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COMPARISON OF DAPAGLIFLOZIN WITH CIDMUS IN HEART FAILURE PATIENTS

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Abstract:

Aim: *The primary goal of this research is to judge against and the safety and effective action of CIDMUS and Dapagliflozin in individuals with heart failure.*

Objectives:

- *To observe the prosperity and sufficiency of Dapagliflozin in contrast to CIDMUS.*
- *To analyze the expense adequacy of both the medications.*
- *To see how much percentage of EF improved after taking Dapagliflozin.*
- *Observe improvement in quality of life after administration of Dapagliflozin.*

Background: *The majority of individuals suffer from heart failure. Dapagliflozin, an anti-diabetic medication that belongs to the Sodium Glucose co-transporter 2 inhibitor family, is currently being used to treat heart failure. The goal of this research is to assess the drug's safety and viability.*

Methodology: *This is a prospective, observational based study done in Aster prime hospital for 6 months in cardiology department. A minimum of 115 cases of heart failure patients were collected. This data was noted in the data collection sheets. Data includes the age, gender, and diagnosis, lab reports (which include HbA1c levels, ejection fraction, pro-BNP and KCCQ-12 score). SAS version 9.4 was used to examine and analyse all of the aforementioned factors.*

Results: *In our study 115 HF patients were first collected and then analyzed with diverse statistical and analytical methods using SAS version 9.4 which includes mean, standard deviation, chi-square test and dependent T-test. Our study showed that 50-59 (35.38%) and 60-69 (32.30%) are more affected with co-morbidities. Whereas safety and efficacy of dapagliflozin compared with CIDMUS was similar (P <0.00001) and 2D ECHO parameters had been improved in similar after both the treatments. CIDMUS was about twice more in price than Dapagliflozin (calculated using cost-effective analysis). Quality of life is similar in both who were used to treat HF patients with Dapagliflozin and CIDMUS.*

Conclusion: *The study reveals that after therapy with Dapagliflozin and CIDMUS in patients with HF and diabetes, dapagliflozin was found to show better safety, efficacy, quality of life, a fair bit of down sizing in hospitalization, mortality, and is also better in an economical aspect when compared with CIDMUS.*

Key Words: *Heart Failure, dapagliflozin, CIDMUS, cost-effectiveness, efficacy and safety*.

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INTRODUCTION:

Heart Failure:

Heart failure sure is a very wrenching and common medical condition treated by medical practitioners, as well as cardiologists in clinical care settings. Due to the advances in research, we now have better understanding of the aetiology, epidemiology, diagnosis, and most significantly, management of HF last 20years [1]. Heart failure (HF) is a condition in which morphological and functional defects in the myocardium impede ventricular filling and blood ejection. However, heart failure may also be caused by malfunctioning pericardium, myocardium, endocardium, heart valves, or great vessels, either alone or in combination [2].

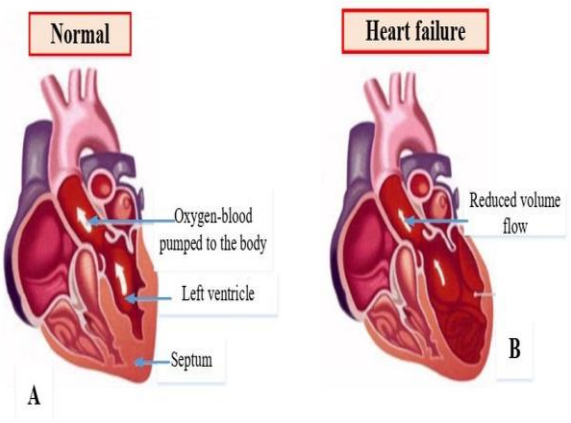


Figure-1: A comparison of Normal Heart versus Heart Failure showing enlarged Left ventricle.

Pathophysiology of Heart Failure:

Heart failure causes the major tissues to decrease blood needed to convene the metabolic needs and a cardiac increase in pulmonary or systemic pressure can lead to organ congestion. Systolic or diastolic dysfunction or more often both, can cause this condition. Although differences in extracellular collagen turnover are an early violation, problems with myocardial function can also occur. HF can also be caused by structural heart problems (such as congenital abnormalities or valve disease), arrhythmias (such as persistent heart rate) and too many metabolic requirements (such as thyrotoxicosis) [3].

Changes with Aging:

As individuals age, changes in their heart and cardiovascular systems reduce the threshold for heart failure. Increases interstitial collagen in the myocardium, tightens the myocardium and prolongs myocardial relaxation. Even in healthy adults, these changes can lead to a significant decrease in left ventricular diastolic function. The systolic function of the heart decreases with age. Age-related decrease in myocardial response to activation of the beta-adrenergic system impairs the efficiency of the circulatory system in response to increased work demands [4]. Peak exercise capacity falls dramatically (approximately 8% per decade after age 30) in response to these changes, although CO decreases more slightly at peak exercise [5]. Usual physical activity helps to slow this decrease. Among the stressors are: treatment non-adherence or low-salt diets (particularly with NSAIDs, Inflammatory medications), infection (especially pneumonia), hyperthyroidism, anemia, hypertension, hyperthermia, heart ischemia, hypoxia, renal failure, intraoperative intravenous fluid load are all danger factors [6].

Catergory:

NYHA classifies Heart Failure into four categories:
Class I:
When done correctly HF has no effect on physical activities and does not cause any symptoms.
Class II:
HF limits physical activities to a minimal, individuals are comfortable at rest but HF symptoms appear due to regular physical activity.
Class III:
HF causes significant physical limitations are better when they rest, but less exercise than usual can cause HF symptoms.
Class IV:
Patients with category 4 may not involve in any physical activity without experiencing symptoms of HF and they may develop symptoms even at rest [7].

Heart Failure Symptoms:

Heart Failure can either be chronic (ongoing) or acute (having a sudden onset). HF signs and symptoms include:

- Weakness and Fatigue
- Swelling in the legs, ankles, and feet
- Chest Pain
- Irregular or fast heart beat
- Reduced Physical Activity
- Abdominal Swelling
- Persistent Cough or Wheezing with white or pink-tinged mucus
- Reduced Appetite and Nausea [8].

Heart Failure types:

Left ventricular hypertrophy is a term used to describe heart failure (LVH). In some people, the

heart failure cause may not be known. In most cases, however, it is caused by a mix of factors, including genetics, age, gender, body size, nutrition and lifestyle. Anyone can get heart failure at any age, but it is more common among the elderly.

Expansion and stiffness in the left side of the heart can be caused by high blood pressure or diabetes mellitus, indicating that the heart is unable to pump enough blood to meet your body's needs. In advanced stages, the right side of your heart, notably the right ventricle, might be compromised, resulting in right heart failure. Because both forms of heart failure are progressive, grouped together as chronic heart failure, but symptoms, progression, and management differ.

Any of the illnesses listed below can induce heart failure by weakening or damaging the heart. The development of fatty deposits in the arteries causes blood flow to be reduced, which might lead to an attack. High blood pressure (HBP), Diabetes Mellitus. Damage to the heart muscle, heart muscle inflammation, and irregular heart rhythms.

Heart disease and diabetes mellitus:

Major effects are exerted by diabetes on the CVS through several mechanisms. Some 2b/3a mechanisms include reduced production and increased activity of endothelin, angiotensin, tissue factor. The overexpression of glycoprotein 2b/3a receptors cause increase in activation and aggregation of platelets. This ultimately causes coronary atherosclerosis. Diabetic patients are at increased risk to develop coronary atherosclerosis leading to multi vessel involvement and even more coronary occlusion. Thus, reduces pumping and doesn't pump enough oxygen to meet the body demands and leads to Heart Failure. Ischemia- and non-ischemic vascular disease in diabetics raises the stakes for them. Diabetes has a decreased predictive value in patients who are admitted in hospitals with ARF, indicating that the degree of cardiac decomposition is more relevant in these people[9].

Dapagliflozin in HF with diabetes mellitus:

Inhibitors of the sodium-glucose cotransporter 2 (SGLT2), which were originally designed as a type 2 diabetes medication, prevent filtered glucose from being reabsorbed. These drugs reduced incident heart failure in type 2 diabetes participants, which occurred early after randomization trials and was baseline independent, as well as changes in glycated haemoglobin, which were time dependent [10].

It was observed that individuals with HF with a lower EF, both with and without type 2 diabetes, were protected by using Dapagliflozin (DAPA-HF). Diabetic and non-diabetic participants in this trial had different reactions to dapagliflozin, with the primary finding of this study pointing to SGLT2 inhibition as a potential treatment. Patients with HF and decreased ejection fraction, both with and without diabetes, were included in an exploratory study to examine the efficacy of dapagliflozin, as well as metabolic and hemodynamic alterations and side effects [11].

CIDMUS in HF with diabetes mellitus:

Angiotensin-nephrotoxin receptor combo inhibitor Sacubitril/Valsartan (ACE inhibitor) is superior to enalapril in patients having less ejection fraction (HFrEF) and coronary heart failure (CHF) in terms of morbidity and mortality. Enalapril and Sacubitril/Valsartan did not lower new-onset diabetes outcomes, even though the number of patients with recently arrived diabetes was quite low.

Sacubutril/Valsartan increases insulin sensitivity and glycemic control in obese hypertensive individuals, whereas omapatrilate, an ACE inhibitor, has substantial benefits on insulin sensitivity and glycemic control.In rats,the amount of fat-zucker increased. We looked and studied the effectiveness and safety of Dapagliflozin and CIDMUS (Sacubitril/Valsartan) in individuals with coronary heart failure and diabetes mellitus [12].

METHODOLOGY:

Table 1: Methods and resources utilized to fulfill each objective

Objective No.	Statement Of The Objective	Method/ Methodology	Resources Utilised
1	Analyze the efficacy and safety of dapagliflozin in comparison to CIDMUS	Prospective observational study	Excel sheet
2	To see how much of an improvement in ejection fraction there was after taking dapagliflozin	Prospective observational study	Dependent t test
3	Quality of life (KCCQ Scale)	Prospective observational study	Dependent t test
4	Study on Cost - Effectiveness	Prospective observational study	Cost effective analysis

Study site:
It was conducted in cardiology department at Aster Prime Hospital,Hyderabad.

Sample size:
A total of 115 individuals were enrolled in the trial, all of whom were being treated for Heart Failure.

Study Design:
Conducted in the Department of Cardiology at Aster Prime Hospital in Hyderabad and was a hospital based prospective observational study.

Study Period:
A 6 months study was conducted from august 2021 toJanuary2022.

STUDY CRITERIA:

a) Inclusion Criteria:

- Patients in between 18–80 years.
- Patients with high blood pressure (Hypertension).
- Patients with an EF of <45%.
- Patients that NYHA class 2, 3 and 4.
- Patients with comorbit conditions including DM.
- Post coronary artery bypass graft surgery(CABG)patients.

b) Exclusion Criteria:

- Patients in between 18 years to 80years.
- Womens who are pregnant and nursing.
- Womens with heart failure who have given birth.
- Patients with viral infection such as hepatitis and HIV.
- Patients with severe hepatic or renal disease.

Source of data:
Patient interview, prescription forms, patient case notes, medication records, nursing notes, and other laboratory investigative data were used to gather patient case history and information on the current illness.

Study Procedure:

1. Patients who met the inclusion criteria were included in an observational research.
2. Patient demographics (name, age, sex, height, weight, and body surface area), patient IP number, admission date, and subject location (inpatient/outpatient) were all gathered. Data was collected using especially constructed data collecting form for the study.
3. The patient's past medical and medication history, as well as treatment throughout his or her hospital stay (brand and generic names, dose, dosage for, duration, and frequency), as well as his or her personal history, were documented. The total number of prescriptions obtained was counted and documented.

Potential Risks And Benefits:

a) **Risks:** Nil

b) **Benefits:**. To reduce mortality , morbidity in patients with heart failure, researchers compared the efficacy and safety of Dapagliflozin with CIDMUS.

Statistical Methods:

a) Descriptive statistics will be applied to

observe the demographics among the study population.

b) Chart sand tables will be made using Microsoft office Excel.

Ethical Considerations And Methods To Address Issues:

The research was carried out in accordance with the Aster Prime Hospital Ethics Committee's guidelines.

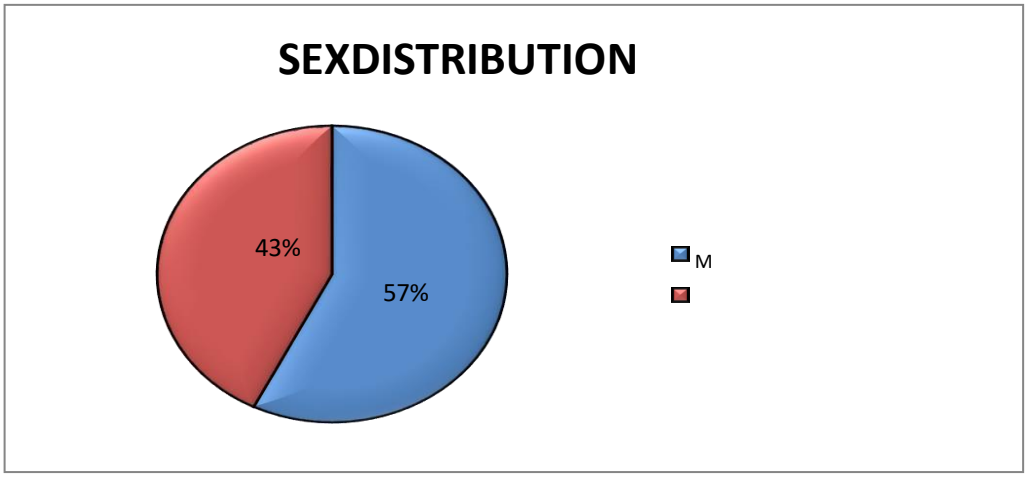
RESULTS:

1) Gender Distribution

The prospective study conducted by us of therapeutic outcome in efficacy of Dapagliflozin compared with CIDMUS in Heart failure in cardiology department, one hundred and fifteen patients enrolled in which the gender distribution was 64(57.39%) were males and 51(42.59%) were females.

Table.2: Shows The Sex Distribution Of Study Subjects In Cardiology Wards.

Sex	Total 115	%
M	64	57.37%
F	51	42.58%



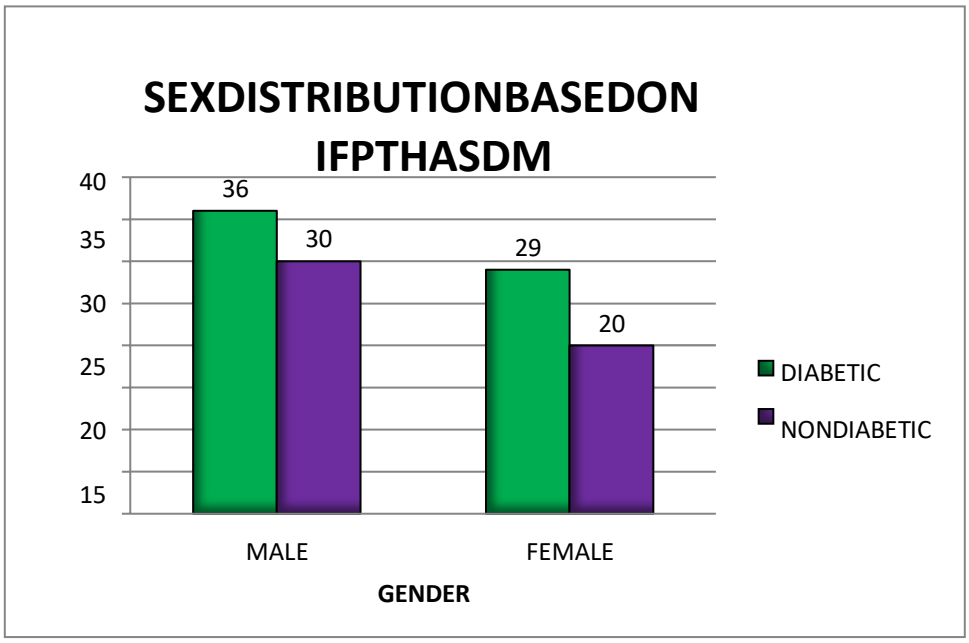
Graph.1:Shows Sex Distribution Of Study Participants In Cardiology Wards

2) Sex Distribution Based On Whether The Patient Has Diabetic Comorbidity

In our study of efficacy of Dapagliflozin compared with CIDMUS in Heart failure diabetic mellitus patients in cardiology,115 patients in which diabetic males: 36(54.54%), non-diabetic males: 30(45.45%), diabetic females:29(59.18%), non-diabetic females: 20(40.81%) were included.

Table 3: Gender Distribution Based On Diabetic Status

Diabetic Status	M		F	
N=115	**66**	**%**	**49**	**%**
True	36	54.54%	29	59.18%
False	30	45.45%	20	40.81%



Graph 2:Sex Distribution Based On Whether The Patient Has Diabetic Comorbidity

3) Age Distribution

The class interval distribution of age among patients was 31–40 : 2(3.59%), 41–50: 18(17.31%), 51–60: 46(41.73%), 61–70:33(28.97%), 71–80: 10(9.37%) have participated.

Table4:Indicates Age Distribution Of Heart Failure With DM And Non DM Patients For Determination Of Efficacy Of Dapagliflozin Compared To CIDM

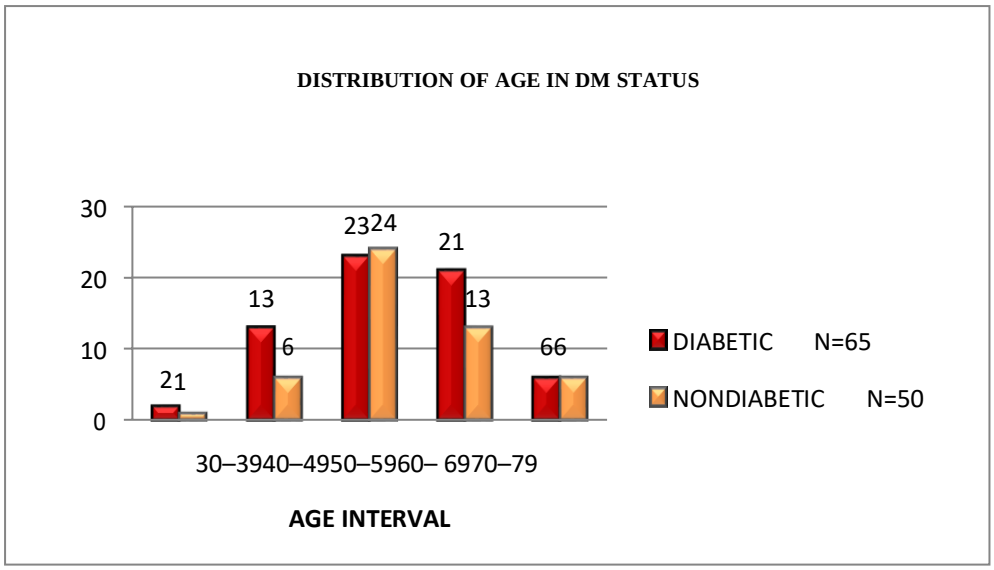
Age Intervals	N= 114	%
31 – 40	3	2.60
41 – 50	19	16.52
51 – 60	47	40.86
61 – 70	34	29.56
71 – 80	12	10.43

4) Distribution Of Age In Relation To Whether A Patient Has Dm

The age distribution in DM patients was 31to 40 years old : 2(2.99%) in DM v/s.2(3%) in non-DM,41–50:12(18%) in DM v/s.5(09%) in non- DM, 51–60:22(32.40%) in DM v/s.23(50%) in non-DM,61–70: 20(31.29%) in DM vs.12(12%) in non DM, 71–80: 5(8.10%) in DM vs.5(08) % in non DM were included.

Table 5:Indicates The Age Distribution Of Diabetics.

AGE INTERVAL	DIABETIC		NON-DIABETIC	
N= 114	N=65	%	N =51	%
31 – 40	2	3.07%	1	2%
41 – 50	12	20%	6	12%
51 – 60	24	35.38%	24	48%
61 – 70	22	32.30%	12	26%
71 – 80	6	9.23%	6	12%



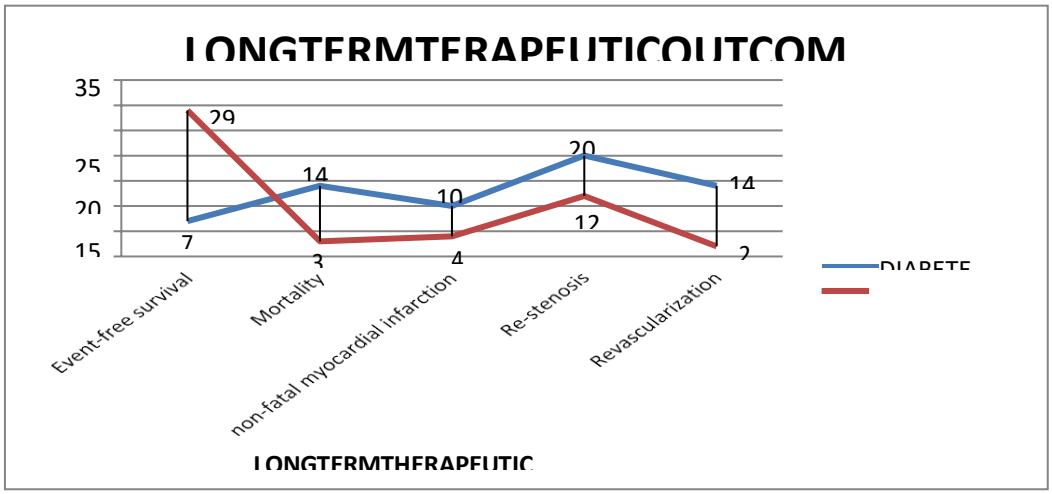
Graph 3: DISTRIBUTION OF AGE IN RELATION TO WHETHER A PATIENT HAS DM

5) Long Term Therapeutic Outcomes After Treatmmet With Dapagliflozin Compared With Cidmus In Hf With Dm

Long- term therapeutic outcomes after therapy with Dapagliflozin versus CIDMUS in HF with Diabetes Mellitus in our prospective clinical study were adverse action – free survival : 6(11.97%) v/s. 30(56%), Mortality:12(20.91%) vs 2(5%), non-fatal MI : 9(14.76%) v/s 3(9%), Re-stenosis: 21(29.2%) v/s.10(21%), revascularization:19(20.33%) v/s 3(6%) were included.

Table 6: Indicates long-term therapeutic outcomes after therapy with Dapagliflozin versus CIDMUS in patients with DM who had heart failure.

Long Term Therapeutic Outcomes	DIABETES		NON-DIABETIC	
	N= 65	%	N= 50	%
Event-Free Survival	7	10.76%	29	58%
Mortality	14	21.53%	3	6%
Non-Fatal Myocardial Infarction	10	15.38%	4	8%
Re-Stenosis	20	30.76%	12	24%
Revascularization	14	21.53%	2	4%



Graph4: Indicates Long Term Therapeutic Outcomes After Treatment With Dapagliflozin Compared With CIDMUS In Heart Failure In Diabetes Mellitus.

6) Prescription Pattern In HF With Dm Patients:

The clinical prospective study of analyzing therapeutic outcomes in HF patients who suffered from diabeties,the prescription pattern was:

Antiplatelets: 59 v/s.42
Dyslipidemic agents: 47 v/s 54,
Beta-blocker :20 v/s.37,
ACE's: 20 v/s.10,
ARB's :7 v/s.9,
CCB's: 9 v/s.5
Benzodiazepines: 51v/s 41
Thyroid drugs:14 v/s 13
Anti-diabetic drugs: 37 v/ 23
Antibiotics: 16 v/s.9,
Diuretics: 11 v/s .35
Anti-anginal: 11 v/s. 4

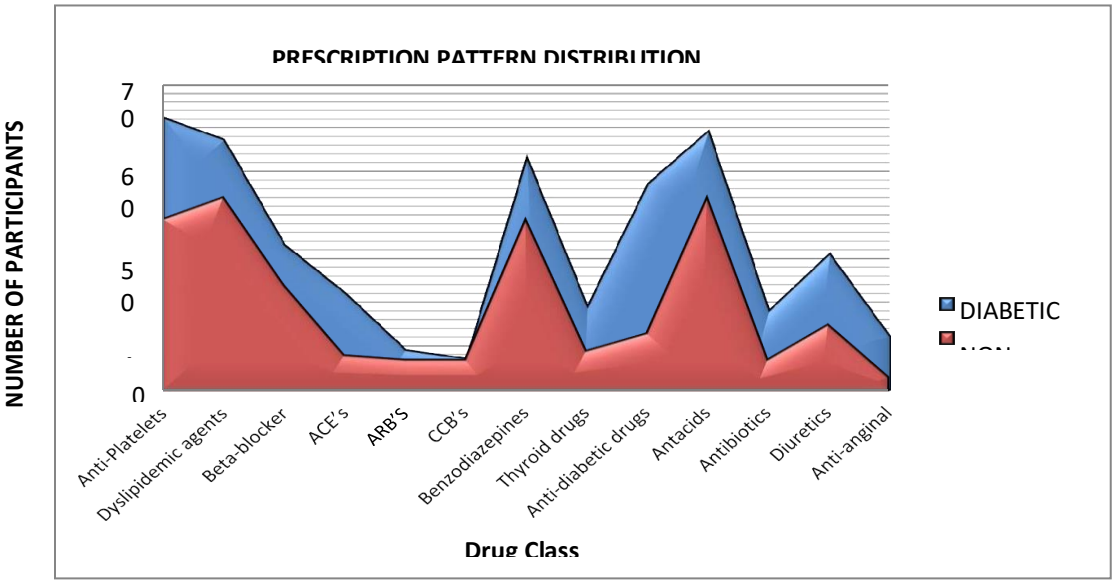


Table6:CHI-SQUARETEST

Therapeutic Outcomes	Dm	Non Dm	In Total
Event-Free Survival	7(20.35)(8.76)	29(15.65)(11.38)	36
Mortality	14(9.61)(2.01)	3(7.39)(2.61)	17
Non-Fatal Myocardial Infarction	10(7.91)(0.55)	4(6.09)(0.72)	14
Re-Stenosis	20(18.09)(0.20)	12(13.91)(0.26)	32
Revascularization	14(9.04)(2.72)	2(5.66)(2.47)	16
Total	65	55	115

Chi-square statistic is seen to be as 30.6978 & the p value is <0.00001. This indicates that there is significant difference if p value is <0.10.

7) Comparison Of Safety And Efficacy Of Dapagliflozin With Cidmus In Heart Failure Patients:

Parameter	Treatment (Dapagliflozin)		P value	Treatment(CIDMUS)		P value
	Before	After		Before	After	
E.F	33.90±5.00	45.34±7.17	<0.0001	35.14± 5.4	38.34± 6.0	<0.001
Mitral Regurgitation						
Value	2	5		2	5	
Normal value	38	55		40	54	
Mild value	40	25	0.0080	39	22	0.0080
Moderate value	14	5		11	4	
Severe						
Diastole Dys-Function						
	16	40				
GradeI	42	42		17	36	
GradeII	21	8	0.0107	42	38	0.0107
Grade III	2	0		24	11	
Grade IV				2	0	

8) Comparison Of Cost Effectivenes Of Dapaglifloz In With Cidmus In Patients Of Hf

Intervention	Cost	Outcomes
Dapagliflozin	420/14tablets	4.2years
Cidmus	939.30/14tablets	4.6years

ICER=C(Dab)–C(Cid)/E(Dab)–E(Cid)

=420-939/4.2-4.6

=-519/-0.4

=1297.5

This shows that Dapagliflozin is better economically viable hence costeffective when evaluated against CIDMUS in HF Patients.

9) In Heart Failure Patients With Kccq Score Of Dapagliflozin And Cidmus

Domain	Cidmus		P Value	Dabagliflozin		P value
	Before	After		Before	After	
Total Symptom frequency Score	14.51± 4.15	20.67± 4.73	<0.0001	13.51± 4.15	19.67± 4.73	<0.0001
Symptom frequency	24.24± 6.80	33.80± 7.71	<0.0001	22.24± 5.80	33.80± 6.71	<0.0001
Overall Score	39.57± 11.51	56.19±12.50	<0.0001	36.57± 11.51	52.19±10.50	<0.0001

- The P-values for the above table, with Mean Standard Deviation, were determined using a dependent t test.
- A considerable variation was noticed in the score before and after Dapagliflozin and CIDMUS treatment.

DISCUSSION:

1) The prospective clinical study which was conducted in Aster Prime Hospital and was deemed according to the ethical considerations had the aim to judge the safety and effective action of CIDMUS and Dapagliflozin in individuals with heart failure. There was a comprehensive evaluation to assess HrQol (Health Related Quality of Life), Economic consideration, therapeutic outcomes after the treatment of heart failure with Dapagliflozin in comparison with CIDMUS.

2) Clinical studies, which have been previously conducted showed a similar efficacy and safety profile in both the drugs in HF patients with DM. A total of 114 patients were selected to be assessed in the study, having fit the inclusion and exclusion criteria. Amongs the patients who were selected, 56.70% were males(59) and 43.30% were females (40). The prospective study conducted by us of therapeutic outcome in efficacy of Dapagliflozin and CIDMUS.

3) In our study of efficacy of Dapagliflozin compared with CIDMUS in Heart failure diabetic mellitus patients in cardiology, a total of 115 in which diabetic males: 36(54.54%), non-diabetic males: 30(45.45%), diabetic females:29(59.18%), non-diabetic females: 20(40.81%) were included.

4) The class interval distribution of age among patients was 31–40:2(3.59%), 41–50:18(17.31%), 51–60: 46(41.73%),61–70:33(28.97%), 71–80: 10(9.37%) have participated.

5) The age distribution in DM patients was 31 to 40 years old : 2(2.99%) in DM v/s. 2(3%) in non-DM, 41 –50:12(18%) in DM v/s.5(09%) in non-DM, 51–60:22(32.40%) in DM v/s.23(50%) in non-DM, 61–70: 20(31.29%) in DM vs.12(12%) in non-DM, 71–80: 5(8.10%) in DM vs.5(08)% in non DM were included.

6) Long-term therapeutic outcomes after therapy with Dapagliflozin versus CIDMUS in HF with DiabetesMellitus in adverse action-free survival : 6(11.97%) v/s. 30(56%), Mortality: 12(20.91%) vs. 2(5%), non-fatal MI: 9(14.76%) v/s.3(9%), Re-stenosis:21(29.2%) v/s.10(21%), revascularization: 19(20.33%) v/s.3(6%) were included.

7) The clinical prospective study of analyzing therapeutic outcomes in HF patients who suffered from diabeties, the prescription pattern was Antiplatelets: 59 v/s. 42, Dyslipidemic agents: 47 v/s 54, Beta-blocker: 20 v/s.37,ACE's:20 v/s.10, ARB's:7 v/s 9, CCB's:9 v/s.5 Benzodiazepines:51 v/s.41 ,Thyroid drugs:14 v/s13
Anti-diabetic drugs: 37v/s.23, Antibiotics: 16 v/s.9, Diuretics:11 v/s.35, Anti-anginal:11v/s.4.

8) Chi-square statistic is seen to be as 30.6978 & the p value is < 0.00001. This indicates that there is significant differenceif p value is <0.10. P-Value is calculated with Standard Deviation +- Average in the above table with dependent T-Test and it illustrates 2D Echo of heart, all parameters after the start of dapagliflozin and CIDMUS. This shows that Dapagliflozin is better economically against CIDMUS in HF Patients.

9) To compare the KCCQ Score Domains before the initiation and after administration with Dapagliflozin compared to CIDMUS in Heart Failure with Diabetes mellitus, the P-values for the above table, with Mean Standard Deviation, were determined using a dependent t test.
A considerable variation was noticed in the score before and after Dapagliflozin and CIDMUS treatment.All the results were incompliance of the previously conducted studies.

CONCLUSION:

In this prospective observational observation of lengthy-term therapeutic consequences, cost-effectiveness,and exceptional life after remedy with Dapagliflozin in comparison to CIDMUS in Heart failure patients, we located that medical outcomes like occasion-unfastened survival became much less favorable in patients with diabetes than in non-diabetic patients. Long-time period complications like revascularization, restenosis, non-fatal myocardial infarction, and mortality have been on the better rate in the patients having diabetes whilst compared with non-diabetic patients. After remedying with Dapagliflozin, coronary heart failure sufferers confirmed better protection, efficacy, Quality of lifestyle, reduction in hospitalization, and mortality.

REFERENCES:

1. Heart Failure Clinical Presentation: History, Physical Examination, Predominant Right-Sided HeartFailure[Internet].Emedicine.medscape.com .2021[cited5June2021].Availablefrom:https://emedicine.medscape.com/article/163062-clinical#b7

2. HeartFailure:Types, Symptoms, Causes&Treatments[Internet].Clevel and Clinic.2021[cited5June2021].Available from:https://my.clevelandclinic.org/health/diseases/17069-heart-failure-understanding-heart-failure#symptoms-and-causes

3. Figure5. Volpe M,Rubattu S, BurnettJ. Natriuretic peptides in cardio vascular diseases:current use and perspectives. European Heart Journal.2013;35(7):419-425.

4 Raikos,A.and Waidyasekara,P.,2014. Howusefulis YouTube in learning heart anatomy?. Anatomical sciences education,7(1),pp.12-18.Anderson, R.H. and Brown, N.A.,1996. The anatomy of the heart revisited. The Anatomical Record: An Official Publication of the American Association of Anatomists,246(1),pp.1-7.

5 Cardiovascular disease: Types, symptoms, prevention, and causes [Internet]. Medical news today.com.2021[cited5June2021]. Available from: https://www.medicalnewstoday.com/articles/257484#types

6 Heartfailure-Symptoms and causes [Internet].Mayo Clinic.2021[cited5June2021]. Available .From: https://www.mayoclinic.org/diseases-conditions/heart-failure/symptoms-causes/syc-20373142

7 Congestive Heart Failure and Heart Disease [Internet]. WebMD.2021[cited5June2021]. Available from https://www.webmd.com/heart-disease/guide-heart-failure

8 Heart failure – Symptoms and causes [Internet]. Mayo Clinic.2021[cited5June2021]. vailable.From:https://www.mayoclinic.org/diseases-conditions/heart-failure/symptoms-causes/syc-20373142

9 Volpe M,Rubattu S, BurnettJ. Natriuretic peptide in cardiovascular diseases: current use and perspectives. European Heart Journal.2013;35(7):419-425.

10 Volpe M,RubattuS, Burnett J. Natriureticpeptides in cardiovascular diseases: current use and perspectives. European Heart Journal.2013;35(7):419-425.

11 KaplinskyE.Sacubitril/valsartan in heartfailure:latest evidence and place in therapy.Therapeutic Advances in Chronic Disease.2016;7(6):278-290.

12 Volpe M,RubattuS,BurnettJ. Natriureti peptides in cardiovascular diseases:current use and perspectives. European Heart Journal.2013;35(7):419-42.