Antidiabetic Prescription and Glycemic Control in Patients With Type 2 Diabetes Mellitus

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ABSTRACT

Objective: To determine the antidiabetic treatment among individuals with type 2 diabetic patients in Mosul city, the number of patients who attained the glycemic target (good glycemic control) and patients who failed to attain glycemic target (poor glycemic control) and to investigate factors that may be associated with poor glycemic control.

Patients and Methods: 299 patients with type 2 diabetes mellitus of both sexes were participated in this study. The patients were divided into 2 groups according to the values of HbA1C: Group 1 (good glycemic control) and group 2 (poor glycemic control). A questionnaire form was prepared to record detailed informations about each patient such as age, drugs used, education level, diabetic family history, adherence to treatment, exercise, and diet. HbA1c level was analyzed using high performance liquid chromatography. Other parameters including total cholesterol, high density lipoprotein-cholesterol (HDL), triglycerides, low density lipoprotein-cholesterol (LDL) and serum glucose concentration were measured using special kits.

Results: The antidiabetic drugs used including metformin, glibenclamide and glimepiride, used alone and in combinations including metformin plus glibenclamide and metformin plus insulin. Fifty patients (16.7%) have good glycemic control and 249 patients (83.3%) have poor glycemic control. Comparison between number of poor glycemic control of metformin and glibenclamide showed non significant difference. Comparison between poor glycemic control of metformin plus glibenclamide and metformin plus insulin showed highly significant difference. Comparison between mono-therapy and combination therapy showed highly significant difference. High proportions of poor glycemic control were obtained with ages >40 males, overweight and obese, low educational level, family history of diabetes, use of herbs, long duration of the disease, low HDL-cholesterol, high atherogenic index, non adherence to treatment, diet and exercise.

Conclusion: This study showed that high proportions of type 2 diabetic patients were on combination therapy and the high proportions of the patients were poor glycemic control. Many factors were found to be associated with poor glycemic control including age >40 males, overweight and obesity, low educational level, family history of diabetes, use of herbs, long duration of the disease, non adherence to treatment, diet, and exercise.

وصف أدوية السكري والسيطرة على مستوى السكر
للمرضى المصابين بداء السكري النوع الثاني

الخلاصة

هدف الدراسة: تعيين أدوية ضد السكري التي تستخدم لعلاج مرض السكري النوع الثاني في مدينة الموصل وعدد المرضى الذين حصلوا على سيطرة جيدة للسكر وعدد المرضى الذين لم يحصلوا على سيطرة جيدة والكشف عن بعض العوامل المرتبطة بالمرضى الذين لم يحصلوا على سيطرة جيدة للسكر.
المرضى و طرق العمل: شارك في الدراسة 299 مريض مصابون بمرض السكري النوع الثاني. تم تقسيم المرضى إلى مجموعتين بناءً على قيمة الهيموكلوبين المسكر. المجموعة الأولى المرضى الذين حصلوا على سيطرة جيدة للسكري والمجموعة الثانية الذين لم يحصلوا على سيطرة جيدة للسكري. وقد حضر شكل استبيان لتسجيل المعلومات العادية لكل مريض مثل العمر والأدوية المستخدمة والنظام الغذائي للعلاقة والمستوى التعليم والعلاج بالادوية والغذاء والرياضة. وقد تم قياس الهيموكلوبين المسكر بواسطة الكولير أكروماتوغرافي عالي الكفاءة. كما تم قياس مستوى السكر وصفة السكر باستخدام عدة.

النتائج: المرضى المصابون بمرض السكري الذين حصلوا على السيطرة الجيدة للسكري وتم استخدام أدوية متعددة مثل الكليبنكل ومتفورمين وكليمبراد ودواء آخر، وتم استخدام أدوية أخرى مثل الكليبنكل ومتفورمين. حصلت المقاومة بين المرضى الذين لم يتمكنوا من السيطرة الجيدة للسكري على مستويات السكر بصور مختلفة، وتم الحفاظ على مستوياتخفضة للايبوبروتين الوعائي، و.ymlت织 كفاءة العلاج.

الاستنتاج: أظهرت الدراسة أن نسبة كبيرة من المرضى يحصلون على السيطرة الجيدة للسكري، ولكن هناك عدد من العوامل المذكورة عن طريق الدراسة، مما يساهم في السيطرة على السكري مع العمر الأكبر من 40 سنة والذكور والوزن العالي والتعليم المنخفض ومستوى السكر الذي تؤخذ لوحدها مع الأدوية المتميزة في مواجهة السكري.

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. DM, long considered a disease of minor significance to world health, is now taking its place as one of the main threats to human health in the 21st century. It is the most common non-communicable disease worldwide and the fourth to fifth leading cause of death in developed countries.

The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. The world prevalence of diabetes among adults (aged 20-79 years) will be 6.4%, affecting 285 million adults, in 2010, and will increase to 7.7%, and 439 million adults by 2030. Between 2010 and 2030, there will be a 69% increase in number of adults with diabetes in developing countries and a 20% increase in developed countries.

Diabetes mellitus is a chronic disease, for which there is no known cure except in very specific situations. Management concentrates on keeping as possible, blood sugar levels as close to normal without causing hypoglycemia. This can usually be accomplished with diet, exercise, and use of appropriate medications (insulin in the case of type 1 diabetes; oral medications, as well as possibly insulin in type 2 diabetes). Patient education, understanding and participation is vital since the complications of diabetes are far less common and less severe in people who have well-managed blood sugar levels.

In clinical practice, optimal glycemic control is difficult to obtain on a long-term basis because the reasons for poor glycemic control in type 2 diabetes are complex. Both patient and health care provider related factors may contribute to poor.
glycemic control\textsuperscript{6}. Despite the evidence from large randomized controlled trials establishing the benefit of intensive diabetes management in reducing microvascular and macrovascular complications, high proportion of patients remain poorly controlled\textsuperscript{7}. Poor and inadequate glycemic control among patients with type 2 diabetes constitutes a major public health problem and major risk factor for the development of diabetes complications. Glycemic control remains the major therapeutic objective for prevention of target organ damage and other complications arising from diabetes\textsuperscript{8}.

Khattab et al.\textsuperscript{9} reported that diabetes was more likely to be poorly controlled among those with increased duration of diabetes, lower level of education, higher body mass index (BMI), hypercholesterolemia, hypertriglyceridemia, and elevated LDL. The highest level of poor glycemic control was among patients on combination of oral antidiabetic agent and insulin. Poor glycemic control was more common among patients who did not follow dietary regimens, did not practice any physical activity, who were not adherent for medications and did not regularly perform home glucose monitoring.

The present study was designed:

- To determine the antidiabetic treatment among individuals with type 2 diabetes mellitus in Mosul city.
- To determine the number of patients who attained the glycemic target (good glycemic control) and patients who failed to attained glycemic target (poor glycemic control) although they continue to take antidiabetic treatment.
- To investigate factors that may be associated with poor glycemic control.

**Patients and Methods:**

A sample of 299 patients with type 2 diabetes mellitus was collected from Al-Salam Teaching Hospital and Al-Wafaa Clinic for Treatment and Researches of diabetes mellitus in Mosul over a period of 5 months. They consist of 121 males and 178 females with a mean ages ±SD of 53.56±9.33 years. The patients were divided into 2 groups according to the values of HbA1C: Group 1 (good glycemic control) and Group 2 (poor glycemic control). Good glycemic control is defined as an HbA1C of ≤ 7 for the past 3 months. Poor glycemic control is defined as an HbA1C value of more than 7% for the past 3 months\textsuperscript{10}.

The data was obtained by direct interviewing of researcher with the patients who visited Al-Salam Teaching Hospital and Al-Wafaa Clinic. A questionnaire form was prepared to record detailed information about each patient. The data involved in the questionnaire form including patient name, age, sex, body weight, length, BMI, education level, diabetic family history, use of herbs, duration of the disease, drugs used, BP, lipid profile, adherence to treatment, adherence to diet and exercise, presence of complications and the use of non diabetic drugs.

Inclusion criteria: including patients with type 2 diabetes mellitus who were on antidiabetic therapy for not less than 6 months.

Exclusion criteria: including type 1 DM, gestational diabetes mellitus, type 2 diabetic patients on antidiabetic treatment for a period of less than 6 months, pregnant and lactating women.

About 10 ml of venous blood samples were taken from each patient after 15 hour fasting. Serum was
obtained from each blood sample and used for the estimation of serum glucose concentration, HbA1C, and lipid profile indices. HbA1C level was analyzed using high performance liquid chromatography. BMI was calculated as weight (kg) divided by the square of the height (m²). BP was measured using standardized sphygmomanometers. Other parameters including total cholesterol, HDL-cholesterol, triglycerides, LDL-cholesterol and serum glucose concentration were measured using special kits.

**Statistical methods:**

P value ≤ 0.05 was considered statistically significant. Data was taken as mean±SD. Chi-square test was used to compare between different parameters.

**Results:**

Two hundred and ninety nine type 2 diabetic patients included in this study. They consist of 121 males and 178 females having a mean ages of 53.56±9.33 years (table 1). They were divided into 2 groups according to HbA1C value: group 1 consist of 50 patients having HbA1C ≤ 7 (good glycemic control) and group 2 consist of 249 patients having HbA1C of >7 (poor glycemic control).

The antidiabetic drugs used by the patients were showed in (table 2). They include metformin, glibenclamide and glippride, used alone and in combinations including metformin plus glibenclamide and metformin plus insulin. Table 3 showed the number of patients with good and poor glycemic control according to the level of HbA1C. Metformin alone was found to be associated with a high number of poor glycemic control patients.

Comparison between number of poor glycemic control of metformin and glibenclamide showed non significant difference (P>0.055). Comparison between poor glycemic control of metformin plus glibenclamide and metformin plus insulin showed highly significant difference (P=0.000). Comparison between mono-therapy and combination therapy showed highly significant difference (Table 4).

Comparison between number of patients with good glycemic control and those with poor glycemic control showed highly significant difference (Table 5).

Tables 6 and 7 showed the proportions of poor glycemic control according to different factors. Highly significant proportions of poor glycemic control were obtained with ages >40 years, males, overweight and obese patients, low educational level, family history of diabetes, use of herbs, long duration of the disease, low HDL, high atherogenic index, non adherence to treatment, diet and exercise.

**Discussion:**

In the present study 70% of patients treated with glibenclamide have poor glycemic control compared with 89% of patients taking metformin. This effect did not reached a statistical significant. Kimmel and Inzucchi reported that most classes of antidiabetic drugs are equally efficacious in reducing HbA1C, with the exception of the α-glucosidase inhibitors and nateglinide. Metformin and glibenclamide have been compared in many studies. Metformin was compared with glibenclamide in 165 type 2 diabetic patients. The study concluded that dose titrated treatment with either metformin or glyburide promotes equal degrees of glycemic control. In another 2 studies comparing the effect of metformin and glibenclamide in type 2
diabetic patients. The 2 drugs had an equivalent effect on glycemic control\textsuperscript{13,14}. The association of poor glycemic control and the use of combination of oral antidiabetic agents and insulin reported in the present study was consistent with the results obtained by other studies\textsuperscript{15-17}. This finding reflects the fact of deteriorations of diabetes over time, and the need for higher doses or additional mediations increases over time. Therefore, patients who were treated by combination therapy of oral antidiabetic agents and insulin had more progressive disease which required more aggressive treatment to provide glycemic control, but this phenomenon could be attributed to delay in applying insulin in the treatment of patients with poor glycemic control\textsuperscript{9}.

There have been consistent reports of incremental decreases in glucose levels by 20% or more when metformin was added to existing sulfonylurea therapy in patients inadequately controlled by maximum doses of the sulfonylurea\textsuperscript{18}. Combination therapy with metformin and sulfonylureas is as effective as combined insulin/sulfonylurea therapy or insulin mono-therapy in individuals presenting with treatment failure\textsuperscript{19}. Consequently, the addition of metformin therapy may reduce the need to add insulin therapy when secondary failure with sulfonylurea drugs occurs.

In the present study mono-therapy with metformin, glibenclamide or glimepiride produced significant less poor glycemic control than combined therapy. These results were in agreement with the results reported by Khattab et al.\textsuperscript{9} who found that compared to patients who were on oral antidiabetic agents alone, those on other treatment modalities were more likely to be poorly controlled. In contrast to this results Blonde et al.\textsuperscript{20} reported that glyburide/metformin combination produced significantly better glycemic control than mono-therapy with either agent.

Of the total 299 patients collected in the present study, 83.3% had HbA1c $\geq$7%, shows the proportion of patients with poor glycemic control. In a similar studies done by other researchers poor glycemic control also found among diabetic patients.

Mafauzy\textsuperscript{21} found poor glycemic control in 80% of 438 diabetic patients. Of the total 917 patients, 65.1% had HbA1c $\geq$7\%\textsuperscript{9}. In Saudi Arabia, only 27% of the patients (404 patients) reached target level of glycemic control\textsuperscript{22}. In United Kingdom, Seventy-six percent of type 2 patients had HbA1c $>7.0\%$\textsuperscript{23}.

In the present study, the proportions of poor glycemic control were associated with many factors including males, overweight and obesity, lower educational level, positive history of diabetes, use of herbs, long duration of diabetes, low HDL level, high atherogenic index, non adherence to treatment, exercise and diet. In the present study poor glycemic control was found more predominant among males. In agreement with the results of this study Almutairi et al.\textsuperscript{24} reported that the percentage of poor glycemic control was highest among male (80.9%), aged 60 years and above, (82.8%), and with results obtained by Gopinath et al.,\textsuperscript{25} who reported that diabetes was more likely to be poorly controlled among male patients.

In the present study the majority of the patients were obese and the proportion of poor glycemic control was increased as BMI of the patients increased indicating a positive correlation between high body weight and poor glycemic control. These results were in consistent with results
reported by Khattab et al.⁹, who also reported a significant correlation between obesity and poor glycemic control. In contrast to the findings of this study Al-Zurfí et al.²⁶ and Miyashita et al.²⁷, reported no correlation between BMI of the patients and poor glycemic control. Obesity is a known risk factor for type 2 diabetes. It has been suggested that patients who reduce their body mass through an increase in physical activity may reduce the risk of developing type 2 diabetes by improving insulin sensitivity²⁸.

The proportion of patients with high poor glycemic control reported in this study was significantly high among those with long duration of the disease (>8 years). This finding was consistent with the results of Almutairi et al.²⁴ who reported that poor glycemic control was significantly higher with those long diagnoses of diabetes mellitus. Also Khattab et al.⁹ reported that longer duration of diabetes was associated significantly with poor glycemic control. Longer duration of diabetes is known to be associated with poor control, possibly because of progressive impairment of insulin secretion with time because of B cell failure, which makes the response to diet alone or oral agents unlikely²⁹.

In the current study poor glycemic control was more common among patients who were not adherent for medications, diet or exercise. These results were in agreement with the results reported by Khattab et al.⁹. Al-Qazaz et al.³⁰ reported that Patients’ knowledge about diabetes is associated with better medication adherence and better glycemic control. An increase in patient education and adherence to treatment has been associated with good glycemic control without any change in medication or dosage³¹. Regular physical activity is recommended for patients with type 2 diabetes since it may have beneficial effects on metabolic risk factors for the development of diabetic complications³². Additional measures are needed to encourage regular physical activity and improve dietary habits in this population³³.

In conclusion: This study showed that high proportions of type 2 diabetic patients were on combination therapy and the high proportions of the patients were poor glycemic control. Many factors were found to be associated with poor glycemic control including age >40, males, overweight and obesity, low educational level, family history of diabetes, use of herbs, long duration of the disease, adherence to treatment, diet, and exercise.
Table 1. Patients characteristics:

| Parameters                              | Mean±SD       |
|-----------------------------------------|---------------|
| patient age (years)                     | 53.56±9.33    |
| Body mass index (Kg/m2)                 | 33.57±5.50    |
| Fasting blood sugar (mmol/L)            | 9.89±3.70     |
| Hemoglobin A1c (%)                      | 8.50±1.78     |
| Triglyceride (mmol/L)                   | 2.21±1.27     |
| Total cholesterol (mmol/L)              | 5.22±1.32     |
| Low density lipoprotein (mmol/L)        | 3.31±1.09     |
| High density lipoprotein (mmol/L)       | 0.96±0.19     |
| Blood pressure systolic (mmHg)          | 133.75±18.46  |
| Blood pressure diastolic (mmHg)         | 80.61±13.43   |
| Duration of the disease (years)         | 7.79±5.81     |
| Duration of using the drugs (years)     | 4.75±4.19     |
| Male / Female                           | 121 / 178     |

Table 2. Antidiabetic drugs:

| Antidiabetic drug                  | Number of Patients | (%)   |
|------------------------------------|--------------------|-------|
| Metformin                          | 38                 | 12.7  |
| Glibenclamide                      | 27                 | 9.0   |
| Glimpiride                         | 5                  | 1.7   |
| Metformin & Glibenclamide          | 125                | 41.8  |
| Metformin & Insulin                | 85                 | 28.4  |
| Other combination                  | 19                 | 6.4   |
| Total                              | 299                | 100   |

Table 3. Good and poor glycemic control patients according to antidiabetic drug:

| Antidiabetic drug                | Good Glycemic Control No. (%) | Poor Glycemic Control No. (%) | Total |
|----------------------------------|-------------------------------|------------------------------|-------|
| Metformin                        | 4(10.5%)                      | 34(89.5%)                    | 38 (100)|
| Glibenclamide                    | 8(29.6%)                      | 19(70.37%)                   | 27 (100)|
| Glimpiride                       | 2(40%)                        | 3(60%)                       | 5 (100) |
| Metformin & Glibenclamide        | 22(17.6%)                     | 103(82.4%)                   | 125 (100)|
| Metformin & Insulin              | 10(11.76%)                    | 75(88.24%)                   | 85 (100) |
| Other combination                | 4(21.1%)                      | 15(78.9%)                    | 19 (100) |
| Total                            | 50                            | 249                          | 299 (100)|

Table 4. Comparison between mono-antidiabetic therapy and combination antidiabetic therapy according to number of poor glycemic control patients:

| Antidiabetic drug              | Total | Poor Glycemic Control No.(%) | P-value |
|--------------------------------|-------|-----------------------------|---------|
| Mono therapy                   | 70    | 56 (80.0%)                  | 0.000   |
| Combination therapy            | 229   | 193(84.3%)                  |         |
| Total                          | 299   | 249                         |         |
Table 5. Number of Good Glycemic Control and Poor Glycemic Control in diabetic patients:

| Parameter                | No. of Patients | %   | P- Value |
|--------------------------|-----------------|-----|----------|
| Good Glycemic Control    | 50              | 16.7| 0.000    |
| Poor Glycemic Control    | 249             | 83.3|          |
| Total                    | 299             | 100 |          |

Table 6. Proportion of patients with poor glycemic control according to different factors:

| Variable                  | Total | Poor Glycemic Control (%) | P- value |
|---------------------------|-------|---------------------------|----------|
| Age (year)                |       |                           |          |
| <40                       | 17    | 14 (82.4)                 | 0.000    |
| 40-50                     | 89    | 77 (86.5)                 |          |
| >50                       | 193   | 158 (81.9)                |          |
| Gender                    |       |                           |          |
| Male                      | 121   | 103 (85.1)                | 0.006    |
| Female                    | 178   | 146 (82.0)                |          |
| BMI (kg/ m2)              |       |                           |          |
| Normal <25                | 13    | 10 (76.9)                 | 0.000    |
| Overweight 25-29          | 60    | 50 (83.3)                 |          |
| Obese > 29                | 226   | 189 (83.6)                |          |
| Educational level         |       |                           |          |
| Illiterate                | 65    | 54 (83.1)                 | 0.000    |
| ≤High school              | 209   | 178 (85.2)                |          |
| >High school              | 25    | 17 (68.0)                 |          |
| Family history            |       |                           |          |
| Positive                  | 184   | 157 (85.3)                | 0.000    |
| Negative                  | 115   | 92 (80)                   |          |
| Use of herbs              |       |                           |          |
| Positive                  | 104   | 88 (84.6)                 | 0.000    |
| Negative                  | 195   | 161 (82.6)                |          |
| Duration of disease       |       |                           |          |
| <4                        | 80    | 62 (77.5)                 | 0.002    |
| 4-8                       | 97    | 80 (82.5)                 |          |
| >8                        | 122   | 107 (87.7)                |          |
| BP (mmHg)                 |       |                           |          |
| Normotensive              | 76    | 67 (88.2)                 | 0.000    |
| Hypertensive              | 223   | 182 (81.6)                |          |
Table 7. Proportion of patients with poor glycemic control according to different factors:

| Variable                | Total | Poor Glycemic Control | P-value |
|-------------------------|-------|-----------------------|---------|
|                         |       | No (%)                |         |
|                         |       | <5.1 (mmol/l)         | ≥5.1 (mmol/l) |
| Total Cholesterol       | 158   | 133 (84.2)            | 116 (82.3) | 0.281 |
| Triglycerides           |       | <1.7 (mmol/l)         | ≥1.7 (mmol/l) |
|                         | 103   | 86 (83.5)             | 163 (83.2) | 0.000 |
| HDL                     |       | >1.3 (mmol/l)         | ≤1.3 (mmol/l) |
|                         | 14    | 11 (78.6)             | 238 (83.5) | 0.000 |
| LDL                     |       | <2.59 (mmol/l)        | ≥2.59 (mmol/l) |
|                         | 78    | 66(84.6)              | 183(82.8)  | 0.000 |
| Atherogenic Index       |       | <5                    | ≥5        |
|                         | 130   | 107(82.3)             | 142(84.0)  | 0.027 |
| Adherence to treatment  |       | Yes                   | No        |
|                         | 249   | 203(81.5)             | 46(92.0)   | 0.000 |
| Adherence to Exercise   |       | Yes                   | No        |
|                         | 204   | 168(82.4)             | 81(85.3)   | 0.000 |
| Adherence to diet       |       | Yes                   | No        |
|                         | 147   | 115(78.2)             | 134(88.2)  | 0.016 |
| Complication            |       | Yes                   | No        |
|                         | 194   | 159(82.0)             | 90(85.7)   | 0.000 |
| Non antidiabetic drugs  |       | Yes                   | No        |
|                         | 174   | 140(80.5)             | 109(87.2)  | .049 |

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