BJPS

Brazilian Journal of
Pharmaceutical Sciences

http://dx.doi.org/10.1590/s2175-97902022e20681

Article

Evaluation of drug utilisation pattern and cost associated with diabetes mellitusType 2 management in Saudi Arabia

Mohammad Daud Ali [1]*, Ayaz Ahmad [1], Nuzhat Banu [1], Munfis Patel [2], Sherihan Ahmad Ghosn [1], Zainab Eltra i [1]

[1]*Department of Pharmacy, Mohammed Al-Mana College for Medical Sciences, Saudi Arabia*
[2]*Foundation year Department, Mohammed Al-Mana College for Medical Sciences, Saudi Arabia*

Diabetic mellitus is an emerging disease in Saudi Arabia. In this regard, a cross-sectional retrospective study was conducted to evaluate drug utilization pattern and the cost associated with non-insulin-dependent diabetes mellitus disease management in Saudi Arabia. Data retrieved from the electronic pharmacy records during the last one year were employed in this study. World Health Organization (WHO) Defined Daily Dose (DDD) method was employed to compute the daily price of each oral hypoglycaemic agent. The American Diabetes Association (ADA) guidelines and protocols were used to evaluate the level of adherence. A total of 17057 patients were enrolled in the study. Out of the 17057 patients enrolled in the study, 60.06 % (10246) were males and the rest females. In monotherapy, biguanides (metformin) were the most recommended and utilised drugs among 5673 patients (33.25%). The most commonly used drug combination was found to be sitagliptin+metformin (1754 units). The cost per unit dose was highest for liraglutide (A10BJ02) 258.32SR (68.79USD), and lowest for metformin (A10BA02) 0.49SR (0.13 USD). Metformin was the choice drug for the diabetes patients; biguanides (metformin) and DPP-4 (sitagliptins) were the most familiar established dose combination employed. Generic drugs should be used in order to reduce overall cost.

Keywords: Antidiabetic agents. Diabetes mellitus Type 2. Drug utilisation pattern. Defined Daily Dose. Cost analysis. Saudi Arabia.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by abnormal high-level blood glucose (BG) (Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997). T2D has the highest incidence rate amongst other forms of diabetes, and it is commonly associated with the development of insulin resistance, as well as a relative dearth of insulin secretion in the early stages of the disease (Van Tilburg *et al*., 2001). There has been a marked upsurge in the prevalence rate of this chronic disease in recent years. The escalation in the incidence of diabetes mellitus type 2 is alarming and of great concern for global public health.

According to the report of the International Diabetes Federation (IDF) in 2019, approximately 463 million adults live with DM and the number is expected to reach 700 million by the year 2045 (https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.htm, https://care.diabetesjournals.org/content/43/Supplement_1/S1). Poorly controlled DM often leads to multiple macrovascular, microvascular, and neuropathic complications that decrease health-related quality of life (HRQOL) culminating in early mortality (Cong *et al*., 2012; Scollan-Koliopoulos *et al*., 2013). The IDF reported that the Gulf Cooperation Council countries are among the top twenty nations in terms of the extensive incidence of diabetes globally (Alzaid, 2012). Furthermore, the WHO estimated an

***Correspondence:** Dr. M. D. Ali. Department of Pharmacy. Mohammed Al-Mana College for Medical Sciences. Abdulrazaq Bin Hammam Street. Al Safa, Dammam 34222, Saudi Arabia. Phone: +966537018749. Email: dali.niper@gmail.com. ORCID: https://orcid.org/0000-0003-3752-2331. Munfis Patel – ORCID: https://orcid.org/0000-0002-8548-6489

approximate increase in diabetes cases from 890,000 in 2000 to 2,523,000 in 2030 (about 300%) in Saudi Arabia (Wild *et al.*, 2004). This prevalence was considerably linked to Gross Domestic Product (GDP), sedentary lifestyle, and energy consumption (Meo, Usmani, Qalbani, 2017).

Many studies have reported the high costs associated with the management of diabetes and its complications (https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.htm). The estimated global growing price of DM medications in relation to health expenditure was 760 billion United State Dollars (USD) in 2019 (https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.htm). In the U.S, the total projected costs of identified diabetes cases reached 327 billion USD in 2017. In Saudi Arabia, the predicted direct cost of DM stood at at 4,5 billion dollars in 2014, with future cost projections reaching 12 billion USD (Mokdad *et al.*, 2015). During the crisis, which drives economic instability, cost analysis in healthcare is a critical factor in decision making on treatment strategy (Hill, 2012). Similarly, drug utilisation evaluation studies are imperative in gauging prescription patterns in comparison with commonly applied guidelines and to assess the quality of care provided to patients (Rafeeq, Murad, 2017).

Pharmacological management options which exist for the treatment of DM type 2 include the use of acarbose, biguanides, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, sodium-glucose co-transporter 2 inhibitors, sulfonylureas, and thiazolidinediones in addition to insulin in the event of uncontrolled cases (Sathananthan, Vella, 2009).

The study was aimed at evaluating the drug utilisation pattern and cost of antidiabetic medications and its relative adherence to the guidelines set by the American Diabetes Association for the management of diabetes mellitus Type 2 disease in Saudi Arabia.

The results of this study can be used to promote rational antidiabetic drug prescription, improve patient adherence, and cost-effective outcome of the therapy in terms of economic cost.

MATERIAL AND METHODS

Study design and data collection

The study was designed as a single centered, cross-sectional retrospective pharmacy database study on utilisation of antidiabetic drug and their cost analysis among diabetes mellitus type 2 patients. Data obtained between the period of 1st January 2019 and 31st December 2019 were retrieved from the electronic pharmacy records in Almana Group of Hospitals, Al Khobar, Saudi Arabia. In-patient and out-patient electronic drug dispensing records of the pharmacy department were reviewed. All retrieved data were archived in Microsoft excel 2013. Patients who were not prescribed and dispensed any medications for type 2 diabetes mellitus disease were excluded from the study. The prices of type 2 diabetes mellitus drugs were also retrieved from the electronic drug dispensing records of the pharmacy. The daily price of each drug was computed based on the World Health Organization (WHO) Defined Daily Dose (DDD), which was established as a universal measure of drug consumption. It provides a rough estimate of the utilisation pattern of different medications taken for various symptoms including type 2 diabetes mellitus. The cost analysis of each studied drug was calculated in terms of the average price of each unit dose of prescription. All the patients' data were categorized into two groups: Saudi and non-Saudi. Lastly, the pattern of prescription was evaluated based on adherence to the guidelines and protocols of the American Diabetes Association (ADA), which are the stipulated guidelines at the study center (hospital) for the treatment of type 2 diabetes mellitus. All the antidiabetic drugs were categorized into eight different groups and coded employing WHO anatomical therapeutic chemical classification code/ATC (https://www.whocc.no/atc_ddd_index/). These included the biguanides (ATC: A10BA) i.e. metformin (A10BA02), sulfonylureas (ATC code: A10BB) i.e. glibenclamide (A10BB01), gliclazide (A10BB09) and glimepiride (A10BB12), thiazolidinediones (A10BG) i.e. pioglitazone (A10BG03), alphaglucosidase inhibitor (ATC code: A10BF) i.e. acarbose (A10BF01), dipeptidyl

peptidase-4 inhibitor (DPP4) (ATC code: A10BH) i.e. linagliptin (A10BH05), saxagliptin (A10BH03), sitagliptin (A10BH01) and vildagliptin (A10BH02), glucagon-like peptide-1 (GLP-1) analogues (ATC Code: A10BJ) i.e. liraglutide (A10BJ02), SGLT2- sodium-glucose co-transporter 2 (SGLT 2) inhibitors (ATC Code: A10BK) i.e. dapagliflozin (A10BK01) and empagliflozin (A10BK03) excluding insulin (ATC code: A10BX).

Data Analysis

Demographic characteristics were presented as frequencies and percentages (employing Wilson 95% confidence intervals for proportions). The Chi-square test (for p-value calculation) was used to compare the utilisation rates of antidiabetic medicines among type 2 diabetes mellitus patients. All statistical analyses were conducted employing SPSS® version 26 (SPSS Institute Inc., Cary, NC, USA) and Microsoft Excel 2013. p-value ≤ 0.05 was considered as statistically significant.

RESULTS

Demographic characteristics of DM Type 2 studied patients

Table I shows the demographic characteristics of DM type 2patients. Data collected showed that males were more affected by DM type 2: 60.06% (10246 of the patients) than females: 39.93% (6811 of the patients). The highest number of patients was recorded among the middle-aged group (41-60 years). The percentage of this group was 55.78%, which indicate that 9515 patients out of the total number of patients were middle-aged. The least number of patients in terms of percentage was recorded among patients aged between 81and100 years (449 patients). Furthermore, other data showed that the number of patients aged from 20-40 years was 10.81% (1828) and 30.86% (5265) for patients aged from 61-80 years out of the total number of patients. The number of Saudi patients was more compared to non-Saudis, which was 9304 (54.45%) and 7753 (45.45%), respectively.

TABLE I - Demographic characteristics of DM Type 2 studied patients

Characteristics	Total 17057% (95% CI) (n)
Gender	
Male	60.06%(59.33-60.8)10246
Female	39.93%(39.2-40.67)6811
Age (Years)	
20-40	10.81%(10.26-11.19)1828
41-60	55.78%(55.03-56.52)9515
61-80	30.86%(30.18-31.57)5265
81-100	2.63%(2.40-2.88)449
Nationality	
Saudi	54.54%(53.8-55.3)9304
Non-Saudi	45.45%(44.7-46.2)7753

Utilisation of DM Type 2 drugs

As displayed in Table II, the overall antidiabetic medications used were divided into 8 groups. These include alpha-glucosidase inhibitors ATC code A10BF, biguanides ATC code A1OBA, DPP-4 ATC code A10BH, GLP-1 ATC code A10BJ, SGLT2 ATC code A10BK, sulfonylureas ATC code A10BB, thiazolidinedione ATC code A10BG, and fixed-dose combinations. Biguanides (metformin) were the most prescribed drugs 5673(33.25%) for monotherapy, followed by sulfonylureas (gliclazide, 10.52%), sulfonylureas (glimepiride, 9.50%), DPP-4 linagliptin (7.09%), SGLT-2 empagliflozin (6.57%), dapagliflozin (4.36%), sitagliptin (2.95%), thiazolidinedione-pioglitazone (2.47%), GLP-1 (liraglutide, 1.41%) and acarbose (0.164%), saxagliptin (0.064%), vildagliptin (0.80%), glibenclamide (0.26%) were prescribed with lower frequency. For fixed-dose combination, antidiabetic drug class with the following number of units were prescribed in decreasing order: sitagliptin+metformin 1754 (10.23%), vildagliptin+metformin 916 (5.37%), empagliflozin+metformin 631 (3.70%), dapagliflozin+metformin 155 (0.90%),

insulin degludec+liraglutide 42 (0.246%), glibenclamide+metformin 35 (0.20%), saxagliptin+metformin HCL 22 (0.12%) and glimepiride+ metformin 3 (0.017%).

Figure 1 shows the overall utilisation rate of DM Type 2 drugs based on the total number of units prescribed. It can be stated that biguanides were the most used drugs with a high percentage of 33.25, followed by fixed-dose combination therapy 20.85%, which was close to the use of sulfonylureas drugs with a percentage of 20.29 based on the total number of units prescribed for overall utilisation of DM Type 2 drugs. There was a marginal difference in the use of SGLT-2 and DPP-4 types of drugs with values of 10.93% and 10.59%, respectively. Least units of utilisation in terms of drug prescription was observed in the use of thiazolidinedione, GLP-1, and alpha-glucosidase inhibitors, with values of 2.47%, 1.50% and 0.16%, respectively.

Figure 2 describes the frequency of antidiabetic drugs used in combination with other antidiabetic drugs. According to the data, the most commonly utilised drug combinations were sitagliptin+ metformin (1754 units). Furthermore, vildagliptin+ metformin (916 units) was the next most commonly prescribed drug, followed by empagliflozin+ metformin (631units), dapagliflozin+metformin (155 units), insulin degludec+liraglutide (42%), glibenclamide+metformin (35%), saxagliptin+ metformin HCL (22 units) and glimepiride+metformin (2 units).

TABLE II - Overall utilization of DM Type 2 Drugs

Anti-diabetic drug class	ATC code	Number of units prescribed (%)
Anti-diabetic drug class	**ATC code**	**Number of units prescribed (%)**
alpha-glucosidase inhibitors	A10BF	
Acarbose	A10BF01	28 (0.164)
Biguanides		
Metformin	A10BA02	5673(33.25)
DPP-4	A10BH	
Linagliptin	A10BH05	1211(7.09)
Saxagliptin	A10BH03	11(0.064)
Sitagliptin	A10BH01	449(2.95)
Vildagliptin	A10BH02	136(0.80)
GLP-1	A10BJ	
Liraglutide	A10BJ02	242(1.41)
SGLT2 inhibitors	A10BK	
Dapagliflozin	A10BK01	744(4.36)
Empagliflozin	A10BK03	1121(6.57)

TABLE II - Overall utilization of DM Type 2 Drugs

Anti-diabetic drug class	ATC code	Number of units prescribed (%)
Sulfonylureas	A10BB	
Glibenclamide	A10BB01	45(0.26)
Gliclazide	A10BB09	1796(10.52)
Glimepiride	A10BB12	1621(9.50)
Thiazolidinedione	A10BG	
Pioglitazone	A10BG03	422(2.47)
Fixed dose combination		
Dapagliflozin, Metformin	A10BD15	155(0.90)
Empagliflozin, Metformin	A10BD20	631(3.70)
Glibenclamide, Metformin	A10BD02	35(0.20)
Glimepiride, Metformin	A10BD02	3(0.017)
Insulin Degludec, Liraglutide	A10AE56	42(0.246)
Saxagliptin, Metformin HCL	A10BD10	22(0.12)
Sitagliptin, Metformin	A10BD07	1754(10.23)
Vildagliptin, Metformin	A10BD08	916(5.37)

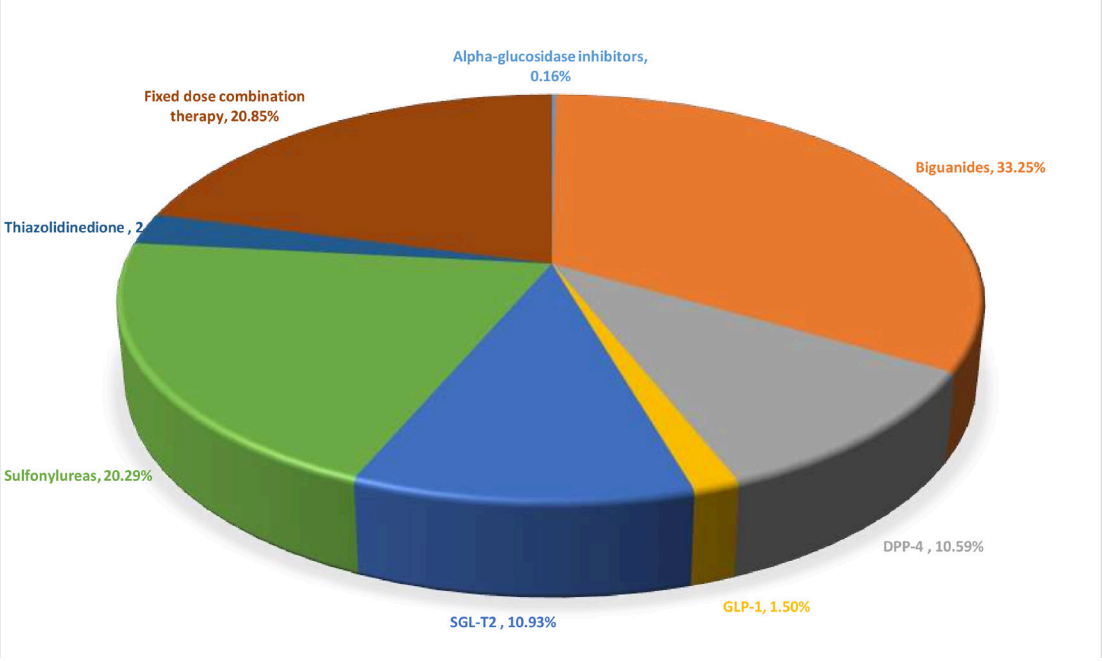

FIGURE 1 - Overall utilization of T2D drugs on the basis of total number of units prescribed

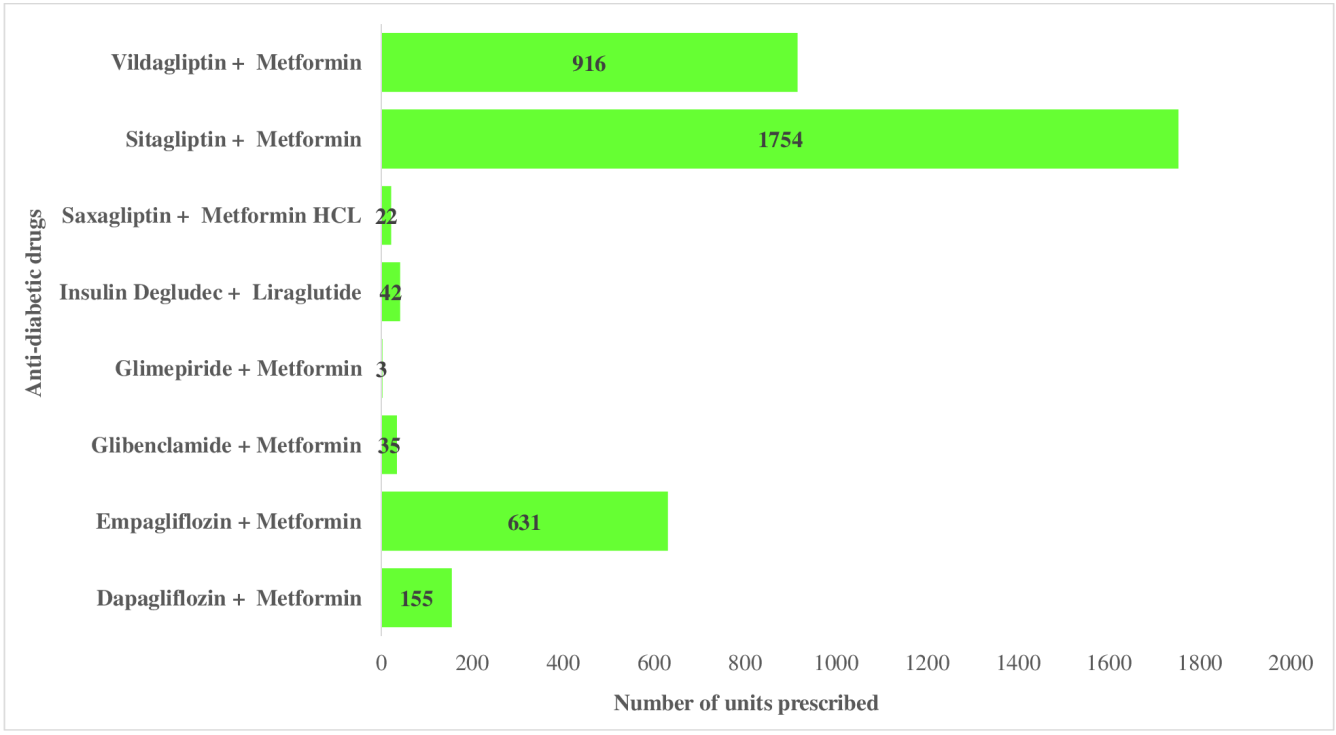

FIGURE 2 - Frequency of anti-diabetic drug combinations used at studied hospital.

DM Type 2 drug use pattern on the basis of age and adherence to ADA

Table III describes the utilisation pattern of antidiabetic drugs based on age, and is presented in terms of percentage, CI and frequency (n). Overall, biguanides {33.25% (32.56-33.97)5673} (p-value=0) were the most commonly prescribed drug class for diabetes among most of the age groups, followed by fixed-dose combinations {20.85% (20.26-21.48)3558 {(p-value=0), and sulfonylureas {20.29% (19.7-20.91)3462} (p-value=0). Alpha-glucosidase inhibitors {0.164% (0.11 0.23)28} (p-value $\leq$ 0.05), and GLP-1 {1.5% (1.25-1.61)242} (p-value $\leq$ 0.05) were among the least prescribed drug class. DPP-4 (p-value $\leq$ 0.05 and SGLT-2 (p-value=0) had similar preference status in terms of prescription; the values were {10.59% (10.14-11.6)1807} and {10.93% (10.46-11.4)1865}, respectively. In age group 20-40, the prescriptions were in the preference order of biguanides{5.31% (4.98-5.66)906}, fixed-dose combination therapy {2.13%(1.93-2.37)365}, sulfonylureas {1.31%(1.16-1.5)225}, SGLT-2 {0.8%(00.68-0.95)136}, DPP-4{0.63%(0.52-0.76)10}, GLP-1{0.3%(0.28-0.46)62}, thiazolidinedione{0.11%(0.09-0.2)23} and alpha-glucosidase inhibitors{0.01%(0.01-0.06)3}. In age group 41-60, the prescriptions were in the preference order of biguanides {17.29% (16.73-17.86)2950}, fixed-dose combination {12.56% (12.08-13.08)2144}, sulfonylureas {11.16% (10.7-11.64)1904}, SGL-T2 {7.15% (6.77-7.55)1220}, DPP-4 {5.28% (4.95-5.28)901}, thiazolidinedione {1.73% (1.26-1.62)244}, and alpha-glucosidase inhibitors {0.03% (0.02-0.08)6}. In age group 61-80, the prescription preference was in the order of biguanides {9.745%(97.52-97.96)1663}, sulfonylureas{7.15%(6.77-7.55}1220), fixed-dose combination {5.8%(5.45-6.15)987}, DPP-4 {4.18%(3.89-4.49)713}, SGLT-2{2.87%(2.63-3.13)490}, thiazolidinedione {0.825%(0.7-0.97)140}, GLP-1{0.2%(0.14-0.28)34}, alpha-glucosidase inhibitors{0.1%(0.07-0.17)18}. In age group 81-100, sulfonylureas {0.66 % (0.55-0.79)113} were the predominant class of drugs prescribed.

TABLE III - DM Type 2 drug use pattern of on the basis of Age (years) and adherence of American Diabetes Association (ADA) (n=17057)

DM Type-2 Agents (ATC code)	Total 17057% (95% CI) (n)	20-40 %(95% CI) (n)	41-60 % (95% CI) (n)	61-80 % (95% CI) (n)	81-100 %(95% CI) (n)	p-Value
Alpha-glucosidase inhibitors (A10BF)	0.164(0.11-0.23)28	0.01(0.01-0.06)3	0.03(0.02-0.08)6	0.10(0.07-0.17)18	-(0-0.04)1	≤ 0.05
Biguanides (A10BA)	33.25(32.56-33.97)5673	5.31(4.98-5.66)906	17.29(16.73-17.86)2950	9.74(97.52-97.96)1663	0.009(0.77-1.05)154	0
DPP-4 (A10BH)	10.59(10.14-11.6)1807	0.63(0.52-0.76)108	5.28(4.95-5.28)901	4.18(3.89-4.49)713	0.49(0.4-0.62)85	≤ 0.05
GLP-1 (A10BJ)	1.5(1.25-1.61)242	0.3(0.28-0.46)62	0.85(0.73-1.01)146	0.2(0.14-0.28)34	0	≤ 0.05
SGLT2 (A10BK)	10.93(10.46-11.4)1865	0.8(00.68-0.95)136	7.15(6.77-7.55)1220	2.87(2.63-3.13)490	0.11(0.07-0.17)19	0
Sulfonylureas (A10BB)	20.29(19.7-20.91)3462	1.31(1.16-1.5)225	11.16(10.7-11.64)1904	7.15(6.77-7.55)1220	0.66(0.55-0.79)113	0
Thiazolidinedione (A10BG)	2.47(2.25-27.1)422	0.11(0.09-0.2)23	1.73(1.26-1.62)244	0.82(0.7-0.97)140	0.08(0.05-0.15)15	≤ 0.05
Fixed dose combination therapy	20.85(20.26-21.48)3558	2.13(1.93-2.37)365	12.56(12.08-13.08)2144	5.8(5.45-6.15)987	0.36(0.28-0.46)62	0

DPP-4: Dipeptidyl peptidase 4 (DPP-4) inhibitors; GLP-1: Glucagon-like peptide-1 (GLP-1) analogues; SGLT2: Sodium-glucose co-transporter 2 (SGLT2) inhibitors

P- Value calculated using chi square test. *P*- Value ≤ 0.05 consider as statistically significant.

DM Type 2 drug utilisation pattern on the basis of gender and adherence to ADA

As shown in Table IV, DM Type 2 drug utilisation pattern on the basis of gender and adherence to ADA is presented in terms of percentage, CI and frequency (n). In males, biguanides were the class of drugs prescribed with the highest percentage {28.34%(27.48-29.22)2904} (p-value= 0.007), followed by FDC therapy {23.65%(22.85-24.49)2424}(p-value ≤ 0.05), sulfonylureas {21.65%(20.87-22.47)2219}(p-value≤0.5), SGLT-2 {12.17%(11.55-12.82)1247}(p-value≤0.5), DPP-4 {9.9%(9.34-10.49)1014} (p-value ≤ 0.05), thiazolidinedione{2.72%(2.42-3.50)279} (p-value ≤0.05), GLP-1 {1.34%(1.14-1.59)138} (p-value=0.02), and alpha-glucosidase inhibitors{0.20%(0.13-0.31)21}(p-value=0.008). In females, biguanides had the highest percentage in terms of prescription{40.65%(39.49-41.82)2769}, followed by sulfonylureas{18.24%(17.35-19.19)1243}, fixed-dose combination therapy {16.64% (15.79-17.56) 1134}, DPP-4 {11.645% (10.19-12.42)793}, SGLT-2{9.07%(8.41-9.78)618}, thiazolidinedione (2.09%(1.79-2.47)143), GLP1{1.52%(1.26-1.85)104}, and alpha-glucosidase inhibitors {0.1%(0.05-0.21)7}.

TABLE IV - Pattern of DM Type 2 drug used on the basis of gender and adherence of American Diabetes Association (ADA)

Anti-diabetic drug class (ATC Code)	Male Total 10246% (95% CI) (n)	Female Total 6811% (95% CI) (n)	p-Value
Alpha-glucosidase inhibitors (A10BF)	0.20(0.13-0.31)21	0.1(0.05-0.21)7	0.008
Biguanides (A10BA)	28.34(27.48-29.22)2904	40.65(39.49-41.82)2769	0.007
DPP-4 (A10BH)	9.9(9.34-10.49)1014	11.64(10.19-12.42)793	≤0.05
GLP-1 (A10BJ)	1.34(1.14-1.59)138	1.52(1.26-1.85)104	0.02
SGL-T2 (A10BK)	12.17(11.55-12.82)1247	9.07(8.41-9.78)618	≤0.5
Sulfonylureas (A10BB)	21.65(20.87-22.47)2219	18.24(17.35-19.19)1243	≤0.5
Thiazolidinedione (A10BG)	2.72(2.42-3.50)279	2.09(1.79-2.47)143	≤0.05
Fixed dose combination therapy	23.65(22.85-24.49)2424	16.64(15.79-17.56)1134	≤0.05

DPP-4: Dipeptidyl peptidase 4 (DPP-4) inhibitors; GLP-1: Glucagon-like peptide-1 (GLP-1) analogues; SGL-T2: Sodium-glucose co-transporter 2 (SGLT2) inhibitors

P- Value calculated using chi square test. *P*- Value ≤ 0.05 consider as statistically significant.

Cost analysis of DM Type 2 drugs

Table V shows all the drugs with their WHO recommended DDD (mg) and cost per unit dose prescribed. DDD ranges from 2000 mg for metformin (A10BA02) to 2 mg for glimepirde (A10BB12), and the duration of therapy ranges from 308.9 days for sitagliptin+metformin combination (A10BD07) to 90 days for glimepiride combination (A10BD02). The cost per unit dose was highest for liraglutide (A10BJ02) 255.32SR (68.79USD), followed by insulin degludec+liraglutide combination (A10AE56) 172SR (45.81USD), and the lowest for metformin (A10BA02) 0.49SR (0.13USD) followed by glibenclamide+metformin combination (A10BD02) 0.72SR (0.19 USD), glibenclamide (A10BB01) 0.75SR (0.20USD), acarbose (A10BF01) 0.78SR (0.21USD), and gliclazide (A10BB09)0.87SR (0.23USD).

TABLE V - Cost analysis of DM Type 2 Drug used among studied patients

Drug	ATC CODE	WHO DDD (mg)	Average therapy of duration in days	Average Cost in Unit dose prescription wise in SR (USD)
Acarbose	A10BF01	300	258.21	0.78(0.21)
Metformin	A10BA02	2000	246.8295	0.49(0.13)
Linagliptin	A10BH05	5	155.1453	3.78(1.01)
Saxagliptin	A10BH03	5	147.2727	4.67(1.24)
Sitagliptin	A10BH01	100	120.1069	5.01(1.33)
Vildagliptin	A10BH02	100	134.4632	2.45(0.65)
Liraglutide	A10BJ02	150	1.772727	258.32(68.79)

TABLE V - Cost analysis of DM Type 2 Drug used among studied patients

Drug	ATC CODE	WHO DDD (mg)	Average therapy of duration in days	Average Cost in Unit dose prescription wise in SR (USD)
Dapagliflozin	A10BK01	10	129.0215	5.67(1.51)
Empagliflozin	A10BK03	17.5	124.1267	5.30(1.41)
Glibenclamide	A10BB01	7	171.0444	0.75(0.20)
Gliclazide	A10BB09	60	144.5512	0.87(0.23)
Glimepiride	A10BB12	2	174.2239	1.22(0.32)
Pioglitazone	A10BG03	30	150.8081	2.37(0.63)
Dapagliflozin, Metformin	A10BD15	Not available	108.225	4.27(1.14)
Empagliflozin, Metformin	A10BD20	Not available	159.962	2.81(0.75)
Glibenclamide, Metformin	A10BD02	Not available	276.5143	0.72(0.19)
Glimepiride, Metformin	A10BD02	Not available	90	1.33(0.35)
Insulin Degludec, Liraglutide	A10AE56	Not available	1.214286	172(45.81)
Saxagliptin, Metformin HCL	A10BD10	Not available	116.5455	4.85(1.29)
Sitagliptin, Metformin	A10BD07	Not available	308.9738	2.68(0.71)
Vildagliptin, Metformin	A10BD08	Not available	263.9148	2.77(0.74)

1USD($)= 3.76 SR

DISCUSSION

Based on the literature review, we believe that this study is one of the very few studies that have been conducted in Saudi Arabia on drug utilisation and cost-effectiveness of antidiabetic medications. Previous studies were conducted based on few published data (Misbahuddin *et al.*, 2018).

Generally, our study revealed that T2D is more prevalent among males, 60.08% (10246) compared to females, 39.93% (6811). The highest number (9515-55.78%) of patients was among the middle-aged group (41-60 years); the elderly people aged 81-100 years were least (449-2.63%) affected by the disease. This finding is in consonance with previous findings (Nordström *et al.*, 2016; Mokdad *et al.*, 2015; Alhowaish, 2013). The number of Saudi patients (9304(54.54%)) were more than non-Saudis (7753(45.45%)). This is in concurrence with studies conducted earlier (Alhowaish, 2013). The key findings suggest that biguanides were the most commonly used drugs with the highest percentage of 33.25, followed by fixed-dose combination therapy, 20.85%. This could be attributed to the low cost and lesser side effects reported in the use of these drugs in addition to the recommendations stipulated by ADA guidelines. Only diarrhea has been reported with the use of some

biguanides like metformin, which can easily ameliorate when the drug is taken with food. Other classes of antidiabetic drugs have been reported to have more side effects such as UTI, which is associated with SGLT-2 inhibitors, hypoglycaemia and nausea with sulfonylureas and liver problems associated with thiazolidinedione (American Diabetes Association. https://www.diabetes.org/diabetes/medication-management/oral-medication/what-are-my-options). The efficacy of monotherapy drugs decrease with years of treatment; in such cases, combination drugs are prescribed. The most frequently prescribed combination drugs are biguanides with sulfonylureas or biguanides with thiazolidinedione in relation to ADA guidelines. This study shows that the drug combination sitagliptin+metformin (1754 units) was the most preferred and commonly prescribed fixed-dose combination therapy, followed by vildagliptin+metformin (916units). The least used combination drug was glimepiride+metformin (3units).

This result is similar to the findings of research conducted earlier (Vijayakumar *et al*., 2017; https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Avandamet/pdf/AVANDAMET-PI-MG.PDF).

Our study results revealed that metformin was the single most frequently prescribed antidiabetic medication (33.25%) for monotherapy followed by gliclazide (10.52%), while sitagliptin and metformin combination (10.23%) was the most prescribed medication for combination therapy.

Combination drugs are used when a single medicine is not able to achieve the desired blood glucose level in the diabetic patient. When the drugs are used in combination, it may allow the use of lower doses of the drugs, which may lower the risk of adverse reaction and keep the patient safe (Okoro *et al*., 2018). Metformin is the most prescribed medication for management of type 2 diabetes mellitus either as monotherapy or combination therapy. The findings of this study is comparable to the findings of a study conducted in a hospital in Nigeria (Okoro *et al*., 2018). A study conducted in Canada showed that 65% of the patients received metformin as first-line treatment (Johnson *et al*., 2006). Our study was also in line with other studies that reported biguanides and sulfonylureas as the most preferable prescription drugs for diabetes (Acharya *et al*., 2013; Satpathy, Datta, Upreti, 2016). In the present study, sitagliptin+metformin (10.23%) was the preferred combination; however, the data published in a research conducted in India showed that sulfonylureas+metformin was the preferred combination when more than one medication was required to control the disease (Satpathy, Datta, Upreti, 2016).

The conclusion of this study that metformin is the most frequently prescribed drug is based on the fact that it is currently the most preferred antidiabetic drug according to recent guidelines. The advantages of metformin as a preferred antidiabetic agent include no risk of hypoglycaemia and the fact that it is less expensive.[31] The collected data showed that the patients were in the age bracket of 20 to 100. In the current study, biguanides (metformin) were the preferred drugs among all age groups between 20 and 60. This is in line with studies conducted previously (Okoro *et al*., 2018). Furthermore, sulfonylureas were the preferred drugs among age group 81-100 and the second most preferred drugs among age group 61-80. According to a study conducted earlier, sulfonylureas were the second most preferred drug for monotherapy (Acharya *et al*., 2013; Satpathy, Datta, Upreti, 2016). A study conducted on drug utilisation among different age groups between 2012 and 2016 showed that sulfonylureas were the second most preferred drug among age groups above 65 except in 2016 (Nathan *et al*., 2009). Sulfonylureas may induce hypoglycaemia and weight gain, which may impede its use and necessitate its replacement with other oral antidiabetic drugs or insulin (Davari *et al*., 2019). Alpha-glucosidase inhibitors were the least prescribed drug class among all age groups and genders. The guidelines available presently did not identify specific preferences for one antidiabetic drug over others in relation to gender. However, the findings of the current study is in consonance with the conclusion of other studies that showed that metformin is the most prescribed drug for both genders in monotherapy and fixed-dose combination therapy, with a higher percentage for females than males (Arnetz, Ekberg, Alvarsson, 2014). Moreover, it was observed that the pattern of antidiabetic prescription for female patients in this study matched the results of another study conducted in Indian where the pattern was in the order of biguanides followed by sulfonylureas (Sharma, Tandon, Roshi Mahajan, 2016).

The nature and complications associated with chronic diseases like diabetes makes it imperative for the cost of prescription to be taken into consideration. In the current study, the average cost per unit dose per prescription ranged from 68.79USD for liraglutide to 0.13USD for metformin; whereas, the average cost of antidiabetic drugs per month was found to be 4.67USD in another study (Shah *et al.*, 2013).

In addition, the results of another study revealed that the monthly cost of glibenclamide monotherapy is the lowest followed by metformin monotherapy (Andayani, Imaningsih, 2007). The report of a study conducted in the UK has shown that the average yearly cost of monotherapy is around 110USD. The cost of combination therapy involving insulin is much more expensive as stated in another study, which is line with our findings (Eibich *et al.*, 2017).

CONCLUSION

This study which was aimed at evaluating the prescription pattern of drugs for the management of DM Type 2 was found to be consistent with the international guidelines set by ADA. Generally, biguanides remain the most highly preferred drug among all the age groups considered in this study followed by sulfonylureas. It was found that DPP-4 had an increased FDC application with metformin in contrast to sulfonylureas with metformin as reported in previous studies. No major difference in prescription pattern was found between both genders. The expenses incurred for the treatment was found to be higher for such chronic disease. Generic drug usage should be promoted to benefit the patients economically; this will improve adherence by the patients to the treatment regimen. More of such studies should be conducted to observe and update data on the drug utilisation pattern.

Since DM Type 2 is prevalent among the middle-aged group, with changes in lifestyles and increase in population, diabetic cases might increase in Saudi Arabia which will increase the burden on healthcare facility, as well as human and financial resources. The Ministry of Health (MOH) should focus more on prevention, awareness creation, and control of the disease in the years to come, concentrating primarily on early detection, sensitization of the public on the risk factors, and advising and promoting healthy lifestyle patterns.

Our study demonstrated the imperativeness for a detailed evaluation of drug utilisation pattern in the management of diabetes and its cost-effectiveness across the kingdom of Saudi Arabia so that proper multidisciplinary management approach can be carried out to avoid complications. Biguanides are the most preferred drug category; consequently, its safety and efficacy should be warranted.

CONFLICT OF INTEREST STATEMENT

None

LIMITATION OF STUDY

This research was conducted based on the principle of retrospective methods. Data for the study were collected from the pharmacy department and other departments of Almana Group of Hospitals. In this regard, the main limitation of the study was lack of patients' follow-up data and lack of patients' biochemical data.

ACKNOWLEDGEMENT

I want to specially thank and appreciate Madam Dr. Aisha Al-Mana, Head of Board of Trustees, MACHS, for giving me the opportunity to publish my research work, providing unpublished data, as well as her unflinching support and encouragement. I would like to also express my gratitude to Prof. Emad AlShwaimi, Dean, MACHS for facilitating the collection of research data.

REFERENCES

Acharya KG, Shah KN, Solanki ND, Rana DA. Evaluation of antidiabetic prescriptions, cost and adherence to treatment guidelines: A prospective, cross-sectional study at a tertiary care teaching hospital. J Basic Clin Pharm. 2013;4(4):82-7.

Alhowaish A. Economic costs of diabetes in Saudi Arabia. J Family Community Med. 2013;20(1):1-7.

Alzaid A. Diabetes: a tale of two cultures. Br J Diabetes Vasc Dis. 2012;12:57.

American Diabetes Association. Oral medication: What are my options? https://www.diabetes.org/diabetes/medication-management/oral-medication/what-are-my-options [Assess on 4th June 2020].

American Diabetes Association. Introduction: Standards of medical care in diabetes 2020. Diab. Care. 2020;43(Suppl.1):S1–S2. https://care.diabetesjournals.org/content/43/Supplement_1/S1. [Assess on 4th June 2020].

Andayani T, Imaningsih I. Cost analysis of antidiabetic drugs for diabetes mellitus outpatient in Kodya Yogyakarta Hospital. Malay J Phar Sci. 2007;5(1):19-23.

Arnetz L, Ekberg NR, Alvarsson M. Sex differences in type 2 diabetes: focus on disease course and outcomes. Diabetes Metab Syndr Obes. 2014;7:409–420.

ATC/DDD Index 2020 https://www.whocc.no/atc_ddd_index/ [Assess on 4th June 2020].

Cong JY, Zhao Y, Xu QY, Zhong CD, Xing QL. Health-related quality of life among Tianjin Chinese patients with type 2 diabetes: a cross-sectional survey. Nurs Health Sci. 2012;14(4):528-34.

Davari M, Bayazidi Y, Esteghamati A, Larijani B, Kebriaeezadeh A. The prescription pattern of antidiabetic medication and glycemic control in type 2 diabetes in Iran: a patient level study. Diabetes Manag. 2019;9(2):57–65.

Eibich P, Green A, Hattersley AT, Jennison C, Lonergan M, Pearson ER, et al. Costs and treatment pathways for Type 2 diabetes in the UK: A mastermind cohort study. Diabetes Ther. 2017;8(5):1031–45.

Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diab Care. 1997;20:1183–97.

Hill SR. Cost-effectiveness analysis for clinicians. BMC Medicine 2012;10:10. https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Avandamet/pdf/AVANDAMET-PI-MG.PDF [Assess on 4th June 2020]

International Diabetes Federation. IDF Diabetes Atlas, 9th ed. Brussels, Belgium: International Diabetes Federation;2019. https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.htm [Assess on 4th June 2020].

Johnson JA, Pohar SL, Secnik K, Yurgin N, Hirji Z. Utilization of diabetes medication and cost of testing supplies in Saskatchewan. BMC Health Serv Res. 2006;6:159.

Meo SA, Usmani AM, Qalbani E. Prevalence of type 2 diabetes in the Arab world: impact of GDP and energy consumption. Eur Rev Med Pharmacol Sci. 2017;21(6):1303–1312.

Misbahuddin MR, Hussam AM, Zohair JG, Ziaullah MS. Anti-diabetic drugutilization patterns in a government hospital in Saudi Arabia. Trop JPharm Res. 2018;17(6):1193–200.

Mokdad AH, Tuffaha M, Hanlon M, El Bcheraoui C, Daoud F, Al Saeedi, et al. Cost of Diabetes in the Kingdom of Saudi Arabia, 2014. J Diabetes Metab. 2015;6(8):575.

Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Medical management of hyperglycemia in type 2 diabetes: 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.

Nordström A, Hadrévi J, Olsson T, Franks PW, Nordström P. Higher Prevalence of Type 2 Diabetes in Men Than in Women Is Associated With Differences in Visceral Fat Mass. J Clin Endocrinol Metab. 2016;101(10):3740–6.

Okoro RN, Nmeka C, Erah PO. Utilization study of antidiabetes medicines at a tertiary care hospital in Nigeria. Future J Pharm Sci. 2018;4(2):109–115.

Rafeeq M M, Murad H. Evaluation of drug utilization pattern for patients of bronchial asthma in a government hospital of Saudi Arabia. Niger J Clin Pract. 2017;20(9):1098-105.

Sathananthan A, Vella A. Personalized pharmacotherapy for Type 2 diabetes mellitus. Per Med. 2009;6(4):417–422.

Satpathy SV, Datta S, Upreti B. Utilization study of antidiabetic agents in a teaching hospital of Sikkim and adherence to current standard treatment guidelines. J Pharm Bioall Sci. 2016;8(3):223-8.

Scollan-Koliopoulos M, Bleich D, Rapp KJ, Wong P, Hofmann CJ, Raghuwanshi M. Health-related quality of life, disease severity, and anticipated trajectory of diabetes. Diabetes Educ. 2013;39(1):83–91.

Shah K, Solanki N, Rana D, Acharya K. Evaluation of antidiabetic prescriptions, cost and adherence to treatment guidelines: A prospective, cross-sectional study at a tertiary care teaching hospital. J Basic Clin Pharm. 2013;4(4):82.

Sharma S, Tandon VR, Roshi Mahajan A. Prescribing pattern of oral antihyperglycaemic drugs, rationality and adherence to American Diabetes Association (ADA) treatment guidelines among type 2 diabetes mellitus (T2DM) postmenopausal women. J Clin Diagn Res. 2016;10(1):11–5.

Van Tilburg J, van Haeften TW, Pearson P, Wijimenga C. Defining the genetic contribution of type 2 diabetes mellitus. J Med Genet. 2001;38(9):569–578.

Vijayakumar TM, Jayram J, Meghana Cheekireddy V, Himaja D, Dharma Teja Y, Narayanasamy D. Safety, Efficacy, and Bioavailability of Fixed-Dose Combinations

in Type 2 Diabetes Mellitus: A Systematic Updated Review. Curr Ther Res Clin Exp. 2017;84:4-9.

Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(5):1047–1053.

Received for publication on 28th July 2020
Accepted for publication on 30th November 2020