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Research Article

TRENDS IN THERAPEUTIC INTERVENTIONS IN PATIENTS WITH DIABETES MELLITUS IN SAUDI ARABIA

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ABSTRACT

Objectives: The aim of the present study is to assess the patterns of therapeutic interventions for diabetes in Hijaz region in Saudi Arabia and compare it with the AACS treatment guidelines for diabetes. Both the pharmacologic and non-pharmacological interventions employed in management of diabetes and the prescribing practices in diabetic patients were evaluated.

Methods: To fulfil this aim, a surveillance and analysis of the physician's prescription habits to diabetic patients was performed. The study was conducted in health centres, hospitals as well as community pharmacies in Taif city. A comparison was done between the therapeutic choices reported in guidelines and those detected in the field study to highlight any possible deviation.

Results: Analysis of prescriptions pattern among diabetics revealed that there is a deviation between the typical reported therapeutic protocol for the management of diabetes and what the physicians actually prescribe. There was a considerable bias towards the use of oral hypoglycemic agents bypassing the necessary life style changes. The impact of life style and nutritional supplements were substantially overlooked. The study revealed that prescription of metformin and glimepiride were found to be maximum among various available antidiabetic drugs. Most common disease associated with diabetes mellitus was found to be hypertension and obesity. Moreover, the study revealed that there is a great need for introducing pharmaceutical care in both hospital and community pharmacy settings.

Conclusion: The physician needs to develop patient care plans and provide effective drug treatments in collaboration with the patient and other caregivers' esp. the pharmacist. It is also important, to discuss and explore other alternative treatment plans / options.

INTRODUCTION

Drug prescribing pattern and/or drug utilization studies are powerful exploratory tools to ascertain the rational usage of drugs in a society [1, 2]. The evaluation of drug use in given health care against predetermined criteria and standards is crucial to assess the appropriateness of drug therapy. Moreover, these studies create a sound sociomedical and health economic basis for healthcare decision making [3]. According to World Health Organization (WHO) drug utilization studies serve as an important marker to measure the clinical and inappropriate drug use over the time and as a control tool in health facilities as well as to measure the effect of a therapeutic intervention [4].

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia and abnormalities in carbohydrate, fat, and protein metabolism [5]. As a chronic illness, DM has a societal impact-both in terms of human lives and economically [6]. In 1996, 8.5 million adults were reported to have diabetes worldwide. This number increased to 13 million in 2002. Furthermore, in 2002 it was estimated that another 5.2 million people had the disease but had not been diagnosed [7]. In Saudi Arabia, diabetes recorded conscious levels compared to other countries. According to International Diabetes Federation, the prevalence estimates of diabetes type II (adjusted to world population) in Saudi Arabia year 2007 was the highest (~20%) compared to other countries and it is expected to increase by the year 2025 [7]. Deaths attributable to diabetes type II is 10-14% of the all deaths in males aging 20-79 years. Surprisingly, diabetes type I in Saudi Arabia has not recorded the highest values in the world as type II has where only 12-14 diabetic child per 100,000 population per year. This figure seems relatively low compared to Canada and Australia where >20 cases were recorded. The mean health expenditure per patient in Saudi Arabia is the highest compared to countries in Middle East amounting to 500-1000 USD (although of course not comparable to the 5000USD expenditure in USA) [7].

The management of type-1 diabetes depends on insulin mainly, whereas the management of type-2 diabetes is mainly managed using oral antidiabetic agents (OADs) [8]. Various guidelines are available and recommended for non-pharmacological management & pharmacotherapy. The new 2013 AACE Comprehensive Diabetes Management Algorithm [9] replaces the 2009 AACE/ACE Diabetes Algorithm for Glycemic Control f diabetes (figure. 1; [10]).

Diabetes, if uncontrolled, leads to several acute and chronic complications (micro-vascular, macro-vascular, and neuropathic complications) [10]. A recent study reported that the majority of patients already developed long-term complications at the time of diagnosis of diabetes [11]. The mortality rate in patients with DM may be up to eleven times higher than in persons without the disease. DM is the leading cause of blindness, renal failure and foot & leg amputations in adults in developed countries[11]. The chronic complications of diabetes make it necessary to prescribe drugs for these patients permanently [12]. Moreover, polypharmacy is commonly expected as a result of concurrently occurring diseases such as hypertension, hyperlipidaemia and ischaemic heart disease [12-14].

Several problems in drug use patterns have been reported worldwide [15]. These include but not limited to use of irrational prescribing, unnecessary multiple drugs, excessive prescription of multivitamins, use of antibiotics in viral infections, etc.[16]. This may lead to adverse drug reactions [17], drug-drug interactions [18, 19], increased cost of drug therapy and/or non-adherence [20, 21]. In diabetes, many cases can be prevented/controlled only by non-pharmacological approaches e.g. life style if the patient maintains strict glycaemic control [22, 23]. Moreover, there is a need to improve patient care by coordinating the activities of various health care providers [24-27]. Currently, a theme of growing interest in the healthcare community is the role of pharmacist. Pharmacists can provide the team with expertise needed to improve a patient's drug therapy and self-care skills [28, 29]. The pharmaceutical care model creates an avenue for collaborative patient care [30]. Carrying out a drug utilisation, prescription-based study can provide valuable information to the researchers, policy makers and the drug and therapeutics committee members to determine the drug use pattern. Upon review of Literature, a study of antidiabetics prescribing pattern in Saudi Arabia was not located. Being a prevalent and acquired disease in Saudi Arabia, preventive measures can be taken against diabetes if proper awareness is given. Drug utilization studies and surveillance of the current therapeutic approaches for

diabetes in Saudi Arabia are warranted for the better management of this prevalent disease.

The aim of the present study is to:

Determine both pharmacologic and non-pharmacological interventions that is be employed in management of diabetes in ordinary and special population (pregnant, obese, geriatrics, patients with renal failure, patients with hepatic diseases)

Compare and analyse the therapeutic choices detected in the field study with the guidelines and to highlight possible deviation (if any)

A surveillance and analysis of the physician's prescription habits was performed regarding diabetic patients in Hijaz region of KSA (in Taif, Makkah, Jeddah and Madinah).

Methodology

Setting: The study was conducted in different sites (n>18) in Hijaz region including hospitals (king Abdul-Aziz hospital, Prince Mansour Military Hospital and Al-Hada Military Hospital), primary-care health centers and different hospital and community pharmacies.

Design: The design was a randomized, multiple-site, cross-sectional controlled study. Retrospective prescribing data was used and patient records were selected using a systematic sampling.

Time/duration: the study was conducted throughout the year 2010 and 2011.

Data collection procedure: Prescriptions (>290) for diabetic patients written by physicians and filled by pharmacists were recorded. Additionally, questionnaires (>120) were filled by physicians, clinical and community pharmacists. The proportions of the different medical specialties visited are the shown in figure 1

Data analysis: Analysis was done by calculating the percentage of antidiabetic drugs prescribed from the total prescriptions issued and filled. Analysis was done by detecting the deviation from the guidelines; Appendix I &II [9, 10]. Scoring of the detected deviation: three degrees were recorded namely: Minor deviation (deviation from guidelines by one step), major (deviation from guidelines by two or more steps) and contra-indicated medications. The role of clinical, hospital and community pharmacists in increasing patients' awareness of the disease management and medication adherence was evaluated.). Statistical analysis was done by Chi-square Test using SPSS version 16.0.1

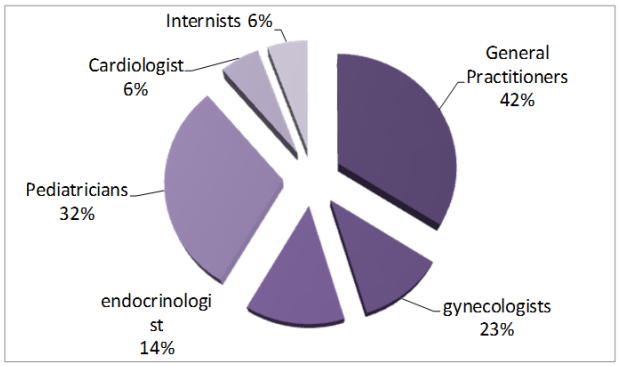

Fig. 1: The proportion (as %) of the different medical specialties included in the medication-use survey of diabetics in Hijaz, KSA

RESULTS

The present study conducted in the western region (Hijaz) in Saudi Arabia revealed that the most commonly diagnosed comorbidities were hypertension (22%) and obesity (21%). The most commonly prescribed antidiabetic medications were metformin (18.4%), sulfonylureas (10.2%), then thiazloidinediones (6.9%). Similar results were previously reported in german patients by Yurgin et al. [31].

Table 1: Age and sex distribution

Age	Male	Female	Total
0-15	39	27	66
15-50	68	59	127
>55	51	46	97
			***n*= 290**

Table 2: Overall pharmacologic and non-pharmacologic treatment for diabetes

Pharmacologic/non-pharmacologic treatment	Comment/Generic drug	Percentage
Life style modification	Diet / Exercise / smoking cessation Patient education Follow up blood glucose level Update medication profile	10.1
Biguanides (MET)	metformin	48.19
Sulfonylureas (SU)	Glimepride, Glipizide, Gliclazide.	31.5
Thiazolidinediones (TZD)	Pioglitazone, troglitazone	5.3
Alpha glucosidase inhibitors (AGI)	Acarbose	0.2
DPP inhibitors (DPP4)	Vildagliptin	18.3
Combinations (dual therapy)	Piogllitazone+Metformin Glimepride+Metformin Pioglitazone+Glimepride	8.9
Insulin	Rapid acting analogue (as insulin Lispro) Short acting (as insulin Actrapid) Intermediate acting (Isophane) Long acting (Human UltraTard) Mixed short/rapid with intermediate acting	50.2

In case of young diabetic patients diagnosed with type I diabetes, the majority of prescriptions (~65%) contained insulin (following the guidelines) as shown in figure 3.

On the other hand, figure 4 shows that prescriptions for adults (11.5%) were detected containing insulin as a first line of treatment before sufficient time is given to OADs (major deviation). Moreover, less than 5% of prescribers gave drug combination (major deviation from guidelines). Only 4% or less of the physicians/pharmacists considered life style modification (diet and exercise) as a first line of treatment of DM (major deviation from guidelines).

The results in figure 5 reveals that biguanides (metformin; Glucophage®) was the major drug prescribed (50.5%) for obese (in agreement with the guidelines). These results corroborated those previously reported by Chiang et al. [32] and Upadhyay et al. [33]. Reports from The Centers for Disease Control and Prevention revealed a marked increase in the number of patients with obesity; additionally, the projected 2050 growth rate in both obesity and diabetes is staggering. It is worth mentioning that the use of Glucobay®; (Acarbose which prevent the digestion of complex carbohydrates) was completely lacking. The glucosidase inhibitors: Acarbose / migilitol / should be used if diabetes is associated with obesity (major deviation from guidelines).

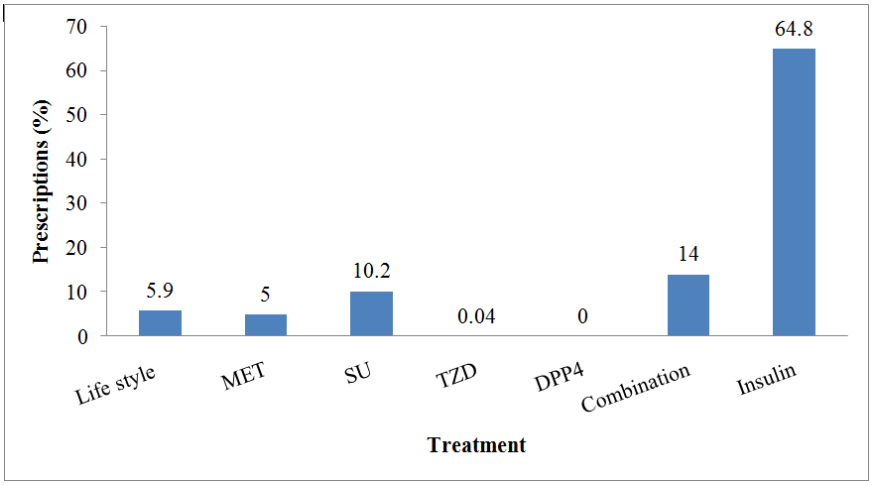

Fig. 2: The different medications prescribed to diabetic children 15 years old or below (n=59).

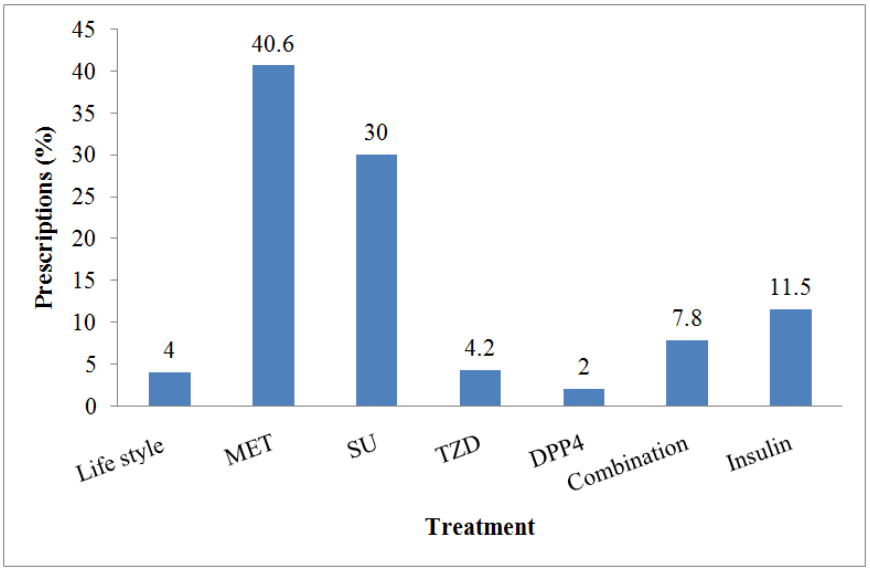

Fig. 3: The different medications prescribed to adult diabetic patients (n=88).

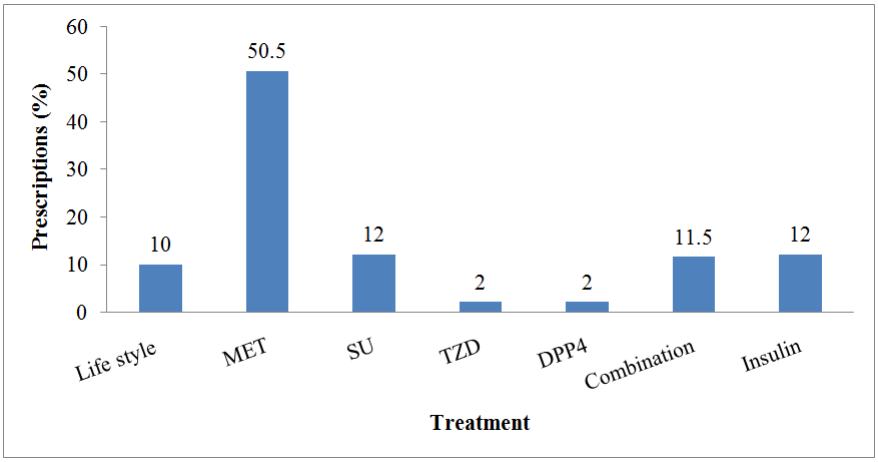

Fig. 4: The different medications prescribed to obese diabetic patients (n=61).

Sulphonylureas monotherapy are associated with increased cardiovascular risk and should not be used as a first line agent [34], nevertheless, they were prescribed at a relatively high percentage (14%) for hypertensive patients (figure 6). This is considered a major deviation. Furthermore, results revealed that 15 % of prescriptions to hypertensive diabetic Saudis contained thiazolidinediones which are known to cause fluid retention or edema [34, 35]. All patients with diabetes and hypertension should be managed with either an angiotensin-converting enzyme or angiotensin receptor blocker [34]

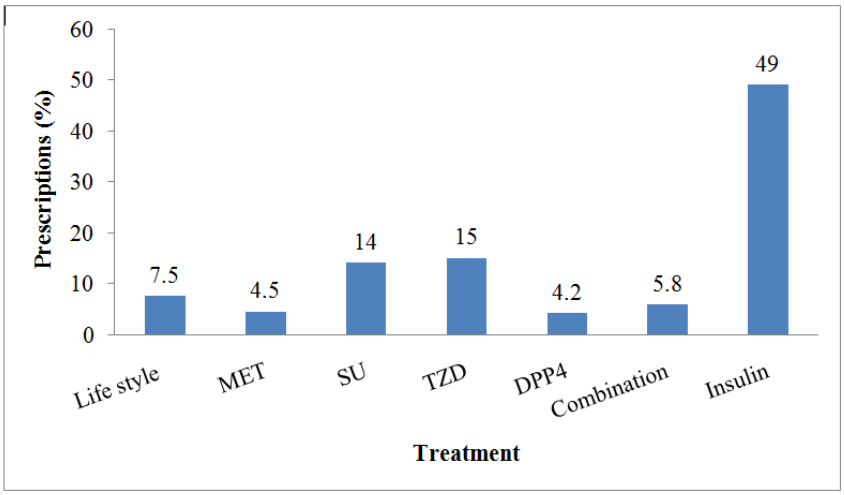

Fig. 5: The different medications prescribed to hypertensive diabetic patients (n=64).

Regarding pregnant women having gestational diabetes, results revealed that more than 82% of the prescriptions contained insulin to pregnant which is in agreement of the guidelines (figure 7). However ~17.5% of prescriptions included some oral antidiabetic drugs (i.e. contra-indicated medications in pregnancy).

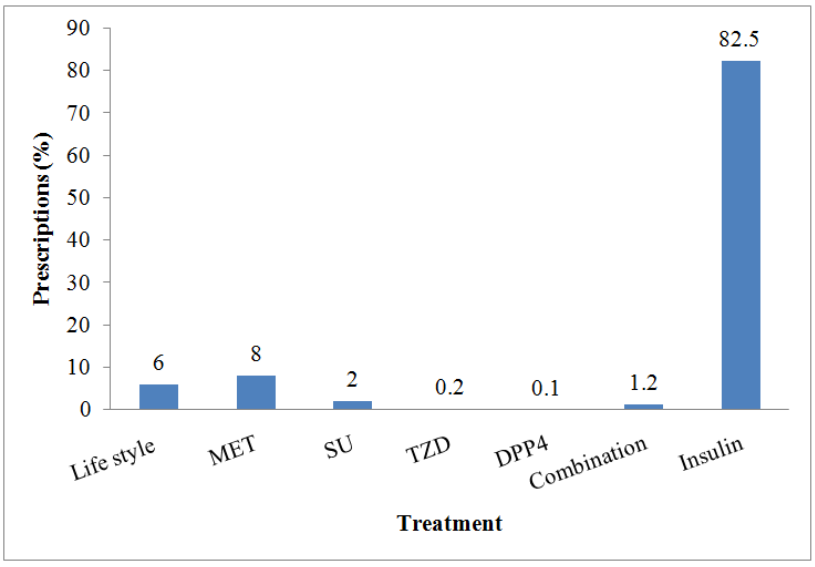

Fig. 6: The different medications prescribed to pregnant diabetic patients (n=41).

Results depicted in figure 8 revealed that 11.5 % of prescriptions to diabetic Saudis with hepatic disease contained sulphonylureas which are absolutely contraindicated in hepatic failure. Moreover, thiazolidinedione drugs were prescribed by 17% despite their hepatotoxicity (contraindicated medication).

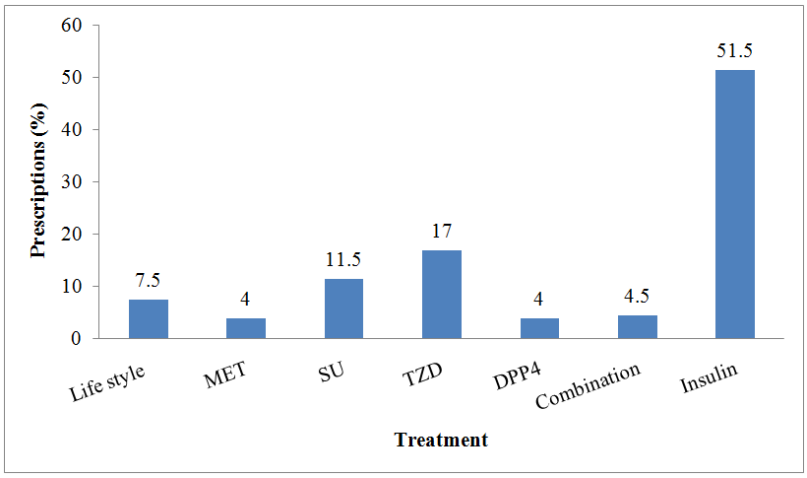

Fig. 7: The different medications prescribed to diabetic patients with hepatic disease (n=44).

Results depicted in figure 8 revealed that 13.5 % of prescriptions to diabetic Saudis with renal disease contained sulphonylureas which are absolutely contraindicated in hepatic failure [34]. In addition, metformin is not a good choice in patients with renal disease or elevated serum creatinine [5]. Nevertheless, it was included in 11.3% of the prescriptions filled by pharmacists to diabetic Saudis with renal impairment. Moreover,the low efficacy and side effect profile of acarbose makes it a poor choice for renal-impaired patients as well

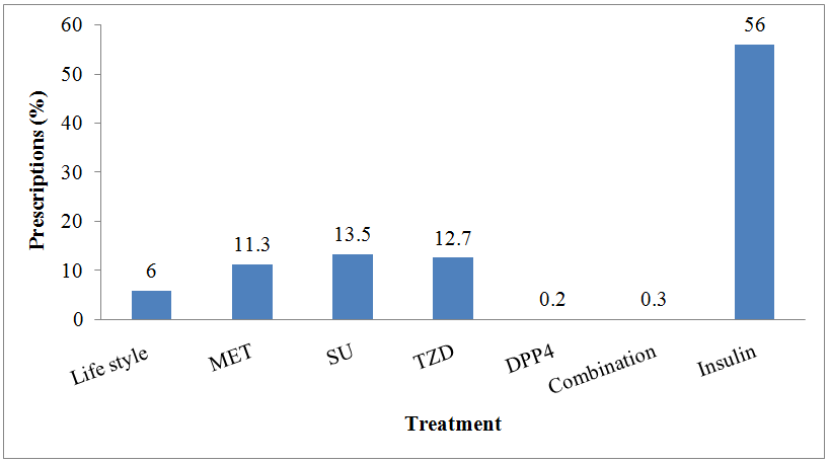

Fig. 8: The different medications prescribed to diabetic patients with renal disease (n=38).

Another noteworthy finding was that the DPP inhibitors; i.e. inhibitor of the enzyme dipeptidylpeptidase-4 responsible for the degradation of the incretin hormone glucagon-like peptide-1 (GLP-1; insulinotropin) , which plays a role in regulating insulin secretion. Among this class of drugs "Vildagliptin and sitagliptin" were detected in 0.2-4.2% of the prescriptions filled and dispensed by pharmacists to different diabetic patients. Sitagliptin is currently approved for use in the United States, whereas vildagliptin has received an approvable letter from the FDA [8, 10]. However more clinical data and full approval by FDA is important before physicians prescribe it. This observation would highlight the potential relationship between physicians' prescribing habits and their exposure to information provided by drug companies [36]. Some reports point out that under the heavy influence of pharmaceutical promotion, doctors may prescribe more expensively, less appropriately and more often.

DISCUSSION

Diabetes mellitus is a chronic illness that is receiving much attention from both the medical community as well as the public. Diabetes has a societal impact-both in terms of human lives and economically. In 1996, 8.5 million adults were reported to have diabetes. This number increased to 13 million in 2002. Furthermore, in 2002 it was estimated that another 5.2 million people had the disease but had not been diagnosed.

As a cause of death, diabetes was ranked seventh on US death certificates in 1996. Despite the increased awareness of the impact that glucose control has on the development and progression of diabetes and its related complications, diabetes has now climbed to sixth place. Some of the reasons for this are the increasing prevalence of the disease: its relationship to other comorbid conditions, an increased awareness of the impact of glucose control on the disease and on these related conditions, as well as the cost of the disease to society. From an economic standpoint, the estimated total cost (direct and indirect) of diabetes in the United States in 2002 was $132 billion. Secondary to the increasing prevalence of this disease, this number has the increased to $156 billion by 2010. In Saudi Arabia, the prevalence of diabetes was estimated as 13.5%; this percentage is expected to increase to 15.7% by year 2025. According to International Diabetes Federation, the prevalence estimates of diabetes (adjusted to world population) in Saudi Arabia is the highest (14-20%). Increased attention to and surveillance of diabetes in Taif city might shed light to better management of this prevalent disease. The present study conducted in the western region (Hijaz) in Arabian Peninsula revealed various degrees of deviation between the pharmacological and non-pharmacological intervention that the physicians follow in reality in diabetics and the therapeutic guidelines. The life style modification (medical diet and exercise) were evidently disregarded. Moreover, recent findings regarding rosiglitazone also have implications for geriatrics. In 2007, rosiglitazone, a thiazolidine-dione, was found to be associated with myocardial infarction, major adverse cardiovascular events, mortality from cardiovascular causes, and all-cause mortality [37]. This was also confirmed by a recent study comparing rosiglitazone with pioglitazone [38]. However, pioglitazone has been associated with a small but significantly increased risk of developing heart failure [39]. Prescription patterns for rosiglitazone changed dramatically when the 2007 meta-analysis [38] was published and the Food and Drug Administration initially issued warnings about the safety of rosiglitazone [40]. A recent study showed up to a 54 percent decrease in rosiglitazone prescription claims across nine commercial plans covering 9 million eligible members, though pioglitazone use was not shown to have changed significantly [41]. The questionnaires gathered from single and chain pharmacies in Hijaz region in Saudi Arabia revealed that 65% of the pharmacists didn't utilize the diabetes education or the "10 facts that the pharmacist should know about diet, exercise and HBMG (i.e. home blood glucose monitoring) in Diabetes management" or "the Diabetes Food Pyramid". As an alternative to the limited number of dieticians in most health care settings in Saudi Arabia, the pharmacists need to be skilled in the dietary management of diabetes and to show commitment to it [42]. Previous studies reported that a physician-supervised, pharmacist-managed primary care clinic has demonstrated improved patient ability to achieve an HbA1c (glycosylated haemoglobin) level of 7% or below, as well as a reduction in the frequency of unscheduled clinic visits [43-45]. Other studies revealed that diabetic patients had greater satisfaction when pharmacists participated in diabetes care by providing education, coordinating care, adjusting medications, and providing constructive guidance [46-48]. According to Garrett and Martin (2003), pharmaceutical care has been associated with decreased direct medical costs per patient per year. Moreover, there was an estimated annual increase in productivity was due to reduced sick time [48]. Although Saudi Arabia is the one of highest in expenditure per diabetic patient in the Middle East, there is a need to allocate more and/or effectively manage these expenditures. There is a great need to launch the "Pharmacist-based diabetes programme" to be integrated into primary care practice where improved patient outcomes are associated with expanded roles of pharmacists[49].

CONCLUSION

The present study conducted in the western region (Hijaz) in Arabian Peninsula revealed various degrees of deviation in prescribing antidiabetics between the therapeutic guidelines and the treatment plan that the physicians follow in reality. Generally there

was a *moderate* implementation of the clinical and therapeutic guideline for the management of DM which may justify the current prescription pattern for the diabetic patients. The life style modification (medical nutrition and exercise) were noticeably disregarded. There is a need to adopt some initiatives to ensure the implementation of the therapeutic guidelines in all the health care settings throughout Saudi Arabia. Such initiatives will not only result in rational and quality use of medicine but also help in reducing the drug-related problems with higher therapeutic outcomes and better control for diabetes mellitus.

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