WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 3, 626-639. Research Article ISSN 2277– 7105

COMPARISON OF EFFECTS ASSOCIATED WITH PIOGLITAZONE AND GLIMEPIRIDE USED IN THE MANAGEMENT OF TYPE 2 DIABETES MELLITUS (T2DM): A PROSPECTIVE STUDY

Neelam Injeti*

Department of Pharm. D, CMR College of Pharmacy, Kandlakoya (V) Hyderabad, 501401, Telangana State, India.

Article Received on
05 Jan 2016,

Revised on 26 Jan 2016,
Accepted on 16 Feb 2016

***Correspondence for Author**
Neelam Injeti
Department of Pharm. D, CMR College of Pharmacy, Kandlakoya (V) Hyderabad, 501401, Telangana State, India.

ABSTRACT

Type 2 diabetes mellitus (T2DM) is a common metabolic disorder primarily either due to insulin hyposecretion and/or resistance. Pioglitazone and Glimepiride are most commonly used oral hypoglycaemic agents (OHAs) to improve insulin sensitivity. Both the drugs possess multiple complications. A prospective case analysis study conducted between October 2010 and September 2011 at Department of Endocrinology, KIMS, Hyderabad after obtaining permission from Institutional Ethics Committee, KIMS, Hyderabad. A total of 292 cases were collected, categorized and analyzed according to inclusion and exclusion criteria by using a structured patient data collection format. 146 cases each were classified in Pioglitazone and Glimepiride group. Data obtained from the study were analyzed by using Chi-square test & T-test to obtain the result. Combination use of Statins and TZDs effectively lower the concentrations of LDL-C, apoB and CRP, as well as increased adiponectin. Hence combination therapy with both Statins and TZDs could be expected not only to improve glycemic control and protect cardiovascular system.

KEYWORDS: Pioglitazone, Glimepiride, Effects, Statistical analysis, Graphical Representation, T2DM.

INTRODUCTION

Diabetes mellitus (DM**)** is a group of metabolic disorders characterized by hyperglycemia associated with abnormalities in carbohydrate, fat and protein metabolism; and results in

chronic complications including micro vascular, macro vascular, and neuropathic disorders. It is characterized with polyuria, polyphagia, and polydipsia.[1]

DM is the leading cause of blindness in adults aged 20 to 74 years, and the leading contributor to development of end-stage renal disease. The vast majority of diabetic patients are classified into one of two broad categories: type 1 diabetes caused by an absolute deficiency of insulin, or type 2diabetes defined by the presence of insulin resistance with an inadequate compensatory increase in insulin secretion. Women who develop diabetes due to the stress of pregnancy are classified as having gestational diabetes. Finally, uncommon types of diabetes caused by infections, drugs, endocrinopathies, pancreatic destruction, and known genetic defects are classified separately.[2]

Autoimmune type 1 DM can occur at any age. Approximately 75% will develop the disorder before age 20 years, but the remaining 25%, including relatives of index patients, develop the disease as adults. Patients with type 2 DM often present without symptoms, even though complications tell us that they may have had type 2 DM for several years. Often these patients are diagnosed secondary to unrelated blood testing. Lethargy, polyuria, nocturia, and polydipsia can be seen at diagnosis in type 2 diabetes, but significant weight loss at diagnosis is less common.[3]

In 2000, according to the World Health Organization, at least 171 million people worldwide suffer from diabetes, or 2.8% of the population. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000.The prevalence of diabetes is higher in men than women, but there are more women with diabetes than men. The urban population in developing countries is projected to double between 2000 and 2030.[4-5]

Surveys were generally performed on middle-aged populations, and data are more limited at younger and older ages. Data on diabetes prevalence are usually presented in broad age bands, which suggest a biologically implausible step-like increase in diabetes prevalence with increasing age.. Taking an urban-rural population distribution of 70:30 and an overall crude prevalence rate of around 4%, at a conservative estimate, India is home to around 40 million diabetics and this number is thought to give India the dubious distinction of being home to the largest number of diabetics in any one country.[6]

Surveys have also shown that the prevalence of Impaired Glucose Tolerance (IGT) is also high. It has been reported that the prevalence of IGT is around 8.7% in urban and 7.9% in

rural areas. Recently, another study has shown the prevalence rates for urban areas is around 6%, whilst the figures in the rural areas was found to be around 5%. Given the observation that around 35% of those with IGT will develop full blown diabetes within five years, the sheer numbers of those with diabetes seems overwhelming. [7-8]

Table 1: Features of FDA approved oral hypoglycemic therapies in type II diabetes [9]

Drug	Advantages	Disadvantages	Lowers HbA1C	Most commonly Reported adverse events	Failure rate
Sulfonylureas (1st &2nd generation): Acetohexamide Glipizide Glyburide Glimepiride	Inexpensive, Improved lipid Profile by lowering Triglycerides	Weight gain, and rare but severe Hypoglycemia	1.5%	Rare allergies, SIADH can be caused by first generation and disulfiram react	10-15%
TZDs Pioglitazone Rosiglitazone	Lower TG, and raises HDL, No hypoglycemia effect	Weight gain, elevated ALT levels, and Edema noted.	0.5-1.5%	Gastrointestinal adverse effects at elevated dosages, rare liver failure, as we mentioned fluid retention (CI in class 3, 4 CHF)	Not known

METHODOLOGY

In this prospective case analysis study, conducted between October 2010 and September 2011 at OPD of Department of Endocrinology KIMS, Hyderabad after obtaining permission from Institutional Ethics Committee KIMS, Hyderabad. A structured patient data collection format was used to document patient related information according to inclusion and exclusion criteria. Format includes; patient demographic details, chief complaints, past medical and medication details, laboratory and other diagnostic investigation details of treatment & management with medication and non-medication. All the collected data were categorized into two groups viz; Pioglitazone used group and Glimepiride used group. Re-visit details of the collected cases were also noted for following details like; blood sugar & lipid profile, BMI, development of pedal edema & bone fracture. Data obtained from the study were analyzed by using Chi-square test & T-test to obtain the final result.

RESULTS

Table 2: Gender Wise Distribution

Drug Name	Male		Female	
PIOGLITAZONE (n=146)	111	76%	35	24%
GLIMEPIRIDE	75	51.3%	71	48.7%

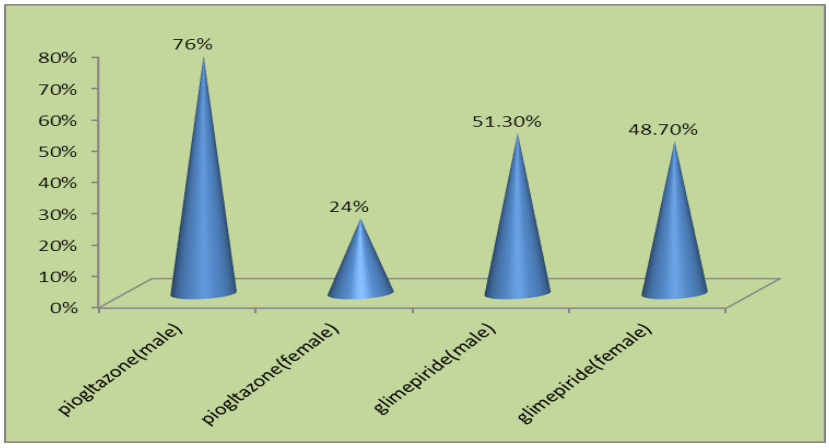

Figure 1: Graphical representation of Gender Wise Distribution

Table 3: Age Wise Distribution

Drug Name	Age group	Number of patients	Percentage of patients
PIOGLITAZONE	40-45yrs	78	53.40%
GLIMEPIRIDE	40-45yrs	40	27.39%
PIOGLITAZONE	46-50yrs	31	21.23%
GLIMEPIRIDE	46-50yrs	35	23.90%
PIOGLITAZONE	51-55yrs	22	15.06%
GLIMEPIRIDE	51-55yrs	25	17.12%
PIOGLITAZONE	56-60yrs	15	10.27%
GLIMEPIRIDE	56-60yrs	46	31.50%

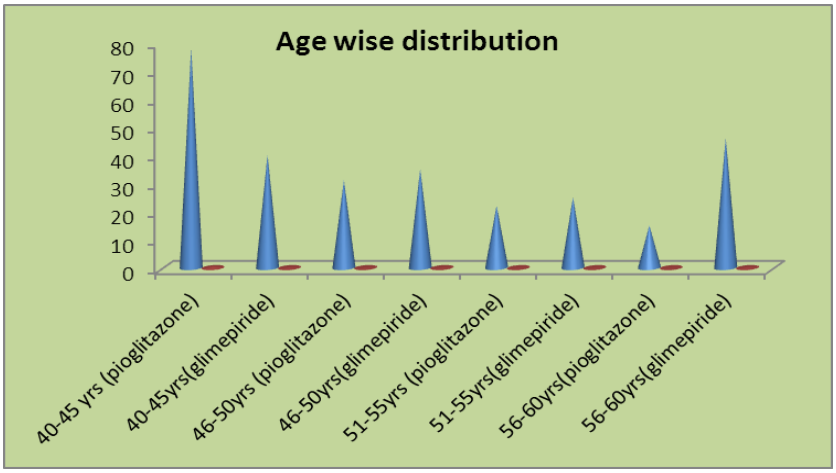

Figure 2: Graphical representation of Age Wise Distribution

Table 4: Analyzing Effects with Laboratory Investigations-Weight Gain

Laboratory investigations	Pioglitazone		Glimepiride	
	No. of patients	%of patients	No. of patients	%of patients
FBG	24	16.40%	26	9.58%
PPBG	30	20.5%	20	13.6%
HbA1C	24	16.4%	4	2.73%
TG	62	42.46%	15	10.27%

TC	93	63.60%	54	36.9%
HDL	62	42.40%	38	26.00%
LDL	97	66.40%	52	35.6%

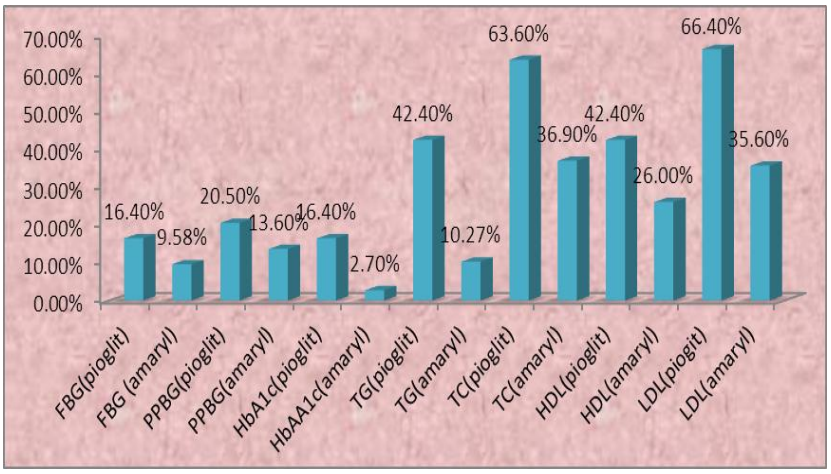

Figure 3: Graphical representation of Analyzing Effects with Laboratory Investigation-Weight Gain

Table 5: Analyzing Effects with Laboratory Investigations-pedal edema

Laboratory investigations	Pioglitazone		Glimepiride	
	No. of patients	%of patients	No. of patients	%of patients
FBG	08	5.47%	7	4.79%
PPBG	11	7.53%	11	5.47%
HbA1C	04	8.21%	09	6.16%
TG	10	13.60%	20	6.80%
TC	62	42.45%	18	12.30%
HDL	27	20.50%	20	13.60%
LDL	62	46.50%	16	10.90%

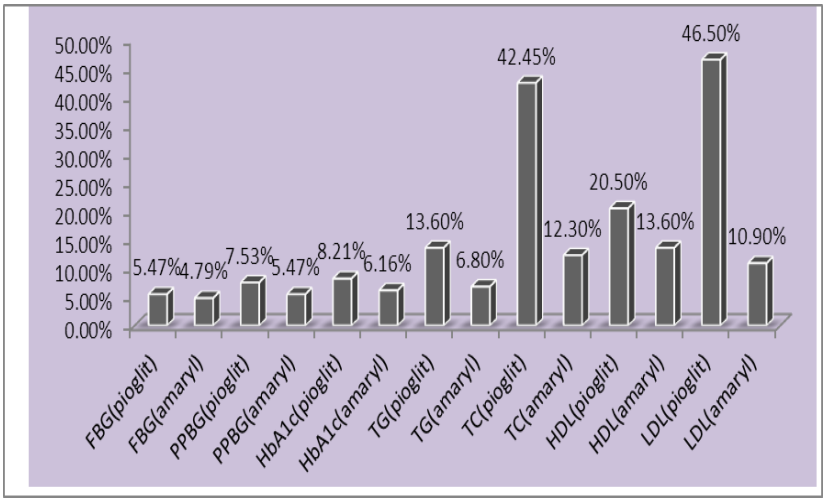

Figure 4: Graphical representation of Analyzing Effects with Laboratory Investigations-Pedal Edema

Table 6: Analyzing Effects with Laboratory Investigations-cardiovascular disorder

Laboratory investigations	Pioglitazone		Glimepiride	
	No. of patients	%of patients	No. of patients	%of patients
FBG	15	10.20%	10	6.84%
PPBG	50	36.98%	20	13.69%
HbA1C	10	6.84%	08	5.47%
TG	50	34.20%	30	20.50%
TC	68	46.57%	52	35.60%
HDL	15	10.27%	25	17.12%
LDL	40	27.30%	14	19.58%

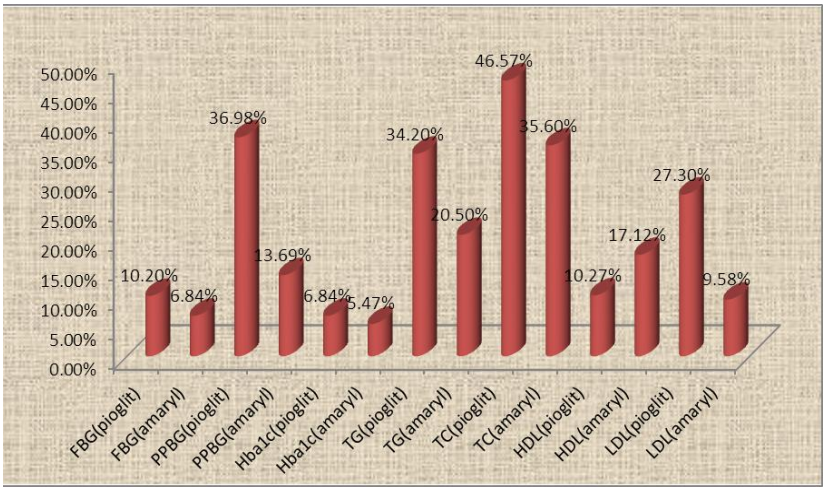

Figure 5: Graphical representation of Analyzing Effects with Laboratory Investigations-Cardiovascular Disorder

Table 7: Analyzing Effects with Laboratory Investigations-bone fracture

Laboratory investigations	Pioglitazone		Glimepiride	
	No. of patients	%of patients	No. of patients	%of patients
FBG	5	3.42%	-	-
PPBG	9	6.16%	-	-
HbA1C	2	1.36%	-	-
TG	6	4.10%	-	-
TC	20	13.60%	-	-
HDL	18	12.30%	-	-
LDL	20	13.60%	-	-

Table 8: Statistical analysis of laboratory investigation FBG

Blood Glucose Profile		No.of Patients	% of Patients	Mean	Standard Deviation	P Value
FGB	Pioglitazone (pioglit)	147	100%	114.1849	12.3601	0.001*
	Glimepiride (amaryl)	147	100%	129.3082	25.1063	

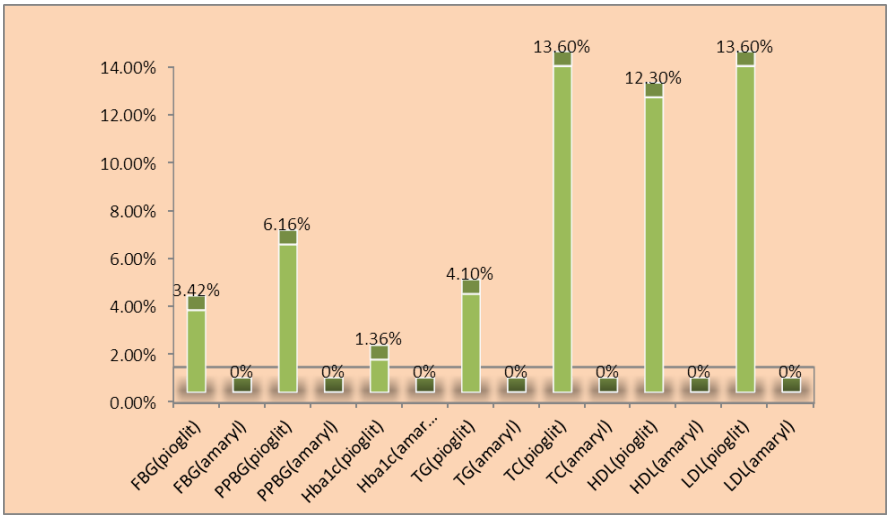

Figure 6: Graphical representation of Analyzing Effects With Laboratory Investigations-Bone Fracture

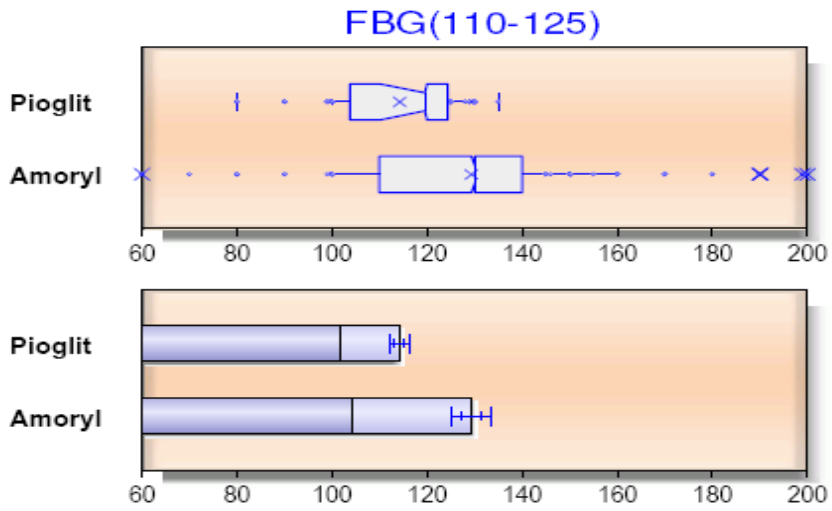

Figure 7: Graphical representation of Statistical Analysis of Laboratory Investigations FBG

Table 9: Statistical analysis of laboratory investigation PPBG

Blood glucose profile		No.of patients	% of patients	Mean	Standard deviation	P value
PPBG	Pioglitazone (Pioglit)	147	100%	183.6370	22.6974	<0.004*
	Glimepiride (Amaryl)	147	100%	213.4110	25.5280	

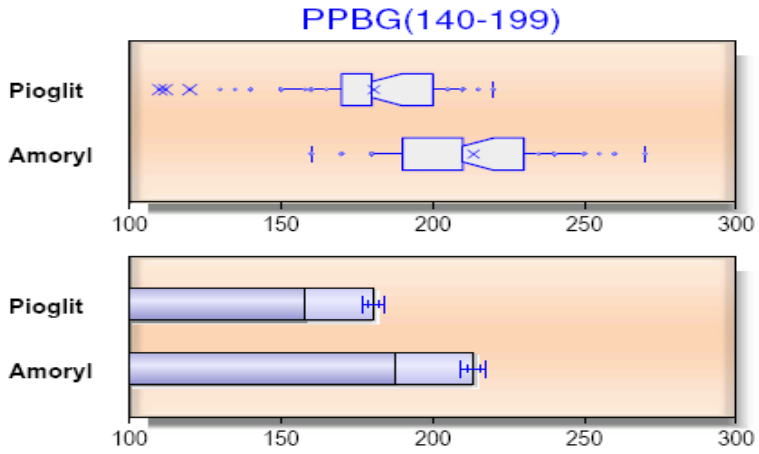

Figure 8: Graphical representation of Statistical Analysis of Laboratory Investigation PPBG

Table 10: Statistical analysis of laboratory investigation HbA1c

Blood glucose profile		No.of patients	% of patients	Mean	Standard deviation	P value
HbA1C	Pioglitazone (pioglit)	147	100%	6.6027	0.7564	<0.001*
	Glimepiride (amaryl)	147	100%	7.8764	1.1913	

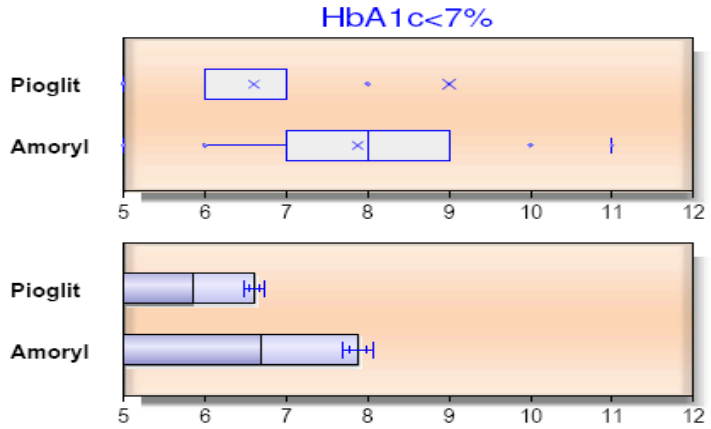

Figure 9: Graphical representation of Statistical Analysis of Laboratory Investigation HbA1C

Table 11: Statistical analysis of laboratory investigation TG

Lipid profile		No.of patients	% of patients	Mean	Standard deviation	P value
TG	Pioglitazone (pioglit)	147	100%	141.8699	17.8361	<0.002*
	Glimepiride (amaryl)	147	100%	237.8090	37.7184	

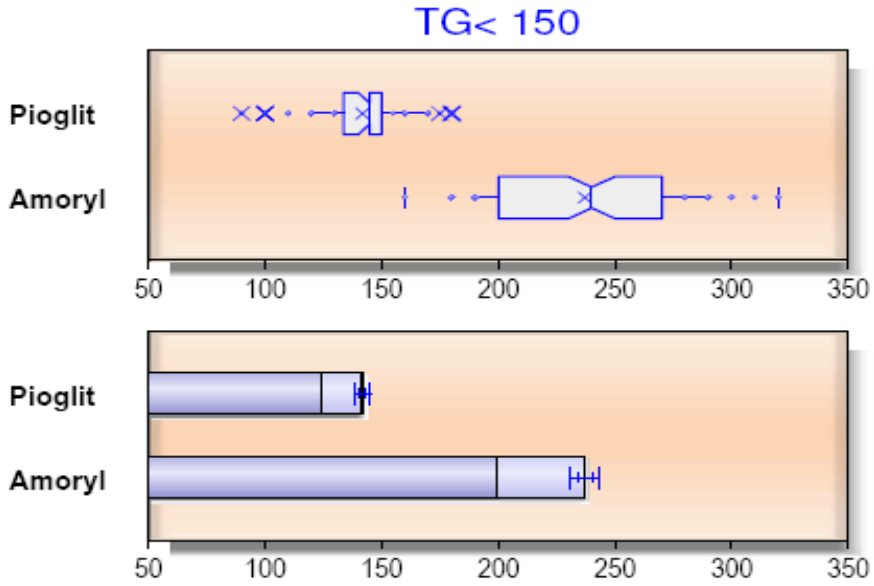

Figure 10: Graphical representation of Statistical Analysis of Laboratory Investigation TG

Table 12: Statistical analysis of laboratory investigation TC

Lipid profile		No.of patients	% of patients	Mean	Standard deviation	P value
TC	Pioglitazone (pioglit)	147	100%	344.0411	39.4060	<0.003*
	Glimepiride (amaryl)	147	100%	279.6164	41.4029	

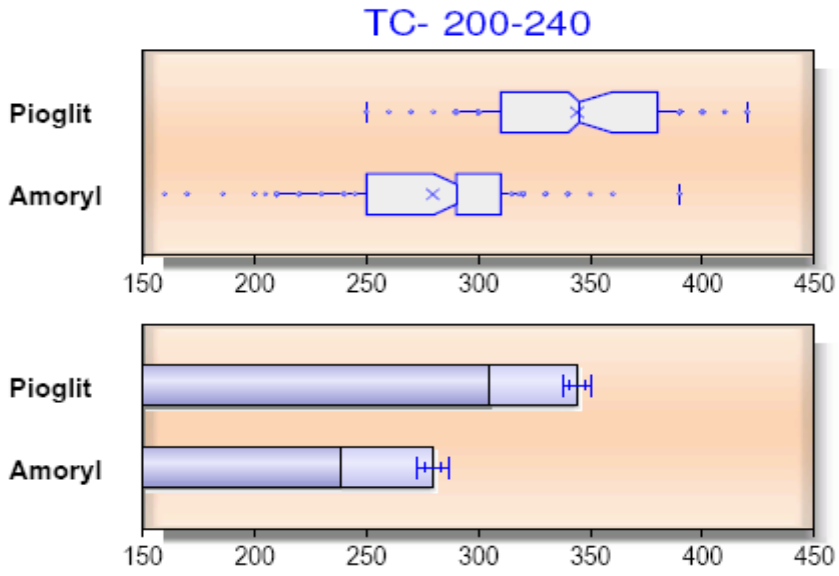

Figure 11: Graphical representation of Statistical Analysis of Laboratory Investigation TC

Table 13: Statistical analysis of laboratory investigation HDL

Lipid profile		No.of patients	% of patients	Mean	Standard deviation	P value
HDL	Pioglitazone (pioglit)	147	100%	59.0959	14.7771	<0.005*
	Glimepiride (amaryl)	147	100%	30.0616	8.030	

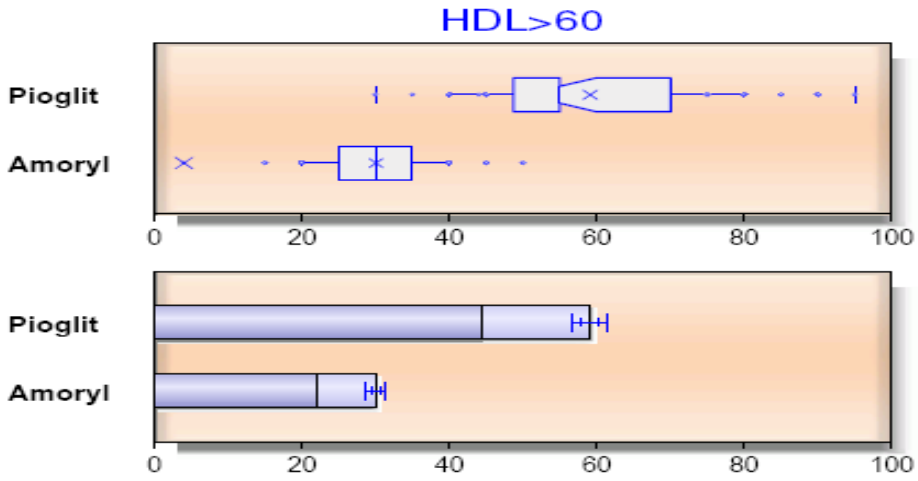

Figure 12: Graphical representation of Statistical Analysis of Laboratory Investigation HDL

Table 14: Statistical analysis of laboratory investigations LDL

Lipid profile		No.of patients	% of patients	Mean	Standard deviation	P value
LDL	Pioglitazone (pioglit)	147	100%	223.8973	55.1033	0.001*
	Glimepiride (amaryl)	147	100%	112.0685	47.2006	

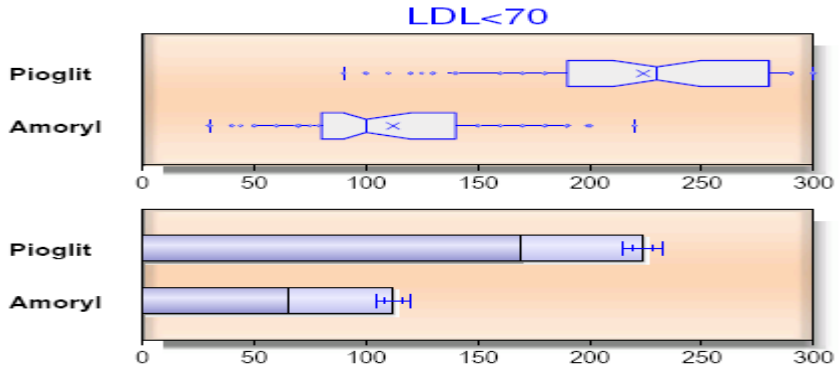

Figure 13: Graphical representation of Statistical Analysis of Laboratory Investigation LDL

Table 15: STATISTICAL ANALYSIS USING T TEST METHOD

Variable	Pioglit	Std.Err.	Amoryl	Std.Err.	T-Test	P value
Age	48.479±	0.389	48.466±	0.390	0.025	0.980
Gender	1.240±	0.035	1.486±	0.042	4.517	<0.001***
FBG(110-125)	114.185±	1.023	129.308±	2.078	6.530	<0.001***
PPBG(140-199)	180.637±	1.878	213.411±	2.113	11.593	<0.004***
HbA1c<7%	6.603±	0.063	7.877±	0.099	10.909	<0.001***
TG< 150	141.870±	1.476	237.089±	3.122	27.576	<0.002***
TC- 200-240	344.041±	3.231	279.616±	3.427	13.678	<0.003***
HDL>60	59.096±	1.223	30.062±	0.665	20.860	<0.005***
LDL<70	223.897±	4.560	112.068±	3.906	18.623	<0.001***

DISCUSSION

In this study a total of 292 diabetic patients were included. The effects caused by glitazones were analyzed by using chi-square method and T test method. Glitazones compared with Sulfonylureas were categorized into two groups using two different drugs with 147 patients in each.

Pandey et al., 2001 [10] studied on drug utilization in diabetes therapy, showed that utilization of thiazolidinediones drug is more in male than in females and utilization of sulphonylureas is almost in equal proportion. Similarly in my study as per table 2 there is a significant difference (P-0.002) showing that the utilization of thiazolidinediones is more in males than in females and sulfonylureas is almost in equal proportionate.

Sayantani Ghosh et al., 2011 [11] studied Pioglitazone induced weight changes in diabetic patients and concluded that weight gain is in males but especially seen in females although triglyceride and lipoprotein levels were not affected. In this present study according to table 4 and fig 3 showed that the blood glucose profile and lipid profile for the weight gain patients, was significant and in lipid profile the HDL C(<0.005), was elevated, TG(<0.002) was reduced and the other parameters remained almost normal.

Richard N et al., 2003 [12] studied on fluid retention or Edema showing that incidence of pedal Edema is more with Thiazolidinediones and it even increases when used in combination with other oral hypoglycaemic drugs. And in my study as shown in the table 5 shows that the blood glucose profile (FBG P value-0.001, PPBG P value-0.004, HbA1C-0.001) was significant and in lipid profile the HDL C, was elevated, TG was reduced and the other parameters remained almost normal.

Frederick A et al., 2005 [13] conducted a retrospective study which shows that Thiazolidinediones drug have less chances of causing cardiovascular disorder when compared with sulfonylureas which have more chances of risk factors. In parallel with article in my study the table 6, showed that the blood glucose profile was significant and in lipid profile the HDL C, was elevated, TG was reduced and the other parameters remained almost normal.

Lars Rejnmark et al., 2008 [14] studies showed that there is a decreased level of biochemical markers of bone formation in subjects treated with Thiazolidinediones indicating a decreased activity of osteoblastic cells and also decrease in plasma levels of bone-specific alkalinephosphatases, which results in loss of bone mineral density, finally leading to bone fracture. In comparison with the above article in present study, in table 8, the blood glucose profile (P value-0.001) showed a significant difference.

Chogtu B, et al., 1999 [15] conducted study on glitazones user's homodynamic parameters. Fasting and postprandial blood glucose levels, glycosylated hemoglobin, lipid profile and blood pressure were recorded. While the pioglitazone group showed significantly better efficacy in improving the lipid profile.

Based on the article my study also includes the lipid profile with elevated HDL, and the fasting .postprandial, glycosylated hemoglobin when compared with sulfonylureas drug as shown from table 13-15 and figure 13-15 showed that the elevated levels were less than the sulfonylureas drug.

Caitlin et al., 2002 [16-17] studied on improvement of Lipid Profiles in Diabetes Patients at High Risk for Cardiovascular Disease reported that HDL C were drastically elevated and TG levels were reduced and there was not much change in LDL and TC levels and in my study as shown in tables from 9-11 and figure 8-10 showed that HDL C was increased followed by increase in LDL (P value-0.001) and TC(P value-0.003) but TG levels were significantly decreased.

Thiazolidinediones, unlike metformin or sulphonylureas, decreases hepatic fat content and increases insulin sensitivity in muscle. These properties would seem to make the drugs particularly useful in patients with insulin-resistant type 2 diabetics. Statins have been shown to reduce cardiovascular events for type 2 diabetic patients. Combination use of Statins and

TZDs effectively lower the concentrations of LDL-C, apoB and CRP, as well as increased adiponectin. Hence combination therapy with both Statins and TZDs could be expected not only to improve glycemic control and protect cardiovascular system. The management for complications includes use of drugs like Statins for maintaining body weight and also some studies showed that it might be beneficial in preventing bone loss or decrease fracture risk. In addition calcium supplements can also be given. The Diuretics can be prescribed for the individuals with edema problem. Along with the above, proper diet maintenance followed by exercise would lead to good results.

CONCLUSION

In my study the complications of glitazones were found to be more and also severe than the sulphonylureas. Number of patients prescribed with pioglitazone between the age group 40-45 years was more, where as in Glimepiride using patients' age limit is not specific. Hence using pioglitazone in elderly patients (>50yrs) should be prescribed with great precaution due to more chances of complications. The ratio of use of glitazones in male and female patients was 3:1, concluding that more number of male patients was prescribed with pioglitazone. There is significance between the two drugs with respect to the complications, weight gain (P value-0.04) and pedal edema (P value-0.0006) which shows that these complications are acutely seen in pioglitazone prescribed patients. Hence regular monitoring and diet maintenance should be included in these drug users.

REFERENCES

1. Harris MI, Flegal KM, Cowie CC. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults: the Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care. 1998; 28: 518-24.
2. Atkinson MA, Eisenbarth GS. Type 1 diabetes: New perspectives on disease pathogenesis and treatment. Lancet. 2001; 358: 221-29.
3. Tataranni PA, Bogardus C. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care. 1997; 20: 1183-97.
4. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998; 21(9): 1414-31.
5. Hogan P, Dall T, Nikolov P. Economic costs of diabetes in the US in 2002, Diabetes Care. 2003; 26: 917-32.

6. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998; 21(9): 1414-31.
7. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. JAMA. 2002; 14: 1723-27.
8. Carroll MD, Flegal KM, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults,1999-2000. JAMA. 2002; 288(14): 1723-27.
9. Neelam I, Kishore BM, Sandeep A. Comparison of complications associated with pioglitazone and glimepiride used in the management of type 2 diabetes mellitus (T2DM): a prospective study. IJIPSR. 2015; 3(9): 1319-29.
10. Pandey A, Tripathi P, Pandey R, Srivatava R, Pandey A Tripathi KD. Drug Utilization Study in Diabetic Patients Essential of Medical Pharmacology, Jaypee Brother Medical Publishers, New Delhi, 2001; 49: 1711-2.
11. Ghosh S, Dey S. Pioglitazone induced weight changes in type 2 diabetic patients. International Journal of Collaborative Research on Internal Medicine & Public Health. 2011; 3(6): 534-40.
12. Richard Nesto R, Libby P. Diabetes mellitus and the cardiovascular system.2003; 41: 611-17.
13. Frederick A. Gerstein.HC, Pogue J, Mann JF, Lonn E, Dagenais GR, McQueen M, Diabetologia 2005; 48: 1749-55.
14. Lars, Rejnmark. 2008. "Bone effects of glitazones and other anti-diabetic drugs." Current drug safety 3 (3): 194-8.
15. Chogtu B, Singh N P, Chawla S, Gupta U Ginsberg H, Plutzky J, and Sobel ARE. Diabetes mellitus J Cardiovascular Risk 1999: 6: 337-46.
16. Caitlin M. Nass, NP; and Roger S. Blumenthal, MD Glitazones and the Potential Improvement of Lipid Profiles in Diabetes Patients at High Risk for Cardiovascular Disease 2000; 6(24): 1247-56.
17. Nathan DM. Initial management of Glycemia in type 2 diabetes mellitus. 2002; N Engl J Med, 2002; 347: 1342-49.