**Glycemic control among patients with Type 2 diabetes mellitus: in relation to medication adherence and life style**

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Abstract

Type 2 diabetes mellitus (DM) is a chronic metabolic disorder in which prevalence has been increasing steadily all over the world. Lifestyle management is a fundamental aspect of diabetes care and it includes nutrition, physical activity, smoking cessation, and psychosocial care. Good glycaemic control among type 2 diabetes mellitus patients involves interplay of self-management measures including physical activity and diet, in addition to medication adherence. One of the major contributing factors is poor medication adherence in type 2 diabetes mellitus which is well documented to be very common and is associated with inadequate glycemic control; increased morbidity and mortality; and increased costs of outpatient care, emergency room visits, hospitalization, and managing complications of diabetes.

Observational cross sectional study, conducted at different major health care facilities in northern Jordan, recruited more than 300 adult patients who had been on the same antidiabetic treatment regimen for a minimum of 3 months. Patients’ data, physical measurements, medications and disease history, dietary carbohydrates and lipids intake data were obtained using pre-validated questionnaires. Fasting blood samples were collected and assessed for HbA1c.

A total of 300 type 2 diabetes mellitus patients were enrolled in this study, 63.7% of them were females and 36.3% were males. The average age of patients was 60.1 years. About 52 (17.3%) of them were smokers, most of them were males (30%). Medication adherence showed that more than two-thirds (69.4%) of the study samples were highly adherent to their medication. Medication adherence was associated significantly with HbA1c level. Only 41.4% of the patients had diet counseling and 58.6% followed a diet plan, both of them were none significantly associated with HbA1c level.

Glycemic control in type 2 diabetes mellitus is not just a matter of proper medications use and dosages, but other factors may contribute to poor glycemic control.

**Key words:** Glycemic control, HbA1c, medication adherence, type 2 diabetes mellitus.

**Introduction:**

Type 2 diabetes mellitus (DM) is a chronic metabolic disorder in which prevalence has been increasing steadily all over the world; with nearly 200 million adults affected along with a 5-fold increased risk of death in developed countries \(^{(14,29)}\). Type 2 diabetes mellitus was firstly described as a component of metabolic syndrome in 1988 \(^{(30)}\). It is characterized by hyperglycemia, insulin resistance, and relative insulin deficiency \(^{(21)}\).

Complex biological elements that influence the development and course of the disease in high-risk populations are important but often insufficient to implement effective prevention and treatment plans. Multiple factors must be addressed in routine diabetes clinical care \(^{(8)}\).

The current DM management therapeutic regimen includes medications, diet, physical activity, adherence; and recently the standards of medical care in diabetes has been updated by American diabetic association (ADA) to address psychosocial issues in all aspects of care including self-management, mental health, communication, complications, co morbidities, and life-stage considerations \(^{(3)}\).
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Lifestyle management is a fundamental aspect of diabetes care which includes nutrition, physical activity, smoking cessation, and psychosocial care. Lifestyle, ethnicity, and age, are other factors partly contributing to high prevalence of DM. A sedentary lifestyle, in addition to consumption of high-fat and high-carbohydrate foods, lead to increased body weight and obesity. Approximately, 90% to 95% of all diagnosed cases of DM have type 2 DM, most of them are overweight. Advancing age is another factor contributing to the increased incidence and prevalence of type 2 DM and mostly occurs in developing countries where the majority of patients are aged between 45 and 64 years.

Physical activity plays an important role in preventing type 2 diabetes. A healthful diet and a moderate exercise program resulting in a 5 to 7 percent weight loss can delay and possibly prevent Type 2 diabetes. Aerobic exercise improves glycemic control, blood pressure and triglycerides level, which lead to reduced cardiovascular mortality and total mortality in patients with type 2 DM and exercise for at least 4 hours per week reduces CVD risk by 40% in women with type 2 DM.

Cigarette smoking is an independent modifiable risk factor for development of diabetes, and smokers are more likely to develop diabetes compared to non-smokers. The medication adherence which is defined as the extent to which a person's behavior agrees with the agreed medication regimen from a health care provider. At least 45% of patients with type 2 DM fail to achieve adequate glycemic control (HbA1c <7%). One of the major contributing factors is poor medication adherence in type 2 DM which is well documented to be very common and is associated with inadequate glycemic control; increased morbidity and mortality, increased costs of outpatient care, emergency room visits, hospitalization, and managing complications of diabetes.

Aims of study:
To examine the role of lifestyle risk factors (diet, exercise and smoking) association with poor glycemic control in type 2 Diabetes mellitus and assess patients medication adherence.

Patients and materials:
This is a cross-sectional observational study conducted during the period of April 2017 to July 2017. The is three hundred fasting patients visiting the outpatient clinics in northern Jordan; at Princess Bassama Ambulatory Care Clinics for follow-up on diabetes management were enrolled. The laboratory work was performed at JUST Medical Health Center lab, during the same period of samples collection.

The Inclusion criteria were:
- Adult patients (Age ≥ 18 years).
- Patient with DM type 2 treated with hypoglycemic medications for a minimum of 6 months on the same DM regimen, and participating patients willing to complete the study surveys.

The exclusion criteria were:
- Recent major trauma.
- Recent surgery, and hospitalization within 12 week, or acute infection requiring antibiotic use.
- Any significant change in the usual diet within the past month.
- Pregnancy, breast feeding or postpartum within 6 months.
- Acute coronary syndrome within 12 weeks.
- Patients unable to provide an informed consent.
- Patients who were not fasting.

The study procedures were explained to eligible patients and an informed consent was obtained prior to enrollment and interview.
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A validated questionnaire was utilized to assess the adherence to hypoglycemic treatment regimen. Medication adherence level categorized into: High, medium and low, according to Morisky medication adherence scale (34,26). Dietary carbohydrates, lipids intake data, and life-style activity were recorded. Physical activity was classified into: light exercise includes activities that not causing sweat breaking or produce shortness of breathless than 3.0 METS (less than 3.5 calories per minute) (One MET is defined as the energy cost of sitting quietly and is equivalent to a caloric consumption of 1kcal/kg/hour). Moderate exercise is an exercise which causing break out in a light to moderate sweat or makes it difficult to carry on a long conversation. Less 3.0-6.0 METS (3.5 – 7 calories per minute). Vigorous exercise causing sweat profusely and makes it difficult to carry on a conversation of any length. (Greater than 6.0 METS (more than 7 calories per minute))9).

Smoking survey was estimated using a pre-validated survey slightly modified to dietary habits in the Jordanian population. Blood samples were obtained after an overnight fasting period (minimum of 10 hours) and 5 ml of patient’s whole blood was obtained in EDTA test tube for the HBA1c measurement.

Data were statistically analyzed using SPSS version 22 software program. General linear model (GLM) was utilized to assess the effect of the predictors on attaining target blood glucose level. All statistical tests were considered significant when P-value of <0.05.

Results:

A total of 300 type 2 DM patients were enrolled in this study, 63.7% of them were females and 36.3 % were males. The average age of patients was 60.1 years. About 52 (17.3%) of them were smokers, most of them were males 33(30%).

Table 1: Association of age and gender with HBA1C goal attainment:

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Elderly patients</th>
<th>Non-elderly</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c target</td>
<td>8.23 ± 1.89</td>
<td>9.7± 2.46</td>
<td>0.03*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>25%</td>
<td>32%</td>
<td>0.028*</td>
</tr>
</tbody>
</table>

➢ Significant association between the subjects’ age and attaining HBA1C target. General linear model (GLM): * Significant P-value of <0.05.

❖ Significant association for one gender with lower HBA1C control. General linear model (GLM):

* Significant P-value of <0.05.

Table 2: Association of life style (Diet counseling, Physical activity, Smoking)

<table>
<thead>
<tr>
<th>Factors</th>
<th>All patients (n=300)</th>
<th>Male (n=109)</th>
<th>Female (n=191)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet counseling</td>
<td>126 (41.4%)</td>
<td>45 (40.2%)</td>
<td>81 (42.2%)</td>
<td>0.067</td>
</tr>
<tr>
<td>Meal plan</td>
<td>178 (58.6%)</td>
<td>66 (58.9%)</td>
<td>112 (58.3)</td>
<td>0.132</td>
</tr>
<tr>
<td>Physical activity</td>
<td>123 (41.1%)</td>
<td>39 (34.8%)</td>
<td>85 (44.8%)</td>
<td>0.737</td>
</tr>
<tr>
<td>Light</td>
<td>161 (53.0%)</td>
<td>65 (58.0%)</td>
<td>96 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>18 (5.9%)</td>
<td>8 (7.1%)</td>
<td>10 (5.2%)</td>
<td></td>
</tr>
<tr>
<td>Vigorous</td>
<td>52 (17.3%)</td>
<td>33 (30.3%)*</td>
<td>19 (10%)*</td>
<td>0.004*</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data represented as number with percentage, statistically significant - p value <0.05

*Calculated from the total male (109) and female (191)

**Calculated from the total of male and female smoking (52)
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Medication adherence showed that more than two-thirds (69.4%) of the study sample were highly adherent to their medication, medication adherence was significantly associated with HbA1c goal attainment (P = 0.035).

Table 3: Frequency of Medications adherence level and HbA1c attainment.

<table>
<thead>
<tr>
<th>Adherence level</th>
<th>N=300</th>
<th>Controlled HbA1c (N= 89)</th>
<th>Non controlled HbA1c (N=211)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High adherence level</td>
<td>209 (69.7%)</td>
<td>64 (72%)</td>
<td>145 (68.5%)</td>
</tr>
<tr>
<td>Medium adherence level</td>
<td>70 (23.4%)</td>
<td>18 (20%)</td>
<td>52 (24.9%)</td>
</tr>
<tr>
<td>Low adherence level</td>
<td>21 (6.9%)</td>
<td>7 (8%)</td>
<td>14 (6.6%)</td>
</tr>
</tbody>
</table>

Discussion:

The relationship between various patients’ related factors, such as age and gender and blood glucose level, revealed a statistically significant association between the subjects’ age and attaining HbA1c target. The mean HbA1c in elderly patients was 8.23 ± 1.89, while it was 9.7± 2.46 (P = 0.03) for non-elderly patient. This finding agrees with Sanal et al (2011) who concluded that glycemic control is better at patients who are 60 years or older. Kayar et al (2017) and Al-Mukhtar et al (2012) also stated that the disease onset younger were related to poor glycemic control with higher HbA1c%, , who suppose that the poor control of blood sugar in the younger population, compared to the elderly, can be linked to the fact that young people do not pay attention to their treatments as elders.

In Our study, gender also showed a significant association with lower HbA1c control in men (25%), compared to women (32%) (P =0.028). This is inconsistent with other findings. Sasishekhar et al (2013) found that males had better glycemic control when compared to females, while Waari et al (2018) found that sex not to be significantly associated with adherence and glycemic control.

Examination patient’s diet (if the patients received diet counseling and/or following a diet plan) showed that only 41.4% of participants had diet counseling (40% men vs. 42% women), and 58.6% of them were following a diet plan, without differences in percentage between men and women. No significant association was found between those having a diet plan and glycemic control. Otherwise; When we examined the relation between the ability of participants to follow their diet plan and glycemic control, a significant association was found with attainment of HbA1c goal (P = 0.003) which is parallel with Kayar et al (2017).

These outcomes cannot be interpreted in isolation of other factors, as most participants were obese or overweight. Yet, they highlight an important factor in poor glycemic control which is an unhealthy diet due to many reasons lack of diet awareness (more than 50%), and this is attributed to lack of medical counseling; unhealthy nutritional habits in Jordan, as many depend mainly on a carbohydrate diet and largely due to low financial income for the majority of the study population. These are the main reasons that impede patients from following a healthy diet. A recent study showed that T2DM patients’ education to enhance national habits and reduce caloric intake in association with increased physical activity for six months was associated with significant reduction in mean HbA1c from 8.5 ± 2.7% to 6.0 ± 1.8%.

Patient life-style, diet, exercise, and patient counseling are the primary non-pharmacotherapy an intervention is recommended for treatment of type 2 DM. This study evaluated patients’ daily activity and the regular exercise. It is found that only 20% of the study samples had exercised on regular basis, and about 38.3% of them attained their target HbA1c, while 27.5% for inactive patients. These results showed a significant association between exercise and attainment of HbA1c target (P = 0.021). This is inconsistent with Kayar et al (2017). Physical activity enhances insulin sensitivity in diabetic patients in the same way as it does in non-diabetic patients. Several studies established that physical exercise reduces cardiovascular risk factors and improves glycemic control in type 2 DM patients.

Smoking is associated with glycemic control in this study’s population sample. A significant association between smoking and poor achievement of HbA1c target (P = 0.004) was observed,
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despite the small percent (17.3%) of smokers with type 2 DM in our sample, several studies support this finding. Nicotine increases the level of circulating insulin-antagonistic hormones (6,20) and decreases insulin sensitivity and insulin-mediated glucose uptake (27). Recent studies support our finding that current smokers with diabetics have higher risk for poor glycemic control than nonsmokers (31) or those who ceased smoking (10).

Diabetes medication adherence is important in helping patients with type 2 diabetes achieving glycemic control. Medication adherence showed that more than two-thirds (69.4%) of the study sample were highly adherent to their medication. Medication adherence was significantly associated with HBA1c goal attainment in parallel with (1,17,40). Poor medication adherence has been reported as one of the important factors associated with inadequate glycemic control (23). Many studies concluded that poor medication adherence to be more common factor of inadequate glycemic control, and its rate was difficult to reduce (3,7). In contrast, a large majority of this study population, 145 (68.5%) were highly adherent to their medications and showed poor controlled HbA1c which is similar to Waari et al (2018) who concluded that a good glycemic control among type 2 diabetics is the interaction of self-management measures including physical activity and diet, in addition to adherence to medication. This excludes adherence as the main factor responsible for poor glycemic control in this population.

Conclusion: Certain factors were significantly associated with glycemic control in patients with type 2 DM. The medication used either the drugs or their doses were one of the most important factors associated with poor glycemic control, especially when combined with the lack of patient counseling and lack of regular and close follow up. Type 2 DM failure or inadequate control could not be explained by a single factor; otherwise those factors are simultaneously associated in a complex manner with poor glycemic control to certain extent. Glycemic control in type2 DM is not just a matter of proper medications use and dosages, but other factors may contribute to medication adherence.

References
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The control on blood sugar level in Type 2 diabetes: what is related to the adherence with drugs and lifestyle?

Type 2 diabetes mellitus (DM) is a chronic metabolic disorder which is increasing its spread all over the world.

The treatment is a combination of diet and lifestyle measures, which include nutrition and physical activity, and discontinuing smoking and psychological and social support.

An unhealthy lifestyle together with the consumption of food rich in fats and carbohydrates, and large portions, leads to weight gain and obesity.

And close to 90% to 95% of all the cases diagnosed with DM are type 2 diabetes, and most of them suffer from obesity.

Physical activity also plays an important role in preventing Type 2 diabetes, and following a healthy diet, and a moderate sports program leads to a weight loss of 5% to 7%, which may delay type 2 diabetes or even prevent it.

With regard to the relationship between smoking and the incidence of diabetes, it is likely that smokers will develop diabetes more compared to non-smokers.

Good control of blood sugar level in Type 2 diabetes is not just a matter of using the suitable medicines and doses, but other factors, compliance with drugs, is an important role of weakened glycemic control in the study community.

Key words: glycemic control, HbA1c, drug adherence.

The investigation involves more than 300 adults in this study, 63.7% of them were women and 36.3% were men.

The average age of the patients was 60.1 years, where 52% (17.3%) of them were men and 48% (36.3%) of them were women.

The average blood sugar level HbA1c was 41.4% of the patients received nutritional counseling and 58.6% follow a diet plan, while 41.4% did not receive nutritional counseling and 41.4% do not follow a diet plan.

HbA1c is a measure of blood sugar level for 2 to 3 months, and it is affected by many factors, including nutrition and physical activity.