Clinical and Laboratory Features of Patients with Impaired Glucose Tolerance (IGT) in Adults of District 13 of Eastern Tehran

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Patients with IGT have increased risk of developing DM type II and non-communicable diseases in the future. The aim of this study was to determine the features of patients with IGT in Tehran and the correlation of IGT with other variables and risk factors of non communicable diseases.

<u>Materials and Methods</u>: This study was a descriptive analytical and cross–sectional one, in which 960 of 9204 persons, participants of the first phase of Tehran Lipid and Glucose Study (TLGS) were found to have IGT in the initial assessment; eight weeks later, a second OGTT was done, and 331 had IGT. DM and IGT diagnosis were based on WHO criteria; in this group, anthropometric indices, BP, serum glucose, and lipid level were assessed after 12 hours of fasting. Obesity was defined as BMI≥30 kg/m² and over weight as BMI between 25 and 29.9 kg/m². WHR over 0.8 in females and 0.95 in males were defined as truncal obesity. Hypertension was defined as SBP≥140 or DBP≥90 mmHg or taking anti hypertensive drugs. Statistical analyses were performed using independent T-test, and ANOVA.

<u>Results</u>: Totally 331 patients with IGT were studied, of whom 232 (70%) were female and 99 (30%) were male. In 43% of cases, BMI was ≥30. WHR was abnormal in 83.7%; total cholesterol level in 32% was ≥240 mg/dL, LDL in 28.1% was ≥130 mg/dL and ≥ 160 g/dL in 24.8%; HDL in 32.9% of cases was <35 mg/dL. In 43.2% of cases, TG was ≥200 mg/dL. Assessment of parameters according to BMI showed that mean cholesterol and triglyceride levels in obese patients were higher than the rest (p<0.05, p<0.001) and mean HDL cholesterol in obese patients was lower (p<0.014). Exercise tolerance test (ETT) was performed in 199 patients, and was positive in 14%.

<u>Conclusion</u>: According to the results of this study, patients with IGT have a high risk of cardiovascular events because of multiple risk factors such as obesity, hypertension, smoking, and hyper lipidemia.

Introduction

Impaired glucose tolerance (IGT) is a dysglycemic condition between normal and diabetic states.[1] The prevalence of IGT according to age, sex, socioeconomic status varies from between 3 and 10% in the European community to between 11 and 20% in North America.[2] It has been reported that its prevalence in Nigeria[3] is 2.2% and in Japenese Americans is 32%.[4] In other studies the prevalence of IGT was borderline.[5,6,7,8,10,11,12,13]

Recently it has been reported that the prevalence of IGT is high among American children and adolescents. In studies from Iran, the prevalence of IGT among persons above 30 years, was 8.2-14.9% in urban and 3.4% in rural areas.[15-16]

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Patients with IGT have a 20 times higher risk of developing diabetes in the future, than do other individuals; 20-50% of individuals with IGT will develop diabetes within 10 years. The risk of developing diabetes following IGT varies from 1.5 to 7% in a year.

In one meta-analysis investigating the data of 6 prospective studies in terms of IGT developing to diabetes, the incidence rate of DM was reported 5.7% in one year.[17] In another study from Taiwan 8.8% of patients with IGT developed DM in one year.[18]

On the other hand, IGT is known as a risk factor for cardiovascular disease, the risk factors for such patients being equal to or exceeding that of diabetics, whereas the evidence of cardiovascular events is between normal tolerance and diabetes.[11]

IGT increases the risk factors of cardiovascular events, independent of common cardiovascular risk factors and patients with IGT have a 40% increased risk of mortality due to cardiovascular diseases.[12] A 12-year follow up of males who participated in the Malmo study (Sweden) showed that IGT increased mortality rates in persons with cardiovascular disease.[20]

One meta-analysis of 20 studies conducted on patients followed for 12.4 years, confirmed that persons with 2 hour plasma glucose of over 140 mg/dL had ircreased risk of cardiovascular events.[21] In the Islamshar study, 22.4% of patients with IGT had positive exercise tests.[22]

The aim of this study was to determine the clinical and laboratory features of patients with IGT and to evaluate the cardiovascular risk factors among this high-risk group of district 13 of eastern Tehran.

Materials and Methods

This was a descriptive, analytic and cross sectional study, the data for which were collected using observation, interviews and questionaires to obtain information on diet and physical activities.

The population consisted of 20-70 year old residents of eastern Tehran who participated in the Tehran Lipid and Glucose Study (TLGS). In our study the patients with IGT were selected as follows; 9204 individuals aged 20-70 yrs underwent oral glucose tolerance test (OGTT) with 75g oral glucose dissolved in 250 ml water. If 2 hour-plasma glucose was 140-199 mg/dL, it was considered as IGT (according to WHO criteria), provided the fasting plasma glucose was under 126 mg/dL; at this stage, 960 persons had IGT; 8 weeks later, a second OGTT was done (among persons with no exclusion criteria) and if they showed IGT in the second OGTT, they were enrolled in the study; 331 persons were found to have IGT. For this group, anthropometric measurements, BP, demographic information and life style were recorded using standard questionnaires. Anthropometric indices including height and weight were obtained; height was measured without shoes using a meter and weight with digital scale with minimum clothing. Waist was measured at the umbilicus, and hip at the area with largest diameter.

BMI was calculated as $\frac{weight(kg)}{height(m^2)}$

The criteria for overweight were: Low weight; BMI < 18.5 kg/m^2, normal weight; BMI $\geq$ 18.5–24.9 kg/m^2, overweight; BMI 24.9-29.9 kg/m^2 and obese BMI $\geq$ 30 kg/m^2.

The distribution of body fat was assessed using waist to hip ratio (WHR); WHR over than 0.8 in females and 0.95 in males were defined as truncal obesity. Blood pressure was measured after the person had rested at least for 15 minutes using a standard sphymomanometer. BP was measured at two 30-minute intervals and the mean was used as the patient's blood pressure.

To determine hypertension and its staging the JNC-VI criteria was used. Criteria of hypertension according to JNC-VJ were: systolic blood pressure <140 mmHg and diastolic $\geq$ 90 mmHg and taking antihypertensive drugs was defined as hypertension.

Smoking is one of the main contributing factors in cardiovascular diseases; for determining different categories of cigarette

smoking, WHO criteria were used. Physical and clinical examinations were done by a trained general physician and ECG was done for all subjects.

Measurement of plasma-glucose was carried out in the Tehran Glucose and Lipid central laboratory on the same day of sampling by an auto analyzer using glucose kits (pars azemoon). Determination of glucose was done using Enzymatic colorimetric glucose oxidase. All measurments were done when the quality control of the system was acceptable. The concentration of total cholesterol, trigyceride was measured using enzymatic colorometric cholesterol esterase, cholesterol oxidase and glycerol phosphate oxidase. After determination of total cholesterol levels, HDL cholesterol were measured using the Friedwald formula. This formula was not used when the triglyceride level was above 400 mg/dL. The staging of lipid and lipoprotein level in adults was done according to the Educational National Cholesterol program (ENCP).

Total cholesterol levels less than 200mg/dL were defined as desirable, between 200-239 mg/dL as borderline and cholesterol >240 mg/dL as high. HDL cholesterol >35 mg/dL was defined as desirable, and less than that as low. LDL cholesterol less 130 mg/dL was desirable, 130-159 mg/dL borderline and >160 mg/dL was high. Triglyceride <200 mg/dL was defined as normal, 200-400 mg/dL borderline, 400-1000 mg/dL high and over 1000 mg/dL as very high.

Measurement of plasma insulin level was done using special kits (DRG company America) using the Elisa Assay.

All the patients underwent exercise tolerance tests (ETT) after assessment of ECG and physical examinations by a cardiologist. Ergospiromety for evaluating the VO_2 max was done in the Masih-Daneshvary research center, Tehran. Data were presented as mean and SD. Independent t-test was used for evaluating and comparing continuous parameters in male and female groups. Anova test was used for assessment of continuous parameters according to BMI levels.

Results

Overall 331 patients, 232 (70%) female and 99 (30%) male, with IGT were studied. The mean age of males was 52.1±20.4 and that of females was 50.4±10.2 years, not statistically significant; 30.2% of the patients were in the 50-59 year age group. Family history of DM was positive in 35% and gestational DM was reported only in one case (table 1).

Table 1. Baseline characteristics of 331 patients with IGT

Variable	
Male	99(30%)
Female	232(70%)
Positive family history of DM	35%
GDM	1
Age (years)	50.9±10.3
Smoker	8%
Weight (Kg)	15.25±12.8
Body mass index (BMI) kg/m^2	29.7±4.83
Waist (Cm)	96.98±10.3
Waist to hip ratio (WHR)	0.92±0.2
Systolic blood pressure (mmHg)	128±20
Diastolic blood pressure (mmHg)	84±11
Fasting plasma glucose (mg/dL)	98.9±11.5
2 hour plasma glucose (mg/dL)	165±16.8
Total cholesterol (mg/dL)	237±50.2
HDL cholesterol (mg/dL)	38.9±9.5
LDL cholesterol (mg/dL)	139.8±36.4
Triglyceride (mg/dL)	220.9±116
Positive Exercise tolerance test (ETT)	14%
Plasma insulin (mu/mL)	10.8±5.6
Vo$_2$ max (mL/kg/minute)	21.27±7.46

Twenty-eight (8%) patients were smokers; 81.4% of the patients with IGT were overweight or obese. WHR was abnormal in 83.7% (Table 2). Exercise test was positive in 14% of the patients with IGT, 65.5% had hypertension, most of whom had stage I. Mean systolic blood pressure was 128±20 and diastolic 84±11 mmHg (Table 1).

Table 2. Some parameters of patients with IGT

Parameters	n	%
Smoker	28	8
Positive family history of DM	115	35
Adequate physical activity	27	12
Body mass index (kg/m^2)		
Lean	1	0.3
Normal	44	13.3
Overweight	141	43.6
Obese	145	43.8
Waist to hip ratio		
Normal	54	16.3
Abnormal	277	83.7
Hypertension		
Normal	148	44.5
High normal	54	16.5
Stage 1	86	26
Stage 2	86	26
Stage 3	13	3.5

Table 3. Laboratory parameters in patients with IGT

Parameters	n	%
Total cholesterol (mg/dL)		
desirable	101	30.3
borderline	124	37.6
high	106	32.1
HDL cholesterol (mg/dL)		
desirable	222	67
low	109	33
LDL cholesterol (mg/dL)		
desirable	115	39.6
borderline	93	32.1
high	82	28.3
Triglycerides (mg/dL)		
desirable	163	49.6
borderline	143	43.3
high	25	1.6
Vo$_2$ max (mL/kg/minute)		
normal	110	60
abnormal	75	40
Exercise tolerance test		
negative	165	83
borderline	6	3
positive	14	28

Mean total cholesterol level was 237±50.2 mg/dL; of patients, 28.3% had high LDL cholesterol levels while 33% had low HDL cholesterol levels. Of the patients 32.1% had high total cholesterol levels (Table 3); 7.6% had high triglyceride levels and mean triglyceride level was 220.9±116 mg/dL.

Vo$_2$ max was abnormal in 40% (Table 4). Mean Vo$_2$ max was 21.3±7.5 mL/kg/minute. Overall mean BMI, total cholesterol, diastolic BP, LDL, HDL, and triglyceride levels were higher in females compared to males, difference being statistically significant (Table 4). Parametric measurements according to BMI showed that mean cholesterol and triglycride levels in obese patients were higher ($p<0.05$, $p<0.001$) and mean HDL cholesterol levels in obese patients were lower ($p<0.05$) (Table 5).

Table 4. Mean and SD of some parameters according to sex, in patients with IGT

Variables	Female Mean ± SD	Male Mean ± SD	P value
Age (years)	50.4±10.2	52.1±10.4	NS
Body mass index (BMI) kg/m^2	30.4±5.1	28.3±3.7	P<0.001
Waist to hip ratio (WHR)	0.9±7.1	0.97±5.4	P<0.001
Systolic blood pressure (mmHg)	128. ±20.9	128.8±19.7	P<0.03
Diastolic blood pressure (mmHg)	82.2±11.8	84.8±11.5	P<0.03
Total cholesterol (mg/dL)	229.8±53.3	209.2±38.3	P<0.042
HDL cholesterol (mg/dL)	40.1±9.5	35.8±8.6	P<0.001
LDL cholesterol (mg/dL)	142.8±35.9	132.6±36.9	P<0.028
Triglyceride (mg/dL)	225±119.6	213.5±110.1	P<0.001
Fasting plasma glucose (mg/dL)	98.2±11.3	100.1±11.9	P<0.069
2- hour plasma glucose (mg/dL)	165.6±11.1	136.6±16.1	P<0.001
Plasma insulin mu/mL	11±5.7	10.2±5.2	P<0.001
Vo$_2$ max (mL /kg/minute)	18.2±6	29.3±4.3	P<0.001

Table 5. Mean and SD of parameters according to body mass index (BMI) in patients with IGT

Variable	BMI (kg/m2)			
	Normal 18.5-24.9	**Overweight 25-29.9**	**Obese >30**	**P value**
WHR (waist to hip ratio)	0.89±1.41 (43)	0.93±6.66 (141)	0.94±6.95 (142)	<0.001
Systolic blood pressure (mmHg)	124.1±23.24 (43)	129.31±18.86 (141)	128.8±20.57 (142)	NS
Diastolic blood pressure(mmHg)	11.65±12.02 (43)	83.22±12.22 (141)	84.61±10.76 (142)	0.003
Total cholesterol (mg/dL)	208.7±42.9 (44)	222.3±54.3 (140)	230±41.2 (145)	0.04
Triglycerides (mg/dL)	157.7±93.1 (44)	220.7±108.5 (140)	240±124.6 (145)	0.001
HDL cholesterol (mg/dL)	42.7±8.9 (44)	38.3±10 (140)	38.2±8.9 (145)	0.01
LDL cholesterl (mg/dL)	132.6±38.6 (40)	138.6±35.4 (124)	143.5±36.6 (125)	NS
Fasting plasma glucose (mg/dL)	97.2±12.1 (44)	97.7±10.6 (140)	100.5±13 (145)	NS
Plasma insulin (mu/mL)	7.1±3.2 (26)	10±5.5 (95)	12.5±5.5 (103)	001
2 hours plasma glucose (mg/dL)	163.9±145 (43)	163.2±17.4 (139)	168.1±16.5 (144)	0.01
Vo2 max (mL/kg/minute)	26.1±7 (23)	21.6±8.3 (76)	19.5±6 (85)	0.001

Discussion

This study, conducted on 331 adult patients with IGT showed that these patients, because of having multiple risk factors, are at higher risk of cardiovascular events. In our study, the proportion of females to males was 2:3, while in some previous studies, the two sexes were equal;[23, 24, 2] in others however, females outnumbered males.[25,13] This discrepancy may be related to the population, sampling methods or males avoiding referring to a physician. Mean age of the patients was 50±10 years, which is similar to some other studies,[2,26,24] in some studies the mean age of the participants was lower.[13,23,27] Family history of diabetes was positive in 34%; in some studies, this was lower[23,22] while in others it was higher.[2,26]

Smoking as a cardiovascular risk factor was positive in 8.5%. In two studies from Sweden[23] and Turkey,[13] the smoking rate was higher. One reason for low rate of cigarette smoking in this study is that most of our patients were female. Mean BMI in our study was 24±4 kg/m^2. In some studies, participants had lower BMI[13,23,21] while in one they had higher BMI.[1]

In assessing WHR and truncal obesity, the rate was similar to the US study.[1] In some studies the WHR was lower.[13] In our study, only 12% had adequate physical activity, while in the Swedish study 23% had adequate physical activity.[23] An assessment of hypertension, showed 26% were hypertensive, similar to findings of some studies;[1,13] In some studies, such as the international study, 43.8% were reported to have hypertension.[2] In assessing plasma lipids, 32% had high total cholesterol level. The mean of fasting plasma glucose in most of the studies was higher than the present study.[1,24] In the Swed-

ish[23] and Chinese studies[27] the participants had higher plasma insulin levels.

Mean Vo_2 max was 21 ± 7 mL/kg/minute in our study. In the Swedish study, the level of Vo_2 max was much higher, one reason being that most of the participants in this study were male. In our study, females had much lower Vo_2 max compared to males, demonstrating that more attention needs to be paid to encouraging physical activity in women.

Comparing risk factors among patients with normal weight, overweight and obese, we observed that systolic and diastolic blood pressure were higher in obese patients (Table 5). Mean total cholesterol, LDL cholesterol, triglyceride, fasting plasma glucose were

higher in obese patients, and HDL cholesterol and mean Vo_2 max was lowest.

It can be concluded that in obese patients with IGT, hypertension, total cholesterol, LDL cholesterol, triglyceride, 2 hour plasma glucose, and insulin levels were all higher compared to patients with normal weight or overweight, and HDL cholestrol level and Vo_2 max rate were lower. According to results of this study, patients with IGT have multiple risk factors such as obesity, hypertension, smoking, hyperlipidemia, which predispose them to cardiovascular events. Therefore in future studies, interventions must be designed to reduce cardiovascular risk ractors in this high risk group.

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