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Latent autoimmune diabetes amongst adults with type 2 diabetes in a Nigerian tertiary hospital

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ABSTRACT

Aims: The aim was to investigate the frequency and characteristics of persons with latent autoimmune diabetes in adults (LADA) amongst patients who had been clinically diagnosed as type 2 diabetes mellitus (CT2DM) in a tertiary care centre.

Methodology: One hundred and sixty patients with CT2DM participated in this cross-sectional study following selection by systematic random sampling. Demographic data, relevant clinical history and anthropometric measurements (weight, height, waist circumference and hip circumference) were taken and blood samples were obtained for analysis of fasting blood glucose, glycated haemoglobin (HbA1c) and glutamic acid decarboxylase antibodies (GADA). The results were analysed using SPSS version 16.

Results: Nineteen (11.9%) out of 160 persons with CT2DM were positive for GADA. 95(59.4%) of the total study population were females. The mean (SD) age, BMI, waist circumference, were 60.49 (10.37) years, 26.47 (4.80) kg/m^2, 92.16 (11.50) cm respectively.

Subjects with CT2DM who were GADA positive had trend towards lower mean BMI (25.64 kg/m^2 vs. 26.59 kg/m^2) and waist circumference (89.80 kg/m^2 vs. 92.47 kg/m^2) than GADA negative subjects. GADA positive subjects also had a trend showing higher mean fasting blood glucose (144 mg/dl vs. 125 mg/dl, $t = 2.20$, $p = 0.14$), higher mean HbA1c (7% vs. 6.1%, $t = 3.19$, $p = 0.077$) and a higher proportion on insulin (31.6% vs. 22%, $\chi^2 = 0.07$, $p = 0.25$) when compared with GADA negative patients.

Conclusion: The prevalence of LADA amongst a subset of Nigerians with CT2DM was 11.9%. There were no distinguishing clinical features to help characterize persons with LADA. The above finding emphasizes the importance of GADA testing for appropriate classification of persons with CT2DM. Early diagnosis of LADA would help direct appropriate therapy to optimize glycaemic control.

Abbreviations: ADA, American Diabetic Association; BMI, body mass index; BP, blood pressure; CT2DM, clinical type 2 diabetes mellitus; DCCT, Diabetes Control and Complications Trial; DM, diabetes mellitus; EDTA, ethylenediamine tetra acetic acid; GAD, glutamic acid decarboxylase; GADA, glutamic acid decarboxylase antibody; HbA1c, glycated haemoglobin; HLA, human leucocyte antigen; IAA, autoantibody to insulin; IA-2A, IA-2β, autoantibody to tyrosine phosphatases; ICA, islet cell antibody; IDDM, insulin dependent diabetes mellitus; IDF, International Diabetes Federation; LADA, latent autoimmune diabetes in adults; MOP, Medical Outpatients Clinic; MRDM, malnutrition related diabetes mellitus; OHA, oral hypoglycaemic agents; Type 1 DM, type 1 diabetes mellitus; Type 2 DM, type 2 diabetes mellitus; UKPDS, United Kingdom Prospective Diabetes Study; WHO, World Health Organization.

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1. Introduction

In routine clinical practice, persons with diabetes are categorized as type 1 or type 2 on the basis of their mode of presentation and phenotypic appearance. Following such classification, the first line of management is usually lifestyle modification followed by medications which may be insulin therapy or oral hypoglycaemic agents (OHAs) or a combination of both. Some patients diagnosed clinically as persons with type 2 diabetes have surprisingly been shown to have autoantibodies, indicating diabetes of autoimmune aetiology.

Latent autoimmune diabetes in adults (LADA) has been described as slowly progressive form of diabetes which results from autoimmune mediated destruction of the beta cells of the pancreas [1]. It is regarded as a sub-classification of type 1 diabetes mellitus (type 1 DM) but patients usually present with an insidious onset of disease suggestive of type 2 diabetes mellitus (type 2 DM). The presence of autoantibodies to islet cell antigens in adults clinically considered to have type 2 DM at the time of diagnosis has been found to be associated with gradual autoimmune β islet cell destruction [1]. Glutamic acid decarboxylase antibody (GADA) has been found to be the most prevalent antibody detected in LADA and in most cases the only detectable autoantibody [2].

The diagnosis of LADA is currently based on three criteria which include adult age at the time of diagnosis of diabetes, the presence of circulating autoantibody to pancreatic islet cell antigens, and the lack of requirement for insulin at the time of diagnosis of diabetes mellitus [3].

It is important to identify this group of patients who may have LADA because its natural history and treatment strategy are different from that of type 2 DM. They often experience marked loss of beta cell function within a few years of diagnosis and much earlier requirement for insulin compared with persons with type 2 DM. Therefore, early identification of LADA may help to convince patients and health care providers on the importance of a quicker and smoother transition to insulin therapy, rather than persistence with oral agents in the face of poor glycaemic control. These measures may help to improve metabolic control and reduce the risk of development of long term complications of DM.

2. Methods

This was a cross-sectional study of 160 consenting persons with type 2 diabetes mellitus based on clinical presentation. It was carried out over a 3-month period after ethical clearance had been obtained from the Joint Institution Review Committee (IRC) of the University College Hospital and the College of Medicine, University of Ibadan. (UI/IRC/07/0068).

3. Sampling technique

The study was conducted at the Medical outpatient clinic, University College Hospital, Ibadan. The calculated sample size was 138 patients using the formula by Lesie & Kisch $n = Z^2pq/d$. An average of 14 patients was selected weekly using systematic random sampling. The first patient was randomly selected and every third patient who satisfied the inclusion criteria was recruited into the study, after obtaining consent.

Anthropometric measurements were taken which included weight (kg), height (m), waist circumference (cm) and hip circumference (cm). Blood samples were obtained for analysis of fasting plasma glucose (FPG), HbA1c and antibodies to glutamic acid decarboxylase.

4. Clinical assessment

4.1. *Weight and height measurement*

Weight was measured (in kilograms) using a beam balance scale with subjects in light clothing and without shoes on. Height was also measured (in metres) using a portable height/length measuring board without the subjects wearing footwear, caps or other head gear. The head was kept in anatomical position and the highest point was taken as the height. Body mass index (BMI) was then calculated using the formula BMI = Weight/Height^2 (kg/m^2). A BMI of 18.5–24.9 was taken as normal. Values of 25–29.9 was in keeping with overweight and obesity with a value >30 [4].

4.2. *Waist circumference measurement*

The waist circumference was measured using a flexible inelastic tape measure with the subject standing and breathing normally using the protocol recommended by the World Health Organization (WHO expert committee 1995). Standing to the side of the subject, without belts or heavy outer clothing, measurement was made directly over the skin. The subject stood comfortably with weight evenly distributed on both feet, and the feet apposed together. The arms hung loosely at the sides while the inferior margin (lowest point) of the last rib and the iliac crest (top of the hip bone) was located and marked with an erasable pen. The midpoint was determined with the use of a tape measure and the point marked. The tape rule was then applied over the marked midpoint and a check was made to ensure that the tape was horizontal across the back and front of the subject. The waist circumference was measured and read at the level of the tape to the nearest 0.1 cm. A waist circumference of ≥80 cm in females and ≥94 cm in males was taken as indicative of truncal obesity [5].

4.3. *Hip circumference measurement*

The hip circumference was measured with the arms relaxed at the sides and standing with their feet together. The measuring tape was placed around the maximum circumference over the buttocks according to the WHO STEPS instrument [6]. The hip circumference was then measured and read at this level to the nearest 0.1 cm. This was measured only once and recorded on the subject's questionnaire. The waist to hip ratio was also calculated and recorded in the questionnaire.

4.4. *Blood pressure measurement*

Blood pressure was measured with the patients seated after at least 5 min rest. A mercury sphygmomanometer with a