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Rom J Diabetes Nutr Metab Dis. **24**(2):119-125
doi: 10.1515/rjdnmd-2017-0016

BODY MASS INDEX AND GLYCAEMIC CONTROL IN PATIENTS WITH DIABETES MELLITUS: A CASE-CONTROL STUDY

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received: April 18, 2017 *accepted*: May 31, 2017
available online: June 15, 2017

Abstract

Background and Aims: *Recent studies have brought evidence on the connection between excess weight and suboptimal glycemic control for Diabetes Mellitus (DM) patients. The aim of this study was to evaluate the association between increased Body Mass Index (BMI) and the likelihood of having suboptimal glycemic control in patients with Type 1 and Type 2 Diabetes Mellitus.* ***Materials and Methods:*** *A case-control study was conducted on 662 patients suffering from Diabetes Mellitus and statistical analysis was performed in order obtain evidence associating BMI and poor glycaemic control. We defined as increased BMI, values >25 kg/m^2 and a hemoglobin A1c (HbA1c) value >7% reflected suboptimal glycemic control.* ***Results:*** *559 (84%) patients had HbA1c >7%. 550 (83 %) patients had a BMI >25 kg/m^2. In case of HbA1c >7%, a BMI >25 kg/m^2 was found in a number of 457 patients (82 %), whereas a normal BMI was present in 102 (18%) patients. For the HbA1c<7% cases, the number of patients associating BMI >25 kg/m^2 was 93 (90%) and a normal BMI was present in 10 (10%) patients. BMI >25 kg/m^2 was not associated with a higher probability of having above-target HbA1c values compared to patients with target HbA1c (OR 0.48, 95% CI: 0.24 to 0.95), with a statistically significant p <0.05.* ***Conclusions:*** *The findings revealed that although in case of suboptimal glycemic control, the number of patients who had a BMI >25 kg/m^2 was significantly higher than the number of patients with a BMI < 25 kg/m^2, a BMI above target was not associated with greater odds of having HbA1c higher than the standard 7% level, compared to individuals with normal HbA1c levels. The results emphasize that a multitude of factors are involved in the process of achieving a targeted glycemic control and a stepped-care approach should be considered for optimum management of Diabetes Mellitus.*

key words: *Diabetes Mellitus, Body Mass Index, glycemic control*

Background and Aims

Diabetes Mellitus (DM) is the most common metabolic disorder worldwide and is characterized by high morbidity rates, low quality of life and premature mortality. Diabetes Mellitus, particularly the Type 2 category is frequently associated with overweight and

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obesity, and has become a public healthcare burden over the last years. Studies estimate that nowadays approximately one third of the world's population is either overweight or obese. A growing body of research describes obesity as issue of concern and a risk factor for developing Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM), as well as other chronic diseases like cardiovascular diseases, respiratory diseases, dyslipidemia, hyper-uricemia, osteo-arthritis and depression [1]. Some studies even suggest that the risk of diabetes increases between 4.5 and 9% for every kilogram of weight gain. Approximately 80% of patients with T2DM are either overweight or obese [1-3]. The PREDATORR study aiming to analyze the prevalence of diabetes mellitus (DM) and prediabetes, and their correlation with cardiometabolic, sociodemographic and lifestyle risk factors in the adult Romanian population from 2012 to 2014 revealed strong correlation between obesity and the presence both prediabetes and DM [4].

Recent clinical trials have brought large evidence regarding diabetes management. These studies illustrated the connection between weight excess and suboptimal glycemic control for DM patients. The results revealed that weight gain tends to worsen glycemic control for patient with T2DM and increase the amount of insulin used in patients with T1DM [1-3]. Furthermore, obesity was shown to be an independent risk factor for dyslipidemia and cardiovascular diseases and weight loss is considered a key measure to the management of T2DM. The prevalence of obesity in patients with diabetes and cardiovascular diseases has been proven to be a major risk factor of premature death. This risk is lower among individuals with normal weight and optimal glycemic control [5-10].

Guidelines for diabetes management now include both optimal pharmacotherapy and lifestyle modifications as recommended measures for diabetic control. Weight loss via exercise and nutrition monitoring may help improve the level of glycemic control, as reported from many studies of medical nutrition therapy [11-13].

In practice, the target level of HbA1c is very difficult to obtain. Except overweight and obesity, many other factors have a negative impact on the attempt of achieving up to standard glycemic control. One of the factors that has lately raised the attention of researchers is the presence of diagnosed depression in patients with DM [14]. Depression as associated comorbidity in patients suffering from diabetes has a great deal of negative implications including poor adherence to medical treatment, poor glycemic control and increased risk of developing vascular complications (micro-vascular and macrovascular complications). Patients associating depression are less likely to be compliant with the recommendations for diabetes management. This could potentially lead to worsening of the symptoms, increased disability, low quality of life and higher rates of mortality [14].

Given all of the above-mentioned, the aim of this study was to evaluate the association between increased BMI as indicator of excess weight and suboptimal glycemic control in patients with both Type 1 and Type 2 Diabetes Mellitus, in order to improve the current understanding of the relationship between the two variables. Furthermore, we also aimed to identify the prevalence of depression among DM patients with poor glycemic control, thus highlighting the importance of individuals' characteristics in diabetes management.

Material and methods

We analyzed a total of 1478 medical records belonging to patients suffering from DM who were admitted to the Diabetes Department of the Emergency County Hospital of Timişoara over

the period of a year, between January and December 2012. We have obtained the permission of the ethic committee of the Timişoara Emergency County Hospital and all the principles of the Helsinki Declaration were fulfilled. Data were recorded from patients charts as follows: demographic data, DM type and duration, DM treatment, weight status (using the Body Mass Index), hemoglobin A1c (HbA1c), presence of complications and comorbidities, including the following: diabetic neuropathy, diabetic retinopathy, myocardial infarction, arterial hypertension, chronic kidney disease and the presence or absence of depression.

However, recorded HbA1c values were found for 662 patients out of 1478, thus we decided to exclude from the present study records with missing HbA1c values.

We thus designed a case–control study on the 662 patients who fulfilled the inclusion criteria, in order obtain evidence associating BMI and poor glycaemic control.

We defined as increased BMI, values higher than 25 kg/m^2, considering the weight status classification according to the World Health Organization: normal (BMI: 18.5-24.9 kg/m^2), overweight (BMI: 25–29.9 kg/m^2), Class I Obesity (BMI: 30-34.9 kg/m^2), Class II Obesity (BMI: 35-39.9 kg/m^2), and Class III Obesity (BMI $\geq$ 40 kg/m^2) [15]. The hemoglobin A1c (HbA1c) level was used to assess glycemic control. Suboptimal glycemic control was described by a HbA1c value higher than 7%, as recent guidelines recommend for non-pregnant adults with diabetes a HbA1c target lower than 7%. We compared the patients who had suboptimal glycaemic control defined by a HbA1c value >7% (cases) with patients who had optimal glycaemic control defined by a HbA1c value <7% (controls) relative to their BMI values, in the attempt of establishing whether a BMI >25 kg/m^2 represents a risk factor for obtaining suboptimal glycemic control.

Also, we evaluated the prevalence of depression among patients with suboptimal glycaemic control. Depression has been diagnosed by the hospital psychiatrist using the Hamilton Depression Scale and the positive diagnosis has been established in case of a score higher than 8 on this specific scale.

All statistical analyses were conducted using descriptive statistics and chi square test of EpiInfo 7.2.1.0. Statistical significance was set at p values <0.05.

Results

The total number of patients enrolled in the study was 662, both male (45%) and female (55%) adults. T1DM was present in 12% (82) of the total cases, while Type 2 Diabetes was found in 88% (580) of the cases. Insulin therapy alone was found in 35% of all patients, oral hypoglycemic medication in 34%, while 25 % of them associated both insulin and oral hypoglycemic drugs as therapy; the rest of 5% managed the disease by lifestyle optimization methods. The presence of associated comorbidities and complications was also assessed in the present study. Arterial hypertension was encountered in 74 % of all patients, with different prevalence for T1DM (29% of all T1DM cases) and T2DM (80% of all T2DM cases) (p <0.001). Similarly, history of myocardial infarction (MI) was found in 1.2% of the T1DM cases, while for T2DM the percentage was higher (7.4%).

Neuropathy was present in a percentage of 63, with 48 % of all T1DM and 65 % of all T2DM, while retinopathy was found in 31% of the patients (40% of all T1DM and 30% of all T2DM). Also, 16% of patients with T1DM and 13% of T2DM patients were found to suffer from chronic kidney disease.

Furthermore, the presence of depression among patients with suboptimal glycemic control was also assessed. A number of 48 (7.2%) patients with HbA1c>7% was found to associate depression, rising the concern that depression may be an additional factor that could negatively influence diabetes control.

All he above-mentioned information is structured in the table below, with further data regarding the exact number of cases corresponding to the percentage and p values (Table 1).

Table 1. Treatment, comorbidities and complications for T1DM and T2DM patients included in the study

Type of diabetes	Total	Percentage	p-value
Type 1 Diabetes Mellitus	82	12%	n/a
Type 2 Diabetes Mellitus	580	88%	
Treatment			
Insulin	236	36%	n/a
Hypoglycaemic drugs	228	34%	
Insulin + hypoglycaemic drugs	165	25%	
Diet	33	5%	
Comorbidities and complications			
Arterial hypertension in T1DM	24	29%	<0.001
Arterial hypertension in T2DM	468	80%	
Arterial hypertension – total	492	74%	
Myocardial infarct in T1DM	1	1.2%	<0.001
Myocardial infarction in T2DM	43	7.4%	
Myocardial infarction – total	44	6.6%	
Neuropathy in T1DM	40	48%	<0.001
Neuropathy in T2DM	378	65%	
Neuropathy – total	418	63%	
Retinopathy in T1DM	33	40%	<0.001
Retinopathy in T2DM	177	30%	
Retinopathy – total	207	31%	
Chronic kidney disease in T1DM	13	16%	<0.001
Chronic kidney disease in T2DM	123	21%	
Chronic kidney disease – total	136	20%	
Depression and glycaemic control			
Depression prevalence for HbA1c > 7%	48	7.2%	<0.001
Depression prevalence for HbA1c < 7%	10	1.5%	

Addressing the main goal of the study, we sought to evaluate the relationship between raised BMI (>25 kg/m^2) and HbA1c values. HbA1c >7 % indicated that glycemic control was not up to standard. 559 (84%) patients out of 662 had HbA1c >7 %. 550 (83 %) patients had a BMI >25 kg/m^2. In case of HbA1c >7%, a BMI >25 kg/m^2 was found in a number of 457 patients (82 %), whereas a normal BMI was present in 102 (18%) patients. For the

HbA1c<7% cases, the number of patients associating BMI >25 kg/m^2 was 93 (90%) and a normal BMI was present in 10 (10%) patients.These results are detailed in Table 2 and Table 3 below, as well as in Figure 1.

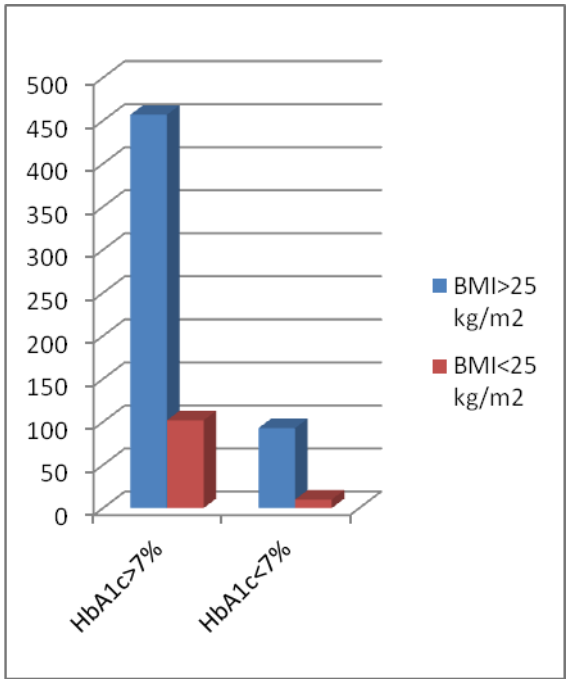

Figure 1. *BMI and HbA1c distribution*

Table 2. BMI distribution

BMI value	Total	Percentage
BMI >25 kg/m^2	550	83%
for which:		
BMI: 25–29.9 kg/m^2	215	39%
BMI: 30–34.9 kg/m^2	188	34%
BMI: 35–39.9 kg/m^2	101	19%
BMI ≥40 kg/m^2	46	8%

Table 3. BMI distribution for HbA1c>7% cases

BMI value for HbA1c >7%	Total	Percentage
BMI >25 kg/m^2	457	69 %
for which:		
BMI:25–29.9 kg/m^2	176	39%
BMI:30–34.9 kg/m^2	150	33%
BMI:35–39.9 kg/m^2	92	20%
BMI ≥40 kg/m^2	39	8%

BMI >25 kg/m^2, classified as overweight or obese, was not associated with a higher chances of having above target HbA1c values (HbA1C>7%) (OR 0.48, 95% CI: 0.24 to 0.95), with a statistically significant p<0.05. Table 4 displays the cases (patients with HbA1c >7%) and the controls (patients with HbA1c <7%) of the study, relative to the presumable risk factor, which for this study was represented by BMI.

Table 4. Contingency table used for correlation analysis between BMI and HbA1c

	HbA1c>7%	HbA1c<7%	Total
BMI >25 kg/m^2	457	93	550
BMI <25 kg/m^2	102	10	112
Total	559	103	662

Discussions

A study assessing data from diabetic patients included in the National Health and Nutrition Examination Survey (NHANES) which took place in US from 1999 to 2006 revealed that mean HbA1c levels were highest in case of diabetics with BMI >25 kg/m^2. The study indicated that approximately half of the adults with diabetes were included in the obesity categories and nearly one fourth of adult diabetes patients struggled with suboptimal glycaemic control. It also pointed out the positive implications of obesity prevention and weight loss through medical or surgical measures in reducing the burden of diabetes on the health care system [12].

A more recent study also conducted in US, analyzing the association between obesity and glycaemic control in patients with DM (with data collected from electronic health records over the course of 3 years from 2009 to 2011), also showed a positive and statistically significant association between obesity and HbA1c >7%, interpreted as poor glycaemic control. The findings from this study revealed that the rates of obesity among diabetes patients were very high, and correspondingly, the percentage of patients with poor glycaemic control was also high, suggesting that lifestyle

changes are mandatory for the treatment of both conditions (diabetes and obesity) [1].

Moreover, recent studies suggest that coexisting depression has also a negative impact on patients suffering from diabetes, as patients struggling with depression are more likely to have poor medication adherence, poor glycemic control, increased risk for diabetic complications, and high rates of premature mortality [14].

Our study confirmed the results of previous studies, showing that the prevalence of overweight and obesity among patients with suboptimal glycemic control was very high, significantly higher than in case normal weight patients. However, when comparing both cases of HbA1c level (lower and higher than 7%), the study failed to provide proof that overweight and obesity are associated with poor glycaemic control. These results could be explained by the multitude of factors associated with the process of achieving a targeted glycaemic control, such as adherence to treatment, the presence of comorbidities and complications, suggesting that a stepped-care approach must be considered in order to obtain successful treatment and of patients with DM. Attention should be paid to all risk factors that could potentially influence DM management, especially to obesity, due to its high prevalence among diabetic patients. Efficient measures should be taken in order to prevent or treat obesity since it is a modifiable factor with major impacts on many chronic diseases including diabetes and cardiovascular pathology.

The present study has limitations; therefore, the results should be interpreted accordingly. First of all, this was a retrospective study, thus data has been collected from patients files, not by direct interview. Secondly, the gathered data do not contain information on medication adherence, patients' behaviors, such as routine physical exercise or diet, which may potentially influence the outcomes.

Future research should focus on capturing all variables that may have an impact on the effort of reaching an up to standard glycemic control. More complex statistical analyses should test the probability of having suboptimal glycemic control for different classes of obesity, as this aspect has not been examined within the present study. We also consider that an active screening for depression in patients with diabetes is important and necessary due to the potential of this complication being overlooked in diabetes centered department.

Conclusions

The main goal of this study was to examine the connection between excess weight and glycemic control among patients with diabetes mellitus. The findings revealed that although in the case of patients with suboptimal glycemic control, the number of patients who were overweight or obese was significantly higher than the number of patient with normal weight, a BMI higher than 25 kg/m^2 was not associated with greater odds of having HbA1c higher than the standard 7% level, compared to individuals with normal HbA1c levels ($p<0.05$). The results of the study did not established high BMI as an independent risk factor associated with poor glycemic control, thus emphasizing that many more other factors contribute to the process of treatment success in patients with type 2 DM. . In conclusion, the present study suggests that identifying other factors linked to poor glycemic control is a reasonable research goal for future investigations, highlighting the importance of individuals' characteristics for optimum management of this disease.

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