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CLINICAL DIAGNOSIS AND SAFETY OF VILDAGLIPTIN VERSUS GLIMEPIRIDE WITH METFORMIN OVER PATIENTS OF TYPE-2 DIABETES MELLITUS

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Keywords:

Beta-cell, Type-2 Diabetes Mellitus, Glimepiride, Vildagliptin, Metformin

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ABSTRACT: The aim of the study to compare the efficacy of vildagliptin (50 mg) and glimepiride (2 mg) metformin (500 mg) for type-2 diabetes mellitus. Vildagliptin and glimepiride are found to be regulated the blood plasma glucose by stimulating beta cell in the pancreas. The treatment course duration of 34 weeks comparative observational study was conducted over 160 patients with type-2 diabetes mellitus was recognized. Group A (n=80) was treated with vildagliptin (50 mg) with a combination of metformin (500 mg). Group B (n = 80) was treated with glimepiride (2 mg) with a combination of metformin (500 mg) with fixed dosage was given daily twice. The baseline of HbA1c from > 7.0% to <10.5%. The tests were performed by the help of vitros 250 and sysmex XN 1000 and 350. Thus, the performance of the t-test was found to play a significant role. Group A and group B have shown a greater reduction in plasma glucose fasting plasma glucose reduced up to 47.9mg/dl ($p<0.000$) in vildagliptin group versus glimepiride group 36.84 mg/dl ($p<0.000$), postprandial glucose reduced up to 54.67 mg/dl ($p<0.000$) in vildagliptin group and glimepiride group reduced up to 42.94 mg/dl ($p<0.000$) and HbA1c reduced up to 1.21%($p<1.0$) in vildagliptin group versus glimepiride group reduced up to 0.90%($p<1.0$). The body weight was increased by 0.93 kg with glimepiride (Group B) and reduced by 0.74 kg with vildagliptin (Group A). In this observation vildagliptin group results were found to be potential treatment with more benefits with comparison to glimepiride. vildagliptinwas good for pancreatic beta cell, with lower risk of hypoglycemia comparison to glimepiride.

INTRODUCTION: Diabetes mellitus (DM) is a complex, chronic metabolic disorder caused by both genetics and environmental factor. Diabetes mellitus is a globally public health problem affecting more than 400 million people globally. Yearly increase in diabetic patients is seen globally, which is expected to rise 629 million by 2045 [1, 2]. The DM is broadly categorized into type-1 and type-2, which are also called as insulin-dependent diabetes mellitus (IDDM) and non-insulin-dependent diabetes mellitus (NIDDM). In case of type-2 diabetes mellitus (T2DM) occurs due to improper production of insulin by the beta cell of pancreas [3].

Blood plasma glucose level increased caused many health complications such as chronic micro-vascular, macrovascular, neuropathic and also food-related disorders, cardiovascular, renal problems. The type-1 is seen due to autoimmune deficiency, or beta-cell destroyed itself, whereas the type-2 is nearly 90% to 95% disorders by variable degrees of insulin resistance and improper insulin secretion leads to increase the glucose production, thus insulin hormone not play an

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effective role to reduce the plasma glucose level due to morphological changes occurs in insulin hormone [4].

If Single anti-diabetic medication not control blood plasma level so many patients needed more than one oral medication for better results. Combination drugs give much better results in newly diabetic patients.

Lately, many new ant-diabetic drugs found [5, 6, 7]. Vildagliptin is a highly effective oral anti-diabetic medicine because it controls blood plasma glucose very effectively in type-2 diabetic patients [8, 9]. Vildagliptin used monotherapy or combination with other medicine such as metformin, thiazolidinedione and insulin [10, 11].

Vildagliptin has not altered blood parameters such as SGOT, SGPT, serum creatinine, HDL, triglycerides, and not effects on body weight.

Some other medicine such as sulfonylurea is the most prescribed medicine as single or combination with other oral anti-diabetic drugs for the care of type-2 diabetic patients [12, 13] but sulfonylurea increased body weight and hypoglycemia.

All guidelines for type-2 diabetic patients follow by American Diabetes Association (ADA), the British National Institute for Health and Care Excellence (NICE), the International Diabetes Federation (IDF), and European Association for the Study of Diabetes (EASD) [14, 15].

The aim of the present study to find the advantages of vildagliptin (50 mg) with metformin (500 mg) with comparison of glimepiride (2 mg) with metformin (500 mg) for type-2 diabetes mellitus patients.

MATERIALS AND METHODS:

Sample Collection: The data of patients were collected randomized, open-label and comparative from Surbhi hospital Noida (U.P., India). The data was carefully analyzed for different variables for the selection of patients to full fill the inclusion criteria.

The patients with a diabetes history of 2 to 3 years with age group between 30 to 70 years were considered. The study of patient data was collected in the duration of 15 November 2019 to 31 October 2020. The ethical committee was approved to analyze the patients' data of T2DM diagnosis with the registration number of NERB/ SOS/CHEM/2018/107 from the hospital record. All patients were given written information for this study.

Study Design: The patients selected for HbA1C range from >7% to <10.5% as a baseline. The exclusion method was type-1 diabetes (T1DM) includes evidence of cardiac failure, renal dysfunction, hepatic dysfunction, malignancy, and history of allergy or pregnancy.

Total number of patients enrolled 175, 15 patients excluded from the study, 7 from group 1 and 8 from group 2. For this study total 160 patients' blood samples were included for testing fasting plasma glucose, postprandial glucose, glycated hemoglobin, creatinine potassium, blood urea, SGPT, SGOT, and Lipid profile for screening.

These tests are performed in Surbhi hospital, Noida, U.P., which is the NABH & NABL accredited for excellence. The patients are equally divided into two groups *i.e.;* group A includes 80 patients undergone the treatment of vildagliptin with metformin), whereas group B includes 80 patients undergone the treatment of sitagliptin with metformin. The methodology of patients was shown in **Fig. 1**.

At the initial phase of treatment, the controlled dosage of vildagliptin (50 mg) with metformin (500 mg) and glimepiride (2 mg) with metformin (500 mg) was given per day. The dosage of drugs was change after the 6 weeks because of glycaemic control as not reached.

After 8 weeks of treatment with vildagliptin (50 mg) with metformin (500 mg) and glimepiride (2 mg) with metformin (500 mg) was given twice a day. The dosage of both group A and group B was kept constant in a due course of 6 weeks and no other antihyperglycemic drugs was added.

Statistics: The collected data was analysed by chi-square test, mean ± standard deviation and calculate the p value, p value <0.05 was considered statistically significant.

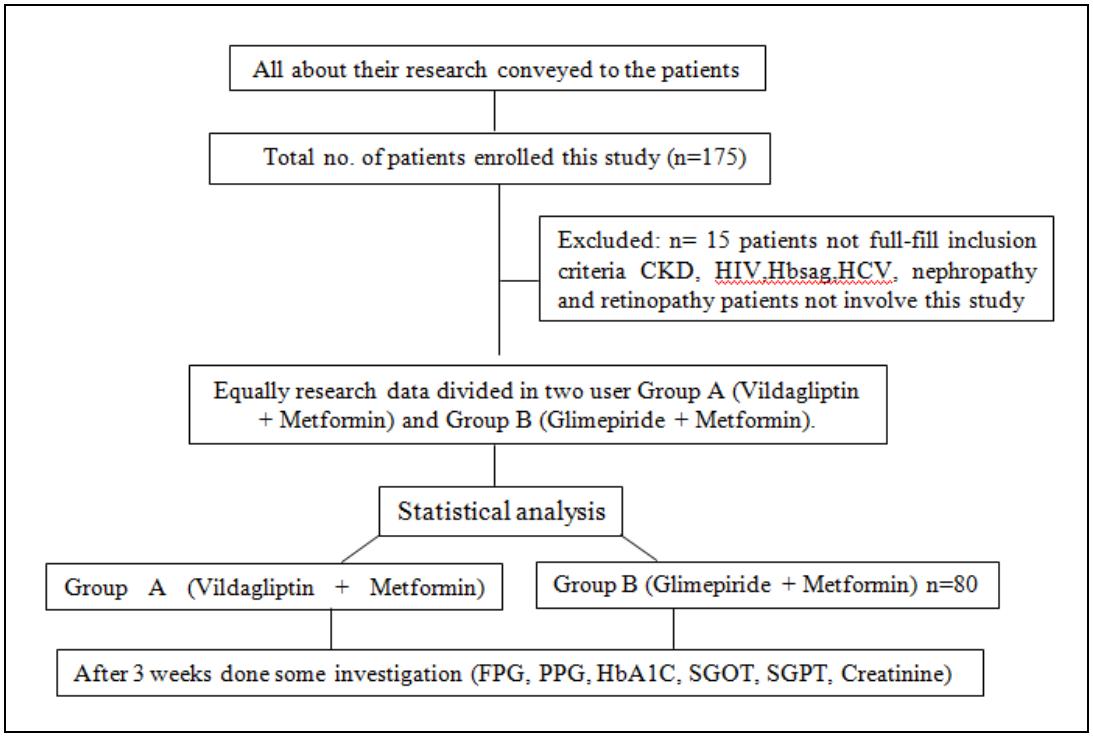

FIG. 1: FLOW CHART OF METHODOLOGY OF PATIENT DISTRIBUTION FOR PRESENT STUDY

RESULTS: The data analysis of 34 weeks of the treatment period, the following results are observed with combination therapy of both groups A and B. Both groups have shown a greater reduction in plasma glucose parameters. The analysis through **Table 1** of both the groups of A and B have shown a greater reduction in FPG, PPG and HbA1c. The treatment with vildagliptin (group A) fasting plasma glucose reduced up to 209.56 ± 31.90 mg/dl to 161.66 ± 27.40 mg/dl a total reduction of 47.90 mg/dl ($p<0.000$).

TABLE 1: PATIENTS RESULT BEFORE AND AFTER TREATMENT OF 34 WEEKS OF THE STUDY.

Parameters	Vildagliptin + Metformin Group (A) N=80		Glimepiride + Metformin Group (B) N=80	
	Before	After	Before	After
Age (Year)	51.8±7.73		53.26±7.66	
Gender (F/M)	37/43		34/46	
FPG (mg/dl)	209.56±31.90	161.66±27.40	217.60±27.73	180.76±25.53
PPG (mg/dl)	259.07±32.27	204.40±30.98	269.65±25.46	226.71±23.69
HbA1c(percentage)	9.37±0.71	8.16±0.69	9.26±0.61	8.36±0.62
Body weight (kg)	66.89±4.67	66.15±4.54	67.89±3.35	68.82±3.03

F: Female, M: Male, mg/dl = milligram per decilitre, N = Total Number, ± = Mean SD.

Fig. 2 shows vildagliptin group works effectively to reduced fasting plasma glucose levels. The postprandial glucose reduced from 259.07 ± 32.27 mg/dl to 204.40 ± 30.98mg/dl a total reduction of 54.67 mg/dl ($p<0.000$) for vildagliptin group shown in **Fig. 4**. Urea (mg/dl) change from 27.10±8.41 to 26.9 2 ± 4.90 in group A and 29.30±6.42 to 30.26 ± 5.31 in group B, serum creatinine (mg/dl) change 0.63±0.22 to 0.63±0.17 in group A and group B 0.63±0.20 to 0.67±0.18. Potassium (meg/dl) alter 4.14±0.49 to 4.23±0.44 in group A, 4.51±0.44 to 4.60±0.38 in group B, SGOT (IU/L) reduction 42.32±18.34 to 37.86±14.88 in vildagliptin group from 43.66±12.02 to 41.91±9.01 in glimepiride group, total cholesterol (mg/dl) change from 173.73±16.29 to 172.55±14.73 in vildagliptin group, and 179.26±15.53 to176.37±13.50 in glimepiride group, triglycerides(mg/dl) change from 149.03 ± 22.32 to148.25 ± 19.30 in vildagliptin group and 159.33 ± 21.79 to 151.22 ± 15.62 in glimepiride group, and HDL (high-density lipoprotein) change from 40.16±8.09 to 42.1±7.53 in vildagliptin group and 40.03±8.53 in glimepiride group shown in **Table 2**.

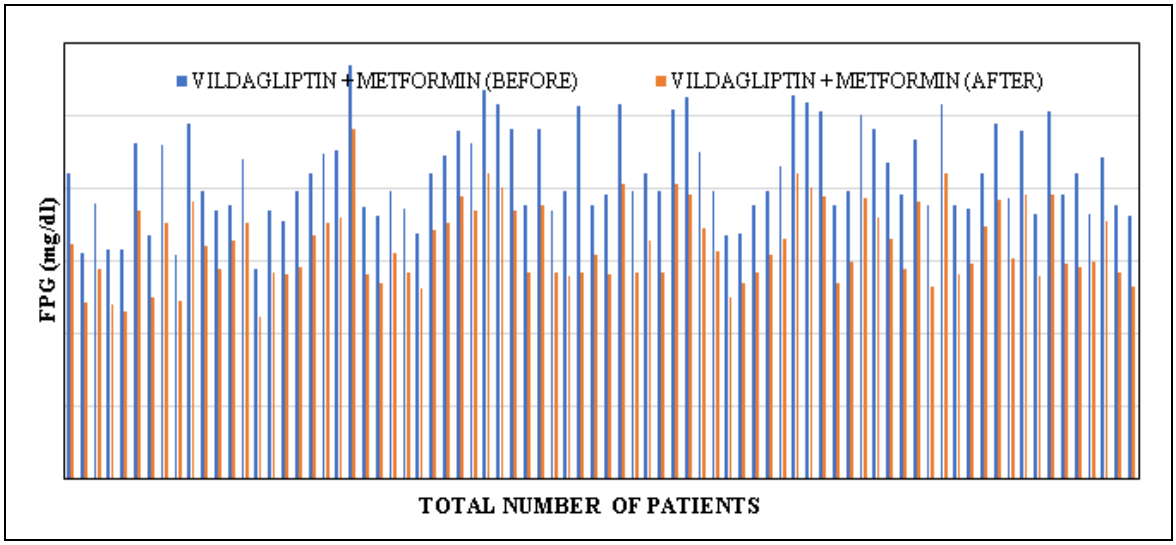

FIG. 2: EFFECT OF FASTING ON PLASMA GLUCOSE RESULTS OF BEFORE AND AFTER TREATMENT OF VILDAGLIPTIN

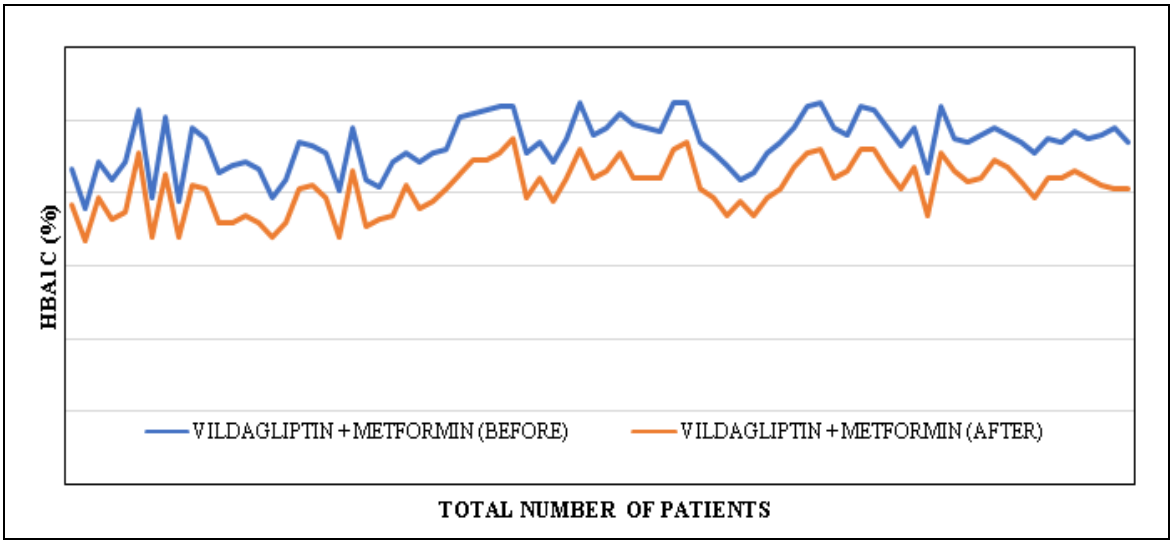

FIG. 3: EFFECT ON HBA1COF RESULTS OF BEFORE AND AFTER TREATMENT OF VILDAGLIPTIN

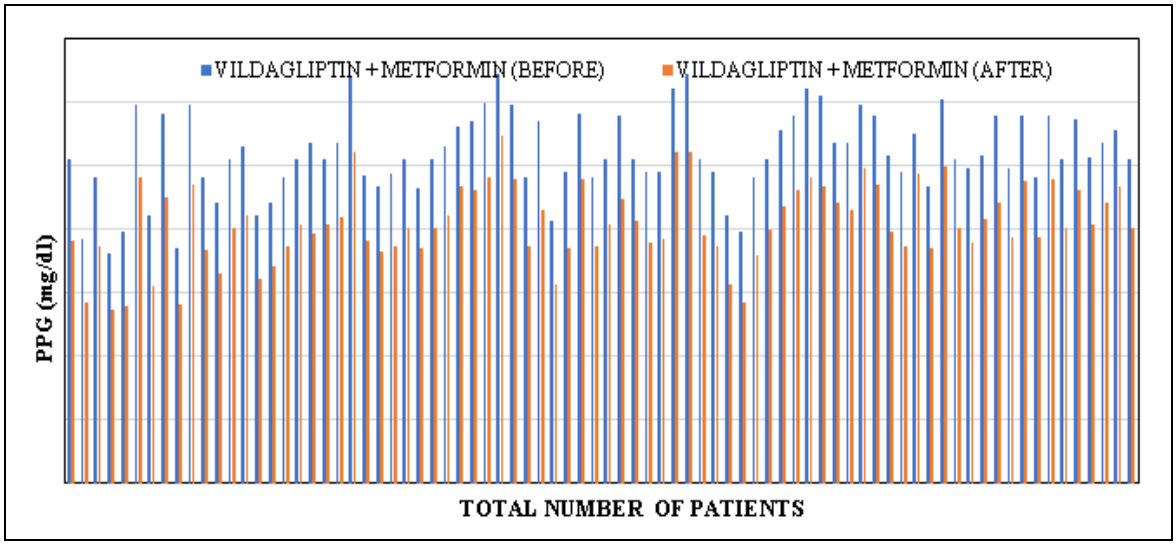

FIG. 4: EFFECT OF POSTPRANDIAL ON PLASMA GLUCOSE RESULTS OF BEFORE AND AFTER TREATMENT OF VILDAGLIPTIN

TABLE 2: PATIENTS PARAMETERS OBSERVED IN GROUP A AND GROUP B BEFORE AND AFTER TREATMENT

Parameters	Group A (N = 80)		Group B (N = 80)	
	Before	After	Before	After
Urea (mg/dl)	27.10±8.41	26.92±4.90	29.30±6.42	30.26±5.31
Creatinine (mg/dl)	0.63±0.22	0.63±0.17	0.63±0.20	0.67±0.18
Potassium (meq/dl)	4.14±0.49	4.23±0.44	4.51±0.44	4.60±0.38
SGOT (IU/L)	42.32±18.34	37.86±14.88	43.66±12.02	41.91±9.01
SGPT (IU/L)	51.95±18.40	48.93±16.54	56.02±19.27	49.16±13.59
CHO (mg/dl)	173.73±16.29	172.55±14.73	179.26±15.53	176.37±13.5
TG (mg/dl)	149.03±22.32	148.25±19.30	159.33±21.79	151.22±15.6
HDL (mg/dl)	40.16±8.09	42.10±7.53	40.03±8.53	44.32±7.86

mg/dl = milligram per decilitre, meq/dl = milliequivalent per decilitre, SGOT = serum glutamic-oxaloacetic transaminase, SGPT = serum glutamic pyruvic transaminase, IU/L = international unit per litre, N = Total Number, ± = Mean SD

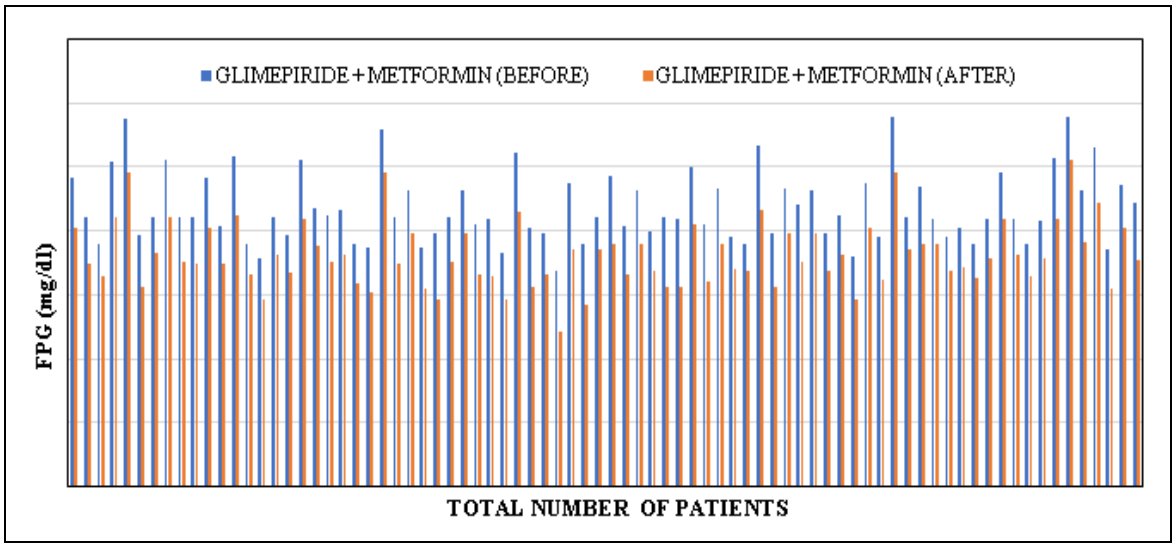

FIG. 5: EFFECT OF FASTING ON PLASMA GLUCOSE RESULTS OF BEFORE AND AFTER TREATMENT OF GLIMEPIRIDE

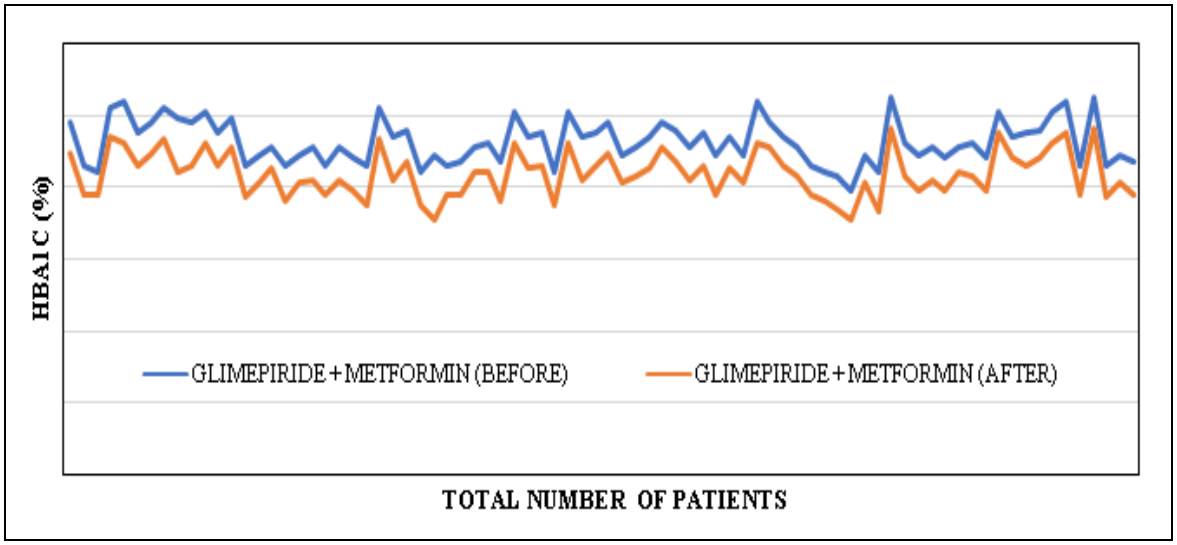

FIG. 6: EFFECT ON HBA1C (%) RESULTS OF BEFORE AND AFTER TREATMENT OF GLIMEPIRIDE

HbA1C reduced from 9.37% ±0.71% to 8.16% ± 0.69% ($p<1.0$) was reduced for vildagliptin group shown in **Fig. 3** and glimepiride group reduced from 9.26±0.61 to 8.36±0.62 shown in **Fig. 6**. Some other test, blood urea, serum creatinine, potassium, SGOT, SGPT, total cholesterol, triglycerides and HDL (high-density lipoprotein) were performed. There was no significant difference in parameters that indicate these drugs were safe for T2DM.

The glimepiride group fasting plasma glucose reduced up to 217.60±27.73 mg/dl to 180.76±25.53 mg/dl. **Fig. 5** shows the glimepiride good control of fasting plasma glucose level. The glimepiride group postprandial plasma glucose reduction from 269.65±25.46 mg/dl to 226.71±23.69mg/dl shown in **Fig. 7** and **Fig. 5** shows the comparison between before and after treatment of glimepiride group, HbA1C reduced from 9.26%±0.61% to 8.36% ± 0.62% (p<1.0). Bodyweight (kg) decreased 66.89±4.67 to 66.15±4.54 from baseline (-0.74kg) in vildagliptin group and increased from 67.89±3.35 to 68.89±3.35 from the baseline (+0.93kg) in glimepiride group shown in **Table 1**. The mean of HbA1C reduction more in the case of vildagliptin group shown in **Fig. 8**.

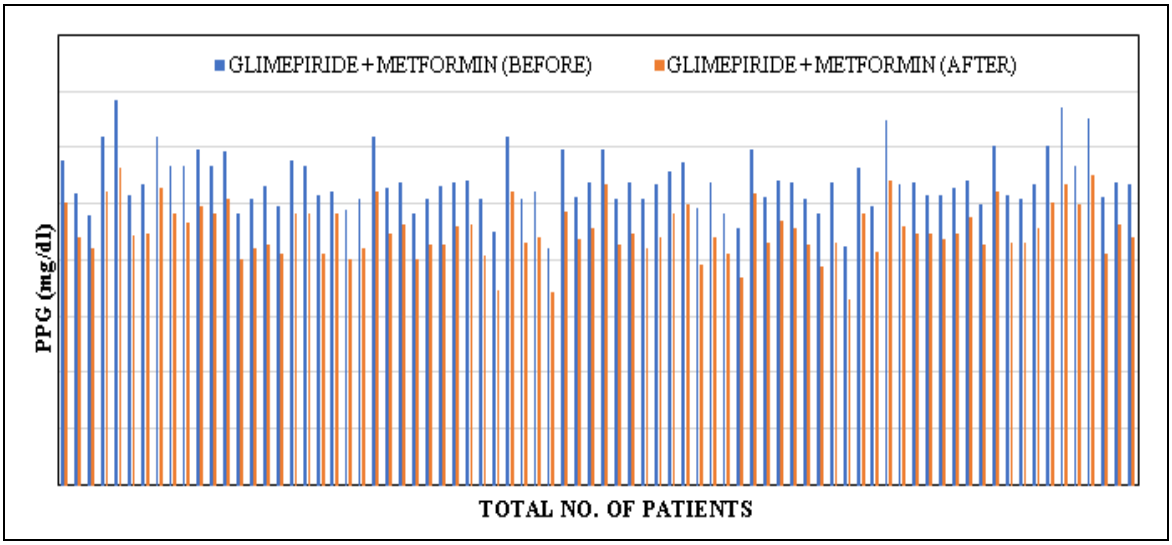

FIG. 7: EFFECT OF POSTPRANDIALON PLASMA GLUCOSE RESULTS OF BEFORE AND AFTER TREATMENT OF GLIMEPIRIDE

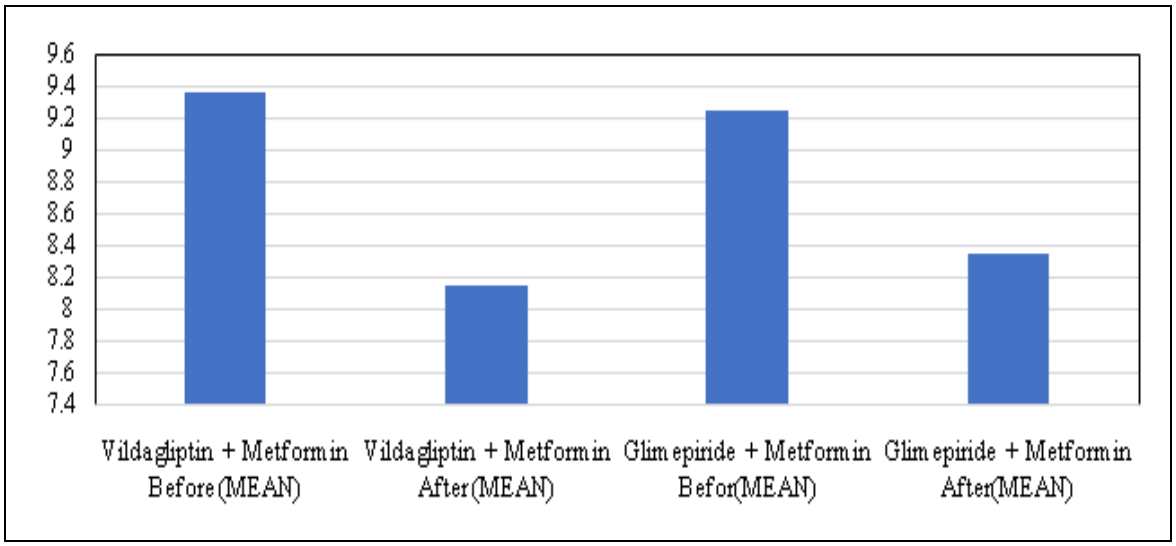

FIG. 8: MEAN GLYCOSYLATED HEMOGLOBIN (HBA1C) COMPARISON BETWEEN VILDAGLIPTIN AND GLIMEPIRIDE GROUP

DISCUSSION: The data analysis results of the present study show the effect of the drug has a considerable effect on the glycaemic control of all the selected patients. The lowering of plasma glucose in group A and group B was statistically significant with the treatment of vildagliptin was found a potential effect in lowering of plasma glucose in due course of 34 weeks. The study on both drugs was comparable with SGOT, SGPT, creatinine, blood urea, potassium, and lipid profile were better controlled at 34 weeks. Vildagliptin with metformin combination drugs did not gain weight, and only 2 patients come under hypoglycaemia, which was similar to the findings of Garber AJ *et. al.* [16]. The type-2 diabetes mellitus frequently occurs in nearly 50 years of age as the

body cells become more resistant to insulin hormone, weight losing capacity slow after 50 years age, and insulin secretion is reduced due to morphological changes in B cell [17]. Many patients complained of gastrointestinal side effects during initial day in both groups but after 4 to 5 weak all patients tolerant. The vildagliptin inhibits DPP-4 enzyme so more and more insulin realized. GLP-1 inhibits the satiety center present in brain so reduced appetite and delay stomach emptying [18].

HbA1C mean standard reduced 1.21% with vildagliptin combination of metformin and glimepiride with metformin also a significant reduction of HbA1C 0.93%, which is quite close to the result of Matthews *et al.* [19]. The difference between vildagliptin group and glimepiride group was found to be 0.31%.

Combination of vildagliptin and metformin decreased weight and low hypoglycaemia [20], which was the safety side of combination drug usage. Similar results also found with our previous study of add-on combination of vildagliptin and metformin with promising efficacy [21].

In the present study, we observed that glimepiride + metformin group caused more hypoglycaemia then vildagliptin + metformin group, which is quite close to Matthews DR *et al.* [22] and Ahrén B *et al.* [23]. Gastrointestinal symptoms significantly more in vildagliptin group competitive to glimepiride group, similar results conducted by HJ *et al.* [24]. Gastrointestinal symptoms were seen starting 2 to 3 weeks, but after 3 weak no symptoms seen, similar result obtains by Nauck MA *et al.* [25]. Different DPP-4 inhibitor such as sitagliptin, vildagliptin showed a effect in different pre-clinical and clinical study for the care of neurodegenerative disorders [26, 27]. No clinically significant difference in Blood Urea, serum creatinine, SGOT, SGPT, serum potassium, total cholesterol, tg, HDL, and no cardiovascular episode was seen during the study, same work observed by Edoardo Mannucci *et al.*, [28]. Finally, vildagliptin with metformin shows superior results compared to glimepiride with the same metformin result observed by Dipti Ranjan Darjee *et al.*, [29]. In nutshells, both vildagliptin with metformin drugs are highly effective to control the plasma glucose level without change a blood parameter.

CONCLUSION: T2DM occurs due to insulin resistance and improper function of beta-cell or both lead to hyperglycaemia. Vildagliptin and glimepiride with metformin comparative study show that both effective drugs regulation of plasma glucose for type 2 diabetes mellitus and no adverse effect seen during study time. Gastrointestinal symptoms significantly more in vildagliptin group competitive to glimepiride group, but after 6 weak both groups give better result in blood parameters. There was no significant difference occurs in blood urea, serum creatinine, SGOT, SGPT, and lipid profile. Vildagliptin group A better effect than glimepiride group B to maintain the plasma glucose level in type 2 diabetes mellitus. Glimepiride + metformin more risk of hypoglycaemia and weight gain comparative to vildagliptin + metformin.

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CONFLICTS OF INTEREST: The authors declare that they have no conflict of interest. The authors are responsible for the content and writing of this article.

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