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

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Received 31.3.2014 Accepted 28.5.2014

ABSTRACT

Objective: To detertmine 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 attained 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 و عدد 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 للسكري.

المرضى و طرائق العمل: شارك في الدراسة 299 مريض مصابون بمرض السكري النوع الثاني. تم تقسيم المرضى الى مجموعتين بناءا 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 استبياني لتسجيل المعلومات العائدة لكل مريض مثل العمروالادوية المستعملة والبيان السكري للعائلة ومستوى التعليم وملازمة العلاج بالادوية والغذاء والرياضة. وقد تم قياس الهيموكلوبين المسكر بواسطة الكروماتوكرافي عالي الكفاءة. كما تم قياس مستوى السكر و صفحة السكر باستخدام عدة خاصة.

النتائج: الادوية ضد السكري التي استعملها المرضى ضمت المتفورمين والكليبنكل أمايد وكليمبيراد اما لوحدهم اواتحاد مع ادوية اخرى مثل متفورمين وكليبنكل أمايد و ميتفورمين مع انسولين.اظهرت الدراسة وجود 50 مريض عندهم سيطرة جيدة للسكري و 249 مريض عندهم سيطرة غير جيدة للسكري.اظهرت المقارنة بين عدد المرضى الذين لهم سيطرة غير جيدة للسكري للمتفورمين مع الكليبنكل أمايد وجود فرق غير معنوي و اظهرت المقارنة بين عدد المرضى الذين لهم سيطرة غير جيدة للسكري للمتفورمين و الكليبنكل أمايد مع المتفورمين والانسولين وجود فرق معنوي و اظهرت المقارنة بين عدد المرضى الذين لهم سيطرة غير جيدة للسكري للادوية التي تؤخذ لوحدها مع الادوية التي تؤخذ متحدة بوجود فرق معنوي. اظهرت الدراسة وجود علاقة للسيطرة الغير جيدة للسكر مع العمر اكثر من 40 سنة والذكور والوزن العالي والتعليم المنخفض و استعمال الاعشاب والبيان العائلي للسكري والمستوى المنخفض للايبوبروتين العالي الكثافة و عدم الملازمة للعلاج بالادوية بالغذاء والرياضة.

الاستنتاج: اظهرت الدراسة ان نسبة كبيرة من المرضى يستخدمون الادوية المتحدة وان النسبة الكبيرة من المرضى يملكون سيطرة غير جيدة للسكري وبوجود عدة عوامل ملازمة للسيطرة الغير جيدة للسكري و التي تضم العمر اكثر من 40 سنة والذكور والوزن العالي والتعليم المنخفض و استعمال الاعشاب والبيان العائلي للسكري والمستوى المنخفض للايبوبروتين العالي الكثافة و عدم الملازمة للعلاج بالادوية بالغذاء والرياضة.

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[1]. 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[2].

The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity[3]. 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[4].

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[5].

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[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[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[8].

Khattab et al.[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 detertmine 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[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 (m^2). 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 glimpiride, 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[11] 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[12]. 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[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[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[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[18]. Combination therapy with metformin and sulfonylureas is as effective as combined insulin/sulfonylurea therapy or insulin mono-therapy in individuals presenting with treatment failure19 . 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.[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.[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 ≥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[21] found poor glycemic control in 80% of 438 diabetic patients. Of the total 917 patients, 65.1% had HbA1c ≥7%[9]. In Saudi Arabia, only 27% of the patients (404 patients) reached target level of glycemic control22. In United Kingdom, Seventy-six percent of type 2 patients had HbA1c >7.0%[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.[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.,[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-Zurfi 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 sensitivity[28].

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 unlikely[29].

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 dosage[31]. 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 complications[32]. Additional measures are needed to encourage regular physical activity and improve dietary habits in this population[33].

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 & Glibinclamide	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(29.63%)	19(70.37%)	27 (100)
Glimpiride	2(40%)	3(60%)	5 (100)
Metformin & Glibinclamid	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 No (%)	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
Overweight25-29	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 No (%)	P- value
Total Cholesterol			
<5.1 (mmol/l)	158	133 (84.2)	0.281
≥5.1 (mmol/l)	141	116 (82.3)	
Triglycerides			
<1.7 (mmol/l)	103	86 (83.5)	0.000
≥1.7 (mmol/l)	196	163(83.2)	
HDL			
>1.3 (mmol/l)	14	11 (78.6)	0.000
≤1.3 (mmol/l)	285	238 (83.5)	
LDL			
< 2.59 (mmol/l)	78	66(84.6)	0.000
≥ 2.59 (mmol/l)	221	183(82.8)	
Atherogenic Index			
<5	130	107(82.3)	0.027
≥ 5	169	142(84.0)	
Adherence to treatment			
Yes	249	203(81.5)	0.000
No	50	46(92.0)	
Adherence to Exercise			
Yes	204	168(82.4)	0.000
No	95	81(85.3)	
Adherence to diet			
Yes	147	115(78.2)	0.016
No	152	134(88.2)	
Complication			
Yes	194	159(82.0)	0.000
No	105	90(85.7)	
Non antidiabetic drugs			
Yes	174	140(80.5)	.049
No	125	109(87.2)	

References

1. American Diabetes Association (ADA). Standards of medical care in diabetes. Diabetes Care 2012; 35: S11-S63.
2. Tripathi BK, Srivastava AK. Diabetes mellitus: complications and therapeutics. Med Sci Monit 2006; 12: 130-147.
3. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27: 1047-1053.
4. Shaw J, Sicree R, Zimmet P. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Research and Clinical Practice 2010; 87: 4-14.
5. Krentz AJ, Bailey CJ. Oral antidiabetic agents: current role in

type 2 diabetes mellitus. Drugs. 2005;65:385-411.
6. Wallace T M, Matthews DR. Poor glycemic control in Type 2 diabetes, conspiracy of disease, suboptimal therapy and attitude.Quarterly J Med 2000; 93: 369-374.
7. Karter A J, Moffet H H, Liu J, et al. Achieving good glycemic control: Initiation of new anti hyperglycemic therapies in patient with Type 2 diabetes from the Kaiser Permanente Northern California diabetes registry. American Journal of Managed Care 2005; 11: 262−270.
8. Koro C E, Bowlin S J, Bourgeois N, et al. Glycemic control from 1988 to 2000 among US adults diagnosed with type2 diabetes: A preliminary report. Diabetes Care 2004; 27: 17−20.
9. Khattab M, Khader YS, Al-Khawaldeh A, et al. Factors associated with poor glycemic control among patients with type 2 diabetes mellitus. Journal of Diabetes and Its Complications 2010; 24: 84–89.
10. American Diabetes Association. Standards of medical care in diabetes-2014. Diabetes Care January 2014; 37 (suppl 1): S14-S80.
11. Kimmel B, Inzucchi SE. Oral agents for type 2 diabetes: AQn Update. Clinical Diabetes 2005; 23: 74-76.
12. Hermann LS, Scherstén B, Bitzen PO, et al. Therapeutic comparison of metformin and sulfonylurea, alone and in various combinations. Diabetes Care 1994; 17:1100-1109.
13. Hermann LS, Karlsson JE, Sjstrand A. Prospective comparative study in NIDDM patients of metformin and glibenclamide with special reference to lipid profiles. Eur J Clin Pharmacol 1991; 41: 263-265.
14. Guthrie R. Treatment of non-insulin dependent Diabetes mellitus with metformin. J Am Board Fam Med 1997; 10: 212-221.
15. Al-Nuaim AR, Mirdad S, Al-Rubeaan K, et al. Pattern and factors associated with glycemic control of Saudi diabetic patients. Annals of Saudi Medicine 1998; 18: 109-112.
16. Valle T, Koivisto A, Reunanen A, et al. Glycemic control in patients with diabetes in Finland. Diabetes Care 1999; 22, 575−579.
17. Goudswarrd AN, Stolk RP, Zuithoff P, et al. Patients characteristics do not predict poor glycemic in type 2 diabetes patients treated in primary care. European J Epidemiology 2004; 19: 541-545.
18. DeFronzo RA, Goodman AM. Efficacy of metformin in patients with non-insulin-dependent diabetes mellitus. N Engl J Med 1995; 333:541-49.
19. Gentile S, Turco S. Glibenclamide-metformin: an alternative in obese type 2 diabetics under abusive insulin treatment. Eur J Clin Invest 1993;23(Suppl 1):A9.
20. Blonde L, Rosenstock J, Mooradian AD, et al. Glyburide/metformin combination product is safe and efficacious in patients with type 2 diabetes failing sulphonylurea therapy. Diabetes Obes Metab 2002; 4: 368-375.
21. Mafauzy M. Diabetes control and complications in private primary healthcare in Malaysia. Med J Malaysia 2005; 60: 212-217.
22. Akbar DH. Low rates of diabetic patients reaching good control targets. Eastern Mediterranean Health Journal 2001; 7: 671−678.

23. Fox KM, Gerber RA, Bolinder B, et al. Prevalence of inadequate glycemic control among patients with Type 2 diabetes in the United Kingdom general practice research data base: A series of retrospective analysis of data from 1998 through 2002. Clinical Therapeutics 2006; 28: 388−395.
24. Almutairi MA, Said SM, Zainuddin H. Predictors of Poor Glycemic Control Among Type Two Diabetic Patients. American Journal of Medicine and Medical Sciences 2013;3: 17-21.
25. Gopinath B, Sri Sai Prasad M, Jayarama N, et al. Study of factors associated with poor glycemic controlin type 2 diabetic patients. Global Journal of Medicine and public health 2013; 2: 1-5.
26. Al-Zurfi BM, AbdAziz A, Abdullah MR, Mohd N . Waist height ratio compared to body mass index and waist circumference in relation to glycemic control in malay type 2 diabetes mellitus patients, Hospital Universiti Sains Malaysia. International Journal of Collaborative Research on Internal Medicine & Public Health (April 1, 2012).
27. Miyashita Y, Nishimura R, Morimoto A, et al. Glycated albumin is low in obese, type 2 diabetic patients. Diabetes Research and Clinical Practice 2007;78: 51-55.
28. Mokdad AH, Bowman BA, Ford ES, et al. The continuing epidemics of obesity and diabetes in the United States. JAMA 2001; 286: 1195 – 200.
29. UK Prospective Diabetes Study (UKPDS) Group. Intensive bloodglucose control with sulphanylureas or insulin compared with conventional treatment and risk of complications in patients with Type 2 diabetes. Lancet 1998; 352: 837−853.
30. Al-Qazaz HK, Sulaiman SA, Hassali MA, et al. Diabetes knowledge, medication adherence and glycemic control among patients with type 2 diabetes. Internat J Clin Pharmacy 2011; 33: 1028-1035.
31. Lee VWY, Leung PY. Glycemic control and medication compliance in diabetic patients in pharmacist-managed clinic in Hong Kong. Am J Health Syst Pharm 2003;60: 2593–2596.
32. Boule NG, Haddad E, Kenny GP. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus. A Meta analysis of controlled clinical trials. JAMA 2001; 286; 1218-1227.
33. Nelson KM, Reiber G, Boyko EJ. Diet and exercise among adults with type 2 diabetes, Diabetes Care 2002; 25: 1722-1728.