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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Assessment of cardiovascular risk factors in persons with impaired glucose tolerance

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SUMMARY

Introduction/Objective The aim of the study was to determine the profile of cardiovascular risk factors in patients with impaired glucose tolerance (IGT) in comparison to patients with impaired fasting glucose (IFG).

Methods The study consisted of 222 adult participants with established fasting blood glucose values within the 5.6–6.9 mmol/L range. IGT was defined as blood glucose of 7.8–11.1 mmol/L in the second hour after the administration of 75 g during oral glucose tolerance test. IFG is the metabolic state between normal and impaired glucose tolerance, where fasting glucose levels are 5.6–6.9 mmol/L, and normal oral glucose tolerance test values. IGT was confirmed in 142 of these individuals (107 females and 35 males; aged 54 ± 13 years). The remaining 80 participants (56 females and 24 males, p = 0.329; aged 53 ± 13 years, p = 0.76) were considered the IFG group. The following parameters were analyzed in both groups: body mass index, waist circumference, blood pressure, fasting glucose, fasting insulin levels, HOMA-IR (homeostasis model assessment – insulin resistance), C-reactive protein, fibrinogen concentrations and lipid profile.

Results Participants in the IGT group were more obese than those in the IFG group (body mass index 30.8 ± 5.5 kg/m^2 *vs.* 26.7 ± 3.8 kg/m^2, p < 0.001), and with greater waist circumference (111 ± 12 cm *vs.* 101 ± 6 cm; p < 0.001). Glucose levels (6.02 ± 0.75 mmol/L *vs.* 5.80 ± 0.62 mmol/L; p < 0.001), and blood insulin levels (21.61 ± 3.46 *vs.* 6.00 ± 2.8 mIU/L; p < 0.001), as well as HOMA-IR (5.78 ± 2.68 mIU/L *vs.* 1.54 ± 1.46 mIU/L; p < 0.001) were also higher in the IGT group. Median levels of HbA1c in IGT subjects were higher compared with those in the IFG group, but the difference was not statistically significant (6.21 ± 0.75% *vs.* 5.92 ± 0.43%; p = 0.105). Median hs-CRP levels in the IGT subjects (6.7 ± 4.88 mg/L) were higher than in the IFG subjects (5.83 ± 6.47 mg/L), but without statistical significance (p = 0.76).

Conclusion Our study indicates the presence of a large number of cardiovascular risk factors in both groups. Still, obesity, hyperinsulinemia, hypercholesterolemia, hypertriglyceridemia, higher diastolic blood pressure, as well as sedentary lifestyle, were statistically significantly more prevalent in patients with IGT.

Keywords: impaired glucose tolerance; impaired fasting glucose; cardiovascular risk factors; diabetes mellitus

INTRODUCTION

Prediabetes is defined as a condition in which blood glucose levels are higher than normal but lower than the established thresholds for diagnosing diabetes [1]. Prediabetes includes impaired glucose tolerance (IGT), impaired fasting glucose (IFG), or glycated hemoglobin levels (HbA1c) in the range of 5.7–6.4% [1, 2]. Patients with isolated IFG can be distinguished from those with isolated IGT by their fasting and two-hour postload glucose values, as well as the shape of their glucose concentration curves obtained during the oral glucose tolerance test (OGTT). By definition, IGT is a condition in which blood glucose reaches levels of 7.8–11.1 mmol/L in the second hour after the administration of 75 g of glucose during the OGTT, with the basal fasting glucose levels < 7 mmol/L. IFG, on the other hand, is defined as an intermediate metabolic state between normal and impaired glucose tolerance, where fasting glucose levels are 5.6–6.9 mmol/L with normal levels of glucose during two hours in OGTT [1, 2, 3].

Prediabetes has started to receive considerable attention recently because individuals with impaired glucose regulation have been shown to be four to six times more likely to develop diabetes than those with normal glucose regulation [4].

Previous studies have shown that IGT when accompanied by other risk factors, such as age, sex, smoking, hypertension, obesity, and dyslipidemia, increases the risk of developing a cardiovascular disease (CVD) [5, 6]. While both IFG and IGT involve insulin resistance, these conditions are distinguished by the site of insulin resistance [5]. High hepatic insulin resistance is a typical finding in patients with IFG, with almost normal values in skeletal muscle. In patients with IGT, the main site of insulin resistance is muscle, with only small changes in liver insulin sensitivity [5]. IGT can easily progress to overt diabetes, whereby macrovascular changes are more pronounced. Thus, there is a

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relevant correlation with the metabolic syndrome (MetS) and, consequently, a higher risk of developing CVD [6].

As individuals with IGT have slightly elevated blood glucose levels, which is a relatively weak risk factor for developing CVD, it is highly likely that other cardiovascular factors are also responsible for increased incidence of macrovascular diseases among individuals with IGT [7, 8, 9].

The aim of the present study was to determine which cardiovascular risk factors, other than elevated blood glucose levels, are present in individuals with IGT in comparison to patients with IFG.

METHODS

This prospective study was conducted with the approval from the Ethics Committee of the Faculty of Medicine, University of Priština, located in Kosovska Mitrovica. Written informed consent was obtained from all subjects involved in the study. The research was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects (WMA Declaration of Helsinki, 2013) [10].

Study participants

This prospective study included participants that were screened in the period from March 2016 to January 2017 at the Department of Endocrinology of the Clinical Hospital Centre in Priština – Gračanica. Criteria for the inclusion into the study were established fasting glucose values in the range of 5.6–6.9 mmol/L based on two measurements and the OGTT findings. The exclusion criteria were as follows: age < 40 years, overt diabetes, and history or presence of clinically significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, neurological, or infectious disorders capable of altering glucose metabolism. The study sample consisted of 222 patients, 142 (107 females and 35 males, mean age 54 ± 13 years) classified to the IGT group, as they met the aforementioned criteria suggested by the American Diabetes Association in 2016 [1]. The remaining 80 subjects (56 females and 24 males, mean age 53 ± 13 years) were classified to the IFG group, as they had isolated IFG and normal OGTT. Medical histories, family histories of CVD, diabetes and obesity, reports on smoking status, and information about current diseases were obtained from all the subjects. Alcohol intake was assessed using the CAGE questionnaire [11]. Physical activity was measured based on the World Health Organization recommendations for healthy adults, and physically inactive participants (exercise < 300 minutes per week) were considered sedentary [12].

Anthropometric, clinical, and biochemical measurements

Nutritional status was determined based on the body mass index (BMI) [13]. The specific distribution of adipose tissue, or the size of abdominal fat pad, was estimated by waist circumference, while the size of abdominal fat depots was determined in relation to the reference values provided by the World Health Organization [14]. Blood pressure was measured using the Riva-Rocci sphygmomanometer. Hypertension was diagnosed if systolic and diastolic blood pressure was ≥ 140/90 mmHg [15]. MetS was diagnosed according to the American Heart Association, National Heart, Lung and Blood Institute – modified Adult Treatment Panel III (ATP III) – criteria [16]. MetS was defined as the presence of at least three of the following conditions: abdominal obesity presented as large waist circumference (men: ≥ 102 cm; women: ≥ 88 cm), elevated triglyceride levels (≥ 1.7 mmol/L), low HDL cholesterol levels (men: < 1.0 mmol/L; women: < 1.2 mmol/L), hypertension (≥ 130/85 mmHg or use of anti-hypertensive medication) or elevated fasting blood glucose level (≥ 5.6 mmol/L or use of glucose-lowering drugs).

All the subjects were on normal diet prior to the biochemical assessments. On the day of testing, venous blood was collected after overnight fasting and was stored in vials with or without anticoagulant. Thereafter, a standardized OGTT was performed in all the subjects following the intake of 75 g of anhydrous glucose. Biochemical measurements, including concentrations of serum glucose, total cholesterol (TC), LDL-cholesterol (LDL), HDL-cholesterol (HDL), and triglycerides (TG), were performed by Olympus AU400 Chemistry Analyzer (Olympus, Tokyo, Japan) using commercial test reagent kits, according to the manufacturer's recommendations [15, 16]. The quality of glycemic control was assessed in terms of HbA1c levels, determined from anticoagulated blood samples by turbidimetric inhibition immunoassay method [17]. Fasting plasma insulin levels were measured by a radioimmunoassay, with a sensitivity of 2 mIU/L (normal range: 0.5–25 mIU/L) [18]. The insulin resistance index (homeostasis model assessment-insulin resistance – HOMA-IR) was calculated using the HOMA model: (fasting insulin × fasting glucose)/22.5 [19]. High sensitivity C-reactive protein (hs-CRP) was measured by a high-sensitivity immunoturbidimetry method (latex) on a Hitachi 902 analyzer (Hitachi, Ltd., Tokyo, Japan) using Roche diagnostic reagents (normal range: 0–5 mg/L). The fibrinogen was measured by the turbidimetric method (normal range: 2–4 g/L). The latest recommendations were adopted as target values [20].

Statistical analysis

The obtained data were analyzed using SPSS Statistics, Version 19.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as prevalence, in percentages, while continuous variables were expressed as mean values and standard deviations (SD) with a confidence interval (95% CI). To analyze the differences between the groups, the χ^2 test or Fisher's exact test was adopted for testing the probability of the null hypothesis (when some of the expected frequencies were lower than five), while conducting the Student's t-test for the independent samples. Pearson correlation coefficient was used to investigate the association between the variables. The level of statistical significance was set at $p < 0.05$.

RESULTS

The study sample included 222 patients, 142 (107 females and 35 males) of whom fulfilled the criteria for IGT diagnosis. The average age of the subjects assigned to the IGT group was 54 ± 13 years. The remaining 80 subjects (56 females and 24 males; mean age 53 ± 13 years, p = 0.76) were assigned to the IFG group, as the OGTT test indicated the isolated IFG diagnosis. Basic demographic, anthropometric and clinical data pertaining to these subjects are shown in Table 1.

The age, sex distribution, fasting blood glucose, HbA1c concentration, and systolic blood pressure levels of the two groups were not statistically significantly different. In addition, no statistically significant differences in the hs-CRP levels and plasma fibrinogen were noted between the individuals with IGT and those diagnosed with IFG. However, the BMI, waist circumference, serum TC, LDL, TG, fasting insulin levels, HOMA-IR, and diastolic blood pressure were significantly higher, whereas HDL cholesterol concentration was significantly lower in the IGT group compared to the IFG group (Table 1). Also, there were more obese subjects (BMI ≥ 30 kg/m^2) in the IGT group than in the group with IFG, and the difference was statistically significant (Table 2).

In addition, we have found that central obesity, hyperinsulinemia, hypercholesterolemia, hypertriglyceridemia, higher diastolic blood pressure, as well as sedentary lifestyle, were statistical significantly more prevalent in patients with IGT, and report family history of type 2 diabetes mellitus (T2DM) (Table 3).

The correlation analysis showed a statistically significant positive correlation between BMI, as well as waist circumference, and the current plasma insulin concentration, while the ratio between these nutritional status values and the current blood glucose levels was not statistically significant (Table 4).

Table 1. Anthropometric, clinical, and laboratory data of studied participants; data are presented either as frequencies (n) or arithmetic mean ± SD; differences between the groups were tested by Student's t-test.

Parameters	IGT group (n = 142)	IFG group (n = 80)	p-value
Male/ Female (n)	35/107	24/56	0.329
Age (years)	54 ± 13	53 ± 13	0.7591
BMI (kg/m^2)	30.8 ± 5.5	26.7 ± 3.8	< 0.001
Waist circumference (cm) Men Women	 111 ± 12 97.6 ± 21.7	 101 ± 6 86 ± 11.3	 0.007 0.019
Total cholesterol (mmol/L)	6.34 ± 0.93	4.52 ± 1.21	< 0.001
HDL-cholesterol (mmol/L)	1.31 ± 0.28	1.42 ± 0.17	0.032
LDL-cholesterol (mmol/L)	4.3 ± 0.92	2.85 ± 1.08	< 0.001
Triglycerides (mmol/L)	2.12 ± 1.25	1.25 ± 0.63	< 0.001
Fasting blood glucose (mmol/L)	6.02 ± 1.26	5.8 ± 0.62	0.852
HbA1c (%)	6.21 ± 0.75	5.92 ± 0.43	0.105
Fasting blood insulin (mIU/L)	21.61 ± 3,46	6 ± 2.8	< 0.001
HOMA-IR	5.78 ± 2.68	1.54 ± 1.46	0.001
Blood pressure (mmHg) Systolic Diastolic hs-CRP (mg/L) Fibrinogen (g/L)	 134.7 ± 17.6 89.7 ± 10 6.7 ± 4.88 3.67 ± 4.88	 129.8 ± 14.4 82.9 ± 9 5.83 ± 6.47 3.36 ± 0.95	 0.159 < 0.001 0.760 0.900

BMI – body mass index; HOMA-IR – homeostasis model assessment insulin resistance; HbA1c – glycated hemoglobin A1c; hs-CRP – high-sensitivity C-reactive protein; IGT – impaired glucose tolerance; IFG – impaired glucose fasting

Table 2. Distribution of anthropometric nutrition measures in studied groups; the differences between the groups in anthropometric measures, body mass index (BMI), and waist circumference, were tested by the χ^2 test

Parameters	IGT group (n = 142)	IFG group (n = 80)	p-value
BMI (kg/m^2)			
18.5–24.9 (%)	4.22	30	< 0.001
25–29.9 (%)	57.75	60	0.835
≥ 30 (%)	38.03	10	< 0.001
Waist circumference – women			
≤ 80 cm (%)	18.69	42.85	0.002
80.1–87.9 cm (%)	39.25	30.36	0.286
≥ 88 cm (%)	42.06	26.79	0.065
Waist circumference – men			
≤ 94 cm (%)	2.86	4.17	0.62
94.1–101.9 cm (%)	57.14	58.33	0.912
≥ 102 cm (%)	40	37.5	0.775

DISCUSSION

The results obtained in the present study have shown a higher incidence of obesity, insulin resistance, dyslipidemias, lower physical activity, positive history of smoking, and positive family history of obesity and T2DM among the subjects with IGT compared with the IFG group. These results confirm the existence of added risk factors for the development of micro- and macrovascular complications in individuals with IGT. In a Danish population-based study of patients with IGT or IFG, the results of fasting laboratory measures and OGTT showed that hypertension, higher BMI, serum TG, and plasma glucose levels predicted the development of T2DM during the 3.5-year follow-up period [21].

Most of the risk factors that were more common in the IGT group are considered modifiable, since they largely depend on the subject's lifestyle and habits. However, several risk factors cannot be modified, especially aging, which is an inevitable biological process associated with overexpression of some and under-expression of other genes. These changes lead to an unstable metabolic control and increased sensitivity to the effects of external factors, such as, for example, poor nutrition and other lifestyle habits [22, 23]. Consistent with previous studies, a strong association of cardiometabolic risk with increasing age in the IGT group was observed in our study. Our subjects were older than 50 years, which, according to some authors, significantly increases the likelihood of developing IGT and CVD risk [21, 22]. The mean age of our subjects with IGT was 53 ± 13.32 years, which is consistent with the findings of other authors [21], while the participants in the Garcia-Alcala's study were somewhat younger [24]. Our results suggest a slightly higher incidence of IGT in

Table 3. Distribution of cardiovascular risk factors in the studied groups; the presence of metabolic syndrome, alcohol intake, physical activity, smoking status, and family history of diabetes were assessed as described in the Methods section; the differences between the groups were tested by the χ^2 test

Risk factors	IGT group (n = 142)	IFG group (n = 80)	p-value
Metabolic syndrome (%)	39.1	11	0.001
Alcohol intake (%)	12.8	13	0.964
Low physical activity (%)	45.3	51.2	0.001
Current smoker (%)	23.1	15	0.001
Family history of diabetes (%)	22.7	15.1	0.001
Hypertension (%)	23.1	20	0.63
LDL cholesterol > 3 mmol/L (%)	32.1	15	0.01
Triglycerides > 1.7 mmol/L (%) hs-CRP 5 mg/L (%) Fibrinogen > 4.0 g/L (%)	31 16 12	12 15 10	0.001 0.85 0.66

LDL – low density cholesterol, hs-CRP – high sensitivity C-reactive protein; IGT – impaired glucose tolerance; IFG – impaired glucose fasting

Table 4. Correlations between body mass index (BMI), waist circumference, and concentrations of glucose, insulin in the group with IGT

	Fasting blood insulin (mIU/L)		Fasting plasma glucose (mmol/L)	
	Pearson's r	p-value	Pearson's r	p-value
BMI (kg/m^2)	0.365	0.010	-0.059	0.102
Waist circumference (cm)	0.402	0.005	-0.260	0.072

women, which is consistent with the data reported by other authors, who also found that its incidence continues to increase with age [5, 6].

Prediabetes carries some predictive power for macrovascular disease, but most of this association appears to be mediated through the MetS [9]. Elevated glucose levels are one component of the current consensus definition of the MetS [16]. IGT and HbA1c appear to correlate more with the CVD risk than the IFG diagnosis [6, 25]. In the present study, patients with IGT (mean glucose 6.02 mmol/L and the HbA1c of 6.2%) had higher glucose levels than the IFG group did (mean glucose 5.8 mmol/L, HbA1c 5.9%), but the difference was not statistically significant.

Our findings further demonstrated that insulin resistance was significantly present in the IGT group, while it was absent in the group with IFG. The patients with IGT had significantly higher levels of fasting insulin, as well as the HOMA index of insulin resistance. An interesting post mortem analysis conducted by Butler et al. [26] revealed that individuals with IGT have 50% fewer β-cells, indicating that there is a significant loss of β-cell mass in individuals with IGT, which occurs long before the onset of T2DM. Accordingly, for the first time, the latest AACE recommendations put emphasis on obesity, stressing that reduction of body weight, not hyperglycemia, should be the primary objective of prediabetes prevention and treatment [27]. In fact, individuals with IGT, in addition to changing their lifestyles, have other options to achieve weight loss including drug therapy and surgical procedures, and consequently reduce insulin resistance and hyperglycemia, as well as successfully prevent progression to T2DM, while improving lipid status and blood pressure levels [28].

Our results not only revealed a high incidence of obesity in the IGT group, but also demonstrated that 38.03% of the subjects had a BMI ≥ 30 kg/m^2, which was statistically significant in comparison to patients with IFG. Obesity plays an important part in the pathogenesis of insulin resistance, which is commonly seen in IGT patients [5]. In addition, our results show that people with IGT tend to exhibit central obesity, which is associated with higher insulin resistance. The risk for prediabetes increases with increasing BMI levels and is particularly significant in individuals with BMI values above 30 kg/m^2 [5, 28]. Importantly, a higher BMI level at baseline, but not BMI change, is associated with IFG/IGT to T2DM transition, as confirmed by the present study [28].

In addition, abdominal obesity is a clinical sign of excessive accumulation of visceral fat and is usually associated with a cluster of cardiovascular risk factors defined by the National Cholesterol Education Program IV Adult Treatment Panel III as the MetS [16]. We noted in the IGT group a significant presence of a cluster of cardiovascular risk factors similar to those associated with the MetS.

Insulin resistance and visceral obesity are associated with high blood pressure. Both cause an increase in blood pressure by activating the sympathetic nervous system and the renin-angiotensin system, with the consequent retention of sodium and water, volume overload, endothelial dysfunction and impaired renal function [29]. Other than an increase in the number of individuals with IGT, the population-based, cross-sectional study of the prevalence of prediabetes in England that was conducted from 2003 to 2011 also revealed an upward trend in the blood pressure in this population [30].

Regarding serum lipid abnormalities in patients with IGT, in most extant studies, statistically significantly increased levels of TC, LDH, and/or TG, and a decrease in HDL were found compared to the group with IFG [31,32]. These findings further confirm atherogenic potential in our patients with IGT.

Some authors have reported that increased levels inflammatory cytokines, such as high-sensitivity C-reactive protein and tumor necrosis factor-alpha, are associated with an increased risk of progression from normoglycemia to prediabetes [33]. In obese individuals, an increase in adipose tissue and abnormal protein with hormone characteristics is common, causing infection of the systemic inflammation type and affecting the metabolic pathway in several processes, resulting in dysglycemia, IFG or IGT, and abnormal blood pressure [34]. The median levels of hs-CRP were increased in both groups, but there was no statistically significant difference between them (p = 0.76). Also, we did not find statistically significant difference in increased CRP prevalence between the groups.

Finally, the impact of smoking and exposure to tobacco smoke on the development of prediabetes must be highlighted, even though it remains insufficiently explored. In fact, one of the few studies that have addressed the influence of smoking on the development of T2DM is the Multi-Ethnic Study of Atherosclerosis (MESA) [35].

This study has certain limitations, one of which is a relatively small sample size. In addition, no control group was

included in the analyses, and the conclusions pertaining to the CV risks are largely based on extant empirical evidence rather than solely on the study results. Moreover, no information was available on whether the patients have taken some measures to prevent CV risk factors. Patients with IGT have a significantly higher number of risk factors for the development of CVD. Their association increases this risk.

CONCLUSION

Our results have shown that, beyond impaired glucose metabolism, individuals with IGT also exhibited obesity, lipoprotein imbalance, hyperinsulinemia, and higher diastolic blood pressure, as well as reported sedentary lifestyle, cigarette smoking, and family history of diabetes, more frequently than patients with IFG, which may be implicated in the development of a cardiovascular disease. Thus, there is an evident need for thorough and systematic application of all preventive measures, including lifestyle changes in the first place, followed by drugs and other treatment modalities, in reducing the risk for the development of type 2 diabetes mellitus and cardiovascular diseases.

Conflict of interest: None declared.

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Процена кардиоваскуларних фактора ризика код особа са смањеном толеранцијом на глукозу

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САЖЕТАК

Увод/Циљ Циљ студије је био да се утврди који су кардиоваскуларни фактори ризика присутни код особа са смањеном толеранцијом на глукозу (СТГ) у поређењу са особама са повишеном гликемијом наште (ПГН).

Методе У студију је било укључено укупно 222 одрасла испитаника са константним налазом концентрације глукозе у распону 5,6–6,9 *mmol/L*. СТГ је стање у којем глукоза у крви достиже ниво 7,8–11,1 *mmol/L* у другом сату после примене 75 *g* у оралном тесту толеранције на глукозу. ПГН је метаболичко стање између нормалне и оштећене толеранције на глукозу, при чему нивои глукозе наште износе 5,6–6,9 *mmol/L*, и са нормалним вредностима оралног теста толеранције на глукозу. Групу са СТГ су чинила 142 испитаника (107 жена и 35 мушкараца; просечне старости 54 ± 13 година) код којих је оралним тестом толеранције на глукозу утврђена СТГ. Осталих 80 испитаника (56 жена и 24 мушкарца, $p = 0,329$; просечне старости 53 ± 13 година, $p = 0,76$) чинило је групу са ПГН. Код свих испитаника анализирани су следећи параметри: индекс телесне масе (ИТМ), обим струка, вредности крвног притиска, гликемије наште, базална инсулинемија, *HOMA-IR* (хомеостазни модел процене инсулинске резистенције), Ц-реактивни протеин (ЦРП), фибриноген и липидни статус.

Резултати Испитаници у групи са СТГ били су гојазнији него они у групи са ПГН (ИТМ: 30,8 ± 5,5 kg/m^2 према 26,72 ± 3,83 kg/m^2; $p < 0,001$), са већим обимом струка (111 ± 12 *cm* према 101 ± 6 *cm*; $p < 0,001$). Концентрације глукозе (6,02 ± 0,75 *mmol/L* према 5,80 ± 0,62 *mmol/L*; $p < 0,001$) и инсулина у крви (21,61 ± 3,46 према 6,00 ± 2,80 *mIU/L*; $p < 0,001$), као и вредности *HOMA-IR* (5,78 ± 2,68 према 1,54 ± 1,46; $p < 0,001$), такође су биле више у групи са СТГ. Средње вредности *HbA1c* код испитаника са СТГ биле су веће у поређењу са особама са ПГН, али није било статистички значајне разлике (6,21 ± 0,75 према 5,92 ± 0,43%, $p = 0,105$). Средњи нивои високо осетљивог ЦРП у групи са СТГ били су већи у поређењу са групом са ПГН (6,70 ± 4,88 *mg/L* према 5,83 ± 6,47 *mg/L*), али без статистички значајне разлике ($p = 0,76$).

Закључак Наша студија указује на присуство великог броја кардиоваскуларних фактора ризика у обе групе. Додатно, потврђено је да су гојазност, хиперинсулинемија, хиперхолестеролемија, хипертриглицеридемија, виши дијастолни крвни притисак, као и седентарни начин живота, статистички значајно чешће заступљени код болесника са СТГ.

Кључне речи: смањена толеранција на глукозу; повишена глукоза наште; кардиоваскуларни фактори ризика; дијабетес мелитус