A Retrospective Study of Medication Utilization Pattern and Clinical Outcome in Middle-Aged and Older Patients with Type 2 Diabetes Mellitus in Qatar

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Abstract

Background: Type 2 Diabetes Mellitus (DM) is a costly illness and general one related with significant mortality and morbidity. In spite of this, there is only small information on the clinical outcome and 'real-world' medication utilization patterns for middle age and older patients with type-2 diabetes. Therefore, the main aim of the study is to evaluate the Medication Utilization Pattern and Clinical outcome in Type2 DM for middle age and older Patients.

Methods: A retrospective longitudinal study was conducted from 1st Jan 2016 to 30 June 2016 in an out-patient department of a tertiary hospital in Doha, Qatar. The outpatients with Type 2 DM and age above 55 years are included in the study. The sample size for the study is selected 150 middle-aged and older patients from a total of 800 patients who attended Rumailah hospital Geriatric outpatient clinic during the study period. Data were compared to find out the associations between DM and socio-demographic and clinical indicators using inferential statistics. ROC analysis, ANOVA, Chi square test and logistic regression were used for analytical purpose. P-value<0.05 was considered to be statistically significant.

Results: Results show that combination anti-diabetic therapy was more used than monotherapy. The study found a significant positive correlation between Age and HbA1C in addition to Fasting Blood Sugar (FBS) and Glycated hemoglobin (HbA1c) levels. Under variable treatment regimens, the majority of 118 older patients were using Metformin as oral hypoglycemic agent; for insulin, the most commonly used treatment regimen is Glargine Insulin; with regards to anti-hypertensive, calcium channel blocker, Amlodipine is the most prescribed medication for patients followed by angiotensin receptor blocker, Valsartan. The use of a combination of Metformin/ Sitagliptin or Vildagliptin shows higher non-insulin anti-diabetic (NIAD) drug prescriptions as per attaining target. ROC analysis showed an elevation in cut off levels of HbA1c with advance in age. Drug utilization pattern of different age groups showed that <65 age group monotherapy was better; 65-74 age group monotherapy and combination therapy was more effective in attaining the target HbA1c. However, drug utilization pattern was comparable in patients above 75 years.

Conclusion: Drug utilization pattern was different according to age group. Monotherapy was found to be most effective in attaining the target HbA1c in middle aged and young elderly population. Metformin (78.7%), Glizalide (32.7%), Sitagliptin (27.3%) and Vildagliptin (17.3%) were the most predominantly prescribed and consumed antidiabetes medicines. The insulin-based therapies were not effective in all age group to attain better glycemic control compared to oral antidiabetic drugs. Our data suggest that standard treatment guideline was followed properly among diabetic older population in Qatar.

Keywords: Drug utilization pattern; Type 2 Diabetes Mellitus; Older persons; Clinical outcome

Introduction

There is a gradual increase in aging population with the high encumbrance of chronic conditions either with a single chronic condition or with multiple conditions. Over the past 20 years, there is a high increase found in the prevalence of Diabetes Mellitus (DM) in various regions of the world and presently it is considered a global health issue [1]. In 2012, around 1.5 million people died due to DM, wherein around 80 percent of these deaths were from low and middle-income nations [2]. In 2014, it was estimated that around 8.5 percent of adults [3] were diagnosed with DM globally and presently around

387 million people are prone to Type 2 Diabetes (T2DM), and by the year 2035, the prevalence of T2DM is predicted to increase up to 592 million. Presently, the count of individuals with T2DM is increasing in every nation. Among them, DM is prevalent and is becoming widespread among older people. Certainly, around 25 percent of the population in the world is affected by DM around the age of 65 years [4]. DM is a chronic metabolic disorder virtually affects almost every cell in the body which in turn leads to pathology in multiple organ systems and consequently leading to higher healthcare expenses. DM is the prominent reason for mortality and morbidity; it is also the main reason for numerous macrovascular diseases (coronary artery diseases, peripheral vascular diseases, stroke) and microvascular diseases (retinopathy, neuropathy, and nephropathy). According to a consensus statement by European Association for the Study of Diabetes (EASD)

and American Diabetes Association (ADA), type 2 diabetes is considered as a progressive loss of β -cell function and a consistent requirement for the progressive and initial accumulation of glucose-lowering plans [5]. It is a challenging task for maintaining and achieving glycemic control as the main treatment goal in managing Type 2 DM (T2DM).

The country which is presently experiencing an alarming increase in the prevalence of T2DM is Qatar, a Middle Eastern country and it is part of the Gulf Cooperation Council. Since 1997, Qatar has been a part of the International Diabetes Federation (IDF) and in 2017, Qatar had around 0.24 million cases of T2DM wherein adult population was around 16.52 percent between the age group 20 to 79 years [4], it was projected that at least one in every four adult Qataris will have diabetes by 2050. These high rates of diabetes in the region have precipitated significant research interest aimed at identifying risk factors that may explain the high diabetes prevalence. A previous study conducted by Bener et al. in Qatar has found a reasonable increase in the prevalence of DM over adult population in Qatar. A severe glycemic control of DM is foremost important for reducing the risk of diabetes-related conditions like ischemic heart disease, stroke, and peripheral cardiovascular diseases [6].

Diabetes mellitus (T2DM) is a chronic metabolic disorder affecting virtually every cell in the body leading to pathology in multiple organ systems with consequent high health care resource expenditures. In the context of Qatar, risk factors associated with diabetes were examined in one study Bener et al. (2009), but there was a lack of investigations related to drug utilization in diabetic adult population. Therefore, the present study is to analyze the effectiveness of the drugs in controlling the glycemic status and to decrease the rate of complications related to diabetes. Hence, the study aims in evaluating the utilization of drugs pattern in geriatric T2DM patients who are at an alarming rate in Qatar. A retrospective longitudinal study is performed in identifying the utilization of combined anti-diabetic therapy rather than using monotherapy for achieving optimal glycemic control.

Research Methodology

Study design

A retrospective longitudinal study was conducted from 1st Jan 2016 to 30 June 2016 in an out-patient department of a tertiary hospital in Doha, Qatar. This study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendment.

This study obtained ethical approval from Research Ethics Committee, at Medical Research Center, Hamad Medical Corporation (HMC), Doha, Qatar (IRB No #15175).

Study population

This Study was conducted in the out-patient department in general geriatric clinic of a Rumailah hospital in Doha, Qatar. The patients with Type 2 DM, around 60 years of age (middle-aged and young old) are included for the study. Non-Type 2 DM, less than 50 years of age are excluded from the study.

Sample size

For 95% confidence interval and, significance level $\alpha=5\%$, $P=90\%$, $Q=10\%$, allowable error=6%, required sample size was 118. P =percentage of Oral hypoglycemic drugs used for the treatment of Type 2 DM. In the pilot study done prior to the original study with 10 patients presented to the out-patient department with Type 2 DM. But we collected 150 middle-aged and older patients.

Data collection

The data collected were age, sex, duration of DM, laboratory findings, vital signs, number of all medicines prescribed, number of medicines prescribed by generic name, number of antidiabetic and antihypertensive medicines prescribed, number of essential antidiabetic medicines name, class, route of administration and comorbidities were abstracted.

Statistical analysis

The gathered data were analyzed using the SPSS v20.0 (Statistical Package for Social Sciences version 20 Inc. USA). Methods for the analysis are Continuous variables analyzing by using student t-test or one-way ANOVA, for skewed continuous data, a non-parametric Mann-Whitney test, and categorical variables compared by using the chi-square test and associations between DM and socio-demographic and clinical indicators were evaluated. ROC analysis was done to find out the cut off for HbA1c level. P -value<0.05 was considered to be statistically significant.

Results

Table 1 shows the demographics, clinical characteristics, comorbidities and laboratory findings in geriatric patients with type 2 DM. From the 150 patients, 80 (53.3%) were female and remaining 70 (46.7%) were male and their mean age was 66.9. From the chosen sample, the number of Qatari was 75 (50%) and 75 belongs to other nationalities. The Comorbidity results show Hypertension was the most common among 108 (72.0%) patients, followed by Dyslipidemia among 66 (44.0%) and the least common was congestive heart failure with 1 (0.7%) patients. The table also shows that the mean score of Systolic blood pressure (146.9), Diastolic blood pressure (73.8) and Body Mass Index (31.1). The laboratory findings show that the creatinine was high with a mean score of 83. The Urine Albumin/Creatinine Ratio of the patients was 3.8. The test on HbA1C level on 146 patients shows that it is $\leq 7.0\%$ among 54 (37%) patients and $>7.0\%$ among 92 (63%) patients. The mean scores 105 patient's Fasting blood sugar level was 7.9 ± 2.3 .

Table 2 shows the percentage of patients with T2DM on anti-diabetic treatment regimens. Under variable treatment regimens, the majority of 118 (78.7%) patients were using Metformin while the least commonly used was Acarbose 1 (0.7%). For insulin, the most commonly used treatment regimens was Glargine Insulin 28 (18.7%) and least commonly used was Human Mixtard Insulin 30/70 by 9 (6.0%) patients. With regards to Anti-hypertensive, Amlodipine was the most prescribed medication for 67 (44.7%), followed by Valsartan by 55 (36.7%) patients and Losartan by 11 (7.3%) patients. For Beta Blocker, the medication was as follows, Metoprolol 6 (4.0%), Atenolol 5 (3.3%), and Bisoprolol 3 (2.0%).

Table 3 shows the baseline characteristics of patients with DM on medication (HbA1C target achieved).

Age group	
55-64	59 (39.3%)
65-74	72 (48%)
≥ 75	19 (12.7%)
Gender	
Females	80 (53.3%)
Males	70 (46.7%)
Nationality	
Qatari	75 (50%)
Duration of DM (years) (n=51)	14.4 ± 7.8
Co-morbidities	
Hypertension	108 (72.0%)
Dyslipidemia	66 (44.0%)
Cerebrovascular accidents	11 (7.3%)
Coronary artery disease(CAD)	10 (6.7%)
Dementia	7 (4.7%)
Chronic kidney (CKD)	6 (4.0%)
Congestive heart failure	1 (0.7%)
Variables	
Aspartate aminotransferase	21.6 ± 9.9
Alanine Aminotransferase	23.4 ± 14.9
Creatinine	83.0 ± 36.1
Urine Albumin/ Creatinine Ratio	3.8 (0.3-350.8)
HbA1c level (n=146)	8.1 ± 1.7
≤ 7.0%	54 (37%)
>7.0%	92 (63%)
Fasting blood sugar (n=105)	7.9 ± 2.3
Total cholesterol	4.2 ± 1.0
Low-Density Lipoprotein-LDL	2.3 ± 1.1
Triglycerides-TG	1.7 ± 0.8
Systolic blood pressure	147.2 ± 20.3
Diastolic blood pressure	74.2 ± 9.3
Body Mass Index	31.1 ± 6.3

Table 1: Demographics, clinical characteristics, co-morbidities and laboratory findings in geriatric patients with type 2 DM (n=150) (Period Jan-June 2016).

It is clear that age was higher in HbA1C ≤ 7.0% at 68.2 ± 5.9; Among gender, female showed higher percentage in 47 (51.1%) in HbA1C>7.0%; Qatari nationals with DM on medication at 42 (45.7%);

BMI range was observed at 31.5 ± 6.8; Systolic blood pressure of patients with DM on medication of HbA1C>7.0% at 147.2 ± 20.2; Diastolic blood pressure was observed higher in HbA1C>7.0% at 74.2 ± 9.6; Body Mass Index was higher in HbA1C>7.0% at 31.5 ± 6.8 and duration of diabetes was noticed as higher in 11.0 ± 7.6 (HbA1C ≤ 7.0%).

Variables	Values n (%)	95% CI
Anti-diabetics		
Metformin	118 (78.7%)	(75.4-82.0)
Gliclazide	49 (32.7%)	(28.9- 36.5)
Sitagliptin	41 (27.3%)	(23.7-30.9)
Vildagliptin	26 (17.3%)	(14.2-20.4)
Glimipride	22 (14.7%)	(11.8- 17.6)
Glibenclamide	7 (4.7%)	(2.9- 6.4)
Glipizide	6 (4.0%)	(2.4- 5.6)
Acarbose	1 (0.7%)	(0.02- 1.4)
Liraglutide	8 (5.3%)	(3.5-7.1)
Various Insulins		
Glargine Insulin	28 (18.7%)	(15.5- 21.9)
Insulin Lispro	20 (13.3%)	(10.5- 16.1)
Insulin Aspart	13 (8.7%)	(6.4- 11)
Human Mixtard Insulin 30/70	9 (6.0%)	(4.1- 7.9)
Anti-hypertensive		
Amlodipine	67 (44.7%)	(40.6- 48.8)
Valsartan	55 (36.7%)	(32.8- 40.6)
Losartan	11 (7.3%)	(5.2-9.4)
Beta Blocker		
Metoprolol	6 (4.0%)	(2.4-5.6)
Atenolol	5 (3.3%)	(1.8- 4.8)
Bisoprolol	3 (2.0%)	(0.9- 3.1)

Table 2: Percentage of patients on various treatment regimens.

The characteristics Chronic diseases of the patients were noted at higher in HbA1C>7.0% as hypertension was higher among 67 (72.8%)patients, Cerebrovascular accidents was higher among 6 (6.5%) patients, Coronary artery disease was 6 (6.5%), Dyslipidemia was higher in 40 (43.5%); Chronic kidney disease was higher in 4 (4.3%). But dementia shown higher among 5 (9.3%) at HbA1C ≤ 7.0%;

Laboratory findings examined the fasting blood sugar was 8.9 ± 2.6; Urine Albumin/ Creatinine Ratio was 4.1(0.8-350.8); High-Density Lipoprotein-cholesterol was 1.2 ± 0.5; Total cholesterol was 4.3 ± 1.1; Triglycerides was 1.7 ± 0.8 at HbA1C>7.0% and slightly high low-density lipoprotein-cholesterol was observed as 2.4 ± 1.1 at HbA1C ≤

7.0%. The findings were not statistically significant related to HbA1c (Table 4).

Out of the total 146 prescribed antidiabetic treatment, 47 (51.1%) were Oral hypoglycemic drugs + Insulin which was the most common treatment among HbA1c>7.0%, preceding was the Oral hypoglycemic drugs in combination with 32.6% in HbA1c>7.0%. Whereas in HbA1c ≤ 7.0%, the most common anti-diabetic treatment was Oral hypoglycemic drugs in combination with 48.1% and the next common treatment was oral hypoglycemic drugs monotherapy with 37.0%.

	HbA1c ≤ 7.0% n=54 (37%)	HbA1c>7.0% n=92 (63%)	P value
Age (mean ± SD) years	68.2 ± 5.9	66.1 ± 5.7	0.03
Females	30 (55.6%)	47 (51.1%)	0.6
Qatari nationals	29 (53.7%)	42 (45.7%)	0.34
Systolic blood pressure	145.5 ± 20.2	147.2 ± 20.2	0.62
Diastolic blood pressure	73.4 ± 10.9	74.2 ± 9.6	0.66
Body mass Index	30.4 ± 5.7	31.5 ± 6.8	0.35
Duration of diabetes	11.0 ± 7.6	7.7 ± 7.0	0.04
Diseases			
Hypertension	39 (72.2%)	67 (72.8%)	0.93
Cerebrovascular accidents	5 (9.3%)	6 (6.5%)	0.54
Coronary artery disease	3 (5.6%)	6 (6.5%)	0.81
Congestive heart failure	0 (0.0%)	1 (1.1%)	0.44
Dementia	5 (9.3%)	2 (2.2%)	0.05
Dyslipidemia	24 (44.4%)	40 (43.5%)	0.91
Chronic kidney disease	2 (3.7%)	4 (4.3%)	0.85
Laboratory findings			
Fasting blood sugar	6.9 ± 1.4	8.9 ± 2.6	0.001
Urine Albumin/ Creatinine Ratio	2.7 (0.3-19.1)	4.1(0.8-350.8)	0.12
Low Density Lipoprotein-cholesterol	2.4 ± 1.1	2.3 ± 1.1	0.7
High Density Lipoprotein-cholesterol	1.2 ± 0.3	1.2 ± 0.5	0.97
Triglycerides	1.6 ± 0.9	1.7 ± 0.8	0.24
Total cholesterol	4.2 ± 0.9	4.3 ± 1.1	0.4

Table 3: Baseline characteristics of patients with DM on medication (HbA1c target achieved).

In Oral hypoglycemic drugs monotherapy, the most commonly utilized drug was Metformin in both HbA1c>7.0% and HbA1c ≤ 7.0%, with 72 (78.3%) and 45 (83.3%) respectively. Gliclazide drug was used more in HbA1c>7.0% with 34 (37.0%) when compared to HbA1c ≤ 7.0% which was 13 (24.1%).

	HbA1C ≤ 7.0% (n=54)	HbA1C>7.0% (n=92)	P value
Anti-diabetic treatment			
Oral hypoglycemic drugs monotherapy	20 (37.0%)	11 (12.0%)	0.001 for all
Oral hypoglycemic drugs in combination	26 (48.1%)	30 (32.6%)	
Oral hypoglycemic drugs + Insulin	5 (9.3%)	47 (51.1%)	
Insulin alone	2 (3.7%)	3 (3.3%)	
No drug	1 (1.9%)	1 (1.1%)	
Oral hypoglycemic drugs monotherapy			
Metformin	45 (83.3%)	72 (78.3%)	0.45
Gliclazide	13 (24.1%)	34 (37.0%)	0.1
Sitagliptin	15 (27.8%)	24 (26.1%)	0.82
Vildagliptin	6 (11.1%)	19 (20.7%)	0.14
Glimipride	5 (9.3%)	16 (17.4%)	0.17
Liraglutide	0 (0.0%)	8 (8.7%)	0.02
Oral hypoglycemic drugs in combination			
Metformin + Vildagliptin	6 (11.1%)	16 (17.4%)	0.3
Metformin + Gliclazide	11 (20.4%)	25 (27.2%)	0.35
Metformin + Sitagliptin	11 (20.4%)	21 (22.8%)	0.72
Metformin + Glimipride	4 (7.4%)	14 (15.2%)	0.16
Metformin + Liraglutide	0 (0.0%)	6 (6.5%)	0.05
Metformin + Glargine Insulin	2 (3.7%)	18 (19.6%)	0.007

Table 4: Type 2 DM patients on medication (HbA1c target achieved).

	No HTN (n=42)	HTN (n=108)	P value
Age (mean ± SD) years	66.5 ± 5.3	67.1 ± 6.0	0.55
Males	18 (42.9%)	52 (48.1%)	0.56
HbA1c level	8.0 ± 1.8	8.1 ± 1.7	0.88
Fasting blood sugar	7.4 ± 1.9	8.2 ± 2.4	0.12
Low Density Lipoprotein-cholesterol	2.7 ± 1.3	2.2 ± 0.9	0.01
High Density Lipoprotein-cholesterol	1.1 ± 0.3	1.2 ± 0.5	0.52
Triglycerides	1.7 ± 0.7	1.6 ± 0.8	0.61
Total cholesterol	4.6 ± 1.2	4.1 ± 0.9	0.03

Table 5: Baseline characteristics of patients with type 2 DM with HTN.

Other drugs such as Sitagliptin, Vildagliptin, Glimipride, and Liraglutide was utilized more in HbA1c>7.0% whereas when compared

with HbA1c $\leq 7.0\%$ these drugs were utilized less frequently. In Oral hypoglycemic drugs combination, the most commonly utilized combinations were Metformin + Gliclazide in HbA1c $>7.0\%$ with 25 (27.2%). In HbA1c $\leq 7.0\%$ the most commonly utilized combinations were Metformin + Sitagliptin with 11 (20.4%) and that was equal to Metformin + Gliclazide with 11 (20.4%) (Table 5).

A major risk factor for cardiovascular diseases in particular with type 2 DM was Hypertension. Hence, on evaluating the presence of hypertension among type 2 DM, it was found that most of the male (48.1%) patients had hypertension with a mean age of $67.1 (\pm 6.0)$. On assessing HbA1c level among patients with and without hypertension; it was found that the levels were having only slight variation among hypertension patients with a mean score $8.1 (\pm 1.7)$ and in not having hypertension, the mean score was $8.0 (\pm 1.8)$. According to fasting blood sugar, the mean score of hypertension was $8.2 (\pm 2.4)$ and with no hypertension, it was $7.4 (\pm 1.9)$. By analyzing low-density lipoprotein-cholesterol, no hypertensive had higher mean value $2.7 (\pm 1.3)$ whereas they are at the risk of heart diseases and stroke but when compared with mean value of $2.2 (\pm 0.9)$ of hypertension it is low. Hence, patients with high levels of low-density lipoproteins are at risk of heart diseases and stroke because lipoproteins carry cholesterol all over the body wherein low-density lipoproteins are also called as high-risk cholesterol making up most of the body's cholesterol. Conversely, in assessing high-density lipoprotein-cholesterol, it was found that there was a slight difference between hypertension and no hypertension was the mean values were $1.2 (\pm 0.5)$ and $1.1 (\pm 0.3)$. On analyzing the levels of triglycerides it was identified that only small variation in the mean values $1.7 (\pm 0.7)$ and $1.6 (\pm 0.8)$ among not having hypertension and hypertensive.

Further on evaluating the total cholesterol level it was found that not having hypertension had a higher mean score of $4.6 (\pm 1.2)$ when compared with a mean score of hypertension $4.1 (\pm 0.9)$ (Figure 1).

On analyzing the percentage of anti-diabetic treatment among patients with T2DM, it was identified that patients with non-insulin anti-diabetic (NIAD) in combination were higher with 38.7%, followed by NIAD + Insulin with 35.3% and NIAD monotherapy with 21.3%. The least percentage was 1.3% with no drug and treatment with no insulin it was 3.3% (Figure 2).

It represents the distribution of HbA1c values in patients with DM and achieving glycaemic control (Figure 3 and 4) was observed. A great number of patients cluster around the median of 7.0%, at 28.71 percent of the patients. 20.55% of patients had HbA1c values within a range of 6.5–7%, 19.86% had HbA1c values within a range of below

6.5%, and 17.12% had HbA1c values with the range of <0.65% and 15.75% shows the glycaemic control as per HbA1c intervals (>10%).

It analyzed the association of different anti-diabetic treatment groups ($P=0.001$) with HbA1c. It was noticed the highest of 149 in NIAD combination, i.e., NIAD combination was significantly associated with median HbA1c%.

Non-insulin antidiabetic drug prescriptions (Sulphonylurea and DPP4i alone or in combination) according to target HbA1c was outlined in Figure 5. The use of a combination of Metformin/Sitagliptin/ Vildagliptin shows higher non-insulin antidiabetic drug prescriptions as per achieving the target HbA1c<7.0% but it was low in HbA1c>7.0%.

Figure 5: Non-insulin antidiabetic drug prescriptions (Sulphonylurea and DPP4i alone or in combination) according to target HbA1c.

The correlation between age and HbA1c levels ($p=0.03$) is shown in Figure 6. The p-value was 0.03 which shows that there was a significant negative correlation between age and HbA1c levels.

Figure 6: Correlation between age and HbA1c levels ($r = -0.18$; $p=0.03$).

The correlation between Fasting blood Sugar (FBS) and HbA1c levels is represented in Figure 7. The p-value is 0.001 which is lower than 0.05. It shows there is a significant positive correlation between FBS and HbA1c levels.

It shows the correlation between SBP and HbA1c levels. The p-value is 0.98 which is higher than 0.05. It shows there is no significant correlation between SBP and HbA1c levels.

The study further analyzed the association of different treatment groups as outlined in Figure 8 with HbA1c: The use of insulin, either alone or in combination with NIAD or NIAD alone or combination was used.

Highest of NIAD alone or combination shows higher combination with target HbA1c ≤ 7% at 86.8%; NIAD and combination of insulin show higher combination with target HbA1c>7% at 51.6% and insulin alone treatment expresses less combination with HbA1c ≤ 7% at 3.8% (Figure 9).

Figure 7: Correlation between FBS and HbA1c levels ($r = 0.47$; $p=0.001$).

Figure 8: Association of anti-diabetic treatment strategies and target HbA1c.

Table 6 show the comparison of baseline characteristics and anti-diabetic treatment of patients with DM based on different age groups. Patients with middle-age were more likely to be prescribed for Metformin as compared to older groups ($p=0.008$).

However, the three groups were comparable for demographics, comorbidities and other anti-diabetic medications.

		B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1a	Age	0.158	0.069	5.167	1	0.023	1.171	1.022	1.342
	BMI	0.112	0.067	2.788	1	0.095	1.118	0.981	1.275
	FBS	-0.403	0.173	5.451	1	0.02	0.668	0.476	0.937
	OHD Mono	1.824	1.714	1.133	1	0.287	6.197	0.215	178.253
	OHD combination	-0.339	1.59	0.046	1	0.831	0.712	0.032	16.068
	OHD	-2.172	1.672	1.688	1	0.194	0.114	0.004	3.019
	Insulin Or alone (1)								
	Gender (1)	0.086	0.672	0.016	1	0.899	1.089	0.292	4.065
	Constant	-10.38	5.953	3.041	1	0.081	0		

a. Variable(s) entered on step 1: Age, BMI, FBS, OHD_Mono, OHD_combination, OHD_Insulin_Or_alone, Gender.

Table 6: Variables in the Equation.

Model Summary						
Model	R	R Square	Adjusted R Square	Std. The error of the Estimate		
1	0.678a	0.46	0.352	1.2175		
a. Predictors: (Constant), BMI, Antidiabetic_3cat, Age, DM_Duration_Cat, FBS						
ANOVAa						
Model		Sum Squares	df	Mean Square	F	Sig.
1	Regression	31.571	5	6.314	4.26	0.006b
	Residual	37.057	25	1.482		
	Total	68.628	30			
a. Dependent Variable: HbA1C level Period Jan Dec 2015, b. Predictors: (Constant), BMI, Antidiabetic_3cat, Age, DM_Duration_Cat, FBS						
Coefficients						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	11.333	4.626		2.45	0.022
	Age	-0.082	0.057	-0.227	-1.445	0.161
	FBS	0.278	0.118	0.408	2.347	0.027
	Antidiabetic 3cat	0.439	0.577	0.134	0.762	0.453
	DM_Duration Cat	0.766	0.593	0.203	1.292	0.208
	BMI	-0.056	0.045	-0.199	-1.238	0.227
a. Dependent Variable: HbA1C level Period Jan Dec 2015						

Table 7: Multivariate linear regression.

The above table shows the multivariate linear regression analysis between HbA1c target level and BMI, antidiabetic medication, age, duration of DM, and FBS. The R-squared value is 0.460, F value is 4.260 and the p-value is 0.05.

Since the p-value is higher than 0.05. After adjusting for relevant covariate, only FBS was found to be an independent predictor of HbA1c target levels.

Figure 10 and ROC analysis yield a cut off value of 7.15 (sensitivity=72.4%, specificity=46.6% and area under the curve=0.055).

Figure 10: ROC curve of HbA1c for 50-64 years.

Figure 11: ROC curve of HbA1c for 65-74 years.

Figure 12: ROC curve of HbA1c for ≥ 75 years.

Figure 11 and ROC analysis yield a cut off value of 7.75 (sensitivity=47.8%, specificity=51.9% and area under the curve=0.471, $p=0.547$).

Figure 12 and ROC analysis yield a cut off value of 7.45 (sensitivity=42.1%, specificity=41.7% and area under the curve=0.365, $p=0.058$).

	HbA1C ≤ 7.0%	HbA1C > 7.0%	P value
Age group 55-64	(n=16)	(n=42)	
Anti-diabetic treatment			
Oral hypoglycemic drugs monotherapy	6 (37.5%)	2 (4.8%)	0.001 for all
Oral hypoglycemic drugs in combination	9 (56.2%)	16 (38.1%)	
Oral hypoglycemic drugs + Insulin	1 (6.2%)	23 (54.8%)	
Insulin alone	0 (0%)	1 (2.4%)	
No drug	0 (0%)	0 (0%)	
Age group 65-74	(n=29)	(n=40)	
Anti-diabetic treatment			
Oral hypoglycemic drugs monotherapy	11 (37.9%)	6 (15.0%)	0.005 for all
Oral hypoglycemic drugs in combination	13 (44.8%)	10 (25%)	
Oral hypoglycemic drugs + Insulin	3 (10.3%)	22 (55%)	
Insulin alone	1 (3.4%)	1 (2.5%)	
No drug	1 (3.4%)	1 (2.5%)	
Age group ≥ 75	(n=9)	(n=10)	
Anti-diabetic treatment			
Oral hypoglycemic drugs monotherapy	3 (33.3%)	3 (33%)	0.963 for all
Oral hypoglycemic drugs in combination	4 (44.4%)	4 (40%)	
Oral hypoglycemic drugs + Insulin	1 (11.1%)	2 (20%)	
Insulin alone	1 (11.1%)	1 (10%)	
No drug	0 (0%)	0 (0%)	

Table 8: Age group wise comparison of Type 2 DM patients on medication (HbA1C target achieved).

Table 8 shows that monotherapy was found to be most effective in attaining the target HbA1c in middle aged and elderly population.

The insulin-based therapies were not effective in all age group to attain better glycemic control compared to oral antidiabetic drugs.

When anti-diabetes medicines consumption was determined with respect to age, it was found that diabetes patients aged 65-74 and ≥ 75 years had significantly higher consumption of Oral hypoglycemic drugs monotherapy compared to 55-64 years.

Discussion

This study aimed to evaluate the drug utilization pattern in geriatric Type-2 DM young older patients in an outpatient setting in Rumailah

Hospital. All patients were under the routine care of endo-geriatrics so that the data have to be interpreted as reflecting specialist care.

In order to examine the Type 2 DM patients on medication, study findings show that combination anti-diabetic therapy was more used than monotherapy. In Oral hypoglycemic drugs monotherapy, the most commonly utilized drug was Metformin in both $HbA1c > 7.0\%$ and $HbA1c \leq 7.0\%$, in Oral hypoglycemic drugs combination, the most commonly utilized combinations was Metformin + Glimepiride in $HbA1c > 7.0\%$ and in $HbA1c \leq 7.0\%$, the most commonly utilized combinations were Metformin + Sitagliptin. This was in line with the previous study findings [7,8]. From this view, it is important to know that 20 percent of the cohort had $HbA1c$ which is less than 6.5% (48 mmol/mol), which could be suggested as either poor health status or overtreatment with a high risk of hypoglycemia [9]. Since the result did not have a significant difference when intensive was associated with the conventional glycaemic control for every causes and mortality which results in lower risk of microvascular complication along with kidney diseases among intensively treated patients with interventional trials [10,11]. If there is a presence of renal anemia then $HbA1c$ levels might be lower due to the short lifespan of erythrocytes [12].

Indeed, the study found a slight but significant positive correlation between age and $HbA1c$ and FBS and $HbA1c$ levels. But when hemoglobin values of the patients were analyzed it was found that majority of the patients were under normal range and it is noted as there is no difference in the mean hemoglobin concentrations among patients with $HbA1c$ values below or above the average. Moreover, hemoglobin but not $HbA1c$ is associated positively with eGFR identified through the findings of [13].

Under variable treatment regimens, majority of 118 (78.7%) patients were using Metformin; for insulin, the most commonly used treatment regimen is Glargine Insulin 28(18.7%); with regards to anti-hypertensive, calcium channel blocker, Amlodipine is the most prescribed medication for patients followed by angiotensin receptor blocker, Valsartan and among Beta Blocker, the medication is Metoprolol 6 (4.0%). It should be noted that there is an ongoing debate about whether the current thresholds for metformin use as suggested by guidelines may be too restrictive [14].

It is noticed the highest of 149 in NIAD combination, i.e NIAD combination was significantly associated with a median $HbA1c$ percentage. The use of a combination of Metformin/Sitagliptin or Vildagliptin shows higher non-insulin antidiabetic drug (NIAD) prescriptions as per the target $HbA1c < 7.0\%$. Treatment with insulin was related to increases in $HbA1c$ (8.3% contrasted with 7.7% towards oral combination group), increased mortality (HR 1.49), increased likelihood of the major large vessel disease event [15]. Additional retrospective study of Type-2 DM from Germany, were patients were recommended with sulfonylurea or insulin, a combination of insulin along with any oral anti-diabetic drugs, a combination of metformin along with sulfonylurea was less likely to attain an intensive $HbA1c$ target [16]. The quality of treatment is better or even comparable than in large cohort studies of patients with Type-2DM in Germany which has identified mean values of $HbA1c$ of 7.0 and 7.2% [17,18]. According to guidelines recommended by Germany, an $HbA1c$ between 6.5% and 7.5% (48 – 58 mmol/mol) for every patient with diabetes associated with kidney disease [8] and our cohort was met with 45% with this criteria. A recent guideline recommendation by U.S. National Kidney Foundation's Kidney Disease Outcome Initiative (K/DOQI) has recommended a target $HbA1c$ of $\sim 7.0\%$ for preventing or delaying the progress of microvascular complications of DM [7].

Hence according to these guidelines many patients were treated. Various studies have also identified that good metabolic control could be attained in patients with DM. Highest of NIAD alone or combination shows higher combination with target $HbA1c \leq 7\%$. The cut off value of $HbA1c$ may vary from older to oldest. Another significant finding of the study is that patterns of Anti-diabetic treatment might differ from general diabetes population and completely highly variable. Overall, moderately more than 50 percent were treated using insulin-based therapies. In Germany, a general Type-2DM population with insulin-based therapy was around 31% wherein 20% is lower than in the patient presently analysed [19]. Around 40% of the patients were treated only with insulin which is particularly higher when compared with general DM cohorts containing along with German cohorts where insulin monotherapy is treated only for 10 – 20% [16,18,20]. Oral glucose-lowering medication (with or without insulin) treatment was only among one-third of the patients. In the General diabetes population of Germany, patients who receive any oral antidiabetic medication were at 60 to 70% of the patients [17–19]. Around one-quarter of the cohort, patients were treated with oral antidiabetic agents alone when compared to 75% of general diabetes cohorts [18,21].

With various levels of metabolic control, diverse treatments were associated. Use of insulin alone or in combination with oral anti-diabetic drugs was supplemented with 4 to approximately 6 times higher probability of having $HbA1c$ values $> 7.0\%$ (53 mmol/mol). In the same way, usage of oral glucose-lowering drugs alone such as glinides, metformin, DPP-4 inhibitors, or combination of metformin along with DPP-4 inhibitors was not related along with such prospect apart from sulfonylureas. From the observation of the study prevents to depict conclusions over effect and cause while identifying these modifications in metabolic control in patients who are under various therapies and numerous factors might take place. Therefore patients with difficulty in treating diabetes were exchanged and treated with insulin or sulfonylureas, describing at least a part higher with $HbA1c$ levels in these patients. Moreover, patients with higher $HbA1c$ targets might be selected intentionally in certain patients. When this recommendation is implemented it might explain higher $HbA1c$ levels in certain patients, improbable it might apply for the majority of the insulin-treated patients, provided in younger age there was no difference in eGFR but the only slight high rate was predominant in CVD. According to ADA and European Association for the Study of Diabetes specified that England National Clinical Guideline for Management in Primary and Secondary Care from NICE (National Institute for Health and Care Excellence) [22] is more evidence-based, usually permitting metformin use down to an eGFR of $30 \text{ mL/min/1.73 m}^2$, with decrease dose advised at $45 \text{ mL/min/1.73 m}^2$ [14,22,23]. Hence the European guideline from 2009 has provoked the German doctors for prescribing metformin in spite of an eGFR of below $60 \text{ mL/min/1.73 m}^2$. Based on the functional status from the study findings, diabetes care has to be addressed through framing national guidelines for overcome hypertension, Dyslipidemia, Coronary artery disease, Cerebrovascular accidents, Congestive heart failure, Diastolic blood pressure, Systolic blood pressure etc.

There are certain limitations of this study apart from observational nature. There is a lack of information on medication history and treatment duration, which might provide a better understanding for reasons of patients with particular therapies. This study couldn't classify older patient's disease complexities and $HbA1c$ level with respect to frailty Index. The backbone of the study is its size and the assessment of various types of anti-diabetic medication. Information

was gathered directly from the patient's e-record, perhaps to overcome certain uncertainties of implementation rationality of prescription orders in patients when treated with more than one doctor. In a central lab utilizing identical methodology, all HbA1c values were determined. However, this study provides the baseline information to the researchers regarding the drug utilization pattern among a cohort of outpatient's older in the Doha province of Qatar.

Conclusion

Drug utilization pattern was different according to age group. Monotherapy was found to be most effective in attaining the target HbA1c in middle aged and young older population. Metformin, Gliclazide, and Sitagliptin were the most predominantly prescribed and consumed anti-diabetes combination medicines. The insulin-based therapies alone were scarce in all age group to attain better glycemic control compared to oral anti-diabetic drugs. Our data suggest that standard treatment guideline was followed properly among older diabetic population in Qatar.

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Author Contribution

NN: study design, Proposal preparation, data review and manuscript writing; HA: study design and manuscript drafting, final review; HS: study design and manuscript editing; SV: study design, data analyzing; NK: manuscript drafting; MR: study design and manuscript editing; FU: manuscript drafting and proofreading; MBR: Proposal preparation, data review; MO: study design and manuscript editing; MA: Datasheet preparation, manuscript drafting; AA: study design, data analyzing; AB: Proposal preparation, data review; ES: study design, data analyzing.

Declaration

We declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere. We know of no conflicts of interest associated with this publication, and there has been no significant financial support for this work that could have influenced the outcome.

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