E-ISSN 2250-0944
ISSN 2250-1150
DOI: 10.31838/ijprt/11.02.10

**Research Article**

# Effect of Sulfonylurea in Patients with Type 2 Diabetes Mellitus

HARINI SIVAKUMAR[1], DR. S. JEGANATH[2*], DR.G.BALAMURUGAN
[1]Department of Pharmacy Practice, School of Pharmaceutical sciences, Vels Institute of Science, Technology And Advanced Studies (VISTAS), Pallavaram, Chennai- 600117, India.
[2]Department of Pharmaceutics, School of Pharmaceutical sciences, Vels Institute of Science, Technology And Advanced Studies (VISTAS), Pallavaram, Chennai- 600117, India.
Corresponding Author Email: harinijillu.001@gmail.com
Received: 23.03.21, Revised: 15.03.21, Accepted: 05.04.21

**ABSTRACT**
Type 2 diabetes mellitus is a chronic metabolic disorder that results from defects in both insulin secretion and insulin action. The major site of action of this drug relies on the ability of the pancreas to secrete insulin and hence requires functioning β-cells to exert a beneficial effect. Sulfonylureas lower blood sugar by increasing pancreatic β-cell sensitivity to glucose, allowing more insulin to be released from storage granules for a given glucose load. Sulfonylureas occupy a central position in the recommendations of many guidelines for treatment of type 2 diabetes mellitus. Concerns, have been raised with respect to possible adverse effects that the use of these drugs might cause. However, sulfonylureas are likely to continue to be a reliable and effective treatment, particularly as combination therapy with metformin hydrochloride.

**Keywords:** Sulfonylurea, type 2 diabetes mellitus, pancreatic beta cell, chronic metabolic disorder, Insulin action.

## INTRODUCTION

According to WHO Diabetes mellitus is defined as a heterogeneous metabolic disorder characterised by common feature of hyperglycaemia with disturbance of carbohydrate, fat and protein metabolism. This is a prospective cohort study with 59 participants in total for the study. Sulfonylurea therapy is also associated with increased tissue sensitivity to insulin, which results in the improvement of insulin action. Few studies suggest that sulfonylureas may promote an increased systemic bioavailability of insulin due to reduced hepatic extraction of insulin secreted from the pancreas. Sulfonylureas are used as the first line therapy for patients and are not well tolerated for a majority of patients due to its adverse effects.

Through this study we try to prove that the ignorance of Sulfonylureas can be minimised. There are 3 generations and here we compare the second and the third generation of sulfonylureas for its better efficacy and practical usage among the patient's i.e. glimepiride and glipizide where both provided glycemic effects but glipizide provided improved glycemic control. A better understanding of sulfonylureas paves way for the effective use of the drug with proper counselling and medication adherence.

## METHODOLOGY

This is an open- labelled, non- randomised prospective cohort study which was carried out in the department of General Medicine at 100 bedded Hospital for a period of 6 months. A data collection form was prepared which includes patient as well as medication related information. The study procedure were followed according to the declaration of Helsinki.

Grouping of patients: The patients were subdivided into 2 groups:

Group A patients taking Glimepiride 1 or 2 mg orally once daily, given with breakfast or the first main meal of the day.

Group B Glipizide 5 mg orally once daily 30 minutes before a meal (preferably breakfast).

Sample size: 59 prescriptions were collected.

All relevant and necessary information for the study was collected from the outpatient department cards, treatment charts, Patient related parameters includes age, sex and drug related data such as name of the drug, dosage form, dosing frequency, duration , route of administration and diagnosis data also noted using the standard data collection form. Descriptive and statistical analysis was performed on all the pooled data. Results and outcome were evaluated.

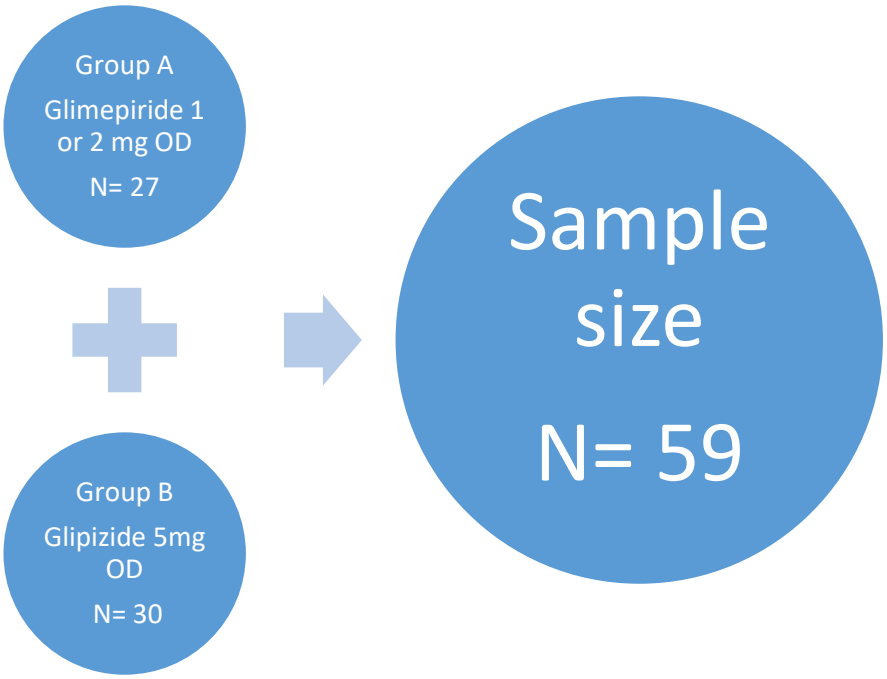
Institutional Review Board Approval was obtained before the commencement of the research work. Informed consent was taken from all the patients who are enrolled for the study and rights to withdraw from the study was provided in the consent.

**Inclusion Criteria**

All patients above 18 years of age who is confirmed with type 2 diabetes mellitus for at least 6 months with a HbA1c levels greater than 6.5% and receiving sulfonylureas as their treatment as single therapy or in addition with another anti-diabetic medication are included in the study.

**Exclusion Criteria**

Patients who are below 18 years of age, allergic to sulfonylurea, obese patients, patients with type 1 diabetes mellitus and who are unwilling to participate in the study are excluded in this study.




2 Participants withdrawn from the research due unwillingness of the patient.

## RESULTS AND DISCUSSIONS

- **Age & Gender wise distribution**

The total number of patients taken into account for evaluation was n=57

There are two groups A and B: Group A: 27 Patients taking Glimepiride (1 or 2 mg once daily).Group B: 30 Patients taking Glipizide (5mg once daily).

From the tables and figures:

Group A: Male patients n=16; female patients n=12

Group B: Male patients n=18; female patients n=12

Which means male patients are higher than female patients which is shown in table 2 and figure1. The majority of the patients were in the age group 46-55 i.e. n=16 and second majority of the patients were in the age group 56-65 i.e. n=15 which is shown in table 1 and figure 1.

**Table 1: Age distribution**

| | 35-45 Years | 46-55 Years | 56-65 Years | 66-75 Years | 76-85 Years |
|---|---|---|---|---|---|
| Group A | 1 | 11 | 8 | 7 | 0 |
| Group B | 9 | 5 | 7 | 5 | 4 |

**Table 2: Gender distribution**

| Total No. of Pts. N=57 | Female (mean patients) | Male (mean patients) |
|---|---|---|
| Group A | 13 | 16 |
| Group B | 12 | 18 |

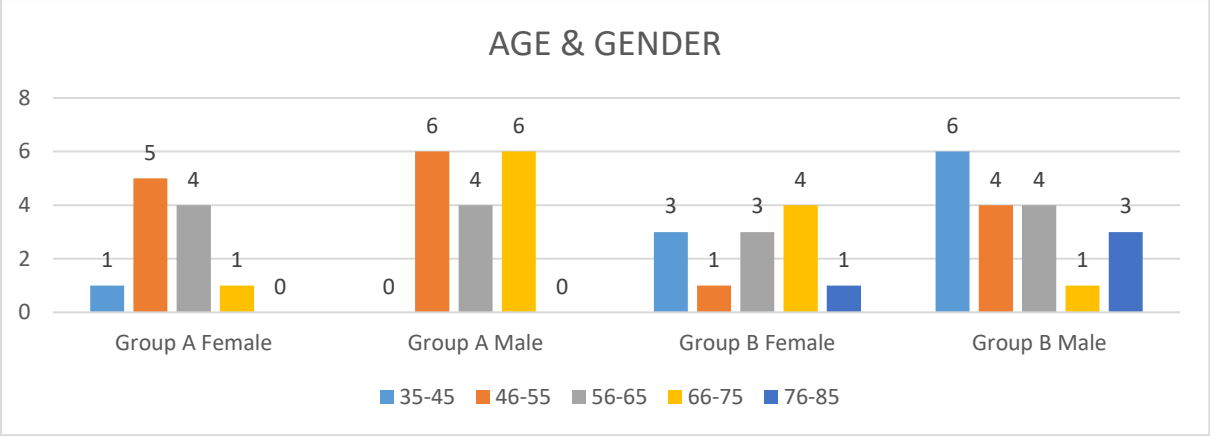



**Fig.1: Age & Gender Distribution**

♦ Weight Gain

As we know that Sulfonylureas has a major adverse reaction of weight gain which makes this graph important for the significant weight gain of the patients. As we look into the first set of graph (figure 2) i.e. Group A (Glimepiride) female patients the weight gain was mostly seen in the age group 50-60 years of age see (table 3)

In the same group the male patients in the age group 71-80 years of age have experienced weight gain. Next if we look at (figure 2) Group B (Glipizide) female patients the weight gain was not much experienced by the patients but when compared with rest of the patients in the same group we can say patients in the age group of 50-70 years have experienced moderate weight gain see (table 3). The last would be Group B male patients where significant weight gain was experienced by the patients in 71-80 years of age. Therefore we can conclude that patients taking Glimepiride experience significant weight gain rather than patients taking Glipizide see (table 3, figure 2).

**Table: 3 weight gain distribution with age**

| | 50-60 Years | 61-70 Years | 71-80 Years | 81-90 Years | 91-100 Years |
|---|---|---|---|---|---|
| Group A | 8 | 10 | 9 | 0 | 0 |
| Group B | 8 | 8 | 8 | 3 | 2 |

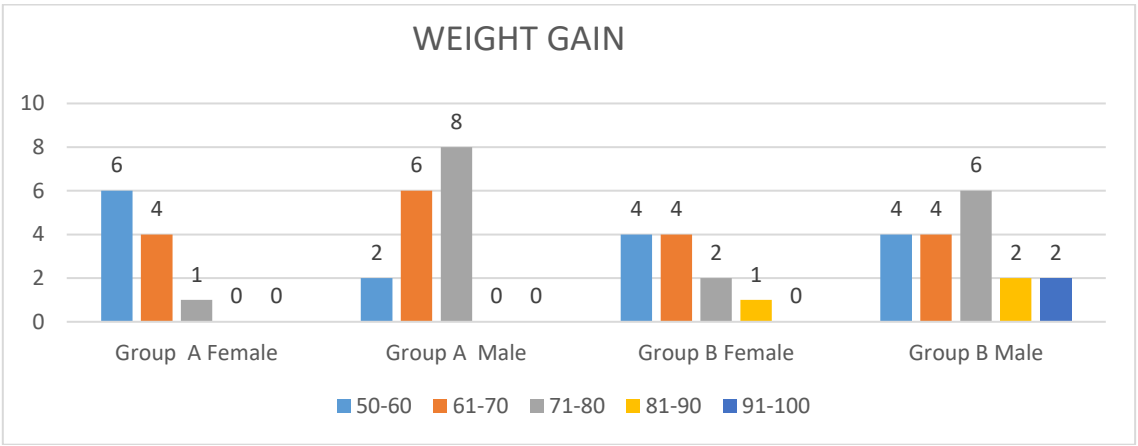



**Fig.2: weight gain distribution**

♦ Insomnia (decreased sleep):

Insomnia or decreased sleep is the important symptom of complaint from diabetes patients. So this graph represents the number of patients who experience decreased sleep or disturbed sleep. From Group A (Glimepiride) female patients the sleep deprivation was not that much significant but experience mild deprivation of sleep i.e. n= 6 see (table 4 figure 3). In Group A male patients there is a significant increase in sleep deprivation than female patients i.e. n= 10see (table 4 figure 3) In Group B (Glipizide) female patients the sleep deprivation is significantly less than female patients in group A i.e. n= 3see

(table 4 figure 3). Group B Male patients have experience significantly more sleep deprivation cases i.e. n=14. From the graph we can conclude that Group B (Glipizide) n= 17 patients experience slight more sleep deprivation than Group A (Glimepiride) n=16 see (table 4 figure 3).

**Table 4: Sleep deprivation distribution**

| | Normal | Decreased sleep |
|---|---|---|
| Group A | 11 | 16 |
| Group B | 12 | 17 |

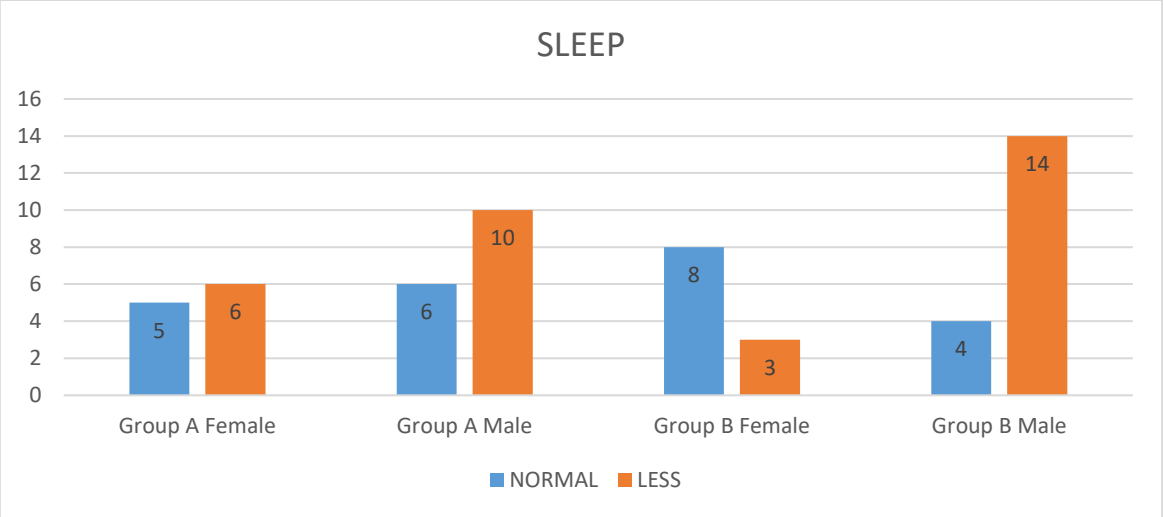



**Fig.3: Sleep deprivation distribution**

- Smoking & Alcohol

Smoking and alcohol consumption is the leading cause for reduced glycemic control and patients must withdraw smoking and alcohol. If we see (table 5 & Figure 4) plotted for smoking the Group A (Glimepiride) male patients n=9 have smoking habits.In Group B (Glipizide) male patients n=10 have smoking habits.From this we can know that both Group A and Group B have similar number of smokers see (table 5 & Figure 4). If we see (table 6 & Figure 4) plotted for alcohol consumption the Group A (Glimepiride) male patients n=9 have alcohol consumption habits. In Group B (Glipizide) male patients n= 11 have alcohol consumption habits. To conclude this both Group A and Group B patients have alcohol consumption habits but Group B patients are slightly increased number see (table 5 & Figure 4).

**Table 5: patients with smoking habits**

| | No | Yes |
|---|---|---|
| Group A | 18 | 9 |
| Group B | 19 | 10 |

**Table 6: patients with alcohol consumption**

| | No | Yes |
|---|---|---|
| Group A | 18 | 9 |
| Group B | 18 | 11 |

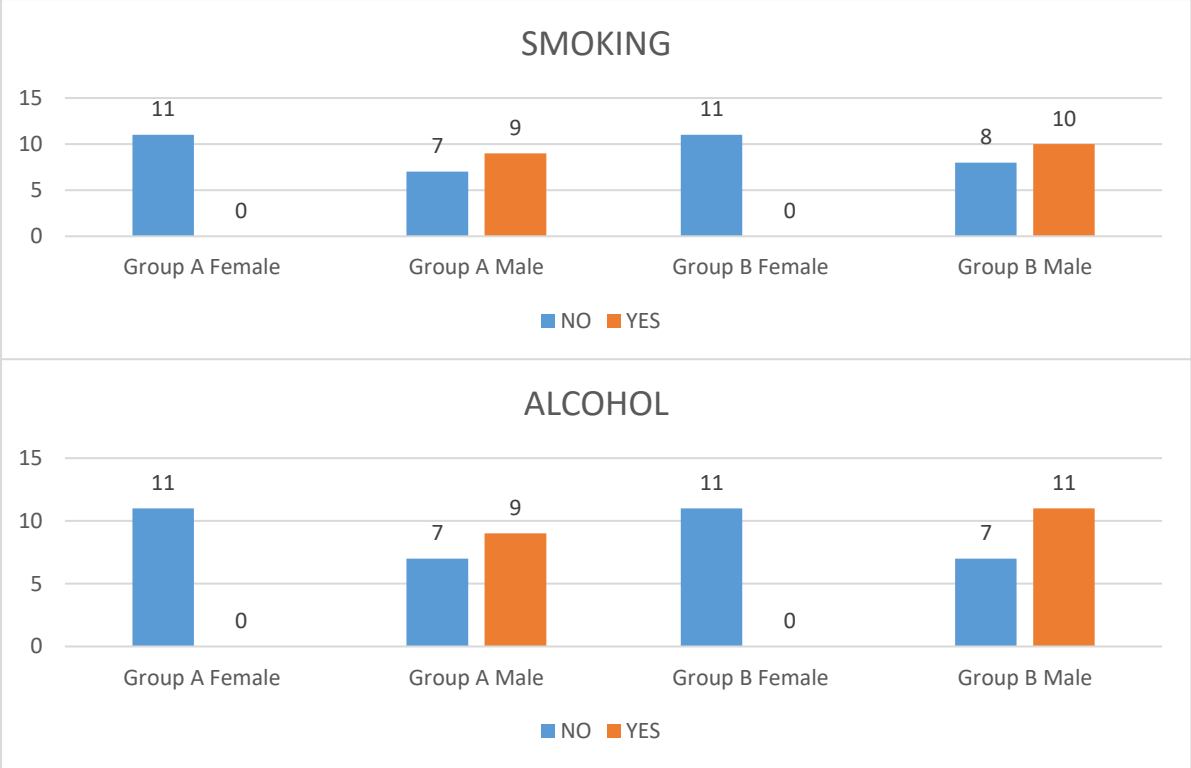



**Fig.4: patients with smoking and alcohol consumption**

♦ Appetite

Appetite is common in most of the Diabetes patients. (Table 7 & figure 5) plotted depicts the number of patients who have decreased appetite. In Group A (Glimepiride) both male n=2 and female patients n=2 have experienced decreased appetite. In Group B (Glipizide) none of the female patients have experienced decreased appetite. And male patients n=3 have experienced decreased appetite. Therefore both Group A and Group B patients have very mild symptom of decreased see (table 7 & figure 5).

**Table 7: Appetite distribution**

| | Normal | Decreased |
|---|---|---|
| **Group A** | 23 | 4 |
| **Group B** | 26 | 3 |

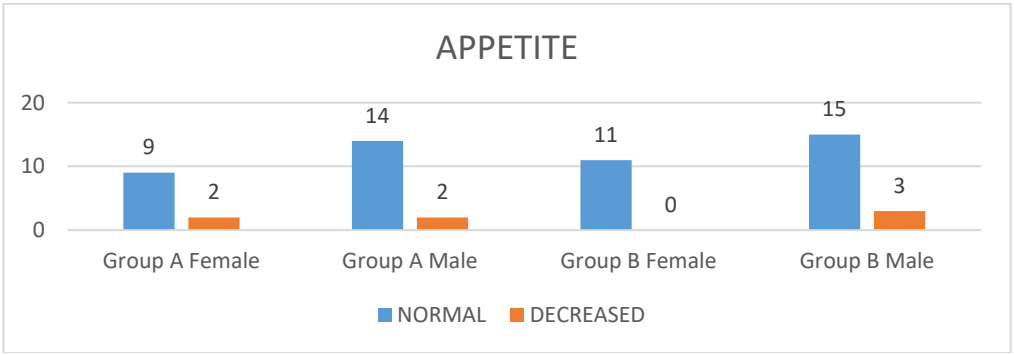



**Fig.5: Appetite distribution**

♦ Co-morbidity

Comorbid conditions are common for Diabetes Patients. In Group A (Glimepiride) both male and female patients n=6 respectively have co-morbid conditions. In Group B (Glipizide) female patients n=1 have co-morbid conditions, whereas male patients n=8 have co-morbid conditions. Hence Group A (Glimepiride) patients have significantly high co-morbid patients than Group B (Glipizide). Shown in table8 and figure 6.

**Table 8: comorbidity distribution**

| | Nil | Yes |
|---|---|---|
| Group A | 15 | 12 |
| Group B | 20 | 9 |

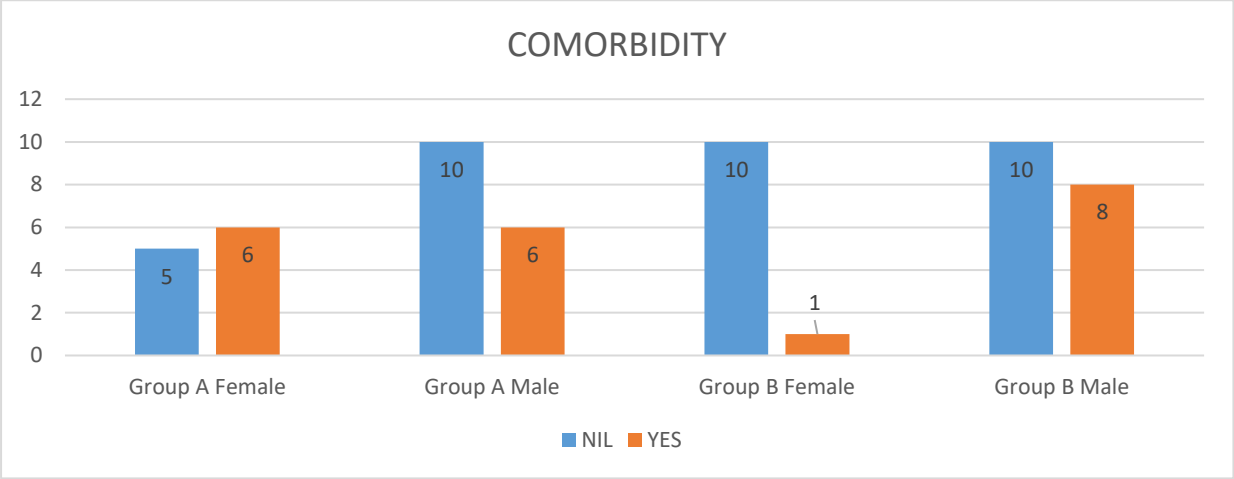



**Fig.6: Comorbidity Distribution**

♦ **Random Blood Sugar Profile:**

RBS Should be below 200 mg/dl and from the (table 9 & figure 7) we can say that
Group A (Glimepiride) has a mean RBS of 196.59
Group B (Glipizide) has a mean RBS of 176.24
Therefore we can say that Glipizide has better glycemic control (RBS). See (table 9, figure7)

**Table 9: Random blood sugar profile**

| | Mean Value |
|---|---|
| Group A | 196.59 |
| Group B | 176.24 |

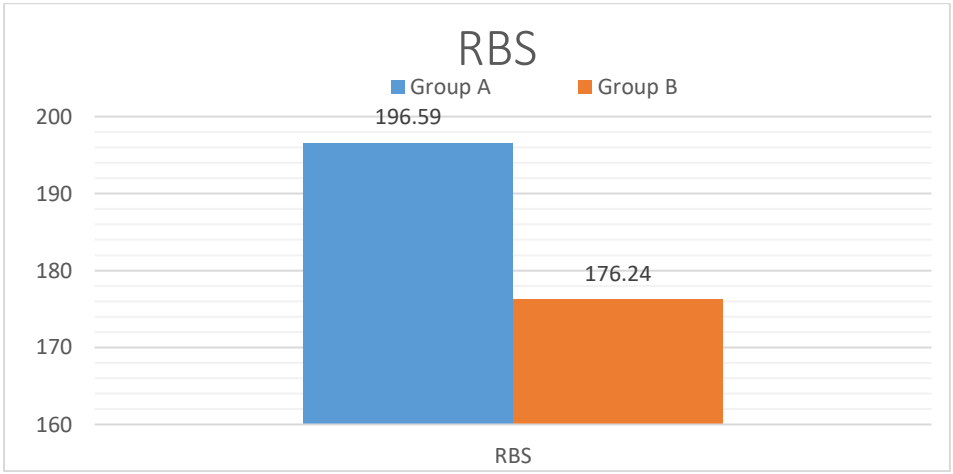



**Fig.7: Random Blood Sugar Profile**

♦ **Fasting Blood Sugar Profile:**

FBS Should be below 100 mg/dl and from the (table10, figure 8) we can say that
Group A (Glimepiride) has a mean FBS of 140.42
Group B (Glipizide) has a mean FBS of 98.33

Hence we can say that Glipizide has better glycemic control (FBS).see (table10, figure8)

**Table 10: Fasting Blood Sugar Profile**

| | Mean Value |
|---|---|
| Group A | 140.42 |
| Group B | 98.33 |

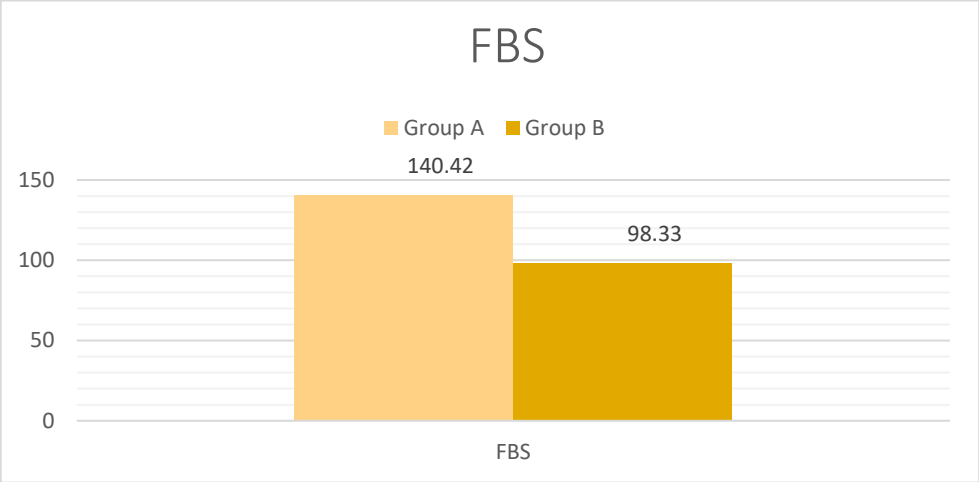



**Fig. 8: Fasting Blood Sugar Profile**

♦ Post-prandial Blood Sugar Profile

Normally PPBS should be below 140mg/dl see (table11, figure 9) which shows similar level of PPBS control but there is a moderate difference between the two groups.
In Group A (Glimepiride) the mean PPBS is 198.04.
In Group B (Glipizide) the mean PPBS is 164.88.

**Table 11: Post- Prandial Blood Sugar**

| | Mean Value |
|---|---|
| Group A | 198.04 |
| Group B | 164.88 |

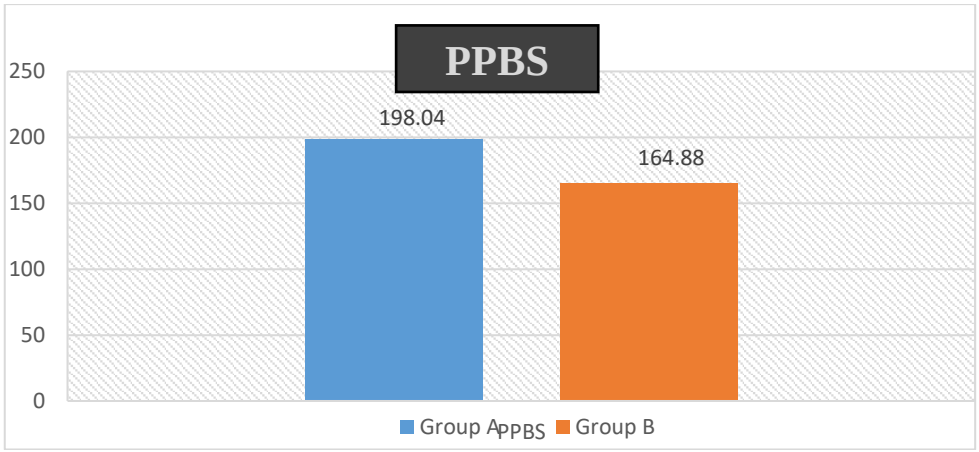



**Fig.9: Post- Prandial Blood Sugar**

♦ Haemoglobin A1c Level

The (table 12, figure 10) shows the haemoglobin A1c level which is taken every 3 months and this is the confirmatory level for the glycemic control of Diabetes Mellitus and has to be less than 6.5%.
In Group A (Glimepiride) the mean HbA1c level is 8.29 %.
In Group B (Glipizide) the mean HbA1c level is 7.82 %.

Therefore both groups doesn't show enough diabetic control but we can say that Group B shows significant decrease in HbA1c level. See (table 12, figure 10)
See (table 11, figure 9)

**Table 12: HbA1c distribution**

| | Mean % |
|---|---|
| Group A | 8.29 |
| Group B | 7.82 |

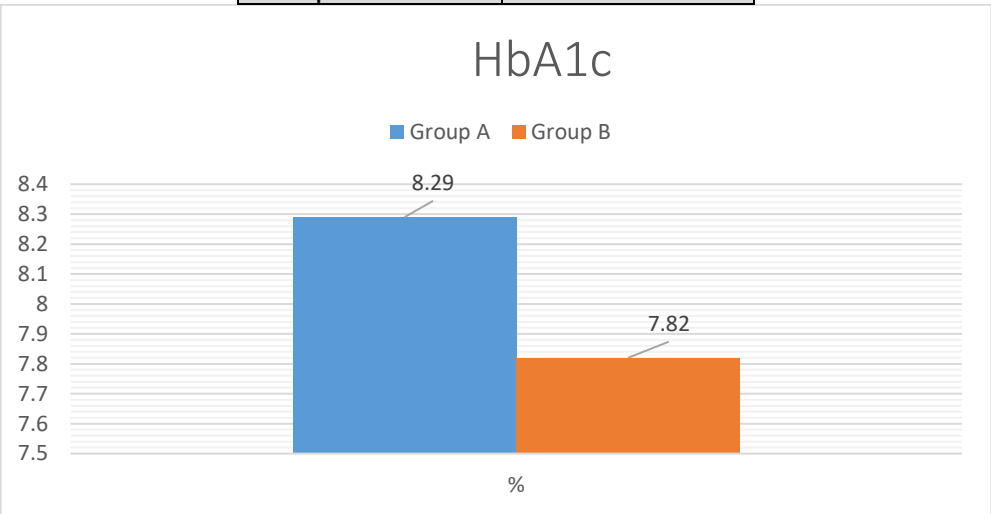



**Fig.10: HbA1c**

♦ Total Cholesterol level

Lipid profile is very important for Diabetes patients. T. Cholesterol should be maintained below 200 mg/dl. See (table 13, figure 11)
Group A (Glimepiride) has mean cholesterol level of 183.22 mg/dl.
Group B (Glipizide) has mean cholesterol level of 184.48 mg/dl.
Therefore both groups have similar glycemic control but very minute difference can be seen in both the groups. We can say that Group A has minute reduced level of cholesterol control. See (table 13, figure 11)

**Table 13: Total Cholesterol**

| | Mean Value |
|---|---|
| Group A | 183.22 |
| Group B | 184.48 |

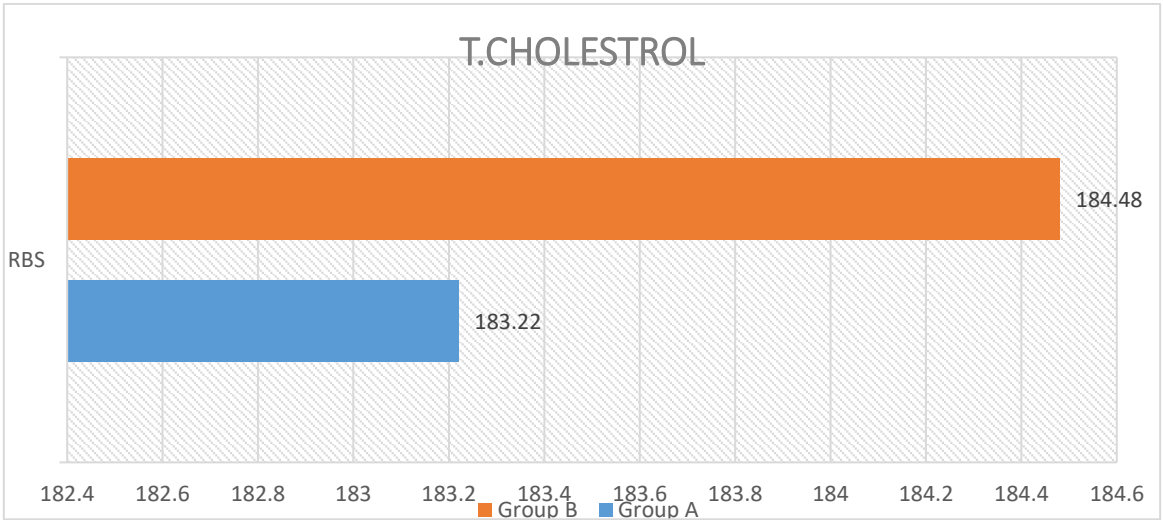



**Fig.11: Total Cholesterol**

## DISCUSSION

Sulfonylureas occupy a central position in the recommendations of many guidelines for treatment of type 2 diabetes mellitus. Concerns, have been raised with respect to possible adverse effects that the use of these drugs might cause. However, sulfonylureas are likely to continue to be a reliable and effective treatment, particularly as combination therapy.

In this study the total number of patients n=59 where it is subdivided into two groups one consuming glipizide and the other glimepiride and according to the tests performed we can say that glipizide provides better glycemic control over glimepiride.

From the study, Group A: male patients n=16; female patients n=12. In Group B: Male patients n=18; female patients n=12. In both groups male patients are higher than female patients. The alcohol and smoking habits are similar in both the groups which means every 1 in 5persons have the habit which may be the trigger factor for hyperglycemia or low glycemic control. When comparing the fasting blood sugar profile, random blood sugar, post-prandial blood sugar, haemoglobin A1C levels and total cholesterol Group B shows significant improvement in glycemic control which means Glipizide has better control over glimepiride.

The appreciation of beta-cell defects in the development and progression of hyperglycemia in type 2 diabetes mellitus has highlighted the need for treatments that may stimulate insulin secretion and preserve the beta-cell mass.

The advancement in the formulation and established non-glucose lowering properties of specific sulfonylurea agents still provide an opportunity for effective treatment of type 2 diabetes mellitus.

## CONCLUSION

- This study provides the effectiveness of sulfonylureas between two generations.
- The second generation sulfonylureas i.e. Glimepiride 5mg P/O OD is compared with the third generation sulfonylureas i.e. Glipizide 1 or 2 mg P/O OD.
- From the results we can say that Glipizide provides better glycemic control than Glimepiride in case of weight gain, blood sugars and lipid profile.

## REFERENCES


1. Hirst JA, Farmer AJ, Dyar A, Lung TW, Stevens RJ. Estimating the effect of sulfonylurea on HbA1c in diabetes: a systematic review and meta-analysis. Diabetologia.2013;56(5):973–984. doi:10.1007/s00125-013-2856-6
2. Ashcroft F. Mechanisms of the glycaemic effects of sulfonylureas. Horm Metab Res. 1996;28:456–463. doi: 10.1055/s-2007-979837. - DOI - PubMed
3. Stefano Del PratoConducted a study on The Place of Sulfonylureas in the therapy for type 2 Diabetes Mellitus and concluded that Advancement in the formation and established Non-glucose lowering properties of specific sulfonylurea agents still provide an opportunity for effective treatment of type 2 diabetes mellitus.
4. Ralph Aconducted a study on Pharmacologic Therapy for Type 2 Diabetes Mellitus and summarizes that Sulfonylureas are very effective glucose-lowering agents that work by enhancing insulin secretion (decrease in HbA1c value, 1.5 to 2.0 percentage points).
5. Martin RidderstraleComparison of empagliflozin and glimepiride as add-on to metformin in patients with type 2 diabetes: a 104-week randomised, active-controlled, double-blind, phase 3 trial [published correction appears in Lancet Diabetes Endocrinol. 2015 Sept;3(9):e7]. Lancet Diabetes Endocrinol. 2014;2(9):691–700. doi:10.1016/S2213-8587(14)70120-2
6. Leif.C Groop LC. Sulfonylureas in NIDDM. Diabetes Care. 1992;15(6):737–754. doi:10.2337/diacare.15.6.737
7. Bruce, Kalra S, Gupta Y. Sulfonylureas. J Pak Med Assoc. 2015;65(1):101–104.
8. Ewan.R.PearsonER, Flechtner I, Njølstad PR, et al. Switching from insulin to oral sulfonylureas in patients with diabetes due to Kir6.2 mutations. N Engl J Med. 2006;355(5):467–477. doi:10.1056/NEJMoa061759.
9. Abraham Nigussie Mekuria AN, Ayele Y, Tola A, Mishore KM. Monotherapy with Metformin versus Sulfonylureas and Risk of Cancer in Type 2 Diabetic Patients: A Systematic Review and Meta-Analysis. J Diabetes Res. 2019;2019:7676909. Published 2019 Nov 19. doi:10.1155/2019/7676909
10. L.A.Harsch IA, Kaestner RH, Konturek PC. Hypoglycemic side effects of sulfonylureas and repaglinide in ageing patients - knowledge and self-management. J Physiol Pharmacol. 2018;69(4):10.26402/jpp.2018.4.15. doi:10.26402/jpp.2018.4.15
11. Zhen Zhang Z, Cao Y, Tao Y, et al. Sulfonylurea and fracture risk in patients with type 2 diabetes mellitus: A meta-analysis. Diabetes Res Clin Pract. 2020;159:107990. doi:10.1016/j.diabres.2019.107990
12. Adesh.K.Jain, Ryan JR, McMahon FG. Potentiation of hypoglycemic effect of sulfonylureas by halofenate. N Engl J Med. 1975;293(25):1283–1286. doi:10.1056/NEJM197512182932503
13. Hagen Kunte, Schmidt S, Eliasziw M, et al. Sulfonylureas improve outcome in patients with type 2 diabetes and acute ischemic stroke. Stroke.

2007;38(9):2526–2530. doi:10.1161/STROKEAHA.107.482216
14. Jen-Hung Chang, Tseng CF, Wang JY. Hypoglycemia-induced myocardial infarction: an unusual adverse effect of sulfonylureas. Int J Cardiol. 2007;115(3):414–416. doi:10.1016/j.ijcard.2006.01.062
15. Rury.R.Holman. Long-term efficacy of sulfonylureas: a United Kingdom Prospective Diabetes Study perspective. Metabolism. 2006;55(5 Suppl 1):S2–S5. doi:10.1016/j.metabol.2006.02.006
16. Cynthia.M.Ripsin, Kang H, Urban RJ. Management of blood glucose in type 2 diabetes mellitus. Am Fam Physician. 2009;79(1):29–36.
17. Gunter Muller, Satoh Y, Geisen K. Extrapancreatic effects of sulfonylureas--a comparison between glimepiride and conventional sulfonylureas. Diabetes Res Clin Pract. 1995;28 Suppl:S115–S137. doi:10.1016/0168-8227(95)01089-v
18. D.M.Nathan, Buse JB, Davidson MB, et al. Medical management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetologia.2009;52:17–30.doi:10.1007/s00125-008-1157-y-DOI- PubMed
19. David.M, Nathan DM. Clinical practice. Initial management of glycemia in type 2 diabetes mellitus. N Engl J Med. 2002;347(17):1342–1349. doi:10.1056/NEJMcp021106
20. M.A.Nauck, Meininger G, Sheng D, Terranella L, Stein PP; Sitagliptin Study 024 Group. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, compared with the sulfonylurea, glipizide, in patients with type 2 diabetes inadequately controlled on metformin alone: a randomized, double-blind, non-inferiority trial. Diabetes Obes Metab. 2007;9(2):194–205. doi:10.1111/j.1463-1326.2006.00704.x
21. Samantha.L Bowker SL, Majumdar SR, Veugelers P, Johnson JA. Increased cancer-related mortality for patients with type 2 diabetes who use sulfonylureas or insulin. DiabetesCare.2006;29(2):254–258 doi:10.2337/diacare.29.02.06.dc05-1558.
22. NICE (2008) CG66 type 2 diabetes: full guideline. In: NICE clinical guideline 66. www.nice.org.uk/nicemedia/pdf/CG66NICEGuideline.pdf
23. Desai NR, Shrank WH, Fischer MA, et al. Patterns of medication initiation in newly diagnosed diabetes mellitus: quality and cost implications. Am J Med. 2012;125(302):e301–e307. - PMC - PubMed
24. DeFronzo RA, Goodman AM. Efficacy of metformin in patients with non-insulin-dependent diabetes mellitus. The Multicenter Metformin Study Group. NEnglJMed.1995;333:541–549.doi:10.1056/NEJM199508313330902.-DOI-PubMed
25. Zhou X, Zhang R, Zou Z, et al. Hypoglycaemic effects of glimepiride in sulfonylurea receptor 1 deficient rat. Br J Pharmacol. 2019;176(3):478–490. doi:10.1111/bph.14553.