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Prescription Patterns for Empagliflozin among Adults with Diabetes Mellitus in Dhaka, Bangladesh

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Objective: To evaluate the prescribing pattern of empagliflozin with respect to other concomitant prescribed drugs in a diabetic patient.
Methods: The present research study was conducted in Dhaka from May 2021 to July 2021 at National Healthcare Network (NHN), Dhaka (Jurain, Uttara and Mirpur Branch). A total of 139 were included in this study by following a simple random procedure.
Results: According to the research criterion, 198 prescriptions were collected and 139 were assessed for the study. 78 (56.12%) were male and 72 (51.8%) belonged to the age group 30-64 years, and 67 (48.2%) were in the age group of 65-79 years. 57 (41%) had normal weight, followed by 33 (23.74%) who were overweight, and 49 (35.25%) patients were obese. Approximately 73 (52.52%) of prescriptions prescribed empagliflozin alone, whereas 76 (54.68%) of prescriptions prescribed the combination of empagliflozin and metformin. Among 202 co-prescribed anti-diabetic preparations other than empagliflozin (either monotherapy or combination therapy), 142 (70.30%) were oral hypoglycemic and 60 (29.70%) were insulin preparations. Apart from anti-diabetics, 396 medications were prescribed in this study, including anti-hypertensives (n=47;11.87%) and lipid-lowering drugs (n=43;10.86%). The number of protein pump inhibitors (PPIs) and nutritional supplements were 106 (26.77%) and 84 (21.21%) prescriptions respectively.

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Conclusion: Empagliflozin is one of the most often recommended anti-diabetic medications in Bangladesh to treat diabetes with or without cardiovascular and obesity-related complications. Other drug classes are prescribed as well, with no apparent contradictions.

Keywords: Empagliflozin; anti-diabetic agents; diabetes mellitus; prescription pattern.

1. INTRODUCTION

Sodium–glucose cotransporter-2 (SGLT-2) inhibition is a non-targeted method to reduce hyperglycemia in type 2 diabetes patients [1]. SGLT-2 plays a role in the regulation of steady-state glycemic control by mediating glucose reuptake from the kidney's proximal tubules. The tendency to reabsorb glucose through the kidney has been shown to be limited when this receptor is inhibited, resulting in glucose excretion in the urine and a reduction in blood glucose levels [2]. Empagliflozin is a potent and selective SGLT-2 inhibitor that improves blood glucose control and has a favorable safety profile in people with type-2 diabetes mellitus [3].

The treatment of type-2 diabetes patients should include not just glycemic management but also the modification of cardiovascular risk factors. Approximately two-thirds of diabetic patients have hypertension, which is a major contributor to cardiovascular problems [4]. Apart from lowering blood glucose effectively, empagliflozin provides additional therapeutic benefits such as reduction in blood pressure [5]. According to a study by Packer M et. al. [6] patients in the empagliflozin group had a decreased risk of cardiovascular death or heart failure hospitalization than those in the placebo group, regardless of whether they had diabetes or not. Moreover, treatment with empagliflozin lasting up to 90 weeks results in long-term benefit in weight management [4]. The weight reduction seen with SGLT2 inhibitor medication could be attributed to calorie loss due to urine glucose excretion [7].

Empagliflozin may be utilized in conjunction with any group of glucose-lowering drugs because SGLT-2 inhibitors have a distinctive and non-insulin-dependent mechanism of action [8]. Empagliflozin and metformin perform together through complementary mechanisms, leading to significant and substantial changes in glucose control as well as considerable weight management [9]. Furthermore, in individuals who have failed to respond to metformin and a sulfonylurea, empagliflozin has the potential to be used as a third-line medication [7]. Because SGLT-2 inhibitors and dipeptidyl peptidase-4 (DPP-4) inhibitors have compatible modes of action, the combination of empagliflozin and linagliptin may provide long-term therapeutic advantages, and no significant hypoglycemic adverse events have been reported with empagliflozin/linagliptin [10]. In those with type-1 diabetes, using a lower dose of empagliflozin as an addition to insulin therapy may provide the optimal balance of safety and efficacy [11].

Diabetes affects 463 million people worldwide, including 88 million in South East Asia (SEA), with the number expected to climb to 153 million by 2045. Bangladesh, one of the 7 countries in the International Diabetes Federation (IDF) SEA region, currently estimates around 8.1% adults with diabetes while the total adult population is 104,015,000 [12].

In 2019, Bangladesh's pharmaceutical market is expected to be worth BDT 260.1 billion (USD 3.1 billion). In recent times, the market has been burgeoning, with a compound annual rate of growth (CARG) of around 15% [13]. Diabetes, the second-largest therapeutic class, will have the highest CAGR of 7-10% in the next five years [14]. Empagliflozin is an example of a patented product in India that has been approved for marketing in Bangladesh by local companies [13]. Boehringer Ingelheim and Lilly co-marketed empagliflozin (Jardiance), which is expected to be the world's third best-selling diabetes medicine in 2024 [15].

Using information available from prescriptions produced by the National Healthcare Network (NHN), Dhaka (Jurain, Uttara, and Mirpur Branch), in this study we assessed prescribing patterns of empagliflozin among the population of Dhaka, Bangladesh. Although there is a fair amount of variance in drug use patterns from country to country and within a single country, [16] Dhaka can be a representative of Bangladesh as it is a diverse city in the country with the maximum number of populations [17].

Therefore, this research may offer valuable insights into current prescribing evaluation of not only empagliflozin but also other anti-diabetic drugs, and it may ultimately lead to rational

medication therapy, better glycemic control, and lower health-care expense for patients and society on a large scale.

2. METHODS

The present research study was conducted in Dhaka from May 2021 to July 2021 at National Healthcare Network (NHN), Dhaka (Jurain, Uttara and Mirpur Branch). Study populations for this study were selected specifically, but the prescriptions were collected randomly from those specific populations. A total of 139 prescriptions were selected for further analysis. Few prescriptions were excluded during the data analysis due to the unreadable handwriting of the concerned prescriber. The prescriptions which did not contain empagliflozin were also not included due to our study design. Descriptive statistics were applied to the collected data using Microsoft Excel software and results are expressed graphically in percentages, mean.

3. RESULTS

A total of 198 prescriptions were examined, with 59 of them being unreadable and containing 120 types of drugs. The majority of study subjects were male (n=78;56.12%) and 72 (51.8%) belonged to the age group of 30-64 years, and 67 (48.2%) were in the age group of 65-79 years.

Among the respondents, on the basis of duration of treatment, most patients were in the group of 5-10 years (n=40;28.78%), followed by 1-5 years (n=36;25.9%), above 10 years (n=37;26.62%) and less than 1 year (n=26;18.71%). According to their BMI, 57 (41%) of the patients were obese, 33 (23.74%) were overweight, and only 49 (35.25%) were normal weight.

Patients were suffering from different types of diabetic complications. 95 (68.24%) had type-2 diabetes and 44 (31.65%) had type-1 diabetes, while 3.92% of patients were suffering from diabetic neuropathy. There was a total of twenty-four different types of anti-diabetic drugs prescribed, with an average of three drugs per prescription, with many of them being multi-drug combinations. Approximately 73 (52.52%) of prescriptions prescribed empagliflozin alone, whereas 76 (54.68%) of prescriptions prescribed the combination of empagliflozin and metformin. There were 10 (7.19%) prescriptions that contained both empagliflozin and a combination of empagliflozin and metformin. In all prescriptions, all medications were prescribed as brand names.

Among all the prescribed anti-diabetic preparations other than empagliflozin (either monotherapy or combination therapy), 142 (70.30%) were oral hypoglycemics and 60 (29.56%) were insulin preparations (Fig. 1).

Patients were predominantly prescribed sulfonylureas (approximately 43.52%) as monotherapy, which includes gliclazide (32.41%) and glimepiride (11.11%). Other antidiabetic drugs included dipeptidyl peptidase -4 inhibitors (linagliptin 27.78%, vildagliptin 4.638%), biguanides (metformin HCl 13.89%), glucosidase inhibitors (voglibose 2.78%, acarbose 0.93%), and meglitinide analogues (repaglinide 1.85%, pioglitazones 0.93%) (Table 1).

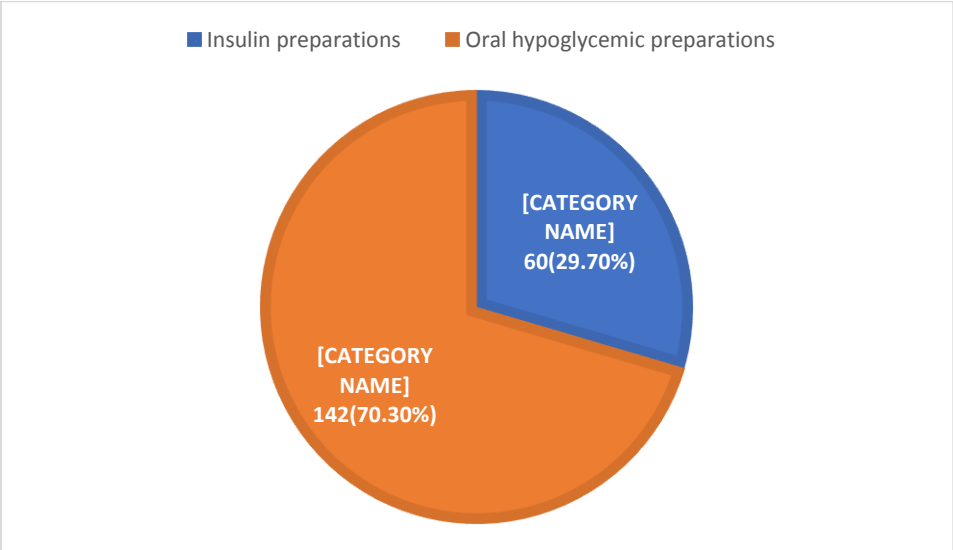

Fig. 1. Distribution of other antidiabetic drugs prescribed with Empagliflozin (n =202)

According to Table 2, besides the empagliflozin plus metformin combination, four types of antidiabetic combination drugs were prescribed. The most commonly used combination drug was linagliptin with metformin HCl (69.44%). Other choices include vildagliptin plus metformin HCl (5%), sitagliptin and metformin (11.11%), and glimepiride plus metformin (5.56%).

With all other oral hypoglycemics, seven different insulin formulations were prescribed. Prescribers recommended short-acting insulin (insulin regular 20%) the most out of all the insulin formulations (short, long, and fast-acting). In comparison to all other insulin preparations, the combination of insulin regular plus insulin isophane was prescribed the most (26.67%) (Table 3).

Cardiovascular drugs (n=91; 22.73%), including anti-hypertensives (n=47;11.87%), and lipid-lowering drugs (n=43;10.86%), accounted for the majority of the 396 prescribed drugs other than anti-diabetics. Along with other classes of medications, 106 (26.77%) proton pump inhibitors (PPIs) and 84 (21.21%) nutritional supplements were recommended. Among the PPIs esomeprazole was mostly prescribed both as monotherapy (n=100;49.06%) and as a combination with naproxen (n=6;5.66%). Apart from anticonvulsants (n=23;5.81%) and antibiotics (n=12;3.03%), miscellaneous drugs (n=81;20.45%) were prescribed, including antihistamines, NSAIDs, anxiolytics, anti-emetics, etc for symptomatic treatments (Figs. 2 and 3).

4. DISCUSSION

Prescription studies and analysis of empagliflozin may facilitate rational drug therapy and effective treatment adaptation, which can assist diabetic patients to achieve optimal glucose control and medication compliance, lowering the disease risk.

Table 1. Distribution of antidiabetic drugs (monotherapy) with Empagliflozin (n=107)

Therapeutic Class	Drug Name	Number (n)	Percentage (%)
Sulfonylureas	Gliclazide	35	32.41
	Glimepiride	12	11.11
Dipeptidyl peptidase -4 inhibitor	Linagliptin	30	27.78
	Sitagliptin	2	1.85
	Vildagliptin	5	4.63
Biguanides	Metformin HCl	15	13.89
Alpha glucosidase inhibitor	Voglibose	3	2.78
	Acarbose	1	0.93
Meglitinide analogues	Nateglinide	2	1.85
	Repaglinide	2	1.85
Thiazolidinediones	Pioglitazone	1	0.93

Table 2. Distribution of antidiabetic drugs (combination therapy) with Empagliflozin (n=36)

Drugs in combination	Number (n)	Percentage (%)
Linagliptin plus Metformin HCl combination	25	69.44
Vildagliptin plus Metformin HCl combination	5	13.89
Sitagliptin plus Metformin HCl combination	4	11.11
Glimepiride plus Metformin HCl combination	2	5.56

Table 3. Distribution of insulin preparations with Empagliflozin (n=60)

Class of drugs	Drugs	Number (n)	Percentage (%)
Short-acting Insulin	Insulin Regular	12	20
Long-acting Insulin	Insulin Glargine	5	8.33
Rapid acting Insulin	Insulin Aspart	9	15
Insulin in combination	Insulin Degludec plus Insulin Aspart	2	3.33
	Insulin Lispro plus Insulin Lispro Protamine	2	3.33
	Insulin Regular + Insulin Isophane	16	26.67

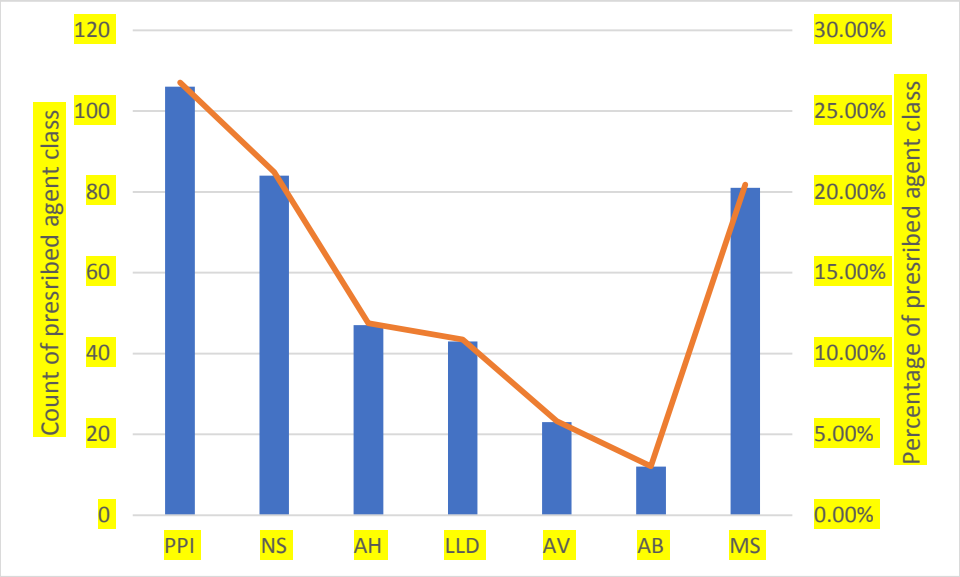

Fig. 2. Distribution of drugs other than anti-diabetic class (n=396)

**PPI=Proton Pump Inhibitors; NS=Nutritional Supplement; AH=Antihypertensive; LLD=Lipid Lowering Drugs; AB=Antibiotic; MS=Miscellaneous*

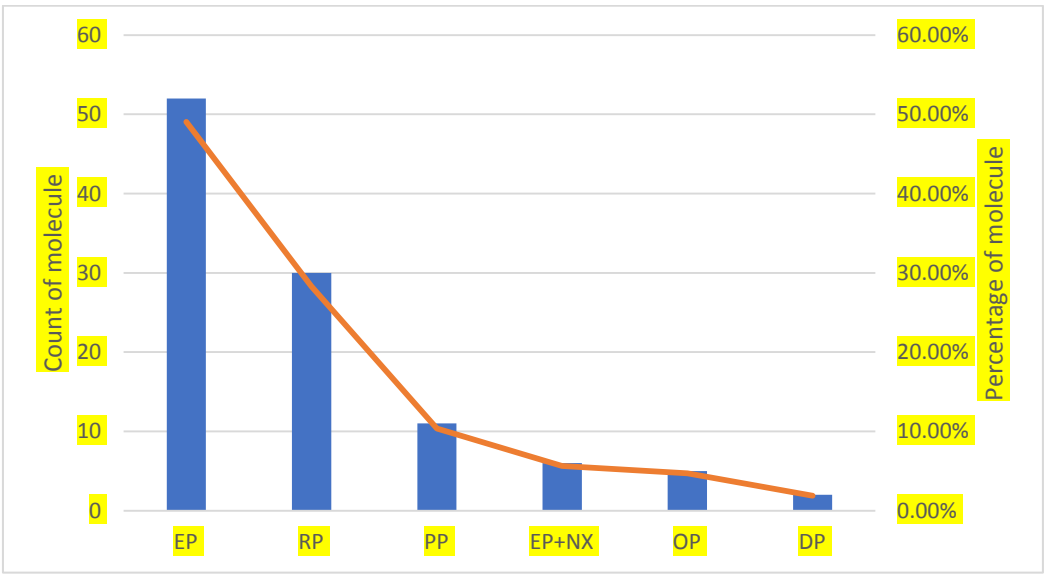

Fig. 3. Distribution of proton pump inhibitors (n=106)

**EP=Esomeprazole; RP=Rabeprazole; PP=Pantoprazole; EP+NX=Esomeprazole+Naproxen; OP=Omeprazole; DP=Dexlansoprazole*

The majority of patients treated with empagliflozin were between the ages of 30-64 years (n=72;51.8%), according to this study. Obese individuals made up the largest percentage of the population in our study, accounting for 57 (41%) that coincides with the fact that treatment with empagliflozin leads to considerable weight reduction, which improves insulin sensitivity and glucose control [7]. The majority of respondents (n=40; 28.78%) had been on diabetic therapy for 5-10 years.

Metformin was often used in combination with empagliflozin to achieve glycemic control because metformin alone often fails to sustain glucose control over time [9]. Other oral anti-diabetics having complementary mechanism of action, such as sulfonylureas and dipeptidyl peptidase-4 inhibitors, were prescribed alongside empagliflozin because of improved glycemic control. This type of combination therapy may provide a treatment option for patients with type 2 diabetes who are intolerant to metformin and/or

have marked hyperglycemia, without the weight gain or increased risk of hypoglycemia [7,10]. Empagliflozin was also given with insulin since it lowers the dose of insulin while improving total glucose levels and body weight without raising the risk of hypoglycemia [18]. Antihypertensives and lipid-lowering drugs were used more frequently, indicating that the patients had cardiovascular issues. And empagliflozin is a critical new therapeutic approach for persons with heart failure with a low ejection fraction who want to lower their risk of cardiovascular death and hospitalization. Empagliflozin is also related to the favorable effect on maintaining lipid profile [19]. Furthermore, PPIs were also the most frequently prescribed therapeutic category of drugs, owing to their potential function in glycemic management as a supplement to other anti-diabetic treatments. It is mostly concerned with the structural similarity of gastrin and incretin [20,21]. Nutritional supplements were recommended as immune booster for patients.

When we inspected the prescription, we detected some anomalies. For example, the World Health Organization (WHO) strongly encourages the prescription of pharmaceuticals by generic name as a safety precaution for patients [22]. But our research found that no medications were prescribed using the generic name. Unfortunately, we had to exclude some prescriptions (n=59) from the study due to poor hand writing of prescribers which is also contradictory according to prescription guidelines of WHO.

To our best understanding, this is the first study to look at empagliflozin prescription patterns in the adult population of Bangladesh. As a result, measuring the degree of rational or irrational drug usage by health care services will be advantageous.

5. CONCLUSION

Since no drugs with severe inconsistencies were identified, the pattern of empagliflozin prescriptions found in this study is pretty satisfactory. Some inaccuracies were also recognized, based on the findings of this investigation. Poor handwriting, on the other hand, was identified as a concern in this study, as did the lack of generic prescribing. Overall, this study could serve as a starting point for future research on both prescribing and patient care indicators to improve medication control.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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