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Review Article

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Correlation Between Glycosylated Haemoglobin and Fasting Plasma Glucose in Africans - A Review

Dr. Ademolu Adegbenga Bolanle

Department of Medicine, Lagos state university teaching hospital (LASUTH), Ikeja, Lagos, Nigeria

***Correspondence to:** Dr. Ademolu Adegbenga Bolanle, Department of Medicine, Lagos state university teaching hospital (LASUTH), Ikeja, Lagos, Nigeria.

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Abstract

Aim/Objectives

In recent times, the use of glycosylated haemoglobin in the diagnosis of diabetes mellitus was adopted by major stakeholder in biochemical definition and management of diabetes mellitus. This includes bodies like World Health Organisation (WHO), American Diabetic Association (ADA). The present consensus is that a glycosylated haemoglobin of 6.5% or more by definition is diabetes mellitus. Furthermore, HbA1c is generally acceptable as a chronic measure of control of diabetes mellitus worldwide.

Fasting plasma glucose (FPG) is an age long biochemical definition of diabetes mellitus with the value presently put at equal to or greater than 126mg/dl (7.0mol/l) prediabetes is FPG equal to or greater than 110mg/dl and less than 126mg/dl (≥6.1 and < 7.0mmol/l).

While correlation in glycosylated haemoglobin and FPG have been done in white population, there is no study on this in Africans to the best of my knowledge. The aim of this review is to sensitise researchers towards a study on correlating these two biochemical parameters in Africans.

Discussion

In a previous pilot study checking the FPG of 120 Africans in Lagos Nigeria, it was affirmed that the range of FPG among Africans is from normal to prediabetes to diabetes. No correlation was done then as HbA1c was not done but was suggested for further expansion of the pilot study.

Different organizations have targets for glycosylated haemglobin. It is generally unacceptable at HbA1c greater than 8%.

If this study is carried out, we will be able to appreciate the distribution of glycosylated haemoglobin among Africans whether they are at highly desirable target or not, and will be able to correlate the normal, prediabetic and diabetic African population using both parameters.

Conclusion

A correlation between glycosylated haemoglobin and fasting plasma glucose is needed in Africans.

Introduction

According to the World Health Organization, the term diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long term damage, dysfunction and failure of various organs [1].

In recent times, the use of glycosylated haemoglobin in the diagnosis of diabetes mellitus was adopted by major stakeholder in biochemical definition and management of diabetes mellitus. This includes bodies like World Health Organisation (WHO) [2], American Diabetic Association (ADA) [3].

Glycated haemoglobin has been in use to monitor control of blood glucose in diabetic patients for about three decades. It provides an average blood glucose level during preceding 10 - 12 weeks. It is a very convenient blood test, can be done in any clinical setting regardless of prandial state. There were thirty different laboratory methods available to measure glycated haemoglobin with significant variability of results on same sample [4].

The use of HbA1c as a test went through nearly three decades of detailed scrutiny before being accepted as a diagnostic test for diabetes.

Researchers had long been searching for test of glycaemia that could be used to screen and diagnose diabetes as well as monitor the chronic glycaemic control; such as test, may also be able to predict the onset of complications. Glycated haemoglobin acquires importance as a test for glycaemia because it has less intra individual variation and is a better predictor of cardiovascular complications compared to fasting plasma

glucose (FPG) and oral glucose tolerance test (OGTT) [4]. In addition, it is used for glucose monitoring of diabetic patients [5,6]. In another study HbA1c and FPG showed continuous relationship with cardiovascular disease [7].

Glycated Hb has been accepted as the gold standard measurement for the assessment of chronic hyperglycaemia for nearly three decades. There are thirty different laboratory methods available to measure glycated haemoglobin. Various analytical methods based on different assays principles, from ion-exchange chromatography to immunoassay and electrophoresis have been used to measure glycated haemoglobin. Such a lack of standardization resulted in wide variability within results (4.0% to 8.1%) on the same sample [8] making it difficult to compare patients results among laboratories. This disparity has always been a source of anxiety among health care providers.

It becomes even more important in this age of heavy economical migration, when people travel long distances and take their native record with them. Therefore, having same method and unit to measure HbA1c is need of the day [4].

Glycosylation is sometimes used for glycation in the medical literature, usually as non-enzymatic glycosylation. In the normal 120-day lifespan of the red blood cell, glucose molecules react with hemoglobin, forming glycated hemoglobin [9]. In individuals with poorly controlled diabetes, the quantities of these glycated hemoglobins are much higher than in healthy people.

Once a haemoglobin molecule is glycated, it remains that way. A buildup of glycated haemoglobin within the red cell, therefore, reflects the average level of glucose to which the cell has been exposed during its life-cycle. Measuring glycated hemoglobin assesses the effectiveness of therapy by monitoring long term serum glucose regulation. The HbA1c is proportional to average blood glucose concentration over the previous four weeks to three months and it is measured in percentage or mmol/mol (millimole per mole) [10].

On the other hand, fasting plasma glucose is an age long biochemical definition of diabetes mellitus and is measured in milligram per deciliter (mg/dl) or millimole per litre (mmol/l).

In taking fasting plasma glucose, it is expected that the patient has fasted for 8 hours'. However, it should be noted that fasting plasma glucose is a dynamic quantitative measure of plasma glucose as its value 8 hours' and 9 hours' post begining of fasting may not be the same, for instance the value at 6.00 am; 7.00 a.m and 8.00 am may all differ in the same patient that begins fasting 10p.m the previous night.

While studies correlating these two parameters have been done among white population [2,3], this has not been replicated in Africans to the best of my knowledge. The aim of this review is to sensitize researchers with interest in African health to correlate these two biochemical parameters to the benefit of Africans in the Africa continent and in diaspora.

Literature Review

Though the disease Diabetes Mellitus has been in existence before the time of Hippocrates, there were no biochemical diagnostic criteria then as diagnosis was majorly clinical.

However, in the last five decades the World Health Organisation has published several guidelines for the diagnosis of Diabetes Mellitus [11-14]. In its 2005 consultation it was emphatically said by WHO that HbAlc should not be adopted as a diagnostic test, as the challenges of measurement accuracy outweighed the convenience of its use [2].

In a sharp contrast in its 2011 consultation, the World Health Organisation said an HbAlc of 6.5% is recommended as the cut off point for diagnosing diabetes. A value less than 6.5% does not exclude diabetes mellitus diagnosed using glucose test. The expert group concluded that there is currently insufficient evidence to make any formal recommendation on the interpretation of the HbAlc levels below 6.5%.

In the light of this paucity of data the challenge of correlating glycosylated haemoglobin with fasting plasma glucose among Africans should be taken up among Africans either by individual researchers, non-governmental organization, governmental organization like African Union or WHO -sponsored.

Nowadays, Diabetes may be diagnosed based on A1C criteria or plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-h plasma glucose (2-h PG) value after a 75-g oral glucose tolerance test (OGTT) [15,16]. The same tests are used to both screen for and diagnose diabetes. Diabetes may be identified anywhere along the spectrum of clinical scenarios: in seemingly low-risk individuals who happen to have glucose testing, in symptomatic patients, and in higher-risk individuals whom the provider tests because of a suspicion of diabetes. The same tests will also detect individuals with prediabetes. The A1C test should be performed using a method that is certified by the National Glycohemoglobin Standardization Programme (NGSP) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay [17].

The A1C has several advantages to the FPG and OGTT, including greater convenience (fasting not required), greater preanalytical stability, and less day-to-day perturbations during stress and illness. These advantages must be balanced by greater cost, the limited availability of A1C testing in certain regions of the developing world like Africa, and the incomplete correlation between A1C and average glucose in certain individuals.

It is important to take age, race/ethnicity, and anemia/hemoglobinopathies into consideration when using the A1C to diagnose diabetes. The epidemiological studies that formed the framework for recommending A1C to diagnose diabetes only included adult populations. Therefore, it remains unclear if A1C and the same A1C cut point should be used to diagnose diabetes in children and adolescents [18-20].

A1C levels may vary with patients' race/ethnicity [21,22]. For example, African Americans may have higher A1C levels than non-Hispanic whites despite similar fasting and postglucose load glucose levels. A recent epidemiological study found that, when matched for FPG, African Americans (with and without diabetes) had higher A1C levels than non-Hispanic whites, but also had higher levels of fructosamine and glycated albumin and lower levels of 1,5-anhydroglucitol, suggesting that their glycemic burden (particularly postprandially) may be higher [23].

Interpreting A1C levels in the presence of certain hemoglobinopathies and anemia may be problematic. For patients with an abnormal hemoglobin but normal red cell turnover, such as those with the sickle cell trait, an A1C assay without interference from abnormal hemoglobins should be used.

In conditions associated with increased red cell turnover, such as pregnancy (second and third trimesters), recent blood loss or transfusion, erythropoietin therapy, or hemolysis, only blood glucose criteria should be used to diagnose diabetes.

In addition to the A1C test, the FPG and 2-h PG may also be used to diagnose diabetes. The concordance between the FPG and 2-h PG tests is imperfect, as is the concordance between A1C and either glucose-based test. National Health and Nutrition Examination Survey (NHANES) data indicate that an A1C cut point of ≥6.5% identifies one-third fewer cases of undiagnosed diabetes than a fasting glucose cut point of ≥126mg/dL (7.0 mmol/L) [24]. Numerous studies have confirmed that, compared with these A1C and FPG cut points, the 2-h PG value diagnoses more people with diabetes. Of note, the lower sensitivity of A1C at the designated cut point may be offset by the test's ease of use and facilitation of more widespread testing [17].

Discussion

In a previous pilot study checking the fasting plasma glucose of 120 Africans in Lagos, Nigeria, it was affirmed that the range of fasting plasma glucose among Africans in Lagos is from normal to prediabetes to diabetes. No correlation was done then as HbA1c was not done but was suggested for further expansion of the pilot study throughout Africa which is what this review is to sensitise on. To the best of my knowledge there is no study on the correlation of glycosylated haemoglobin with fasting blood sugar in Africans for epidermiological and clinical purposes. By definition, diabetes mellitus is defined as fasting plasma glucose of equal to or greater than 126mg/dl (7.0mol/l), prediabetes (impaired fasting glucose) is fasting plasma glucose equal to or greater than 110mg/dl and less than 126mg/dl (≥6.1 and < 7.0mmol/l). Also by definition, a glycosylated haemoglobin of less than 5.7% is normal; prediabetes is HbA1c between 5.7% to 6.4% while diabetes is HbA1c equal to or greater than 6.5% (HbA1c 6.5% = 48mmol/mol). Different organizations have targets for glycosylated haemglobin. It is generally unacceptable at HbA1c greater than 8%.

American Diabetes Association recommends that a target of HbA1c of less than 7% is desirable while the European Association for the study of Diabetes, (EASD), American Association of Clinical Endocrinologist (AACE), International Diabetic Federation (IDF) and World Health Organisation all recommended that a glycosylated haemoglobin of less than 6.5% is highly desirable [25].

At the practical conclusion of this study in Africans, we will be able to appreciate the distribution of glycosylated haemoglobin among African whether they are at highly desirable target or not, and will be able to correlate the normal, prediabetic and diabetic African population using both parameters that is fasting plasma glucose and glycosylated haemoglobin.

Conclusion

A correlation between glycosylated haemoglobin and fasting plasma glucose is needed in Africans to see the pattern among normal, prediabetes and diabetic African population.

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