



Prescription Pattern Study in Type 2 Diabetes Mellitus in Diabetic out Patients in Private Clinics in Kerman, Iran

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Authors' contributions

This work was carried out in collaboration between all authors. All authors have substantial contributions to conception and design, acquisition of data or analysis and interpretation of data. Author GY designed the study and wrote the protocol. Author GS managed the analyses of the study and wrote the first draft of the manuscript. Author MS performed the statistical analysis. Author HG collects the data and managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: Diabetes mellitus (DM) is a chronic disease associated with significant morbidity and mortality. The present study was carried out to assess prescribing practice for oral antidiabetic drugs in type 2 diabetes mellitus patients seen in diabetic outpatients in private clinics in Kerman, Iran.

Study Design: Retrospective analysis of prescription pattern for type 2 diabetic outpatients.

Place and Duration of Study: Diabetic clinics in Kerman city, Iran, (from 1st September 2012 to 31st August 2013).

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Methodology: Prescription pattern of 1118 diabetic outpatients were analyzed for age, percentage of male and female patients, antidiabetic drug category, name of prescribed drug, most frequently prescribed antidiabetic drug and percentage of one/two drug combination.

Results: Out of the 1118 prescriptions of antidiabetic drugs studied, 424 (37.9%) were for women and 694(62.1%) were for men with mean age of 56.2 ± 11 years. Oral antidiabetic drugs were prescribed for 777(69.5%) and 30.5% of patients received insulin. Biguanides were the most frequently prescribed drugs (61.7%) followed by sulfonylurea (59.9%), alpha-glucosidase inhibitors (4.5%), repaglinide (NovoNorm®) (2.7%) and thiazolidinediones (1.7%). Metformin 690 (61.7%) and glibenclamide 670 (59.9%) were the most frequently prescribed antidiabetic drugs. About 46.9% of patients received monotherapy and a total of 594 (53.1%) patients were on combination therapy of 2 or more antidiabetic drugs. The Combination of glibenclamide plus metformin (41.5%) was the most commonly prescribed antidiabetic drug combination in diabetic outpatients. Most common prescribed drugs associated with DM were found to be antihypertensive/antianginal (65%) and lipid lowering drugs (33.3%).

Conclusions: Oral hypoglycemic agents were the main form of antidiabetic therapy in type 2 DM patients. Metformin was the most frequently prescribed biguanides and combination of metformin with glibenclamide has been most widely used. This suggests the need for development of evidence-based guidelines for oral antidiabetic prescription by health professionals.

Keywords: Antidiabetic drugs; prescription pattern; diabetic outpatients; Kerman; Iran.

1. INTRODUCTION

Diabetes mellitus (DM) is one of the most common chronic diseases in nearly all countries. The prevalence of DM among adults in the world was approximately 6.4% (285 million adults) in 2010, and will increase to 7.7% (439 million adults) by 2030 (1-2).

The most important demographic change to diabetes prevalence across the world appears to be the increase in the proportion of people >65 years of age [1]. The numbers of adults with DM between 2010 and 2030 will increase by 69% in developing countries and a 20% increase in developed countries [1,2].

It is reported that the prevalence of DM (defined as fasting blood sugar equal to or more than 126mg/dL) in Iran is 5.5percent (5.1% in women and 5.8% in men),with a significantly higher prevalence among urban dwellers (7%) compared to that of the rural subgroup (3%) and in those over 40 years old the prevalence was 24% [3,4]. A major burden of this disease would be shared by developing countries like Iran. The major complications of diabetes are both acute and chronic. Acute complications include diabetic coma, abnormally low blood sugar due to diabetes medications. Chronic complications are related to both macrovascular and microvascular complications, which can damage the eyes, kidneys, nerves, and heart [5-8]. Also peripheral arterial disease (PAD) is one of the macrovascular complications of type 2 diabetes mellitus [5]. Uncontrolled hyperglycemia in diabetic patients will increase the risk of myocardial infarction, stroke, amputation (including death from PAD), and microvascular disease (predominantly retinopathy), non-fatal heart failure and cataract extraction [9]. Glycemic control is related to the incidence and progression of diabetic microvascular complications in both IDDM and NIDDM [9,10]. Advanced glycation end products (AGEs) have been implicated as important factors in the pathogenesis of diabetic vascular complication [7].

Medications for DM need to be taken for the entire life and factors like efficacy, side effects, drug interactions and cost of therapy need to be taken into consideration. Prescribing patterns and indicators of prescription quality for DM patients show wide variability in different parts of the world [11-15].

The burden of diabetes is projected to rise in the very near future. Despite an extensive range of available and effective treatments, inadequate adherence or non-adherence to oral antidiabetic prescribed drug is common and less than 50% of diabetic patients achieve a glycaemic target of ideal HbA1c value (<7.0%) and about two-thirds of diabetic patients mortality is due to premature cardiovascular disease [15-17].

More importantly, the lack of a functional institutionalized system for monitoring and assessing the effectiveness and safety of the medication use process in most developing countries, including Iran, is a key factor for conducting the studies for the evaluation of pattern of prescription in diabetic patients. However, to date, there is no reliable evidence on the prescription pattern of antidiabetic drugs in type 2 diabetes mellitus in Iran, so this study was performed to evaluate antidiabetic prescribing pattern in type 2 diabetic outpatients attending in private clinics in Kerman city, Iran during 1 year period.

2. MATERIALS AND METHODS

Most of Iranians are supported mainly by two Iranian insurance organization. Iranian Social Security Insurance Organization provides coverage of workers and employees in the private sector where coverage is compulsory by law, as well as voluntary coverage of self-employed persons. Iranian Medical Services Insurance Organization covers a wide range of individuals including governmental employees and all individuals of the community with various socioeconomic levels that were not eligible to be covered by other health insurance organizations. Therefore most of our patients seek private treatment using insurance coverage. So the findings from such settings may be more representative of the actual practice. An observational study conducted for one year from 1st September 2012 to 31st August 2013 in Kerman city, the center of Kerman Province of Iran, to survey the prescription pattern of 1118 diabetic outpatients attending different diabetic clinics in Kerman city, Iran. The prescriptions of outpatients which contained at least one antidiabetic agent were selected for further analysis. Using World Health Organization (WHO) drug use indicators [18], we evaluated the quality and quantity of prescriptions in Kerman. Before collecting the prescriptions data, an informed verbal consent was taken from the patients. Ethical approval for this study (K/89/86) was provided by local Ethical Committee of Kerman University of Medical Sciences which permits and confirms that the institute gives approval to release the data. The brand names of drugs in prescriptions were decoded to generic names of drugs. Drug selection indicators selected for present study includes age, percentage of male and female patients, antidiabetic drug category, name of prescribed drug, most frequently prescribed antidiabetic drug, percentage of one/two drug combination.

3. RESULTS

Out of the 1118 prescriptions of antidiabetic drugs studied, the rate of prescription for men 694 (62.1%) was significantly higher than women 424 (37.9%), ($P=0.01$). The average ages of the study population was 56.2 ± 11 years. Statistical analysis using t-test showed that there was no significant difference between the age of males (55.8 ± 10.7) and females (56.9 ± 10.5), ($P=0.9$).

The frequency of the oral antidiabetic drug classes were as follow: biguanides (61.7%), Sulfonylurea (59.9%), alpha- glucosidase inhibitors (4.5%), repaglinide (NovoNorm®) (2.7%) and thiazolidinediones (1.7%) (Table 1).

(Table 1) show that 341(30.5%) of diabetic outpatients received insulin alone (23.7%) or in combination with oral antidiabetic drugs (6.8%) and 777(69.5%) of diabetic outpatients received oral antidiabetic drugs.

Table 1. The frequency of the antidiabetic drug classes prescription of diabetic outpatients in private DM clinics in Kerman, Iran (n=1118)

Drug category	Frequency*	Percentage*
Biguanides	690	61.7
Sulfonylurea	670	59.9
Alpha-glucosidase inhibitors	30	2.6
Repaglinide	30	2.7
Thiazolidinediones	9	0.7
Insulin Preparations	341	30.5

*:Patients may receive more than one drug category in each prescription

(Table 2) indicates that metformin (the only prescribed biguanides) 690(61.7%) and glibenclamide 670(59.9%) were the most prescribed drugs. Both drugs were prescribed most commonly in combination (41.5%). Other commonly prescribed drugs were, repaglinide (2.7%), acarbose (2.6%) and pioglitazone (1.7%).

Statistical analysis using chi-square test showed that the rate of biguanides (61.7%) and sulfonylurea (59.9%) prescription was significantly higher than other antidiabetic drug classes (Table 1) (P=.001).

Metformin was the only prescribed biguanides. Almost 46.9% of patients received monotherapy as follow: insulin 265(23.7%), glibenclamide (10.6%), metformin 115(10.3%). A total of 594(53.1%) patients were on combination therapy of 2 or more antidiabetic drugs. The Combination of glibenclamide plus metformin (41.5%) was the most commonly prescribed antidiabetic drug combination in diabetic outpatients.

Insulin was prescribed for 30.5% of patients with type 2 diabetes mellitus and combination of NPH and regular insulin (20.7%) was the most frequently prescribed Insulin therapy (Table 3).

From the data collected (Table 2), it was observed that among the antidiabetic drug category, drugs were found to be prescribed in following order: combination of metformin and glibenclamide>insulin>metformin>glibenclamide>Insulin+oral antidiabetic drugs>glibenclamide plus metformin plus acarbose.

Antihypertensive/antianginal or both drugs were prescribed in the 727(65.0%) of patients with diabetes. Angiotensin converting enzyme inhibitors (ACEIs) were the most frequently prescribed antihypertensive/antianginal (34.2%) followed by beta-blockers (18%) and calcium-channel blockers (11.1%). Diuretics were prescribed for a total of 185(16.5%) patients, either for treatment of hypertension or congestive heart failure (CHF). Also lipid lowering drugs were prescribed for 372(33.3%) of patients and statins or HMG-CoA reductase inhibitors (27.6%) was prescribed frequently (Table 4). Atorvastatin was the most frequently prescribed statins.

Table 2. Most frequently prescribed antidiabetic medications of diabetic outpatients in private DM clinics in Kerman, Iran (n=1118)

Type of drug therapy	Name of drug	Total prescriptions N(%)*	Men N=694	Women N=424
Monotherapy:	Metformin	115 (10.3)	71	44
	Glibenclamide	118 (10.6)	71	47
	Repaglinide	12 (1.1)	8	4
	Acarbose	6 (0.5)	3	3
	Pioglitazone	8 (0.7)	5	3
	Insulin	265 (23.7)	157	108
Polytherapy:	Glibenclamide plus metformin	464 (41.5)	280	184
	Glibenclamide plus repaglinide	7 (0.6)	4	3
	Metformin plus repaglinide	11(1.0)	9	2
	Insulin plus oral antidiabetic drugs	76 (6.8)	55	21
	Glibenclamide plus metformin plus acarbose	24 (2.1)	16	8
	Glibenclamide plus metformin plus other oral antidiabetics	12 (1.1)	7	5

*:Patients may receive more than one drug in each prescription

Table 3. Most frequently prescribed insulin preparations of diabetic outpatients in private DM clinics in Kerman, Iran (n=1118)

Type of insulin	Frequency (N)	Percentage (%)
NPH+regular	231	20.7
NPH	50	4.5
Insulin as part	40	3.6
Regular	10	0.9
Insulin glargine	7	0.6
Lansulin N (human NPH insulin)	3	0.2
Total	341	30.5

Table 4. Frequency of antihypertensive/antianginal and lipid lowering agents prescription of diabetic outpatients in private DM clinics in Kerman, Iran (n=1118)

Type of prescribed drugs	Frequency N (%) [*]
Antihypertensive/antianginal drugs:	727(65.0)
ACEIs/ARBs	383(34.2)
Beta blockers	201(18)
Calcium channel blockers	124(11.1)
Alpha blockers	19(1.7)
Diuretics:	185(16.5)
Furosemide	92 (8.2)
Other diuretics	93 (8.3)
Lipid lowering agents:	372(33.3)
HMG-CoA reductase inhibitors(statins)	309(27.6)
Fibrates(gemfibrozil)	51(4.6)
Omega-3	10(0.9)
Niacin	2(0.2)

**:Patients may receive more than one drug in each prescription. ACEIs=Angiotensin converting enzyme inhibitors ARBs=Angiotensin receptor blockers*

4. DISCUSSION

The present study showed that total frequency of prescriptions of antidiabetic medications in diabetic outpatients was significantly higher in men (62.1%) than in women (37.9%). The results are in agreement with those previously reported in different countries [3,19-21]. However, other studies reported higher prevalence of DM in women [4,22,23].

To our information, the factors underlying the gender difference in DM prevalence is not determined yet, however, different life styles of men and women in different countries which results in steady increase in body weight, higher energy intake and reduced energy expenditure in some developed countries and in oil producing countries such as Saudi Arabia and Kuwait may have a decisive role in the prevalence of overweight and DM [24].

The present study revealed that biguanides were the most frequently prescribed drug class followed by sulfonylureas for diabetic outpatients in Kerman province of Iran. Our results are in agreement with some previous reports [15,21,25,26]. Metformin (biguanides category) was the most frequently prescribed oral antidiabetic drug followed by glibenclamide (second generation sulfonylurea) which is in accordance with most of previous reports [15,21,25-29]. At present, glibenclamide and glimepiride are the second- generation's sulfonylureas most widely used in the United States [30,31].

Our results showed that combination of metformin and glibenclamide was the most commonly prescribed medication in type 2 diabetic patients followed by insulin, metformin and glibenclamide. Pioglitazone was prescribed in a minority of diabetic patients. The prescription rate for thiazolidinedione derivatives, mainly pioglitazone, in this study was only 0.7% which was much lower than similar studies in other countries. The frequency of use of pioglitazone hydrochloride and rosiglitazone maleate (21%) were higher in the United States and in Europe (5%) [32]. The reasons for the lower use of thiazolidinedione oral antidiabetic drugs in our study is not known and suggest the need for development of evidence-based guidelines for oral antidiabetic prescription by health professionals [27].

Investigators reported the beneficial effects of pioglitazone on other cardiovascular risk factors associated with the insulin resistance syndrome [33]. On the contrary, other studies revealed that the probability of an increased risk for CHF with these agents remains high. Even though, their efficacy still need to be demonstrated in outcome trials [33,34,35,36].

In our study, the number of patients with type 2 diabetes treated with insulin was higher than previously reported studies (3-15%) [12,36]. This is one of the most noteworthy findings in our study.

The factors underlining this high incidence of use are not determined yet. However, it could be an indication of poor glycemic control among the type 2 diabetics or it could be due to other factors such as non-adherence with self-management practices and/or prescribed oral anti-diabetic medications, inappropriate dose, regimen of the medicines prescribed or potential drug interactions. Also others reported that non-adherence or inadequate adherence to oral anti-diabetic medications is an important factor in the management of type 2 diabetes [16,17].

In the present study, 46.9% of the diabetic outpatients were treated with only one drug and 53.1% were on combination therapy. Previous reports in the literature indicated a higher prevalence of monotherapy (69.6%, 61.8% and 51.5%) of the patients [27,35,36]. Our study showed that a combination of glibenclamide and metformin were the most frequently prescribed antidiabetic drugs in type 2 DM patients. Several studies showed that a combination of sulfonylurea with metformin has been most widely used, although a relative increase occurred in the prescription of thiazolidinediones (pioglitazone) in some countries [15,21,24-25,28,37].

Antihypertensive /antianginal and lipid lowering drugs were the most frequently prescribed drugs in diabetic outpatients. This could be due to the association of microvascular complications and peripheral arterial disease, hypertension and lipid profile abnormality in type 2 diabetes mellitus [5,7,9,10]. Our study had a few limitations. Our data did not include patients' main diagnoses and co-morbidities that may affect how prescription patterns are interpreted. The diabetes patients admitted in the hospital were not included in the study. Also we had not recorded the socio- economic status of the patients which may affect the prescription pattern [38].

5. CONCLUSION

In summary, the results of this study revealed that metformin was most frequently prescribed antidiabetic drug followed by glibenclamide which is very similar to previous studies [15,21,24-28]. The use of newer thiazolidinediones (pioglitazone) and improved insulin preparations was reported in a minority of DM patients. This study shows the need of continuous education for a progressive change in the prescription of antidiabetics in accordance with guidelines. In this way, it will also reduce the adverse effects of long term treatment with antidiabetic drugs.

ETHICAL APPROVAL

Ethical approval for this study (K/89/86) was provided by local Ethical Committee of Kerman University of Medical Sciences which permits and confirms that the institute gives approval to release the data.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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