Assessment of Adherence to Guidelines in the Treatment of Patients with Type 2 Diabetes Mellitus at Selected Clinics in Punjab: A Retrospective Observational Study

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Abstract

Purpose: To identify the drug prescription patterns in patients with type 2 diabetes mellitus (DM). Other objectives were to analyze demographic data and HbA1c levels of patients and assess their pharmacological therapy plans.

Methods: A retrospective observational study was conducted at diabetes clinics in the Punjab region of India. The subjects who fulfilled the inclusion criteria were enrolled in the study. The collected data were analyzed with the help of SPSS ver. 24.

Results: As per the disposition data, the number of female patients with DM was greater than the male patients. Type 2 DM was found to be common among the patients over the age of 60 years and 54 patients have had the disease for 5-10 years. A majority of the patients enrolled in the study had normal renal functions. A significant relationship was found between HbA1c levels and age ($p<0.001$) and disease duration ($p<0.005$). Evaluation report of the drug prescription pattern revealed that the long-acting insulin analogs were widely prescribed to the patients along with metformin.

Conclusion: Any standard prescribing pattern was not found which was advised by the national or international standard guidelines. This can be attributed to the population size, different prescribers, and inter-individual variation and may be due to some factors not found in the patient's medical record. Regardless of the cause, there has to be adherence to the most recent standard guidelines that are supported with evidence to improve the health of patients. With regard to the International Diabetes Federation (IDF) guidelines, there was no adherence to these sets of standard guidelines in most of the prescription patters for patients.

Keywords: Type 2 diabetes mellitus, Prescription pattern, International diabetes federation guidelines, Medication adherence.

Introduction

Type 2 diabetes mellitus (DM), also known as insulin non-dependent diabetes mellitus (INDDM), affects the individual in an old age, obesity, and insulin resistance. If left untreated, type 2 DM may lead to nephropathy, neuropathy, retinopathy, and cardiovascular complications.[1-3] Type 2 DM constitutes about 85% to 95% of the population with diabetes in developed countries and even higher in the developing countries. In 2003, 194 million people (aged 20 to 79 years) had diabetes and a quarter of them belonged to the developing countries. There is a rapid increase in the prevalence of diabetes in the Asian countries.[4] Diabetes, if not well controlled, may cause blindness, kidney failure, lower limb amputation, and several other long-term consequences that impact significantly on the quality of life.[5,6] Where data are available – mostly from high-income countries – prevalence, incidence, and trends vary hugely between countries.[7] In 2010, diabetic retinopathy caused 1.9% of moderate or severe visual impairment globally and 2.6% of blindness.[6,8] Pharmacological approach involves medication therapy while the non-pharmacological approach involves reduction of weight, alcohol intake, and smoking, and increase in exercise.[9] Proper use of the drug has an enormous contribution to the reduction of death and diseases all over the world due to its subsequent checkup, and public and economical reimbursement.[10] Irrational use of drugs will lead to failure of treatment, resistance, and toxicity of drug as well as affect the quality of drug therapy.[11] One-half of all the drugs that are prescribed, dispensed, and sold worldwide are inappropriate, while half of the patients fail to take the drugs properly and 1/3rd of them fail to access to the essential drug list. This is why it is necessary to

introduce drug use patterns and focus on the irrational prescribing pattern.[12] The pattern of drug use is different in different countries. Problems related to drug use may be due to practitioner, distributer, and consumer and may be due to health care facility that further worsens the medication management.[13] Thus, the overall aim of this study was to explore the current status of the adherence of anti-diabetic drugs to the international guidelines (as prescribed by the international federation) by medical practitioners and the current status of prescription.

Methodology

A retrospective observational study was conducted at selected clinics in the Malwa region of Punjab, India. A total of 103 patients diagnosed with type 2 DM were enrolled in the study by considering the inclusion criteria of both genders and signing the informed consent form. The investigation was carried out for 6 months after obtaining approval from the Institutional Ethics Committee (IEC) and the data of consecutive 5 years were collected from the Medical Record Department (MRD) with the help of a data collection form. Steps required for the evaluation of the prescription are mentioned in **Figure 1**.

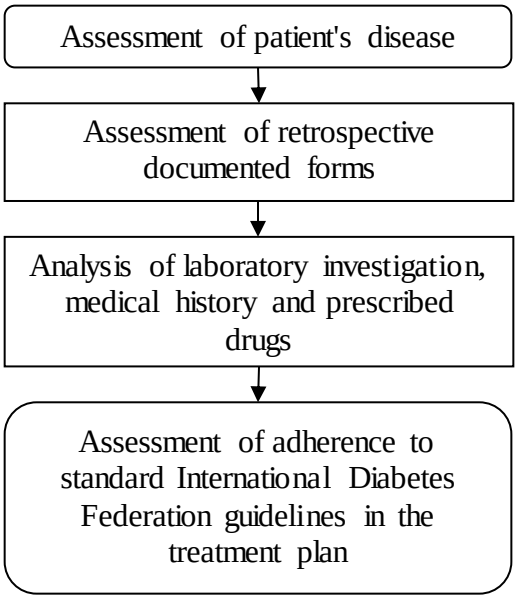

Figure 1 Evaluation of Prescriptions

Data Analysis

The collected data was analyzed via SPSS Ver. 24. Descriptive statistics were used to analyze various parameters taken in the study.

Results

Demographic and Baseline Characteristics

An aggregate of 103 cases were enrolled in the study. The number of female patients with type 2 DM was higher than the male patients (56 [57.2%] vs 44 [42.7%]). The highest rate of type 2 DM was found to be among patients >60 years of age (41 [39.8%]), followed by patients between the age of 50-59 years (32 [31.0%]; **Table 1**).

Table 1 Demographic and Baseline Characteristics

Characteristic **Statistic**	**N=103**
Age	
Mean ± SD (years)	56.02 ± 10.944
Age distribution, n (%)	
20-29 yrs	2 (1.9)
30-39 yrs	6 (5.8)
40-49 yrs	22 (21.3)
50-59 yrs	32 (31.0)
>60 yrs	41 (39.8)
Gender, n (%)	
Male	44 (42.7)
Female	59 (57.2)
BMI, (kg/m^2)	
Median	26.47
Interquartile range	8.62
BMI distribution	
<18.5 kg/m^2 (underweight)	2
18.5-25 kg/m^2 (normal)	28
25-30 kg/m^2 (overweight)	47
>30 kg/m^2 (obese)	26
Disease duration, n (%)	
<2 yrs	1 (0.9)
2-5 yrs	18 (17.4)
5-10 yrs	54 (52.4)
>10 yrs	30 (29.1)
eGFR for Renal function, n (%)	
>90 mL/min/1.73 m^2 normal kidney function	97 (94.17)
89-60 mL/min/1.73 m^2 mild kidney damage	1 (0.97)
59-30 mL/min/1.73 m^2 mild to moderate kidney damage	4 (3.88)
29-15 mL/min/1.73 m^2 severe kidney damage	1 (0.97)
<15 mL/min/1.73 m^2 severe kidney damage	0 (0)
HbA1c, n (%)	
6-8%	6 (5.8)
8-10%	12 (11.6)
10-12%	74 (71.8)
12-14%	11 (10.6)
Age distribution of HbA1c, n (%)	
6-8%	
20-29 yrs	2 (33.3)
30-39 yrs	1 (16.7)
40-49 yrs	1 (16.7)
50-59 yrs	1 (16.7)

Characteristic Statistic	N=103
>60 yrs	1 (16.7)
8-10%	
20-29 yrs	0 (0)
30-39 yrs	3 (25)
40-49 yrs	4 (33.3)
50-59 yrs	3 (25)
>60 yrs	2 (16.7)
10-12%	
20-29 yrs	0 (0)
30-39 yrs	2 (2.7)
40-49 yrs	17 (23)
50-59 yrs	26 (35.1)
>60 yrs	29 (39.2)
12-14%	
20-29 yrs	0 (0)
30-39 yrs	0 (0)
40-49 yrs	0 (0)
50-59 yrs	2 (18.2)
>60 yrs	9 (81.8)
Route of administration of anti-diabetic drug, n (%)	
Tablet (Oral)	40 (38.8)
Injection	8 (7.7)
Tablet + Injection	55 (53.3)

N = No. of subjects; BMI = body mass index; SD = Standard deviation.

Body Mass Index (BMI)

Upon evaluation of the patient's body mass index (BMI), patients with a BMI of 25-30 kg/m^2 had the highest prevalence of DM with 19.4% and 26.2% for male and female, respectively.

Disease Duration

Over 30 (29.1%) patients have had the disease for more than 10 years, while 54 (52.4%) patients have had it for 5-10 years.

Renal Function

A majority of the patients (97 [94.17%]) had normal kidney function, while 1 (0.97%) patient had severe kidney damage that required an adjusted therapy plan. Based on the outcomes of the study, renal functioning was significantly related to age ($p<0.005$).

HbA1c Test Evaluation

A total of 74 (71.8%) patients had high HbA1c levels (10-12%), and 11 (10.6%) had very high levels (12-14%; **Figure 2**). There was a significant relationship between HbA1c levels and age *(*$p<0.001$*)* and disease duration ($p<0.005$).

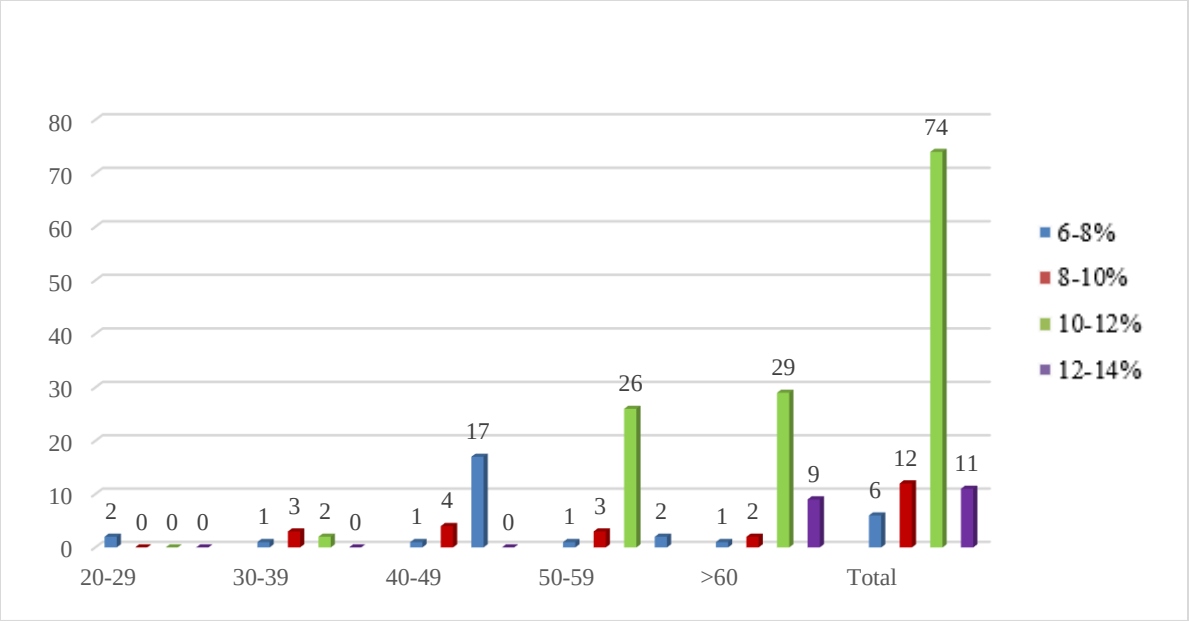

Figure 2 HbA1c levels

Evaluation of Route of Administration

Of 103 patients with anti-diabetic prescriptions, 40 (38.8%) patients were taking oral prescriptions (tablets), 8 (7.7%) patients were taking injections, and 55 (53.3%) patients were taking both oral prescriptions (tablets) and injections.

Drug Prescription Pattern in Patients with Type 2 DM

Most of the patients (40 [38.8%]) were prescribed long-acting insulin analog injections (insulin detemir and insulin glargine) and metformin tablets (**Table 2**), and 22 (21.3%) of the patients were prescribed a combination of metformin and sulfonylurea. Few patients had metformin only or sulfonylurea only prescriptions, comprising 2 (1.9%) and 3 (2.9%), respectively, while 13 (12.6%) patients had a prescription of metformin with rapid-acting insulin. Three-drug therapy or two drugs plus insulin were also observed that made up 15 (14.5%) of the total patients.

Table 2 Drug Prescription Pattern

Antidiabetic drugs used by patients	**n (%)**	**Glycated hemoglobin (HbA1c) test (%)**			
		6-8	**8-10**	**10-12**	**12-14**
Metformin (GC2)	2 (1.9)	2	0	0	0
Sulfonylurea (GC2)	3 (2.9)	1	2	0	0
Metformin + sulfonylurea (GC3)	22 (21.3)	3	10	9	0
Metformin + α-glucosidase inhibitor / DPP-4 inhibitor / thiazolidinedione (GC3)	0	0	0	0	0
Metformin + rapid-acting insulin secretagogue (GC3)	13 (12.6)	0	0	13	0
3-drug therapy or 2 drugs + insulin (GC4)	15 (14.5)	0	0	11	4
NPH insulin, insulin glargine or insulin determir + metformin (GC5)	40 (38.8)	0	0	36	4
Biphasic insulin + metformin (GC5)	8 (7.7)	0	0	5	3
Basal plus mealtime insulin regimen + metformin (GC5)	0	0	0	0	0

GC2 - First-line therapy; GC3 - Second-line therapy; GC4 - Third-line therapy; GC5 - Fourth-line therapy

Treatment Concerning Disease Duration

Based on the results of the study, antidiabetic agent treatment was significantly associated with the disease duration of the patient ($p<0.005$; **Table 3**).

Table 3 Treatment Concerning Disease Duration

Antidiabetic drugs used by patients	**Disease duration (years)**			
	<2	**2-5**	**5-10**	**>10**
Metformin	0	2	0	0
Sulfonylurea	0	3	0	0
Metformin + Sulfonylurea	1	7	14	0
Metformin + α-glucosidase inhibitor / DPP-4 inhibitor / thiazolidinedione	0	0	0	0
Metformin + rapid-acting insulin secretagogue	0	1	10	2
3-drug therapy or 2 drugs + insulin	0	0	3	12
NPH insulin, insulin glargine or insulin determir + metformin	0	5	23	12
Biphasic insulin + metformin	0	0	4	4
Basal plus mealtime insulin regimen + metformin	0	0	0	0

Treatment for Renal Function

Patients with moderate to low renal function constituted 4.85% of the total subjects under study and required special care for their treatment as per their renal condition. **Figure 3** depicts the treatment plan given to patients with renal disease.

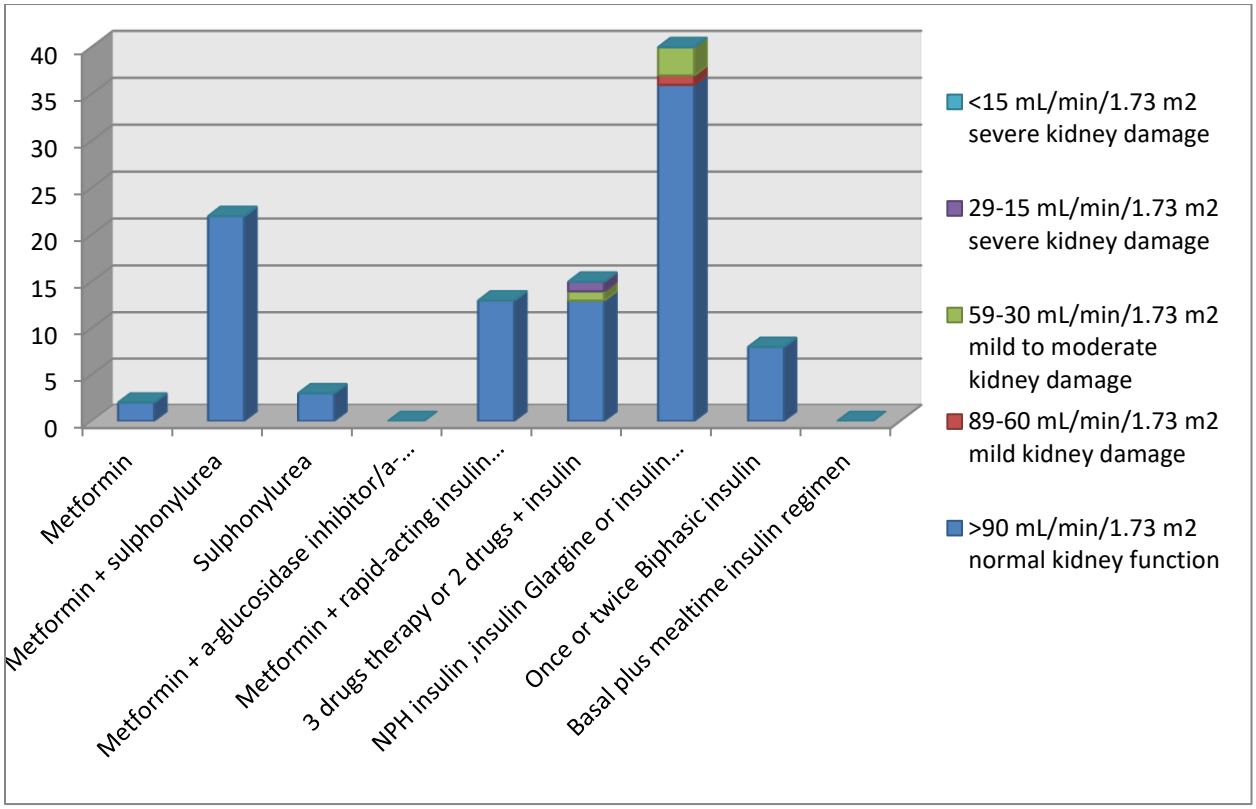

Figure 3 Drug therapy plan for patients with a renal condition

Glycated Hemoglobin vs. Disease Duration

Our investigation also reported that glycated hemoglobin was strongly related to disease duration ($p<0.005$). The following **Table 4** illustrates the effectiveness of the therapy over the years.

Table 4 Drug Response of Patients

HbA1c (%)	Disease duration (years)			
	<2	**2-5**	**5-10**	**>10**
6-8	1	5	0	0
8-10	0	4	8	0
10-12	0	8	44	22
12-14	0	1	2	8

Discussion

After collecting data from 103 patients, evaluating and analyzing their prescriptions and disease state, these results do not indicate the actual prevalence of diabetes among men and women, due to sample size restriction. With the highest BMI values belonging to women, 26.2% of the total population was women who were overweight (25-30 kg/m^2). Women with obesity (>30 kg/m^2) were also higher than to men (13.5% vs 11.6%). Nevertheless, previous studies show that men are more at risk of developing type 2 DM compared to women of the same age.[14] This was confirmed by evaluating the BMI of both genders. Men tend to develop the condition at lower BMI than women of the same age do.

As the body grows over time, there is a gradual change in physiology due to wear and tear that occurs over time. This makes the elderly population more susceptible to illnesses. For that reason, it is no surprise that the highest prevalence of type 2 DM is found in elderly population in this study (39.8% and 31.0% for patients over 60 and 50-59 age groups, respectively). Limited physical activity, co-morbidities, and patient compliance adversely affect the progression of the disease and treatment to a greater extent in the elderly population compared to the younger population.

Glycated hemoglobin (HbA1c) is one of the most important tests to indicate how well the disease is controlled.[15] It provides a long-term indicator for blood sugar levels. Many national and international guidelines recommend a target level of <7%. Analyzing the test results collected from patients, 94% patients had high HbA1c levels (≥8% to 14%), which indicate ineffective treatment, poor patient compliance to therapy, exercise, and diet recommendations.

According to patients' renal function, the prescribed treatment to the six patients which includes metformin, was not as per IDF guidelines as the mild and moderate kidney damage could be aggravated by metformin. However, the FDA announced a revised warning use of metformin in certain patients with reduced kidney function. They have concluded from the review of studies published in the medical literature that metformin can be used safely in patients with mild impairment in kidney function and some patients with moderate impairment in kidney function.[16] It was observed that 2 out of 6 patients with a relatively low HbA1c (6-8%) were prescribed metformin only therapy, which was not per IDF guidelines. Three metformin + sulfonylurea prescriptions were also observed and identified as irrational since this combination can cause hypoglycemia. One patient was receiving a sulfonylurea only treatment, which, according to guidelines, can be chosen as an alternative to metformin.

Second-line therapy of two anti-diabetic drugs (metformin + sulfonylurea, metformin + α-glucosidase inhibitor / DPP-4 inhibitor / thiazolidinedione, metformin + rapid-acting insulin

secretagogue) was prescribed to 35 patients, while only 12 patients had HbA1c levels of 8-10%. We conclude that some patients were either overprescribed or under-prescribed. In both cases, it is considered as an irrational treatment that may lead to severe consequences to the patients. Third-line and fourth-line therapies as per the IDF guidelines include adding insulin to the treatment plans, which is justified in patients who have high levels of HbA1c to control their blood glucose levels. Prescribers use different strategies regarding insulin, and treatment should be individualized as per the patients' health state taking particular note of the cost and availability of generic drugs. However, 24 patients who have had high HbA1c levels and have not been prescribed any form of insulin, which can aggravate the disease complications. As per the recommended guidelines GC6, insulin therapy should not be unduly delayed.

Type 2 DM is known to be a progressive disease, and as such treatment should be adjusted according to the blood glucose levels. It was observed that the HbA1c levels were 10-12% high in patients who have had the disease for 5-10 years (44 patients) and over 10 years (22 patients), 12-14% in eight patients who have had the disease for more than 10 years. These numbers indicate inefficient treatments and/or poor patient compliance. The overall status of control of the disease is less than satisfactory.

Conclusion

After careful analysis of data, we conclude that the treatment practices for type 2 DM were not as per the IDF guidelines. Irrationality in treatment and disease management were detected which, can lead to decreased patient satisfaction, high therapy costs, aggravating the disease state, and possible failure of therapy. Many patients require rectification of therapy plans to control their rather high blood glucose levels regardless of current oral antidiabetic agents and put to insulin regimen as per the prescribed guidelines to avoid further complication. It must be noted that all studies of this kind must be considered as a feedback to the policy makers, physicians, hospital administrations, governments, organizations, and related parties in the health care system for future references and the betterment of patient's health.

Improper control of diabetes can put patients at a risk of advancement of long-term physiological and psychological complications. Therefore, it is of utmost importance to provide the best care to patients. This can be achieved only by following the evidence-supported standard guidelines in the diagnosis and treatment of diabetes to provide optimum health care and ensure maximum benefit utilization of available choices of drugs.

Regardless of the cause, there has to be adherence to the most recent standard guidelines which are supported with evidences to improve health care provided. With regard to the IDF guidelines specially, there was no adherence to these sets of guidelines in most patients.

Conflict of interest

The authors whose names are listed in the paper have no confederations with or involvement in any organization or entity with any financial interest (similar to honoraria, educational grants, participation in speakers' divisions, membership, employment, consultancies, stock ownership, or other equity interest; and expert evidence or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, confederations, knowledge, or beliefs) in the subject matter or accouterments bandied in this paper.

Data availability statement

The data can be made available upon request from the author.

Ethics statement

This study was approved by the ethics committee. Participants were informed at the beginning of the study that it was voluntary and that they could quit at any time. All study participants gave written informed consent.

Acknowledgement

Not applicable.

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