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The Association of Obesity and Microvascular Complications with Glycemic Control in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: According Type 2 diabetes mellitus is a chronic metabolic disease with a high prevalence characterized by elevated blood glycemic values and with progressive development of micro and macrovascular complications. Glycemia control is a very important factor in the process of „delaying“ the onset of complications by glycated hemoglobin (HbA1c) analysis. **Aim:** The aim of the study is to determine the association of obesity, microvascular complications with glycemic control in patients with type 2 diabetes. **Methods:** The study was prospective, involving 105 patients with type 2 diabetes. It was conducted at the University Clinical Center of the Republic of Srpska from January 2016 to January 2018. The patients were adults, of both sexes, suffering from type 2 diabetes, in whom complications of this disease are present. Glycemic control was evaluated based on a target HbA1c value of 7%. **Results:** Out of the 105 patients in the study, 45.8% were male, 54.2% female. The mean age of the patients was 68.3%±10.7 years. The mean HbA1c level was 8.32±1.57%. Of the total number of patients, in 25.7% the HbA1c levels were ≤7.0%, while in 74.3% the HbA1c were ≥7.0% (p<0.001). There were 57.1% of obese patients, of whom 37.0% had HbA1c ≤7.0%, and 64.1% had HbA1c ≥7.0% (p<0.014). Depending on the duration of diabetes, the study found that ≥7.0% HbA1c was more present in patients with an diabetes duration over 20 years (24.4%) compared with those who had had the diabetes for less than 20 years (3.8%) (p<0.037). Microvascular complications were present in 58 patients (55.2%), of which 33.3% had normal HbA1c values, while unregulated glycemia had 62.8% (p<0.008). Retinopathy was present in 40.9%, polyneuropathy 37.1% and nephropathy 32.4% from which the unregulated glycemia (HbA1c ≥7.0%) was present in 39.7% of patients compared to normal glycemic values in 11.1 % of respondents (p<0.006). In 88 patients, certain diseases were present: hypertension in 76.2% of patients, cardiovascular disease 58.0% and hyperlipidemia 35.2%. **Conclusion:** Glycemia control in obese patients with type 2 diabetes mellitus is important especially for the prevention of serious microvascular complications that significantly affect the quality of life of patients.

Keywords: glycemic control, diabetes mellitus, microvascular complications.

1. INTRODUCTION

Type 2 Diabetes mellitus is a chronic multisystemic disease characterized by impaired carbohydrate metabolism (hyperglycemia, increased blood glucose level), fat and protein due to absolute or relative disturbance in biological insulin secretion, insulin action, or both (1-3). One in eleven adults in the world population is suffering from diabetes and one in two is unaware that he/she has diabetes (4-6). Therefore, type 2 diabetes mellitus is one of the most significant public health problems of modern times and is a growing pandemic (7). Due to the specific etiopathogenesis of the disease and the influence of genetic and environmental factors in patients, there is

often a progressive development of complications, which can be acute and chronic, affecting vital organs causing significant percentage of disability and mortality in the population (8, 9).

The most common complications associated with diabetes are chronic complications in the heart, blood vessels, kidney damage and failure, impairment and loss of vision, which are due to insufficient glycemic control in patients (10). In clinical practice, glycated hemoglobin (HbA1c) is used as a maker of good glycemic control and according to the recommendations of the American Diabetes Association (ADA), the target values for the prevention of microvascular complications are HbA1c below or equal to 7% (11).

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Also, more and more scientific studies indicate that early detection of the disease and good glycemic control can improve long-term outcomes, or “delay” the onset of complications and improve the quality of patient’s life (12).

2. AIM

The aim of our study was to determine the association of obesity, the presence of microvascular complications with glycemic control according to the values of glycosylated hemoglobin (HbA1c) in patients with type 2 diabetes mellitus.

3. MATERIAL AND METHODS

The study was prospective, involving 105 patients with type 2 diabetes mellitus. It was conducted at the University Clinical Center of Republic of Srpska in Banja Luka, from January 2016 to January 2018 at the Clinic for Cutaneous and Sexually transmitted Diseases of University Clinical Center of Republic of Srpska. This study was approved by the University Clinical Center of Republic of Srpska Ethics Committee.

The patients were adults, both sexes, suffering from type 2 diabetes mellitus. They were referred for hospital treatment or treated as outpatients by patients referred by a family physician. All patients were assessed for glycemic control based on HbA1c (%). In accordance with the ADA recommendations for 7% HbA1c target values, good glycemic controls, patients were divided into two groups.

Group I consisted of patients with good glycemic control, HbA1c≤7%, while Group II consisted of patients with unregulated glycemic values, HbA1c≥7.1%. To all respondents were determined a body mass index (BMI) and anamnestic data that related to the duration (in years) of diabetes and the therapy they used (insulin dependent/independent therapy). In the clinical study, we used relevant laboratory analyzes of blood and urine, and in addition to endocrinologists’ examinations, consultative examinations by other specialists were used to confirm the diagnosis of microvascular complications or the presence of certain comorbidities (hypertension, cardiovascular disease, hyperlipidemia).

Statistical analyses were carried using SPSS 22 software package. The data were described by mean values and standard deviations (SD) for continuous variables and incidence, and percentage for categorical variables. The differences between subgroup mean values were analyzed by the t-test and the one-way analysis of variance (ANOVA) depending on the number of groups. The chi-squared test was used to determine whether there was a significant difference between incidences of categorical variables. P-values lower than 0,05 were considered as significant.

4. RESULTS

This study included 105 adult patients who were diagnosed with type 2 diabetes mellitus, with various microvascular complications and comorbidities. There were 48 males and 57 females in the study (45.8% and 54.2%, respectively) whose mean age was 68.3±10.7 years. According to the HbA1c values, the patients were divided into two groups, group I with well-regulated glycemic values (HbA1c ≤ 7%) and group II with unregulated glycemic values (HbA1c ≥ 7.1%). Mean HbA1c was 8.3 ± 1.6%.

In the first group, 27 patients (25.7%) with HbA1c 6.7±0.2% had well-regulated glycemic control. The mean age in this group was 70.4±8.1%. In the second group, 78 patients (74.3%) had unregulated glycemic control; values for HbA1c were 8.9±1.4%, while the mean age was 67.6±11.4 years, representing a statistically significant difference between the two groups (p<0.001). (Table 1). There was no correlation between gender (p=0.547) and mean age of the patients (p=0.244) between the two groups.

There were 60 patients on insulin therapy (57.1%), 40.8% of patients had good glycemic control, and 62.9% of patients had poor glycemic control, which was a significant statistical difference (p=0.046). Most of the patients with unregulated glycemic control (24.4%) had been diagnosed with diabetes mellitus over 20 years ago compared to well controlled glycemia (3.8%), which was a statistically significant difference (p=0.037) (Table 1).

According to BMI values, the obese patients (BMI >25 kg/m²) in the study were 60 (57.1%), while the normal body weight (BMI 18.5-24.9 kg/m²) had 45 patients (42.2 %). 37.0% had good glycemic control (HbA1c≤7%) in obese patients, while 64.1% had unregulated glycemia (HbA1c≥7.1%), which is a statistically significant difference (p=0.014) (Table 1).

| Variables | All patients N=105 | Group I (HbA1c ≤7.0%) N=27 | Group II (HbA1c ≥7.1) N=78 | p value |
|------------------------------------|-----------------------|----------------------------------|----------------------------------|---------|
| Number of patients. (n. %) | 105 (100%) | 27 (25.7%) | 78 (74.3%) | 0.000 |
| Age. mean±SD | 68.36±10.72 | 70.44±8.08 | 67.64±11.45 | 0.244 |
| Gender (n.%) | | | | |
| Male | 48 (45.8%) | 11 (40.8%) | 37 (47.4%) | 0.547 |
| Female | 57 (54.2%) | 16 (59.2%) | 41 (52.6%) | |
| Duration of diabetes (years) | | | | |
| < 1 year | 8 (7.6%) | 3 (11.1%) | 5 (6.4%) | 0.466 |
| 1-9 years | 33 (31.4%) | 13 (48.1%) | 20 (25.6%) | 0.130 |
| 9-19 years | 44 (41.9%) | 10 (37.0%) | 34 (43.6%) | 0.700 |
| >20 years | 20 (19.0%) | 1 (3.8%) | 19 (24.4%) | 0.037 |
| Insulin dependency (n.%) | | | | |
| Insulin independent | 45 (42.9%) | 16 (9.2%) | 29 (37.2%) | 0.053 |
| Insulin dependent | 60 (57.1%) | 11 (40.8%) | 49 (62.9%) | 0.000 |
| HbA1c % (n. mean. DS) | 8.32±1.57 | 6.67±0.21 | 8.89±1.43 | 0.000 |
| Obesity. BMI >25 kg/m ² | | | | |
| Yes | 60 (57.1%) | 10 (37.0%) | 50 (64.1%) | 0.014 |
| No | 45 (42.9%) | 17 (63.0%) | 28 (35.9%) | |

Table 1. Characteristics of the respondents in the study. n (%) - total number (percentage) of patients, X- mean, SD- standard deviation

| Variables | All Patients | HbA1c ≤7.0 % | HbA1c ≥7.1 % | P-value |
|--|--------------|--------------|--------------|---------|
| Microvascular complication (n, %) | | | | |
| Total | 58 (55.2%) | 9 (33.3%) | 49 (62.8%) | 0.008 |
| Polyneuropathy | 39 (37.1%) | 6 (22.2%) | 33 (42.3%) | 0.063 |
| Nephropathy | 34 (32.4%) | 3 (11.1%) | 31 (39.7%) | 0.006 |
| Retinopathy | 43 (40.9%) | 8 (29.6%) | 35 (44.9%) | 0.165 |
| Comorbidity (n, %) | | | | |
| Total | 88 (83.8%) | 22 (81.5%) | 66 (84.6%) | 0.703 |
| Cardiovascular disease | 61 (58.0%) | 17 (63.0%) | 44 (56.4%) | 0.552 |
| Hypertension | 80 (76.2%) | 20 (74.0%) | 60 (76.9%) | 0.765 |
| Hyperlipidemia | 37 (35.2%) | 6 (22.2%) | 31 (39.7%) | 0.100 |

Table 2. Frequency of microvascular complications and comorbidities in patients with type 2 diabetes mellitus

Examining the presence of microvascular complications and comorbidities, which progressively develop in patients with diabetes mellitus type 2, in our study, out of a total of 105 patients, 58 patients (55.2%) had microvascular complications. Of these, 33.3% of patients had good glycemic control, while unregulated glycemic values were present in 62.8% of the patients, representing a statistically significant difference (p=0.008) (Table 2).

Polyneuropathy was present in 39 patients (37.1%); 22.2% for well-regulated glycemia and 42.3% for unregulated glycemic values, which does not represent a statistically significant significance (p=0.0063). Of total, 34 patients, or 32.4%, had nephropathy. With well-controlled glycemia, HbA1c≤7% there was 11.1% of patients, while 39.7% of patients with nephropathy had HbA1c values ≥7.1%, which represents a statistically significant difference (p=0.006) (Table 2). Retinopathy had 43 patients or 40.9%, with good glycemic control was 29.6% of patients, while in 44.9% of the HbA1c values ≥ 7.1%, there was no significant difference (p = 0.165) in the statistic (Table 2).

In our study, of the 105 patients, comorbidities were present in a total of 88 patients (83.8%). Of these, hypertension was most prevalent in 76.2% of the patients, cardiovascular disease (heart failure, myocardial infarction) in 58.0% of the patients, while hyperlipidemia was present in 35.2% of the patients. The glycemic control values of HbA1c showed no statistically significant differences (Table 2).

5. DISCUSSION

Our study has shown that type 2 diabetic patients who are obese (BMI >25 kg/m²) and who have some chronic microvascular complications have statistically significantly more often unregulated glycemic values (HbA1c ≥7.1%) with scientific studies highlighting obesity as a significant risk factor for microvascular complications (9, 13, 14). In our study, there was no statistically significant difference in gender compared to glycemic control, which is confirmed by other studies, although, on the other hand, some studies report that glycemic control is worse in women due to differences in glucose homeostasis, response to treatment and certain psychological factors (15, 16, 17).

The mean age of the patients in our study in both groups was 68±11 years and in most patients the values of HbA1c were ≥7.1%. These results are in line with other studies showing that the mean age of patients with micro/macrovascular complications and comorbidities in patients with type 2 diabetes mellitus is approximately the same and that the prevalence of macrovascular complications in older diabetics is higher, while microvascular complications are more present in younger diabetics with unregulated glycemia (18).

In our study, patients with diabetes duration over 20 years had statistically significantly more often poor glycemic control, with a mean HbA1c value of 8.89±1.43%, compared to those with a diagnosis of diabetes for less than 20 years. This is confirmed by other scientific studies indicating that the previously confirmed diagnosis of diabetes and insufficient glycemic control, combined with hypertension and hyperlipidemia, are a risk factor for the increased incidence of micro/macrovascular complications in patients with long-standing disease (14, 19, 20).

In our study, 57.1% of patients were on insulin therapy. A large percentage had unregulated glycemia and correlated positively with the duration of diabetes, older age of the patients, and the presence of other risk factors for this disease (obesity), which is consistent with the results of other scientific studies (18, 20).

In our study, 58 or 55.2% of the patients had some of the microvascular complications that were associated with poor glycemic control, which was statistically significant and in line with the results of other studies indicating that 35% had type 2 diabetes by the time of diagnosis, one of the complications of this disease had already developed. Gedebjerg et al. point out that 12% had microvascular complications, 17% had macrovascular complications, while 6% had both types of complications (21, 22). Also, scientific studies indicate that a longer period of exposure to HbA1c ≥8% is associated with increased microvascular and macrovascular events and increased mortality (22).

In our study, polyneuropathy was not significantly associated with unregulated glycemia. Literature data indicate that, in the comparison of less good and good glycemic control of HbA1c, there is no absolute reduction in the relative risk of developing diabetic neuropathy whose onset depends on other factors (duration of diabetes, lipid status, age of the patient) (23). Nephropathy in our study was statistically significantly associated with unregulated glycemia, which is consistent with other scientific studies showing that good glycemic control reduces the risk or slows the progression of diabetic kidney disease, which is present in 20-40% of patients with diabetes and is a leading cause terminal kidney disease. Also, studies show that it is important to maintain optimal values of systolic blood pressure in order to reduce this complication as well as former smokers (24, 25).

Diabetic retinopathy is a very common microvascular complication of patients with diabetes and depends mainly on the duration of the diabetes. It is equally represented in type 1 and type 2 diabetes (24). In our study, this vascular complication was not statistically significantly associated with glycemic control of HbA1c, although scientific studies have shown different results. In a study by Jelinek et al., Retinopathy was the most common complication in elderly patients over 65 years with poor glycemic control, and that lipid values, obesity, waist circumference was significantly associated with diabetic retinopathy (26, 27). Other studies indicate that retinopathy was significantly present in patients with diabetes and that the associated risk factors for this microvascular complication were, among others, female sex, older age, hypertension, inadequate glycemic control, physical inactivity, long duration of the disease, insulin use (28).

The presence of certain comorbidities (cardiovascular disease, hypertension, hyperlipidemia) in our study was verified in 83.8% of the total number of patients. Hypertension was more prevalent but was not statistically significantly associated with glycemic control of HbA1c. Basit et al. found in their study that hypertriglyceridemia and hypertension were significantly associated with unregulated glycemic values (29). Other scientific studies suggest that hypertension is twice as common in a diabetic patient compared to non-diabetic individuals. Moreover, insulin resistance is often present in patients with hypertension, which poses a higher risk of developing diabetes than in normotensive individuals (30).

The cardiovascular diseases identified in the patients in our study (diabetic myocardiopathy, myocardial infarction) were not significantly correlated with glycemic control of HbA1c, which is in agreement with the research by Grenier et al., who proved that diabetics with cardiovascular disease and diabetics diseases achieved a similar glycemic control to HbA1c (31). Scientific studies show that these diseases are often prevalent in patients with diabetes due to the relatively long preclinical detection period in which insulin resistance and hyperglycemia gradually worsen causing vascular complications and are positively correlated with glycemic control (32, 33). These diseases, in the presence of other risk factors (obesity, hypertension, dyslipidemia), can significantly affect the quality of life of patients with type 2 diabetes, and therefore early detection of the disease and adequate therapy are imperative to prevent complications; cardiovascular risks should be evaluated on an annual basis in all patients with diabetes (12, 34).

In our study, hyperlipidemia was not statistically significantly associated with glycemic control, although there are scientific studies indicating that hyperglycemia adversely affects lipoproteins through increased glycosylation and oxidation leading to the development of atherosclerosis, which is associated with other risk factors (obesity, hypertension) cardiovascular disease in patients with diabetes (21, 35). Glycemic and lipid control in patients with type 2 diabetes is therefore very significant because it reduces the overall risk of complications

that are leading causes of morbidity and mortality in patients (2, 36, 37). The results of scientific studies indicate that different therapeutic modalities, in addition to pharmacological therapy, can significantly influence the correction of dyslipidemia, and thus hyperglycemia (36). The first and most important step is a lifestyle change (diet change), weight reduction in case of obese patients, and an increase in physical activity under the control of a professional (38).

6. CONCLUSION

Unregulated glycemic values of HbA1c in obese patients suffering from type 2 diabetes mellitus for many years can cause certain microvascular complications in patients and increase the overall risk of developing cardiovascular events. Early identification of risk factors as well as the disease itself through an adequate prevention program and better patient education can contribute to reducing the development of these complications and improve the quality of life of patients.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Author's contribution:** RB, JB and SUŠ collected the data. RB analyzed them and wrote the text. SM assisted in writing the text including final editing and critical revision of the scientific content. All authors have read the text and approved the final manuscript.
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