**Original Article**

# Glycemic Status of Type 2 Diabetic Patients Treated with Different Single Anti-diabetic Agents

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**Abstract**

***Objective:*** *The study was aimed to describe the patterns of single anti-diabetic agents used by type 2 diabetic patients and their glycemic status during hospital admission.*

***Study design and methods:*** *This cross-sectional study was carried out in BIRDEM among hospitalized type 2 adult diabetic patients of different ages and both sexes. Data were collected during admission that included detailed history, medical records review, clinical examination and laboratory investigations.*

***Results:*** *Subjects (n=253; 174 female, 79 male) had age (years) as mean ± SD: 55.28 ±13.45 (15-90 years), BMI (kg/m$^2$) as mean ±SD: 24.67±4.97 and HbA1c (%) as mean ±SD: 10.56±2.98. Use of pre-mixed insulin 90 (35.57%) and split-mixed insulin 70 (27.66%) were more common than other drugs. Glycaemic control was poor in all age groups as evidenced by raised HbA1c, significantly higher in patients <40 years age group. Blood glucose profiles were also high among the all age groups. HbA1c and blood glucose profiles both were high irrespective of type of anti-diabetic agents used during admission. It was also found that patients with increasing age groups were using insulin more frequently. BMI categorization had no significance within treatment groups. (p=0.453).*

***Conclusion:*** *There was no significant difference in blood glucose control among the different single anti-diabetic drug users, that might be due to treatment of diabetes includes medical nutrition therapy with judicious and individualized dietary plan, lifestyle modification, effective exercise plan, and individualized target oriented use of anti-diabetic agents. Along with proper selection of anti-diabetic agents, patient's self-management education and disease-specific awareness is essential to achieve good glycemic control.*

***Key Words:*** *Anti-Diabetic Drugs, Glyemic Control, Type 2 Diabetes.*

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## Introduction

Diabetes mellitus is a global burden for both developed and developing countries affecting all age groups and both sexes. It is one of the most common non-communicable diseases world-wide and its socio-economic impact is enormous especially in developing countries like Bangladesh. It is defined as a group of metabolic diseases characterized by persistent hyperglycemia resulting from defects in insulin secretion and/or action and or both that arises from genetic as well as environmental factors.[1] Number of people with diabetes is increasing day by day and is projected to rise from 171 million in year 2000 to 366 million by the year 2030.[2] Its global prevalence was 6.6% in 2010, which is projected to rise up to 7.8% by the year 2030 [3]. Once known as disease of affluent society, it has been speculated that by the year 2030, most of diabetic cases will be found among population from Asia and Africa.[2] Estimated national prevalence of diabetes mellitus of Bangladesh was 6.1% for the year 2010.[3] Among sub-types, type 2 diabetes is by far the commonest (85% to 95%) among all cases both globally[4,5,6] and in

Bangladesh.[7] In Bangladesh, the crude prevalence of type 2 diabetes is 4.3% and impaired fasting glucose is 12.4 %.[7]

People with diabetes have a substantially reduced life expectancy with age specific mortality rates twice than that of non-diabetic population in developed countries due to development of early complications.[8] Complications are less common and less severe among those diabetic subjects who had well controlled glycemic status. Two primary techniques are recommended to assess effectiveness of treatment plan on glycemic control: patient's self-monitoring of blood glucose (SMBG) and HbA1c%.[9] DCCT,[10] Kumamoto,[11] UKPDS,[12,13] confirmed that intensive glycemic control was associated with significant reduction of micro vascular complications of diabetes. With some exceptions and along with some metabolic parameters, main goal of treatment in diabetes is to keep HbA1c <7%.[9] Frequency and timing of SMBG depends upon type of diabetes, need and goal of treatment. SMBG monitored treatment strategy can reduce HbA1c by 0.25%.[14] A well planned treatment approach to a diabetic patient encompasses patient-centered strategy taking into account patient body weight, glycemic target, individual preference, cost, potential adverse effects, availability etc.[9] Based on above factors single or multiple non-pharmacological and pharmacological interventions are applied to meet glycemic targets. This study was designed to assess pattern and frequency of use of various treatment modalities as a single agent and to find out their achieved glycemic status along with role of diabetic education on glycaemic control among type 2 Bangladeshi subjects who got admitted into Endocrinology Department for better management of their glycemic status and other metabolic components.

**Study design and methods**

This cross-sectional observational study was done in Endocrinology Department of BIRDEM, a tertiary care hospital located in Dhaka, Bangladesh from January to August, 2014. Total 253 hospitalized type 2 adult diabetic patients of different ages and both sexes were purposively recruited into the study who remained on single anti-diabetic drug for at least three months prior to admission. Type 2 Diabetic subjects who were minor, pregnant, suffering from severe and multiple co-morbid conditions, using multiple anti-diabetic drugs or who declined to participate into study were excluded. Data were collected in preformed case record form after admission of patient by means of detailed history, medical records review, clinical examination and laboratory investigation that included blood glucose levels using standard glucometer and simultaneous HbA1c level by modified HPLC (Variant, Bio-Rad). Statistical analyses were done with SPSS software 17.0 for Windows version.

**Results**

Among 253 subjects, 174 were female and 79 were male. Subjects had age (years) as mean ± SD: 55.28 ±13.45 (15-90 years) and BMI (kg/m$^2$) was mean ±SD: 24.67 ±4.97. Almost all patients had uncontrolled blood glucose levels evidenced by mean HbA1c 10.55%. Other values like FBS, 2 hABF, 2 hAL and 2 hAD are shown in table I.

**Table I**

*Clinical and Glycemic Parameters of Study Subjects*

| Features | Results |
|---|---|
| Female (n) | 174 |
| Male (n) | 79 |
| Age (years) as mean ± SD | 55.28 ±13.45 |
| BMI (kg/m2) as mean ±SD | 24.67 ±4.97 |
| FBS (mmol)as mean ±SD | 10.79 ±5.2 |
| 2 hABF (mmol) as mean ±SD | 14.99 ±6.08 |
| 2 hAL (mmol )as mean ±SD | 14.98 ±6.20 |
| 2 hAD (mmol ) as mean ±SD | 13.97 ±5.65 |
| HbA1c (%)as mean ±SD | 10.56 ±2.98. |

*N.B.: FBS: fasting blood glucose; 2h ABF: 2 hour after breakfast blood glucose; 2h AL: 2 hour after lunch blood glucose, 2h AD: 2 hour after dinner blood glucose; SD: standard deviation*

As a single agent, most patients were using insulin [pre-mixed insulin 90 (35.57%) and split-mixed insulin 70 (27.66%)]. Among study subjects pattern of use of anti-diabetic agents are shown in table II.

It was seen that with increasing age group, frequency of using insulin was more (Table III). BMI categorization had no significance within treatment groups (p=0.453). (Table IV).

All the study subjects had uncontrolled blood glucose levels (Table V). It was seen that, patients using sulphonylurea had a relatively favourable glycaemic levels. It was also seen that younger patients (<40 years age group) had worst control (Table VI).

Among the study population 75 (29.64%) had disease specific education and 178 (70.36%) had no such exposure before admission. Fifty five (21.73%) patients used to do SMBG for monitoring glycemic status, 198 (78.26%) were not. Among patient who did SMBG, 10 (18.19%) did weekly (Table VII).

**Table II**

*Observe use of anti-diabetic agents among the study subjects*

| Subjects | Anti-Diabetic agents | | | | | | |
|---|---|---|---|---|---|---|---|
| | Metformin N (%) | Sulphonyl -urea N (%) | Pre mixed Insulin N (%) | Split mixed Insulin N (%) | Basal bolus N (%) | Other anti diabetic agents | No drugs N (%) |
| Male (79) | 2 (11.8) | 15(34.9) | 26(28.9) | 22(31.4) | 6(50) | 5(33%) | 3(50) |
| Female (174) | 15(88.2) | 28(65.1) | 64(71.1) | 48(68.6) | 6(50) | 10(66%) | 3(50) |
| Total(253) | 17 (6.72) | 43(16.99) | 90(35.57) | 70(27.66) | 12(4.74) | 15(5.91) | 6(2.37) |

**Table III**

*Distribution of different drugs among the study group according to age*

| Age limit | Metformin N (%) | Sulphonyl -urea N (%) | Pre mixed Insulin N (%) | Split mixed Insulin N (%) | Basal bolus N (%) | Other anti diabetic agents | No drugs N (%) |
|---|---|---|---|---|---|---|---|
| Gr-1(<40y) | 3 (17.6) | 6(14.0) | 10(11.2) | 10(14.3) | 1(8.3) | 2(13.3) | 3(50.0) |
| Gr-2(40-49y) | 2(11.8) | 8(18.6) | 15(16.9) | 13(18.6) | 3(25) | 0 (o.o) | 1(16.6) |
| Gr-3(50-59y) | 5(29.4) | 15(34.90 | 25(27.0) | 14(20.0) | 5(41.7) | 3 (20.0) | 1(16.6) |
| Gr-4(>60y) | 7(41.2) | 14(32.6) | 40(44.9) | 33(47.1) | 3(25) | 10 (66.6) | 1(16.6) |

**Table IV**

*BMI category among the different anti-diabetic drug user*

| BMI | Anti-diabetic drug | | | | | | |
|---|---|---|---|---|---|---|---|
| | Metformin N (%) | Sulphonyl -urea N (%) | Pre mixed Insulin N (%) | Split mixed Insulin N (%) | Basal bolus N (%) | Other anti diabetic agents | No drugs N (%) |
| <23 | 6(35.3) | 16(37.2) | 38(42.3) | 38(54.3) | 1(8.4) | 11(73.3) | 3(50) |
| >23 | 11(64.7) | 27(62.8) | 52(57.7) | 32(45.7) | 11(91.6) | 4 (26.7) | 3(50) |
| Total (253) | 17 | 43 | 90 | 70 | 12 | 15 | 6 |

**Table V**

*Glycemic status among the different anti- diabetic drug user during admission*

| | Different anti-diabetic agents | | | | | | |
|---|---|---|---|---|---|---|---|
| | Metformin N (%) | Sulphonyl -urea N (%) | Pre mixed Insulin N (%) | Split mixed Insulin N (%) | Basal bolus N (%) | Other anti diabetic agents | No drugs N (%) |
| $HbA_{1c}$ | 11.0 ±2.4 | 8.1 ±1.2*[a] | 10.3±3.9 | 11.2±3.2 | 10.3±2.4 | 10.4±5.6 | |
| FSG | 11.4 ±6.8 | 8.8±2.5*[b] | 9.4±2.9 | 10.7±4.9 | 10.8±3.5 | 7.5±1.6 | |
| 2h ABF | 15.1 ± 4.8 | 15.2±5.7 | 15.8±5.8 | 14.1±5.4 | 12.4±2.8 | 9.6±3.4 | |
| 2h AL | 15.9 ±9.1 | 15.3±6.7 | 15.6±6.3 | 14.1±5.2 | 14.3±4.2 | 10.3±1.6 | |
| 2h AD | 13.7 ±5.7 | 11.3±2.0*[b] | 14.7±5.1 | 13.1±5.5 | 13.7±4.3 | 9.5±3.3 | |

FBS, Fasting serum glucose; 2h ABF, serum glucose at 2hrs after breakfast; 2h AL, serum glucose at 2hrs after lunch; 2h AD, serum glucose at 2hrs after dinner. *a significantly different ($p<0.05$) compared to basal bolus and split mixed insulin; *b significantly different compared to basal bolus.

**Table VI**

*HbA1c of Different age groups*

| Age category | Number/% | HbA1c (Mean) | Std. deviation |
|---|---|---|---|
| Gr 1 (<40y) | 36 (14.22%) | 12.371 | 4.2279 |
| Gr 2(40-49y) | 42(16.62%) | 10.511 | 2.7386 |
| Gr 3 (50-59y) | 68(26.87%) | 10.183 | 2.7423 |
| Gr 1 (>60y) | 107(42.29%) | 10.026 | 2.6675 |
| P- value (significance at the level 0.05) | | | |
| Gr 1 vs Gr 2 | 0.028 | | |
| Gr 1 vs Gr 3 | 0.002 | | |
| Gr 1 vs Gr 4 | 0.000 | | |
| Gr 2 vs Gr 3 | 1.000 | | |
| Gr 2 vs Gr 4 | 1.000 | | |
| Gr 3 vs Gr 4 | 1.000 | | |

**Table VII**

*Disease specific education status of the study population*

| | | | |
|---|---|---|---|
| Diabetic Education | YesNo (%) | NoNo (%) | TotalNo (%) |
| | 75 (29.64%) | 178(70.36%) | 253 |
| Home monitoring | YesNo (%) | NoNo (%) | TotalNo (%) |
| (SMBG) | 55 (21.73%) | 198 (78.26%) | 253 (100%) |
| | Weekly | Monthly | |
| | No (%) | No (%) | |
| | 10(18.19%) | 45(81.81%) | |

**Discussion**

Proper control of glycemic status, prevention, prompt identification and treatment of complications are key essence of management of diabetes. Chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart and blood vessels. Patient's education, motivation and active participation are equally important while managing this chronic disorder.

Various classes of anti-diabetic agents including different types, formulations of insulin are available for pharmacological treatment of diabetes. Patient's individual glycemic status, co-morbidities, availability of a drug, economic status and follow up facilities often influence treatment options. Despite choosing appropriate medication, glycemic targets may not be achieved due to other confounding factors especially while the treatment are implied in a poor resource setting like Bangladesh. Lack of education and awareness may impair glycemic status as well.

Several hospital based studies have been done to find out trend of use of anti-diabetic agents among diabetic patients. A Study conducted to find out pattern of use of anti-diabetic agents revealed that, as a monotherapy, metformin, sulphonylureas, and insulin were used in 40.35%, 12.28%, and 22.8% cases respectively.[15] In that study total 114 patients were enrolled with male to female ration as 0.72: 1 and with mean age of 56.8 ± 10.5 years. Fasting and postprandial blood glucose levels

were 147.5 ± 73.1 and 215.6 ± 97.3 mg/dl respectively. In another study, as monotherapy, use of metformin was also found to be overtaken by insulin. (32.2% for insulin versus 29.6% for metformin).[16] Similar results were obtained in other study as well that revealed that prescription of metformin (27%) and glimepiride (22.60%) were maximum as single anti-diabetic drugs. Category wise the maximum prescribed drugs are glimepride (22.60%, sulfonylurea category), metformin (27%, biguanide category) and pioglitazones (13.90%, glitazone category) and insulin prescription was found to be very less (4.5%).[17] However, in a study, use of insulin as a monotherapy was found as high as 81% patients among hospitalized patients.[18]

Our study revealed that metformin as a single agent was used in 6.72% subjects. Use of sulphonylurea, and insulin were 16.99% and 75.07% respectively. Among prescribed regimen, pre-mixed insulin (90, 35.57%) and split-mixed insulin (70, 27.66%) were two most frequent groups. In this study among different treatment groups BMI categorization and HbA1c% showed no significant difference [p=0.453 and 0.063 respectively]. However HbA1c% was found highest and lowest among long acting insulin analogue [as mean ± SD: 13.00±1.5]. Though HbA1c% was high in all age groups, those who aged less than 40 years had highest value (as mean ±SD: 12.37± 4.22) and difference of HbA1c% values were significant among different age groups (Group 1 versus group 2, 3 and 4 as p=0.028, 0.002 and 0.000 respectively). This study was conducted in a tertiary care hospital among subjects who sought medical care for their impaired glycemic control. So this might not represent whole community.

## Conclusion

There is no significant difference in blood glucose control among the different single anti-diabetic drug users among the study population, that might be due to treatment of diabetes includes medical nutrition therapy with judicious and individualized dietary plan, lifestyle modification, effective exercise plan, and individualized target oriented use of anti-diabetic agents. To accomplish these multi-level treatment strategies successful and to achieve target glycemic status, service should be provided by a team consisting of physicians, nurse, diabetic educators, nutrition experts, pharmacists and mental health professionals. Patient self management education and disease-specific awareness is fundamental for better outcome. If these potential issues are not addressed with equal importance, choice of anti-diabetic agents may not solely a pivotal factor in achieving targets.

Selections of appropriate agent/agents are very much important in the management of diabetes with optimization of life style modification**.** Type of ant diabetic agent is not sole answer for glycemic control. Disease specific education, monitoring along with proper dose adjustment of any agent is equally important for optimum blood glucose control.

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