



Original Article

Trends of Prescriptions of Anti-Diabetic Drugs in Type-2 Diabetic Patients

Saibal AA¹, Begum SA², Islam MZ³, Akter MS⁴

Abstract:

The purpose of this study was to evaluate the prescription trend and pattern of oral anti-diabetic drugs which are extensively used in recent years due to increased number of Type-2 diabetic patients. Study of prescribing pattern is a component of medical audit for evaluating the prescribing practice of the prescribers and recommends necessary modification to achieve rational medical care. It was a cross sectional observational study which was conducted at medicine outpatient department in a tertiary medical college hospital during two years from the period of July 2016 to June 2018. Total 450 prescriptions were enrolled. Majority of the study subjects (68.9%) were male and (31.1%) were female. 41-61 years of age group were mostly affected. Amongst all the available Oral Antidiabetic Drug (OAD) Glimperide was the most commonly prescribed drugs (10%) followed by Metformin (8.9%). Use of new generation OAD like Dipeptidyl Peptidase-4 inhibitors (DPP-4 Inhibitors) also increased dramatically (8.9%). Among the prescriber GP/Qualified physician prescribe mostly (27.8%) followed by village doctor (26.7%). Diabetologist prescribed (24%) and specialist physician (21%) respectively. Our study found increased number of combination therapy. Two drug combination were (34.9%) and more than two drug combination were (9.8%). OAD plus Insulin were (6.7%). We also found early initiation of insulin in Type-2 diabetic patients. In combination with OAD mostly intermediate acting insulin analogue was used. In conclusion, the trend of use of anti-diabetic drugs in Type-2 diabetic patients has changed dramatically due to increased prevalence of Diabetes Mellitus (DM) over last couple of years. Newer generation anti-diabetic drugs were commonly used. Region wise more data needed to make a guideline to use more rational and uniform use of anti-diabetic drugs in Type-2 DM.

Key words: Type-2 Diabetes Mellitus (DM), Anti-Diabetic Drugs, Prescription

Received: September 11, 2018; **Accepted:** December 15, 2018

Introduction:

Among all the non-communicable diseases Diabetes Mellitus (DM) is a leading cause of death and disability worldwide¹. Its global prevalence was about 8% in 2011 and predicted to rise to 10% by 2030². Nearly 80% of people with DM live in low and middle income countries. In Bangladesh which had a population of 149.8 million in 2011, a recent meta-analysis showed that the prevalence of diabetes among adult had increase substantially. According to the International diabetes federation the prevalence will be 13% by 2013³. In recent years Bangladesh has experienced rapid urbanization. A number of population based studies conducted in Bangladesh have revealed an increasing prevalence of DM in both rural and urban population⁴.

Prescription pattern means exploring the insight regarding the existing drugs usages to ensure rational drug therapy. It is one of the most important tools that communicate between physician and the patient and also a written order of medication schedule to the patient⁵. Apart from Type-1 diabetes which is treated only by insulin, different type of

drugs were developed for the treatment of Type-2 DM over last couple of decades. Most commonly used oral-anti diabetic drugs (OAD) includes Sulfonylurea (SU), Biguanides (Metformin), Alpha glucosides inhibitors, Thiazolidinediones (TZD), Dipeptidyl Peptidase-4 inhibitors (DPP-4 Inhibitors), Glucagon-like Peptide (GLP-1) agonist and Sodium Glucose Co-transporter-2 inhibitors (SGLT-2 Inhibitors)^{6,7}. Sudden introduction of this drugs in the market made a dramatic change in the pattern of prescription writing by physician⁸. The question of rational use of these drugs also arises.

The aim of our study was the better understanding of prescription writing with OAD usages and also to understand the pattern of the prescription for the population residing in this region. Many of the current drugs using for treatment of DM are costly for the people of this particular area. Many cannot continue the medications due to financial constrain. Several drugs utilization studies on glucose lowering drugs have been previously conducted in the United States, United kingdom and other European countries^{8,9}. Most of the study revealed

¹ Dr. Md. Arif Akbar Saibal, Associate Professor, Dept. of Internal Medicine, Eastern Medical College & Hospital, Cumilla, Bangladesh.

² Dr. Shamsi Ara Begum, Assistant Professor, Department of Radiology & Imaging, BIRDEM, Dhaka, Bangladesh.

³ Dr. Md. Zakirul Islam, Associate Professor, Dept. of Pharmacology & Therapeutics, Eastern Medical College, Cumilla, Bangladesh.

⁴ Dr. Musammat Shamima Akter, Associate Professor, Department of Gynaecology & Obstetrics, EMCH, Cumilla, Bangladesh.

Address of Correspondence: Dr. Md. Arif Akbar Saibal, Associate Professor, Dept. of Internal Medicine, Eastern Medical College & Hospital, Cumilla, Bangladesh. Mobile: +8801711354428, Email: saibalakbar@gmail.com

substantial increased in the prescription of anti-diabetic medications as well as decrease SU usage and increased Metformin & DPP-4 Inhibitor usages and also combination therapy^{9,10}. Because of the increasing number of OAD medication choices, we can be able to evaluate considerably more specific circumstances that may influence clinical OAD uses such as changes region wise guideline, drugs used in aged population, new adverse effects of drugs and changing health insurance policy. More such study in region wise is needed to explore the actual status of prescription writers of Type-2 DM which may be helpful for the choice of drugs and make a guideline.

Trends of use of insulin in Type-2 DM is also changed over last 10-15 years. Many insulin analogue came into market which are bio-similar, cause less hypoglycemia and having more predictable course. So apart from co morbid condition in Type-2 DM, physician are writing many insulin analogue. Early initiation of insulin is also recommended by many current guidelines. So adding insulin with OAD or use of only insulin analogues also available in many prescriptions with good control of blood sugar.

Materials and Methods:

It was a cross sectional observational study. The study was conducted in the department of Medicine at Eastern Medical College Hospital (EMCH), a tertiary medical college hospital situated in Cumilla, Bangladesh. The study period was two years from July 2016 to June 2018. This study was approved by the ethical review committee of the respective Institution. According to the selection criteria only Type-2 diabetic patients attending in the medicine Out Patient Department (OPD) of EMCH were included in this study. Verbal consent was taken from every patient prior to collecting data. 450 prescriptions of Type-2 diabetic patients were enrolled in this study. Data were collected from prescriptions and preformed questionnaires were filled up. Then data were tabulated and analyzed with SPSS (Statistical Package for Social Science) version 23.

Results:

Most of the 450 prescriptions of Type-2 diabetic patients were received from rural, sub urban and urban area.

Table-I: Gender wise distribution of Type-2 diabetic patients

Gender	Number of Patient (Total = 450)	Percentage
Male	310	68.89%
Female	140	31.11%

Table I & II revealed the demographic profile of the study subjects. The majority of the study subject

[310 (68.9%)] were male and rest of them [140 (31.1%)] were female. Majority of the study subjects were belong to the age group 41-60 years (47%) and second most belong to age group 61-80 years (33.33%).

Table-II: Age wise distribution of Type-2 diabetic patients

Age in years	Number of Patient (Total = 450)	Percentage
20-40	85	18.89%
41-60	215	47.78%
61-80	150	33.33%

On the basis of the HbA1c level 37.8% patient had HbA1c level 6.5-8.5% where as 27.8% patient had HbA1c level <6.5% (Table-III). Considering the HbA1c level 27.8% subjects had well controlled DM, rest of the subjects were either moderately controlled or uncontrolled.

Table-III: HbA1c levels in diabetic patients

HbA1c level (%)	Number of Patient (Total = 450)	Percentage
<6.5	125	27.78%
6.5-8.5	170	37.78%
8.5-10	110	24.44%
>10	45	10.00%

We tried to categorize the prescriber by seeing the prescription where Table-IV showed most of our prescriptions (27.8%) came from GP (Qualified Physicians, MBBS). The village doctors mostly the paramedics and diploma doctors prescribe 26.7% prescriptions. Diabetologist occupied third position that is 24%. Specialist doctors or medicine specialist did 21%.

Table-IV: Types of prescribers

Prescription done by	Number of Patient (Total = 450)	Percentage
Specialist doctor/ Medicine specialist	95	21.11%
Diabetologist	110	24.44%
Qualified General physician (GP)	125	27.78%
Village doctor (Diploma & others)	120	26.67%

We found both new and old generations of OAD from our prescribers. Among all the available anti-diabetic medications Glimepiride was the most commonly prescribed OAD (10%) followed by Metformin 8.9% (Table-V). New generation OAD like DPP-4 inhibitors getting more popular day by day (Vildagliptin 8.9%, Sitagliptin 7.5% and

Linagliptin 7.8%). Combination of OAD getting more popularity in recent trends. Metformin was the most commonly prescribed in combination therapy (Table-V). Our study revealed Metformin and Glimpiride were the most common combination (8.44%); Gliclazide 4.4%, Vildagliptin 8%, Sitagliptin 6.7%, Linagliptin 6.2% respectively. Three drug combinations were also found in some prescription like Metformin + Vildagliptin + Glimpiride (5.3%). We found OAD + Insulin in 6.7% cases. 1.1% cases were found as combination of SGLT-2 inhibitors, Pioglitazone and some traditional Herbal medicine (Table-V).

Table-V: Different anti-diabetic drugs and their combination in the prescription

Name of drug	No. of Patient	Percentage
Metformin	40	8.9%
Glimpiride	45	10.0%
Gliclazide	20	4.44%
Metformin + Glimpiride	38	8.44%
Metformin + Gliclazide	25	5.56%
Vildagliptin	40	8.89%
Sitagliptin	34	7.56%
Linagliptin	35	7.78%
Metformin + Vildagliptin	36	8.00%
Metformin + Sitagliptin	30	6.67%
Metformin + Linagliptin	28	6.22%
Metformin + Vildagliptin + Glimpiride	24	5.33%
Metformin + Sitagliptin + Glimpiride	20	4.44%
Others (SGLT ₂ inhibitors, Pioglitazone, Voglibose, Herbal medicine)	5	1.11%
OAD+ Insulin	30	6.67%

Table-VI: Number of patients taking single and combination anti diabetic drugs

Drug	No. of Patient	Percentage
Single drug	214	47.55%
Two drug combination	157	34.89%
Three drug combination	44	9.78%
OAD + Insulin	30	6.67%
Others	5	1.11%

Table-VI, revealed 47.6% patient prescribed by single drug, 34.9% patient prescribed by 2 drug combination, 9.8% patient prescribed by 3 drugs combinations, 6.7% patient prescribed by OAD plus

Insulin and 1.1% patient prescribed by others (SGLT-2 inhibitors, Pioglitazone, Herbal medicine/Ayurveda).

Table-VII: Different types of Insulin and their combination in the prescription

Types of Insulin used in Prescription	No. of Prescription	Percentage
Short acting	6	20.00%
Intermediate acting	8	26.67%
Short + Intermediate	7	23.33%
Long acting	5	16.67%
Insulin analogue -ultra short acting -ultra long acting	4	13.33%

Our study also revealed use of different types of Insulin (Table-VII). Short & Intermediate acting Insulin combination were mostly used (23%) followed by Short acting Insulin (20%). Use of modern Insulin like insulin analogue was also increased in recent years. We found 13.33% patients were on Insulin analogue.

Discussion:

We investigated in this study the trend in the prescription pattern of OAD medications for Type-2 diabetes in a tertiary medical college hospital. Most of the prescriptions recruited here were from the rural, sub urban and few urban areas. A prescription based survey is considered to be one of the most effective method to assess and evaluate the prescribing attitude of the physician and dispensing practice of the pharmacist¹¹. In our study the incidence of diabetes was seen 310 (68.9%) in male and 140 (31.1%) in female patients and 41-60 years age range was the most commonly affected diabetic patient. This was comparable with previous study done by Guercil *et al.* where male was mostly affected by Type-2 DM¹². The cause of male predominance and particular age group involvement with diabetes is still uncertain.

Most of our patient has uncontrolled DM (37.8%). That may be due to poor compliance to OAD and irregular follow up to doctor. We found most of our prescription done by general practitioner (27.8%) followed by village doctor (26.7%). ICDDR,B reported that in rural area of Bangladesh, village doctors (unqualified practitioner) played an almost equal roll to graduate medical doctors¹³. Village doctors and pharmacy supply as much as 67% of the primary health care in Bangladesh as they are the preferred health care provider because they are perceived to be more available, accessible and affordable than other public health care options^{14,15}.

That could be important explanation that village doctors are writing more prescriptions due to easy access and availability of doctors for the patients. Diabetologist and specialist physicians prescribed 24% and 21% prescriptions respectively. This may be due to prescription received from rural and sub urban areas where GP/ qualified physicians and village doctors are handling the patient primarily. Secondly new generations anti-diabetic drugs are safer and causes less hypoglycemia. Although these group of doctors are not aware of different guidelines of using anti diabetic medication but encouraged and motivated by different pharmaceuticals companies particularly the village doctors. So primary health care physicians are more interested to prescribe anti diabetic drugs than any time before.

Our study found that third generation secretagogue, Glimpiride was most commonly prescribed (10%) followed by Metformin (8.4%). Many guideline still advocate Metformin as a first line drug. Some studies carried out in India and Hong Kong which reported that secretagogue was most commonly prescribed their which is similar to our study^{16,17}. But Xavier *et al.* found Metformin was the most commonly prescribed drug¹⁶. Our prescriptions revealed no big differences between use of Metformin and Glimpiride. Among other secretagogue Glimpiride causes less hypoglycemia.

In this study we found use of new generation OAD for Type-2 diabetic patients like DPP-4 Inhibitors e.g. Vildagliptin (8.9%), Sitagliptin (7.5%) and Linagliptin (7.8%). Many studies in different parts of the world revealed similar results that is more use of DPP-4 Inhibitors¹⁸. Recent trends in using more DPP-4 Inhibitor may be due to that, they cause less hypoglycemia, more tolerable and predictable course. Although costly but many patients are more interested to use new generation OAD like Gliptin group but many guideline do not recommend Gliptin group as a first line drugs. Our study revealed dramatic incremental use of DPP-4 inhibitors for Type-2 diabetic patients.

Treatment goal setting for Type-2 diabetes has undergone a major shift since 2006¹⁹. The target HbA1c level was set to 7 since then. In 2008, the American Diabetes Association (ADA) published standard medical care in diabetes and changed the pre-prandial glucose target to 70-130mg/dl²⁰. Amongst use of OAD medication Metformin became the most widely used drugs since 2010. By contrast the usages rate of SU dropped gradually. However clinical physician raised concern about the side effects of such drug as hypoglycemia and weight gain may explain the decline in the prescription of such drug. Regarding the new

generation anti-diabetic medication DPP-4 Inhibitors are one of the most widely used drugs²¹. Result from previous studies have revealed that the prescription trend for this drug group is increased rapidly and this trend is consistent with that, observed in our study. Rafuniello *et al.* in their study determined the increase in the proportion of mono therapy treatment, particularly for DPP-4 Inhibitor in recent years²².

In the analysis of our prescription pattern the proportion of combined therapy constituted 51% of all prescriptions. Which was very close to a study conducted by Chu WM *et al*²³. They found 60% prescription had some form of combination therapy.

In recent years, early combination therapy has become increasingly crucial in diabetes treatment. Current guidelines also encourage the early use of combination therapy involving sub maximal doses of each drug to lower blood glucose more effectively with less adverse outcome²⁴. Many study revealed that fixed dose combination therapy could lower the adherence rate to 26%²⁵. One systematic review indicated that fixed dose combination therapy increased the patient adherence and satisfaction in addition to lowering treatment cost²⁶. Our study observed the trend of prescribing a fixed dose combination therapy over the past years.

Our study also found use of different types of Insulin particularly use of modern Insulin or Insulin analogue in Type-2 diabetic patients apart from use of OAD. That may be due to less hypoglycemic effect and predictable course with Insulin analogue. That could be possible cause of break of barrier of using such Insulin than that of conventional Insulin which also revealed in our study.

Conclusion:

Third generation anti diabetic, Glimpiride is the most prescribed OAD followed by Metformin. Regarding combination therapy Metformin is the most commonly prescribed drug where it is combined with all types of OAD and Insulin. DPP4-Inhibitors are an emerging OAD due to their less side effects and more tolerability. Although we received most of our prescriptions from rural and suburban areas and few urban areas, qualified physician/ GP playing an important role to initiate new generation anti-diabetic drugs followed by village doctors. Region wise different studies should be done for more data on the basis of which a guideline can be made which will guide us to follow a uniform treatment pattern for the treatment of Type-2 DM in our country.

Conflict of Interest: The authors declared no conflict of interest during conducting the study.

References:

1. Lorazno R, Naglavi M, Foreman K, et al. Global & regional mortality from 235 cases of death for 20 age group in 1990 & 2010: A systematic analysis for the global burden of disease study 2010. *Lancet*. 2012; 380 (9859): 2095-128
2. International Diabetes Federation (IDF) country estimates table 2011. *IDF diabetes atlas 6th ed*, 2012. Available at: <http://www.idf.org/diabetesatlas> [Accessed on July 02, 2018]
3. Saquib N, Saquib J, Ahmed T, et al. Cardiovascular disease & type 2 diabetes in Bangladesh: a systematic review & meta-analysis of studies between 1995 and 2010. *BMC public health*. 2012; 12: 434.
4. Abu Sayeed M, Ali L, Hussain MZ, et al. Effect of socioeconomic risk factors on the differences in prevalence of diabetes between rural and urban population in Bangladesh. *Diabetes Care* 1997; 20 (4): 551-5.
5. Mohammad M, Reddy CR, JR Sounya, et al. Prescription pattern analysis of antidiabetic drug in diabetes mellitus & associated comorbidities. *Clin Invest*. 2018; 8 (1): 5-12.
6. Hampp C, Borders-Hemphill V, Money DG, et al. Use of antidiabetic drugs in U.S., 2003-2012. *Diabetes Care*. 2014; 37 (5): 1367-74.
7. Wilkinsons S, Douglas I, Stirnadel-Farrant H, et al. Changing use of antidiabetic drugs in the UK: trends in prescribing 2000-2017. *BMJ Open*. 2018; 8 (7): 1-3.
8. National Institute for Health Care Excellence (NICE). NG28: Type 2 diabetes in adult: management national for health and care excellence, 2015. Available at: <https://www.nice.org.uk/guidance/ng28> [Accessed on July 02, 2018]
9. Gallwitz B. New therapeutic strategies for the treatment of type 2 diabetes mellitus based on Incretins. *Rev Diabet Stud*. 2005; 2 (2): 61-9.
10. Filion KB, Joseph L, Boivin JF, et al. Trends in the prescription and cost of diabetic medications in the United Kingdom: A population-based analysis. *Pharmacoepidemiol Drug Saf*. 2009; 18 (10): 973-6.
11. Yuen Yh, Chang S, Chong CK, et al. Drug utilization in a hospital general medical outpatient clinic within particular reference to antihypertensive and antidiabetic drugs. *J Clin Pharm Ther*. 1998; 23 (4): 287-94.
12. Guerci B, Drouin P, Grange V, et al. Self-monitoring of blood glucose significantly improves metabolic control in patients with type 2 diabetes mellitus. *Auto surveillance intervention active study (ASIA)*. *Diabetes Metab*. 2003; 29 (6): 587-94.
13. Determinants of qualified hypertension diagnosis in a surveillance sites of Bangladesh: findings from a cross sectional study. *Health Sci Bull*. 2011; 9: 15-8.
14. Mahmood SS, Iqbal M, Hanif SM, et al. Are Village Doctors in Bangladesh a curse or a blessing? *BMC Int Health Hum Rights*. 2010; 10: 18.
15. Cockcroft A, Andersson N, Milne D, et al. What did the public think of health service reform in Bangladesh? Three national community based survey 1999-2003. *Health Res Policy Syst*. 2007; 5: 1.
16. Xavier D, Nugarani MA, Srishyla MV. Drug utilization study of antihypertensive & antidiabetic in an Indian referral hospital. *Indian J Pharmacol*. 1999; 31: 241-2.
17. Lau GS, Chan JC, Chu PL, et al. Use of antidiabetic and antihypertensive drugs in hospital and outpatient settings in Hong Kong. *Ann Pharmacother*. 1996; 30 (3): 232-7.
18. Ramesh, Gupta DD. Role of DPP-4 Inhibitors in the management of type 2 diabetes. *Int J Basic Clin Pharmacol*. 2018; 7 (12): 2488-95.
19. Nathan DM, Buse JB, Davidson MB, et al. Management of hyperglycemia in type2 DM: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the study of Diabetes. *Diabetes Care*. 2009; 32 (1): 193-203.
20. American Diabetes Association. Standards of Medical Care in Diabetes 2019 abridged for primary care providers. *Clin Diabetes*. 2019; 37 (1): 11-34.
21. Chiang CW, Chiu HF, Chen CY, et al. Trends in the use of oral antidiabetic drugs by outpatients in Taiwan: 1997-2003. *J Clin Pharm Ther*. 2006; 31 (1): 73-82.
22. Rafaniello C, Arcoraci V, Ferrajolo C, et al. Trends in the prescription of antidiabetic

- medications from 2009 to 2012 in general practice of southern Italy: a population based study. *Diabetes Res Clin Pract.* 2015; 108 (1): 157-63.
23. Chu WM, Ho HE, Huang KH, et al. The prescribing trends of oral antidiabetic agents for type 2 diabetes in Taiwan: An 8-year population based study. *Medicine (Baltimore).* 2017; 96 (43): e8257.
24. Del Prato S, Felton AM, Munro N, et al. Improving glucose management: ten steps to get more patients with type 2 diabetes to glycaemic goal. *Int J Clin Pract.* 2005; 59 (11): 1345-55.
25. Bangalore S, kamalakkannan G, Parker S, et al. Fixed-dose combinations improve medication compliance: a meta-analysis. *Am J Med.* 2007; 120 (8): 713-9.
26. Hutchins V, Zhang B, Fleurence RL, et al. A systematic review of adherence, treatment satisfaction and cost in fixed-dose combination regimens in type 2 diabetes. *Curr Med Res Opin.* 2011; 27 (6): 1157-68.

Citation of this article:

Saibal AA, Begum SA, Islam MZ, Akter MS. Trends of Prescriptions of Anti-Diabetic Drugs in Type-2 Diabetic Patients. *Eastern Med Coll J.* 2019; 4 (1): 3-8.