

# Comparative Study Of Safety, Efficacy, Tolerability And Cost Of Glimpiride And Gliclazide In Type-2 Diabetes Mellitus Patients With Hypertension

<sup>1</sup>G. Jhansi, <sup>1</sup>P. Swathi, <sup>1</sup>A. Makarandh, \*K. Devender

<sup>1</sup>Pharm. D, \*Associate Professor  
Department of Pharmacy Practice,  
St. Peter's Institute of Pharmaceutical Sciences, Warangal, India

**Abstract:** Type-2 Diabetes Mellitus is a progressive condition in which the body becomes resistant to the normal effects of insulin and/or gradually loses the capacity to produce enough insulin in the pancreas. Diabetic ketoacidosis, retinopathy, nephropathy, neuropathy, diabetic foot, cardiovascular and cerebrovascular complications are associated with Type-2 Diabetes Mellitus, since past few decades the prevalence of Type-2 Diabetes Mellitus has increased and this has led to an increase in need to identify the better choices of drugs used along with the 1st line drugs in Type-2 Diabetes Mellitus in lowering the blood glucose levels to optimum level. Sulphonylureas have been increasingly used as second-line therapy in combination with Metformin. Glimpiride is generally prescribed as the drug of choice along with Metformin but newer Sulphonylureas like Gliclazide are equally/more efficacious and safer than Glimpiride. The aim of the study is to identify the better choice of drug by comparing Glimpiride and Gliclazide in terms of their safety, efficacy, tolerability and cost.

**Index Terms** – Type-2 Diabetes Mellitus, Glimpiride, Gliclazide, Safety, Efficacy.

## INTRODUCTION:

In Diabetes Mellitus ability of the pancreas to produce to the hormone insulin is impaired and body's ability to respond to insulin is also impaired, which results in abnormal metabolism of carbohydrates and blood glucose levels are elevated. Diabetes Mellitus is a cluster of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. If left untreated or improperly treated Diabetes Mellitus might cause several complications which include diabetic retinopathy, diabetic foot, diabetic ketoacidosis, nephropathy, neuropathy, cardiovascular complications etc.

Type 2 diabetes mellitus increases the risk of major cardiovascular complications by two times in patients with and in patients without established cardiovascular disease, such that the majority of patients with diabetes die due to cardiovascular diseases<sup>1</sup>, Globally diabetic nephropathy is a significant cause of chronic kidney disease and end-stage renal failure<sup>2</sup>, Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20–74 years<sup>3</sup>, It is estimated that 15% of all diabetic individuals experience diabetic foot ulcers<sup>4</sup>.

Diabetes mellitus type 2 is generally treated with Insulin and Oral hypoglycemics which include Biguanides (Metformin, Phenformin etc.) and Sulphonylureas (Glimpiride, Gliclazide, Glipizide etc.) these drugs lower the blood glucose levels by stimulating the pancreas to secrete more insulin.

## METHODOLOGY:

**Study site:** The proposed site was carried out in outpatient department of Rohini Super Specialty Hospital and Samraksha Endocrinology Department Hospital.

Rohini Super Specialty Hospital, a Tertiary Care Hospital, located in Hanamkonda. It is a 300 bedded hospital with departments like General medicine, Cardiology, Neurology, Urology, Gastroenterology, Orthopedics, Pediatrics, General Surgery and Gynecology. It provides all the facilities along with adequate laboratory needs.

Samraksha Diabetic, Thyroid Super Specialty Hospital, located in Warangal. It provides services for complicated diabetes, Diabetology, Diabetic management, Thyroid management, Preventive Medicine, Endocrinology. It provides all the facilities along with adequate laboratory needs. The present study was conducted in Diabetology department of this hospital. The study was performed under the supervision of Dr. B. Sridhar M.D. general medicine (NIMS), D.M.D. Endocrinology (OSMANIA).

**Study design:** Prospective observational study.

**Study period:** 6 months (November 2018 to April 2019).

**Sample size:** 200 patients suffering from Diabetes Mellitus Type 2 with Hypertension were considered and patient information was collected.

**Study population:** Patients arrived with Diabetes Mellitus Type 2 with HTN to Endocrinology outpatient Department of Rohini Super Specialty Hospital and Samraksha Diabetic and Thyroid Super Specialty Hospital were enrolled in the study.

Study criteria: The outpatients who were diagnosed with Diabetes Mellitus Type 2 with Hypertension were enrolled into the study by considering following inclusion and exclusion criteria.

Inclusion Criteria:

- Patients with Diabetes Mellitus ype-2 and Hypertension.
- Patients who are at age of 25-80 years old.
- Both inpatients and outpatients.
- Patients using Glimepiride/Gliclazide with Metformin.

Exclusion Criteria:

- Patients with other comorbidities except Hypertension.
- Pediatric patients.
- Pregnant and lactating women.
- Patients using other oral hypoglycemics/Insulin along with Glimepiride or Gliclazide with Metformin.

Study procedure:

- Enrolment into the study: Diabetes Mellitus type-2 patients fulfilling the inclusion criteria were enrolled into the study after obtaining consent from them. Patient's interview was done to determine disease outcome before and after the treatment. Their detail clinical history was obtained regarding demographic details (age, gender, and occupation), weight, height (for BMI) and chief complaints, past medical history, medication adherence, past medication history, family history, social history, allergies, site and severity of condition.
- Follow up was done on 2nd visit.

Sources of the data:

All the relevant and necessary data was collected from the following:

- Patient Medication Chart.
- Patient Profile Form.
- Patient and Attendant Interview.

#### STATISTICAL ANALYSIS:

1. Mean: It is used to derive the central tendency of the data in question. It is determined by adding all the data points in the subjects and then dividing the total by the number of points. The resulting number the mean of data.
2. Average Reduction Percentage: It is used to estimate the percentage of reduction of blood glucose levels among subjects after treatment. The difference between the two average numbers are calculated then the number is divided with its initial average and it is multiplied by 100.

#### RESULTS:

This study consists of the complete data of 200 patients with Diabetic mellitus type 2 from two different hospitals viz., Rohini Super Specialty Hospital, Hanamkonda, Warangal and Samraksha Super specialty Hospital, Hanamkonda, Warangal.

Sample:

Age Wise Distribution of Subjects:

Data was collected for a total of 200 patients. Out of which 7 patients were from the age group of 20-30 years, 46 patients between the age of 30-40 years, 79 patients in between the age of 40-50 years, 51 patients were 50-60 years of old and 17 patients are 60-70. The percentage of a study sample was calculated and mentioned.

Table 1. Age wise Distribution of Subjects

S. No	Age (Years)	No. of patients	Percentage
1	20-30	7	3.5%
2	30-40	46	23%
3	40-50	79	39.5%
4	50-60	51	25.5%
5	60-70	17	8.5%

The maximum number of patients are under the age group of 40-50, followed by 50-60 years.

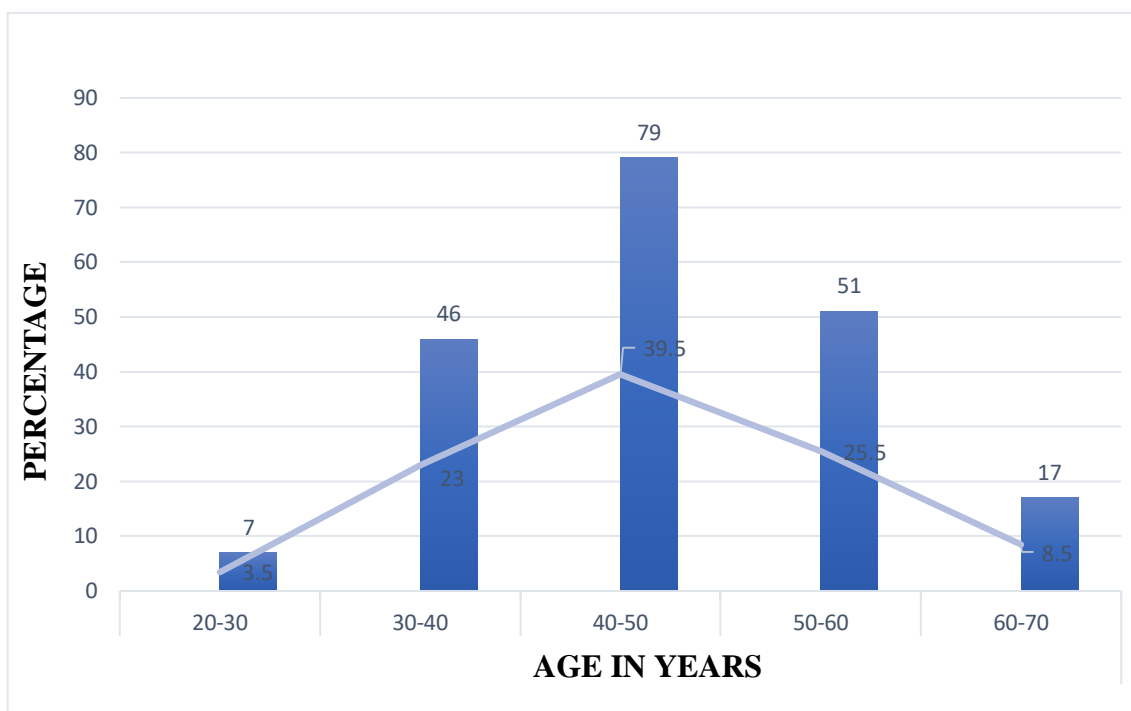


Fig 1: Age Wise Distribution of Subjects.

Gender Wise Distribution of Subjects:

The study sample included 107 male (53.5%) and 93 female (46.5%) patients.

Table 2: Gender Wise Distribution of Subjects.

S. No	Gender	Frequency	Percentage
1	Male	107	53.5%
2	Female	93	46.5%
Total	Male + Female	200	100%

Among the 200 patients, the male population found to be greater than that of the female population. Males were 107 out of 200 patients that contributes to 53.5% and females were 93, which contributes to 46.5% of the total samples collected.

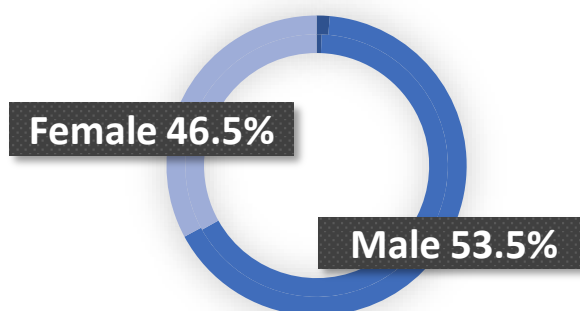


Fig 2: Gender wise Distribution of Subjects

Demographic data:

Treatment for the patients in the study Glimperide (78) and Gliclazide (122) and their distribution among male and female.

Table 3: Demographic data in the treatment groups.

S. No	Parameters	Glimepiride group [n=78]	Gliclazide group [n=122]
1	No. of patients	78	122
2	Male: Female	44:34	64:57
3	Average Age [Years]	47.94	45.59

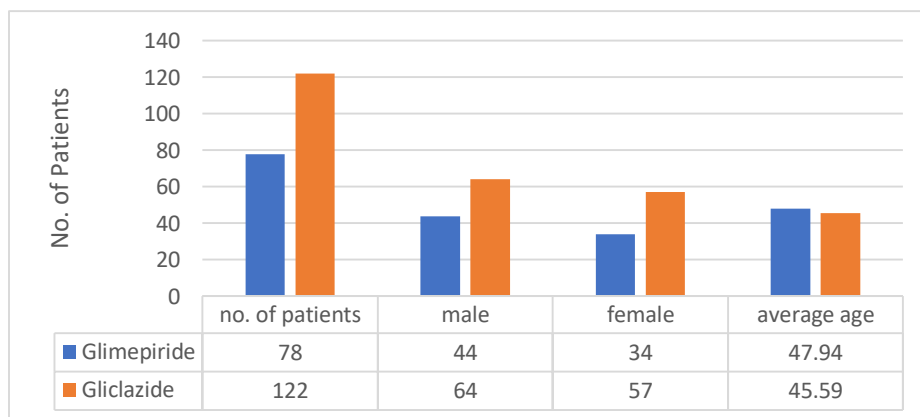


Fig 3: Demographic data in the treatment groups.

Prescription pattern of Glimepiride and Gliclazide:

Glimepiride are prescribed in total patients of male and female as 44 and 34 respectively. Gliclazide are prescribed in total patients of male and female as 64 and 57 respectively. A total of 78 Glimepiride and 122 Gliclazide.

Table 4: Prescription pattern of Glimepiride and Gliclazide.

Gender	Glimepiride	Gliclazide
Male	44	65
Female	34	57
Total	78	122

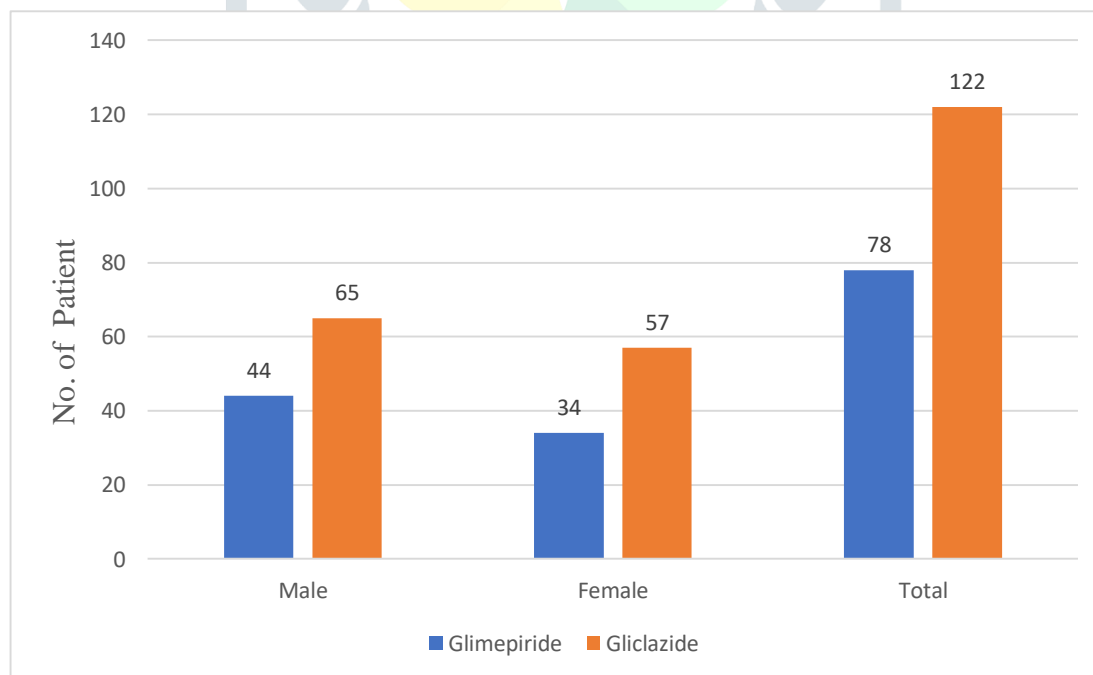


Fig 4: Prescription pattern of Glimepiride and Gliclazide

**EFFICACY:**

In terms of blood glucose levels.

FBS, PPBS and HbA1c were calculated and evaluated in patients before and after treatment of both the drugs Glimepiride and Gliclazide respectively. The blood glucose levels were calculated on the basis of average reduction percentage.

Table 5: Comparison of mean FBS Pre and Post Treatment of Glimepiride

Glimepiride patients	Pre-treatment FBS	Post treatment FBS
Mean Value	147.84	122.17

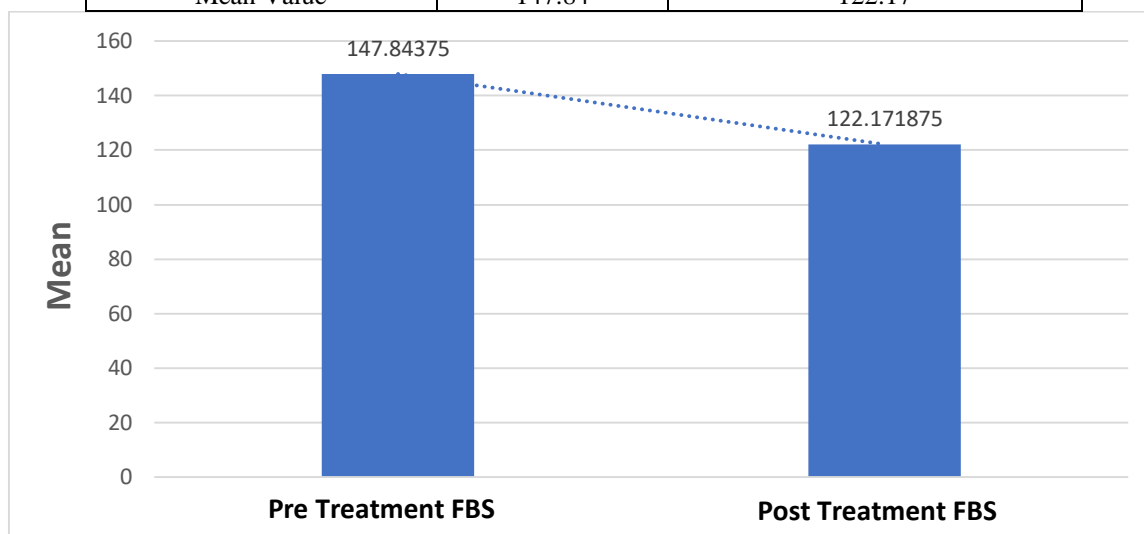


Fig 5: Comparison of mean FBS Pre and Post treatment of Glimepiride

Table 6: Comparison of mean PPBS Pre and Post treatment of Glimepiride

Glimepiride patients	Pre-treatment PPBS	Post treatment PPBS
Mean Value	247.40	152.65

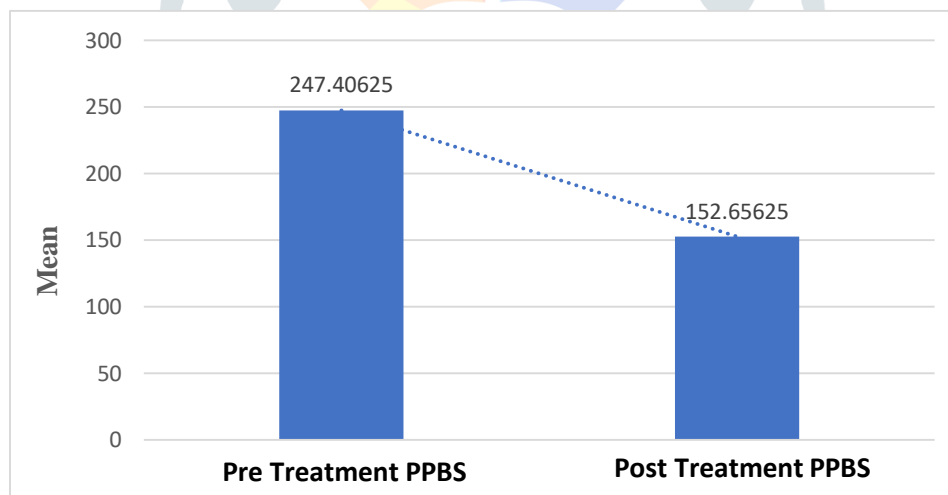


Fig 6: Comparison of mean PPBS Pre and Post Treatment of Glimepiride.

Table 7: Comparison of Average reduction percentage Of FBS and PPBS of Glimepiride.

Glimepiride patients	FBS	PPBS
Average Reduction %	22.17	52.65

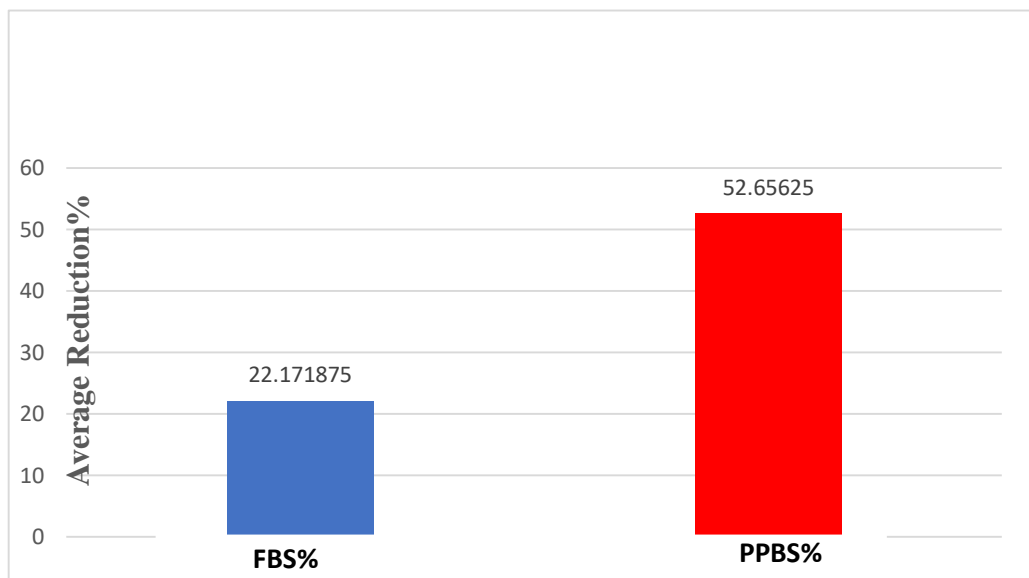


Fig 7: Comparison of Average Reduction Percentage Of FBS and PPBS of Glimepiride.

Table 8: Comparison of HbA1c mean values of pre and post treatment of Glimepiride.

Glimepiride patients	Pre-treatment HbA1c	Post treatment HbA1c
Mean Value	8.72	7.4

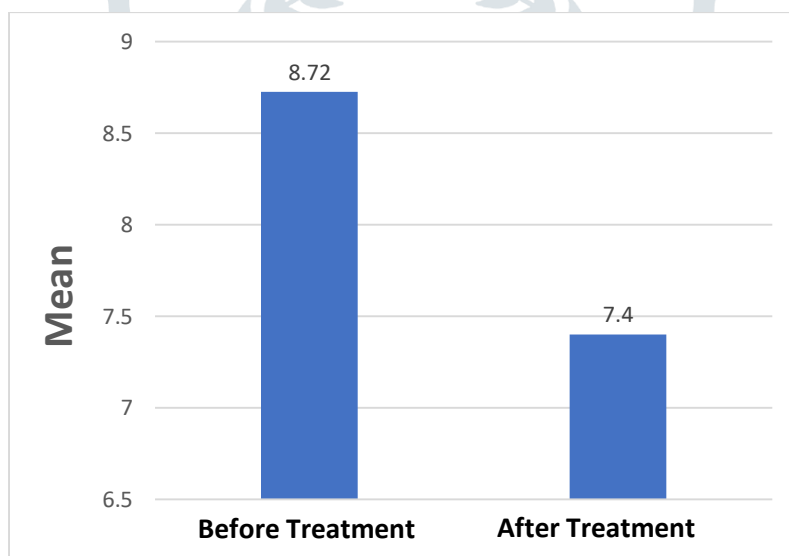


Fig 8: Comparison of HbA1c mean values of pre and post treatment of Glimepiride

The Mean and Average reduction percentage of Glimepiride for pre and post treatment FBS and PPBS were evaluated for efficacy. The HbA1c mean values for the same were calculated.

Table 9: Comparison of mean FBS for pre and post treatment of Gliclazide.

Gliclazide patients	Pre-treatment of FBS	Post treatment of FBS
Mean Value	162.53	124.79

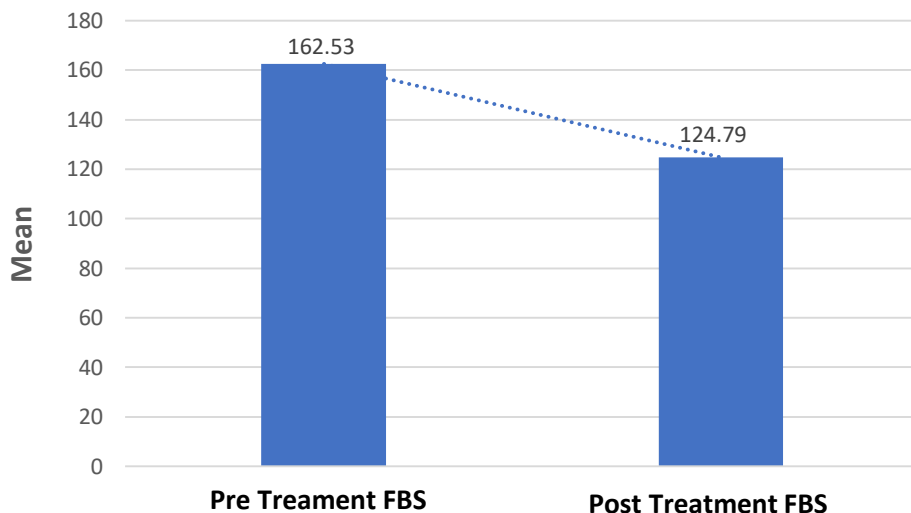


Fig 9: Comparison of mean FBS for pre and post treatment of Gliclazide.

Table 10: Comparison of mean PPBS for pre and post treatment of Gliclazide.

Gliclazide patients	Pre-treatment for PPBS	Post treatment For PPBS
Mean Value	247.47	159.82

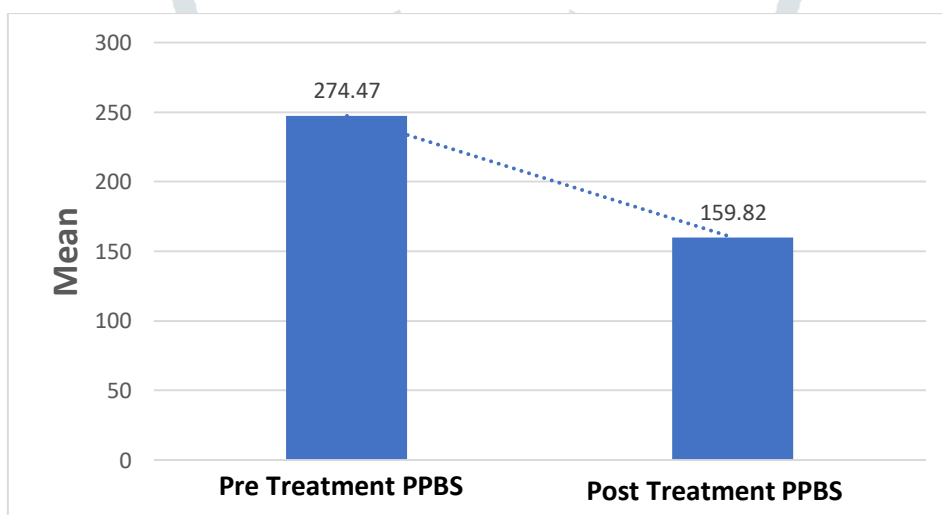


Fig 10: Comparison of mean PPBS for pre and post treatment of Gliclazide.

Table 11: Comparison of Average Reduction % for FBS and PPBS of Gliclazide.

Gliclazide patients	FBS	PPBS
Average Reduction %	24.79	59.82

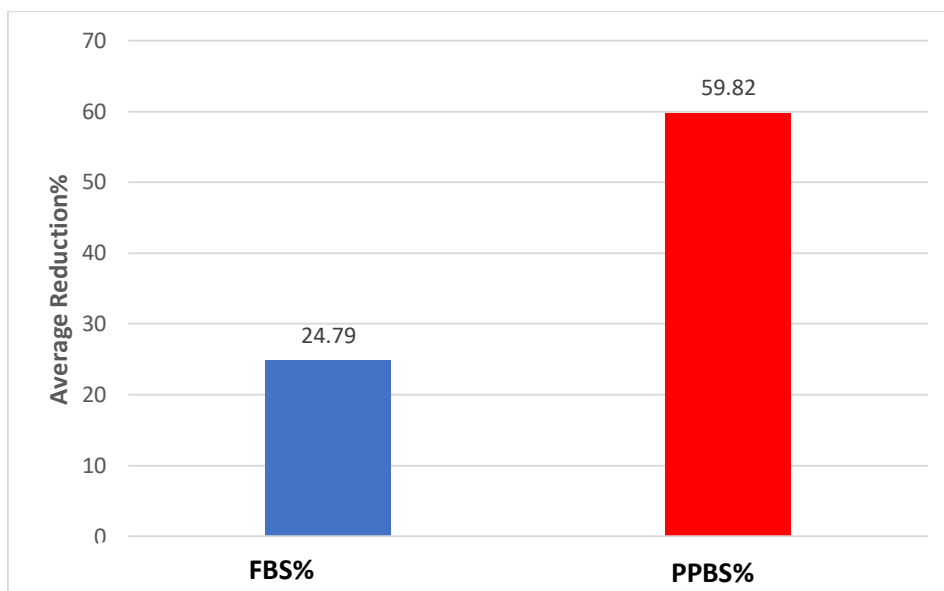


Fig 11: Comparison of Average Reduction % of FBS and PPBS of Gliclazide

Table 12: Comparison of mean HbA1c for pre and post treatment of Gliclazide.

Gliclazide patients	Pre-treatment for HbA1c	Post treatment For HbA1c
Mean Value	8.90	7.21

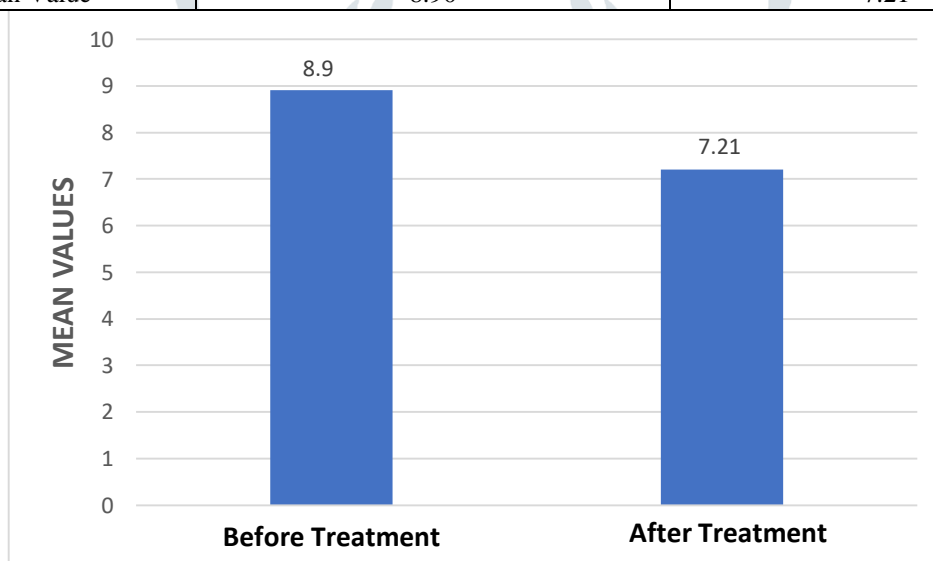


Fig 12: Comparison of mean HbA1c for pre and post treatment of Gliclazide.

Table 13: Comparison of mean HbA1c for Glimepiride and Gliclazide in patients after treatment.

Post Treatment of Glimepiride Mean HbA1c	Post Treatment of Gliclazide Mean HbA1c
7.4	7.21



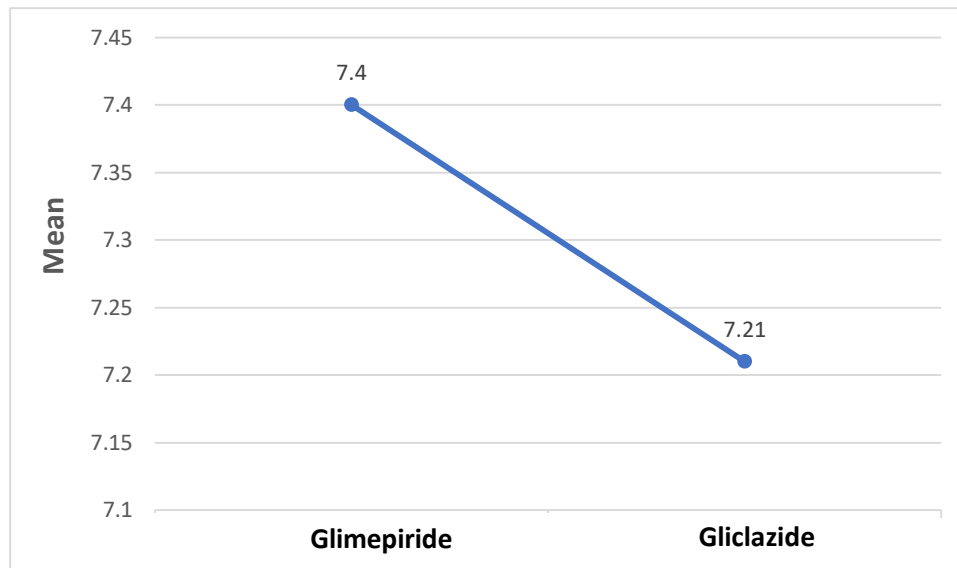


Fig 13: Comparison of mean HbA1c for Glimepiride and Gliclazide in patients after Treatment.

The efficacy of Glimepiride and Gliclazide for lowering the blood glucose levels in the patients were evaluated based on FBS, PPBS and HbA1c. Gliclazide was found to more efficacious than Glimepiride in lowering the blood glucose levels.

**SAFETY:**

In terms of ADRs.

Safety of glimepiride and gliclazide were evaluated on the basis of Adverse Drug Reactions in patients.

Most common adverse drug reaction that were observed in patients were hypoglycaemia, Weight gain, palpitations, diarrhoea, dizziness, itching, sweating, blurred vision in both treatment procedure.

Table 14: The Observed ADRs in Glimepiride.

Hypoglycaemia	Weight Gain	Diarrhoea	Palpitation
12	4	2	1

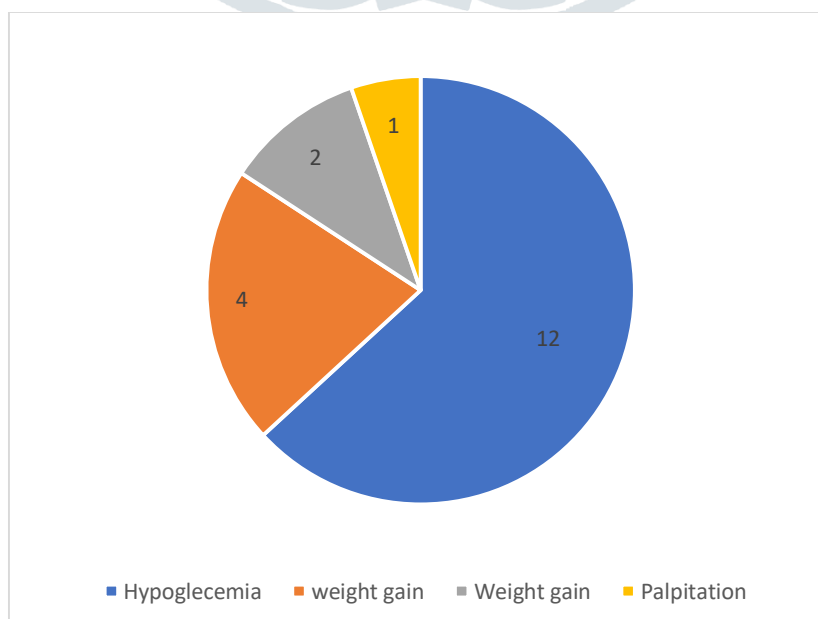


Fig 14: The Observed ADRs in Glimepiride.

During our study period, the major Adverse Effects with Glimpiride were found to be hypoglycaemia (12) and weight gain (4) in 68 patients.

Table 15: The Observed ADRs in Gliclazide.

Hypoglycaemia	Dizziness	Itching	Palpitation
2	1	1	1

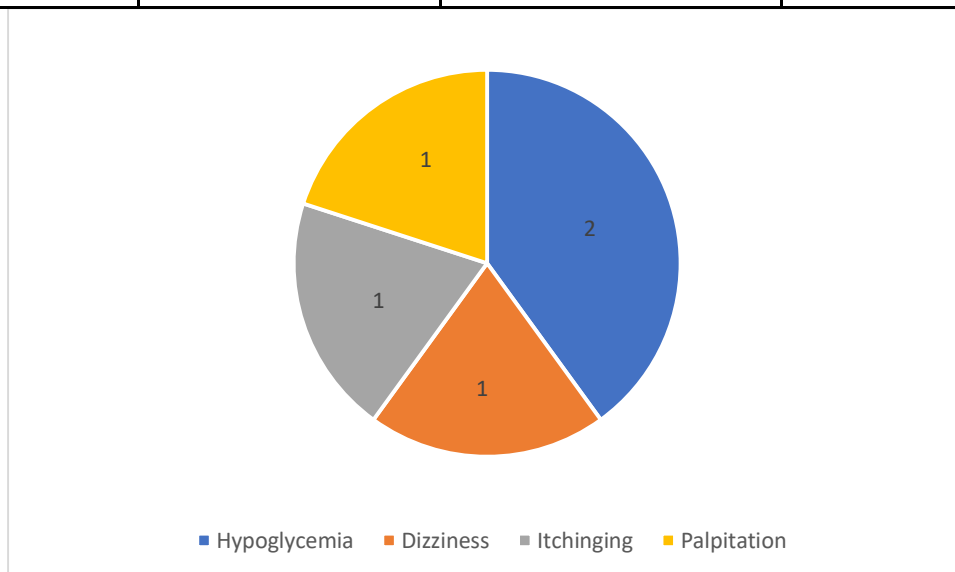


Figure 15: The Observed ADRs in Gliclazide.

During our study period, the major Adverse Effects with Gliclazide were found to be hypoglycaemia (2) and weight gain (1) in 84 patients. Gliclazide was found to be safer than glimepiride.

**TOLERABILITY:**

In terms of Patient Satisfaction.

With regard to tolerability both drugs were found to be equally tolerable by the patients.

**COST:**

Comparison of Cost:

Table 16: Comparative cost between Glimpiride and Gliclazide.

Name of Drugs	Dose	Cost per day in INR 1 tab in strip of 10 tablets	Mean Cost
Glimpiride + Metformin	2mg+500mg OD		
Brand A Gluconorm G2		13.16	10.97
Brand B Glycomet-2		9.46	
Brand C Gemer-2		10.3	

Gliclazide+ Metformin	80mg+500mg		
Brand A Prizide M 80		7.00	
Brand B Claz- M		3.118	4.69
Brand C Gliclamet 1		3.96	

The study sample showed that the mean cost of treatment per day with Glimepiride was INR 10.97 which was significantly higher than mean cost of therapy per day with Gliclazide INR 4.69.



Fig 16. Comparison of cost between Glimepiride and Gliclazide.

**DISCUSSION:** Over the past few decades the prevalence of Diabetes Mellitus has increased, and this has led to a growing recognition of need to identify the better choices of drugs used along with the 1<sup>st</sup> line drugs used in Diabetes Mellitus in lowering the blood glucose levels to optimum level. Sulphonylureas have been increasingly used as second line therapy in combination with Metformin, Newer Sulphonylureas like Gliclazide have equal efficacy to standard/traditional Sulphonylureas like Glimepiride. However safety of these drugs was found to be greater when compared to standard/traditional Sulphonylureas.

Gliclazide has been evaluated in international studies and is indicated for increased blood glucose levels associated with Diabetes Mellitus Type-2.

Aim of the study was to compare safety, efficacy, tolerability and cost of Glimepiride and Gliclazide in Diabetes Mellitus Type-2 patients with Hypertension. This study not only evaluates its efficacy and tolerability in patients but also compare it with Glimepiride which is of the widely used drug for Diabetes Mellitus patients.

In this present study of 200 Patients medical data collected out of which 153 patients' after treatment data was collected. 109 were found to be males and 91 were females in gender wise distribution and most of them were found to be in the age group of 40-50 followed by 50-60 years of age. As reported in the literature, the incidence of Diabetes is higher in males than in females.

Evaluation of anti-diabetic activity between the two drugs was done by comparing Mean values and Average reduction percentage in FBS, PPBS, HbA1c before and after treatment.

In the present study Gliclazide was found to be more efficacious in reducing blood Glucose levels than Glimepiride, these results were similar to Chipirishetti et al<sup>9</sup> study on Safety, Efficacy and Tolerability of Glimepiride and Gliclazide<sup>9</sup>.

Similarly, Schernthaner G et al <sup>10</sup> study concluded that gliclazide is at least as effective as glimepiride, either as monotherapy or in combination.

In current study more AE's occurred in patients treated with Glimepiride (16) when compared to Gliclazide (5), similar incidence of AE's was observed in Chipirishetti et al <sup>9</sup>-study conducted on 40 patients where Glimepiride caused 8 ADR's where Gliclazide caused none.

Similarly, Schernthaner G et al <sup>10</sup> study concluded that safety of gliclazide was significantly better, demonstrating approximately 50% fewer confirmed hypoglycaemic episodes in comparison with glimepiride.

Merck Sharp & Dohme. corp <sup>11</sup> study showed that among 550 patients using Glimepiride 75 Hypoglycemic events occurred and among 550 patients using Gliclazide only 35 Hypoglycemic events occurred.

The present study showed that Glimepiride and Gliclazide were equally tolerable by patients which coincides with the previous conducted on 40 patients by Chipirishetti et al <sup>9</sup>.

The present study sample showed that the mean per day treatment cost with Glimepiride was INR 10.97 which was significantly higher than mean per day cost therapy with Gliclazide INR 4.69.

A study by Scott Klarenbach <sup>12</sup> et al conducted in 2011 also concluded that addition of sulphonylurea as an additive therapy to metformin will result in more cost-effective therapy

**CONCLUSION:** Over the past few decades, the prevalence of Diabetes Mellitus has increased, and this has led to a growing recognition of the need to identify the better choices of drugs used along with the 1st line drugs used in Diabetes Mellitus in lowering the blood glucose levels to an optimum level. Sulphonylureas have been increasingly used as second-line therapy in combination with Metformin, Newer Sulphonylureas like Gliclazide have equal efficacy to standard/traditional Sulphonylureas like Glimepiride. However, the safety of these drugs was found to be greater when compared to standard/traditional Sulphonylureas.

Analysis of results of all the parameters of safety and efficacy explores the probable superiority of Gliclazide over Glimepiride in Diabetes Mellitus Type-2 patients with Hypertension. Since long term Oral hypoglycaemic agents (Sulphonylureas) treatment is indicated for Diabetes Mellitus Type-2 the ideal agent should have good efficacy and low propensity to cause an adverse effect. This study concludes that Males have more occurrence of Diabetes Mellitus Type-2 when compared to females among overall subjects. Our results concluded that patients with Gliclazide treatment were found to be more efficacious in terms of FBS, PPBS and HbA1c than patients taking Glimepiride treatment. The results of the study revealed a smaller number of patients with ADRs were seen with Gliclazide treatment as compared to Glimepiride treatment.

The study showed that Glimepiride and Gliclazide were equally tolerable in patients. As there was a significant difference between the cost of Gliclazide and Glimepiride. It can be safely assumed and quoted that Gliclazide can be a good alternative among Sulphonylureas as an oral hypoglycaemic agent in the treatment of Diabetes Mellitus Type-2.

**ACKNOWLEDGMENT:** We owe our profound gratitude to our guide Dr. Devender Kodati, M. Pharmacy, Ph. D., Associate professor, HOD, Dept. Of Pharmacy Practice. We thank him for his help, support and encouragement throughout the process of this work which enable us to carry out the work successfully.

We express our heartfelt gratitude to Dr. Bathula Sridhar, consultant Endocrinologist, Samraksha Hospital Warangal for his precious support, insightful comments and stimulating suggestions throughout the duration of this work. We thank him for providing us the opportunity to complete the research.

Finally, but immensely, we thank all the Patients who participated in the study and Hospital staff without whom the study would not been possible.

**FUNDING:** This research did not receive any specific grant from funding agencies in public, commercial, or not-for-profit sectors.

**CONFLICTS OF INTEREST:** No

**REFERENCES:**

1. The ACCORD Study Group. Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus. *The New England Journal of Medicine*. 2010; 362:1575-1585
2. Andy KH Lim. Diabetic nephropathy – complications and treatment. *International Journal of Nephrology and Renovascular disease*. 2014; 7: 361–381.
3. Donald S. Fong. Retinopathy in Diabetes. *Diabetes Care*. 2004 Jan; 27(suppl 1): s84-s87.
4. Sharad P. Pendsey. Understanding Diabetic Foot. *International Journal of Diabetes in Developing Countries*. 2010 Apr-Jun; 30(2): 75–79.
5. Alexandria VA. Expert committee on the diagnosis and classification of Diabetes Mellitus care. *American Diabetes Association*.1997; 1183 – 1197.
6. Sarwar N et al. Diabetes Mellitus, fasting blood glucose concentration, and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies. *Lancet J*. 2010; 26:375(9733): S0140-6736.
7. K.D. Tripathi 7 Edition *Essentials of Medical Pharmacology*. 270, 272, 280.
8. American Diabetic Association: Standards of medical care in Diabetes – abridged for primary care providers in 2019; 42(Supplement 1): S1-S194
9. Raju Chipirishetti. Comparative Study Of Glimpiride And Gliclazide In Type 2 Diabetes Patients On Safety, Efficacy And Tolerability. *Journal of Drug Delivery and Therapeutics*.2015; 5(3):10-12.
10. Scherthaner G. Double-blind comparison of once daily gliclazide MR and glimepiride in type 2 diabetic patients. *European Journal of Clinical Investigation*. 2004 Aug;34(8):535-42.
11. Merck Sharp & Dohme Corp. A Study of the Safety and Efficacy of Glimepiride, Gliclazide, Repaglinide or Acarbose When Added to Sitagliptin + Metformin Combination Therapy in Chinese Participants With Diabetes (MK-0431-313). U.S. National Library of Medicine. *ClinicalTrials.gov Identifier: NCT01709305*
12. Scott Klarenbach. Cost-effectiveness of second line antihyperglycemic therapy in patients with type 2 diabetes mellitus inadequately controlled on metformin *Canadian Medical Association Journal*, E1220 November 8, 2011, 183(16).