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Cardiovascular risk factors in relatives of type 2 diabetics with normal glucose tolerance test and elevated one-hour plasma glucose

Czynniki ryzyka chorób sercowo-naczyniowych u krewnych osób chorujących na cukrzycę typu 2 z prawidłowym testem tolerancji glukozy i zwiększonym stężeniem glukozy w pierwszej godzinie po obciążeniu

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Abstract

Introduction: To investigate the effect of elevated one hour post-load plasma glucose on cardiovascular risk factors, in normal glucose tolerance (NGT) people, who are first degree relatives of type 2 diabetics.

Material and methods: A cross-sectional study on 1475 NGT subjects (Arian ethnicity), who had one hour post-load plasma glucose was carried out. We compared the mean of age, sex, body mass index, waist circumference, blood pressure, lipid profile, and area under the curve of glucose (AUC-G) of 1190 out of 1475 NGT subjects with one hour plasma glucose (1hpG) ≥ 155 mg/dL, and 285 NGT subjects with 1hpG < 155 mg/dL.

Results: The mean age, body mass index, waist circumference, blood pressure, lipid profile (but not low HDL-cholesterol), and area under the curve of glucose (AUC-G) was significantly higher in NGT subjects with 1hpG ≥ 155 mg/dL ($P < 0.05$). Normal glucose tolerance people (first degree relatives of type 2 diabetic patients) with 1hpG ≥ 155 mg/dL were older and heavier than those with 1hpG < 155 mg/dL. Cardiovascular risk factors (but not low HDL and hypertension) were more prevalent in those with elevated one hour post-load group ($P < 0.05$).

Conclusions: NGT subjects with elevated one hour post-load plasma glucose (1hpG ≥ 155 mg/dL) had higher prevalence of most cardiovascular risk factors in comparison with those with 1hpG < 155 mg/dL. **(Pol J Endocrinol 2010; 61 (4): 359–363)**

Key words: *type 2 diabetes mellitus, glucose tolerance test, risk factors*

Streszczenie

Wstęp: Celem badania była ocena wpływu podwyższonej glikemii w pierwszej godzinie po obciążeniu glukozą na czynniki ryzyka sercowo-naczyniowego u osób z prawidłową tolerancją glukozy (NGT, *normal glucose tolerance*) będących krewnymi pierwszego stopnia chorych na cukrzycę typu 2.

Materiał i metody: Badanie wieloośrodkowe objęło 1475 osób z prawidłową tolerancją glikemii (etniczni Arianie), u których oznaczono stężenie glukozy w osoczu w godzinę po doustnym obciążeniu glukozą. Wszystkich chorych podzielono na dwie grupy w zależności od wartości glikemii: 1190, u których glikemia 1 godzinę po obciążeniu glukozą wynosiła ≥ 155 mg/dl i 285 osób < 155 mg/dl. W obu grupach porównano średnie wartości następujących parametrów: wieku, płci, wskaźnika masy ciała, obwodu talii, ciśnienia tętniczego, profilu lipidowego i pola pod krzywą stężenia glukozy.

Wyniki: U osób z prawidłową tolerancją glikemii (będących krewnymi pierwszego stopnia chorych na cukrzycę typu 2), u których glikemia na czczo w godzinę po doustnym obciążeniu glukozą wynosiła ≥ 155 mg/dl ($p < 0,05$) stwierdzono istotnie wyższe wartości następujących parametrów: średni wiek, wskaźnik masy ciała, obwód talii, ciśnienie tętnicze, stężenia lipidów (z wyjątkiem cholesterolu frakcji HDL) i pola pod krzywą stężenia glukozy. Osoby, u których glikemia w godzinę po obciążeniu glukozą wynosiła ≥ 155 mg/dl były starsze i cięższe niż osoby z niższym poposiłkowym stężeniem glukozy (< 155 mg/dl). Czynniki ryzyka sercowo-naczyniowego (z wyjątkiem niskiego stężenia cholesterolu frakcji HDL i nadciśnienia tętniczego) występowały częściej u osób z wyższymi wartościami glikemii w godzinę po obciążeniu glukozą ($p < 0,05$).

Wnioski: U osób z prawidłową tolerancją glukozy i wyższymi wartościami glikemii w godzinę po obciążeniu glukozą (≥ 155 mg/dl) stwierdzono częstsze występowanie czynników ryzyka chorób sercowo-naczyniowego niż u osób, u których glikemia w godzinę po obciążeniu glukozą wynosiła < 155 mg/dl. **(Endokrynol Pol 2010; 61 (4): 359–363)**

Słowa kluczowe: *cukrzyca typu 2, test tolerancji glukozy, czynniki ryzyka*

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Introduction

The number of type 2 diabetic patients is expected to increase to ~300 million by the year 2025, in comparison with 150 million diabetics in the year 2000 [1].

Type 2 diabetes mellitus (T2DM), as a chronic disease, not only causes serious morbidity and mortality due to vascular complications but also imposes a heavy economic burden on countries [2].

Changes in lifestyle and drug therapy decrease the incidence of T2DM in high-risk subjects. Therefore, it is essential to identify the high-risk people to establish a successful primary prevention program for T2DM [3–5].

Among the high-risk subjects for T2DM and related cardiovascular complications are people with impaired glucose tolerance (IGT) test [6]. However, some longitudinal epidemiological surveys show that ~40% of subjects with T2DM have normal glucose tolerance (NGT) test at baseline [7]. Therefore, it is necessary to investigate which category of normal glucose tolerance people is at high risk of developing T2DM [6].

Recently, some studies have demonstrated that elevated one-hour plasma glucose levels (1hPG) during oral glucose tolerance test (OGTT) are a suitable predictor for the development of type 2 diabetes in future [2, 8], and NGT subjects with 1hPG at or above 155 mg/dl are at high-risk of T2DM development [8–10].

Also, one study has demonstrated that NGT subjects with elevated 1hPG develop early atherosclerosis in the carotid artery as a sign of cardiovascular atherosclerosis [6].

Meanwhile, another study has shown that in NGT subjects with 1hPG ≥ 155 mg/dL, cardiovascular risk factors are more prevalent in comparison with 1hPG < 155 mg/dL NGT subjects [11].

Based on these results, the aim of our study was to compare the demographic characteristics and cardiovascular risk factors in NGT subjects with 1hPG ≥ 155 mg/dL and those with 1hPG < 155 mg/dL who are first degree relatives of T2DM patients.

Material and methods

From 2005 to 2008, of 2952 people (Arian ethnicity) who were first degree relatives of type 2 diabetics, 1526 individuals (1140 females, 386 males) had normal glucose tolerance test based on two-hour plasma glucose less than 140 mg/dL and fasting plasma glucose less than 100 mg/dL [12]. Of these 1526 NGT participants, one-hour plasma glucose concentration was measured in 1475 people. Participants were 30–55 years old and were first degree relatives of T2DM patients who had already been registered at the Isfahan Endocrine and Metabolism Research Centre (IEMRC). After 10 hours of overnight fasting, oral glucose tolerance test (OGTT) with 75 g glucose was performed. Plasma glucose was measured at 0, 30, 60, and 120 minutes. Then, according to American Diabetes Association (ADA) criteria [12], the subjects were divided into prediabetics (n = 1140), normal glucose tolerant (NGT) (n = 1526), and diabetics (n = 284). Prediabetics and diabetic patients were excluded from the study. People with normal glucose tolerance test were divided into two groups, one with 1hPG ≥ 155 mg/dL (n = 1190) and the other with 1hPG BS < 155 mg/dL (n = 285).

Plasma glucose was measured with GOD-PAP method (by BT 3000 PLUS autoanalyzer, Italy).

All participants signed a written consent form to enrol in the study. The study was designed according to the Ethics Regulations of the Helsinki Declaration, and its protocol was approved by the IEMRC Medical Ethics Committee.

Total cholesterol, HDL-cholesterol, and triglyceride were measured at fasting state by GHOD-PAP and GPO-PAP methods, respectively (by BT3000 autoanalyzer, Italy). LDL-cholesterol was calculated based on the Friedewald formula. In our study, we defined metabolic syndrome according to ATP ^{222} criteria [13].

Demographic and anthropometric characteristics (age, sex, weight, height, waist circumference) and blood pressure were measured for all participants. Body mass index (BMI) was calculated by body weight (kg)/height (m^2). Blood pressure was measured after 15 minutes of rest in a seated position with a standard mercury sphygmomanometer (ALPK2, Japan) and recorded in mmHg.

Statistical analysis

Data are shown as mean (SD). Student's t -test was used to compare quantitative variables (cholesterol, triglyceride, HDL-c, LDL-c, blood pressure, waist, BMI, age, area under the curve of mean plasma glucose (AUC-G) during OGTT, and Chi square test was used to compare the qualitative variable (sex) between two groups (NGT subjects, with 1hPG ≥ 155 mg/dL and 1hPG < 155 mg/dL). To know the effect of one hour plasma glucose level on the coronary heart disease risk factors (BMI ≥ 25 kg/m^2, cholesterol ≥ 200 mg/dL, HDL ≤ 40 mg/dl in men or HDL ≤ 50 mg/dL in women, LDL ≥ 130 mg/dL, triglycerides ≥ 150 mg/dL, blood pressure ≥ 140/90 mm Hg, and waist ≥ 102 cm in man or ≥ 88 cm in women), age, sex, and BMI were adjusted by multiple logistic regression. The area under the curve of mean plasma glucose during OGTT was calculated by the trapezoid rule. P values less than 0.05 were considered statistically significant.

Table I. *The means of demographic and laboratory data in first degree relatives of type 2 diabetics with normal glucose tolerance, based on one-hour post-load plasma glucose levels*

Tabela I. *Dane demograficzne i laboratoryjne osób z prawidłową tolerancją glikemii w zależności od poziomu glikemii w godzinę po obciążeniu glukozą będących krewnymi chorych na cukrzycę typu 2*

Data	1hpG < 155 mg/dL		1hpG ≥ 155 mg/dL		P value
	Number 1190	Mean (SD)	Number 285	Mean (SD)	
Age	1177	41.9 (6.54)	282	43.5 (6.75)	0.001
Sex					
Man	289	24.3%	89	31.2%	0.017
Woman	899	75.7%	196	68.8%	
BMI [kg/m^2]	1175	28.3 (4.28)	280	29.4 (4.52)	0.001
SBP [mm Hg]	1139	112 (15.4)	278	116 (18.0)	0.001
DBP [mm Hg]	1139	72 (11.9)	278	75 (12.8)	0.001
Triglyceride [mg/dL]	1154	156.4 (97.57)	282	174 (84.2)	0.001
Cholesterol [mg/dL]	1159	191.0 (37.98)	281	204 (39.0)	0.001
HDL-cholesterol [mg/dL]	1130	45.7 (11.91)	273	45.0 (11.5)	0.38
LDL-cholesterol [mg/dL]	1089	115.1 (33.56)	269	124 (35.6)	0.001
Waist [cm]	1157	87.1 (9.56)	280	90.6 (9.9)	0.001
AUC-G [mg/h/dL]	1142	731 (99.68)	268	954 (78.29)	0.001

1hpG — one-hour post-load plasma glucose; SD — standard deviation; SBP — Systolic Blood Pressure; DBP — Diastolic Blood Pressure; AUC-G — Area under the curve of glucose

Results

From 1526 participants who were first degree relatives of T2DM, with normal glucose tolerance test , 1190 and 285 subjects, had one hour plasma glucose level (1hPG) less than 155 mg/dL and equal or more than 155 mg/dL, respectively.

Table I illustrates the demographic and laboratory characteristics of normal glucose tolerance test (NGT) individuals, with one hour plasma glucose (1hPG) < 155 mg/dL and those with 1hPG ≥ 155 mg/dL. The mean age, BMI, blood pressure, triglyceride, cholesterol, LDL-cholesterol, waist, AUC-G, and HDL-cholesterol were significantly higher in NGT subjects with 1hPG ≥ 155 mg/dL.

Table II shows that the mean plasma glucose in 0, 30, 60, and 120 minutes, during OGTT, in the 1hpG ≥ 155 mg/dL NGT group is significantly higher than in the 1hpG < 155 mg/dL NGT group.

Table II also shows that the mean plasma glucose during OGTT in NGT subjects with 1hPG ≥ 155 mg/dL is significantly higher.

AUC-G is significantly higher in the 1hPG ≥ 155 group (Table I).

Table III illustrates the prevalence and odds ratio (OR) of the cardiovascular risk factors by glucose category, after adjusting for age, sex, and BMI. The prevalence of most ischaemic heart disease risk factors (but low HDL and hypertension) is increased in the 1hpG ≥ 155 mg/dL group.

Discussion

This study investigates the association of one-hour post-load plasma glucose level with cardiovascular risk factors in first degree relatives of type 2 diabetics with normal glucose tolerance test. Normal glucose tolerance subjects with 1hPG ≥ 155 mg/dL have higher blood pressure and more abdominal and generalized obesity. The blood pressure difference between two groups is not remarkable clinically; however, it is statistically significant, probably due to the large sample size (Table I).

They were older than those with 1hPG < 155 mg/dL. Males have a higher prevalence of 1hPG ≥ 155 mg/dL (Table I).

In 1hPG ≥ 155 mg/dL NGT subjects, most of the cardiovascular risk factors were significantly, more prevalent than those with 1hPG < 155 mg/dL (Table II).

In concordance with our study, in the GENFIEV study [11] the prevalence of most of the cardiovascular risk factors (but not low HDL-c) in NGT subjects with 1hpG ≥ 155 mg/dL was higher in comparison with 1hpG < 155 mg/dL. In another study [16], 1hPG ≥ 155 mg/dL NGT subjects had higher BMI and lipid ratio (triglyceride/HDL and total cholesterol/HDL) and were older, in comparison to NGT subjects with 1hPG < 155 mg/dL. However, in one study in Japan [14], there were no significant differences in triglyceride, total cholesterol, and HDL-cholesterol levels between two NGT groups (with or without elevated 1hpG levels).

Table II. *The means of plasma glucose at 0, 30, 60, and 120 minutes (during OGTT) based on one-hour post-load plasma glucose group in first degree relatives of type 2 diabetics with normal glucose tolerance*

Tabela II. *Średnie stężenie glukozy w osoczu 0, 30, 60 i 120 minut (podczas doustnego testu obciążenia glukozą) u krewnych pierwszego stopnia osób chorych na cukrzycę typu 2 w zależności od glikemii 1 godzinę po obciążeniu glukozą*

Time (min)	1hpG < 155 mg/dL		1hpG ≥ 155 mg/dL		P value
	Number 1190	Mean (SD)	Number 285	Mean (SD)	
0	1190	87 (7.57)	285	90 (6.86)	0.001
30	1143	124 (23.09)	270	154 (25.43)	0.001
60	1190	115 (23.39)	285	175 (17.94)	0.001
120	1189	97 (21.23)	283	110 (21.31)	0.001

1hPG — one-hour plasma glucose

Table III. *Prevalence of coronary heart disease risk factors in first degree relatives of type 2 diabetics with normal glucose tolerance according to one-hour post-load plasma glucose*

Tabela III. *Występowanie czynników ryzyka choroby wieńcowej u krewnych pierwszego stopnia osób chorych na cukrzycę typu 2 w zależności od glikemii 1 godzinę po obciążeniu glukozą*

Cardiovascular risk factors	Number	Prevalence (%)	OR (CI 95%)
BMI ≥ 25 kg/m²	1172		
1hpG < 155 mg/dL	933	79	1
1hpG ≥ 155 mg/dL	239	85	1.5 (1.0–2.1)
Hypertension*	209		
1hpG < 155 mg/dL	156	13	1
1hpG ≥ 155 mg/dL	53	19	1.1 (0.7–1.6)
Triglycerides ≥ 150 mg/dL	612		
1hpG < 155 mg/dL	460	39	1
1hpG ≥ 155 mg/dL	152	53	1. 4 (1.0-1.8)
Cholesterol ≥ 200 mg/dL	591		
1hpG < 155 mg/dL	439	37	1
1hpG ≥ 155 mg/dL	152	54	1.7 (1.3–2.2)
LDL-c ≥ 130 mg/dl	446		
1hpG < 155 mg/dL	333	30	1
1hpG ≥ 155 mg/dL	113	42	1.4 (1.1–1.9)
HDL-c ≤ 40 mg/dl (male)	190		
1hpG < 155 mg/dL	148	53	1
1hpG ≥ 155 mg/dL	42	51	0.97 (0.7–1.3)
HDL-c ≤ 50 mg/dl (female)	691		
1hpG < 155 mg/dL	564	66.2	1
1hpG ≥ 155 mg/dL	127	66.5	0.97 (0.7–1.3)
Waist > 102 cm (male)	49		
1hpG < 155 mg/dL	34	12	1
1hpG ≥ 155 mg/dL	15	17	1.6 (1.2–2.1)
Waist > 88 cm (female)	383		
1hpG < 155 mg/dL	292	33	1
1hpG ≥ 155 mg/dL	91	46	1.6 (1.2–2.1)
Metabolic syndrome	281		
1hpG < 155 mg/dL	203	17.1	1
1hpG ≥ 155 mg/dL	78	27.4	1.8 (1.3–2.4)

*Blood pressure ≥ 140/90 mm Hg; OR — odds ratio; CI — confidence interval

Our cross-sectional study cannot explain why cardiovascular risk factors are more prevalent in NGT subjects with elevated 1hPG.

However, to the best of our knowledge, based on some studies, elevated one-hour plasma glucose level during OGTT, similar to some other cardiovascular risk factors, not only increases the risk of future T2DM [8–10] but also increases cardiovascular mortality and morbidity [6, 15, 16] and all cause mortality in the general population [15, 16].

Therefore, it is suggested that a cohort study be designed to investigate the causal relationship between elevated 1hPG and cardiovascular risk factors. Our study is among the few studies which concentrate on the 1hPG in NGT people. However, none of them have been carried out on first degree relatives of T2DM.

AUC-G and the mean plasma glucose at 0, 30, 60, and 120 minutes were significantly higher in the 1hPG ≥ 155 mg/dL NGT group. We can explain these results, based on the greater prevalence of metabolic syndrome and decreased early-phase insulin secretion in 1hPG ≥ 155 mg/dL NGT subjects.

In another study, the same results demonstrate defective β-cell function and insulin resistance in 1hPG ≥ 155 mg/dL NGT subjects[17].

Conclusions

The prevalence of most cardiovascular risk factors (but not low HDL and hypertension) was higher in NGT subjects with 1hpG ≥ 155 mg/dL. It is recommended that a cohort study be designed to investigate the causal relationship between cardiovascular risk factors and increased related mortality in NGT subjects of first degree relatives of T2DM with elevated 1hpG.

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