

Comparison of Outcome of Combined Oral Anti-Diabetics to that of Insulin Therapy in the Management of Type II Diabetes Mellitus

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ABSTRACT

Background: The prevalence of diabetes mellitus has increased due to urbanization, lifestyle changes and genetic susceptibility. Management of diabetes required lifestyle modification and anti-diabetic pharmacotherapies. Purpose of this study was to compare the outcome of combined oral anti diabetic to that of insulin therapy in the management of Type II diabetes mellitus.

Materials and Methods: An observational study was conducted at Endocrinology Outpatient Department of Dhaka Medical College Hospital, Dhaka and Outpatient Department of Ibrahim General Hospital, Mirpur, Dhaka over a period of one year (July 2018 to June 2019). Total 110 Type II diabetic patients were selected purposively. The patients were divided into two groups. In group I, 55 patients treated with gliclazide (80mg) and metformin (500mg) combination therapy twice daily for consecutive 12 weeks and in group II, 55 patients treated with Insulin (premixed 30/70) twice daily for consecutive 12 weeks.

Results: After 12 weeks of treatment HbA1c level reduced from (mean \pm SD) $8.94 \pm 0.91\%$ to $7.82 \pm 1.86\%$ in group I and $10.07 \pm 1.28\%$ to $7.90 \pm 1.01\%$ in group II. FBG level reduced from 10.05 ± 1.57 mmol/l to 7.96 ± 1.62 mmol/l in group I and 11.61 ± 2.62 mmol/l to 7.60 ± 1.23 mmol/l in group II. Blood glucose 2 hours ABF level reduced from 14.00 ± 2.04 mmol/l to 10.99 ± 1.41 mmol/l in group I and 16.70 ± 3.61 mmol/l to 10.71 ± 1.52 mmol/l in group II. In group I, 36.4% patients achieved HbA1c target level, 40% patients achieved FBG target level and 25.5% patients achieved blood glucose 2 hours ABF target level. In group II, 29.1% patients achieved HbA1c target level, 56.4% patients achieved FBG target level and 29.1% patients achieved blood glucose 2 hours ABF target level. But on comparison there was statistically no significant difference between two groups.

Conclusion: Metformin and gliclazide combination therapy showed less hypoglycemic effect, greater patient compliance and better adherence than premixed insulin. So, they may be prescribed to the patients who are prone to be hypoglycemic and insulin for patients in whom too strict glycemic control is needed.

Keywords: Type II DM, Glycaemic Control, Oral Hypoglycaemic agent Vs Insulin.

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INTRODUCTION

Diabetes is a chronic metabolic disease characterized by insulin secretion or action abnormalities that cause hyperglycemia. The two main kinds of diabetes mellitus are type II, which is more frequent and type I, which usually develops in childhood or adolescence and produces absolute insulin insufficiency due to pancreatic beta cell death¹. The prevalence of diabetes mellitus is rising globally. According to IDF 2025 an

estimated 589 million adults aged 20-79 years are currently living with diabetes that represent 10.5% of world's population of this age and by 2045, the number may rise to 852.5 million. Around 3.4 million deaths worldwide per year due to diabetes and its complications. In Bangladesh about 13.9 million people are diabetic with a prevalence of 14.2% in adult population (20-79 years). Bangladesh is in the 8th position in the world by the total number of people

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with diabetes and by the year 2050 it is projected to move to the 7th position with 23.1 million type II DM patients².

Severe micro- and macrovascular complications are common in patients with diabetes, particularly in those with poor glycemic control. Most adults with diabetes have at least one comorbid chronic disease and up to 40% have at least three. Up to 75% of adults with diabetes also have hypertension. Other common comorbidities of diabetes are dyslipidemia, cardiovascular disease, kidney disease, non-alcoholic fatty liver disease and obesity³. Type II diabetes is the most common form of diabetes mellitus which accounts for 90% to 95% of all diabetes patients. Lifestyle has a great importance to development of type II diabetes mellitus such as obesity, sedentary life style, physical inactivity, smoking, alcohol consumption⁴. Dietary and Life style modification are the first approach to maintain optimum glycemic control. If the desired level of glycemic control is not achieved with diet and exercise, pharmacological intervention is required. Oral and injectable anti diabetic drugs are used on the basis of effectiveness, cost, risk of hypoglycemia, weight gain and patients preference⁵.

Metformin is established as first line monotherapy. It reduced hepatic glucose production, increasing uptake and utilization of glucose in tissues and improve insulin sensitivity in type II diabetic patients. Metformin does not cause weight gain and hypoglycemia. Gliclazide is a second-generation sulfonylurea drug. It stimulates the production of insulin from beta cell of pancreas and improves insulin resistance in peripheral target tissues. It causes hypoglycemia and weight gain⁶. Metformin plus gliclazide combination therapy is effective at improving glycemic control in patients with type II diabetes insufficiently controlled by monotherapy⁷.

Insulin therapy reduces microvascular complications and lowers macrovascular risk in type II diabetes. Weight gain and hypoglycemia is associated with insulin therapy. Hypoglycemia may occur from a mismatch between insulin and diet⁸.

This study gives an idea about effects & outcome of glycemic control by combination therapy of gliclazide-metformin versus insulin in type II diabetes mellitus patients.

MATERIALS & METHODS

This observational outdoor-based study was conducted at Endocrinology Outpatient Department of Dhaka Medical College Hospital, Dhaka and the Outpatient Department of Ibrahim General Hospital, Mirpur, Dhaka. The study was carried out for a period of one year (July 2018 to June 2019). Ethical clearance was taken from ethical review committee of Dhaka Medical College Hospital and Ibrahim General Hospital authority. Total 110 type II diabetic patients of 30 to 70 years old were selected purposively. The patients were divided into two groups. In group I, 55 patients treated with gliclazide (80mg) and metformin (500mg) combination therapy twice daily for consecutive 12 weeks and in group II, 55 patients treated with Insulin (premixed 30/70) twice daily for consecutive 12 weeks. Baseline data of glycemic status HbA1c, fasting blood glucose (FBG), blood glucose 2 hours after breakfast and weight were recorded in a data collection form during first visit. About 110 patients were interviewed in each group and their baseline data were recorded during first visit. Then the patients were counseled for a follow up visit in the same diabetes center after 12 weeks with their investigation reports. In follow-up visit, information of HbA1c, fasting blood glucose (FBG), blood glucose 2 hours after breakfast, weight and any history of hypoglycemia in last 12 weeks were recorded in the data collection form. During follow-up visit about 55 patients were dropped out in each group because some patients did not come in follow up and some did not have any investigations which were advised.

All relevant information were collected, completed and compiled. Collected data was analyzed by SPSS 25.0. Student 't' test and chi-square test were done. The p value ≤ 0.05 was considered as statistically significant at 95% CI (confidence interval).

RESULTS

Demographic profile:

In this study mean age of the patients were 47.69 ± 8.58 years in group I and 50.78 ± 10.19 years in group II. Out of 110 cases male patients were predominant in both groups. In group I male were 31 and female were 24 and in group II male were 29 and female were 26. In group I family history positive 20 (36.4%) and in group II 23 (41.8%) respondents had positive family history. Mean duration of diabetes of the patients were 3.93 ± 2.6 years in group I and 5.38 ± 4.96 years in group II.

Table I: Demographic Profile of Study participants.

Demographic variable	Group-I (n=55)	Group-II (n=55)
Mean age (year)	47.69 ± 8.58	50.78 ± 10.19
Gender (Male/Female)	31/24	29/26
Family history positive (%)	20 (36.4%)	23 (41.8%)
Mean Duration of DM (year)	3.93 ± 2.6	5.38 ± 4.96

Glycemic comparison of the groups:

In this study it was observed that after 12 weeks of treatment mean HbA1c level significantly reduced from 8.94 ± 0.9% to 7.82 ± 1.86% in group I and 10.07 ± 1.28% to 7.90 ± 1.01% in group II (Figure 1). After 12-weeks of treatment HbA1c 7.82 ± 1.86% in group I and 7.90 ± 1.01% in group II. On comparison between two groups, statistically no significant difference (p = 0.711). Mean FBG level significantly reduced from 10.05 ± 1.57 mmol/l to 7.96 ± 1.62 mmol/l in group I and 11.61 ± 2.62 mmol/l to 7.60 ± 1.23 mmol/l in group II (Figure 2). After 12-weeks of treatment FBG, 7.96 ± 1.62 mmol/l in group I and 77.60 ± 1.23 mmol/l in group II. On comparison between two groups statistically no significant difference (p = 0.186). Mean blood glucose 2hrs ABF level significantly reduced from 14.00 ± 2.04 mmol/l to 10.99 ± 1.41 mmol/l in group I and 16.70 ± 3.61 mmol/l to 10.71 ± 1.52 mmol/l in group II (Figure 3). After 12-weeks of treatment blood glucose 2hrs ABF, 10.99 ± 1.41 mmol/l in group I and 10.71 ± 1.52 mmol/l in group II. On comparison between two groups statistically no significant difference (p = 0.308).

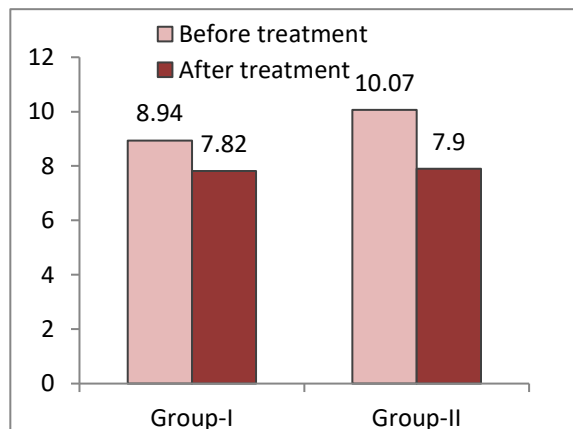


Figure 1: Changes in mean HbA1c before and after treatment.

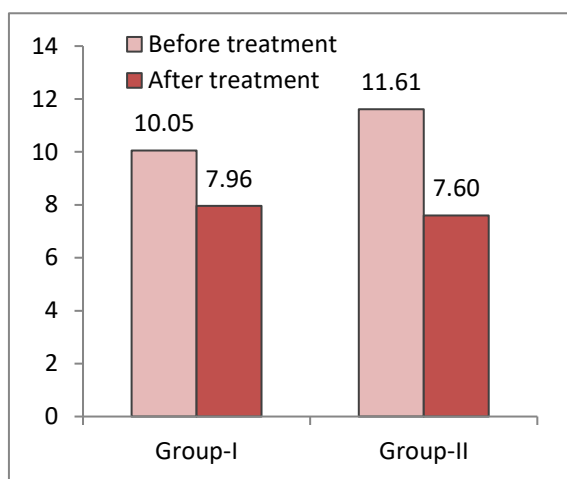


Figure 2: Changes in mean FBG before and after treatment (mmol/l)

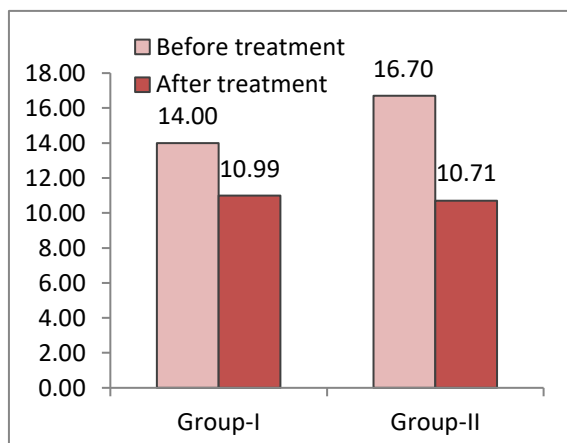


Figure 3: Changes in mean blood glucose level 2 hours after breakfast before and after treatment (mmol/l)

In this study, target level of HbA1c was set <7%, FBG 4.4-7.2 mmol/l and blood glucose 2hrs ABF <10 mmol/l according to American Diabetes Association guideline 2022. In group I, 20 (36.4%) patients achieved HbA1c target level, 22 (40%) patients achieved FBG target level, 14 (25.5%) patients achieved blood glucose 2 hours ABF target level. In group II, 16 (29.1%) patients achieved HbA1c target level, 31 (56.4%) patients achieved FBG target level, 16 (29.1%) patients achieved blood glucose 2 hours ABF target level.

Table II: Individuals achieved target glyceimic control (according to American Diabetic Association guideline, 2022) during study period. (Duration of treatment 12 weeks)

Investigations	Group I (n=55)	Group II (n=55)
	n (%)	n (%)
HbA1c (Diabetic ≥7%)	20 (36.4)	16 (29.1)
FBG (DM ≥7.0 mmol/l)	22 (40.0)	31 (56.4)
Blood glucose 2hrs ABF (DM≥11.1mmol/l)	14 (25.5)	16 (29.1)

Frequency of Hypoglycemic Episodes:

It was observed that 12 (21.8 %) patients had experienced hypoglycemia in group I and 15 (27.3%) patients experienced hypoglycemia in group II during the study period (Table III).

Table III: Distribution of respondents by hypoglycemia

Hypoglycemia	Group I (n=55)	Group II (n=55)	‘P’value
	n (%)	n (%)	
Present	12 (21.8)	15 (27.3)	0.658
Absent	43 (78.2)	40 (72.7)	

Weight change:

In group I, mean body weight was increased from 65.22 ± 9.36 kg to 65.27 ± 9.32 kg and in group II, mean body weight was increased from 63.07 ± 10.41kg to 63.67 ± 10.35 kg (Table IV). The change in mean body weight was not statistically significant after 12 weeks of treatment.

Table IV: The mean body weight changes in two study groups during the study period.

Body weight (kg)	Group I (n=55)	Group II (n=55)
	Mean ± SD	Mean ± SD
Before Treatment	65.22 ± 9.36	63.07 ± 10.41
After 12-wks treatment	65.27 ± 9.32	63.67 ± 10.35
‘p’ value	0.321	0.081

Patient Compliance and Adherence:

Adherence to therapy was better in the oral antidiabetic group, with 84% of patients reporting regular intake and minimal missed doses. In contrast, only 71% of patients in the insulin group demonstrated consistent compliance (table V). The complexity of insulin administration and fear of injections were the main reasons for reduced adherence in Insulin group.

Table V: Compliance and Adherence

Group	Good Compliance	Poor Compliance
Group I (n=55)	46 (84%)	09 (16%)
Group II (n=55)	39 (71%)	16 (19%)

DISCUSSION

This observational hospital-based study was carried out to comparison of the outcome of combined oral anti diabetic versus insulin therapy in type II diabetes mellitus management. This study showed highest respondents in age group 41 – 50 years which occupied 26 (47.3%) in group I and highest respondents in age group 51-60 years which occupied 17 (30.9%) in group II. These results are near to findings of Zakia, et al., 2013, in which that majority (50.7%) of patients was in age group 41-55 years⁹. Majority of patients were male. In group I male were 31 (56.4%) and in group II male were 29 (52.72%). Similar findings were found to the study done by Afroz, et al., 2019, which shown male 54.4% but Safita, et al., 2016, showed female patients (56.9%) are more than male patients (43.1%)^{10,11}. Educational status revealed maximum patients in both groups 21 (38.2%) respondents had completed their SSC. These results are near to findings of Latif, et al., 2017, in which that majority 34.6% were SSC¹². In case of occupation, predominant occupation was housewife, 40% in both groups. These results are near to findings of Vanderlee, et al., 2016, in which that predominant occupation 56% was housewife¹³. In this study family history positive 20 (36.4%) in group I and in group II 23 (41.8%) respondents had positive family history. Similar findings were found to the study done by Afroz, et al., 2019, in which showed that 34.6% patients have a positive family history¹⁰. In this study showed that duration of diabetes was (Mean ± SD) 3.93 ± 2.6 years in group I and 5.38 ± 4.96 years in group II, which was around similar to the study done by Zakia, et al., 2013, where duration of diabetes was (Mean ± SD) 6.3± 5.6 years⁹. Another study done by Afroz, et al., 2019, where duration of diabetes was (Mean ± SD) 10.7 ± 7.7 years¹⁰.

In this study it was observed that after 12 weeks of treatment mean HbA1c level significantly reduced from $8.94 \pm 0.9\%$ to $7.82 \pm 1.86\%$ in group I who were treated with metformin plus gliclazide and $10.07 \pm 1.28\%$ to $7.90 \pm 1.01\%$ in group II who were treated with premixed insulin. After 12-weeks of treatment, on comparison between two groups, statistically no significant difference ($p = 0.711$). Similar type of study was conducted by Vaughan, et al., 2017, in USA for 12 months found that there was significantly decreased HbA1c level by oral and insulin treated group. $11.25 \pm 2.1\%$ to $7.73 \pm 2.1\%$ in insulin group and $9.40 \pm 2.1\%$ to $7.22 \pm 1.7\%$ in oral group. But on comparison statistically no significant difference between two groups¹⁴.

Mean FBG level significantly reduced from 10.05 ± 1.57 to 7.96 ± 1.62 in group I and 11.61 ± 2.62 to 7.60 ± 1.23 in group II. After 12-weeks of treatment, on comparison statistically no significant difference ($p = 0.186$). This result is also similar to study done by Pasquel, et al., 2015 also showed that significant reduction of FBG in both groups. But there was statistically no significant difference between oral group and insulin group¹⁵. Mean blood glucose 2hrs ABF level significantly reduced from 14.00 ± 2.04 to 10.99 ± 1.41 in group I and 16.70 ± 3.61 to 10.71 ± 1.52 in group II. After 12-weeks of treatment, on comparison between two groups statistically no significant difference ($p = 0.308$). This result is also similar to the study done by Pasquel, et al., 2015 also showed that significant reduction of blood sugar 2 hours ABF in both groups. But there was statistically no significant difference between oral group and insulin group¹⁵.

In this study, target level of HbA1c was set $<7\%$ according to ADA guideline, 2022. 20 (36.4%) patients achieved HbA1c target level ($<7\%$) in group I and 16 (29.1%) patients achieved HbA1c target level ($<7\%$) in group II. Which was around similar to the study done by Pandit, 2016, in India also found that 7 of 26 patients (26.92%) of oral therapy achieved HbA1c target level ($<7\%$) and 11 of 34 patients (32.35%) of premixed insulin therapy achieved HbA1c target level ($<7\%$)¹⁶. Respondents experienced more hypoglycemia who were treated with premixed insulin than with metformin plus gliclazide (27.3% and 21.8% respectively) in this study, which was around similar to the study done by Pandit, 2016, in India¹⁶.

In present study mean baseline body weight was (Mean \pm SD) 65.22 ± 9.36 kg in group I and $63.07 \pm$

10.41 kg in group II. After 12 weeks of treatment there was increased mean body weight. From 65.22 ± 9.36 kg to 65.27 ± 9.32 kg in group I and from 63.07 ± 10.41 kg to 63.67 ± 10.35 kg in group II. The change in mean body weight was not statistically significant in both study groups. Similar type of study was conducted by Bharti, et al., 2025, in India with type II diabetes patients found there was significant increase in body weight in oral and insulin groups¹⁷.

Adherence to therapy was better in the oral antidiabetic group, with 84% of patients reporting regular intake and minimal missed doses. In contrast, only 71% of patients in the insulin group demonstrated consistent compliance. This result is also similar to the study done by Bharti, et al., 2025, in India where adherence to therapy was better in the oral antidiabetic group¹.

Conclusions

In the study both groups of drugs were found effective in controlling blood glucose. On comparison between two groups there was statistically no significant difference but individual group has unique beneficial effect. Metformin and gliclazide combination therapy showed less hypoglycemic effect, greater patient compliance and better adherence than premixed insulin. So, they may be prescribed to the patients who are prone to be hypoglycemic (elderly people, working people who do not take their meal properly). Premixed insulin causes higher reduction of HbA1c, FBG, blood glucose two ours ABF than metformin and gliclazide combination. So premixed insulin may prefer for patients in whom too strict glycemic control is needed. Patient education, frequent monitoring, and support systems, especially for insulin users, increase results.

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The authors have **No Conflict of Interest** with this article.

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