs & Beta Blockers.
- **Stage C:** Prior symptoms of Stage A & B. Drug of choice for this stage is Isosorbide Dinitrate, ACE inhibitors, ARBs, Digoxin. If diuretics causes fluid retention, then beta blockers should be avoided.
- **Stage D:** It's the end stage of heart failure, requires advanced treatment option [3].

Reliable estimates of heart failure are few in India due to the lack of a surveillance program to track incidence, prevalence, outcomes, and primary causes. We conservatively estimate that the prevalence of heart failure in India due to coronary heart disease, hypertension, obesity, diabetes, and rheumatic heart disease ranges from 1.3 to 4.6 million, with an annual incidence of 491 600-1.8 million based on estimates of the prevalence and incidence of heart failure for individual diseases. Nearly half of the increase in heart failure patients globally between 1990 and 2017 was attributed to China (29.9%) and India (16.6%), according to a paper from the European Society of Cardiology (ESC). the leading cause of hospital admissions worldwide, affecting more than 64 million people globally [4]. In 2017, 63% Non-communicable disease (NCDS) deaths occurred in India among those 27% deaths occurred due to Heart failure, main affected age group was found to be 40 to 69 years of age groups [5]. Heart failure is responsible for: Coronary artery disease, Myocardial infraction, Hypertension, Heart muscle disease (Dilated cardiomyopathy, hypertrophic cardiomyopathy) or Inflammation (Myocarditis), Diabetes and Obesity like Comorbidities [6]. β adrenergic receptor antagonists also known as β blocker developed in the year of 1960 to treat angina pectoris. In the year of 1963 pronethalol first introduce in the market but use of these drug limited only for life threatening condition because of its huge side effect. Propranolol was launched in the year of 1965 and it become best-selling drug in the market and this drug used in for hypertension, angina, arrythmia and hypertrophic cardiomyopathy. In the year of 1976 atenolol known as ideal beta blocker launched and become best-selling drug. Metoprolol, Bisoprolol and carvedilol launched in the year of 1978,1986 and 1995 respectively. Dr James black was awarded Nobel prize in the year of 1988 for invention of propranolol [7]. Beta Adrenergic Blockers, group of medications that have shown promise in controlling the course of heart failure. These medications have a high affinity for β-adrenergic receptors, which prevents endogenous catecholamines from interacting with them [8]. Beta blockers has two properties Lipophilic and Hydrophilic.

Lipophilic:

- Selective Beta Blocker- Propranolol, Metoprolol, Oxprenolol, Bisoprolol, Carvedilol.
- Readily absorbed from GI, metabolized in Liver
- Large Volume of distribution, and penetrate BBB well.

Hydrophilic:

- Acebutolol, Atenolol, Betaxolol, Carteolol, Nadolol, Sotalol.
- Less easily absorbed, not extensively metabolized.
- Plasma half-lives is long.

Hepatic failure prolong t ½ lipophilic, renal failure prolongs hydrophilic [9]. There are three different types of Beta blocker: Selective Beta Blockers: Metoprolol, Bisoprolol, Atenolol. This selective beta blockers are given to heart failure patients who are having COPD and Asthma. It is mainly given in Stage B & C, In Stage C if any patients experience fluid retention in body because of diuretic drugs or other

cause then beta blockers are avoided. Non-Selective Beta Blockers: Labetalol, Sotalol. Non-Selective beta blockers are avoided in heart failure patients who are having COPD and Asthma, because it can occur Bronchoconstriction. Mixed Alpha and Beta Blocker: Carvedilol. It is mixed Alpha and Beta Blocker (Selective alpha and non-selective beta-blockers) Selectively antagonized alpha-1 adrenergic receptors, antagonized beta1 and beta 2 adrenergic receptors [10]. According to the AHA/ACC/HFSA guideline Beta blockers are mostly prescribed for Heart failure patients who all are in stage B and C [11]. This study is significant to find that the prescription pattern of beta blockers is following the guidelines or not. Beta blockers are more frequently used in stage B and C, but in collective cases where beta blockers cause fluid retention in stage C, there it got stopped by immediate effect. This study will be helpful to detect the accuracy of correct dosage form, frequency of beta blockers. Drugs should be prescribed while measuring the safety parameters with respect to the co morbidities, if there is any. If patients are having co morbidities like hypothyroidism, hypertension, type 2 diabetes mellitus they are very prone to get Heart failure. Beta blockers should be prescribed, respective with the symptoms that occurred specifically to a particular patient. This study helped to detect the parameters of prescribing beta blockers in different symptoms and co morbidities. It will help to improve the quality of treatment and patient quality of life.

2. Materials and Methods

This is an observational study and was carried out for a period of 6 months. The study was carried out in the In-patient Department of General medicine, ESIC MC - PGIMSR, Rajajinagar, Bengaluru for 6 months. A total of 39 participants, satisfying the inclusion/exclusion criteria were recruited in the study The sample size was calculated by using the following formula $N = Z^2 * P(1-P) / M^2$

Study tools:

- Patient profile form: Data will be collected using Proforma from which contains details like demography, chief complaints, history of present illness, co morbidities, clinical data such as various laboratory reports.
- Medication chart

Inclusion criteria:

1. Subjects who have confirmed diagnosed with Staging of heart failure.
2. Subject above 18 years.
3. Subjects with other comorbidities leading to heart failure.

Exclusion criteria:

1. Pregnant women.
2. Patient with congenital heart disease.
3. patient not willing to participate in the study.
4. Comatose and Unconscious patients.
5. Patients with not giving beta blockers.

Statistical Analysis:

All recorded data were entered and analyzed using MS Excel for determining for the statistically significant. Descriptive statistics were computed for percentages were calculated. Column charts, bar graphs were made to find the nature of data distribution.

2. Results

A total of 39 patients were enrolled in the study, out of the 23 male patients, 12 (52.17%) male patients

having heart failure were from 48-57 age group, 1(4.37%) male patient having heart failure were from 78-87 age group and out of 16 female, 6(37.5%) female patients having heart failure were from both 48-57& 58-67 age group, 2(12.5%) female patients having heart failure were from both 38-47& 68-77 age group.

Age	Number of Male (23)	percentage (%)	Number of Female (16)	Percentage (%)
38-47	5	21.73	2	12.5
48-57	12	52.17	6	37.5
58-67	5	21.73	6	37.5
68-77	0	0.00	2	12.5
78-87	1	4.37	0	0.00

Table 1: Distribution of patients by gender according to age

Out of 39 patients, 27(65%) patients given metoprolol and 6(15%) patients given carvedilol.

Beta blockers	Numbers of patients (39)	Percentage (100%)
Metoprolol	27	65
Bisoprolol	9	22
Carvedilol	6	15

Table 2: Distribution of patients by beta blockers

Out of 39 patients, 26 patients were given metoprolol they experienced fatigue and 1 patient were given amlodipine who experienced swelling in feet, ankles, legs or abdomen.

Symptoms	Metoprolol	Furosemide	Telmisartan	Amlodipine	Aspirin	Clopidogrel	Atorvastatin	Pantoprazole	Aldactone	Insulin R	Metformin	Digoxin
Swelling in the feet, ankles, legs or abdomen	18	17	3	1	9	2	10	12	13	6	6	5
Fatigue	26	25	6	2	11	4	14	18	19	10	8	8

Shortness of breath	21	20	2	2	11	3	11	12	13	8	6	5
Chest pain	12	12	3	0	6	2	7	8	7	4	7	5
Increased heart rate	23	22	5	2	9	4	10	15	16	9	7	8

Table 3: Distribution of patients given other drugs and metoprolol according to symptoms

Out of 39 patients, 8 patients were given bisoprolol they experienced fatigue and minimum 1 patient were given amlodipine (Fatigue), Telmisartan (Fatigue), Atorvastatin (Increased heart rate), Insulin (Swelling in the feet, ankles, legs or abdomen), Metformin (Swelling in the feet, ankles, legs or abdomen, Fatigue, Chest pain, Shortness of breath), Digoxin (Swelling in the feet, ankles, legs or abdomen, Chest pain, Increased heart rate).

Symptoms	**Bisoprolol**	**Furosemide**	**Telmisartan**	**Amlodipine**	**Aspirin**	**Clopidogrel**	**Atorvastatin**	**Pantoprazole**	**Aldactone**	**Insulin R**	**Metformin**	**Digoxin**
Swelling in the feet, ankles, legs or abdomen	5	5	0	0	2	0	3	3	4	1	1	1
Fatigue	8	7	1	1	2	0	4	5	6	3	1	2

Shortness of breath	7	6	0	0	2	0	3	4	5	2	1	2
Chest pain	5	5	0	0	2	0	3	2	3	0	1	1
Increased heart rate	6	5	0	0	0	0	1	2	4	2	0	1

Table 4: Distribution of patients given other drugs and bisoprolol according to symptoms

Out of 39 patients, 6 patients given with Carvedilol (Fatigue) & Furosemide (Fatigue). While minimum 1 patient is given with Digoxin (Swelling in the feet, ankles, legs or abdomen, Chest pain, Increased heart rate, Shortness of breath, Fatigue).

Symptoms	**Carvedilol**	**Furosemide**	**Telmisartan**	**Amlodipine**	**Aspirin**	**Clopidogrel**	**Atorvastatin**	**Pantoprazole**	**Aldactone**	**Insulin R**	**Metformin**	**Digoxin**
Swelling in the feet, ankles, legs or abdomen	5	5	0	0	3	0	3	3	3	3	3	1
Fatigue	6	6	0	0	4	0	3	4	3	4	4	1
Shortness of	5	5	0	0	3	0	2	3	3	3	3	1

breath												
Chest pain	5	5	0	0	3	0	2	3	3	3	3	1
Increased heart rate	5	5	0	0	4	0	3	4	2	4	4	1

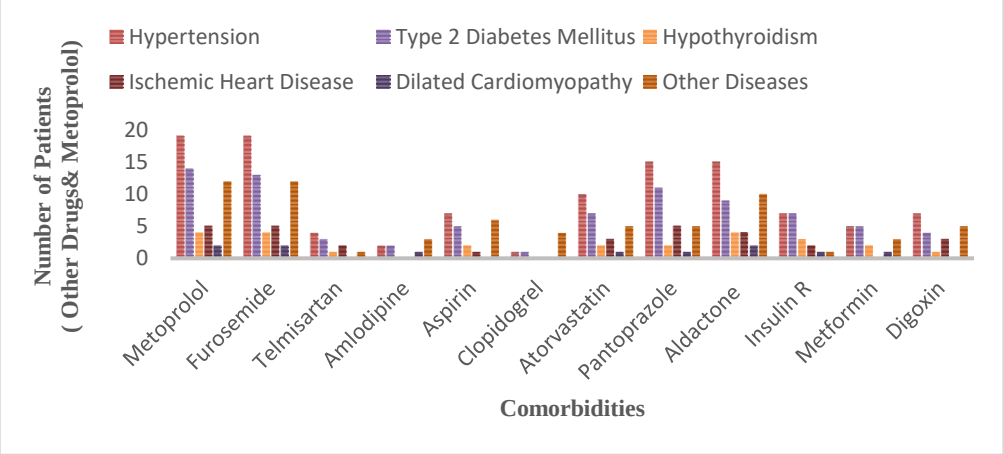
Table 5: Distribution of patients given other drugs and carvedilol according to symptoms

Out of 39 patients, 25 patients were having HF with reduced EF(HFrEF) and 1 patient were having HF with improved EF(HFimpEF)

Class of Heart Failure	Number of Patients (39)	Percentage (100%)
HF with reduced EF (HFrEF)	25	64.10%
HF with mildly reduced EF(HFmrEF)	6	15.38%
HF with preserved EF (HFpEF)	7	17.96%
HF with improved EF (HFimpEF)	1	2.56%

Table 6: Distribution of patients according to the class of heart failure

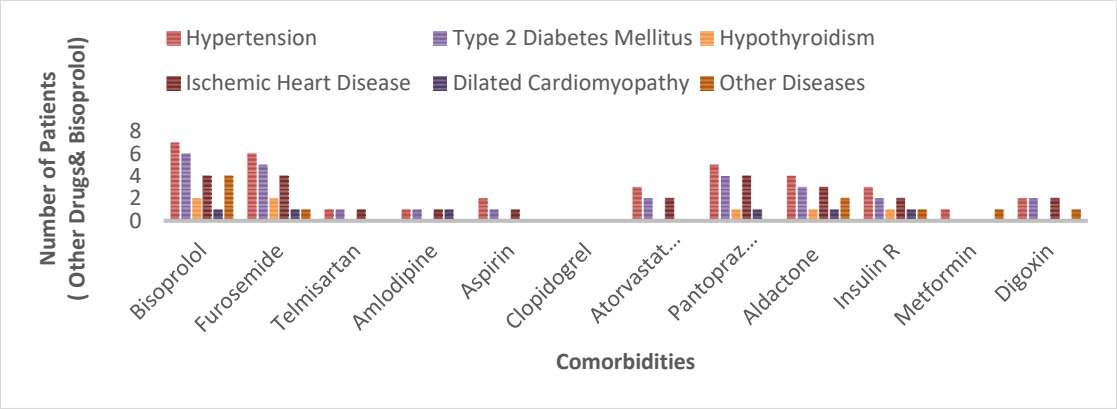
Fig 1: Distribution of patients given other drugs and metoprolol according to comorbidities



Out of 39 patients, 19 patients given metoprolol and furosemide they were having hypertension. In the other hand Minimum 1 patient is given with Telmisartan (Hypothyroidism, other diseases), Clopidogrel

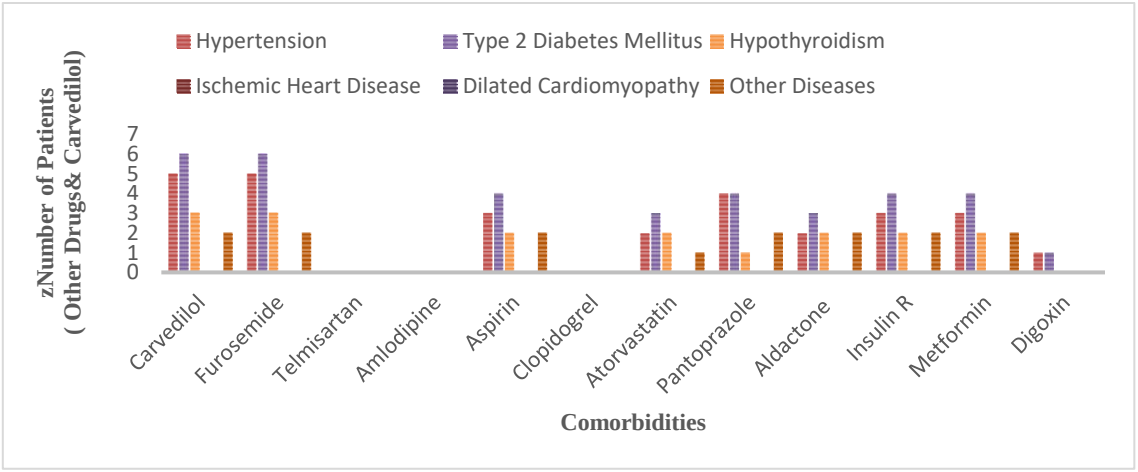
(Hypertension, T2DM), Amlodipine (Dilated cardiomyopathy), Atorvastatin (Dilated cardiomyopathy), Pantoprazole (Dilated cardiomyopathy), Insulin (Dilated cardiomyopathy, other disease), Metformin (Dilated cardiomyopathy) Digoxin (Hypothyroidism).

Fig 2: Distribution of patients given other drugs and bisoprolol according to comorbidities



Out of 39 patients, 7 patients given bisoprolol they were having hypertension. In the other hand Minimum 1 patient is given with Furosemide (Dilated cardiomyopathy, other disease), Telmisartan (Hypothyroidism, Hypertension, ischemic heart disease), Aspirin(T2DM, ischemic heart disease), Amlodipine (Hypertension, ischemic heart disease,T2DM, Dilated cardiomyopathy), Atorvastatin (Dilated cardiomyopathy), Pantoprazole (Hypothyroidism, Dilated cardiomyopathy), Insulin (Dilated cardiomyopathy, Hypothyroidism), Metformin (Hypertension, other disease), Aldactone (Hypothyroidism), Digoxin (other disease).

Fig 3: Distribution of patients given other drugs and carvedilol according to comorbidities



Out of 39 patients, 6 patients given carvedilol and furosemide they were having type 2 diabetes mellitus. In the other hand Minimum 1 patient is given with Atorvastatin (other disease), Pantoprazole (Hypothyroidism), Digoxin (Hypertension, T2DM).

4. Discussion

This study was conducted in general medicine department in ESIC MC- PGIMSR & Model Hospital, Raj-

ajinagar, Bengaluru among who all are diagnosed with heart failure. A total of 39 patients were included in the study which spanned 3 months from April 2023 to June 2023. The objectives of the study include investigating the demographic details, of which age is a factor. AGE & GENDER: Total number of patients were 39, of that (46.05%) patients having heart failure were from age group 48-57, followed by (2.5%) of 78-87 age group of which the males (58.96%) proportion where seems more than the females (41.04%), 57.17% male patients were having heart failure from 48-57 age group followed by (4.37%) were having from 78-87 group and (32.5%) female patients were having heart from both 48- 57 and 58-67 age group followed by (12.5%) female patients having heart failure from both 38-47 and 68-77, Male patients had higher coronary artery disease and anemia in the PSF group found in study conducted by Harish T et al., (2016) [12]. SYMPTOMS: Fatigue (94.87%), Chest pain (56.41%), Swelling in the feet, ankles, legs or abdomen (66.66%), Shortness of breath (79.48%), Increased heart rate (82.05%). Fatigue is a common and distressing symptom of heart failure (HF) and has important implications for patient-reported and clinical outcomes found in study conducted by Noelle V et al, (2022) [13]. COMORBIDITIES:100% patients were having cardiovascular disease (hypertension-76.92%, ischemic heart disease - 17.94%, Dilated cardiomyopathy-5.14%). 84.61% were hormonal disease (Type 2 DM-75.75%, Hypothyrodism-24.25%), Other diseases (51.28%). Patients having diabetes mellitus and hypertension are more prone to get heart failure found in study conducted by Harish T et al., (2016) [14]. PRESCRIPTION PATTERN: The prescription pattern for heart failure patients were found as 100% Beta adrenergic blockers (metoprolol-65%, bisoprolol-22%, Carvedilol-15%), (96.29%) patients were given metoprolol, they experienced fatigue, (44.44%) chest pain, (88.88%) patients were given bisoprolol they experienced fatigue, (55.55%) chest pain & swelling in the feet, ankles, legs or abdomen, these 6 patients, 6(100%) patients were given carvedilol, they experienced fatigue and 5(55.55%) patients experienced chest pain, swelling in the feet, ankles, legs or abdomen, shortness of breath & increased heart rate, comparing metoprolol and carvedilol after acute myocardial infarction found that overall survival was similar for both treatments found in study conducted by Ghaith Z et al., (2021) [15]. Metoprolol was given (70.37%) patients having hypertension & (14.81%) patients having hypothyroidism, bisoprolol were given (77.77%) patients having hypertension & (22.22%) patients having hypothyroidism, β1-adrenoceptor selectivity in β- blockers' utility in managing hypertension and cardiovascular disease found in study conducted by AlHabeeb W et al., (2022) [16]. 15% carvedilol prescribed patients were having type 2 diabetes mellitus (100%) & (33.33%) patients having other disease, Patients treated with carvedilol were older and had more comorbidities found in study conducted by Ghaith Z et al., (2021) [17]. Other drugs (Fuesemide-94.87%, Telmisartan-15.38%, Amlodipine-7.69%, Aspirin- 4.02%, Clopidogrel-10.25%, Atorvastatin-48.75%, pantoprazole-64.10%, Aldactone-64.10%, insulin R-43.28%, Metformin-28.20%, Digoxin-33.33%), Spironolactone, a mineralocorticoid receptor antagonist, in heart failure patients with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) found in study conducted by Austin c et al., (2022) [18]. From the total number of patients 34 are those who all are given with furosemide and experienced fatigue, followed by 1 patient given amlodipine who experienced swelling in feet, ankles, legs and abdomen. 28 patients given with furosemide while having hypertension, 1 patient who is given with telmisartan (hypothyroidism, other disease), clopidogrel (hypertension, T2DM), amlodipine (ischemic heart disease, dilated cardiomyopathy), Insulin (dilated cardiomyopathy), metformin (dilated cardiomyopathy), ARB treatment may reduce slightly heart failure hospitalizations (moderate- certainty evidence) found in study conducted by Nicole M et al., (2021) [19]. From total number of patients, 26 were given metoprolol and experienced fatigue, followed by 1 patient given with amlodipine who experienced swelling in feet, ankle, legs or

abdomen, 8 patients were given bisoprolol and they experienced fatigue, followed by 1 patient were given with amlodipine (fatigue), telmisartan (fatigue), atorvastatin (increased heart rate), insulin (swelling in the feet, ankles, legs or abdomen), metformin (swelling in the feet, ankles, legs or abdomen, fatigue, chest pain, shortness of breath), Digoxin (swelling in the feet, ankles, legs or abdomen, chest pain, increased heart rate), and 6 patients given carvedilol (fatigue), furosemide (fatigue), followed by 1 patient given with digoxin (swelling in the feet, ankles, increased heart rate, shortness of breath, fatigue), Beta-blockers reduce mortality at all studied heart rates in patients with HFrEF in sinus rhythm Kotecha. D.et al., (2017) [20]. 19 patients out of 39 given metoprolol and furosemide who were having hypertension, followed by 1 patient is given with telmisartan (hypothyroidism, other diseases), clopidogrel (hypertension, T2DM), amlodipine (dilated cardiopathy), atorvastatin (dilated cardiomyopathy), pantoprazole (dilated cardiomyopathy), Insulin (dilated cardiomyopathy, other diseases), metformin (dilated cardiomyopathy, other diseases), digoxin (hypothyroidism). Among 39 patients, 7 patients given bisoprolol were having hypertension. 1 patient is given with furosemide (dilated cardiomyopathy, other diseases), telmisartan (hypothyroidism, hypertension, ischemic heart disease), aspirin (T2DM, ischemic heart disease), amlodipine (Hypertension, ischemic heart disease,T2DM, Dilated cardiomyopathy), Atorvastatin (Dilated cardiomyopathy), Pantoprazole (Hypothyroidism, Dilated cardiomyopathy), Insulin (Dilated cardiomyopathy, Hypothyroidism), Metformin (Hypertension, other disease), Aldactone (Hypothyroidism), Digoxin (other disease). Among total 39 patients, 6 patients given carvedilol and furosemide they were having type 2 diabetes mellitus. In the other hand Minimum 1 patient is given with Atorvastatin (other disease), Pantoprazole (Hypothyroidism), Digoxin (Hypertension, T2DM) depicted in, In a contemporary clinical cohort of HFrEF patients with and without T2D, carvedilol was not associated with a reduction in long-term mortality compared with metoprolol found in study conducted by Brian. S. et al., (2021) [21]. Among 39 patients, total 49 times cardiovascular symptoms have shown and at least 1 time edema, fatigue, respiratory has been shown in gastrointestinal disease and 1-time Respiratory symptom showed in hepatic disease, Out of 39 patients, 25 patients were having HF with reduced EF (HFrEF) and 1 patient were having HF with improved EF (HFimpEF), According to the WHO guideline average number of medicines per encounter is 5.589, Percentage of medicines prescribed by generic name 68.80%, Percentage of encounters with an antibiotic prescribed 0, Percentage of encounters with an injection prescribed 24.77%, and Percentage of medicines prescribed from the essential medicines list 74.31%.

5. Conclusion

The study entitled Prescription pattern of beta blockers in patients diagnosed with heart failure was conducted in general medicine department of ESIC MC- PGIMSR& Model hospital, Rajajinagar, Bengaluru for 3 months. During the study it was observed that the mostly prescribed beta blocker was Metoprolol, followed by other beta blockers such as bisoprolol & carvedilol. The study conducted the following major patterns, such as, Prescription pattern for Heart failure Stage B and C according to the guidelines For Stage C the most prescribed drug was ARNI in [NYHA (II & III)], ACE inhibitor or ARB in [NYHA II- IV], Beta blockers, MRA (Mineralocorticoid receptor antagonists), SGLT2 inhibitor (Sodium glucose transport proteins - 2), Diuretics, Hydral- nitrates. And then, For Stage - B prescribed drugs is- ACEI, ARB if intolerant, Beta blockers. In this study it was observed that they are also following the same prescription pattern for stage B & C heart failure which is mentioned as per guidelines. It was observed all patients were given spironolactone when the EF <25%. Those who were prescribed with statin, majority of them experienced fatigue, it might be happened because of statins quickly metabolized HMG-CoA, and this

time very quickly cholesterol level decrease in blood and blood pressure fluctuation is seen, so due to this condition patients may be experience fatigue. It was observed that digoxin is given only in Stage C specific condition, such as hyperthyroidism, fatigue and shortness of breath. The study found that the beta blockers are mainly prescribed according to the symptoms, carvedilol exhibits a more pronounced BP lowering effect as a consequence of its α1-receptor blocking activities and thus causes more frequent dizziness and hypotension. In patients predisposed to symptomatic hypotension, metoprolol succinate may be the more desirable whereas in patients with uncontrolled hypertension, carvedilol may be preferred. Patients' reactive airway disease may still use β-blockers; however, considerable caution should be made in those who display active respiratory symptoms. A selective β1-blocker such as metoprolol succinate is a reasonable option for patients with reactive airway disease.

6. Conflict of Interest

The authors declare that no conflict of interest.

7. Acknowledgement

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