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The relationship between homeostasis model assessment and cardiovascular risk factors in Iranian subjects with normal fasting glucose and normal glucose tolerance

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Abstract

Background: Insulin resistance is a complex problem which may not always correlate with all its cardiovascular risk factors in various populations. We investigated the relationship between homeostasis model assessment of insulin resistance (HOMA-IR) with cardiovascular risk factors in Iranian subjects with normal fasting glucose (NFG) and normal glucose tolerance (NGT).
Methods: Of the 605 subjects aged 25–79 y enrolled in this study, after the oral glucose tolerance test, 366 subjects aged 25–50 y and 135 aged >50 y were classified as NFG and NGT. Insulin resistance was estimated by the HOMA-IR.
Results: Women had higher values of body mass index (BMI), insulin and HOMA-IR than men in both age groups. The prevalence of insulin resistance, general and abdominal obesity, low HDL-C and physical inactivity was higher in women than men in the 2 age groups. Men had a higher prevalence of hypertension and hypertriglyceridemia in the group with age 25–50 y. The Pearson correlation controlled for age, BMI, waist circumference and physical activity showed that HOMA-IR had significant correlation with triglyceride and inversely associated with HDL-C in both sexes. In addition, the results of HOMA-IR quartiles demonstrated that the prevalence of hypertension, obesity, and low HDL-C was particular high in women with HOMA-IR >2.39. Multiple regression indicated that log HOMA-IR was independently predicted by BMI, triglyceride and HDL-C in men and BMI, HDL-C and waist-to-hip (WHR) ratio in women.
Conclusions: HOMA-IR is associated with the features of metabolic syndrome with a sex difference in the degree and predictors of HOMA-IR and the frequency of cardiovascular risk factors.
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Keywords: Insulin resistance; Normal glucose tolerance; Normal fasting glucose; Cardiovascular risk factors; Homeostasis model assessment

1. Introduction

Insulin resistance has an important role in pathogenesis of a number of human disorders, including type 2 diabetes, obesity, hypertension, and dyslipidemia. These disorders, which also are risk factors for cardiovascular disease, together are referred to as metabolic syndrome or insulin resistance syndrome [1,2].

There is increasing evidence supporting the fact that insulin resistance is a predictor of diabetes development even in individuals with normal glucose tolerance. Predicting insulin

Abbreviations: NGT, normal glucose tolerance; NFG, normal fasting glucose; IR, insulin resistance; HOMA-IR, homeostasis model assessment of insulin resistance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; WHR, waist-to-hip ratio; CVD, cardiovascular disease; BMI, body mass index.

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resistance in normoglycemic individuals is important, as diabetes intervention programs are more likely to be successful at this stage rather than after the development of impaired glucose tolerance. Therefore, a simple test to identify insulin-resistant individuals is important both for population-based research and clinical practice. Because abnormal glucose tolerance affects insulin sensitivity, we excluded abnormal glucose tolerance and type 2 diabetes subjects to investigate the relationship between insulin resistance and cardiovascular risk factors in normal glucose tolerance (NGT) and normal fasting glucose (NFG) subjects.

Differences between ethnic groups in insulin resistance and β-cell function have been suggested in a number of studies [3,4]. Epidemiological studies showed notable differences in coronary heart disease (CHD) mortality rate among countries. Racial discrepancies have also been reported for type 2 diabetes and insulin concentrations [5,6].

Several studies have illustrated an increasing incidence of impaired glucose tolerance and type 2 diabetes in Iran. In Iran, there were 1.6 million people with type 2 diabetes in 1995 and this number is expected to increase to >5.0 million by 2025 [7]. Also, over the last 20 y, coronary artery disease mortality increased by 20–45% in Iran [8,9]. Change in lifestyle, especially high fat diet and decreased physical activity, is a major contributor to the increase of type 2 diabetes and cardiovascular disease in Iran. However, all of these studies focused on estimating the population distribution of major risk factors for cardiovascular diseases (CVDs). Thus, given the increasing rates of impaired glucose tolerance, type 2 diabetes and obesity in Iran, our aim in this study was to investigate homeostasis of model assessment of insulin resistance (HOMA-IR) and its relationships with cardiovascular risk factors in an Iranian population with NFG and NGT.

2. Materials and methods

2.1. Subjects

The survey was conducted at the Pasteur Institute of Iran, Tehran between September 2003 and March 2004 and includes subjects of both sexes. A total of 605 subjects aged 25–79 y were studied. After oral glucose tolerance test, according to WHO criteria in 1997, 32 were found to be type 2 diabetic patients, 64 were borderline-type subjects, those who were of neither the diabetic nor normal type and 501 were NFG and NGT (266 men and 235 women). For the purpose of the present study, subjects with diabetes and borderline-type subjects included those with impaired fasting glucose (IFG) and impaired glucose tolerance were excluded. 8 subjects who had heart and kidney failure and chronic liver disease or endocrine disease were excluded from the study. Written informed consent was obtained from all subjects before enrollment in the study.

2.2. Data collection

Subjects were advised to refrain from severe physical activity, smoking, eating, and drinking for at least 12 h before the screening visit. Screening included standardized questionnaires on personal data and clinical measurements such as age, sex, personal medical history, any history of coronary heart disease, high blood pressure, dyslipidemia, diabetes, and physical activity. Physical activity was graded into 4 categories, from 1 to 4, according to an increasing order of physical activity [10]. The questionnaire also asked about smoking habits (never, past or current smoker).

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice on the right arm of subjects who had been resting for at least 10 min in a comfortable position. Two consecutive measurements of SBP and DBP were recorded, and the mean values of these were used for the present analysis. Height was measured without shoes to the nearest centimeter. Weight was measured to the nearest 0.5 kg. Waist and hip circumference were measured to the nearest 0.5 cm with a measuring tape while all subjects were standing in a relax position. The waist circumference (WC) was taken at the midpoint between the iliac crest and the lower rib margin, and the hip circumference was taken around the maximum circumference of the buttocks posteriorly and the symphysis pubis anteriorly.

All subjects not taking diabetes medication had a 2 h 75 g (glucose monohydrate) oral glucose tolerance test after an overnight fast. Normal subjects were defined as having a fasting plasma glucose <6.1 mmol/l and a 2 h plasma glucose <7.8 mmol/l. Diabetes was diagnosed if subjects reported a history of diabetes and were taking oral hypoglycemic medication or insulin or if the fasting plasma glucose level was ≥7.0 mmol/l or the 2 h glucose value was ≥11.1 mmol/l [11]. Subjects who did not meet the criteria for diabetes, normal fasting glucose and normal glucose tolerance were defined as borderline-type (IFG, IGT).

2.3. Laboratory measurements

Blood samples were taken at 0 and 120 min and plasma preserved with EDTA and serum was separated immediately by centrifugation at 2500 rpm for a period of 10 min. The samples were processed immediately or in the first week following preservation at −20 °C. Glucose measurements (intra-assay CV 2.1%, inter-assay CV 2.6%) were carried out using the glucose oxidase method. Total cholesterol (TC) and total triglycerides (TG) were determined using enzymatic methods. HDL-cholesterol was measured in the supernatant after precipitation of the lipoprotein containing Apolipoprotein B (Apo B) with phosphotungstic acid and magnesium chloride. LDL-cholesterol was calculated using Friedewald's formula. LDL-cholesterol was not calculated for individuals with TG >4.5 mmol/l. All of the measurements were carried out in a Technicon® analyzer RA™ 1000. Insulin was determined by RIA assay. The intra- and inter-assay coefficients of variation for insulin were 4.8% and 5.5%, respectively. No cross-reactivity was observed between insulin and proinsulin. Apolipoprotein B was determined by an immunoturbidometric assay.

2.4. Classification criteria

Insulin resistance was assessed from glucose and insulin concentrations by the use of homeostasis model assessment (HOMA)

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