Original Article

The profile of hypertension and dyslipidemia in prediabetic subjects; results of the Isfahan Diabetes Prevention program: A large population-based study

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Abstract

Background: The present study was designed to evaluate hypertension and dyslipidemia in prediabetic subjects with a family history of type 2 diabetes (first-degree relatives), and they were compared with the normal glucose-tolerance subjects.

Materials and Methods: Three thousand and eighty-six (788 men and 2298 women) subjects were selected from a consecutive sample of patients with Impaired Glucose Tolerance (IGT), Impaired Fasting Glucose (IFG), and Combined (IFG and IGT), and their first-degree relatives formed the control group. Potential risk factors for diabetes including age, gender, body size, HbA1c, cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, blood pressure (BP), urine microalbumin, and family and personal medical history were assessed.

Results: The studied participants included 300 IGT patients (9.7%), 625 IFG patients (44.9%), 411 combined patients (13.3%), and 1750 (56.7%) normal subjects. Aging led to increase in hypertension. Increase in body mass index (BMI) led to an increase in the prevalence of hypertension significantly in all groups. The mean triglyceride in the normal group was different in comparison with that of the IGT ($P < 0.05$) and combined ($P < 0.001$) groups. Differences in total cholesterol were observed in the normal group when compared with the IGT ($P < 0.05$) and combined ($P < 0.001$) groups, and of the combined group in comparison with the IGT ($P < 0.05$) group. The difference in LDL level was related to the combined group in comparison with IGT, marginally ($P < 0.1$), and normal in comparison with the combined group ($P < 0.05$).

Conclusion: Prevalence of hypertension was not significantly different between the groups, however, in prediabetic patients it was higher than in the normal group, and prevalence of dyslipidemia in prediabetic subjects was significantly higher than in the normal group.

Key Words: Dyslipidemia, glucose tolerance, hypertension, prediabetic

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INTRODUCTION

Prevalence of diabetes, which is associated with increase in morbidity and mortality, is increasing and it is one of the major healthcare problems in the world.[1] According to the pathogenesis and natural history of diabetes, it has a prolonged prediabetic phase.[2] Studies have shown that heart disease and

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atherogenic progression in diabetic patients have presented in the prediabetic phase.[3] Prediabetes generally refers to an intermediate stage between the clinical entity of type 2 diabetes and normal glucose levels.[4,5]

Prediabetes increases the risk of developing diabetes. Prospective and observational studies showed that diabetes developed approximately in 25-40% of prediabetic patients after three to eight years.[6-8] Prediabetes is considered as a risk factor for cardiovascular disease and macrovascular disease development and is not only a significant risk factor for progression of type 2 diabetes. Evidence advocates that prediabetic patients have a significantly greater risk for cardiometabolic disease and death, when compared with normal subjects.[9-12]

Prediabetic individuals are more likely to be obese than others, and unrelated to their age or body mass index, are additionally expected to have multiple risk factors for cardiovascular disease (CVD), including dyslipidemia and hypertension.[3] The goal of blood pressure is the same in diabetes, as in prediabetic patients. It is noticeable that hypertension and dyslipidemia, as important risk factors of CVD, are common in prediabetic states and should be managed as aggressively.[13]

The exact relationship between prediabetes and CVD is still unclear and controversial. However, studies show the relationship between prediabetes and morbidity and mortality.[14-17]

Screening program, preventive strategy, and risk factor detection are important for prediabetic patients. Hypertension and dyslipidemia are well-recognized markers of cardiovascular risk. The present study is designed to evaluate hypertension and dyslipidemia in prediabetic subjects with a family history of type 2 diabetes (first-degree relative) and compare them with those of normal subjects.

MATERIALS AND METHODS

This case-control study was carried out on 3086 (788 men and 2298 women) patients, with first-degree relatives with diabetes, in an Outpatient Clinic in Isfahan Endocrinology and Metabolism Research Center (IEMRC), Iran. The Ethics Committee of Isfahan University of Medical Sciences had approved the study and an informed consent was obtained from each participant.

Patients with Impaired Fasting Glucose (IFG) or Impaired Glucose Tolerance (IGT) and patients with a combination of these disorders (IFG and IGT) were selected as the case groups and their first-degree relatives were chosen as the control group. The control group included siblings and children of patients with type 2 diabetes.

The participants completed the laboratory tests, including standard 75 g -two-hour oral glucose tolerance test (OGTT), HbA1c (measured with the help of a spectrophotometer), microalbuminuria, serum creatinine, triglycerides cholesterol, HDL (measured using standardized procedures), LDL (calculated by the Friedwald equation, provided the total triglyceride did not exceed 400 mg/dL),[14] and BP (systolic and diastolic), at registration. In addition, a questionnaire on health status and the various potential risk factors of diabetes was completed. This questionnaire included gender, age at diagnosis, age, educational level, duration of diabetes (time between diagnosis and baseline examination), BMI (weight/height^2 (kg/m^2)), and smoking status (never, current).

Patients with IGT, IFG, combined, and diabetes were identified from the baseline and follow-up OGTTs were performed according to American Diabetes Association criteria.[17] For the present study, the analyses were limited to the IGT, IFG, combined, and patients' first-degree relatives groups.

According to American Diabetes Association (ADA) criteria, the participants were divided into groups as follows: Normal glucose tolerance (NGT) was defined as fasting plasma glucose (FPG) of less than 100 mg/dL and two-hour post load glucose of <140 mg/dL.

The prediabetic state was defined as a state with an Impaired Fasting Glucose (IFG) (a fasting plasma glucose (FPG) of 100-125 mg/dL) and/or an impaired glucose tolerance (IGT) (two-hour post load glucose of 140-199 mg/dL).[17] All blood sampling procedures were performed in the Central Laboratory of the Isfahan Endocrine and Metabolism Research Center.

Height and weight were measured in light clothes and without shoes, using the standard apparatus. The weight was measured with a 0.1 kg accuracy on a calibrated beam scale. The height was measured with a 0.5 cm accuracy with a measuring tape. The height was measured only at the start of the study. The systolic and diastolic blood pressures were measured after 10 minutes of resting by using a calibrated mercury sphygmomanometer and standard techniques. All clinical measurements for patients and normal participants were made using the same standardized protocol.

Statistical analysis

The quantitative variables are represented as a mean (±SD or SE), while the qualitative variables as a number (percent). The Chi-square test or linear-by-linear Chi-square test as appropriate, were used for comparing the prevalence rates and the association between the qualitative variables, respectively. For age, sex, and body mass index (BMI), the Multivariate Analysis of Variance (MANOVA) stratified analysis was considered for comparing the quantitative dependent variables along with the Bonferroni post-hoc test. All statistical calculations were carried out with the SPSS for Windows (SPSS Inc., Chicago, IL, USA). The level of significance was considered to be less than 0.05.

RESULTS

According to the baseline characteristics of the 3086 participants, they included 300 (9.7%) IFG patients, 625 (44.9%) IGT patients, 411 (13.3%) combined patients, and 1750 normal subjects; the control group had older participants compared to the others. The number of females was significantly more than men in all the groups in the study. There was no significant difference in BMI across all groups.

Table 1 shows the prevalence of hypertension in the glucose-tolerance groups, in terms of age, sex, and BMI variables. Aging led to an increase in hypertension. However, it was significant only in the normal group. There was a significant association between the BMI and prevalence of hypertension in all groups. An increase in BMI led to an increase in the prevalence of hypertension.

The triglyceride (TG) level in glucose-tolerance groups was significantly more than in the normal group. The effect of the age variable was statistically significant at $P < 0.001$. An older age led to higher TG levels in all groups. There was no significant interaction effect between the age and glucose tolerance status on the triglyceride level.

Triglyceride level difference in the level of the sex variable was statistically significant ($P < 0.001$). The mean triglyceride level in women was higher than in men, in all levels of the glucose tolerance variable. The difference was more notable in the combined and IGT groups. There was no significant interaction effect between sex and the glucose-tolerance groups. Also, the BMI affected the TG level significantly in all groups [Table 2].

The total cholesterol level was higher in older and obese subjects. The result of Bonferroni post-hoc test demonstrated that the mentioned difference is related to the normal with IGT ($P < 0.05$), normal with combined ($P < 0.001$), and combined with IGT ($P < 0.05$) groups. In addition, the effect of the age variable was statistically significant. No significant interaction effect was found between the age and glucose tolerance status, on the total cholesterol level. The total cholesterol level in women was higher than in men in most levels of the glucose tolerance variable; however, no statistically significant difference was detected. There was no significant interaction effect between sex and the glucose-tolerance groups [Table 3].

Table 4 shows the mean LDL level in the normal and glucose-tolerance groups at different levels of age, sex, and BMI variables. The effect of the age variable was statistically significant across groups. It was also shown by the Bonferroni test the all pairwise comparison age groups were significantly different. The interaction effect between the age and glucose-tolerance status on the LDL level was not statistically significant. Although the LDL level in all glucose-tolerance groups was higher in men than in women, the differences were not statistically significant. Also, no significant interaction effect between the sex and glucose-tolerance groups was

Table 1: The prevalence of hypertension in the glucose-tolerance groups in terms of age, sex, and BMI variables

Variables	Glucose tolerance							
	Normal (%)		IFG (%)		IGT (%)		Combined (%)	
Age								
<40	37.4	*P*<0.001	48.8	*P*=0.09	47.7	*P*=0.09	45.9	*P*=0.18
40-49	46.3		53.2		46.8		48.9	
≥50	57.1		57.9		62.8		55.1	
Sex								
F	48.9	*P*=0.02	56.2	0.19	71.1	*P*=0.002	47.2	*P*=0.68
M	42.2		50.6		46.5		49.8	
BMI								
Normal	30.3	*P*<0.001	39.5	*P*<0.001	38.2	*P*=0.005	46.3	*P*=0.02
Overweight	43		49.6		45.6		41.6	
Obese	54.2		60.9		61.5		57.2	

BMI: Body mass index, IFG: Impaired Fasting Glucose, IGT: Impaired Glucose Tolerance

Table 2: The mean triglyceride level (standard error) in normal and glucose-tolerance groups in different levels of age, sex and BMI variables

Variables	Glucose tolerance				p^1	p^2	p^3
	Normal	IFG	IGT	Combined			
Age							
<40	152.5 (3.8)	167.59 (7.0)	164.9 (9.8)	171.2 (9.3)	0.007	<0.001	0.8
40-49	156.4 (3.9)	168.9 (6.4)	170.3 (9.6)	187.1 (7.6)			
≥50	164.1 (6.2)	175.3 (8.7)	197.1) 12.6)	198.1 (10.1)			
Sex							
F	184.7 (4.8)	190.9 (6.7)	211.9 (14.4)	230.2 (11.6)	<0.001	<0.001	0.5
M	145.9 (2.8)	157.8 (5.1)	165.9 (6.5)	173.8 (5.5)			
BMI							
Normal	126.9 (17.5)	154.4 (10.8)	128.4 (17.5)	159.5 (15.5)	<0.001	<0.001	0.3
Overweight	158.5 (3.5)	170.3 (6.1)	185.4 (8.2)	190.4 (7.6)			
Obese	160.9 (4.4)	173.5 (6.6)	171 (10.1)	184.6 (7.4)			

p^1s are related to the main effects of row variables (age, sex and BMI), p^2s are related to the main effects of glucose-tolerance groups, p^3s are related to the interaction between row variables and glucose-tolerance groups, BMI: Body mass index, IFG: Impaired Fasting Glucose, IGT: Impaired Glucose Tolerance

Table 3: The mean total cholesterol levels (standard error) in the normal and glucose-tolerance groups at different levels of age, sex, and BMI variables

Variables	Glucose tolerance				p^1	p^2	p^3
	Normal	IFG	IGT	Combined			
Age							
<40	186.8 (1.4)	194.8 (2.7)	188.4 (3.7)	199.8 (3.6)	<0.001	<0.001	0.87
40-49	195.8 (1.5)	200.8 (2.5)	198.1 (3.7)	204.7 (2.9)			
≥50	208.5 (2.4)	209.6 (3.3)	209.9 (4.9)	217.4 (3.9)			
Sex							
F	193.1 (1.9)	198.6 (2.7)	192.3 (5.7)	211.1 (4.6)	0.64	<0.001	0.43
M	194.3	202.0 (1.9)	197.6 (2.6)	205.2 (2.2)			
BMI							
Normal	184.7 (2.2)	193.2 (4.2)	185.8 (6.8)	194.2 (6.1)	<0.001	<0.001	0.92
Overweight	194.5 (1.4)	198.0 (2.4)	197.5 (3.2)	205.5 (2.9)			
Obese	198.9 (1.7)	206.7 (2.6)	199.4 (3.9)	210.2 (2.9)			

p^1s are related to the main effects of row variables (age, sex and BMI), p^2s are related to the main effects of glucose-tolerance groups, p^3s are related to the interaction between row variables and glucose-tolerance groups, BMI: Body mass index, IFG: Impaired Fasting Glucose, IGT: Impaired Glucose Tolerance

Table 4: The mean LDL levels (standard error) in the normal and glucose-tolerance groups at different levels of age, sex, and BMI variables

Variables	Glucose tolerance				p^1	p^2	p^3
	Normal	IFG	IGT	Combined			
Age							
<40	111.6 (3.3)	116.6 (2.4)	111.2 (3.3)	121.1 (3.2)	0	0.006	0.92
40-49	120.5 (1.3)	123.8 (2.2)	120.4 (1.3)	124.3 (2.6)			
≥50	128.1 (2.2)	130.6 (2.9)	125 (4.4)	132.9 (3.5)			
Sex							
F	118.2 (0.9)	124.2 (1.8)	118.7 (2.3)	125.1 (1.9)	0.29	0	0.61
M	116.9 (1.7)	120.6 (2.4)	112.5 (5.1)	127.6 (4.2)			
BMI							
Normal	111.4 (1.9)	119.3 (3.8)	111.7 (6.1)	116.8 (5.5)	0.001	0.004	0.80
Overweight	118.4 (1.2)	119.7 (2.1)	117.5 (2.9)	124.8 (2.7)			
Obese	121.5 (1.6)	128 (2.3)	119.9 (3.5)	128.5 (2.6)			

p^1s are related to the main effects of row variables (age, sex, and BMI), p^2s are related to the main effects of the glucose-tolerance groups, p^3s are related to the interaction between row variables and glucose-tolerance groups, BMI: Body mass index, IFG: Impaired Fasting Glucose, IGT: Impaired Glucose Tolerance, LDL: Low-density lipoprotein

observed. BMI led to a significant effect. The difference was attributed to normal with obese ($P < 0.01$) and to obese with overweight ($P < 0.05$) groups, by using the Bonferroni post-hoc test.

DISCUSSION

Prevalence of hypertension and dyslipidemia in prediabetic subjects with a family history of type 2

diabetes (first-degree relative) in comparison with the normal groups was questioned in the present study. Results of our study showed that the prevalence of dyslipidemia in prediabetic subjects was significantly more than in the normal group, but hypertension in prediabetic patients was similar to the normal group. IFG and IGT were associated with obesity and dyslipidemia, such as, high triglycerides, high total cholesterol, and hypertension.

Findings of the previous studies were inconsistent. Some studies showed lack of difference in the lipid profile between the IFG and normal subjects. However, another reported similar changes of lipid profile in prediabetic patients and normal subjects.[18-20]

These wide fluctuations may be partially due to the different cut-off points that were used for defining IFG, according to American Diabetes Association (ADA) and World Health Organization (WHO). However, most studies showed that the IFG group presented significant pro-atherogenic changes in all lipid parameters in comparison with the NGT group.

Our study showed that the prevalence of IFG was lower than IGT. Similarly, IGT was found to be more prevalent compared to IFG in Mauritius (USA) and in the Pima Indians.[21-22]

There are few studies that reported the prevalence of hypertension and dyslipidemia in prediabetic subjects with a family history of diabetes, however, results of the present study showed that aging led to an increase in the prevalence of hypertension, and male patients showed a greater prevalence of hypertension than female patients. With respect to the lipid profile, the triglyceride level was higher in the IGT and combined groups compared to the normal group. Total cholesterol was higher in the IGT and combined groups compared to the normal group, and LDL cholesterol was significant between the IGT and combined groups and the normal group. An important result was that all the assessed variables were similar in the IFG group with the normal group, and it was possible that these differences between the groups were related to the IGT.

Obesity, hypertension, and dyslipidemia are important cardiovascular risk factors in prediabetic patients. Our results showed differences between prediabetic patients and normal subjects, therefore, assessing and treating these risk factors is an important aspect for reducing cardio metabolic risk.

In summary, the prevalence of hypertension and dyslipidemia in prediabetic patients in comparison with normal groups was assessed in the present study, however, prevalence of hypertension was not significantly different between the groups, but in prediabetic patients it was higher than in the normal group. Prevalence of dyslipidemia in prediabetic subjects was significantly higher than in the normal group. However, further studies need to be conducted, to assess hypertension and dyslipidemia in prediabetic subjects based on the glucose-tolerance status in these subjects.

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