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Original scientific paper

STATISTICAL RESEARCH ON THE CORRELATION BETWEEN BMI AND GLYCOSYRED HEMOGLOBIN IN PATIENTS WITH DIABETES

Merije ELEZI*, Vlatko TANEVSKI, Besnik ELEZI, Enesa NESIMI, Mirsade TAIRI, Enisa RAHMANI, Zuliha AVDIYI, Mustafa MUSTAFI

Faculty of Food Technology and Nutrition, University of Tetova, st. Ilindenska nn., 1200 Tetovo, Republic of North Macedonia
**Corresponding author e-mail: merije.elezi@unite.edu.mk*

Abstract

Diabetes is a significant global challenge to the health and well-being of people, families and countries. The main objectives of this research are: to statistically determine the correlation between BMI and the value of glycated hemoglobin (HbA1c) and to analyze the eating habits and lifestyle of the 109 subjects who were included in this study. The research was conducted in the period from 01.06.2023-30.06.2023. by the Faculty of Food Technology and Nutrition at the University of Tetovo and VT Diet Club - Bitola. The data from the 109 respondents (35 men and 74 women) aged from 5 to 81 years. were collected by an online questionnaire. Information about minors was obtained from their parents - guardians. The following statistical methods were used: Pearson's correlation coefficient and relative numbers. 68% of the respondents suffer from diabetes type 2, and 32% of the respondents suffer from diabetes type 1. Most of the patients with diabetes (29.4%) are aged 45-54 years. The value of the correlation coefficient r = 0.04 indicates that there is a very weak correlation between BMI and the value of glycated hemoglobin. This means that the value of glycated hemoglobin is influenced by other factors such as: diet, physical activity, use of therapy with oral antidiabetics and/or insulin, etc. 41.3% of respondents are overweight (BMI = 25-29.9 kg/m2), and the same percentage of respondents are obese (BMI = 30 and more kg/m2). Crucial negative food habits practiced by the respondents are: 69% of the respondents indicated that they have 3-4 meals a day (diabetics should have 3 main meals and 2 snacks) and the same % of respondents indicated that they consume food with a high glycemic index. From this study, it can be concluded that a healthy and balanced diet and physical activity are crucial for leveling glycemia in diabetics, as well as for the prevention of complications caused by diabetes.

Keywords: diabetes, glucose, hemoglobin, nutrition, activity, BMI.

1. Introduction

Diabetes mellitus is defined as a clinical syndrome that is followed by a state of chronically elevated blood glucose concentrations, both on an empty stomach and after consuming carbohydrates, during which the appearance of glucose in the urine can also be registered.
Diabetes is a consequence of an absolute or relative lack of insulin. Experts from the World Health Organization (WHO - World Health Organization, 1999) define diabetes mellitus based on laboratory findings, namely:

- If the fasting venous plasma glucose concentration is 7.0 mmol/L and more and/or
- If the concentration of glucose in the venous plasma is 11.1 mmol/L or more two hours after a meal with carbohydrates or an oral load of 75 g of glucose.

According to the WHO categorization, there are three types of diabetes mellitus clinically:

- Primary (idiopathic),
- Secondary and
- Gestational.

Primary diabetes mellitus includes:

- Diabetes mellitus type 1 and
- Diabetes mellitus type 2.

There are several potential causes for the occurrence of secondary diabetes mellitus, namely:

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- Damage to the pancreas or during its surgical removal,
- Various endocrinological diseases, etc.

Gestational diabetes mellitus occurs for the first time during pregnancy.

Diabetes mellitus type 1 is also called juvenile diabetes, and the older name - insulin-dependent diabetes mellitus (IDDM) is still found. It usually occurs in young people, although its occurrence is not excluded at any age. In the largest number of newly discovered patients with diabetes mellitus type 1 (even over 90%), autoantibodies directed at the β-cells of the islets of Langerhans of the pancreas can be detected in the serum, which indicates the autoimmune nature of the disease. In most patients, these autoantibodies disappear after a few years. There are data that diabetes mellitus type 1 can also occur after a viral infection that causes the destruction of β-cells.

So, diabetes mellitus type 1 is characterized by an absolute lack of insulin, severe hyperglycemia and ketoacidosis, which, if not treated in time, can result in death. By applying an adequate dose of insulin in these patients, a satisfactory regulation of the blood glucose concentration is achieved, although microvascular complications develop over time.

Of all cases of diabetes mellitus type 1 account for 5 to 10%.

Diabetes mellitus type 2 is also called diabetes in adults, and the older name - non-insulin dependent diabetes mellitus (NIDDM) is still found. It most often occurs in people over 40 years of age who are overweight and have a sedentary lifestyle, although its occurrence in younger people is not excluded. Insulin concentrations that are higher than normal are detected in the plasma of these patients, but their cells are resistant to insulin, so it is not able to maintain the normal concentration of glucose in the blood.

So, diabetes mellitus type 2 is characterized by a relative lack of insulin. Ketoacidosis rarely occurs. Treatment is with oral hypoglycemic drugs and body weight regulation, and only in some patients in the later stage of the disease, insulin treatment is required due to the secondary development of absolute insulin deficiency.

Of all cases of diabetes mellitus type 2 account for 80-90% [1].

2. Goals

Diabetes is a significant global challenge to the health and well-being of people, families, and countries. New figures from the International Diabetes Federation reveal an alarming rise in the prevalence of diabetes. 537 million adults worldwide live with diabetes. It is predicted that 643 million adults will be living with diabetes by 2030 [2]. Therefore, the main objectives of this research are:

- To statistically determine the correlation between BMI and the value of the three-month average (HbA1c) in the representative sample that was included in this study;
- To make a detailed statistical analysis of the food habits and lifestyle of the respondents who were included in this study.

3. Material and methods

3.1. Research material: One in 10 adults has diabetes [2]. Since diabetes is a global problem, we decided to research the correlation between BMI and the value of the three-month average (HbA1c) in diabetics (type 1 diabetes and type 2 diabetes) who were included in this study, as well as their eating habits and lifestyle. The research was conducted by: The Faculty of Food Technology and Nutrition at the University of Tetovo and VT Diet Club - Bitola. The research was conducted in the period from June 1, 2023. – June 30, 2023 through an online survey. The research we conducted is of a prospective type. Also, below is the survey questionnaire that we used to conduct this research.

The research was conducted on a representative sample of 109 respondents. The study included male and female subjects aged 5 to 81 years. To be able to use the obtained data in our study, we obtained consent from the respondents who were included in the research and the parents - guardians of the minor respondents.

3.2. Research Methodology: The study was conducted with a quota sample: of 35 men and 74 women. The selection of the sample was systematic, i.e. it was necessary to meet certain criteria:

- The study should include both sexes;
- Respondents should be between the ages of 5 and 81;
- The subjects should suffer from diabetes (type 1 diabetes, type 2 diabetes, gestational diabetes).

We would also like to point out that the data for the minors who were included in this study were obtained from their parents - guardians.

3.3. Statistical method of data processing: To determine the correlation between BMI and the value of the three-month average (HbA1c) as a statistical method of work, Pearson's correlation coefficient was used. Also, relative numbers were used to process the data related to the food habits and lifestyle of the respondents. The data are presented tabularly and graphically.

4. Results

Chart 1 shows the percentage distribution of diabetes patients by gender.

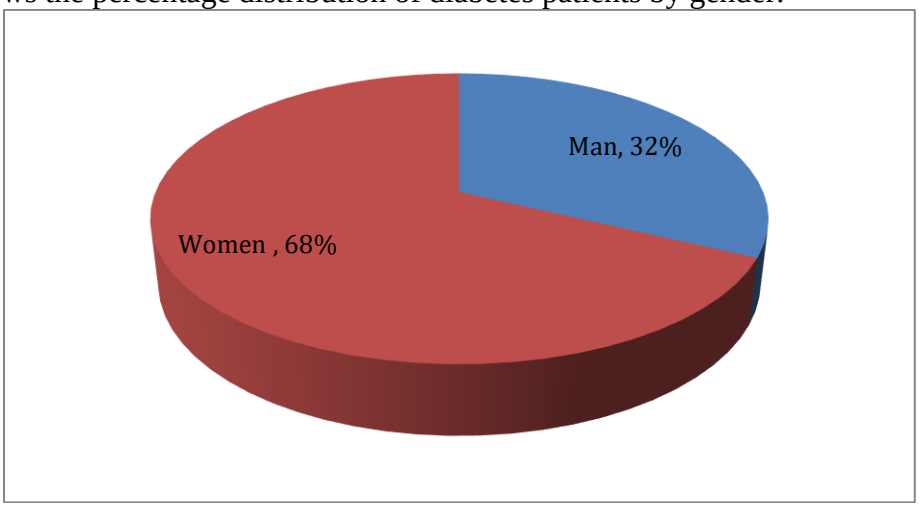


Chart 1: Percentage distribution of diabetes patients by gender

From graph 1, it can be concluded that diabetes as a pathology is much more prevalent in the female population, i.e. 68% of the diabetics who were included in this study were women.
Graph 2 shows information on the number of respondents who were included in the study, distributed by age group.

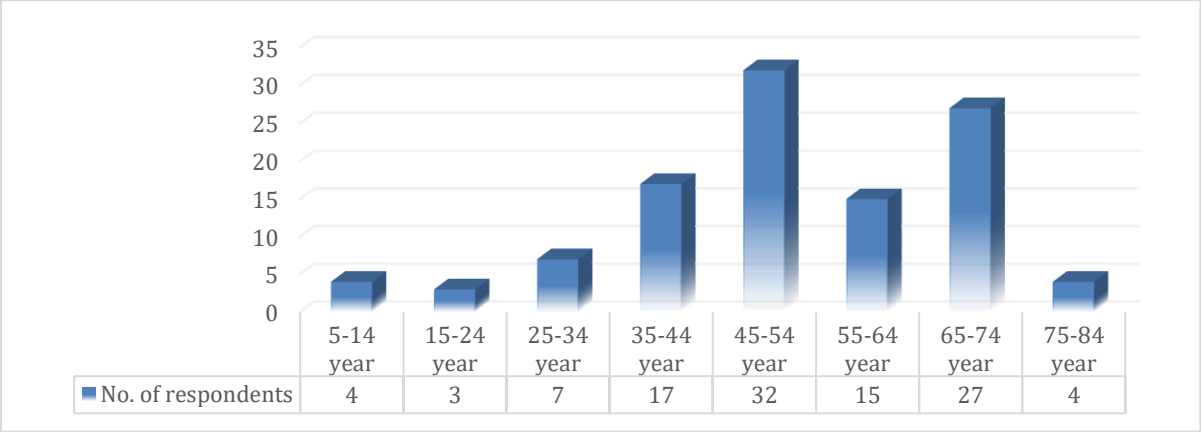


Chart 2: Distribution of diabetes patients by age group

From graph 2, it can be seen that the majority of people with diabetes are aged 45-54 (32 respondents).
Table 1 shows information about the number of respondents who were included in this study, distributed by the type of diabetes they suffer from.

Table 1: Distribution of diabetes patients by type of diabetes

Types of diabetes	**No. of respondents**	**%**
Type 1 diabetes	35	32%
Type 2 diabetes	74	68%
Gestational diabetes	0	0%
In total	109	100%

From Table 1 it can be seen that 68% of the respondents are suffering from type 2 diabetes, while 32% of the respondents are suffering from type 1 diabetes.
Graph 3 shows the percentage distribution of diabetes patients according to the age at which they were first diagnosed with diabetes by a medical person - a doctor.

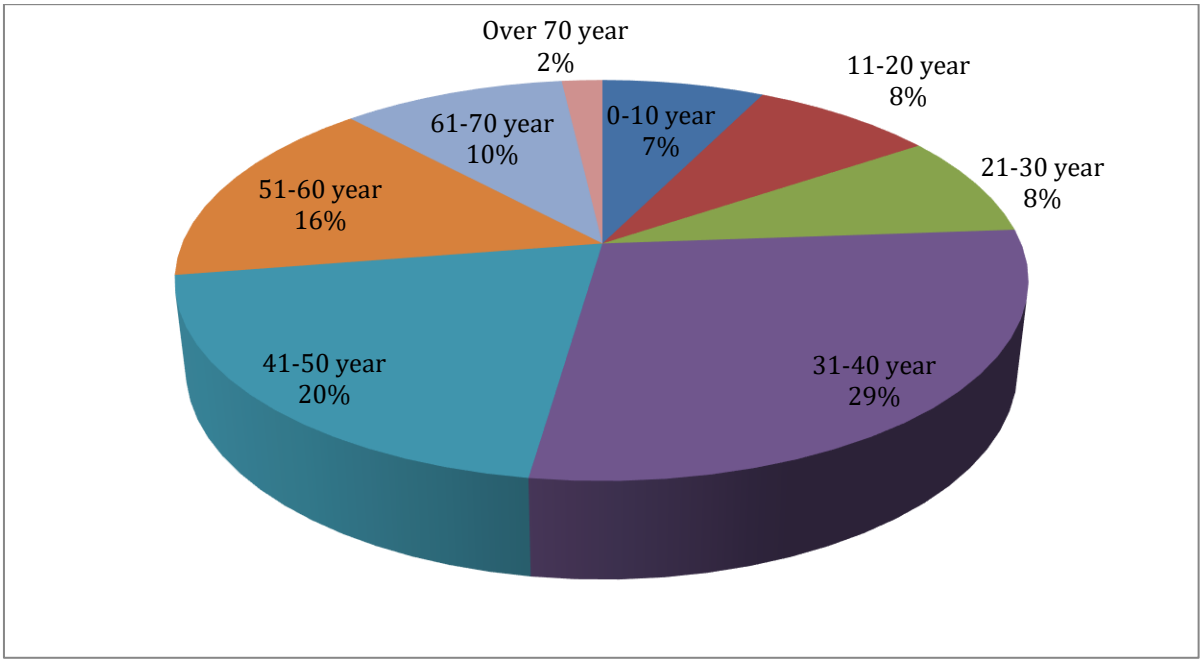


Chart 3: Percentage distribution of diabetes patients by age at which the disease was first diagnosed

From graph 3, it can be concluded that the majority of respondents (29%) were diagnosed with diabetes for the first time by a doctor at the age of 31-40.

To determine the correlation between BMI and glycated hemoglobin (HbA1c) levels in subjects, we used Pearson's correlation coefficient (r). With correlation, we examine the relationship of mutual changes of two or more phenomena. In the case of inanimate phenomena, there is a mathematical relationship, that is, the constant cause under the same conditions causes the same consequence (effect). In medicine, there is no strict mathematical relationship with mass phenomena, that is, it is not possible to completely remove (separate) the action of random factors from the action of the "main factor". It could be said that correlation in medicine examines the relationship between the influence and interdependence of changes in two or more phenomena. In the series with numerical marks, by examining the relationship, it is seen how the changes in the average values of one phenomenon affect the changes in the average values of other phenomena. Correlation can be simple (simple), multiple, linear, and curvilinear. The value and strength of the correlation are determined by Pearson's correlation coefficient (r). The correlation coefficient varies from -1 (minus one) to +1 (plus one). The closer the value of the correlation coefficient is to 1 (one), the stronger the correlation. If r = 0 then correlation does not exist. The interpretation of the correlation coefficient values is performed based on the following scale:

0.00 to 0.19 weak correlation;
From 0.20 to 0.39 low correlation;
From 0.40 to 0.69 mean correlation;
From 0.70 to 0.89 high correlation;
0.90 to 1.00 very high correlation.

Table 2 shows the methodology of determining a simple linear correlation. We determine the correlation coefficient using the formula:

$$r = \frac{Cxy}{\delta x \times \delta y}$$

In the formula C is covariance, x shows one (dependent) and y the other (independent) phenomenon. δ represents the standard deviation. The covariance C is determined by the formula:

$$Cxy = \frac{\sum xy}{N} - \overline{x} \times \overline{y}$$

Table 2: Examination of the relationship between BMI and mean value of glycated hemoglobin

BMI kg/m^2 (x)	X	f	fx	d(x) (X-$\overline{X}$)	fd	d^2(x)(X-$\overline{X}$)^2	fd^2	Average value of glycated hemoglobin %(y)	d(y)(y-$\overline{y}$)	d^2(y)(y-$\overline{y}$)	xy
0-18,4	9.7	0	0	-21.1399083	0	446.8957211	0	0	-6.38333333	40.74694	0
18,5-22,9	21.2	8	169.6	-9.63990826	-77.1192661	92.9278312	743.42265	8	1.616666667	2.613611	169.6
23-24,9	24.45	11	268.95	-6.38990826	-70.2889908	40.83092753	449.140203	7.2	0.816666667	0.666944	176.04
25-29,9	27.95	45	1257.75	-2.88990826	-130.045872	8.351569733	375.820638	6.9	0.516666667	0.266944	192.855
30-39,9	35.45	38	1347.1	4.610091743	175.183486	21.25294588	807.611943	8.8	2.416666667	5.840278	311.96
40-49,9	45.45	7	318.15	14.61009174	102.270642	213.4547807	1494.18347	7.4	1.016666667	1.033611	336.33
∑		109	3361.55		554.908257	823.7137762	3870.1789	38.3		51.16833	1186.79
$\overline{x}$	30.8399083							$\overline{y}$	6.383333333		

First, the average values of BMI ($\overline{X}$=30.8) and glycated hemoglobin ($\overline{Y}$=6.4) are determined. Determining the standard deviation of the two occurrences is the next step in the process.

$$\delta x = \sqrt{\frac{\sum fd^2}{\sum f}}$$

$$\delta x = \sqrt{\frac{3870,18}{109}} = 5,96$$

$$\delta y = \sqrt{\frac{\sum d^2}{N}}$$

$$\delta y = \sqrt{\frac{51,17}{6}} = 2,92$$

The value of the standard deviation for BMI is δx = 5.96, while for glycated hemoglobin δy = 2.92. The individual products between BMI and glycated hemoglobin values are determined, as well as their sum ∑1186.79. The obtained values from table 2 are substituted in the covariance formula:

$$Cxy = \frac{\sum xy}{N} - \overline{x} \times \overline{y}$$

$$Cxy = \frac{1186,79}{6} - 30,8 \times 6,4 = 197,8 - 197,12 = 0,68$$

The value of the covariance is Cxy = 0.68. If the values are replaced in the formula for creating the correlation coefficient, we get:

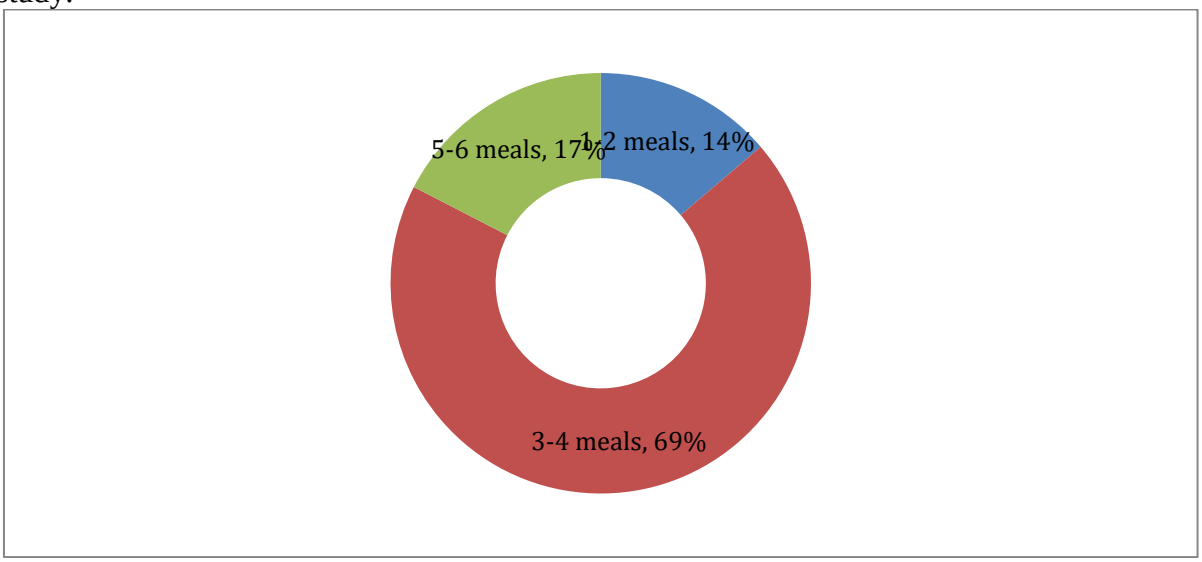
$$r = \frac{Cxy}{\delta x \times \delta y}$$

$$r = \frac{0,68}{5,96 \times 2,92} = \frac{0,68}{17,4} = 0,04$$

Based on the obtained value of the correlation coefficient r = 0.04, it can be said that there is a very weak correlation between BMI and the value of glycated hemoglobin in the 109 subjects [3].

Also, from Table 2 it can be seen that 41.3% of the respondents are overweight (BMI = 25-29.9 kg/m2), the same percentage of people who fall into the obese category (BMI = 30 and more kg/m2).

Chart 4 shows information on the number of meals eaten by diabetics who were included in this study.



Graph 4: Number of meals that diabetics have

From Graph 4, it can be seen that 69% of the diabetics who were included in this study declared that they eat 3-4 times a day.

Table 3 shows information on the distribution of respondents who answered the question: "Do you consume sweetened soft drinks (carbonated and non-carbonated)?".

Table 3: Distribution of diabetics who answered the question: "Do you consume sweetened soft drinks (carbonated and non-carbonated)?"

Consumption of sweetened soft drinks (carbonated and non-carbonated)	**No. of respondents**	**%**
Yes	30	28%
No	79	72%
In total	109	100%

The results in Table 3 are encouraging as they suggest that 72% of the diabetics included in this study reported not consuming sweetened soft drinks (carbonated and still).
Table 4 shows the distribution of respondents who answered the question: "Do you eat food that has a high glycemic index (white bread and pastries, cornflakes, snacks, white rice, pasta, potatoes, sugar, biscuits, cakes, chocolate, etc.)? ".

Table 4: Distribution of diabetics who answered the question: "Do you eat food with a high glycemic index (white bread and pastries, cornflakes, snacks, white rice, pasta, potatoes, sugar, biscuits, cakes, chocolate, etc.)?

Consumption of high GI foods	No. of respondents	%
Yes	75	69%
No	34	31%
In total	109	100%

According to the results of Table 4, it is worrying that 69% of the respondents declared that they consume foods with a high glycemic index such as: white bread and pastries, cornflakes, snacks, white rice, pasta, potatoes, sugar, biscuits, cakes, chocolate, etc.
Table 5 shows the distribution of respondents who answered the question: "Do you practice light physical activity (walking, jogging, cycling, etc.) every 30 min. daily?".

Table 5: Distribution of diabetes patients who answered the question: "Do you practice light physical activity (walking, jogging, cycling, etc.) after 30 min. daily?

Practicing 30 minutes of light physical activity	No. of respondents	%
Yes	85	78%
No	24	22%
In total	109	100%

From Table 5, it can be concluded that 78% of the respondents suffering from diabetes declared that they practice light physical activity for 30 minutes a day, such as: walking, jogging, cycling, etc.

5. Discussion

Diabetes mellitus represents a complex group of disorders with different etiology, pathogenesis, clinical picture and treatment. Improper diet, obesity, and insufficient physical activity are considered the main risk factors for the occurrence of insulin-independent diabetes, which accounts for 90% of the total number of patients. This type of diabetes is characteristic of developed countries, where food offers and energy density are abundant, and the physical activity of the population is insufficient [4]. According to the results of our study, 68% of the respondents who were included in the study suffer from insulin-independent diabetes. The number of people with diabetes in the world was 100 million in the year 2000, and by 2020, it exceeded the figure of 300 million [4].
In the Republic of North Macedonia, 7432 new diabetes patients were registered in 2020. 53.5% of newly diagnosed cases in 2020 were women, and 46.5% of newly diagnosed cases in 2020 were men [2]. Also, from the results of our study, it can be concluded that diabetes as a

pathology is much more prevalent in the female population, i.e. 68% of the diabetics who were included in this study were women.
When it comes to our neighborhood, a 2012 study from Bulgaria indicates that the prevalence of diabetes is significantly higher in men than in women – 56.7% male diabetics versus 43.3% female diabetics ($p < 0.001$) [5]. Overall, the global prevalence of diabetes is higher in men, but there are more women with type 2 diabetes than men [6].
According to age, the participation of newly registered persons in 2014 at the age of 0 to 15 years is 37 persons or 1.43% of the total number of patients, and the most registered cases are in the age group of 55 to 60 years and is 898 persons or 34.8% [7]. But the data from our study is worrying that most of the diabetics who were included in this study (29.4%) are aged 45-54 years. Also, most of the respondents (29%) stated that they were diagnosed with diabetes for the first time by a doctor at the age of 31-40. These startling numbers say that diabetes is no longer a disease characteristic of the third age, but, unfortunately, is increasingly present in younger people.
In type 2 diabetes, diet therapy with reduction of body mass is a priority, given that over 80% of these diseases are associated with obesity [4]. From the results of our study, it can be seen that 41.3% of the respondents are overweight (BMI = 25-29.9 kg/m2), the same percentage of people who fall into the obese category (BMI = 30 and more kg/m2). Although not all obese people develop diabetes, nor are all people with diabetes obese, about 80% of people with diabetes are well-nourished and obese. It has been established that for a 1 kg increase in body weight, the risk of developing type 2 diabetes increases by 7.3% [8].
The main objective of this study was to statistically determine the correlation between BMI and the value of glycated hemoglobin (HbA1c) in the representative sample that was included in this study. Hemoglobin A1c is formed by the non-enzymatic binding of glucose (glycosylation) to the valine residues of the N-terminal end of the β-chain of hemoglobin A. Hemoglobin A1c has two important characteristics that make it suitable for wide clinical use as an indicator of glycemic control in the previous two to three months:

- The concentration of hemoglobin A1c is proportional to the concentration of glucose in the blood and this is seen in the long term.
- Hemoglobin A1c is not broken down, but remains present in the blood until the erythrocytes themselves are destroyed [1].

Based on the obtained value of the correlation coefficient $r = 0.04$, it can be said that there is a very weak correlation between BMI and the value of glycated hemoglobin in the 109 subjects. In medicine, there is no strict mathematical relationship with mass phenomena, that is, it is not possible to completely remove (separate) the action of random factors from the action of the "main" factor [3]. The value of the Pearson's correlation coefficient $r = 0.04$ indicates that the value of glycated hemoglobin is influenced by other factors such as: diet, physical activity, therapy with oral antidiabetics and/or insulin, etc. A scientific study was made based on data from the US database for the period from 2012 to 2019. indicates that mean BMI increased significantly and there was a decrease in the proportion of adults with type 2 diabetes who achieved glycemic control. Also, for all years studied, higher BMI classification was associated with higher HbA1c values [11]. Also, a Japanese longitudinal retrospective study that included 5325 subjects aged 20-75 years. found that in 405 obese subjects with normal baseline HbA1c (BMI ≥ 27.0 kg/m2, HbA1c 5.2-5.6%), mean HbA1c levels increased over the study period, and 50.9% developed prediabetes/diabetes. In contrast, in 77 underweight subjects with high-normal HbA1c levels (BMI ≤ 18.9 kg/m2, HbA1c 5.7-6.4%), the mean HbA1c level remained constant. Similar changes occurred in other groups during the study, resulting in a linear increase in HbA1c levels with increasing BMI [12].
Proper nutrition is an integral component in the treatment of diabetes, but despite this, there are many differences in the conception of the proper nutrition plan for people with diabetes.

Therefore, there is a need to provide nutritional recommendations based on principles that have already been proven in practice and supported by scientific evidence. Of course, all recommendations for proper nutrition must be applied, considering individual circumstances, cultural and ethnic differences, and the basic involvement of people with diabetes in the decision-making process when choosing a nutritional plan [8]. 69% of the diabetics who were included in this study declared that they eat 3-4 times a day. It is a completely wrong concept. Diabetics should follow the rule of 3 main meals and 2 snacks. Snacks are very important meals that contribute to maintaining blood sugar levels [9]. The results of a scientific study suggest that in patients with type 2 diabetes, the levels of HbA1c and glucose after 120 min. of the OGTT (oral glucose tolerance test) decreased with 6 vs. 3 meals ($p < 0.001$ vs. $p = 0.02$, respectively). Also, subjects' subjective hunger and desire to eat were reduced with 6 versus 3 meals per day [10].

It is encouraging that 72% of diabetics included in this study reported not consuming sweetened soft drinks (carbonated and non-carbonated). ADA recommendations for people with or at risk of diabetes are to avoid sugar-sweetened beverages (soft drinks, fruit drinks, energy and vitamin drinks that contain sucrose, high fructose corn syrup, and/or fruit juice concentrates) to reduce the risk of worsening the glycemic profile and prevent weight gain [13].

Worryingly, 69% of the respondents who were included in this study declared that they consume foods with a high glycemic index such as: white bread and pastries, cornflakes, snacks, white rice, pasta, potatoes, sugar, biscuits, cakes, chocolate, etc. GI (glycemic index) is a measure of how the body reacts to foods containing carbohydrates. To determine the GI, all foods are compared to a reference food, usually glucose, and tested in equivalent carbohydrate amounts. Glucose has a GI value of 100. Foods with a high GI cause a rapid rise in blood glucose levels and have a GI value above 70 [14]. In one scientific study that followed 3,800,618 subjects, 15,027 cases of type 2 diabetes were documented. In pooled multivariable analyses, those in the highest quintile of energy-adjusted GI had a 33% greater risk of developing type 2 diabetes than those in the lowest quintile. In conclusion, this study states that high GI food intake is associated with an increased risk of type 2 diabetes [15].

Diabetes and cardiovascular health are closely related and interact in many ways. In people who already have diabetes, it is especially important to introduce some form of physical activity, because it will help in using and "wasting" the excess sugar circulating in the blood. Namely, elevated sugar levels can damage blood vessels and thus worsen cardiovascular health. Regular movement also affects the level of insulin, its efficiency, and concentration in the blood. By reducing insulin resistance (increasing sensitivity), body weight regulation is improved, thus maintaining and improving cardiovascular health [16]. The fact that 78% of the subjects suffering from diabetes and who were included in this study declared that they practice light physical activity for 30 minutes a day such as: walking, jogging, cycling, etc. is encouraging.

6. Conclusion

According to the International Diabetes Federation, the prevalence of diabetes has increased from 30 million to 230 million in the last 20 years, and in 2025, the number is expected to increase to 350 million people, and more in developed countries. Such epidemic proportions are due to an increase in the percentage of adults and the population with increased body weight, as well as the absence of physical activity. Diabetes increases the risk of cardiovascular diseases, including mortality. Every year, 6 million new people get diabetes, and 3 million die, i.e. every 10 seconds someone dies from diabetes, so diabetes is the 4th leading cause of death in the world. Also, 5-10% of the national budget of the countries goes to the treatment of diabetes and its complications. Therefore, it is better to give more means for the prevention of diabetes [17]. From everything previously stated, one general conclusion can be stated that a

healthy and balanced diet and physical activity are key to leveling the glycemia in diabetics, as well as to the prevention of the complications caused by diabetes.

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