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Oral Glucose Tolerance Test 90-Min Values in Prediabetes Detection: Using of Multiple Regression Analyses for Diagnostic Criteria Determination

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ABSTRACT

Purpose: The aim of this study was to determine the possibility of PG90 using as an indicator of PD and reveal the optimal cut-off point for separation of normal glucose metabolism (NGM) and impaired (PD+DM) glucose metabolism (IGM) by PG90 level.

Methods: 134 persons (32 men and 102 women) aged 20-79 years were examined. Glycemic levels after 30, 60, 90,120 minutes after 75 g glucose loading was performed. The HbA1C examined by the SDA1c Care (SD biosensor, Korea). Fasting and post load venous plasma glucose was determined by Precision PCx Medi Sense (Abbot, USA). Equations obtained Bby linear and multiple regression method; by applying these equations 90 minutes glycemic level post-load 75 g glucose was calculated. Qualitative characteristics of the diagnostic test were used for the evaluation of cut-off point for 90 minutes glycemic level post-load 75 g glucose.

Results: The relationship between PG90 and HbA1C, PG90 and FG, PG90 and PG120 was studied by using correlation analyses. The relationship between PG90 and HbA1C (r=+0.71 [95%CI +0.615, +0.785]), PG90 and FG (r=+0.53 [95%CI +0.397, +0.641]) was as well as between PG90 and PG120 (r=+0.85 [95%CI +0.796, +0.891]). All three correlation coefficients were statistically significant, p<0.001.
The equation for PG90 cut-off point was calculated by applying multiple regression analyses.
It was obtained the quality characteristics of received cut-off point by equation.
Maximal Index Youden had FG cut-off point ">109 mg/dl" (67.9%). Index Youden for PG90 cut-off point ">168 mg/dl" was higher than 50.0 %.

Conclusion: The cut-off point PG90 may be used for NGM and PD differentiation.

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Abbreviations
AAEDTE - Azerbaijan Association of Endocrinology, Diabetology and Therapeutic Education
BMI - Body Mass Index
CI - confidence interval
DBP - diastolic blood pressure
DM - diabetes mellitus
FG - fasting glucose
HbA1C - glycated hemoglobin
IGM - impaired glucose metabolism
IGT - impaired glucose tolerance
NGM - normal glucose metabolism
OGTT - oral glucose tolerance test
PD - prediabetes
PG30 - plasma glucose level after 30 min.
PG60 - plasma glucose level after 60 min.
PG90 - plasma glucose level after 90 min.
PG120 - plasma glucose level after 120 min.
SBP - systolic blood pressure
WC - waist circumference
WHO - World Health Organization

Introduction

Prediabetes is a serious health condition where blood sugar levels are higher than normal, but not enough yet to be diagnosed as type 2 diabetes. It is considered to be an at risk state, with high chances of developing diabetes [1]. The International Diabetes Federation (IDF) estimates that, worldwide, 541 million individuals aged 20–79 years have impaired glucose tolerance (IGT) and 319 million have impaired fasting glucose. These numbers are projected to increase to 730 million and 440 million by 2045 [2]. Prediabetes not only is associated with high risk of progression to type 2 diabetes; it also confers an increased risk for cardiovascular morbidity and mortality [3]. Prediabetes occurs in individuals

as IGT, impaired fasting glucose (IFG), and high-risk glycated hemoglobin (HbA1c). HbA1c, FG, and 2-h plasma glucose value during 75-g oral glucose tolerance test (OGTT) are used for DM diagnostics. The same tests applied also for PD detection are used [3]. The OGTT, which is used to diagnose DM, takes longer than the others. OGTT has evolved over the past decades glucose load varied 50, 75, and 100 g; glucose measurement times also varied after 30 (PG30), 60 (PG60), 90 (PG90) and 120 (PG120) minutes [4]. In 1985 two points were determined during the test: FG and PG120 [5, 6]. The significance of post-loading glucose is emphasized by the fact of the relationship between PG120 values (≥11.1mmol/l) and cardiovascular mortality, shown in DECODE and HOORN studies. At the same time, there was no such relationship between FG (≥7.0mmol/l) and cardiovascular mortality [7, 8]. There have not been extensive studies of PG90 compared to other points. The 2016 study showed that glycemic levels at 60 and 90 minutes were more important for detecting DM [9]. in 2020 a study conducted by Turkish scientists showed that plasma glucose levels at 90 minutes had better correlation with HbA1c than plasma glucose levels at other time points. It is also noted that as a result of the study PG90 would be beneficial to investigate whether plasma glucose at 90 minutes is a more important parameter in predicting diabetes [10].

The aim of this study was to find out the capability of PG90 using as an indicator of PD and determine the optimal cut-off point for separation of normal glucose metabolism (NGM) and impaired (PD+DM) glucose metabolism (IGM) by PG90 level.

Materials and Methods

Subjects and clinical examination

To carry out this research we used a data from database of Azerbaijan Association of Endocrinology, Diabetology and Therapeutic Education (AAEDTE). The study was conducted on 134 cases (32 men and 102 women).

Inclusion criteria:

- Age from 20 to 79 years;
- Availability of registered anthropometric data: height (cm), weight (кg), waist circumference (cm);
- Office blood pressure measurement: systolic blood pressure (SBP), diastolic blood pressure (DBP) in mmHg;
- Laboratory examination: HbA1c, FG, and PG30, PG60, PG90, PG120;

Exclusion criteria:

- Pregnancy and lactation;
- The presence of severe comorbid diseases affected the glucose metabolism state;
- Availability of previously known DM or PD;
- Absence of any inclusion criteria.

Body Mass Index (BMI) was figured dividing the weight (kg) by the height in meters squared (m2) and classified by the criteria of WHO [11].

OGTT was performed by using of 75 g glucose. Samples of FG, PG30, PG60, PG90, PG120 after glucose loading where measured in venous plasma by Precision PCx Medi Sense (Abbot, USA) and presented in mg/dl.Glycohemoglobin (HbA1c) was studied by the SDA1c Care (SD biosensor, Korea) and measured in mmol/mol.

We used the average values ± Standard Deviation in this study. The statistical significance of the differences between the average values was determined by the Student's T-test. Chi-square tests were applied to compare categorical variables [12]. A correlation analysis of the relationship between PG90 and HbA1C, FG, PG120 was performed [13]. Confidence interval (CI) 95% was determined for correlation coefficient [14].

PG90 cut-off point was calculated by using of the multiple linear regression method [15].

The following indicators were used for determinate the qualitative characteristics of the diagnostic tests: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Overall Diagnostic Accuracy and Youden Index [16, 17].

Diagnosis of PD and DM was carried out in accordance with the proposed for discussion AAEDTE Standards [18], presented in Table 1.

Table 1: Diagnostic criteria for NGM, DM and PD according to AAEDTE [18].

Parameters	Units	NGM	PD	DM
HbA1c	%	≤ 5,6	5,7-6,4	≥ 6,5
	mmol/mol	≤38	39-47	≥48
FG	mg/dl	<110	110 – 125	≥126
	mmol/l	<6,1	6,1-6,9	≥7,0
OGTT 2-hour glucose	mg/dl	≤ 139	140 – 199	≥ 200
	mmol/l	≤ 7,7	7,8 – 11,0	≥11,1

According to these standards, DM was detected in 6 persons, PD - in 41 cases (n of IGM=6+41=47) and NGM – in 87 persons.

The gender characteristics of NGM and IGM (PD+DM) groups are shown in Fig. 1.

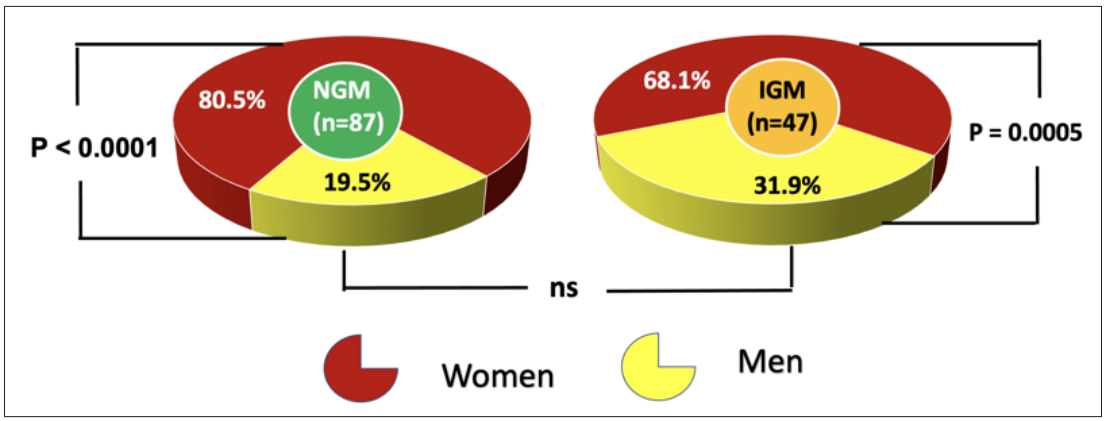

Figure 1: Gender characteristics of NGM and IGM (PD+DM) groups

As it is seen from Fig.1 in all three groups prevalence of female was higher than prevalence of male: 80.5%/19.5% in NGM group, 68.1%/31.9% in IGM (PD+DM) group. At the same time, there were no statistically significant gender differences between the analyzed groups.

The main characteristics of three groups are presented in Table 2.

Table 2: The main characteristics of NGM, PD and DM groups

Parameters	Research groups		p
	NGM (n=87)	IGM(PD+DM) (n=47)	
Age in years (M ± SD)	43.5±13.1	54.4±13.3	<0.001
Height in cm (M ± SD)	163.3±8.5	163.5±9.5	ns
Weight in kg (M ± SD)	76.6±18.7	83.9±17.8	<0.05
WC in cm (M ± SD)	91.6±14.7	100.7±12.2	<0.001
BMI in kg/m^2 (M ± SD)	28.8±6.8	31.6±6.8	<0.05
SBP in mmHg (M ± SD)	121.6±16.3	134.4±16.7	<0.001
DBP in mmHg (M ± SD)	78.9±9.6	85.3±9.9	<0.001
HbA1c (mmol/mol)	33.0±2.8	39.5±6.0	<0.001
FG (mg/dl)	92.8±10.2	113.6±10.7	<0.001
PG30 (mg/dl)	184.7±20.3	202.6±21.3	<0.001
PG60 (mg/dl)	172.1±21.0	199.9±22.0	<0.001
PG90 (mg/dl)	139.1±13.9	170.1±27.4	<0.001
PG120 (mg/dl)	107.9±14.3	137.8±25.6	<0.001

As it is seen from Table 2 NGM group was younger, thinner and had lower blood pressure and glucose metabolism indicators than IGM group.

Results

The relationship between PG90 and FG, PG90 and PG120, PG90 and HbA1c was studied by using correlation analyses. Data on the correlation between them are shown at Fig. 2.

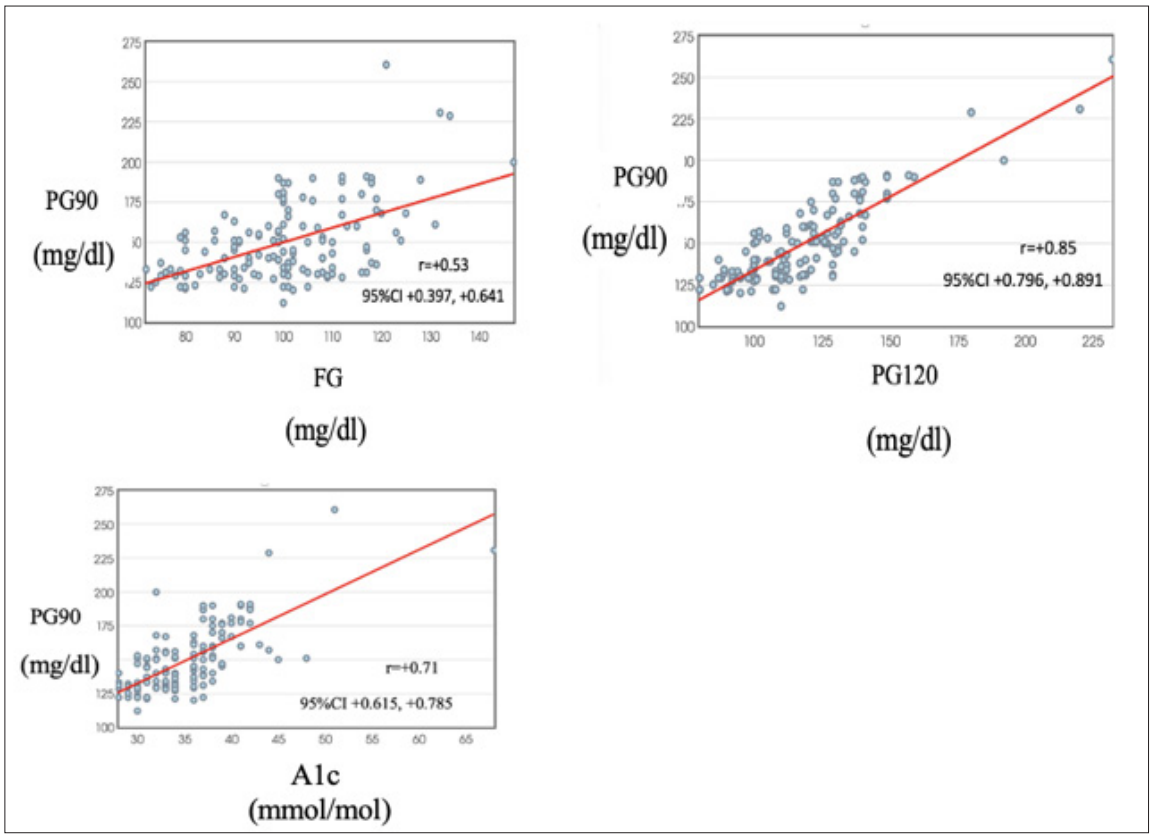

Figure 2: Correlation and confidence interval between PG90 and FG, PG90 and PG120, PG90 and HbA1c

As it is seen from Fig. 2, the relationship between PG90 and HbA1C (r=+0.71 [95%CI +0.615, +0.785]), PG90 and FG (r=+0.53 [95%CI +0.397, +0.641]) was as well as between PG90 and PG120 (r=+0.85 [95%CI +0.796, +0.891]). All of three correlation coefficients were statistically significant, p<0.001 for each of them. Differences between correlation coefficients were non statistical (p >0.05 in all cases).

The equation for PG90 cut-off point was calculated by applying multiple regression analyses.
PG90= 34.3115+ 0.8913*HbA1c - 0.064*FG + 0.7651*PG120

The upper limits of the norm for HbA1c (38mmol/mol), FG (109mg/dl), PG120 (139mg/dl) were used.
The received answer was 168 mg/dl/. Thus, all of points PG90 above 168 mg/dl must be consider appropriate for IGM (PD+DM).

Table 3 shows the comparative qualitative characteristics of the PG90, PG60, PG120, FG and HbA1C.

Table 3: Comparative qualitative characteristics of the PG90, PG60, PG120, FG and HbA1C.

Indicator	Cut-off point*	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Overall Diagnostic Accuracy (%)	Overall Diagnostic Accuracy (%)
PG90	168 (mg/dl)	55.3	97.7	92.9	80.2	82.8	53.0
PG60	197 (mg/dl)	68.1	82.8	68.1	82.8	77.6	50.8
PG120	139 (mg/dl)	44.7	100	100	77.0	80.6	44.7
FG	109 (mg/dl)	70.2	97.7	94.3	85.9	88.1	67.9
HbA1C	38 (mmol/mol)	66.0	100	100	84.5	88.1	66.0

*the upper limit for NGM

Table 3. Comparative qualitative characteristics of the PG90, PG60, PG120, FG and HbA1C.

As it is seen from Table 3 the maximal Youden Index had FG cut-off point “>109 mg/dl” (67.9 %). The Youden Index for HbA1C cut-off point “>38 mmol/mol” was 66.0%. The Youden Index for PG90 “>168 mg/dl” was higher than 50.0 %.

Discussion

Previously, we used multiple regression equations for clarify of FG and HbA1C PD cut-off points [19, 20].At the present study this technique was used to determine the PG90 cut-off point for PD and ">168 mg/dl" result was obtained.

So, the highest normal value for PG90 was 168 mg/dl and had Sensitivity (55.3%), Specificity (97.7%), Positive Predictive Value (92.9%), Negative Predictive Value (80.2%) and Overall Diagnostic Accuracy (82.8%), Youden Index (53.0%).

As it is seen from Table 3 the Youden Index was maximal for FG ">109 mg/dl" (67.9%), below for HbA1C ">38 mmol/mol" (66.0%) and minimal for PG120 ">139 mg/dl" (44.7%). It is necessary to note that Youden Index below 50.0% shows not so good quality of using cut-off point [21]. It is very interesting that "PG120 >139mg/dl" cut-off point is only generally accepted indicator for PD diagnostics [4, 22-24]. Low quality characteristics of this indicator were noticed by DECODE and HOORN studies [7, 8].

Until today only two research studies were conducted for the study of PG90 for IGM identification [9, 10]. In our study we used multiple regression analyses for determination the lowest border of PD. Principally, it is possible to use for this purpose the other statistical methods, such as study of Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Overall Diagnostic Accuracy, Youden Index, which can be the matter for future research studies.

There was disparity in number of females and males, which would limit the result of our study, if the aim of research was to assess the frequency of occurrence of prediabetes in males and females. As our aim was to study diagnostic criteria of prediabetes diabetes gender differences are irrelevant.

Conclusion

The cut-off point PG90 may be used for NGM and PD differentiation.

Acknowledgements

There is no any financial interest and conflict of interest to declare.

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