Research Article

Pattern of Statin use in patients with diabetes mellitus type 2 for primary and secondary prevention of cardiovascular disease in Saudi Arabia

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Abstract

Background: Statins have been recommended by contemporary guidelines to be used in all diabetic patients regardless of the baseline cholesterol; more real-world data are needed to know about the actual pattern of statin use. We aimed to determine the pattern of statin use in the diabetic population in Almadinah Almunawwarah, Saudi Arabia.

Results: This was a cross-sectional study on 167 Saudi adult diabetic patients attending the outpatient diabetes clinic through interviewing the patients and filling-in a questionnaire. Multivariate binary logistic analysis was used to assess the predictors of poor adherence to statin.

Statins were prescribed to 122 (73.1%) patients. There were 109 (65.3%) patients who were aged 40 years or above and had no cardiovascular disease (CVD), of those, 70.6% were receiving statins for primary prevention. Whilst, CVD was diagnosed in 44 (26.3%) patients, of those, 97.7% were receiving statins for secondary prevention. After adjustment of confounders, there was a significant association ($p<0.05$) between low adherence to statin and three predictors; diabetes duration ≥ 15 years, OR=5.09, (95% CI: 2.06-12.59), age range (45-54.9 years), OR=4.66, (95% CI: 1.63-13.36), and polypharmacy of ≥ 5 drugs, OR=3.44, (95% CI: 5.09-7.93).

Conclusions: Even though the rate of statin prescription in our study was higher than the world-wide numbers, it is far below the clinical guidelines recommendations. Efforts are needed to improve adherence to the updated guidelines to use statin for all diabetic patients above the age of 40 years to prevent CVD. Moreover, cost-effectiveness studies are needed to evaluate the impact of using statins in all diabetic patients.

Keywords: Statins; Adherence; Cardiovascular diseases; Prevention; Diabetes mellitus

Abbreviations: Cardiovascular Disease (CVD); Diabetes Mellitus (DM); International Diabetes Federation (IDF); Middle East and North Africa (MENA); Coronary Artery Disease (CAD); Myocardial Infarction (MI); Low-Density Lipoprotein (LDL); 3-Hydroxy-3-Methyl Glutaryl Coenzyme A (HMG-CoA); Triglycerides (TG); High-Density Lipoprotein (HDL); Justification for The Use of Statins In Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER); High-Sensitivity C-Reactive Protein (Hs-CRP); American Diabetes Association (ADA); Peripheral Artery Disease (PAD); Blood Pressure (BP); Body Mass Index (BMI); Statistical Package for Social Science (SPSS); Standard Deviation (SD); Odds Ratio (OD); Confidence Interval (CI); Fasting Blood Glucose (FBG); Glycated Hemoglobin (HbAIc); World Health Organization (WHO); Cholesterol Treatment Trialists (CTT); American Heart Association/American College of Cardiology (AHA/ACC); National Cardiovascular Data Registry Practice Innovation and Clinical Excellence (NCDR PINNACLE); Proportion-Of-Days Covered (PDC).

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Introduction

Worldwide, the overall diabetes mellitus (DM) prevalence rises steadily. In 2017, it was assumed that about 60 million adult Europeans had type 2 DM (half of them undiagnosed). This increase leads to the prediction that by 2045, more than 600 million individuals worldwide would be developing type 2 DM, with pre-DM developing around the same number.[1]

The International Diabetes Federation (IDF) in 2014[2] has reported that DM prevalence in Saudi Arabia was 24% in 2013 and is expected to increase to 24.5% in 2035. In the updated 9th edition of IDF, in 2019, Saudi Arabia was reported to be one of the countries with the highest estimated number of children and adolescents with DM in the Middle East and North Africa (MENA) region. In the same edition, undiagnosed diabetes in the region was as high as 44.7%. Moreover, DM was responsible for 418,900 regional deaths in adults aged 20-79 years. Notably, nearly 53% of deaths from DM in the region occurred in those under the age of 60.[3]

Diabetic dyslipidemia has a two to three-fold rise in coronary artery disease (CAD) risk, and a four-fold rise in the post-myocardial infarction (MI) mortality rate.[4] CAD prevention has been dependent on controlling the traditional risk factors, including the management of dyslipidemia through statin therapy,[5] which has

contributed significantly to the reduction of CVD especially among diabetic patients or those with existing CVD.[6]

Statin therapy has proved successful in lowering the likelihood of serious cardiovascular events and mortality by 27% and 15% respectively.[4] Statins can decrease low-density lipoprotein (LDL) as much as 53-55% through inhibiting 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase enzyme. Beside decreasing LDL, statins also can lower triglycerides (TG) and increase high-density lipoprotein (HDL) however to a lesser extent.[7] Statins also reduce inflammation through their pleiotropic effects on multiple pathways.[8] Moreover, the JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) trial recruited 18,802 patients with normal level of LDL and high inflammatory marker, high-sensitivity C-reactive protein (hs-CRP), rosuvastatin significantly reduced the incidence of cardiovascular events over a median follow-up period of 1.9 years.[9] The American Diabetes Association (ADA), recently in 2020, advised to use statin treatment in diabetic patients aged 40 years or above, irrespective of the baseline cholesterol level.[10]

The efficacy of statins, as with any drug treatment, can be greatly impaired by patients inability to comply with treatment criteria.[11] It has been suggested that failures to meet LDL goals are due to many reasons, including insufficient dose titration, and poor follow-up. Notably, poor adherence to the drug is the most significant cause.[12]

Numerous patients, health care providers, and medical factors may affect the compliance behavior of statin users. Patient-related variables, such as demographic profiles and clinical components, usually provide higher adherence estimates than physician-related or financial considerations. Patient-related data can be obtained from case notes and records. Registered interventions, however, have only a limited capacity to clarify statin compliance, largely because there is an additional provision for contextual variables such as personal and social conduct toward statins.[13]

We aimed to determine the pattern of statin use in the diabetic population in Almadinah Almunawwarah, Saudi Arabia.

Methods

Study design and population

We conducted this cross-sectional study at Al-Ansar Hospital which is a secondary care hospital of 100 beds located in Almadinah Almunawwarah, Saudi Arabia.

The inclusion criteria were all Saudi adult patients aged more than 18 years, with DM, living in Almadinah Almunawwarah region. We excluded patients diagnosed with the following conditions: chronic liver disease, nephrotic syndrome, and patients with malignancy.

A total of 167 subjects were recruited using a simple random sampling technique for diabetic patients who attended the outpatient diabetic clinic at Al-Ansar Hospital in the duration from May to September 2019.

Data collection through a questionnaire

We interviewed the patients and filled in the self-made questionnaire. The first part was concerned about demographic details (age, gender, address). We inquired about the diagnosis of DM, duration of the disorder, follow-up, and glycemic control. We asked about the diagnosis of atherosclerotic CVD and its risk factors. Diagnosis of atherosclerotic CVD included CAD, stroke, and peripheral artery disease (PAD). We asked about risk factors that included hypertension with reporting blood pressure (BP) readings, smoking, and obesity with reporting body mass index (BMI). Other comorbid conditions were also reported. The details on the statin drug used, dosage, side effects, and adherence to the medication were interrogated. If the patient did not take a statin drug, the explanation was questioned.

Adherence was evaluated by the patient self-reporting of his/her behavior towards statin therapy. The patients were asked during the interview about the number of missed daily doses per the last year via the designed questionnaire. If the number of missed doses was below 20% this is considered good adherence, otherwise, it was considered poor adherence. Notably, Garber and colleagues found that adherence, assessed by questionnaires and diaries, showed moderate to high correlation with non-self-measures, for example, electronic reporting.[14]

The validity of the questionnaire was verified by content validation, since the questionnaire covered the aim of the study, which is "the assessment of the pattern of statin usage in diabetic patients in Almadinah Almunawwarah, Saudi Arabia". Validity has been confirmed by the opinion of 2 adult cardiology consultants, and has been accepted for use in the Saudi community.

Ethical considerations

This work was accepted by the academic ethics committee. All patients who engaged in the study agreed on written consent of Taibah University, Saudi Arabia. Patients were told that their details would show no patient identification and would be confidential.

Statistical analysis

Data from questionnaires have been collected, extracted, and entered into the SPSS (Statistical Package for Social Science) program for statistical analysis, (version 21; Inc., Chicago. IL). Qualitative data has been presented as numbers and percentages, and the Chi-Squared test was carried out to determine the relationship between the variables. For 2 × 2 qualitative variables, Fisher exact test was used when more than 25% of the cells have expected count less than 5. The normally distributed continuous variables were defined as mean and standard deviation (SD), and independent student t-test assessed the difference between variables. The nonparametric continuous data were expressed as median and inter-quartile range and tested by the Mann Whitney U test. The normality of data was also assessed using the Shapiro-Wilk test. Stepwise logistic regression model was used to give the adjusted odds ratio and 95% confidence interval of the effect of different factors on the compliance of diabetic patients to treatment. A p-value of below 0.05 was considered to be statistically significant.

Results

In the current study, we recruited 167 Saudi adult diabetic patients as seen in the flowchart in Figure 1. The mean age and SD was (55.4 ± 9.3). Baseline characteristics of our study population were reported in Table 1, and Table 2. Notably, more than one-

third of our patients (39.5%) were diabetics for duration of more than 15 years.

CVD was diagnosed in 44 (26.3%) patients, 26 (15.6%) patients have CAD, 32 (19.2%) has PAD, and 8 (4.8%) patients has a stroke. It was found that some patients have combined diseases of CAD, PAD, and/or stroke.

Regarding the status of statin use, we found that statins were prescribed by the treating health care provider in 122 patients (73.1%), and not prescribed for the rest of the population 45 (26.9%) (Figure 1). Notably, almost all patients with CVD [43 of 44 CVD patients (97.7%)] were receiving statins for secondary prevention. There were 123 patients without CVD, 79 (64.23%) of them were taking a statin. Whilst, patients without CVD and age of 40 years or above were 109 patients, we found that 77 (70.64%) of them were using statin for primary prevention (Figure 2).

Figure 3 showed the side effects due to statin treatment that were reported in 50 patients. Myalgia was reported in 36 patients (72%), elevation of transaminases was reported in 8 (16%) patients, Arthralgia was reported in 2 (4%) patients and GIT upset was reported in 4 (8%) patients.

Figure 1: Flowchart of recruited patients

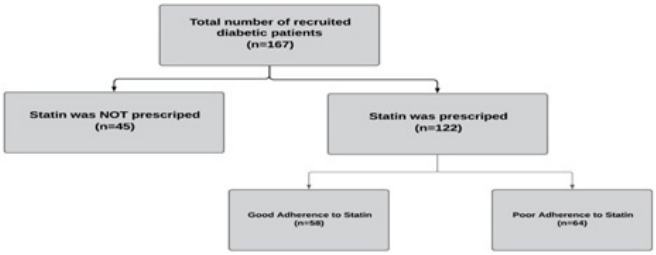


Figure 2: Use of statin as primary prevention and secondary prevention in patients aged 40 years or above.

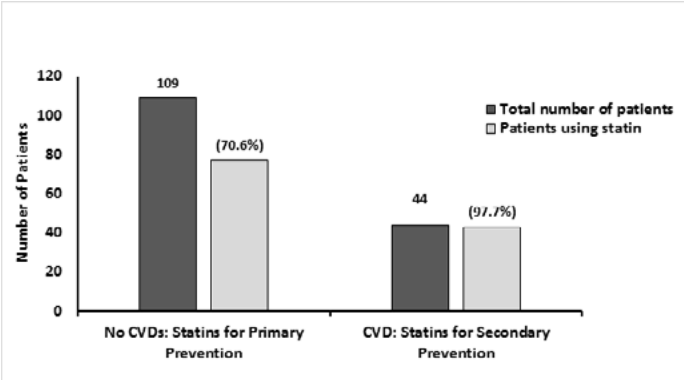


Figure 3: The reported statin side effects (frequency and percentage).

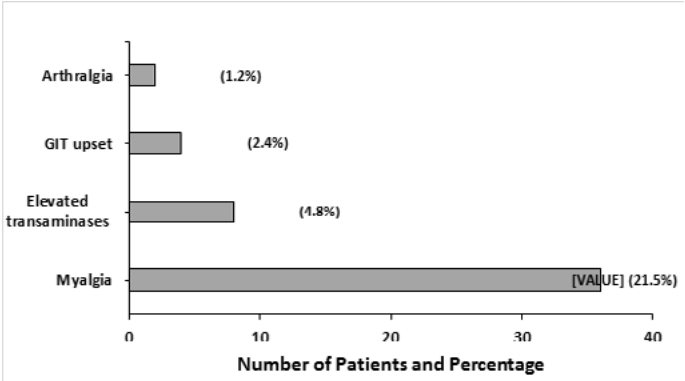


Table 1: *Main baseline characteristics of patients*

Characteristics	Median	Interquartile range (IQR)
Age (years)	57	50-61
BMI (Kg/m2)	28.04	25.6-31.1
Height (cm)	165	160-170
Weight (Kg)	77	70-86
HbAIc	8.7	7.4-9.6
Fasting plasma glucose	200	162.5-2
Systolic BP	154	137-169
Diastolic BP	83	78-93
Total cholesterol	4.9	4.3-5.6
LDL	3.2	2.9-4.1
HDL	1	0.76-1.2
Triglycerides	2.35	1.9-3.1
Abbreviations: BMI, body mass index; HbAIc, Glycated hemoglobin; BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density-lipoprotein		

Table 2: *Distribution of the studied patients according to different parameters (n=167)*

Characteristics	Frequency	Percent
Gender:		
Male	114	68.3
Female	53	31.7
Duration of diabetes		
1-3 years	12	7.2
4-5 years	16	9.6
6-10 years	31	18.6
11-15 years	42	25.1
> 15 years	66	39.5
Treatment		
Oral hypoglycemics (only)	62	37.1
Insulin (only)	57	34.1

Oral hypoglycemics and insulin	48	28.7
Smoking:		
Yes	34	20.4
No	133	79.6
HTN		
Yes	79	47.3
No	88	52.7
Cardiovascular disease		
Yes	44	26.3
No	123	73.7
CAD		
Yes	26	15.6
No	141	84.4
PAD		
Yes	32	19.2
No	135	80.8
Stroke		
Yes	8	4.8
No	159	95.2
Abbreviations: HTN, hypertension; CAD, coronary artery disease; PAD, peripheral artery disease.		

Among those who have received a prescription of statins, statin non-persistence (stopping taking statin) was reported in one-quarter of them (25.4%) (Table 3). Myalgia was accused in 20 (64.5%) patients, and elevation of hepatic transaminases was reported in 8 (25.8%) patients. While 3 (9.7%) of those who stopped statin did not report any side effects.

We found that nearly half (47.5%) of statins users were taking rosuvastatin. Atorvastatin and simvastatin were used by 46 (37.7%), and 18 (14.8%) of patients, respectively. Regarding potency, most of the studied subjects used moderate-potency statins 96 (78.7%), while high-potency statins were used by 16 (13.1%), as were the low potency statins in 10 (8.2%) of patients (Table 3). Regarding statin adherence among patients who received statin, 58 (47.54%) patients showed good adherence, while 64 (52.46%) stated poor adherence.

Table 3: *Status of statin use among statin prescribed patients*

Study data	Overall N (%) (n=122)
Status of statin use	
Current user	91 (74.6)
Non-persistent (stopped statin due to side effect)	31 (25.4)
Compliance state	
Good adherence	58 (47.5)
Poor adherence	64 (52.5)
Statin drug used	
Atorvastatin	46 (37.7)
Rosuvastatin	58 (47.5)
Simvastatin	18 (14.8)
Potency of statin	
High	16 (13.1)
Moderate	96 (78.7)
Low	10 (8.2)

Results of the binary logistic regression, after adjustment of confounders, indicated significant associations ($p<0.05$) between having age ranging from 45-54.9 years, being diabetic for 15 years or more, polypharmacy of 5 drugs or more, and the low adherence to statin therapy among diabetics. Polypharmacy of 5 drugs or more and being diabetic for 15 years or more significantly predicted low adherence to statin, OR=3.44, (95% CI: 5.09-7.93), OR=5.09, (95% CI: 2.06-12.59), respectively. Moreover, age (45-54.9 years) significantly predicted the likelihood of low adherence to statin, OR=4.66, (95% CI: 1.63-13.36). The other age groups, gender, CAD, PAD, presence of CVD, or hypertension did not significantly predict the low adherence to statin among our diabetic participants (Table 4).

Table 4: *Binary Logistic Regression for poor adherence to statin therapy in diabetic patients including adjusted odds ratios and 95% confidence intervals*

	Adjusted (OR)*	**95% CI**	**p value**
Age Group			
18-44.9	6.56	(0.89-48.00)	0.064
45-54.9	4.66	(1.63-13.36)	0.004
More than 55 (Ref)			
DM duration			
≥15 years	5.09	(2.06-12.59)	<0.001
<15 years (Ref)			
Polypharmacy			
≥ than 5	3.44	(5.09 – 7.93)	0.004
< than 5 (Ref)			
*** OR has been adjusted for age, gender, CAD, PAD, CVD, and hypertension.**			

On comparing the statin non-persistence versus active statin users, as can be seen by the frequencies cross-tabulated in Table 5, there is a significant relationship between hypertension and statin non-persistence, ($p=0.01$). Hypertensive patients were found to be 74.2% of the statin non-persistence group, while they were only 48.4% of the statin current users.

As seen in Table 5, being diabetic for a duration of more than 15 years was significantly associated with statin non-persistence among the studied population, ($p=0.002$). Patients who have been diabetic for over 15 years make up 71% of the statin non-persistence group, although they make up just 39.6% of active statin users.

Table 5: *Comparison between current statin user versus non-persistent categorical variables*

		Statin Users (n=122)		p value
		Current statin user	Non-persistent users	
		n=91 (%)	n=31 (%)	
Gender	Male	61 (67.0%)	20 (64.5%)	0.79
	Female	30 (33.0%)	11 (35.5%)	
Smoking	Smoker	15 (16.5%)	8 (25.8)	0.25
	Non-smoker	76 (83.5%)	23 (74.2%)	
Hypertension	Hypertensive	44 (48.4%)	23 (74.2%)	0.01
	Non-hypertensive	47 (51.6%)	8 (25.8%)	
DM duration	≤15 years	55 (60.4%)	9 (29.0%)	0.002
	>15 years	36 (39.6%)	22 (71.0%)	
Cardiovascular disease (CVD)	Diagnosed CVD	26 (28.6%)	17 (54.8%)	0.008
	No CVD	65 (71.4%)	14 (45.2%)	
Coronary artery disease (CAD)	Diagnosed CAD	14 (15.4%)	12 (38.7%)	0.006
	No CAD	77 (84.6%)	19 (61.3%)	
Peripheral artery disease (PAD)	Diagnosed PAD	16 (17.6%)	16 (51.6%)	0
	No PAD	75 (82.4%)	15 (48.4%)	
Stroke	Diagnosed stroke	4 (4.4%)	4 (12.9%)	0.20*
	No stroke	87 (95.6%)	27 (87.1%)	
Polypharmacy	Polypharmacy > 5	27 (29.7%)	30 (96.8%)	< 0.001*
	Polypharmacy < 5	64 (70.3%)	1 (3.2%)	

(a) Categorical data expressed as number (percent) and tested by the chi-square test.

(*) Exact Fisher test.

The diagnosed CVDs were significantly different between the statin current users and statin non-persistence (p=0.008). In the statin non-persistence group, 54.8% of the patients had CVD, while just 28.6% of them had CVD in the statin active users. Similar findings were also found in patients with diagnosed CAD, and PAD, (p=0.006, and p<0.001) respectively. On the other hand, there were no significant associations between the statin therapy non-persistence and gender, smoking history, or the patient diagnosed with the stroke, (p>0.05).

Results of Table 6 showed no significant effect of age, and weight on the probability of statin non-persistence (p>0.05). However, diabetes control showed a significant effect on statin non-persistence. Fasting blood glucose (FBG) was significantly higher in the statin non-persistence, (p=0.01), and as was glycated hemoglobin (HbAIc), (p=0.01).

Table 6: *Selected personal, medical, and laboratory parameters among statin prescribed patients distributed by their state of statin use*

	Current Statin Users	**Non-persistent Users**	**P value**
	n=91	**n=31**	
	mean (SD)	**mean (SD)**	
Age [a]	58.28 (7.15)	57.44 (7.74)	0.58 [b]
Weight [a]	77.35 (12.99)	75.32 (12.03)	0.45 [b]
HbAIc [a]	8.38 (1.4)	9.14 (1.46)	0.01 [b]
FBG [a]	192.25 (38.58)	211.39 (39.33)	0.01 [b]
	median (IQR)	median (IQR)	
Systolic BP [b]	156 (140-169)	169 (157-175)	0.002
Diastolic BP [b]	83 (78-91)	92 (79-98)	0.01
TC [b]	4.78 (4.33-5.2)	5.9 (4.8-6.32)	<0.001
LDL [b]	3.16 (2.86-3.65)	4.27 (3.04-4.72)	0.001
HDL [b]	1 (0.83-1.2)	0.8 (0.7-1.2)	0.04
TG [b]	2.3 (1.9-2.86)	3.1 (2.35-4)	0

(a) continuous and normally distributed data, expressed as mean (SD: standard deviation) tested by student t-test

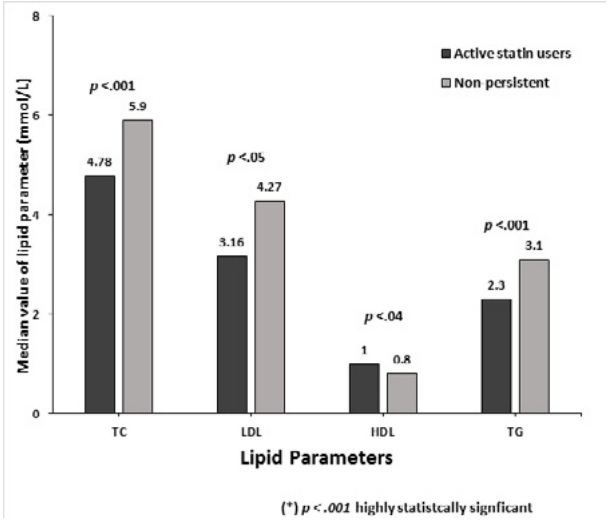
(b) Continuous and non-normally distributed tested by Shapiro Wilk test, expressed as median (IQR: interquartile range).

Abbreviations: HbAIc, glycated hemoglobin; FBG, fasting blood glucose; BP, blood pressure; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density-lipoprotein; TG, triglycerides.

There was a significant relationship (p<0.05) between the blood pressure and lipid profile as independent variables, and the statin non-persistence as an outcome (dependent variables). There was a statistically significant difference in the systolic blood pressure (p=0.002) between active statin users and statin non-persistence, as was the diastolic blood pressure (p=0.01). For the non-persistence of statin, the median of systolic and diastolic blood pressure was higher.

Figure 4 shows the lipid profile distribution according to the active statin users versus non-persistent group. There were statistically significant differences between the active statin users and stain non-persistence in all studied lipid profile parameters as following, total cholesterol (TC) (P<0.001), low-density lipoprotein (LDL) (p=0.001), high-density lipoprotein (HDL) (p=0.047), and triglycerides (TG) (p<0.001). The median values of all studied lipid parameters were significantly higher in the statin non-persistence than the active statin group. TG showed a highly significant difference (p<0.001).

Figure 4: Lipid profile distribution according to the active statin users versus non-persistent group.



Discussion

World health organization (WHO)[15] reported that DM prevalence is growing globally, having quadrupled, and having reached pandemic rates in the Middle East and around the world.[16] This presents a significant challenge for health care authorities as diabetes raises the risk of multiple diseases especially cardiovascular disease.[17]

CVDs are the major cause of morbidity and mortality worldwide, including Saudi Arabia.[18] The Cholesterol Treatment Trialists' (CTT) Collaborators [19] reviewed more than [18] thousand diabetic patients in a meta-analysis of [14] randomized statin trials involved, followed up for more than 4 years. It was stated that reducing the LDL by one mmol/l has decreased total mortality by 9% and vascular mortality by 13%. Moreover, they concluded that the benefits were proportionally related to the absolute LDL reduction without a lower level of LDL below which benefits were absent.

DM, type 2, is not only considered to be a major risk factor for CAD, and but also equal to CAD in risk.[20] Patients with diabetes are 2 to 4 fold more likely to develop CAD than patients without diabetes.[21] The ADA stated that patients with age more than 40 should receive moderate-intensity statin, which is well-established in the reduction of all cardiovascular major events and total mortality, not only in the general population,[22] but also in patients with diabetes mellitus.[23] These major benefits of statin is mainly dependent on adherence.[20]

Therefore, we aimed to know the pattern of statin use in diabetic patients in Almadinah Almunawwarah, Saudi Arabia.

Our study reported that for patients aged 40 years or above, there were 70.6% of diabetic patients were prescribed statin for primary prevention. This statin prescription practice has demonstrated that the use of statin needs to be increased following the recommendations of the contemporary clinical guidelines. The 2013 American Heart Association/American College of Cardiology (AHA/ACC) lipid management guidelines suggested that all patients with diabetes should receive statins regardless of cholesterol levels.[24] More recently, the ADA 2020 guidelines noted that diabetic patients, of 40 years of age or above, should receive moderate-intensity statins with lifestyle changes, whereas high-intensity statins should be reserved for patients with CVD or other risk factors.[23]

Similar results were stated by the NCDR PINNACLE (National Cardiovascular Data Registry Practice Innovation and Clinical Excellence) registry data from 2008 to 2012, they found 67.6% of the patients were using statins.[25] As in Elnaem et al. study,6 in Malaysia, 65% of patients admitted to the hospital statin treatment were prescribed for primary prevention.

In 2019, the Demoz et al.[26] found that 55.7% of the diabetic patients had received statins. In the Indian Heart Watch-2, Gupta et al.[27] reported that 55.2% of the diabetic patients had statin treatment. The prescribing rate in Hong Kong was as small as 33.8%.[28]

The reported rates of statin use in diabetes in the western countries were much lower. Mortensen et al.,[29] in Denmark, studied 1622 patients presented with first MI, and they found that 47% of the patients were not receiving statin before MI. In the US, Steen et al.[30] found that only 40% of diabetic patients have been taking statins for primary prevention. The difference in the number of risk factors in subjects participating in the research and study design may explain this discrepancy. In the Danish study, the mean TC and LDL were 4.5 mmol/l and 2.5 mmol/l, respectively, while in our cohort the mean TC and LDL were much higher 4.95 mmol/l, and 3.45 mmol/l. Moreover, they stated that the insurance plan for their diabetic cohort was 40.9%.

In our study, statins and other diabetes medications were obtained for free from the Saudi Ministry of Health the responsible body for health care in Saudi Arabia. According to the IDF report 2017,[31] patients who have diabetes suffer from their medications not being available and unaffordable, which continues to be a major obstacle to diabetes in Africa and many other middle-income countries.

In our study, for primary prevention moderate-intensity statin was prescribed in 63%, this is compared to Demoz et al.,[26] they reported that moderate statins were used in 46.1%. Regarding secondary prevention, we found in the present study that statins were prescribed in 97.7%. High potency statins were used in only 11.4%, and moderate potency statins were used in 75%. This is consistent with Gupta et al,[27] they reported that high dose statins were used in only 14.5% of the high-risk patients (they are diabetics and microvascular or macrovascular complications), whereas most of their high-risk patients 84.4% were using moderate doses. In the US, Steen et al.30 found that statins were used in only 49% for secondary prevention. As agreed with Lin et al.,[32] the use of high-intensity statin was from 13.3% to 31.4%, while the use of moderate-low potency was from 86.6 to 86.7%.

In the Nilsson et al. study 33 that was conducted on 931 patients in Sweden, they reported statin use as low as 34.5%. This can be explained as the mean age of their cohort was 74.7 years in women and 68.2 years in men, whereas in our cohort the mean age was 54.3 years and 55.9 years for men and women respectively. It is known that with rising age, statin therapy has been shown to decline and be substantially lower in people over the age of 75, indicating potential discrepancies in prescribing and compliance.[34]

The widespread use of statin suboptimal-intensity therapy has been routinely reported in high-risk populations,[35,36] this was consistent with our results. In addition, our results agreed with that of Arnold et al.,[35] they found that statin initiation is very common in a large, multicenter, contemporary prospective cohort of acute MI patients, with 87% of statin-naïve patients starting statin therapy during hospitalization. However, statin maximization (discharge on a high potency statin) was reported in only 23%.

We found in our study; statins were stopped in 18.6% due to side effects (non-persistence group). In this group, we found some clinical and laboratory characteristics. They are older people, with higher rates of hypertension (higher median systolic BP and diastolic BP), CAD, stroke, with higher median total cholesterol, LDL, triglycerides, and lower HDL. Moreover, they have poorer indices of DM control, as they have a higher median FBG and HbAIc. This showed that the non-persistence group was sicker and had more comorbidity. Moreover, polypharmacy of at least 5 drugs or more was reported in 96.8% in the non-persistent

group compared with just 22% in the active statin user group. In addition, we found that the most important predictor for statin poor adherence was the polypharmacy of 5 drugs or more, which increases the rate of poor adherence more than 6-fold. Therefore, we concluded that polypharmacy is associated with inadequate adherence in diabetic Saudi patients. Our data agreed with those published by Alwhaibi et al. in 2018. By cross-sectional retrospective study, in Saudi Arabia, they recruited 8932 diabetic patients and found that nearly 78 percent of patients were at risk of polypharmacy, particularly in patients with medical comorbidities such as cardiovascular, respiratory and mental illness.[37] Our results were also consistent with several studies that confirmed that the strong association between poor adherence to statins and the use of multiple medications, polypharmacy.[38,39]

In Swiss University primary health care centers, Aubert et al.[40] studied more than one thousand patients, about 29% were diabetics, and reported a clear correlation between polypharmacy and DM (OR=4.47; 95 percent CI=3.23 − 6.20). In addition, hypertension (OR=8.49; 95% CI=5.25−13.73) showed a stronger association. While in Canada, McCracken and her colleagues [41] enrolled nursing home residents and found that at least nine drugs prescribed for 48% of these patients, particularly in patients with hypertension or congestive heart failure. They concluded that aggressive treatment of cardiovascular risk factors increases the risk of polypharmacy.

Limitations

Observational studies have some limitations;including small sample size therefore, it is difficult to infer any causal relationships. Adherence was assessed by patients reporting the use of statins through a patient interview via a questionnaire, not via an electronic proportion-of-days covered (PDC). That might lead to some inaccuracy. We only included drugs related to DM and/or cardiovascular diseases, and we did not include other classes of therapeutic drugs, such as over the counter drugs, herbs, and vitamins. This may have underestimated the rate of polypharmacy. We conducted the present study in the outpatient clinic of a secondary care hospital in Almadinah Almunawwarah, Saudi Arabia; therefore, the findings of this study cannot be generalized to different care settings or other regions of Saudi Arabia.

Despite these limitations, this study has an advantage that is considered the first study, to the best of our knowledge, in Almadinah Almunawwarah, Saudi Arabia to evaluate the pattern of statin use in the diabetics which is going to help the health care authorities to define the magnitude of the problem with adherence and helps in planning preventive strategies for dyslipedemia for type 2 diabetic Saudi patients.

Conclusion

Despite the fact, the rate of statin use for primary and secondary prevention for diabetics in Saudi Arabia was higher than that reported internationally. It is below the practical and clinical guidelines recommendations. Efforts are needed to increase adherence to the contemporary guidelines for all diabetic patients to use a statin to prevent CVD. Furthermore, public health campaign on the importance of statin for diabetic patients, for both primary and secondary prevention, is urgently needed to improve the adherence to statins. These results highlight the need for large scale studies and cost-effectiveness studies to examine the effect of the use of statin on all diabetic Saudi patients. In addition, a multidisciplinary policy strategy for managing diabetes mellitus considering statin as a pivot in the treatment should be established between health care providers and health care systems.

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