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Prevalence of insulin resistance and cardiometabolic risk in Korean children and adolescents: A population-based study

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ABSTRACT

Aims: We aimed to establish normal reference values of serum insulin and the homeostasis model assessment of insulin resistance (HOMA-IR). We also aimed to verify HOMA-IR "cut-off values" in predicting cardiometabolic risk among Korean children and adolescents.
Methods: Data from 2716 Korean subjects (1421 male and 1295 female, aged 10–20 years) were evaluated. Insulin resistance was defined as HOMA-IR >95th percentile. The odds ratios of cardiometabolic risk were assessed based on the state of insulin resistance.
Results: Reference values of insulin and HOMA-IR were determined according to sex and age, based on data obtained from normal-weight subjects with normal fasting glucose levels. HOMA-IR values appeared to peak at the age of 14–15 years in male subjects and at the age of 12–13 years in female subjects. The prevalence of insulin resistance in the subjects was 9.8% (male = 10.9%, female = 8.6%). The prevalence of insulin resistance in normal-weight, overweight, and obese subjects were 4.7%, 25.6%, and 47.1% respectively. Subjects with insulin resistance had a higher prevalence of metabolic syndrome (odds ratios = 18.33; 95% confidence interval, 9.62–34.94) and its components, especially hyperglycemia and hypertriglyceridemia.
Conclusion: We established reference values of serum insulin and HOMA-IR according to age and sex. Obesity is the most important risk factor for insulin resistance and metabolic syndrome. However, insulin resistance independently increases cardiometabolic risk. This information may be useful for Korean as well as other Asian in planning programs for the prevention of type 2 diabetes.

1. Introduction

Insulin resistance or hyperinsulinemia precedes type 2 diabetes mellitus and cardiovascular disease (CVD), and plays a major role in the pathogenesis of these diseases [1,2]. Insulin resistance precedes the development of impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), which has been shown to predict the development of type 2 diabetes mellitus [3,4]. Insulin resistance also plays a pivotal role in

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metabolic syndrome, which precedes the development of CVD, leading to morbidity and mortality [1,2]. Thus, insulin resistance has been proposed as a strategic target for type 2 diabetes mellitus and CVD prevention interventions [5,6].

Metabolic syndrome, also called insulin resistance syndrome, is a surrogate marker of type 2 diabetes mellitus and CVD in children and adolescents, as well as adults [7]. Prospective studies have shown that metabolic syndrome develops during childhood and progresses to adulthood type 2 diabetes mellitus and CVD [8–10]. Thus, many studies have investigated the prevalence of metabolic syndrome in children. The pediatric prevalence of metabolic syndrome varies widely depending on ethnicity, ranging from 0.7% to 4.5% in population-based studies using the International Diabetes Federation (IDF) definition [11–14]. Furthermore, the clinical features of metabolic syndrome differ according to race or ethnicity. Asians experience higher rates of type 2 diabetes mellitus and CVD, despite much lower levels of obesity, than their non-Asian counterparts [15,16]. Insulin resistance in Asians is thought to be an important contributor to the increasing rates of these diseases along with increasing prevalence of obesity in this region.

Fasting insulin and the homeostasis model assessment of insulin resistance (HOMA-IR) have been proposed as surrogate markers of insulin resistance for epidemiology studies, outcomes of therapeutic interventions, and clinical applications [17]. Thus, many recent studies have proposed reference ranges and cut-off values for insulin and HOMA-IR [18–21]. However, population-based studies of insulin concentrations and HOMA-IR in Asian children and adolescents are lacking.

The objectives of this study were as follows: (1) to establish normal reference values of serum insulin and HOMA-IR in healthy Korean children and adolescents, (2) to estimate the prevalence of insulin resistance by HOMA-IR cut-off, and (3) to verify the HOMA-IR ''cut-off values'' in predicting cardiometabolic risk among a nationally representative population.

2. Subjects and methods

This study was performed using data acquired during the Fourth Korea National Health and Nutrition Examination Survey (KNHANES IV) (2007–2009). These surveys have been conducted periodically since 1998 to assess the health and nutritional status of the non-institutionalized civilian population of Korea. KNHANES IV was a cross-sectional and nationally representative survey with a multistage and stratified sampling design conducted by the Division of Chronic Disease Surveillance, Korea Centers for Disease Control and Prevention [22]. A total of 31,705 individuals (11,520 families from 500 sectors based on region and economic status) were included in the KNHANES IV; among them, 74.5% families participated in health surveillance and blood sampling. For this study, 3023 subjects aged 10–20 years (representing 5,956,228 individuals) were identified as potential subjects.

All subjects and their parents were interviewed at home after providing informed consent; they underwent various examinations including blood sampling. Weight was determined to the nearest 0.1 kg on a medical balance (GL-6000-20, CAS, Seoul, Korea); height was measured to the nearest 0.1 cm with a wall-mounted stadiometer (Seca 220, Seca, Hamburg, Germany). Body mass index (BMI) was calculated by dividing the weight (kg) by the height squared (m^2). Waist circumference (WC) was measured using a flexible tape at the narrowest point between the lowest rib and the uppermost lateral border of the right iliac crest. Blood pressure (BP) was measured after the subject had rested for 5 min in a sitting position. Three readings each of the systolic and diastolic blood pressure were recorded, and the average value was used in the analyses.

The blood samples were taken by a trained nurse and transported daily to the Central Laboratory (NEODIN Medical Institute, Seoul, Korea). The concentrations of fasting glucose, triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) were determined according to standard procedures using a ADIVIA1650 (Siemens, Washington, DC, USA) in 2007 and a Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan) in 2008–2009. Insulin concentrations were measured by an immunoradiometric assay (INS-IRMA; Biosource, Nivelles, Belgium) using a 1470 WIZARD gamma-counter (PerkinElmer, Turku, Finland). The sensitivity and the intra-assay and inter-assay variation coefficients (CV) were 1.0 μIU/mL, 1.6–2.2%, and 6.1–6.5%, respectively. Insulin sensitivity was evaluated by the HOMA-IR index using a standard formula: fasting insulin (μIU/mL) × fasting glucose (mmol/L)/22.5 [23].

Of the 3023 subjects, a subsample ($n = 2815$) had glucose and insulin concentrations measured. A total of 99 subjects who had not fasted for a minimum of 8 h were excluded. Thus, the final analytical sample consisted of 2716 subjects (1421 male; 1295 female), which included 2573 with normal fasting glucose (NFG) levels (glucose < 100 mg/dL (5.5 mmol/L)), 141 with impaired fasting glucose (IFG; glucose ≤ 100 or < 126 mg/dL (≤5.5 or < 7.0 mmol/L)), and 2 patients with newly identified type 2 diabetes mellitus (glucose ≥ 126 mg/dL (7.0 mmol/L)). Subjects aged 20–30 years without chronic disease such as type 2 diabetes mellitus, thyroid disease, rheumatic arthritis, cancer, and CVD were also included in normal reference of serum insulin and HOMA-IR as a comparison of adult insulin concentrations and HOMA-IR. Among them, 1469 subjects had a BMI < 25 and 1130 subjects had a BMI < 23 (normal-weight in the Korean population). Age- and sex-specific reference for HOMA-IR was made in normal-weight subjects with NFG. Subjects were classified as normal-weight if BMI was <85th percentile, overweight if BMI was ≥85th and <95th percentile, or obese if BMI was ≥95th percentile, based on Korean reference data [24].

For the prediction of type 2 diabetes mellitus and CVD risk, we used the metabolic syndrome definition of the International Diabetes mellitus Federation (IDF) for subjects older than 10 years of age [7]. Central obesity was defined as waist circumference ≥90th percentile on the basis of Korean waist reference data [24]. Two or more of the following clinical features were also required: fasting TG concentrations ≥150 mg/dL, fasting glucose concentration ≥ 100 mg/dL (5.5 mmol/L), systolic BP ≥ 130 mm Hg or diastolic BP ≥ 85 mm mm Hg, and HDL-C concentration < 40 mg/dL for both genders, except in girls aged ≥16 years (HDL-C concentration < 50 mg/dL).