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THE EFFECT OF SGLT2 INHIBITORS IN HEART FAILURE PATIENTS

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Abstract

The study aimed to observe the effect of SGLT2 inhibitors in heart failure patients. It is a prospective observational study design; with this method, the researcher selected 40 samples from department of cardiology at Banjara Hills, Hyderabad Care Hospital. The result showed that after the addition of SGLT2 inhibitors in cardiac patients (subset of HFpEF and HFrEF) has reduced symptomatic effect of heart failure,SGLT2 inhibitors Proven to lower blood pressure by 2%,SGLT2 inhibitors reduced HbA1C levels by 2%,Its incidental observation of Reduction in body weight with SGLT2 inhibitors usage ,Diuretic effect observed by correction of dilutional hyponatremia and reduction inserum potassium levels with SGLT2 inhibitors,5% ADRs observed like increased incidence of UTI in patients with SGLT2 inhibitors, Appropriate measures for screening in at risk population should be suggested before initiating the drug.so, the usage of SGLT2 inhibitors is a new pharmacological application effective in the treatment of DM and NON- DM and associated with heart failure.

Keywords: Heart Failure, Cardiology, SGLT2 Inhibitors, Blood Pressure, Diabetes Mellitus.

1.INTRODUCTION TO SGLT2 INHIBITORS:

The inhibitor of selective sodium-glucose transporter-2 (SGLT2), expressed in the proximal renal tubules, is responsible for most of the filtered sugar that is reabsorbed from the tubular lumen. SGLT2 inhibitors decrease glucose reabsorption and lower the renal threshold for glucose, which increases urine glucose excretion in addition to decreasing sodium reabsorption and boosting the transport of sodium to the distal tubule. [2] Because of this, they hardly ever result in hypoglycemia when there are no treatments that might otherwise do so. SGLT2 inhibitors slightly lower blood pressure and weight. [1] There is ongoing research to explore the mechanistic effects of SGLT-2 inhibitors in HF and

evaluate their use in worsening Heart Failure. This research focuses on the evidence for SGLT-inhibitors from type 2 diabetes cardiovascular outcome and primary HF trials and discusses ongoing research related to their use in cardiovascular disease.

1.1 EMPAGLIFLOZIN:

It does not have a beta- cell capacity or an insulin pathway, empagliflozin does not pose a risk of hypoglycemia.[3]Empagliflozin is a tabletthat is taken orally, empagliflozin has a molecular weight of 450.91 g/mol [4] its Bioavailability is 78% and is orally active, reaches highest plasma concentration administration after 1.5 hours [5] its T ½is 12.4 hrs and Total body clearance is 10.6 L/hrs., Empagliflozin is prescribed at a dose of 10 mg followed by 25 mg.[5], its adverse effects include UTI, myotic infections, diabetic ketoacidosis, and urosepsis are all interrelated.[6][7], Empagliflozin is not for patients who suffer from hypersensitivity, severe renal impairment, or need dialysis. [8], . Empagliflozin has cardiovascular and extracardiac protective effects, including improved diuretic efficacy, renal protection, increased heart substrate digestion (i.e., improved ketone arrangement and utilization), and diminished vascular firmness.[9] , empagliflozin has the ability to inhibit fibroblast initiation induced by changing development factor-beta- Prompted the start of fibroblasts collagen synthesis and fibrosis also reduce the production ofthe pro-inflammatory adipokine leptin and increase the production of the anti-inflammatory adipokine adiponectin.[10][11],] A reduction in preload, left ventricular (LV) filling weight, and LV wall stress—the last of which is the primary driver for the production of N-terminal expert mind natriuretic peptide (NT-proBNP)—has been proposed as a possible explanation for the observed cardiovascular benefits of SGLT2 inhibitors.[12][13]

1.2 DAPAGLIFLOZIN

Dapagliflozin can be purchased as 5 mg or 10 mg tablets for oral use. For those who require additional glycaemic control, the recommended daily dose, 5 mg, can be increased to 10 mg. [14], its Bioavailability is 78% and its Protein binding is 78%, Half life is 12.9hrs , 75% excretion through urine, 21% through faeces [15] Dapagliflozin by showing metabolic shifting it reduces fatty acid oxidation and increasesglucose oxidation and 3 beta hydroxybutyrate thus Dapagliflozin increases cardiac efficiency and decreases cardiac effects and improves heart failure outcome.[15][16] ,it also Decreases hypertrophy, fibrosis and remodeling, its used to lower the risk of cardiovascular death, in adults with HFrEF and heart failure (NYHA classii - iv) with T2DM, established cardiovascular disease(CVD), or multiple CV risk factors to suffer from HF.[15] , adverse effects include female genital mycotic infections , nasopharyngitis ,elevated urination ,urinary tract infections.

1.3 CANAGLIFLOZIN

Apart from lowering blood sugar, it also has Pasitve effect on kidneys and heart.[17] ,its Bioavailability is 65% , C_{MAX} is 1-2 hrs , Protien binding is 99%(mainly to albumin)and its Vd is 119lit, recommended doses are 100 mg and 300mg ,drug Half life are 100mg dose - 10.6 hrs,300mg dose-13.1hrs ,it is used to improve glycemic control ,reduce the occurrence end stage kidney disease, cardiovascular death .Adverse reaction of canagliflozin are increased urination ,thirst , constipation, male genital mycotic infections ,female genital mycotic infections ,urinary tract infections [18] Canagliflozin shows the effect to transiently decrease plasma volume during the initial first weeks of treatment. After 12 weeks, however, this effect was significantly weakened. Therefore, a diuretic dose effect of SGLT2i with consequent beneficial effects on blood volume was suggested. Thus, it affects the BP and shows the cardio protective action and reduces the reoccurrence of cardiovascular events. [19][20].

2.METHODOLOGY:

The aim of the study is to find the impact of SGLT2 inhibitor medications on individuals with heart Failure**.**

The Primary Objective of the study is to observe and quantify the effect of SGLT2 inhibitors drugs in heart failure patients with Heart failure with reduced ejection fraction (HFrEF) and Heart failure with preserved ejection fraction (HFpEF).

The secondary objective of the study is to observe the symptomatic effects in patients using SGLT2 inhibitors. To observe the diuretic dose effect in patients using SGLT2 inhibitors. To find the adverse effects such as UTI in Patients using SGLT2inhibitors.To observe the Patients with weight loss in Patients using SGLT2inhibitors.To observe the length of hospital, stay and mortality in patients using SGLT2inhibitors.

This is a Prospective and Observational Non-interventional study was applied to achieve the aim of the current study. The study was conducted in the department of cardiology at the tertiary care hospital, located at banjara hills road no.1 Hyderabad, Telangana. The sample size was determined as 40 in this study. Python software will be used for statistical analysis. A P value of less than 0.05 was deemed statistically significant. Descriptive statistics will be used to present all of the results: the median and interquartile range (IQR) for skewed distributions and the mean and standard deviation (SD) for regularly distributed data. Counts and percentages will be used to display binary and category variables. Statistical test was used are paired t-test.

3.RESULTS AND DISCUSSION

The study showed that SGLT2i was shown to significantly reduce heart failure hospitalizations and heart disease mortality in type 2 and non-diabetic patients at
high cardiovascular risk**.** In addition, the benefits of SGLT2i in terms of heart failure hospitalizations and cardiovascular deaths were evident despite a significant reduction in HbA1c or a baseline HbA1c. These results suggest that the effect of SGLT2i is independent of glycaemic control. SGLT2i significantly lowers systolic and diastolic blood pressure, helping to relieve stress on the heart. SGLT2i treatment also alters fuel and improves the heart's energy state by increasing ATP production. SGLT2i significantlyimproved ejection fraction, obesity, and diffuse fibrosis in patients with or without T2DM

3.1. GENDER DISTRIBUTION:

In the study of the results of using SGLT2i in patients with heart failure, 40 cases were recorded. Among them, 23 patients are men and 17 women. Of the 40 patients, 57% were male and 43% female. The Below Fig 1 Represents percentage of gender distribution in heart failure patients.

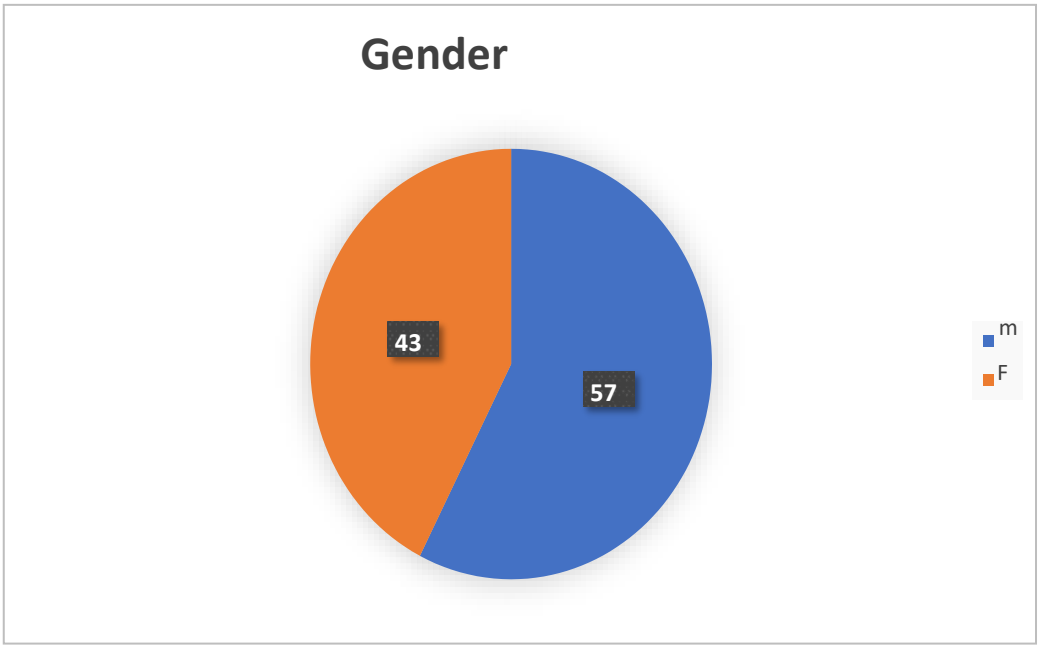


Fig (1): percentage of gender distribution in heart failure patients

3.2.AGE DISTRIBUTION IN PATIENTS:

Total 40 patients included in the study. Among these; 2 patients were found between 40 - 50years, 9 patients between 50 - 60 years, 13 patients between 60 - 70 years, 12 patients 70 -80 years and 4 patients were between 80 - 90 years. The Below Figure 2 Shows Bar representation of Patients according to their age.

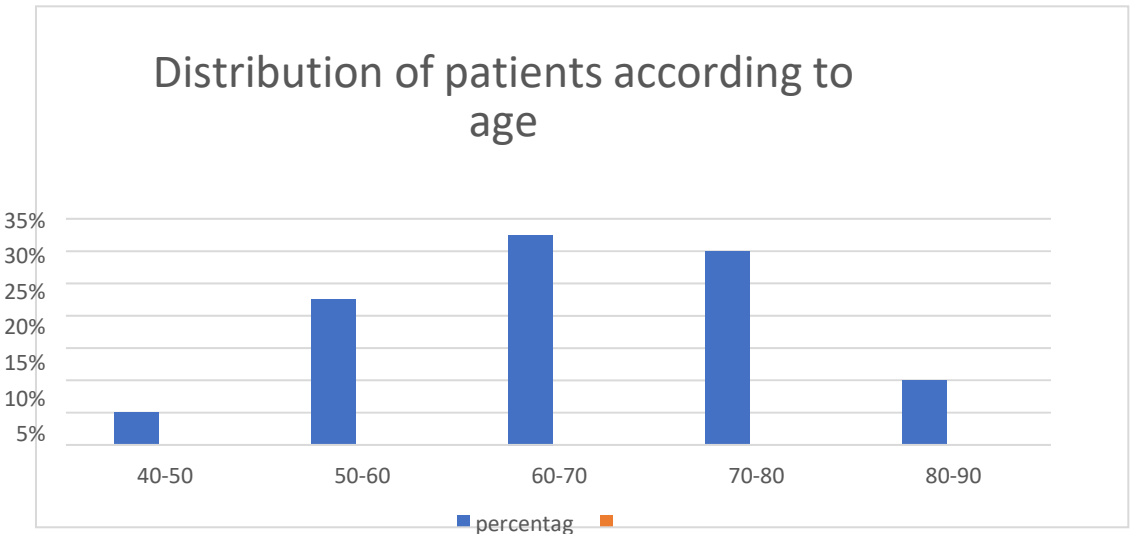


Fig (2): Bar representation of patients according to age group

3.3. DISTRIBUTION OF HEART FAILURE PATIENTS:

Among total 40 heart failure patients we found 24 patients with HFREF and 16 patients with HFPEF. The below figure 3 represents Percentage of Patients based on type of heart failure.

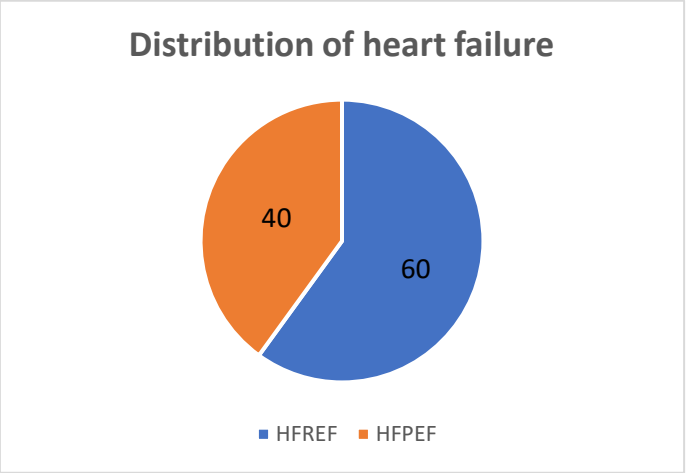


Fig (3): percentage of patients based on the type of heart failure

3.4. DISTRIBUTION OF COMORBIDITIES:

Among 40 heart failure patients we found 1 HTN; 3 T2DM; and 36 patients with both the comorbidities. The below bar representation in Figure 4 shows the number of patients with Comorbidities.

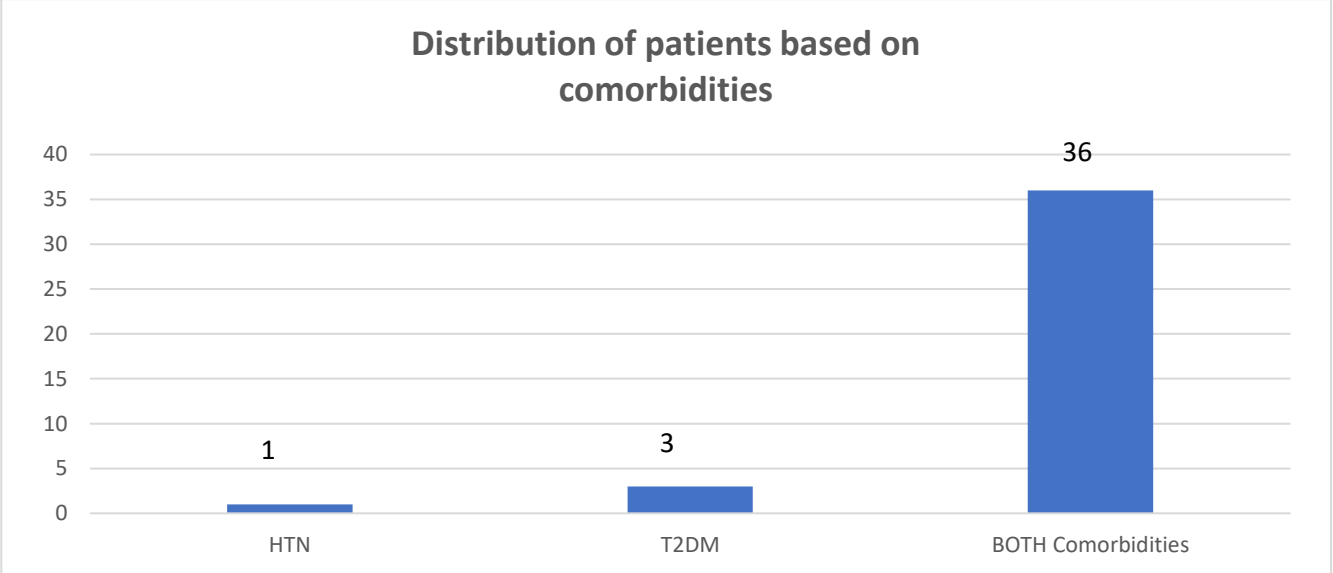


Fig (4): number of patients based on comorbidities

3.5. DISTRIBUTION OF EJECTION FRACTION:

Ejection fraction values were taken for 40 patients; from those we found 16 patients having ejection fraction >40%(HFpEF) and remaining 24 patients with ejection fraction <40% (HFrEF). Figure 5 shows Bar representation of distribution of ejection fraction.

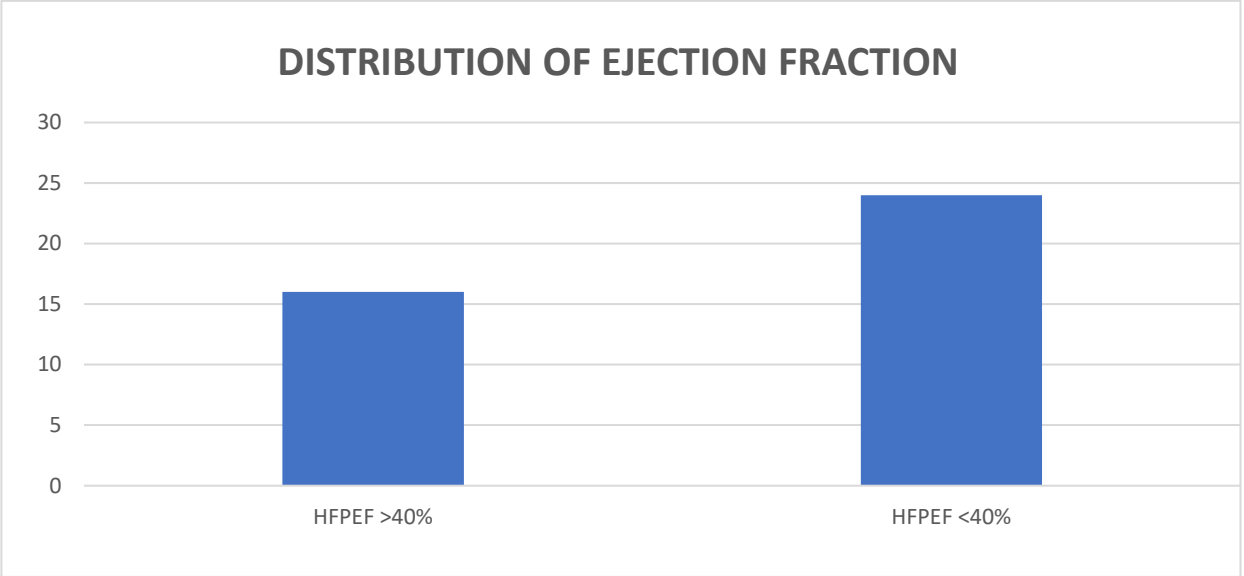


Fig (5): Distribution of patients based on LVEF

3.6. EFFECT OF SGLT2 INHIBITORS IN WEIGHT REDUCTION:

Patients with HF nearly recovered and plan to discharge from ICU, prescribed with SGLT2 inhibitors. 40 subjects were taken in our project. Patients who are taking SGLT2i has been observed minor reduction of weight. Before taking the drug the average weight was 70.42kg and after the drug use 69.55kg. So, the average weight reduction after the drug use found to be 0.87kg. Figure 6 shows Bar representation of efficacy of sglt2 inhibitors in weight reduction.

Paired t test is used. P-value is insignificant.

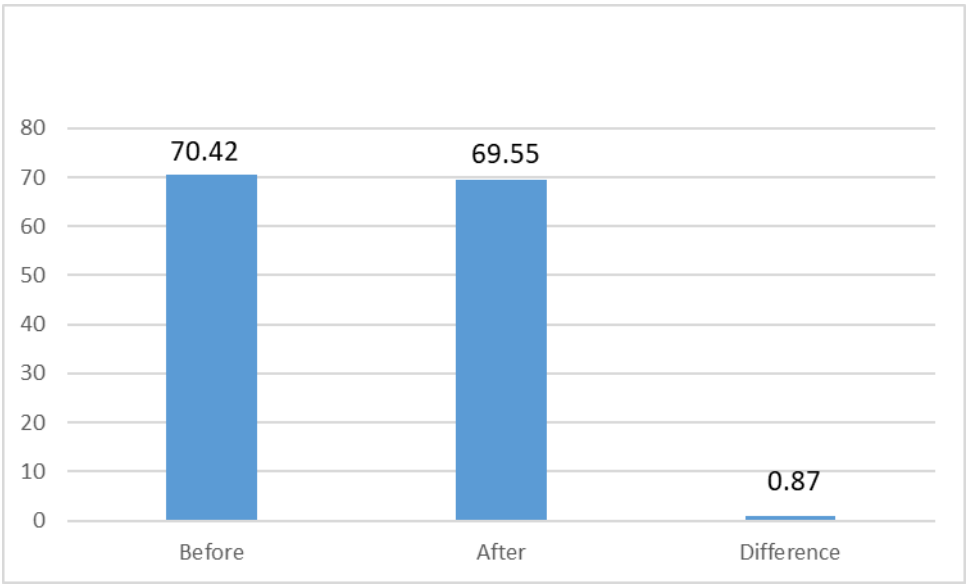


Fig (6): Bar representation of efficacy of sglt2 inhibitors in weight reduction

3.7. EFFECT OF SGLT2 INHIBITORS IN BLOOD PRESSURE:

Patients with HF nearly recovered and plan to discharge from ICU, prescribed with SGLT2

inhibitors. 40 subjects were taken in our project. Patients who are taking SGLT2i has been observed reduction of blood pressure. Before taking the drug the average mean arterial pressure was 96.25 and after the drug use 91.83.
So, the average reduction of mean arterial pressure after the drug use found to be 4.42. Figure 7 Shows Distribution of mean arterial Pressure.

Paired t test is used. P-Value is highly Significant.-

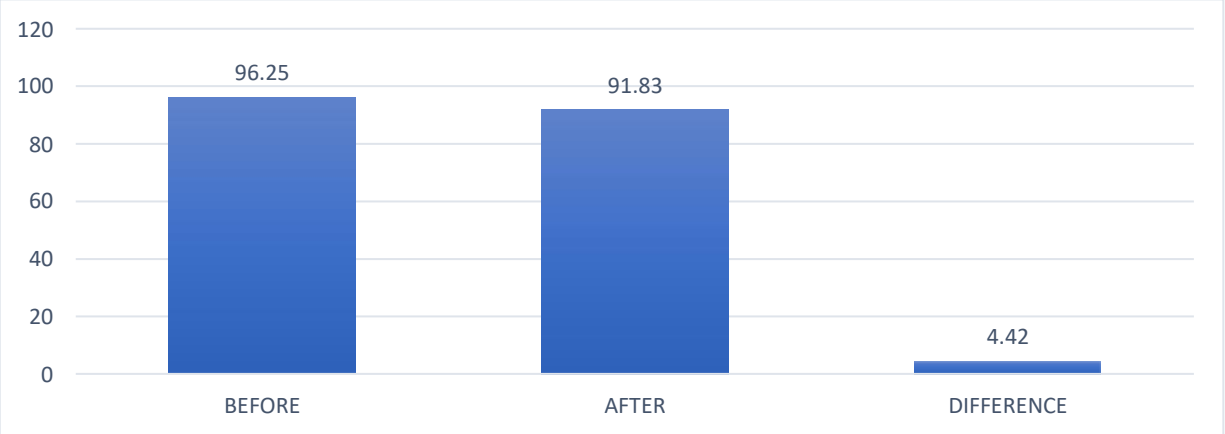


Fig (7): Bar distribution of mean arterial pressure

3.8. EFFECT OF SGLT2 INHIBITORS IN HbA1C:

Patients with HF nearly recovered and plan to discharge from ICU, prescribed with SGLT2 inhibitors. 40 subjects were taken in our project. Patients who are taking SGLT2i has been observed that reduction of HbA1C Before taking the drug the average HbA1C was 7.74 and after the drug use 7.59.
So, the average HbA1C reduction after the drug use found to be 0.15. Figure 8 Shows Distribution of HbA1C .

Paired t test is used. P-value is insignificant.

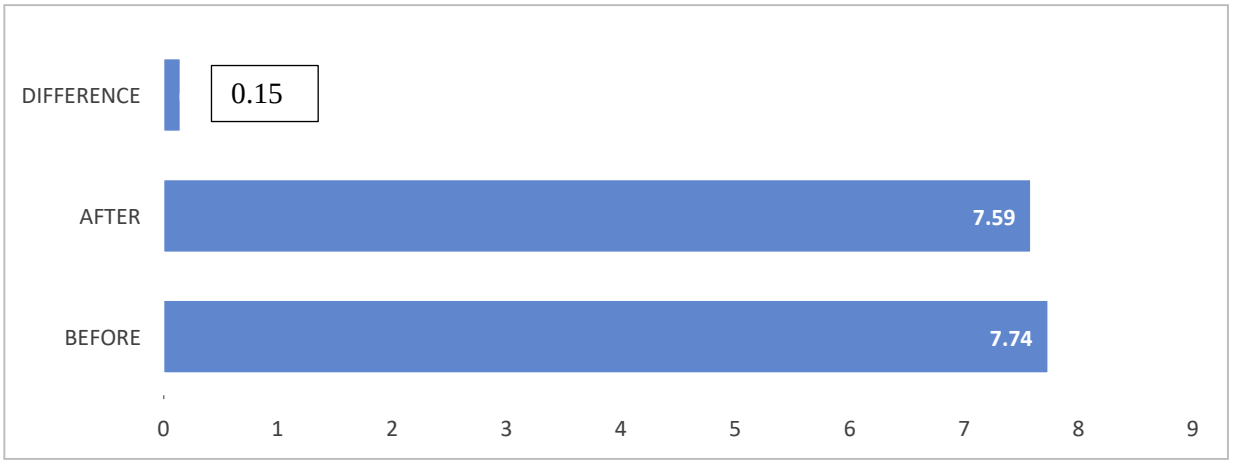


Fig (8): Bar distribution of HbA1C

3.9. EFFECT OF SGLT2 INHIBITORS IN SERUM SODIUM:

Patients with HF nearly recovered and plan to discharge from ICU, prescribed with SGLT2 inhibitors. 40 subjects were taken in our project. Patients who are taking SGLT2i has been observed

that reduction of Sodium Before taking the drug the average Sodium was 134.85 and after the drug use 132.32.
So, the average Sodium reduction after the drug use to be 2.53. Figure 9 shows Bar distribution of Serum Sodium.

Paired t test is used. P-value is highly Significant.

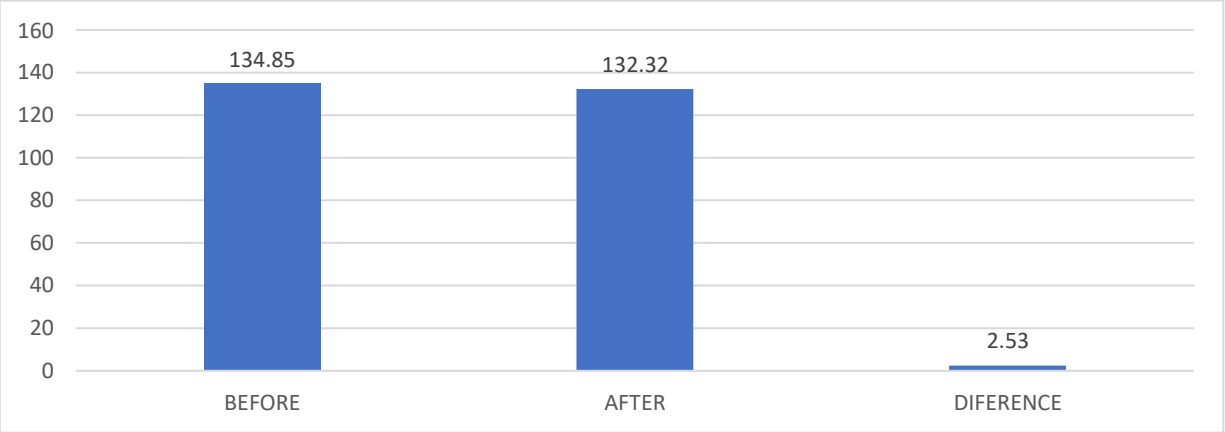


Fig (9): Bar distribution of serum sodium

3.10. EFFECT OF SGLT2 INHIBITORS IN POTASSIUM:

Patients with HF nearly recovered and plan to discharge from ICU, prescribed with SGLT2 inhibitors. 40 subjects were taken in our project. Patients who are taking SGLT2i has been observed that reduction of potassium Before taking the drug the average potassium was 4.2 and after the drug use 4.0
So, the average potassium reduction after the drug use to be 0.2. figure 10 shows bar distribution of serum potassium

Paired t test is used. P-value is border line significant

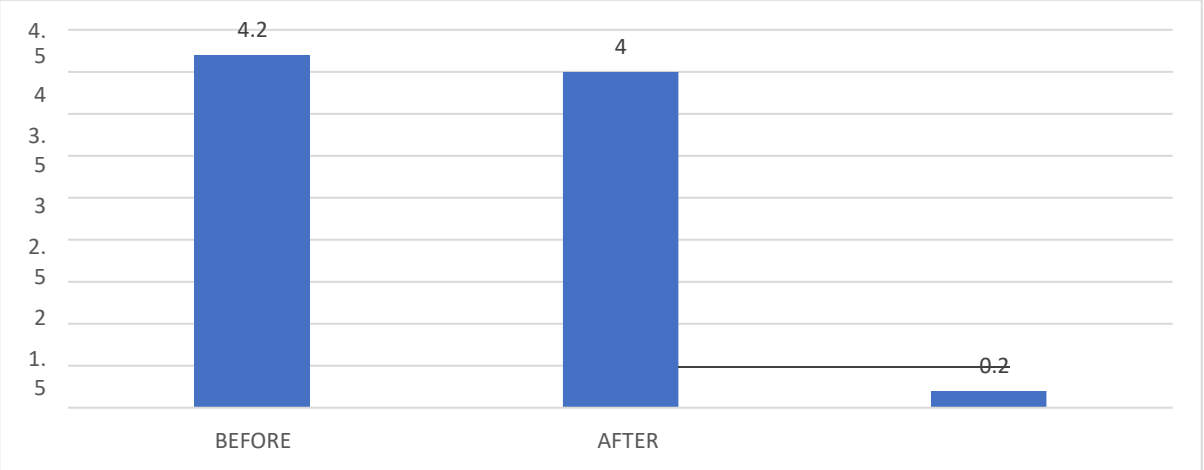
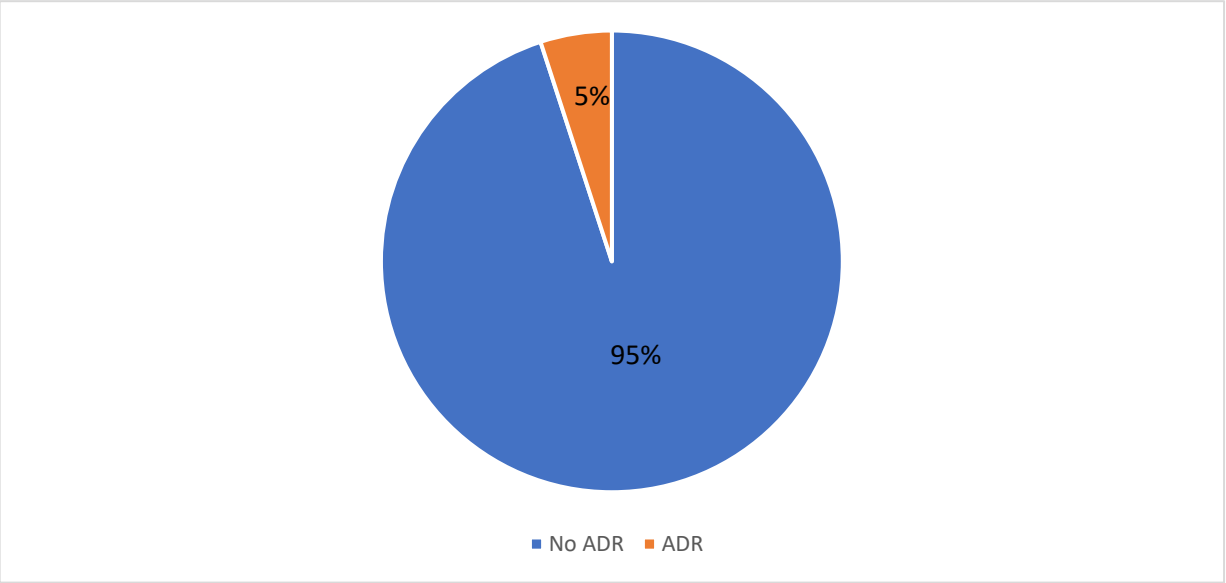


Fig (10): Bar distribution of serum potassium

3.11. EFFECT OF SGLT2 INHIBITORS IN ADVERSE REACTION:

Patients with HF nearly recovered and plan to discharge from ICU, prescribed with SGLT2 inhibitors. 40 subject were taken in our project. Among them 2 patients were developed ADR[Urinary Tract Infections]. Figure 11 Represents percentage of ADRS.



Fig(11): percentage of ADRs

4.CONCLUSION

- This observational study has shown us that after the addition of SGLT2 inhibitors in cardiac patients (subset of HFpEF and HFrEF) has reduced symptomatic effect of heartfailure.SGLT2 inhibitors Proven to lower blood pressure by 2%.SGLT2 inhibitors reduced HbA1C levels by 2%.Its incidental observation of Reduction in body weight with SGLT2 inhibitors usage.Diuretic effect observed by correction of dilutional hyponatremia and reduction in serum potassium levels with SGLT2 inhibitors.5% ADRs observed like increased incidence of UTI in patients with SGLT2i. Appropriate measures for screening in at risk population should be SUGGESTEDbefore initiating then drug.

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