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Evaluation of the impact of abdominal obesity on glucose and lipid metabolism disorders in adults with Down syndrome

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ABSTRACT

We aimed to describe anthropometric differences in weight-related disorders between adults with Down syndrome (DS) and healthy controls, as well as their disparate impact on glucose and lipid metabolism disorders. We underwent a cross-sectional study of 49 consecutively selected, community-residing adults with DS and 49 healthy controls in an outpatient clinic of a tertiary care hospital in Madrid, Spain. Siblings of adults with DS were studied as controls in 42 cases. Epidemiological data (age and gender), anthropometric data (body mass index, waist circumference, and waist-to-height ratio [WHR]), coexisting clinical conditions, and laboratory data (fasting glucose, insulin, glycated hemoglobin, creatinine, thyroid hormones, and lipid profile) were measured and compared between the groups. Adults with DS were significantly younger and more often male, with a higher prevalence of overweight and obesity than controls. Adults with DS also had a higher WHR, and more frequently presented abdominal obesity. Moreover, insulin resistance measured using the homeostatic model assessment was more prevalent among adults with DS and abdominal obesity. However, lipid profiles were similar between groups. The kappa correlation index for the diagnosis of abdominal obesity between waist circumference and WHR was 0.24 (95%CI: 0.13–0.34). We concluded that the prevalence of overweight, obesity, and abdominal obesity was higher in adults with DS than in controls. Adults with DS and abdominal obesity showed higher indexes of insulin resistance than their non-obese peers. WHR was a useful tool for the evaluation of abdominal obesity in this population.

1. Introduction

Atherosclerosis is the main pathophysiological substrate of cardiovascular disease, which is the leading cause of morbidity and mortality in Western countries (WHO, 2009). The prevalence of cardiovascular disease increases with age and with the presence of various concomitant risk factors, such as arterial hypertension, diabetes mellitus, dyslipidemia, obesity, and sedentary lifestyle (Asia Pacific Cohort Studies Collaboration, 2005; Multiple Risk Factor Intervention Trial Research

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Group, 1986). High blood pressure and metabolic risk factors interact to give rise to metabolic syndrome, which leads to a greater total cardiovascular risk than the sum of its individual components and is associated with an augmented risk for cardiovascular morbidity and mortality (Alberti et al., 2009; Moreno-Palanco et al., 2011). Obesity, particularly abdominal obesity (measured by waist circumference) and oxidative stress are considered to be an early stage in the development of metabolic syndrome and play a central role in its pathogenesis (Giacchetti, Sechi, Rilli, & Carey, 2005; NCEP-ATPIII, 2001). In recent decades, the prevalence of obesity and the prevalence of metabolic syndrome have increased in all age groups and are now considered major public health problems (Ervin, 2009).

Since the 1980s, the gradually improving survival of children with Down syndrome (DS) has dramatically increased life expectancy in a growing number of adults with DS (Irving, Basu, Richmond, Burn, & Wren, 2008; Yang, Rasmussen, & Friedman, 2002). This "new" population of adults with DS poses unique clinical problems that differ from those of the pediatric population with DS or the general population (Kerins, Petrovic, Bruder, & Gruman, 2008). Adults with DS present multiple immunologic and metabolic disturbances, which in turn lead to increased oxidative stress in several cellular systems and to premature tissue aging (Corsi et al., 2009; Licastro et al., 2007). Obesity and dyslipidemia also appear to be more prevalent in the population with DS, both in children and in adults (Adelekan, Magge, Shults, Stallings, & Stettler, 2012; Fujiura, Fitzsimons, & Marks, 1997; Melville, Cooper, McGrother, Thorp, & Collacott, 2005; Prasher, 1995; Rubin, Rimmer, Chicoine, Braddock, & McGuire, 1998). Although the initial studies found no significant differences in mean total cholesterol and triglyceride levels between adults with and without DS, recent research has revealed a more atherogenic lipid profile in individuals with DS than in the general population (Adelekan et al., 2012; Melville et al., 2005; Murdoch, Rodger, Rao, Fletcher, & Dunnigan, 1977). Furthermore, a higher incidence of type 1 diabetes mellitus has also been observed in the DS population (Bergholdt, Eising, Nerup, & Pociot, 2006). However, despite the possible coexistence of multiple cardiovascular risk factors, subclinical atherosclerotic damage or cardiovascular events are still extremely rare in adults with DS (Draheim, Geijer, & Dengel, 2010; Rodrigues et al., 2011; Yla-Herttuala, Luoma, Nikkari, & Kivimaki, 1989).

Among the various cardiovascular risk factors, obesity has received little attention in adults with DS, and early studies focus solely on the evaluation of body mass index (BMI). Therefore, the prevalence of abdominal obesity and the appropriateness of waist circumference for diagnosing obesity in this population are unknown. We hypothesized that adults with DS would have a different profile of weight-related disorders than the general population; yet this profile would not lead to the development of significant metabolic disorders. Anthropometrical differences in body fat distribution could be key to explaining this discrepancy. We therefore designed a cross-sectional study based on a comprehensive assessment of several anthropometric parameters, with the following objectives: (a) to describe the prevalence of weight disorders (overweight, obesity, and abdominal obesity) in a cohort of adults with DS; (b) to evaluate any differences with a cohort of healthy controls; and (c) to study the differential influence of abdominal obesity on the prevalence of metabolic disorders (states of glycemic dysregulation such as impaired fasting glucose, insulin resistance or diabetes mellitus, dyslipidemia, and/or metabolic syndrome) between groups (DS vs. controls and abdominally obese vs. non-obese).

2. Materials and methods

2.1. Study design

We performed a cross-sectional study of 49 adults with DS and 49 healthy controls. The former were consecutively selected at the Adult Down Syndrome Outpatient Clinic of the Department of Internal Medicine Hospital Universitario de La Princesa, Madrid, Spain. The recruitment period ran from January 2012 to March 2013. The study was conducted in accordance with the provisions of the Declaration of Helsinki and Good Clinical Practice guidelines, and the study protocol was approved by the local institutional review board. All subjects and family members were extensively informed by two of three investigators (DRA, PP, and/or RC) before the initial evaluation and provided written informed consent to undergo study procedures. Patient data protection and confidentiality were ensured according to the most recent Spanish data protection legislation.

2.2. Patients

The inclusion criteria were age over 18 years and the presence of DS documented by karyotype. All adults with DS included in the study had a full trisomy 21 (we found no Robertsonian translocations or mosaics). Control participants were race-matched healthy individuals. Family members and legal guardians of adults with DS were invited to participate in this study. Siblings of adults with DS were used as controls in 42 cases (42/49, 86%); as for the remainder, two were parents of adults with DS, and five were unrelated healthy individuals. The exclusion criteria were as follows: severe congenital heart disease not treated with surgery, severe sensory impairment, inability to provide consent, pregnancy, and a known diagnosis of diabetes mellitus or metabolic syndrome.

2.3. Measurements

The following variables were collected in all study subjects: age (years), gender, height (cm), weight (kg), BMI (kg/m^2), waist circumference (cm), waist-to-height ratio (WHR), and total body fat percentage. Height was measured with a