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STUDY TO EVALUATE SAFETY AND EFFICACY OF METFORMIN MONOTHERAPY AS COMPARED TO DUAL AND TRIPLE COMBINATION WITH SULPHONYLUREAS AND PIOGLITAZONE IN TYPE 2 DIABETES MELLITUS.

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ABSTRACT

Background: This observational study was intended to evaluate safety and effectiveness of metformin Monotherapy with sulphonylureas and pioglitazone in routine clinical practice in type 2 diabetes mellitus. **Material and method:** This was a 26 week, multicentre, parallel group, open label, non-randomized, observational study carried out in T2DM patients from Gujarat India. **Result:** A total of 105 subjects with T2DM, mean age 57.28 ± 6.17years and mean duration of diabetes, 2.63 ± 1.83 years were completed study. 82 patients enrolled in age between 51 to 65 years. Metformin combination with sulphonylurea and thiazolidinedione significantly reduced HbA1c%, FBG and PPBG. Triple combination of metformin, sulphonylurea and thiazolidinedione achieved highest percentage of HbA1c% goal at <6.5 and ≤7.0 as well as Fasting and postprandial blood glucose. Among all group percentage minor hypoglycaemic events occurs in dual combination of metformin and thiazolidinedione. **Conclusion:** In Gujarati people, triple combination therapy with metformin, Sulphonyluea and thiszolidinedione having good glycemic control as compare to dual combination.

KEYWORDS: Diabetes mellitus, HbA1c, glycemic control, sulphonylurea, pioglitazone.

1. INTRODUCTION

Population studies all over the world have clearly showed that the prevalence of diabetes mellitus (DM) is escalating and very likely we are heading towards epidemic proportions.[1]

According to the International Diabetes Federation, there were an estimated 387 million individuals with diabetes worldwide in 2014 and this will increase to 592 million by the 2035. The incidence of diabetes in the Asian population is on the rise; hence the incidence of late diabetes complications is also expected to increase correspondingly. Amongst the countries in Asia, India has got the highest number of people suffering from diabetes.[2]

The next challenge in India is that the quality of diabetes care varies considerably depending on expertise, awareness, attitude and perceptions among health care professionals in diabetes.[3]

India has diverse lifestyle pattern and ethnic variations, thus epidemiological profile of Type 2 diabetes mellitus (T2DM) may be considered at one of the rich and developed states of India. A diet rich in oil and sugar content has pushed Gujarat to the forefront of contributors of diabetic patients in India. Ethnic Gujarati people are presumed to have high prevalence of obesity, metabolic syndrome, diabetes, hypertension because of traditional Gujarati food and less physically active lifestyle.[4]

Despite a broad range of antidiabetic therapies, a majority of T2DM patients are not achieving the recommended glycaemic target. It has been recommended that, when managing glycaemia in patients with T2DM, physicians should aim to minimise the risk of weight gain and hypoglycaemia.[5,6,7,8]

Metformin is the first-line therapy in type 2 diabetes. In patients inadequately controlled with metformin, the additions of sulfonylurea or pioglitazone are equally plausible options to improve glycemic control.[9]

Metformin is a drug from the biguanide compound group which acts to lower plasma glucose levels without increasing the circulating insulin concentrations.[10]

Sulphonylurea (SU), which has been available for 50 years, is still primarily used because of its efficacy and low cost, but it has known side effects such as hypoglycemia and weight gain.[11]

Pioglitazone, is member of the class of the thiazolidinediones (TZDs). TZDs, potent and selective ligands for peroxisome proliferator-activated receptor gamma (PPARγ), are widely used clinically in the treatment of type 2 diabetes as insulin-sensitizing agents.[12]

In addition to the concept of glycaemic control, there is a heightened awareness that diabetes therapies should also address cardiovascular risk factors such as obesity, hypertension and lipids.[13,14,15,16]

Surveillance of diabetes is a necessary primary step toward its prevention and control and is fundamental to any improvement program. Furthermore, to control and prevent the T2DM epidemic, it must be approached in an appropriate manner but very little data are available from Gujarat to support this and for the prevention of diabetes, it is also vital to know the profile of diabetes in Gujarati people.

The aim of this observational study was to investigate the effectiveness of sulphonylurea or pioglitazone adding to metformin in Gujarati patients with type 2 diabetes.

2. MATERIALS AND METHODS

2.1 Study Design

The study was performed in accordance with the Declaration of Helsinki and good clinical practices and approval was gained from independent ethics committees. All participants gave written informed consent.[17,18]

Study design was a 26 week multicentre, parallel group, open label, non-randomized, observational study to compare safety and efficacy profile of SU Vs. Pioglitazone, as add on to metformin in subject with T2DM inadequately controlled on metformin monotherapy. Data was collected from 8 centers across Gujarat state, India.

Data were collected at Baseline (Visit 1), approximately after 13 weeks (Visit 2) and at approximately 26 weeks (Visit 3). The frequency and timing of visits were based on accepted standard of care for T2DM management.[19]

Only those patients with type 2 diabetes mellitus and were willing to sign the informed consent form were eligible to participate in this study. All patients, >18 years of age, men or women and willing to participate and comply with the study requirements were enrolled in the study. Inclusion criteria included subject have type 2 diabetes, HbA1c > 9.0% at time of diagnosis and > 7.0% even after 6 months of therapy with other anti-diabetic agents.

Prior to any study related activity, the investigator gave the oral information to subject or parents/the subject's legally acceptable representative, as applicable. The subjects were

informed of study related risks and benefits and they could withdraw from the study at any time. The responsibility for seeking informed consent (IC) remained with the investigator. The written IC was signed and dated by the investigator. A voluntary, signed and dated informed consent from (ICF) was obtained at Visit-1 prior to any study related activities.

Sulphonylureas (SU) and Pioglitazone were prescribed by the physician as part of routine treatment, depending on the patient's needs; the dosage was also adjusted individually, as required and information about the dose was recorded at baseline, 3 months and at the final visit (after 6 months).

2.2 Treatment administered

Treatment prescribed by the physicians to the patients during their routine clinical evaluation was in the form of study groups, which are listed below.

Group 1: Metformin monotherapy

Group 2: Metformin + SU

Group 3: Metformin + TZDs (Pioglitazone)

Group 4: Metformin + SU + TZDs

2.3 Data collection

The data was collected by reviewing patient's medical records and clinical examination reports for the past one year and by personal interviews for further information. Patient data included demographic parameters such as age, sex, BMI, and diabetes duration; while efficacy variable included glycaemic parameters (glycosylated haemoglobin [HbA1c], fasting blood glucose [FBG], postprandial blood glucose [PPBG]); while safety variable includes adverse events and hypoglycemic events and other safety variable parameter including Fasting lipid variables**.** Data obtained from these patients were systematically recorded into a case report form designed for the study.[18,20,21]

2.4 Statistical methods

Continuous variables were summarized with descriptive statistics expressed as Mean ± Standard Deviation (SD). The data was analyzed using ANOVA followed by Tukey's multiple comparison tests and Paired t-test. $p<0.05$ were considered as statistically significant. Categorical data was summarized with the number (N) and percentage (%) of subjects in each category. The continuous endpoints were defined as change from baseline to week 26.

3. RESULTS

3.1 Treatment administered

The study was a survey in patients with T2DM being treated at diabetes clinics and referral clinics in Gujarat. Since it was open label and non randomised study, considering treatment allocation to the patient during their routine clinical evaluation by the investigator.

Table 1 shows of 184 patients, 24 (13.04%) were on Metformin alone, 53 (28.80%) patients were on oral dual combination of metformin and SU, while 46 (25.00%) patients on oral dual combination of metformin and Pioglitazone and 61 (33.15%) on triple combination of metformin, SU and Pioglitazone.

Table: 1 Summary of Diabetes management. * Study group considered for data evaluation.* Study group consider for data evaluation

	Baseline		26 Week	Male	Female
Anti-diabetic Medication	**N (184)**	**%**	**N (105)**	**N (63)**	**N (42)**
Biguanide (Metformin)*	24	13.04	23	16	7
Dual Combination of Metformin					
Metfromin+Sulphonylurea (Glimepiride, Glibenclamide, Gliclazide, Glipizide)*	53	28.80	30	18	12
Metformin+Thiazolidinedione (Pioglitazone)*	46	25.00	20	11	9
Triple combination of Metformin					
Metformin + Sulphonylurea + Thiazolidinedione*	61	33.15	32	18	14

3.2 Study subjects

3.2.1 Disposition of study subjects

Table 2 summarises study completion status for all enrolled subjects. A total of 184 subjects constituted for full analysis set. Of 184 enrolled subjects, 105 (57.06%) completed the study and were considered as effective and safety analysis set, and 79 (42.93%) discontinued the study where 38 (20.6%) and 41 (22.28%) subjects were discontinued at weeks 13 and 26, respectively. The major reason for study discontinuation was loss to follow-up and change in medication in their respective routine checkup.

3.2.2 Characteristics / demographic data of study subjects

Table 3 summarized subject demographics at baseline. Of the 184 enrolled subjects, 106 (57.60%) were male and 78 (42.39%) were female. The mean (SD) age, height and Type 2 DM duration were 57.28 (6.17) years, 164.58 (5.58) cm and 2.63 (1.83) years respectively of

the subjects who completed study. The mean (SD) age and duration of diabetes for enrolled male was 57.03 (6.26) and 4.53 (2.96) respectively, while in female 57.67 (6.09) and 2.83 (1.73) respectively (Table 4).

Table: 2 Summary of subject study completion status full analysis set.

Population/Disposition reason	**Overall (N=184) N (%)**
Population[1]	
Full Analysis Set	184 (100.0)
Effectiveness Analysis Set/Safety Analysis Set	105 (57.06)
Disposition Reason[1]	
Total number of subjects completed the study	105 (57.06)
Total number of subjects discontinue from the study	79 (42.93)
At 13 week	38 (20.6)
At 26 week	41 (22.28)
Reason for subject early termination[2]	
Lost to follow up	56 (70.88)
Adverse drug reaction	0.0 (0.0)
Drug therapy discontinue	23 (29.11)
Note:[1] Respective column header counts were used as denominator for percentage. [2] Percentages were calculated using early termination subjects' count as denominator.	

Table: 3 Summary of subject Demographic information visit wise full analysis set.

Parameters	**Baseline (N=184)**	**Visit-2 (N=146)**	**Visit-3 (N=105)**
Gender			
Male	106 (57.60%)	94 (64.38%)	63 (60.00%)
Female	78 (42.39 %)	52 (35.61%)	42 (40.00%)
Age (Years)			
Mean			57.28
SD			6.17
Median			57.00
Range (Min: Max)			42:74
Missing			0
Height (cm)			
Mean			164.58
SD			5.58
Median			166
Range (Min: Max)			152:175
Missing			0
Type 2 diabetes mellitus duration (years)			
Mean			2.63
SD			1.83
Median			2
Range (Min: Max)			0.5:9
Missing			0

Table: 4 Average age and duration of diabetes in year vs. Gender.

Parameters	Enrolled subject (N=105)	Male (N=63)	Female (N=42)
Age (Years)			
Mean	57.29	57.03	57.67
SD	6.17	6.26	6.09
Median	57	57	57
Range (Min: Max)	42:74	42:74	47:70
Missing	0	0	0
T2DM duration (Years)			
Mean	2.63	4.53	2.83
SD	1.83	2.96	1.73
Median	2	4	3
Range (Min: Max)	0.5:9	0.5:12	0.5:8
Missing	0	0	0

3.2.3 Summary of Diabetes Duration versus Age in year of subject completed study at baseline visit.

In the present study randomly patients were enrolled during their routine check up for T2DM at various clinics. We found that maximum patients has been enrolled at the age between 51 and 65, particularly highest 30 patients from the age between 56 and 60. Still it has been worried about patients of T2DM having age 42 to 50 total enrolments is 13 (Figure 1).

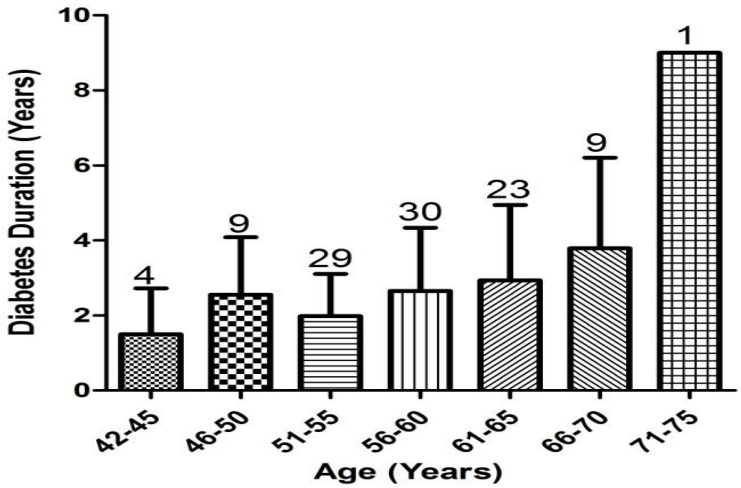

Figure: 1 Summary of average diabetes duration versus age in years. Above bar graph number indicating number of patients in particular age group.

If we go through the duration of diabetes and male age in year shows highest enrolment at age between 51 and 65, particularly highest 21 patients enrolled at the age between 56 and 60. The lowest age 42 to 45, 4 patients enrolled. While in female the lowest age 47 to 50, 5

patients enrolled. The highest female patients enrolled at the age between 51 and 55 (Figure 2 & 3).

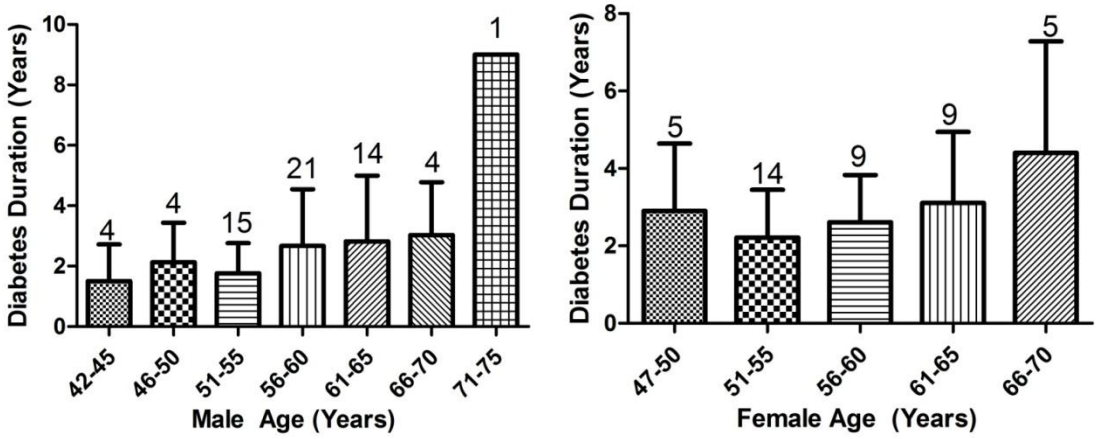

Figure: 2 Summary of average diabetes duration versus average male age in years. Above bar graph number indicating number of patients in particular age group.

Figure: 3 Summary of average diabetes duration versus average female age in years. Above bar graph number indicating number of patients in particular age ratio.

3.3 Efficacy variables

3.3.1 Effect on HbA1c% from Baseline to Week 26 Effective analysis set.

Table 5 and figure 4 shows when patient treated with metformin and its combination with sulphonylurea, effect on HbA1c % from baseline to week 26; visit 2 and visit 3 significantly reduced from baseline ($p<0.001$).

Table: 5 Summary of HbA1c% from baseline to Week 26 effective analysis set. Values are Mean±SD. One way ANOVA followed by Tukey's multiple comparison tests. p value from baseline to 26 weeks visit.

Study Group	HbA1c % (mean ± SD)			
	Baseline	Week 13	Week 26	p value
Metformin	7.73±0.45	6.81±0.60	6.92±0.28	<0.001
Metformin + SU	8.42±0.95	7.60±0.77	7.16±0.33	<0.001
Metformin + TZD	8.71±0.93	7.90±0.74	7.24±0.36	<0.001
Metformin + SU + TZD	9.27±0.79	7.88±0.75	6.89±0.35	<0.001

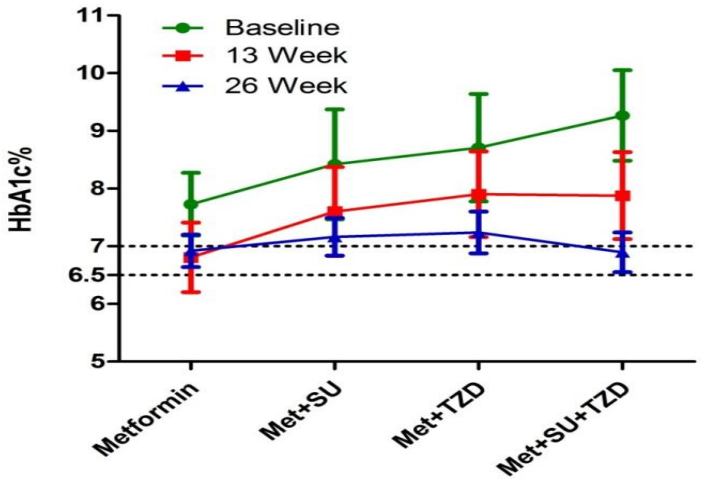

Figure: 4 Effect of all group combination with Metformin on HbA1c% from Baseline to Week 26 Effective analysis set. Values are Mean ± SD.

Metformin plus thiazolidinedione combination therapy, visit week 13 ($p<0.01$) and week 26 ($p<0.001$) significantly reduced as compared to baseline visit, while week 26 visit significantly reduced HbA1c% as compared to 13 week visit ($p<0.05$). Metformin, sulphonylurea and thiazolidinedione combination shows significantly reduced HbA1c as compared to baseline visit ($p<0.001$).

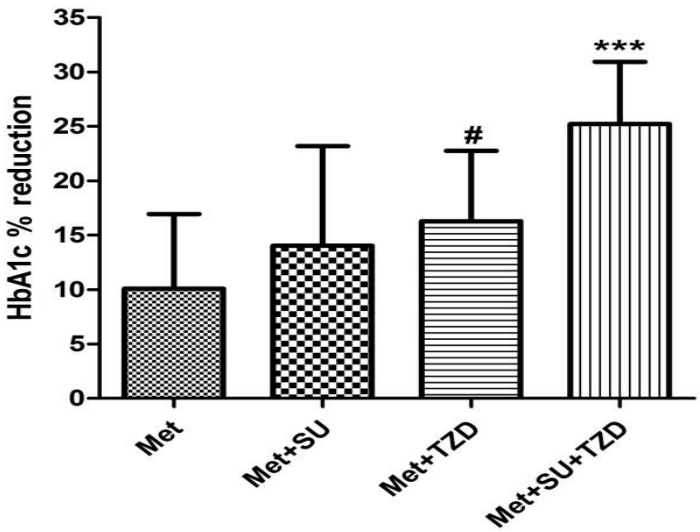

Figure: 5 Effect of all group combination with Metformin on % reduction of HbA1c from Baseline to Week 26 Effective analysis set. Values are Mean ± SD. One way ANOVA followed by Tukey's multiple comparison tests. # indicates $p<0.01$ as compared to Metformin, *** indicates $p<0.001$ as compared to Met+SU group and Met+TZD group of subjects.

Figure 5 comprises comparison of HbA1c% reduction. Dual combination of metformin and thiazolidindions significantly reduced HbA1c% as compared to metformin alone ($p<0.01$). Tripal combination of sulphonylurea and thiazolidinedione with metformin significantly reduced as compared to dual combination with metformin and sulphonylurea ($p<0.001$).

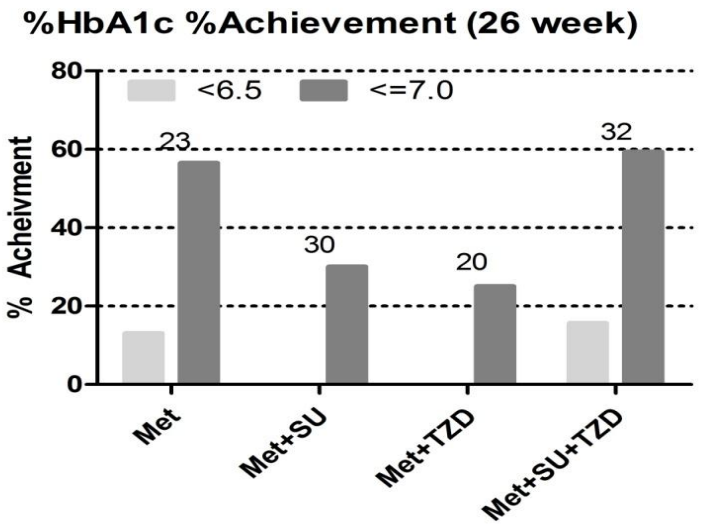

Figure: 6 Effect of all group on % achievement 6.5 and 7.0 based on American diabetes association and American college of Endocrinology on HbA1c% from Baseline to Week 26 Effective analysis set. Above bar graph number indicating number of patients in particular group.

Figure 6 comprises % Achievement of HbA1c% <6.5 or ≤7.0 from the total number of patients enrolled in respective group as per guideline of American Diabetes Association and American college of Endocrinology.[22,23] Result show that Metformin group achieve 13.04% and 56.52% of the total 23 patients respectively. The dual combination of sulphonylurea and thiazolidinedione with metformin not achieved at <6.5, while achieve 30% and 25% at ≤7.0 respective group, While triple combination shows 15.63% and 59.38% achieved respectively by total number of patients 32.

3.3.2 Effect on Fasting Blood Glucose (FBG) from Baseline to Week 26 Effective analysis set.

Patients treated with metformin Fasting blood glucose level of 26 week visit was significantly decrease as compared to baseline visit ($p<0.01$), While adds on to sulphonylurea given second and third visit significantly reduce fasting blood glucose level as compared to baseline visit ($p<0.001$). Metformin combination therapy with pioglitazone significantly decrease

second and third visit as compared to baseline visit ($p<0.05$ and $p<0.001$ respectively), While triple combination significantly reduced fasting blood glucose level from baseline ($p<0.001$) (Table 6 & Figure 7).

Table: 6 Summary of Fasting Blood Glucose (FBG) from baseline to Week 26 effective analysis set. Values are Mean±SD. One way ANOVA followed by Tukey's multiple comparison tests. p value from baseline to 26 weeks visit.

Study Group	Fasting Blood Glucose (mean ± SD) mg/dl			
	Baseline	Week 13	Week 26	p value
Metformin	138.3±21.22	122.4±29.03	114.2±17.09	<0.01
Metformin + SU	154.6±25.24	128.8±22.46	116.4±20.3	<0.001
Metformin + TZD	163.7±30.49	140.9±26.73	121.2±22.41	<0.001
Metformin + SU + TZD	164.8±28.34	127.8±23.37	112.7±20.34	<0.001

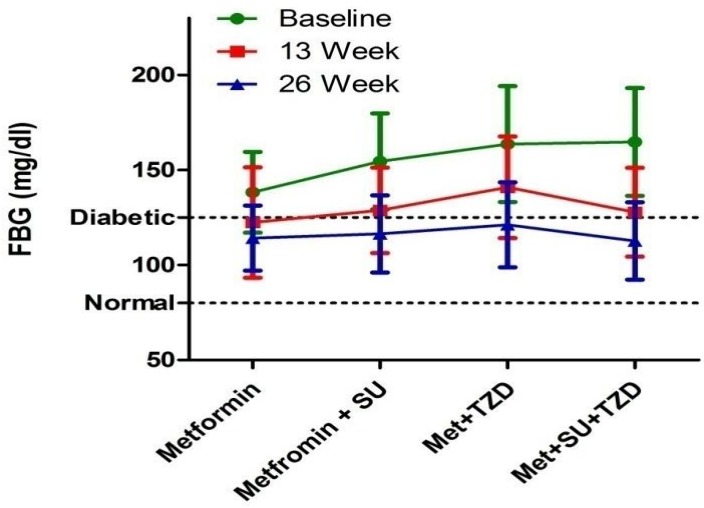

Figure: 7 Effect of all group combination with Metformin on Fasting Blood Glucose (FBG) from Baseline to Week 26 Effective analysis set. Values are Mean ± SD.

3.3.3 Effect of on Postprandial Blood Glucose (PPBG) from Baseline to Week 26 Effective analysis set.

Patient treated with metformin significantly reduced postprandial blood glucose at second and third visit as compared to baseline visit. Metformin combination therapy with pioglitazone significantly reduced on second and third visit $p<0.01$ and $p<0.001$ respectively, While add on to sulphonylurea significantly reduced on 13 and 26 week visit $p<0.001$ (Table 7 & Figure 8).

Table: 7 Summary of Postprandial Blood Glucose (PPBG) from baseline to Week 26 effective analysis set. Values are Mean±SD. One way ANOVA followed by Tukey's multiple comparison tests. Analyse p value from baseline to 26 weeks visit.

Study Group	Postprandial Blood Glucose (mean ± SD) mg/dl			
	Baseline	Week 13	Week 26	p value
Metformin	171.9±21.09	157.3±23.8	154.4±11.09	<0.01
Metformin + SU	193.5±25.03	182.9±24.49	141.8±15.95	<0.001
Metformin + TZD	197.7±24.67	172.3±26.7	147.5±24.0	<0.001
Metformin + SU + TZD	216.3±34.06	174.9±23.82	137.5±16.84	<0.001

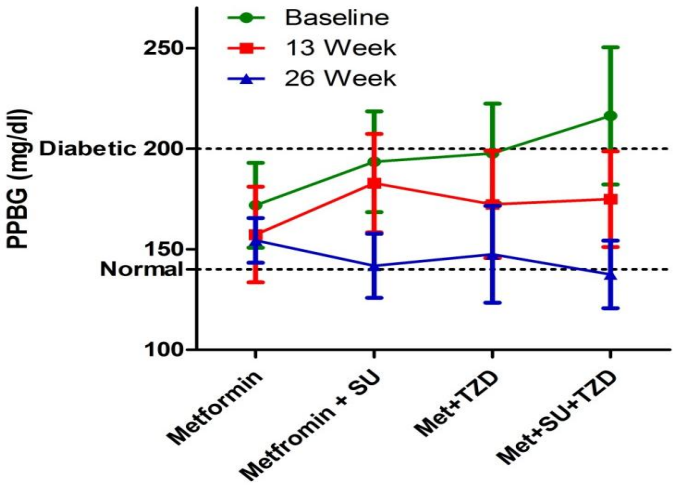

Figure: 8 Effect of all group combination with Metformin on Postprandial Blood Glucose (PPBG) from Baseline to Week 26 Effective analysis set. Values are Mean ± SD.

3.4 Safety variables

3.4.1 Adverse event/Serious Adverse Event

There was not observed adverse event or serious adverse event reported during study period.

3.4.2 Hypoglycemic events

No major hypoglycemic event occurs during the study. Table 8 shows summary of percentage minor hypoglycemic event occurs during the study. No statistical analysis was confirmed hypoglycemic episodes as too few events were reported in the study.

Table: 8 Summary of percentage minor hypoglycaemic events occurs in study groups.

Study Group	No. of subjects	Minor Hypoglycemic event	% minor hypoglycemic event occur
Metformin	24	1	4.17
Metformin + SU	53	1	1.89
Metformin + TZD	46	4	8.70
Metformin + SU + TZD	61	1	1.64

3.5 Other safety variables

3.5.1 Fasting lipid variables

Effect on Total Cholesterol (TC) from Baseline to Week 26 safety analysis set.

Figure 9 shows group wise mean±SD changes in total cholesterol are mentioned. Results show that in group of combination of pioglitazone and metformin, total cholesterol level is slightly increased. Metformin group shows baseline 173.9±15.92 mg/dl and 26 week 166.7±12.64 mg/dl (p<0.1113). Metformin and SU combination group shows baseline 195.9±21.44 mg/dl and 26 week 187±23.07 mg/dl (p<0.0425). Metformin and Thiazolidinedione combination group shows baseline 187.5±14.87 mg/dl and 26 week 195.6±23.6 mg/dl (p<0.1410) while triple combination shows at baseline 201±21.18 mg/dl and 26 week 205.8±19.21 mg/dl (p<0.2097).

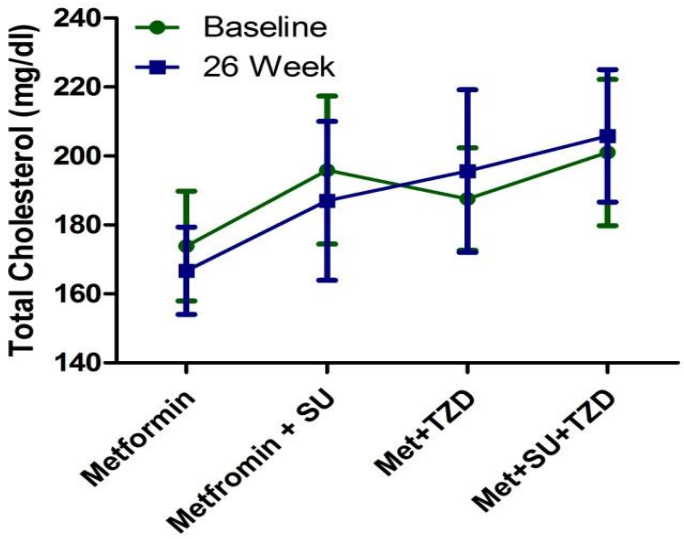

Figure: 9 Effect of all group combination with Metformin on Total Cholesterol (TC) from Baseline to Week 26 safety analysis set. Values are Mean ± SD followed by paired t tests.

Effect on HDL-cholesterol (HDL-C) from Baseline to Week 26 safety analysis set.

Results shows group wise mean±SD changes in HDL- cholesterol from base line to week 26. Metformin group shows baseline 50.47±2.23 mg/dl and 26 week 50.63±3.69 mg/dl (p<0.7776). Metformin and SU combination group shows baseline 50.11±4.16 mg/dl and 26 week 51.40±3.77 mg/dl (p<0.0183). Metformin and Thiazolidinedione combination group shows baseline 47.86±3.30 mg/dl and 26 week 49.67±3.04 mg/dl (p<0.0058) while triple combination shows at baseline 50.70±2.12 mg/dl and 26 week 51.74±3.47 mg/dl (p<0.0306) (Figure 10).

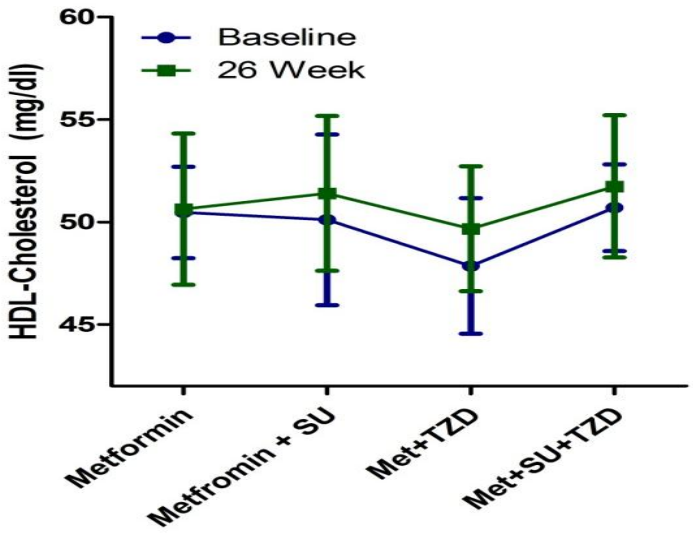

Figure: 10 Effect of all group combination with Metformin on HDL-Cholesterol (HDL-C) from Baseline to Week 26 safety analysis set. Values are Mean ± SD followed by paired t tests.

Effect on LDL-cholesterol (LDL-C) from Baseline to Week 26 safety analysis set.

Figure 11 shows mean ±SD change in LDL-Cholesterol from baseline. Metformin group shows baseline 112.9±11.09 mg/dl and 26 week 108.3±8.17 mg/dl ($p<0.1436$). Metformin and SU combination group shows baseline 118.8±12.64 mg/dl and 26 week 110.0±10.60 mg/dl ($p<0.0017$). Metformin and Thiazolidinedione combination group shows baseline 116.7±11.02 mg/dl and 26 week 117.5±12.50 mg/dl ($p<0.6782$) while triple combination shows at baseline 120.2±10.4 mg/dl and 26 week 122.0±9.47 mg/dl ($p<0.4800$).

Effect on Triglyceride (TG) from Baseline to Week 26 safety analysis set.

Results shows group wise mean±SD changes in triglyceride from baseline to week 26. Metformin group shows baseline 157.2±15.77 mg/dl and 26 week 144.8±16.77 mg/dl ($p<0.0036$). Metformin and SU combination group shows baseline 173.7±18.20 mg/dl and 26 week 156.3±15.74 mg/dl ($p<0.0001$). Metformin and Thiazolidinedione combination group shows baseline 177.1±15.75 mg/dl and 26 week 158.7±18.0 mg/dl ($p<0.0079$) while triple combination shows at baseline 188.0±14.06 mg/dl and 26 week 164.0±15.03 mg/dl ($p<0.0008$) (Figure 12).

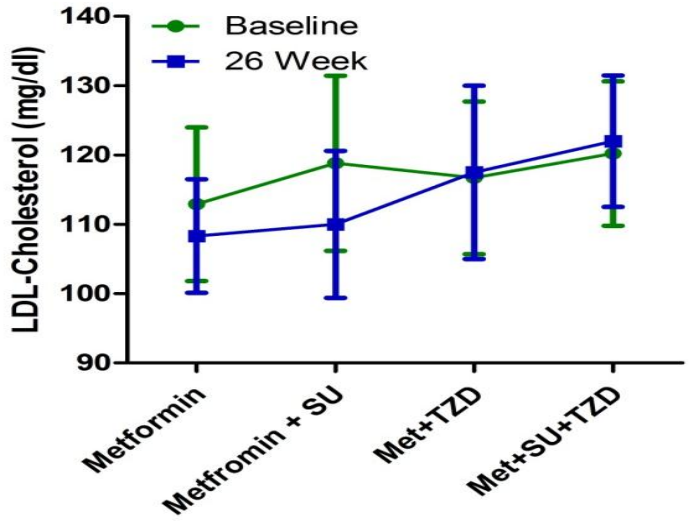

Figure: 11 Effect of all group combination with Metformin on LDL-Cholesterol (LDL-C) from Baseline to Week 26 safety analysis set. Values are Mean ± SD followed by paired t tests.

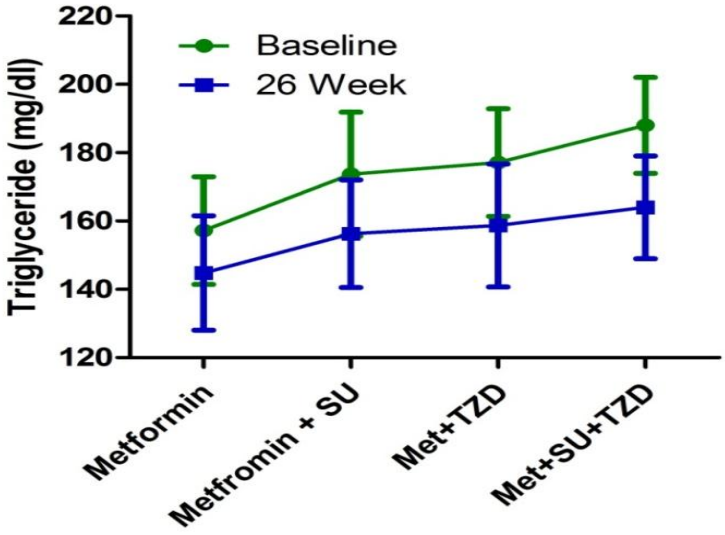

Figure: 12 Effect of all group combination with Metformin on Triglyceride (TG) from Baseline to Week 26 safety analysis set. Values are Mean ± SD followed by paired t tests.

4. DISCUSSION

Diabetes mellitus is reaching potentially epidemic proportions in India. The level of morbidity and mortality due to diabetes and its potential complications are enormous and pose significant healthcare burdens on both families and society. Worryingly, diabetes is now being shown to be associated with a spectrum of complications and to be occurring at a relatively younger age within the country.[24]

In India, limited studies have focused on diabetes care and provide an insight into the current profile of patients and their management. In DiabCare Asia, a multi-centre collaborative observational study in Asia shows that T2DM begins at an early age amongst Indians and the mean age of diagnosis among Indian respondents was 43.6 years. 50% had poor control as measured by HbA1c and 54% had late severe complications.[25]

DiabCare India 2011 has shown that type 2 diabetes sets in early in Indians and glycaemic control is often sub-optimal in these patients. These results indicate a need for more structured intervention at an early stage of the disease and need for increased awareness on benefits of good glycaemic control. It cannot be overemphasized that the status of diabetes care in India needs to be further improved.[26]

This trial was designed to assess and compare the efficacy and safety after 26 weeks of treatment with oral hypoglycaemic agents in subjects with T2DM. To the best of knowledge, no such type of profiles has been reported from Gujarat. Nonetheless, literature on the prevalence of diabetes is available from South and North India.[27] The main motivation for this analysis was to obtain the risk profile so as to prevent or decrease the burden of T2DM at Gujarat.

In present observational study, total 184 T2DM patients from the specified study group were recruited and 105 patients were completed the study. When patients were treated with metformin and other combinations in other treatment groups the HbA1c% level reduced effectively from the baseline to week 26. A statistically significant reduction in HbA1c% was seen. Triple combination of sulphonylurea and thiazolidinedione with metformin significantly reduced as compared to dual combination with metformin and sulphonylurea ($p<0.001$).

As per guidelines of American diabetes association and American college of endocrinology %HbA1c is <6.5 and ≤7.0 respectively, which shows optimum glycemic target achieved.[22,23]

Study results showed that 15.63% patients achieved <6.5%HbA1c in group of metformin, sulphonylurea and thiazolidinedione, which indicates that optimum glycaemic target was achieved in maximum patients in triple combination group. Triple combination of sulphonylurea and thiazolidinedione increases the percentages reduction of fasting blood glucose and postprandial blood glucose as compared to dual combination of metformin individually with sulphonylurea and thiazolidinedione.

In conclusion, the results indicate a need for more structured intervention at an early stage of the disease and need for increased awareness on benefits of good glycaemic control. It cannot be overemphasized that the status of diabetes care in India needs to be further improved.

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