

AUTOIMMUNITY DOES NOT CONTRIBUTE TO THE HIGHLY PREVALENT GLUCOSE METABOLISM DISTURBANCES IN A JAPANESE BRAZILIAN POPULATION

The Japanese Brazilian population has one of the highest prevalences of diabetes worldwide. Despite being non-obese according to standard definitions, their body fat distribution is typically central. We investigated whether a subset of these subjects had autoantibodies that would suggest a slowly progressive form of type 1 diabetes. A total of 721 Japanese Brazilians (386 men) in the 30- to 60-year age group underwent clinical examination and laboratory procedures, including a 75-g oral glucose tolerance test and determinations of serum autoantibodies. Antibodies to glutamic acid decarboxylase (GADab) were determined by radioimmunoassay and to thyroglobulin (TGAb) and thyroperoxidase (TPOAb) by flow-cytometry assays. Mean body mass index was 25.2 ± 3.8 kg/m², but waist circumference was elevated according to the Asian standards. Diabetes, impaired glucose tolerance, and impaired fasting glycemia were found in 31%, 22%, and 22%, respectively, and 53% of the subjects had metabolic syndrome. Glutamic acid decarboxylase (GADab) was positive in 4.72%, TGAb in 9.6%, and TPOAb in 10% of the whole sample. When participants were stratified according to the presence of thyroid antibodies, similar frequencies of GADab were found in positive and negative groups. The prevalence rates of glucose metabolism disturbances did not differ between GADab positive and negative groups. Our data did not support the view that autoimmune injury could contribute to the high prevalence of diabetes seen in Japanese Brazilians, and the presence of co-morbidities included in the spectrum of metabolic syndrome favors the classification as type 2 diabetes. (*Ethn Dis.* 2007;17:78–83)

Key Words: Diabetes, Glutamic Acid Decarboxylase Antibodies, Thyroid Antibodies, Metabolic Syndrome, Japanese Migrants

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INTRODUCTION

Japanese Brazilians have one of the highest prevalences of diabetes mellitus worldwide: 36.2% and a seven-year incidence of 30.9 per 1000 persons.¹ Environmental and lifestyle changes have been implicated in the increasing prevalence of diabetes among Japanese migrants. Weight gain is a direct consequence of changes in diet and physical activity, and obesity is one of the strongest risk factors for type 2 diabetes.⁴ The World Health Organization (WHO) defines obesity as a body mass index (BMI) of 30 kg/m²,⁵ while the Japanese Society for the Study of Obesity defines it as ≥ 25 kg/m².⁶ Japanese Brazilians are relatively non-obese when compared to the Brazilian general population,^{7,8} but although overweight and obesity are more common in the Brazilian general population, the prevalence of diabetes is much higher in Japanese descendants living in Brazil under the same environmental conditions.⁹ Such an intriguing situation has motivated a number of investigations.

Slight weight gain in Japanese people is associated with insulin resistance and diabetes.¹⁰ Type 2 diabetic subjects are commonly non-obese and have reduced insulin response to glucose stimulation even during the preclinical phase.¹¹ The disease is markedly different from the classical type 2 diabetes seen in Caucasians, which is associated with obesity-induced insulin resistance.¹² Beta-cell deficiency occurs early in the course of the disease in Japanese subjects even in the prediabetic phase.¹¹ Proinsulin was predictive of diabetes in Japanese Americans¹³; this hormone

could reflect primary lesions in beta cells during pathogenesis of type 2 diabetes. Reduced insulin secretion in response to oral glucose is found before the accumulation of intra-abdominal fat, which suggests that, in the natural history of the disease in Japanese subjects, beta-cell injury could occur before insulin resistance, which could be a consequence of hyperglycemia or obesity.¹⁴ Genetic susceptibility could also play a role, since the general Brazilian population has less than half of the diabetes prevalence detected in Japanese Brazilians.¹⁵

Incidence of type 1 diabetes in Japanese persons is lower than in Caucasians. The subtype of slowly progressive type 1 diabetes – latent autoimmune diabetes (LADA)—is reported in both Japanese¹⁶ and Caucasians¹⁷ who tend to be classified as having type 2 diabetes. Latent autoimmune diabetes (LADA) could be diagnosed by circulating specific autoantibodies, such as the glutamic acid decarboxylase antibody (GADab), which is a sensitive and specific marker for autoimmune diabetes.¹⁸ Type 1 diabetes may be associated with other autoimmune diseases. The Belgian Diabetes Registry found a 22% prevalence of thyroperoxidase antibodies in patients with type 1 diabetes.¹⁹ Thyroid autoantibodies are common and may be present for years without progression to overt thyroid disease.²⁰ We hypothesized that autoimmune factors present among the Japanese Brazilian population could indicate an insulin secretion deficiency induced by immunologic injury that, in association with the genetic predisposition to metabolic syndrome, may account for the high prevalence of diabetes.