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EVALUATING THE THERAPEUTIC OUTCOMES OF GLIMEPIRIDE VS THE COMBINATION OF SITAGLIPTIN AND METFORMIN FOR THE TREATMENT OF UNCOMPLICATED TYPE 2 DIABETICS

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ABSTRACT

Present study was to assess the clinical outcomes of glimepiride and sitagliptin+metformin in patients with simple Type 2 diabetes. A 6-month prospective observational study was conducted in Dr. Raghu Diabetes and General Clinic on 60 patients with Type 2 DM. Participants were randomly assigned to Group 1(sitagliptin+metformin 50+500 mg/day) and Group 2 (glimepiride 1mg/day). Follow-up began 15 days after the patient became stable, with data recorded at this point considered as Zero months. Our study assessed Fasting Plasma Glucose (FPG), Post-prandial Plasma Glucose (PPG), and HbA1c levels within each group from zero to six months and compared these parameters between groups at the six-month mark. Adverse drug events were documented and summarized for each treatment group. After six months, Group 1 (sitagliptin+metformin 50+500 mg/day) demonstrated significant reductions in FPG, PPG, and HbA1c (all $P<0.001$) compared within the group. Group 2 (glimepiride 1mg/day) also exhibited significant decreases in FPG, PPG, and HbA1c (all $P<0.01$) within the group. A statistically evident difference (all $P<0.05$) favouring Group 1 was noted at 6 months. Adverse drug events, such as hypoglycaemic episodes and gastrointestinal issues, were more prevalent in Group 2. Additionally, Group 1 experienced weight loss, while Group 2 showed weight gain. Our study concludes that there is a notable difference between glimepiride and the sitagliptin+metformin combination in type-2 diabetic patient's medical outcomes, notably glycaemic control and adverse events. These results

highlight the possible significance of taking into account these drug selections in light of their various impacts on glucose control and safety profiles for those with diabetes mellitus.

Keywords : Sitagliptin, metformin, Glycemia control, Glimepiride, Type 2 DM patients.

INTRODUCTION:

Diabetes mellitus is a chronic metabolic disease that is characterized by hyperglycemia. This metabolic disorder is caused by a defect in insulin secretion or insulin action, or both.[1-4] According to the World Health Organization (WHO), more than 200 million people worldwide had diabetes in the year 2000. By 2025, this number is expected to rise to 300 million and this number would increase to 80 million by the year 2030.[5-7]The escalating global burden persists as the occurrence and prevalence of type 2 DM continues to rise. This can be attributed to factors such as population growth, aging, obesity, physical inactivity, and the extended lifespan of individuals with DM. Type 2 diabetes mellitus (DM) poses a significant risk for the development of various complications. These complications can be categorized into two types: microvascular complications, which include retinopathy, nephropathy, and neuropathy, and macrovascular complications, which encompass coronary heart disease, cerebrovascular disease, and peripheral vascular disease.[9] The main objective of variable treatments is to minimize hyperglycemia and enhance insulin sensitivity. These methods are theoretically appealing as they directly target the underlying problems associated with type 2 DM. However, despite the extensive range of available treatment options, glycemic control tends to decline over time.[10] Targeting glucose management and keeping the HbA1C level between 6 and 7% as the major treatment objective will reduce the risk of microvascular and macrovascular complications without predisposing individuals to hypoglycemia.[11] Using just one treatment, antihyperglycemic medication frequently fails at reaching and/or preserving sustained control of blood sugar levels. In individuals with type 2 diabetes, numerous patients need combined treatment.[12] Metformin monotherapy or sulfonylurea is the most widely prescribed first oral hypoglycaemic agent (OHA) regimen to treat patients with Type 2 diabetes.

For the treatment of type 2 diabetes, several novel medications have been launched in fixed dose combinations and as monotherapy. One such recently developed medication class is dipeptidyl peptidase-IV (DPP IV) inhibitors. Sitagliptin is a once-daily, oral, powerful, and extremely selective (DPP-4) inhibitor that has been authorized in numerous nations for therapy of type-2 diabetes.[13] It is currently being used either as a stand-alone treatment or in conjunction with continuous oral antidiabetic medications in individuals with type 2 DM with glycemic levels significantly reduced in a short period of time. The use of DPP IV inhibitors as monotherapy or in addition to continuous oral antidiabetic medications in individuals with type 2 DM. However, there is a lack of academic research on their comparative clinical results. Therefore, it was deemed valuable to investigate and contrast the clinical results of DPP IV inhibitor combination therapy i.e. sitagliptin+metformin and Glimepiride for the treatment of uncomplicated type 2 diabetics.

METHODOLOGY:

The study research was done at Dr. Raghu Diabetes and General Clinic on type 2 DM. The evaluation of blood glucose levels with patient history and other clinical evaluations are tested to identify DM. The patient at the age between 18 and 70 years those who are identified by type 2 DM. Type 2 Diabetes Mellitus patients who are uncontrolled on glimepiride or single therapy. (Fasting Plasma Glucose [FPG] level of ≥126 mg/dL& ≤ 200 mg/dL and/or two hours Post Prandial Plasma Glucose [PPG] ≥200 mg/dL and/or glycosylated haemoglobin [HBA1c] levels ≥7.5% and ≤10 % at screening) were included in the study.

Hence, Type 1 DM, pregnant and breastfeeding women, patients with hepatic and renal disease, and patients with any cardiovascular problems who are taking medicines and planning for surgery during the expected study timescale were also excluded from the study. The approval of the protocol and informed consent form are given by the Ethics Committee of the respective hospital which is performed in this study.

STUDY DESIGN AND STUDY PROTOCOL:

The entire group of 60 participants who suffered from type 2 Diabetes Mellitus was screened and were split up into groups of two i.e., Group 1 was given sitagliptin+metformin (50/500) mg/day and Group 2 was given glimepiride (1mg)/day appropriately.

Fasting blood sugar level (FBS) and post-prandial blood sugar (PPBS) levels were assessed on the day before starting the treatment. The patient is suggested to consult after 15 days of every month till 6 months for the quantification of blood glucose levels. Moreover, HBA1c was assessed along with it. If the patient experiences any hypoglycemic symptoms, then assessment should be required at any time, and any health difficulties should also documented.

Daily investigation of the blood sugar levels of participants is needed, and they come up with a good diet plan and adhere to physical activity. In the hospital laboratory, the glucose oxidase test was used to estimate blood glucose levels. FPG and PPG and HBA1c are assessed for the endpoints from the starting month to 6 months of the study period. Retrospective analysis is applied as a technique for studying records. This was done to give additional information on the data documented.

The power of the trial is greater than 80%, and the patient sample was determined based on the incidence of Type 2 Diabetes Mellitus in the anticipated area. The data was signed for statistical analysis using the unpaired t-test. A statistically significant value was defined as one with a probability value less than ($p<0.05$). SPSS was utilized to perform each statistical analysis that was conducted on the window.

RESULTS AND DISCUSSION:

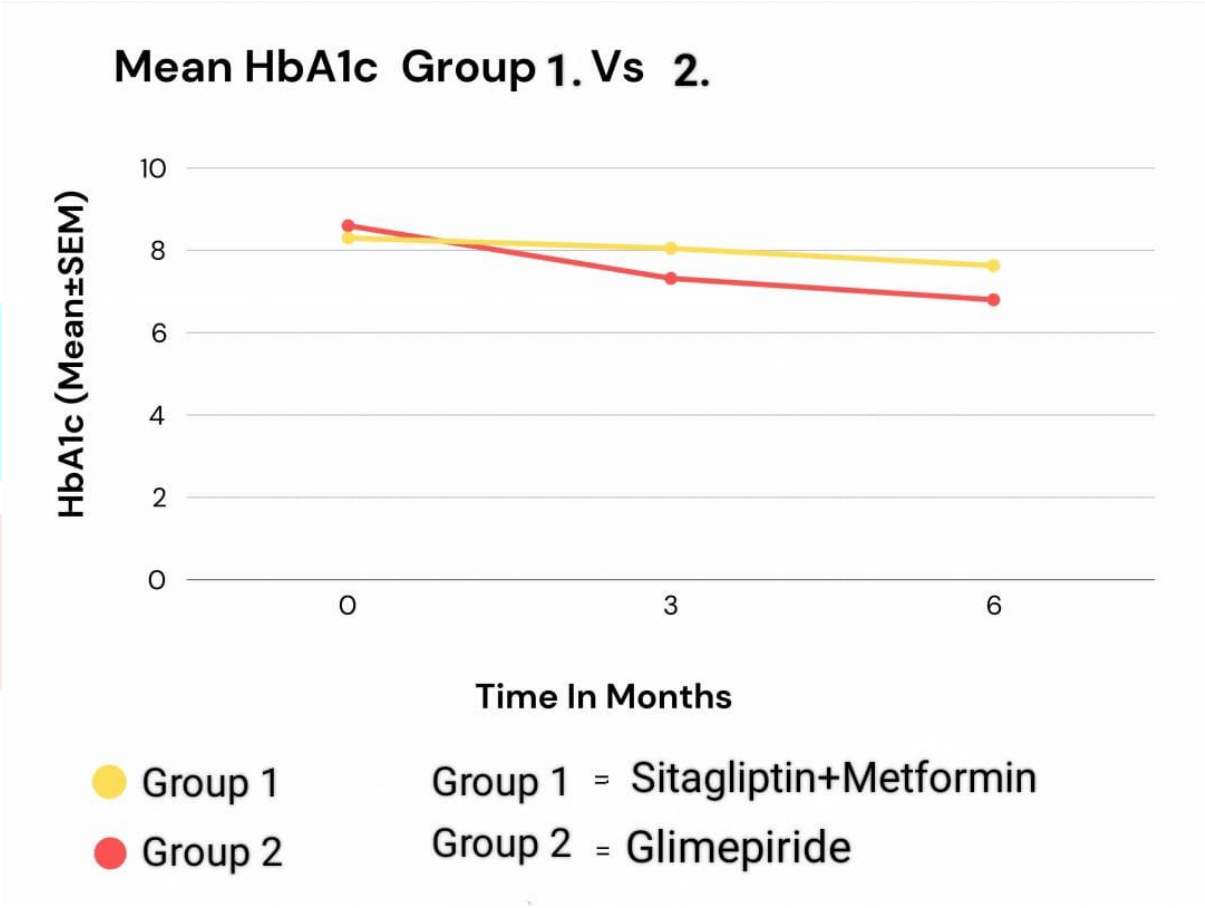
Mean fasting blood glucose levels should be obtained before the treatment has been received, and they were considerably decreased upon analyzing the fasting blood glucose levels, ranging from zero to six months, both within and between the groups post treatment. Notable differences have been discerned. There has been significant variation in the mean blood glucose levels among the different treatment groups.

In assessing the glycemic control, there was a notable($p<0.001$), yet minor reduction in the average glucose levels recorded over a period of zero to six months, relative to the initial fasting and post-prandial glucose levels

noted prior to the start of treatment in the group. A highly notable ($p<0.001$) glycemic control Comparing to the mean fasting and post-prandial blood glucose levels within the zero to six month therapy period in group 1, an exceptionally noteworthy glycemic control was observed.

A minor reduction in all recorded blood glucose levels which were tracked from the commencement of treatment until six months later. These levels were compared to the average blood glucose levels obtained one day prior to the initiation of therapy. A striking difference ($p<0.001$) in glycemia was observed when comparing the average fasting and post-prandial blood glucose measurements between the onset of therapy and after six months within group 2.

Fig.1: **Graph Difference Between HbA1c Group A Vs B**



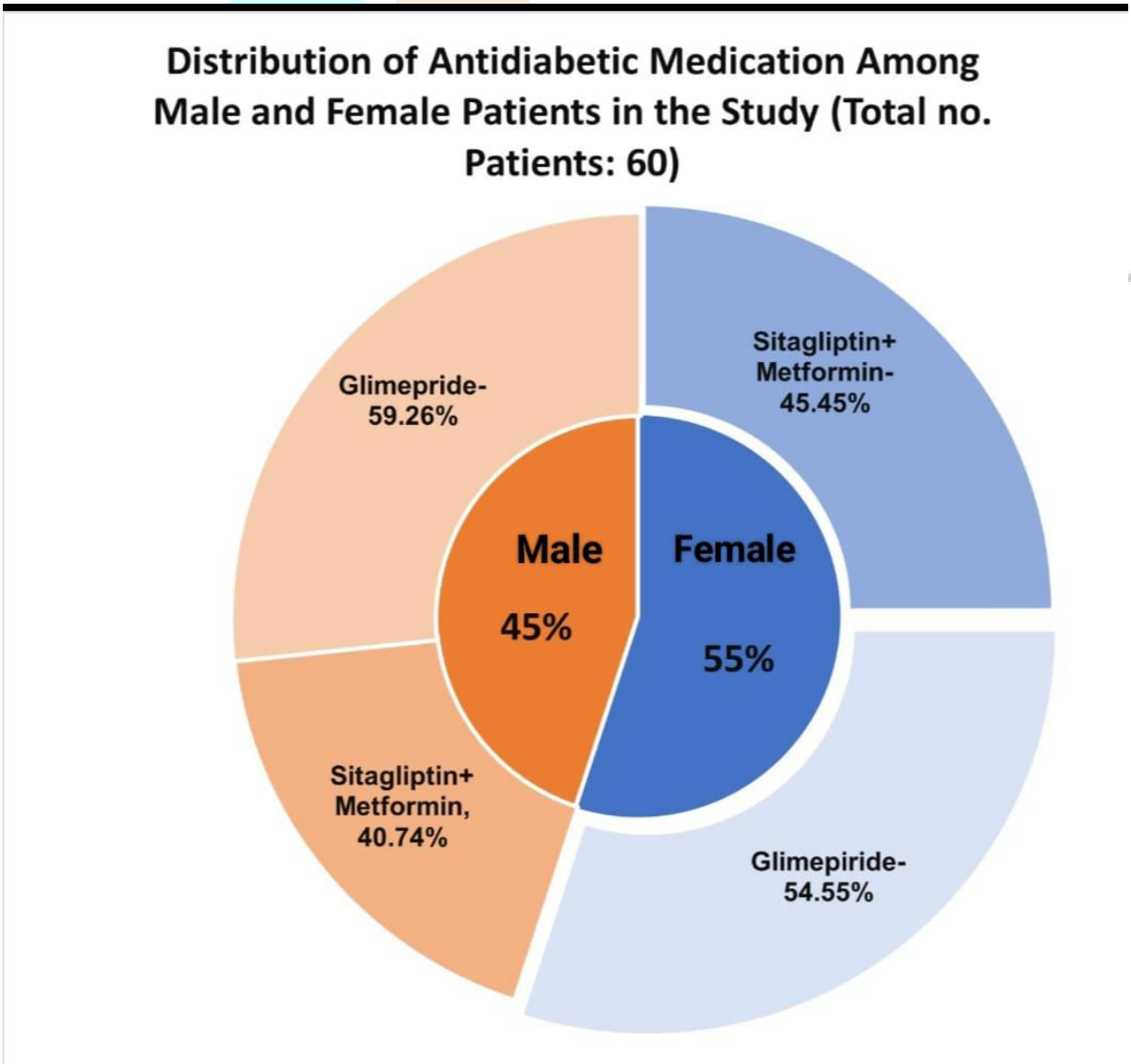
In the assessment of attained glycemic control across both treatment groups, we observed a significant reduction ($p<0.001$) between Group 1 and Group 2. In our evaluation, each patient's HBA1c level was utilized as a standard measure to gauge glycemic control within both patient groups. A considerable variation was observed in the HBA1c levels after three and six months compared to the initial HBA1c reading taken at the beginning of the treatment (zero-month) in Group 1, who were administered a combination therapy of sitagliptin and metformin. Similarly, a notable difference ($p<0.001$) was detected in the HBA1c readings pre- and post-treatment for patients of Group 2 who were treated solely with glimepiride. Upon comparison of HBA1c levels between the two groups, a significant disparity ($p<0.001$) was evident at six month.

Diabetes mellitus, which is considered the most common endocrine disorder globally, is characterized by a partial or complete deficit in insulin production. Given that India has the highest rate of diabetes worldwide, according to WHO estimates, India is in the first rank in the world. India is projected to have 80 million people

with diabetes by 2030. Even though there has been no cure for diabetes up to this point, the present management methods are only means to an end; they cannot heal. Consequentially, several more novel medications are made available as monotherapy and set dosage regimens for the management of type 2 diabetes mellitus. Individuals diagnosed with Type 2 Diabetes Mellitus are managed with DPP IV inhibitors. As a result, several additional novel medications have been developed and are now available as monotherapy with established dosage regimens for the management of Type 2 Diabetes Mellitus. DPP-4 inhibitors.

Individuals diagnosed with Type 2 Diabetes Mellitus are managed with DPP IV inhibitors. These can be used as a standalone treatment or in conjunction with continued oral anti-diabetic drugs. A recently developed class of medications, are a worthy mention in this context. However, there is not much scientific literature comparing the clinical outcomes of these. Therefore, it was deemed valuable to examine and contrast the clinical results for glycemic management with sitagliptin plus metformin and glimepiride alone, as well as the frequency of negative medication responses.

Fig.2: **Distribution of Antidiabetic Medication Among Male and Female patients**

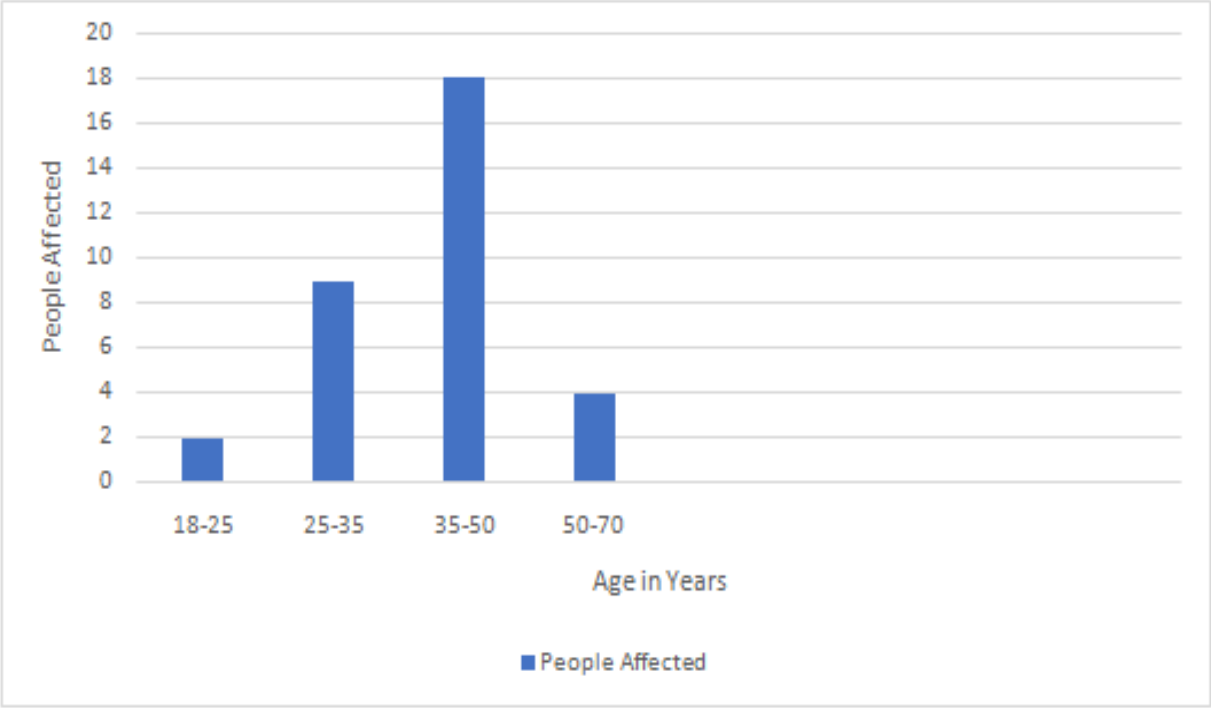


In our study, we included 60 patients diagnosed with Type 2 Diabetes Mellitus, comprised of 27 males and 33 females. Among 33 females, 15 were treated with a Sitagliptine+Metformin combination and 18 were treated with

Glimepiride. Among 27 males, 11 were treated with a Sitagliptine+Metformin combination and 16 were treated with Glimepiride.

Fig.3: **Bar graph presentation according to the age of females with effected people**

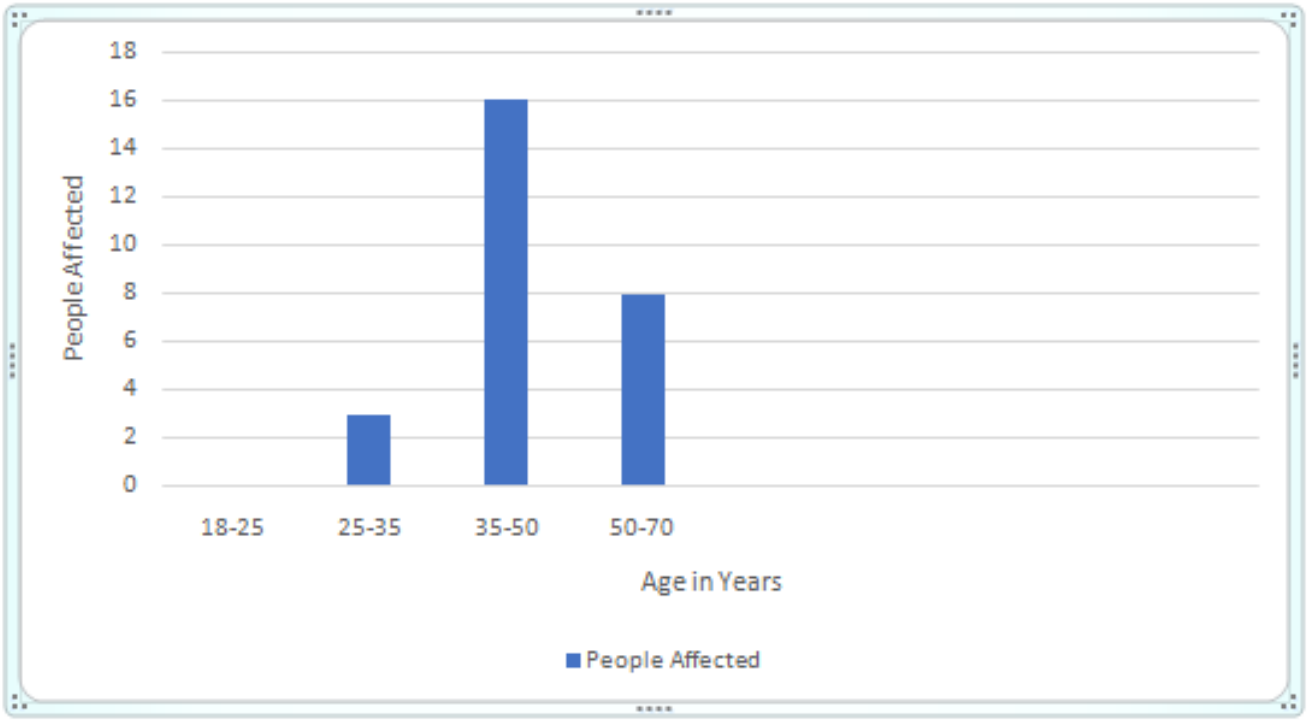
Females Age Group	People Affected
18-25	2
25-35	9
35-50	18
50-70	4



The above bar graph represents information about how the female was affected by the drugs. While accessing their glycemic control, the number of people affected among the female group is indicated in the above bar graph. A total of 33 people were affected between the ages of 18 and 70. In this, 2 people were affected between the ages of 18 and 25, 9 people were affected between the ages of 25 and 35, 18 people were affected between 35 and 50, and 4 people were affected between the ages of 50 and 70.

Fig.4: **Bar graph presentation according to the age of males with effected people**

Males Age Group	People Affected
18-25	0
25-35	3
35-50	16
50-70	8



The above graph represents information about how the males were affected by the drugs. While assessing their glycemic control, the people affected by the male group are indicated in the above graph. A total of 27 people were affected between the ages of 18 and 70. In this, 0 people were affected between the ages of 18 and 25, 3 people were affected between the ages of 25 and 35, 16 people were affected between 35 and 50, and 8 people were affected between the ages of 50 and 70.

The clinical trial encompassed a collective of 60 individuals suffering from type 2 Diabetes mellitus. Our esteemed patients were categorized into two distinct cohorts, labeled as Group 1 and Group 2, which each got a mix of glimeperide and sitagliptin + metformin respectively. The glycemic control was the most often evaluated admission result, control as well as the frequency of unfavourable medication responses. When contrasting the average blood levels after eating and fasting glucose measured before beginning of the therapy using mean recording of postprandial glucose levels and fasting, a statistically significant difference after one month exists in the two groups.

These findings corroborate research that found that individuals receiving a combination of therapies had a considerable drop in their mean blood glucose levels: Glimepiride on its own and sitagliptin with metformin.[15-17] When contrasting the glycemia control attained by Sitagliptin with metformin treatment, it is statistically significant. A variation in the average blood glucose levels was noted, for a duration of six months to zero months. An important There was a difference ($P<0.001$) between the HbA1c comparisons. Upon the initiation of therapy, the HbA1c was measured at zero. Month-long therapy in group A, Who received care with metformin

+ sitagliptin. These outcomes are consistent with research highlighting the significant drop in HbA1c levels among those receiving a mix of simultaneous Metformin.[18-21]

Additionally, a significant discrepancy was observed among the HbA1c levels gathered at the third and sixth month, as compared to the HbA1c level recorded during the initial(0) month period in Group 2, patients who underwent exclusive Glimepiride therapy.[17] These findings are consistent with research that mentioned the significant drop in HbA1c levels among those receiving treatment for glimepiride alone. When contrasting the occurrence of medication side effects, decreased prevalence of hypoglycaemia in patients being treated with a regimen consisting of metformin and sitagliptin.

On the other hand, patients treated with glimepiride alone experienced more hypoglycemic episodes compared to those treated with sitagliptin+metformin combination. A statistically significant difference in hypoglycemic episodes is important. These outcomes are consistent with earlier research.[22,23] However, the frequency of negative medication responses such as GIT issues, which include nausea and vomiting, and both groups reported experiencing stomach pain. However, there was no clinically relevant difference observed.

Weight loss was noted in individuals receiving treatment with metformin + sitagliptin. These outcomes resemble previous research that revealed a notable decrease in weight.[24] However, weight growth rather than weight decrease was seen. It was noted in those receiving glimepiride treatment alone. These results are in agreement with earlier research indicating a notable increase in weight managed with glimepiride.[22]

CONCLUSION:

Our study shows that there is a notable difference between the usage of glimepiride alone in type-2 DM patients and combination therapy of sitagliptin+metformin in terms of clinical outcomes related to control of glycemic levels and the incidence of unfavorable drug reactions. More specifically, when glimepiride was administered alone, the combination of sitagliptin and metformin showed superior control over blood sugar and a lower rate of adverse drug reactions. Based on these findings, it can be concluded that, in contrast to glimepiride single therapy, the sitagliptin+metformin combination could offer type-2 diabetes patients with improved glycemic control and potentially decreased risk of adverse drug reactions.

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