

# The characteristics of pre-diabetic patients associated with body composition and cardiovascular disease risk factors in the Iranian population

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**Background:** Different populations have shown various patterns of association between impaired fasting glucose (IFG) and body composition parameters and risk factors of cardiovascular disease (CVD). The current study aimed at investigating the differences between persons with prediabetes and healthy people in terms of CVD risk factors including body composition parameters, blood pressure, and lipid profile in a sample of the Iranian population. **Materials and Methods:** In a case-control setting, a sample containing 386 (193 prediabetic subjects and 193 normal subjects) of the first-degree relatives of diabetic patients aged 35-55 years were investigated. Samples were assessed using glucose tolerance categories. Prediabetes was defined according to the American Diabetes Association (ADA) criteria. Body composition parameters, blood pressure, glucose parameters, and lipid profile were measured and compared between the two groups. **Results:** Prediabetic patients had higher body mass index (BMI), waist circumference (WC), and body fat (BF) in comparison to the control group ( $P < 0.05$ ). In addition, prediabetic subject had a higher intake of energy, carbohydrate, protein, fat, and cholesterol and it seems that these patients had an unhealthy dietary intake ( $P < 0.05$ ). Fasting blood glucose (FBG) ( $P < 0.001$ ), total cholesterol ( $P = 0.007$ ), low-density lipoprotein cholesterol (LDL-C), and triglyceride ( $P = 0.021$ ) were higher in prediabetic patients ( $P < 0.05$ ) than in the controls. **Conclusion:** Both the risk factors of CVD and body composition parameters were different between the prediabetic and normal groups; total cholesterol (TC), triglyceride (TG), and FBS were predictors of the risk of prediabetes.

**Key words:** Body composition, cardiovascular disease risk factors, lipids, prediabetes, risk factors

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## INTRODUCTION

Prediabetes is the precursor stage to diabetes mellitus in which not all of the symptoms required to label a person as diabetic are present but the blood sugar is abnormally high. In recent years, prediabetes prevalence has increased, especially in developing countries. Its prevalence is higher than diabetes mellitus type 2.<sup>[1]</sup> Probably more than 400 million people would be affected in 2030.<sup>[2]</sup> Prediabetic patients have a high risk for developing diabetes.<sup>[3]</sup>

Prediabetes includes impaired fasting glucose (IFG) [fasting blood glucose (FBG) levels between 100 mg/dL and 125 mg/dL] and impaired glucose tolerance (IGT) (2 h postglucose load, plasma glucose levels between 140 mg/dL and 199 mg/dL). IFG and IGT represent the various metabolic defects. IFG is strongly associated with increased risk of cardiovascular disease (CVD) and all-cause death.<sup>[4]</sup>

In addition to IFG, other common risk factors associated with diabetes and CVD as obesity and lipid disorders are considered for the prevention of noncommunicable diseases. The prevalence of obesity is increasing in

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the world and according to evidences, obesity and body composition parameters associate with CVD and risk factors for vascular disease.<sup>[5]</sup> Higher body mass index (BMI) and waist circumference (WC) are associated with increase in the risk of metabolic diseases such as type 2 diabetes and insulin resistance. However, it is not clear whether anthropometric indices in prediabetic patients and healthy subjects are different or not. Lipid disorders are shown as risk factors for CVD.<sup>[6,7]</sup>

Studies showed that abnormal lipid profiles and central obesity were considered as important factors for prognostic IFG before the onset of diabetes symptoms.<sup>[8,9]</sup> Also, high serum uric acid level was related to some cardiometabolic risk factors in prediabetic individuals compared to normal persons.<sup>[10]</sup>

Different populations have various patterns of association between IFG and obesity and lipid profiles;<sup>[11]</sup> it is important to assess the characteristics of relationship between IFG and other related risk factors in the Iranian population. Also, because IFG is the initial stage of diabetes and CVDs development, determination of preventable risk factors related to IFG is very important in the prevention and control of these diseases. Therefore, in the present study we investigated the differences of body composition parameters and CVD risk factors between prediabetic patients and a sample of healthy participants in a community-based case-control study in the Iranian population.

## MATERIALS AND METHODS

### Study participants

The Isfahan Diabetes Prevention Study (IDPS) is an ongoing cohort study that was performed between 2003 and 2005. This study was conducted to determine efficacy of intensive diet and exercise to prevent or delay the beginning of type 2 diabetes mellitus in first-degree relatives of patients with type 2 diabetes. Six hundred and fourteen men and 1,754 women participated in IDPS in Isfahan Endocrine and Metabolism Research Center, which depends on the Isfahan University of Medical Sciences, Isfahan, Isfahan Province, Iran.<sup>[12]</sup> This study was approved by Ethics Committee of Isfahan University of Medical Sciences.

The participants were monitored annually. Clinical data were collected for all consecutive patients including an examination of the ocular fundus and lens, the limbs, and blood pressure (BP), measurement of height, weight, and FPG, glycosylated hemoglobin (HbA1c), urine protein, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), total cholesterol (TC), and serum creatinine levels at the first visit and at the next monitoring stages. Follow-up tests were performed based on the

Standards of Medical Care in Diabetes to update participant information regarding anthropometric, demographic, and lifestyle factors and diabetes, IFG, and IGT.

We performed a case-control study based on the recorded data collected from participants in the cohort study in IDPS. The cases and controls were matched for age and gender. Finally, 193 subjects were selected in each group.<sup>[13]</sup> Healthy people or prediabetic patients had been recognized by oral glucose tolerance test (OGTT) test, FPG test, and HbA1C test according to the American Diabetes Association (ADA) criteria.<sup>[14]</sup> IFG was defined as FBS  $\geq 100$  mg/dL and  $< 126$  mg/dL. IGT was diagnosed as 2-h plasma glucose concentration  $\geq 140$  mg/dL and  $< 200$  mg/dL using OGTT after an intake of 75 g oral glucose. Those with normal range of blood glucose level had been selected as the control group (FBS  $< 100$  mg/dL, 2-h plasma glucose concentration  $< 140$  mg/dL and HbA1C  $< 5.7\%$ ).<sup>[14]</sup> Information including the participant's lifestyle, sociodemographics, family history of type 2 diabetes mellitus in first-degree relatives, occupation, education, smoking, medication use, medical history, and disease history were collected by a trained interviewer. Each participant provided written informed consents before participation. We explained the protocol of the study regarding the probable side effects during preparation of the blood samples. Participants could leave the study at any stage of the research. The total metabolic equivalent (MET) in min/week was calculated by multiplying the frequency, duration, and intensity of each physical activity in 24 h. Usual dietary intake was assessed using a validated semi-quantitative food frequency questionnaire (FFQ).<sup>[15,16]</sup> Drug information, medical history, and biochemical information were extracted from medical records of patients at the center and the latest presentation was recorded.

### Anthropometric assessment

Body weight was measured by seca (Hamburg, Germany) scale while subjects were lightly clothed and without shoes, and they were recorded to the nearest 100 g. Height was measured by Seca stadiometer while the subjects were in a standing position with their shoulders in the normal position. BMI was computed as weight (kilograms) divided by height (meters); subjects with squared BMI of less than  $25 \text{ kg/m}^2$  were considered as normal, between  $25 \text{ kg/m}^2$  and  $30.0 \text{ kg/m}^2$  as overweight, and greater than  $30 \text{ kg/m}^2$  as obese.<sup>[17]</sup> WC was measured at the level midpoint between the lowest of the rib cage and upper border of the iliac crest.

Body composition of all participants was assessed using bioelectrical impedance analysis (Jawon Medical Company, Korea). Parameters that were determined included body fat (BF), total body water (TBW), visceral fat (VF), mineral, protein, soft lean mass (SLM), lean body mass (LBM), and abdominal circumference (AC).

Blood pressure assessment

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were taken using a standardized mercury sphygmomanometer (Suzhou Sunmed Co., Ltd. Jiangsu, China, Mainland) on the right arm, after a 15-min rest in a sitting position. The SBP was defined as the appearance of the first sound (Korotkoff phase 1), and DBP was defined as the disappearance of the sound (Korotkoff phase 5).

Biochemical assessment

A fasting blood sample was collected after at least 10 h overnight fasting for biochemical investigations. FBS was measured by the glucose oxidase method (Clinical Chemistry Analyzer Liasys, Roma, Italy). A 75-g oral glucose was administered and plasma glucose concentrations were measured at 120 min after glucose taking. All biochemical parameters were performed using enzymatic kits. HbA1c was measured by ion-exchange chromatography; high-density lipoprotein cholesterol (HDL-C), triglyceride, and total cholesterol were measured by the enzymatic method. Low-density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald equation.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) software for Windows, version 20 (SPSS Inc., Chicago, IL) was used for statistical analyses. Means and their standard deviations (SDs) were used for the continuous variables, and frequencies and percentages were used for the categorical variables. The normality distribution of the studied variables was investigated using one-sample Kolmogorov–Smirnov test. Independent sample *t*-test or analysis of covariance (ANCOVA) and chi-square test were used to compare the quantitative and qualitative studied variables, respectively, between the groups. The level of significance was considered to be less than 0.05.

RESULTS

The total number of subjects included in the present study was 386, of whom 193 were cases of prediabetic patients and 193 were matched controls with normal blood glucose.

There was no statistically significant difference in age, gender, and educational level between the prediabetic subjects and controls. However, the control group had more significantly physical activity than prediabetic patients (*P* < 0.0001). A comparison of sociodemographic characteristics between the two groups is shown in Table 1. More number of control subjects (24.9%) reported smoking than prediabetic subjects (8.30%) (*P* < 0.0001, Table 1).

Energy, carbohydrate, protein, total fat, saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, and

cholesterol intake in prediabetic patients were significantly more than in the control group. However, the control group had a higher intake of fiber than prediabetic patients [Table 2].

Prediabetic patients had significantly higher weight, BMI, and WC than the control group (*P* < 0.0001). As expected, total BF, percentage of BF (*P* < 0.0001), and VF in the abdomen (*P* = 0.007) in prediabetic patients were higher than in the control group. In addition, body mineral content in prediabetic patients was higher than in the control group (*P* = 0.04). The control group had higher TBW than prediabetic subjects (*P* < 0.0001) [Table 3]. Table 4 shows the results of comparing the CVD risk factors between prediabetes and the control group. As can be seen, there are significant differences between the two groups in terms of all the studied variables except SBP.

DISCUSSION

In this community-based case-control study of prediabetes in the Iranian population, we confirmed previous reports

Table 1: Sociodemographic characteristics of prediabetic subjects and controls in the Iranian population

Variables	Prediabetic patients (n = 193)	Control group (n = 193)	P value*
Age (years)	47.78±7.80	46.56±8.03	0.134
Gender, n (%)			
Male	62 (32.10%)	77 (39.90%)	0.112
Female	131 (67.90%)	116 (60.10%)	
Education level			
Middle and high school	100 (51.80%)	100 (51.80%)	0.99
College and higher level	93 (48.20%)	93 (48.20%)	
Smoking			
Yes	16 (8.30%)	48 (24.9%)	<0.001
No	177 (91.70%)	145 (75.10%)	
Physical activity (MET h/day)	26.41±4.52	32.64±5.61	<0.001

\*Resulted from independent *t*-test or chi-square test

Table 2: Comparison of dietary intakes between prediabetic patients and the control group

Variables	Prediabetic patients (n = 193)	Control group (n = 193)	P value*
Energy (kcal)	2376.60±587.39	1813.96±465.23	<0.001
Carbohydrate (g)	356.99±92.73	278.54±76.12	<0.001
Protein (g)	86.40±28.57	68.66±20.51	<0.001
Fat (g)	77.68±36.05	51.87±22.08	<0.001
Fiber (g)	44.27±18.44	57.70±28.10	<0.001
SFA (g)	22.76±11.93	13.53±6.98	<0.001
MUFA (g)	19.14±10.02	15.70±7.37	<0.001
PUFA (g)	20.14±13.16	13.96±7.55	<0.001
Cholesterol (mg)	208.25±74.73	158.72±70.82	<0.001

SFA = Saturated fatty acid; MUFA = Monounsaturated fatty acids; PUFA = Polyunsaturated fatty acids; \*Resulted from independent *t*-test or chi-square test

**Table 3: Comparison of body composition parameters between prediabetic patients and the control group**

Variables	Prediabetic patients (n = 193)	Control group (n = 193)	P value*
Weight (kg)	76.08±11.76	70.33±11.26	<0.001
Height (cm)	161.51±8.17	162.76±9.53	0.18
Body mass index (kg/m <sup>2</sup> )	29.20±4.25	26.65±4.31	<0.001
Waist circumference (cm)	91.63±8.72	87.45±8.63	<0.001
Total body fat (kg)	40.27±6.83	34.56±6.31	<0.001
Percentage of body fat (%)	52.94±3.84	49.09±4.00	<0.001
Visceral fat in the abdomen (cm <sup>2</sup> )	122.82±42.59	112.53±38.86	0.007
Lean body mass (kg)	35.81±6.37	35.76±6.15	0.94
Soft lean mass (kg)	31.58±5.91	31.67±5.80	0.87
Body mineral content (kg)	4.22±0.66	4.08±0.63	0.04
Total body water (kg)	23.59±5.15	28.46±8.33	<0.001
Body protein (kg)	8.92±2.096	8.81±1.86	0.41

\*Resulted from ANCOVA

**Table 4: Comparison of CVD risk factors between prediabetic patients and the control group**

Variables	Prediabetic patients (n = 193)	Control group (n = 193)	P value*
SBP (mmHg)	115.26±16.07	112.79±13.69	0.15
DBP (mmHg)	78.36±12.11	73.98±12.00	<0.001
Mean arterial blood pressure (mmHg)	90.66±12.10	86.92±37.09	<0.001
TC (mg/dL)	207.89±37.78	178.01±37.09	<0.001
LDL-C (mg/dL)	124.76±26.13	109.44±23.80	<0.001
HDL-C (mg/dL)	42.31±8.98	48.41±9.32	<0.001
TG (mg/dL)	163.45±54.75	128.89±43.09	<0.001
2hpp (mg/dL)	140.58±27.96	112.24±18.96	<0.001
FBG (mg/dL)	105.79±9.99	91.34±5.59	<0.001
HbA1C (%)	5.49±0.42	5.03±0.35	<0.001

SBP = Systolic blood pressure; DBP = Diastolic blood pressure; TC = Total cholesterol; LDL-C = Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG = Triglyceride; 2hpp = 2-h postprandial plasma glucose; FBG = Fasting blood glucose; \*Resulted from ANCOVA

that risk factors of CVD and body composition parameters in prediabetic patients were higher than normal subjects. These factors including high BF, obesity, abnormal lipids, and high blood pressure may work together and reinforce the development of IFG.

Evidences consistently showed that high BF and BMI are risk factors for CVD, coronary heart disease, diabetes, and premature death.<sup>[18,19]</sup> Also, abdominal obesity is associated with an increased risk for coronary heart disease and type 2 diabetes, independent of overall adiposity.<sup>[20,21]</sup>

The classical perception of adipose tissue as a storage place of fatty acids has been replaced by the notion that adipose tissue has a central role in lipid and glucose metabolisms,

and produces a large number of hormones and cytokines. Therefore, the increased prevalence of excessive visceral obesity and obesity-related cardiovascular risk factors is closely associated with the rising incidence of type 2 diabetes. BF distribution, especially intraabdominal adipose tissue accumulation, is a key correlate of a cluster of diabetogenic, atherogenic, prothrombotic, and inflammatory metabolic abnormalities, increasing the risk for type 2 diabetes and CVD.<sup>[20]</sup>

The occurrence of rapid and major lifestyle changes in many countries has increased the prevalence of obesity and other noncommunicable disease risk factors such as hypertension and dyslipidemia, which have been reported to be the major etiologic factors for the rising incidence of type 2 diabetes across the globe.<sup>[22]</sup>

The data presented in this study confirm the increasing risk factors of CVD and abnormal body composition in prediabetes. Therefore, preventing or ameliorating obesity once it has developed is likely to help prevent the development of diabetes risk factors. Several cardiovascular risk factors are found concomitantly, along with risk factors of diabetes in an individual. Those risk factors are obesity, hypertension, low HDL-C, increased triglycerides level, and glucose metabolism disorder, which is known as the metabolic syndrome.

No study has yet prospectively examined the predictive ability of this anthropometric measure for diabetes or prediabetes.

Studies showed that TC, LDL-C, and TG were higher and HDL-C was lower in prediabetic patients in comparison to normal subjects.<sup>[23,24]</sup> Insulin resistance may lead to the abnormality of lipid and lipoprotein in the hyperglycaemic state, which is the main pathophysiological feature of type 2 diabetes. Hyperinsulinemia, enhanced hepatic gluconeogenesis, and glucose output occur in an insulin-resistant status. In addition, insulin resistance decreases the suppression of lipolysis in adipose tissue, leading to high free acid flux and enhances hepatic very-low-density lipoprotein secretion. These condition leads to hypertriglyceridemia and reduces the levels of HDL-C. Many studies have reported that abnormality of fatty acid metabolism plays the major role in the etiology of IFG.<sup>[25,26]</sup>

In the present study after adjustment with confounders, there was no significant association between blood pressure and prediabetes. The relationship between hypertension and prediabetes may probably be related to the metabolic syndrome and hyperinsulinemia.<sup>[27]</sup> One cohort study showed that CVD mortality and total



mortality were significantly higher in prediabetic patients with hypertension.<sup>[28]</sup> The close association between blood pressure and prediabetes may be because of similar molecular mechanisms in insulin resistance and hypertension and may be the reason for their close relationship.<sup>[29,30]</sup>

## CONCLUSION

Our findings showed that the risk factors of CVD and body composition parameters were different in prediabetes subjects and healthy subjects. TC, TG, and FBS were predictors of the risk of prediabetes.

## Ethical approval

All procedures performed in the present study involving human participants were in accordance with the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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## Conflicts of interest

There are no conflicts of interest.

## AUTHOR'S CONTRIBUTION

ZGh collected the data. MHB and ZGh wrote the manuscript. AF analyzed the data. BI and GhA managed the research project and revised the manuscript.

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