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Alternative indices of glucose homeostasis as biochemical diagnostic tests for abnormal glucose tolerance in an African setting

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ABSTRACT

Aims: Accurate diabetes diagnosis is important in Africa, where rates are increasing, and the disease largely undiagnosed. The cumbersome oral glucose tolerance test (OGTT) remains the reference standard, while alternative diagnostic methods are not yet established in Africans. We assessed the ability of fasting plasma glucose (FPG), HbA1c and fructosamine, to diagnose OGTT-based abnormal glucose tolerance in mixed-ancestry South Africans.

Methods: Mixed-ancestry adults, residing in Cape Town were examined between February and November 2015. OGTT values were used to classify glucose tolerance status as: screen-detected diabetes, prediabetes, dysglycaemia (combination of diabetes and prediabetes) and normal glucose tolerance.

Results: Of the 793 participants included, 65 (8.2%) had screen-detected diabetes, 157 (19.8%) prediabetes and 571 (72.0%) normal glucose tolerance. Correlations of FPG and 2-h glucose with HbA1c ($r = 0.51$ and 0.52) were higher than those with fructosamine (0.34 and 0.30), both $p < 0.0001$. The highest c-statistic for the prediction of abnormal glucose tolerance was recorded with 2-h glucose [c-statistic = 0.997 (screen-detected diabetes), 0.979 (prediabetes) and 0.984 (dysglycaemia)] and the lowest with fructosamine (0.865, 0.596 and 0.677). At recommended or data-specific optimal cut-offs, no combination of FPG, HbA1c and fructosamine did better than 2-h glucose, while FPG was better than HbA1c and fructosamine on a range of performance measures.

Conclusions: Abnormal glucose tolerance in this population is overwhelmingly expressed through 2-h glucose's abnormalities; and no combination of FPG, HbA1c and fructosamine was effective at accurately discriminating OGTT-defined abnormal glucose tolerance. Tested

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non-glucose based strategies are unreliable alternatives to OGTT for dysglycaemia diagnosis in this population.

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1. Introduction

Diabetes mellitus has reached epidemic proportions worldwide, with the fastest relative growth of the population with diabetes occurring in sub-Saharan Africa (SSA). Another distinctive feature of diabetes in SSA is the high proportion of people with diabetes whose disease remains undiagnosed. According to the 7th International Diabetes Federation (IDF) Diabetes Atlas, nearly two-third of the 14.2 million SSA adults with diabetes in 2015, were undiagnosed [1]. The ill-prepared health care system to efficiently address non-communicable diseases in general, contributes to some extent to the unfavourable prevailing diabetes prevention and control performances across Africa. The situation is compounded by the challenging applicability and performance of existing tools for diabetes screening and diagnosis in the African setting [2,3].

The combination of a fasting and 2-h blood glucose values during an oral glucose tolerance test (OGTT) has been for decades, the reference standard to diagnose diabetes and abnormal glucose tolerance in general [4]. However, recommendations for diabetes diagnosis vary, with the American Diabetes Association (ADA) for instance recommending the use or either fasting glucose or 2-h glucose, and not necessarily their combination [5]. It has been shown that the use of fasting glucose alone would fail to diagnose diabetes in a significant proportion of individuals with the disease [6]. In recent years, glycated haemoglobin (HbA1c) measurement was also introduced as an alternative to glucose-based diabetes diagnosis [5]. HbA1c based strategies have multiple advantages: being less time demanding, and not requiring fasting. However, HbA1c measurement is limited by factors that can interfere with red cells longevity, membrane permeability, haemoglobin content and quality. As a consequence, variable performances of HbA1c to diagnose abnormal glucose tolerance, have been reported across ethnic diversities and settings [7,8]. Evidence from few studies performed in Africa as well as in migrant Africans do not support an uncritical applicability of ADA [5] recommended standards to diagnose diabetes using HbA1c in African populations. Other suggested indices of glucose homeostasis for abnormal glucose tolerance detection include fructosamine, glycated albumin and 1,5-anhydroglucitol. But, their diagnostic utility for abnormal glucose tolerance has yet to be established in the African setting. Studies elsewhere have reported racial differences in the levels of glycated proteins, not always reflecting phenomenon related to glucose metabolism, with Africans Americans for instance reported to display higher levels of HbA1c than Caucasian Americans [9]. These racial variations in HbA1c levels could lead to race-specific discordances between HbA1c (and glycated proteins in general) and glucose-based tests in classifying glucose tolerance statuses.

In the current study, we have tested the capability of HbA1c, fructosamine and fasting plasma glucose, singly or in combination, to diagnose OGTT-based abnormal glucose tolerance including screen-detected diabetes, prediabetes (i.e. impaired fasting glycaemia and/or impaired glucose tolerance) and the combination of both (dysglycaemia) in mixed-ancestry South Africans. In a clinical setting, the interest resides in accurately distinguishing people with prediabetes and those with diabetes for the prescription of measures to prevent the full development or progression of diabetes. In community-based settings however, the interest likely reside in picking up people requiring confirmatory test in clinical setting for suspected abnormal glucose tolerance (dysglycaemia).

2. Subjects, material and methods

2.1. Study design, and population

The current study uses data from the ongoing Cape Town Vascular and Metabolic Health (VMH) study, an extension of the Cape Town Bellville South study, which has been described in detail previously [10]. The wave of cross-sectional data collection for the current analysis took place between February 2015 and November 2015 during a community-based survey involving Mixed-ancestry South Africans residing in the Township of Bellville South in Cape Town. According to the 2011 population census, its population stands at approximately 29,301. The population is predominantly of mixed ancestry or coloured (76%) followed by black Africans (18.5%) and Caucasian and Asians making only 1.5%. The study was approved by the Research Ethics Committees of the Cape Peninsula University of Technology (CPUT) and Stellenbosch University (respectively, NHREC: REC—230 408–014 and N14/01/003), and conducted in compliance with the code of ethics of the World Medical Association (Declaration of Helsinki). All included participants voluntarily signed a written consent after the procedures had been fully explained in the language of their choice. Permission to conduct the study was also obtained from relevant authorities including the city and community authorities.

2.2. Interviews and physical examination

All interviews and physical examinations took place starting at 8 am at a research clinic located within the study suburb. Self-selected participants were asked to fast overnight and were transported to the clinic and back home by a minibus. All interviews and examinations were conducted by trained research team. The field workers collected data on demographics, personal and family medical histories, ongoing treatments, and habits including smoking using a questionnaire on a password-protected personal digital assistant

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