# Research in Pharmacy and Health Sciences

## Prescribing trends of antidiabetic drugs in diabetic and hypertensive diabetic patients in an urban tertiary care hospital of Bangladesh

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**ABSTRACT**

**Objective:** The present epidemiological study was conducted with the objectives of providing an insight into the current use of antidiabetic medications to diabetics and hypertensive diabetics in urban areas and determining how the patient factors influence the prescribing of antidiabetic medications. **Methodology:** Data of patients of past two years were collected from Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, Bangladesh. The details were entered in the structured patient profile form. Data were statistically analyzed using the Microsoft Excel 2007 software. **Result:** A total of 958 patient's data were collected and analyzed of which 632 (65.97 %) were males and 326 (34.03 %) were females. These patients were further categorized based on their age. 330 patients (34.45 %) belonged to the age group 20 - 44 years, 504 (52.61 %) to the age group 45 - 65 years and 124 (12.94 %) to the age group 65 – 80 years. 684 (71.4%) patients out of the 958 patients studied were suffering from coexisting hypertension. Co-existing hypertension was found to be more prevalent in the age group 45 - 65 years (67.69%) and was found more in females (84.04%). **Conclusion:** Metformin was the oral hypoglycemic which was the highest prescribed. In hypertensive diabetics Metformin and Pioglitazone were most frequently prescribed drugs. Biguanides and Insulin were the most commonly prescribed antidiabetics. A combination of two or more drugs of different classes was prescribed to hypertensive diabetics. It is necessary to have an improved understanding of the etiology and pathophysiology of diabetes to focus on research efforts appropriately.

**Keywords:** *Diabetic drugs, Diabetes, Hypertensive diabetes, Metformin, Insulin injection*.

## INTRODUCTION

Diabetes is a life-threatening global public health problem, afflicting approximately 5% population worldwide.[1,2,3] It is estimated by the World Health Organization that the number of people with diabetes would reach 300 million by 2025 throughout the world.[3] After cardiovascular and cancer diseases, diabetes is becoming the third 'killer' of mankind, because of its high prevalence, morbidity and mortality.[4] Actually the term diabetes mellitus (DM) describes a group of metabolic disorders characterized by a chronic hyperglycemic condition with disturbances of protein, fat and carbohydrate metabolism.[4] Two main types of diabetes mellitus are: i. Type 1 diabetes, is caused by lack of insulin secretion by beta cells, ii. Type 2 diabetes, is caused by decreased sensitivity of target tissues to insulin.[5] The reduced sensitivity to insulin is often called insulin resistance.[5] Insulin initiates its physiological effects by binding to a high affinity specific receptor

located on the plasma membrane. After binding to the receptor, insulin transmits its signal to the interior of the cell through a second messenger that influences enzymatic processes.[6] Insulin exhibits a multitude of effects in many tissues, with liver, muscle, and adipose tissue being the most important target organs for insulin action. The effects of insulin on carbohydrate metabolism include stimulation of glucose transport across muscle and adipocyte cell membranes, regulation of hepatic glycogen synthesis, and inhibition of glycogenolysis and gluconeogenesis.[6] Insulin regulates blood glucose levels by its effects on the liver and skeletal muscles. Normal blood glucose levels are maintained by sustenance of balance between hepatic glucose production and glucose utilization by the peripheral tissues.[7] The chronic hyperglycemia arising from uncontrolled diabetes mellitus accompanies long-term damage, dysfunction, and failure of various organs. Diabetes is a major risk factor for cardiovascular disease.[6] More than 75% of adults with diabetes have blood pressure (BP) levels >130/80 mm Hg. Hypertension is already evident in most patients with diabetes. Mortality is increased 7.2-fold when hypertension is present in patients with diabetes. [8, 9]

Life style management is apparently the cornerstone of management of diabetes mellitus. It is recognized as being an essential part of diabetes and cardiovascular disease prevention.[6] Lifestyle changes should have a significant role in managing hypertension in all patients with BP. These include weight loss, increase in physical exercise, reduction of alcohol intake, smoking cessation and, low sodium intake.[9, 10] It has a positive effect on long term health and quality of life. Moreover, the treatment of diabetes and hypertensive diabetes is based on oral hypoglycaemic or antidiabetic agents and insulin.[4] Different oral hypoglycemics have been in use to aid in maintenance of blood glucose level at the requisite threshhold in diabetics through distinct mechanisms.[11] It is hypothesized that all classes of oral antidiabetic drugs have significant glycemic control effect along with lipid lowering effect.[3] Metformin, glibenclamide, glipizide, glyburide, gliclazide, glimepiride, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol,voglibose, repaglinide, nateglinide, sitagliptin, saxagliptin, vildagliptin, and linagliptin all are effective oral antidiabetic drugs.[3] The present study was designed with the objectives of providing an insight into the current use of antidiabetic drugs to diabetic and hypertensive diabetic patients in urban areas and determining how the patient factors influence the prescribing of antidiabetic medications.

## METHODOLOGY

*Study Area:* The study was carried out in the Department of Endocrinology at Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, Bangladesh. It is a tertiary care teaching hospital. It runs a separate endocriology department supported by a separate ward and outpatient department (OPD). *Study period and study population:* The study was conducted from October, 2014 to March, 2015. The patients admitted in the department of Endocrinology and treated with antidiabetic drugs during the study period were included in the present study. A total of 1642 diabetic patients were registered during this time frame, of which 684 were suffering from coexisting hypertension. Hence, 958 diabetic and 684 hypertensive diabetic patients were considered for inclusion in this study. *Study design and study tools:* It was a hospital based descriptive observational study based on retrospective evaluations of the medical records at the Endocrinology Outpatient Department of BSMMU Hospital, Dhaka. Prescriptions of diabetic patients being treated at the hospital were included in this study. All registered patients medical records from October 2014 to March 2015 at the Endocrinology Outpatient Department were reviewed. A data collection form was used to collate the information from the patients' records, such as socio-demographic data, family and personal medical history and co-morbid medical complications. After collecting the data, the details were entered in the structured patient profile form. The patients were classified into different age groups. The data was classified as: 1- The different oral hypoglycemic drugs prescribed to diabetic patients depending on various factors such as age, sex etc. 2- The different oral hypoglycemic drugs prescribed to hypertensive diabetics based on factors such as age and sex. *Inclusion and exclusion criteria:* Patients suffering from Diabetes mellitus of both sexes attending outpatient department (OPD) of Endocrinology Department were included in the study. Diabetic patients having concurrent illnesses like hypertension were also included. Pregnant females suffering from Diabetes were excluded from the study. *Data analysis:* Descriptive statistics were used to analyze the data (frequency and percentages). Microsoft Office Excel 2007 software package was used for statistical analysis. Moreover, Chi square test was applied on data where the *p* value less than 0.05 were considered significant. The study protocol was approved by ethical research committee of Bangabandhu Sheikh Mujib Medical University Hospital, Dhaka, Bangladesh.

## RESULTS

*Characteristics of study population:* Data of 958 diabetic patients were collected and analyzed of which 632 (65.97 %) were males and 326 (34.03 %) were females (Table 2). These patients were further categorized based on their age. 330 patients (34.45 %) belonged to the age group 20 - 44 years, 504 (52.61 %) to the age group 45 - 65 years and 124 (12.94 %) to the age group 65 – 80 years (Table 1). 684 diabetic patients out of the 958 patients studied were suffering from coexisting hypertension. Co-existing hypertension was found to be more prevalent in the age group 45 - 65 years (67.69%) and was found more in females (84.04%) (Table 3 and 4).

**Table 1: Frequency distribution of anti-diabetic drugs based on age group of diabetic patients**

| Medicines | 20-44 years | | 45-65 years | | > 65 years | | Total | | Chi-square result |
|---|---|---|---|---|---|---|---|---|---|
| | number | % | number | % | number | % | number | % | P-value |
| Insulin Injection | 172 | 53.42% | 135 | 26.52% | 43 | 33.86% | 350 | 36.53% | 0.1886 |
| Glibenclamide | 7 | 2.17% | 32 | 6.29% | 11 | 8.66% | 50 | 5.22% | 0.9944 |
| Gliclazide | 87 | 27.02% | 358 | 70.33% | 60 | 47.24% | 505 | 52.71% | 0.0354* |
| Metformin | 165 | 51.24% | 251 | 49.31% | 105 | 82.68% | 521 | 54.38% | 0.0293* |
| Glimepiride | 111 | 34.47% | 193 | 37.92% | 49 | 38.58% | 353 | 36.85% | 0.1831 |
| Pioglitazone | 53 | 16.46% | 90 | 17.68% | 49 | 38.58% | 192 | 20.04% | 0.6542 |
| Repaglinide | 13 | 4.04% | 27 | 5.30% | 7 | 5.51% | 47 | 4.91% | 0.9959 |
| Acarbose | 18 | 5.59% | 62 | 12.18% | 10 | 7.87% | 90 | 9.39% | 0.9056 |
| Vildagliptin | 80 | 24.84% | 277 | 54.42% | 46 | 36.22% | 403 | 42.07% | 0.1105 |
| Sitagliptin | 90 | 27.95% | 129 | 25.34% | 79 | 62.20% | 298 | 31.11% | 0.3034 |
| Number of patients | 330 | | 504 | | 124 | | 958 | | |

*[ * Statistically significant results; P value < 0.05 ]*

**Table 2: Frequency distribution of anti-diabetic drugs based on sex of diabetic patients.**

| Medicines | Males | | Females | | Total | | Chi-square result |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | P-value |
| Insulin Injection | 242 | 38.29% | 108 | 33.13% | 350 | 36.53% | 0.1886 |
| Glibenclamide | 36 | 5.70% | 14 | 4.29% | 50 | 5.22% | 0.9944 |
| Gliclazide | 324 | 51.27% | 181 | 55.52% | 505 | 52.71% | 0.0354* |
| Metformin | 322 | 50.95% | 199 | 61.04% | 521 | 54.38% | 0.0293* |
| Glimepiride | 198 | 31.33% | 155 | 47.55% | 353 | 36.85% | 0.1831 |
| Pioglitazone | 110 | 17.41% | 82 | 25.15% | 192 | 20.04% | 0.6542 |
| Repaglinide | 28 | 4.43% | 19 | 5.83% | 47 | 4.91% | 0.9956 |
| Acarbose | 54 | 8.54% | 25 | 7.67% | 90 | 9.39% | 0.9556 |
| Vildagliptin | 282 | 44.62% | 121 | 37.12% | 403 | 42.07 | 0.1105 |
| Sitagliptin | 180 | 28.48% | 118 | 36.20% | 298 | 31.11 | 0.3034 |
| No. of patients | 632 | | 326 | | 958 | | |

*[ * Statistically significant results; P value < 0.05 ]*

**Table 3: Frequency distribution of various oral hypoglycemic drugs based on age group of hypertensive diabetic patients.**

| Medicines | 20-44 years | | 45-65 years | | > 65 years | | Total | | Chi-square result |
|---|---|---|---|---|---|---|---|---|---|
| | Number | % | Number | % | Number | % | Number | % | P-value |
| Insulin Injection | 9 | 10.23% | 28 | 6.05% | 7 | 5.26% | 44 | 6.43 | 0.8659 |
| Glibenclamide | 5 | 5.68% | 18 | 3.89% | 6 | 4.51% | 29 | 4.24% | 0.9624 |
| Gliclazide | 13 | 14.77% | 81 | 17.49% | 36 | 27.07% | 130 | 19.01% | 0.1351 |
| Metformin | 19 | 21.59% | 145 | 31.32% | 38 | 28.57% | 202 | 29.53% | 0.0117 * |
| Glimepiride | 23 | 26.14% | 91 | 19.65% | 23 | 17.29 | 137 | 20.03% | 0.1090 |
| Vildagliptin | 21 | 23.86 | 72 | 15.55% | 29 | 21.80% | 122 | 17.84 | 0.1711 |

| Pioglitazone | 17 | 19.32% | 67 | 14.47% | 22 | 16.54% | 106 | 15.50% | 0.2666 |
| Repaglinide | 8 | 9.09% | 29 | 6.26% | 14 | 10.53% | 51 | 7.46% | 0.8021 |
| Acarbose | 12 | 13.64% | 35 | 7.56% | 24 | 18.05 | 71 | 10.38% | 0.589 5 |
| Sitagliptin | 9 | 10.23% | 42 | 9.07% | 9 | 6.77% | 60 | 8.77% | 0.7092 |
| No of Patients | 88 | | 463 | | 43 | | 684 | | |
| *[ \* Statistically significant results; P value < 0.05 ]* | | | | | | | | | |

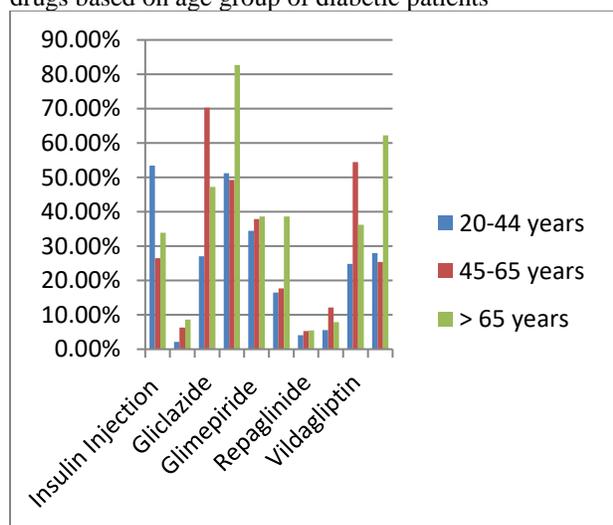**Table 4: Frequency distribution of oral hypoglycemic drugs based on sex of hypertensive diabetic patients.**

| Medicines | male | | Female | | Total | | Chi-square result |
|---|---|---|---|---|---|---|---|
| | Number | percent | Number | Percent | Number | percent | P value |
| Insulin Injection | 31 | 7.56% | 13 | 4.74% | 44 | 6.43% | 0.8870 |
| Glibenclamide | 21 | 5.12% | 8 | 2.92% | 29 | 4.24% | 0.9693 |
| Gliclazide | 77 | 18.78% | 53 | 19.34% | 130 | 19.01% | 0.1696 |
| Metformin | 111 | 27.07% | 61 | 33.21% | 202 | 29.53% | 0.0181 * |
| Glimepiride | 127 | 30.98% | 70 | 25.55% | 197 | 28.80% | 0.0215 * |
| Vildagliptin | 69 | 16.83% | 53 | 19.34% | 122 | 17.84% | 0.2102 |
| Pioglitazone | 61 | 14.88% | 45 | 16.42% | 106 | 15.50% | 0.3134 |
| Repaglinide | 35 | 8.54% | 16 | 5.84% | 51 | 7.46% | 0.8308 |
| Acarbose | 48 | 11.71% | 23 | 8.39% | 71 | 10.38% | 0.6354 |
| Sitagliptin | 35 | 8.54% | 25 | 9.12% | 60 | 8.77% | 0.7470 |
| Total | 410 | | 274 | | 684 | | |
| *[ \* Statistically significant results; P value < 0.05 ]* | | | | | | | |

*Frequency distribution of anti-diabetic drugs to the diabetic patients:* We observed that metformin was the highest prescribed antidiabetic in patients of all the age groups. Also it was observed that Insulin was prescribed more in the age group 20-44 years and as the age advanced the number of patients prescribed Insulin decreased. This result is statistically significant and indicates that age is an important factor influencing the prescription of insulin. Graph 1 show that age influences the prescription of oral hypoglycemic drugs like glibenclamide, gliclazide, acarbose, vildagliptin and sitagliptin. (Table 1 and Graph 1). Moreover, table 2 describes the frequency distribution of anti-diabetic drugs based on sex of diabetic patients. Metformin was the highest prescribed antidiabetic drug and repaglinide was the least prescribed antidiabetic to patients of both the sexes (Table 2 and Graph 2).

**Graph 1:** Comparative distribution of anti-diabetic drugs based on age group of diabetic patients



**Graph 2:** Comparative distribution of anti-diabetic drugs based on sex of diabetic patients.
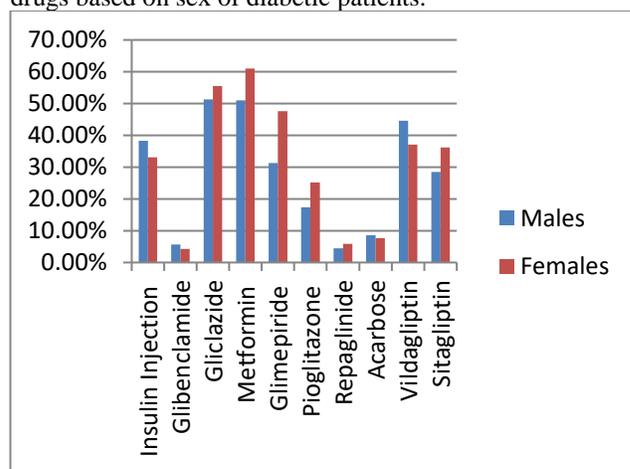


*Frequency distribution of hypoglycaemics to the hypertensive diabetic patients:* Metformin was the

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highest prescribed drug in total population of hypertensive diabetics and also in all the age groups and the age of the patient does not influence its prescription. Also glibenclamide was the least prescribed drug in total population of hypertensive diabetics. (Table 3 and Graph 3). Furthermore, it was found that glimepiride and metformin were the highest prescribed antidiabetics to male and female respectively. And glibenclamide was the least prescribed antidiabetic to patients of both the sexes (Table 4 and Graph 4).

**Graph 3:** Distribution of various oral hypoglycaemics among hypertensive diabetic patients.
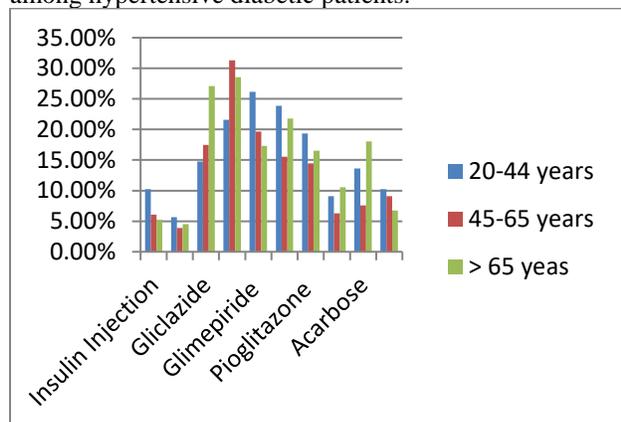


**Graph 4:** Distribution of oral hypoglycaemics based on sex of hypertensive diabetic patients.
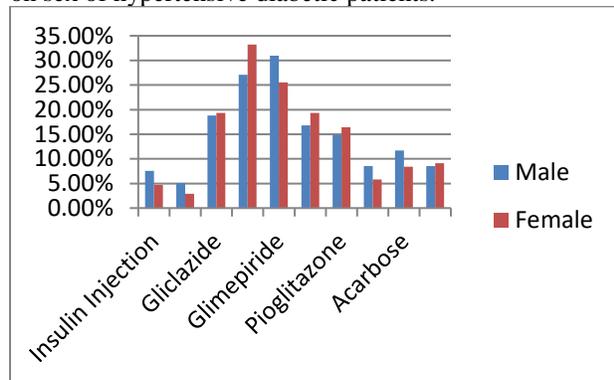


## DISCUSSION

In recent decades, significant increases in the incidence and prevalence of diabetes have occurred in many parts of the world especially in the newly industrialized and developing countries.[12] Generally, such dramatic changes in the prevalence or incidence of diabetes (type 2 diabetes) have been noticed in communities where people take typical 'Western' diet. [13] The lowest rates of diabetes (type 2 diabetes) are observed in rural areas where people practice traditional lifestyles. Actually, diabetes has reached epidemic proportions in many newly industrialized countries.[14,15] Besides, diabetes is a major risk factor

for cardiovascular disease and hypertensive diabetes is probably the fastest growing disease with an increasing global prevalence and incidence.[9] The main purpose of the present study was to further evaluate the prescribing trends of antidiabetic agents to diabetic and hypertensive diabetic patients. This study also identified the factors affecting the implementation and use of the antidiabetic medications.

The prevalence of diabetes varies considerably among populations of different ethnic origins. High prevalence rates of diabetes have been found among Asian Indians.[13] The empirical risk of having type 2 diabetes is increased 2 to 6-fold if a parent or sibling has the disease. Furthermore, the prevalence or incidence of diabetes also varies to some extent between the sexes from one population to another.[13] In the present study majority (65.97 %) of the diabetic patients were male. However, significant number of female (84.04%) was found to have hypertensive diabetes as compared to males. In terms of age, the incidence of diabetes and hypertensive diabetes was significantly higher in this study (52.61% and 67.69% respectively) mainly in older individuals (e.g. 45–65 years of age), confirming a previous report.[13] In our study, a decrease in prevalence was also observed in the oldest age groups (e.g. > 65 years) because of may be higher mortality rates in those with the disease.

Diabetes mellitus is a very expensive disease and creates different complications which reduce both quality of life and life expectancy.[6] Hence, management of diabetes is utmost important. Meta-analyses demonstrate that lifestyle management led to a 63% reduction in diabetes incidence in those at high risk. Such management has a positive effect on long term health and quality of life.[6] Besides, different oral hypoglycemics have been in use to aid in maintenance of blood glucose level at the requisite thresh hold in diabetics through distinct mechanisms.[11] By upregulating endogenous insulin secretion, sulfonylureas and nonsulfonylurea secretagogues establish normoglycemia.[6] Metformin is a widely used drug of choice for the treatment of diabetic patients.[3] In our study, metformin was the highest prescribed drug in diabetic and hypertensive diabetic patients (54.38% and 29.53% respectively) of all the age groups. It was found that Metformin was prescribed more to hypertensive females (33.21 %) than to hypertensive males (27.07%). Metformin works by decreasing hepatic gluconeogenesis. Combination of sulphonylureas and metformin were found to exhibit significant effect.[6] Metformin is normally given along with insulin. The present study also observed that age is an important factor influencing the prescription of insulin. Moreover, repaglinide and glibenclamide were the least prescribed antidiabetics to diabetic and hypertensive diabetic patients respectively of both sexes. Anyway,

various antidiabetic drugs have serious side effects. Hence, we should search newer hypoglycemic agents that retain therapeutic efficacy and are devoid of side effects. [4] And plants provide a promising source of anti-diabetic medicines.[16]

## CONCLUSION

It can be concluded from this study that insulin and biguanides (metformin) were the most commonly used hypoglycemic agents. A combination of two or more drugs of different classes was prescribed to hypertensive diabetics. The prescribing pattern shows that combination of antidiabetics are prescribed more to achieve a better glycemic control in order to avoid long term complications. Our study has established a baseline data regarding the prescribing pattern in diabetic and hypertensive diabetic patients in an urban tertiary care hospital. Since diabetes and co-existing hypertension in diabetes is widespread problem in Bangladesh, this study has provided a scope for further research in this area.

**Conflict of Interest:** Authors had declared no conflict of interest.

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