**ORIGINAL ARTICLE**

# Comparison of mean HbA1c with Sitagliptin plus Metformin Versus Glimepride plus Metformin for the Management of Uncontrolled Type 2 Diabetes Mellitus

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## ABSTRACT

**Aim:**To compare the mean HbA1c with Sitagliptin plus Metformin versus Glimepiride plus Metformin for management of cases presenting due to Uncontrolled Type 2 Diabetes Mellitus**.**

**Methods:** This was a research randomized control trial that was planned and executed at Department of Medicine, Mayo hospital Lahore for 6 months (Date: 1st June 2016 to 31st November).The Non-probability purposive sampling was used. All patients were randomly divided in two equal groups by using lottery method. Blood sample was obtained and was sent to laboratory of hospital for assessment of baseline HbA1c. Patients in S group were given sitagliptin and patients in G group were given glimepiride. Initially patients were given dose of 50/100mg per day sitagliptinand of1/2 mg per day glimepiride. Dose of metformin was not changed throughout research.

**Results:** The mean age of the patients was 57.36±11.91 years, the male to female ratio of the patients was 1.7:1. The mean HbA1c baseline was 8.30±0.72 and the mean HbA1c at 12th week was 6.39±1.13. The mean HbA1c at 12 week in sitagliptin group was 5.39±0.45 and meanHbA1c in glimepiride group was 7.38±0.61. Significant difference was found between the study groups and HbA1c at 12th week i.e. p-value=0.000.

**Conclusion:** It has been proved by our study that at 12thweek significant lower mean value of HbA1c with Sitagliptin plus Metformin was found as compared to Glimepiride plus Metformin for controlling the level of diabetes mellitus in the cases of Uncontrolled Type 2 Diabetes Mellitus.

**Keywords:**Type 2 Diabetes Mellitus, Metformin, Sitagliptin, Glimepiride, HbA1c

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a perpetual dynamic morbidity that regularly requires blend of anti-diabetic medications with various mechanism of activity to accomplish glycaemic targets[1,2,3]. In Pakistan, out of 19211 subjects, 1677(8.73%) patients were found to have T2DM, with a total of 1258 (6.55%) were of known while few 419(2.18%) were those who were not having history of T2DM[4].

The comprehensively utilized combination of metformin and a sulphonylurea (SU) remained non activated to keep up glycaemic control after some time and the incorporation of a 3rd anti-hyperglycaemic drug is required[5].

Metformin is the most broadly endorsed first-line specialist for the administration of T2DM and is standard first-line pharmacotherapy, alongside eating routine and exercise[6].

Treatment with a solitary antihyperglycemic medicine is regularly unsuccessful in accomplishing as well as keeping up glycemic control in patients with T2DM, and numerous patients require a combination of antihyperglycemic agents.[7] When metformin alone remains non effective to keep up adequate glycaemic control, the secondary option is opted by addition of sitagliptin or glimepiride might be powerful in controlling glycemic contro[8].

Sitagliptin is an oral, once-day by day, strong, and profoundly particular dipeptidyl peptidase-4 (DPP-4) inhibitor for the treatment of T2DM[7].

One study has reported that mean HbA1c (%) after 12 weeks of addition of Sitagliptin plus Metformin in uncontrolled T2DM was 7.784±0.423% (n=25) while with Glimepiride plus Metformin was 7.480±0.398% (n=25). It was not the groups were statistically different in terms of effectiveness. (P=0.012)[9].

But another study found that mean HbA1c (%) after 12 weeks of addition of Sitagliptin plus Metformin in uncontrolled T2DM was 6.93±0.31% (n=21) while with Glimepiride plus Metformin was 6.98±0.31% (n=19). The dissimilarity between both the groups was insignificant (P=0.678) and authors concluded that Sitagliptin is not superior that the glimepiride in reducing HbA1C[10].

Some studies supported this evidence and reported that in patients with type 2 diabetes and insufficient glycaemic control on metformin monotherapy, the expansion of sitagliptin or glimepiride prompted comparable change in glycaemic control even following 30 weeks[11].

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Rationale of this study is to compare the mean HbA1c with Sitagliptin plus Metformin versus Glimepiride plus Metformin for management of patients presenting with Uncontrolled Type 2 Diabetes Mellitus. It has been observed through literature that if Sitagliptin is given alongwith metformin for management or control of uncontrolled T2DM, it is more beneficial that glimepiride plus metformin. But controversial evidences have also been observed which showed that both have equal effectiveness in controlling the uncontrolled T2DM as two studies have been mentioned above[9,10].

## MATERIALS AND METHODS

One hundred consecutive patients were selected for this study. By design, it was randomized control trial was done at Medical Department of Mayo hospital Lahore. The study was conducted for 6 months from 1st June 2016 to 31st November. Non probability sampling was used in this study. Informed consent was contained from all patients. Their demographic information(name, age, gender, address and contact) was also noted.100 patients who fulfilled specific criteriafor selection were enrolled in the study. All patients were randomly divided into two equal groups. Blood samples were obtained and sent to the laboratory of hospital for assessment of baseline HbA1c. Both groups were compared by using t-test for mean HbA1c after 12 weeks. P-value ≤ 0.05 was considered significant. Patients in S group were given sitagliptin and pts in G group were given glimepride. Starting dose of sitaglitin was 50/100mg once daily and for glimepride was 1/2mg once daily. Dose of metformin wasbarely kept constant. Patients were advised to visit OPD after 6 weeks and then after 12 weeks. Blood was obtained on 12th week and samples were sent to laboratoryof the hospital for assessment of HbA1c.

## RESULTS

Average age of participants was 57.36±11.91 years with a age range of 40 & 78 years respectively (Table 1). In our study 64% patients were males and 36% patients were females. The male to female ratio of the patients was 1.7:1 (Fig.1).The study results showed that the mean T2DM duration was 4.81±2.87 years with minimum and maximum duration of 1 & 9 years respectively(Table 2).

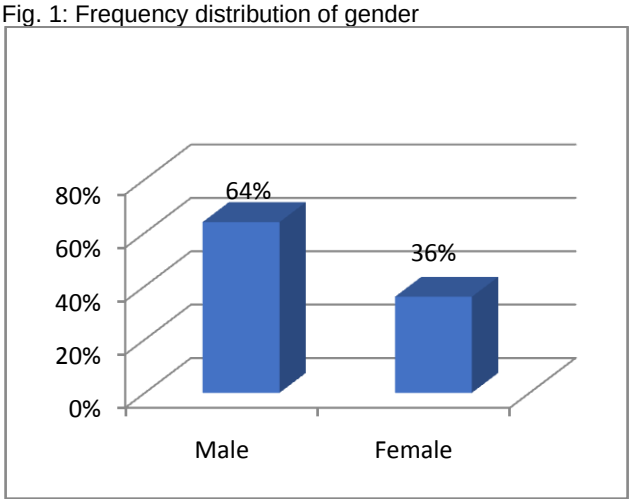
The study results showed that the mean HbA1c baseline was 8.30±0.72 and the mean HbA1c at 12th week was 6.39±1.13 (Table 3).

In this study the mean value of HbA1c at 12 week in sitagliptin group was 5.39±0.45 and its mean value in glimepiride group was 7.38±0.61. Statistically significant difference was found between the study groups and HbA1c at 12th week of the patients. i. e p-value=0.000 (Table 4).

The study results showed that in below 55 years patients, the mean HbA1c value at 12th week in sitagliptin group was 5.38±0.46 and its mean value in glimepiride was 7.25±0.58, similarly in above 55 years patients, the mean HbA1c value at 12th week in sitagliptin group was 5.41±0.45 and its mean value in glimepiride was 7.48±0.62. Statistically significant difference was found between the HbA1c at 12th week and study groups of the patients stratifying by age. i. e p-value=0.000, 0.000 (Table 5).

The study results showed that male patients, the mean HbA1c value at 12th week in sitagliptin group was 5.34±0.45 and its mean value in glimepiride was 7.39±0.61, similarly in female patients, the mean HbA1c value at 12th week in sitagliptin group was 5.50±0.45 and its mean value in glimepiride was 7.37±0.63. Statistically significant difference was found between the HbA1c at 12th week and study groups of the patients stratifying by gender i.e., pvalue=0.000, 0.000 (Table 6).

Fig. 1: Frequency distribution of gender




The study results showed that in below 5 years DM duration patients, the mean HbA1c value at 12th week in sitagliptin group was 5.46±0.45 and its mean value in glimepiride was 7.31±0.59, similarly in above 5 years DM duration patients, the mean HbA1c value at 12th week in sitagliptin group was 5.31±0.44 and its mean value in glimepiride was 7.46±0.64. Statistically significant difference was found between the HbA1c at 12th week and study groups of the patients stratifying by DM duration i.e., p-value=0.000, 0.000 (Table 7). The study results showed that in below 8 HbA1c at baseline patients, the mean HbA1c value at 12th week in sitagliptin group was 4.91±0.32 and its mean value in glimepiride was 6.84±0.39, similarly in above 8 HbA1c at baseline patients, the mean HbA1c value at 12th week in sitagliptin group was 5.61±0.32 and its mean value in glimepiride was 7.78±0.41.

Statistically significant difference was found between the HbA1c at 12th week and study groups of the patients stratifying by HbA1c at baseline i.e., p-value=0.000, 0.000 (Table 8).

Table 1: Descriptive statistics of age (years)

| | | |
|---|---|---|
| Age (years) | N | 100 |
| | Mean | 57.36 |
| | SD | 11.91 |
| | Minimum | 40 |
| | Maximum | 78 |

Table2: Descriptive statistics of duration of DM

| | | |
|---|---|---|
| DM duration | n | 100 |
| | Mean | 4.81 |
| | SD | 2.87 |
| | Minimum | 1 |
| | Maximum | 9 |

Table3: Descriptive statistics of duration of DM at baseline and at 12th week

| HbA1c | At baseline | At 12th week |
|---|---|---|
| n | 100 | 100 |
| Mean | 8.30 | 6.39 |
| SD | 0.72 | 1.13 |
| Minimum | 7.1 | 4.5 |
| Maximum | 9.5 | 8.6 |

Table4: Comparison of DM duration at 12th week with study groups

| HbA1c at 12th week | Study Groups | |
|---|---|---|
| | Sitagliptin | Glimepiride |
| n | 50 | 50 |
| Mean | 5.39 | 7.38 |
| SD | 0.45 | 0.61 |

Pvalue=0.000 Tvalue=-18.35

Table5: Comparison of DM duration at 12th week with study groups stratifying by age

| Age (years) | Study Groups | HbA1c at 12th week | p-value |
|---|---|---|---|
| < 55 | Sitagliptin | 5.38±0.46 | 0.000 |
| | Glimepiride | 7.25±0.58 | |
| ≥ 55 | Sitagliptin | 5.41±0.45 | 0.000 |
| | Glimepiride | 7.48±0.62 | |

Table6: Comparison of DM duration at 12th week with study groups stratifying by sex

| Gender | Study Groups | HbA1c at 12th week | p-value |
|---|---|---|---|
| Male | Sitagliptin | 5.34±0.45 | 0.000 |
| | Glimepiride | 7.39±0.61 | |
| Female | Sitagliptin | 5.50±0.45 | 0.000 |
| | Glimepiride | 7.37±0.63 | |

Table7: Comparison of DM duration at 12th week with study groups stratifying by DM duration

| DM duration | Study Groups | HbA1c at 12th week | p-value |
|---|---|---|---|
| < 5 years | Sitagliptin | 5.46±0.45 | 0.000 |
| | Glimepiride | 7.31±0.59 | |
| ≥ 5 years | Sitagliptin | 5.31±0.44 | 0.000 |
| | Glimepiride | 7.46±0.64 | |

Table8: Comparison of DM duration at 12th week with study groups stratifying by HbA1c (baseline)

| HbA1c (Baseline) | Study Groups | HbA1c at 12th week | p-value |
|---|---|---|---|
| <8% | Sitagliptin | 4.91±0.32 | 0.000 |
| | Glimepiride | 6.84±0.39 | |
| ≥ 8% | Sitagliptin | 5.61±0.32 | 0.000 |
| | Glimepiride | 7.78±0.41 | |

## DISCUSSION

T2DM is a dynamic sickness portrayed by debilitated beta cell work, and decreased insulin affectability and secretion. Metformin, an ordinarily utilized oral antihyperglycemic specialist, both as monotherapy and in mix with different operators diminishes increased blood glucose levels by lessening hepatic glucose yield and furthermore by enhancing insulin resistance[9].According to our study results mean value of HbA1c at 12 week in sitagliptin group was 5.39±0.45 and its mean value in glimepiride group was 7.38±0.61. Noteworthy distinction was found between the review groups and HbA1c at twelfth week of the patients i.e., p-value=0.000. A portion of the reviews are talked about beneath demonstrating the outcomes for our review as.

Janssen-Cilag International NV (Janssen) today reported outcomes from a post-hoc examination which demonstrated that at 52 weeks, canagliflozin gave diminishments in both HbA1c and body weight in more patients with type 2 diabetes mellitus as an extra to metformin, when contrasted and sitagliptin 100mg or glimepiride[12].

The combination has additionally been very much endured in 24-week clinical trials with insulin and glimepiride (Amaryl, Sanofi). The sitagliptin/metformin mixture (Janumet) might be most proper in patients near their HbA1c objective who are taking double antihyperglycemic operators or in those encountering hypoglycemia with their present regimen[13,14].

Hermansen et al[15] followed up a 24-week examination of sitagliptin versus placebo treatment in patients insufficiently controlled on glimepiride±metformin treatment. At 24 weeks, sitagliptin treatment had fundamentally decreased HbA1c by 0.74% general contrasted and placebo treatment, with the most articulated mean lessening in HbA1c (0.89%) found in the group that had been treated with each of the three dynamic medications.

One study has reported that mean HbA1c (%) after 12 weeks of addition of Sitagliptin plus Metformin in uncontrolled T2DM was 7.784±0.423% (n=25) while with Glimepiride plus Metformin was 7.480±0.398% (n=25). The difference between both the groups was significant (P=0.012)[9].

Some studies supported this evidence and reported that in patients with T2DM, furthermore,

insufficient glycaemic control on metformin monotherapy, the expansion of sitagliptin or glimepiride prompted comparable change in glycaemic control even following 30 weeks[11].

A review directed by Chwieduk CM[16] demonstrated that extra treatment in treatment-experienced patients with deficient glycaemic control, the HbA(1c)- bringing down adequacy of sitagliptin in addition to metformin was noninferior to that of glimepiride in addition to metformin in a 30-week, twofold visually impaired trial.

One review by Chung et al[17] introduced that impacts of sitagliptin kept going over 12 weeks in more seasoned patients with a higher pattern HbA1c, and slower lessening of HbA1c amid 12 weeks. Then again a post-hoc investigation of pooled information from three randomized, twofold visually impaired investigations of 373 elderly (matured ≥65 years) patients analyzed the impacts of sitagliptin versus glipizide or glimepiride added to metformin or eating regimen alone. At 30 weeks, both HbA1c and FBG levels had diminished in both the sitagliptin and sulfonylurea treatment groups, with no factually noteworthy contrasts between treatment modalities[18].

But another study found that mean HbA1c (%) after 12 weeks of addition of Sitagliptin plus Metformin in uncontrolled T2DM was 6.93±0.31%% (n=21) while with Glimepiride plus Metformin was 6.98±0.31% (n=19). The mean change in the glycemic level was in groups was insignificant (P=0.678) and authors concluded that Sitagliptin is not superior that glimepride in controlling the blood sugar level assessed by HbA1C[10].

## CONCLUSION

It has been proved by our study that at 12$^{th}$week significant lower mean value of HbA1c with Sitagliptin plus Metformin was found as compared to Glimepiride plus Metformin for management of patients presenting with Uncontrolled Type 2 Diabetes Mellitus. So we can say that Sitagliptin plus Metformin is suitable combination therapy for the management of uncontrolled type 2 DM.

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