COMMENTARY: IMPROVING PERSISTENTLY ELEVATED HbA1c IN DIABETES MELLITUS PATIENTS IN NIGERIA

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Glycated hemoglobin (HbA1c) level in patients with diabetes reflects quality of disease control and propensity to develop hyperglycemic complications. During more than 12 years of using HbA1c for monitoring of glycemic control among patients at Nigerian hospitals, the mean glycated hemoglobin ranged from 7.9% ± 2.4 to 8.3% ± 2.2. Most of these patients (63% to 68%) had poor glycemic controls with mean HbA1c greater than 7%.

Factors that are implicated in this scenario are: 1) high cost of HbA1c testing, 2) ineffective management of risk factors, 3) poor patient compliance, 4) improperly managed diabetes education program, and 5) health care system defect.

Central to improving diabetes glycemia is education of doctors, other health workers and patients, within the confines of an overhauled national health system. Physicians need to increase adherence to diabetes mellitus management guidelines and patients must be enrolled into a well-structured education program at health centers. Doctors, as leader of the health team, should drive such education schemes, which must be based on standard training curriculum, sufficient number of trained diabetes educators, and effective monitoring of patients. The most appropriate diabetes education model features small-to-moderate sized participant groups and makes use of motivational interviewing rather than a traditional advice-giving format.

Improved health care funding is mandatory given the issue of cost and this can be helped by increased participation of patients in Nigeria's National Health Insurance Scheme. Failure to address the persistently elevated HbA1c will affect long-term quality of life, longevity and health care services in Nigeria. (*Ethn Dis*. 2014;24[4]:502–507)

Key Words: HbA1c, Diabetes Mellitus, Nigeria, Health Care System, Diabetes Education

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INTRODUCTION

Compared to most Western European countries, Africa is reported to have a higher age-specific level of diabetes mellitus (DM), especially in urban areas of sub-Saharan Africa.[1] A published update on diabetes in Africa by the International Diabetes Federation in 2013, noted that the region is witnessing a surge in DM cases,[2] with a disease prevalence of 4.99% among those 20–79 years. The majority of DM patients in the region are aged <60 years and more than 76% of deaths due to the disease occur in same age bracket.[2] It is predicted that Africa will witness a 110% increase in DM prevalence between 2013 and 2035, with most of the affected people suffering from type 2 diabetes mellitus (DM2). This worrying level of disease burden in Africa is compounded by the observation that the region has a 7.3% prevalence of impaired glucose intolerance (IGT) and 50.7% of DM patients are undiagnosed,[2] a fact that is reflected by the increased level of morbidity and mortality among affected Nigerian patients.[3–5]

Among countries in Africa, Nigeria has the highest number of cases of DM with 3.9 million people (4.99%) affected. The country has an IGT prevalence of 7.13%, a level that makes it imperative for action to be taken now given the aging population and increasing levels of obesity, sedentary lifestyle and Westernization of local diet.[6,7] In Nigeria, studies have related DM-associated complications and mortality to suboptimal glycemic control in patients. Such complications include diabetic retinopathy, diabetic nephropathy, diabetic foot disease and cardiovascular diseases.[4,8,9]

Since earlier studies that measured HbA1c in Nigerian diabetics in the 1980s,[10,11] various other studies[8,12,13] have shown that this biomarker outweighs fasting plasma glucose measurement in the evaluation and monitoring of glycemia in our patients.

In DM, excess circulating glucose molecules cause glycation of hemoglobin (Hb) molecules in a non-reversible process that involves the condensation of glucose to the N-terminal lysine and valine of the beta-chain of HbA.[12,14] This is a slow process that takes places over the lifespan of the erythrocyte, such that blood level of HbA1c represents the integrated value for blood glucose over the preceding 6–8 weeks.[12,15] The higher the value of HbA1c, the poorer the glycemic control of a diabetic patient and the greater likelihood of diabetic complications. This makes knowledge of level of a patient's HbA1c very important in the management of diabetes mellitus. Until recently, there was no widespread use of HbA1c testing in most of our hospitals, hence diabetes mellitus patients were monitored using fasting plasma glucose testing, a test that has been manipulated by some patients in Nigeria.[13] Additional benefits of using HbA1c level for monitoring DM patients includes its freedom from day-to-day glucose fluctuations, stable pre-analytical phase, and being unaffected by exercise or recent food ingestion.[16,17] Caution must be taken in the application of HbA1c in our environment due to its variability with race/ethnicity. This is of particular significance in African-Americans and persons of African ancestry who have been found to have a higher HbA1c than Whites for comparable fasting plasma glucose (FPG).[8] Another important factor that needs monitoring in our environment is the application and interpretation of HbA1c, and its variations in the presence of high red cell turnover

conditions such as sickle cell hemoglobinopathy. This fact was recognized very early in the evolution of HbA1c testing in Nigeria when, in 1991, it was demonstrated that patients with sickle cell anemia and sickle cell traits had different values during microchromatographic measurement of glycated hemoglobin.[18]

Despite these shortcomings, HbA1c has been found useful for monitoring of diabetic patients in the country and its relationship to prevalence of diabetic complications has been established in various studies. The purpose of my review was to determine the level of HbA1c in Nigeria's diabetic population, show the extent to which use of HbA1c has reflected diabetic complications and suggest ways to address issues related to high mean levels of HbA1c in various Nigerian studies.[8,12,13]

ASSESSMENT OF GLYCEMIA

The British and American Diabetes Associations recommend regular HbA1c measurements in DM patients for improved care, especially for the purpose of reducing complications of the disease.[17] Results from the Diabetes Control and Complication Trial (DCCT) further emphasized the importance of HbA1c estimation in the long-term monitoring of diabetic patients.[19] Indeed, both the DCCT study and UKPDS[20] findings make HbA1c the gold standard in the assessment of glycemia in DM patients especially for the reasons mentioned above.[21]

For the primary assessment of glycemia in DM patients, physicians are expected to measure the HbA1c level, thus making the use of blood glucose determination, pre- or/and post-prandial glucose measurements, as secondary assessment tool in DM management. Such secondary measurements include fasting plasma glucose (FPG) and random plasma glucose (RPG) levels.[21] It is important to note that the use of a secondary glucose assessment tool is primarily for self-monitoring of blood glucose, a factor that can influence day-to-day decision making in DM management.[22,23]

HbA1c target goals are set at $<7.0\%$ (53 mmol/mol), with some suggesting set target value of HbA1c $<6.5\%$ (48 mmol/mol). If possible, individualization of these targets is advised, so as not to over-treat and tip patients into hypoglycemia, especially those who have hypoglycemia unawareness or history of severe hypoglycemia. In patients who achieve set monitoring targets, measurement of HbA1c should be performed at least twice a year, but for those outside the target, testing of blood glycated level should be more frequent, with the rate dependent on clinic-laboratory status of the patient.[21,24] Elevated blood level of HbA1c ($\geq 7.0\%$) does not only infer poor glycemic control, it also mean that affected patients are more prone to developing complications from the disease,[20] and this should ring the alarm bell for both doctor and patient.

LONG-TERM BENEFITS OF USING HBA1C IN DM MONITORING

The advantages of HbA1c allow prompt disease diagnosis and commencement of treatment, thus allowing for improved monitoring of the disease for good glycemic control.[25] If we can fully take advantage of these benefits of HbA1c, it has the potential to reduce observed high prevalence (50%) of complications of DM reported at the time of diagnosis,[26] particularly when intense effort is applied to the patient's treatment.

The knowledge of HbA1c level and commencement of appropriate treatment can result in the reduction of diabetic complication. This has been demonstrated in the DCCT, Kumamoto Study and UKPDS, where it was reported that 1% absolute reduction in HbA1c will result in 30–35% reduction in microvascular complications.[19,20,26] In patients treated intensively for hyperglycemia and able to achieve up to 1% decrease in HbA1c level, Okhubo et al found an associated 14% reduction in macrovascular complications.[27] This further emphasizes the importance of measuring blood HbA1c in diabetes patients as it serves as a useful guide for disease treatment.

WHAT IS THE STATE OF HbA1c LEVELS IN NIGERIAN PATIENTS WITH DIABETES?

During the study period, 2003 to 2012, the level of control of HbA1c in Nigerian patients with diabetes mellitus did not show improved glycemia with time. In 2003, among diabetic patients attending University of Ilorin Teaching Hospital Diabetic Clinic in Ilorin, Nigeria, we recorded a mean HbA1c concentration of $8.1\% \pm 1.4$.[12] By 2012, two separate studies recorded mean HbA1c levels of $8.2\% \pm 2.2$ in Edo State, Nigeria[14] and $8.3\% \pm 2.2$[8] in a multi-center study involving seven teaching hospitals in Nigeria, thus suggesting widespread poor glycemic control among diabetic patients in the country. (Table 1) In the Ilorin study, 64% of the study population had a mean HbA1c $\geq 7.2\%$; this was similar to the Edo study and Nigeria multicenter study, which had 63% and 68%, respectively, of patients with mean HbA1c $>7.0\%$.[8,13]

This persistent long-term poor glycemic control in Nigeria's diabetics is responsible for increasing burden of diabetic complications in our patients. The prevalence of diabetic retinopathy in the country was 15.1% in 1989 in Ilorin, Nigeria.[28] By 2003, a multicenter study found diabetic retinopathy prevalence of 24%, 20.9% and 16% in Lagos, Ibadan and Enugu cities respectively in Nigeria, and these are comparable to the 24% noted in Accra,

Table 1. The level of mean HbA1c found in studies of Nigerian patients with diabetes

Study	Level of HbA1c Mean ±SD	% of Population with Poor Glycemia
Adebisi SA et al. *WAJM*. 2003[12]	8.0% ± 1.4	64
Edo AE et al. *NJCP*. 2012[13]	8.2% ± 2.2	63
Adesina OF et al. *AJDM*. 2012[33]	7.9% ± 2.4	-
Chinenye S et al. *Int J Endocrinol Metal*. 2012[8]	8.3% ± 2.2	68

Ghana.[29] About two decades after the 15.1% retinopathy prevalence recorded in Ilorin, a study carried out at the Eye Clinic, University College Hospital, Ibadan, Nigeria found a diabetic retinopathy prevalence of 42.1%.[30] These findings indicate that, in less than 25 years, the prevalence of diabetic retinopathy in Nigerian diabetes patients increased by 200% to 300% (Table 2). This increase could be due to the possibility that Africans are more at risk of developing diabetic retinopathy than other races, even with comparable disease duration.[31]

It is known that diabetes mellitus creates a huge burden on health care systems in Nigeria and other countries. In one study, it was noted that 15% of admissions in a Nigeria tertiary hospital were due to diabetes mellitus[5] and 15% of such admitted patients had foot ulcers, of which one third would result in amputation.[4] It is also reported that 30% of mortality cases from DM are prompted by diabetic foot ulcer, a complication related to hyperglycemia, peripheral neuropathy and made worse by infection.[4,5] At its current prevalence, diabetes mellitus and associated complications have a significant negative impact on the quality of life and longevity of affected Nigerians as well as creating a strain on existing health care resources.

Possible Reasons for Poor Glycemic Control in Nigerian Diabetics

In Africans, including Nigerians, poor glycemic control is due primarily to such factors as poor compliance, inadequate access to appropriate care and reduced affordability of treatment.[32] The factors that underlie the poor long-term glycemic control in Nigerian diabetes mellitus patients and by extension the associated high burden of disease complications in Nigeria include: 1) high cost of HbA1c testing, 2) ineffective management of risk factors for complications, 3) poor patient compliance, 4) poor patient education, and 5) health system defects.

High Cost of HbA1c Testing

The importance of HbA1c in monitoring of DM is appreciated by many Nigeria doctors especially those in tertiary health care centers where most studies mentioned in this article were performed. Yet, the high cost of the HbA1c test is one factor that prevents its widespread use. This problem thrives more in our cash-for-care health care practice in which patients have to pay out of pocket for treatment received including laboratory testing. In a study at Federal Medical Centre, Abeokuta, Nigeria, only 25% of diabetic patients could afford HbA1c testing ordered by the doctor. Among the 25% of patients who could afford to pay for the testing, the mean HbA1c was 7.9% ± 2.4.[33] This inability to pay for laboratory test is not unexpected given that 90.2% of Nigerians live on ≤US $2 per day,[34] thus making it difficult to expect such patients to pay for laboratory tests, drugs and consultation services.[8] To address this problem, we must increase patient participation in the National Health Insurance Scheme.

Table 2. Changes in prevalence of retinopathy as an index of diabetic complications in Nigeria

Study	% Retinopathy
Erasmus RT et al. *EAJM*. 1989[28]	15.1%
Rotimi C et al. *Ethn Dis*. 2003[29]	24%
Ashaye A et al. *Clinical Opthalmology*. 2008[30]	42.1%
Chinenye S et al. *Indian J. Endocrinol Metab*. 2012[8]	35.5%

Ineffective Management of Risk Factors for Complications

Clearly, both microvascular and macrovascular complications of DM are related to level of dysglycemia and HbA1c. The high mean level of HbA1c in our diabetic population[8,12,13] and associated complications such as diabetic retinopathy,[8,28–30] nephropathy[8] and diabetic foot ulcers[4] are established facts.

Beyond hyperglycemia,[30,35,36] hypertension,[37] hyperlipidemia,[38] and obesity,[39,40] diabetics also suffer from an increase in risk of developing diabetic retinopathy. Some studies in the country found hypertension prevalence of 61.8%[30] and 79.2%[4] among diabetic populations. The Nigeria multicenter study of diabetics[8] found that only 11% of the hypertensive diabetics had good blood pressure control. This may explain why high blood pressure has been found to be a major contributor to stroke mortality in diabetic patients in the country.[41]

Hyperlipidemia, another risk factor for retinopathy has been recorded in Nigeria diabetics,[8,42] and hypertriglyceridemia in particular has been identified as a risk factor of note in Nigerian diabetics.[43] Apart from contributing to retinopathy and other complications of DM, hypertension and hyperlipidemia contribute significantly to observed increased mortality among diabetics

admitted in Nigeria hospitals.[41] Efforts should be made to increase treatment compliance by patients and adherence to treatment guidelines by doctors in the management of these patients,[44] as good management can help ameliorate risk factors known to worsen glycemia and complications in DM patients.

The high prevalence of overweight or obesity in Nigeria diabetics, especially among female patients[12,45] is another factor needing attention as it contributes to worsening HbA1c.[11,13] In a previous study, we discussed management strategies that would improve glycemia and health outcomes of obese diabetes patients.[45]

Poor Patient Compliance

One problem solved by the use of HbA1c rather than FPG in the management of DM patient is lack of patients' compliance with doctors' instruction before visiting the laboratory for measurement of FPG.[13]

Diabetic patients in the country have been found to have poor response to referrals for further assessment of their conditions. For example, among a group of patients seen at a diabetes clinic and sent for eye examination, only 57% of them reported to the eye clinic for assessment.[30] The issue of poor compliance by some patients has been related to their finding it difficult to accept a medical condition needing lifelong treatment.[8]

Ineffective Patient Education

The benefit of effective patient education include reduced glycated hemoglobin, reduced body weight, reduced systolic blood pressure and decreased need for medication.[46] In most of our diabetes clinics, education programming on diabetes is not optimum as it is not curriculum driven; and, there is often lacking a proper record of a patient's attendance to effectively monitor the program. Despite these shortcomings, patients who attend some form of diabetic education program in the country have been found to have better glycemic control.[8]

Studies carried out in the Western Cape Province of South Africa revealed a population with poor glycemic levels similar to ours with more than 80% of their patients having HbA1c >7.0%.[45,47] To address the dismal picture of diabetes care in South Africa, a chronic care team was established and helped to implement a structured diabetes education program for the country.[48] Such a structured program, which is professionally driven and based on a proven curriculum, has been found to be effective in improving patients' glycemic control and reducing risk factors such as obesity and high blood pressure.[49]

While some authors have canvassed the coaching approach of a stepped-cared model tailored to individual patient's preference,[50] this form of diabetes education may be too expensive in our environment where trained personnel are insufficient. The use of motivational interviewing methods that clearly outperform traditional advice-giving methods in diabetes education[51] could benefit our patients.

Nigeria should consider setting up a chronic care team at the national, regional or state levels to anchor these evidence-based suggestions, in a systematic manner. This team would evaluate the unmet needs in diabetes care in the country and recommend strategies and solutions, including availability of diabetes educator and training curriculum, which would be monitored for effectiveness. Based on others' successes, the education component would be wise to adapt motivational interviewing methods and small patient education groupings that would take into consideration local experiences and culture, as was done in South Africa.[52]

Health Care System Defect

A significant contributor to the problem of poor glycemic control is Nigeria's defective health care system, which is not prepared to implement population wide preventive strategies for non-communicable diseases (NCD). The health system in Nigeria is structured into primary, secondary and tertiary levels of care, and these are operated on the local, regional/state and national/federal levels of government, respectively. However, this division of care is not strictly adhered to, with most regions/states investing heavily in tertiary level care to the detriment of others, particularly primary health care (PHC).[53]

The various problems identified with PHC in the country includes insufficient number of health centers, inadequate health professionals, inadequate funding, poor community involvement and abuse of scarce resources by political leadership at this level.[54–58] Implications of poor management of PHC are delayed diagnoses, ineffective preventive services, and undue pressure on secondary and tertiary level health care services. This pressure is reflected in the poor state of glycemic control as indicated by elevated mean glycated hemoglobin over the years. For example, studies have revealed that most Nigerian health care workers whose primary assignment is outside tertiary health care institutions are not familiar with current practice guidelines, including diabetes education, for the management of DM patients.[59,60]

Addressing the issues presently identified with PHC needs the attention of policy makers and government, for a reappraisal and reorganization of our health priorities and PHC system. This effort might not immediately bring down the high levels of glycated hemoglobin in our diabetic population, but it will, in the long run, put the health system in shape for effective management of NCDs. Failure to restructure our health care system may result in Asuzu's 2004 warning[53] coming true: "The neglect of the primary health care system, its mal-distribution as well as the secondary health care, will result in an inverted health care pyramid. This will not produce any health

for the people but will always have the threat to collapse on itself.''

CONCLUSION

As in most developing countries, the prevalence of DM is rising rapidly in Nigeria due to urbanization, Westernization of life styles, obesity, increased longevity and possible genetic predisposition. This portends huge health care challenges for our country, especially in the presence of high prevalence of poor glycemic control and associated disease complications. There is an urgent need for a health care system overhaul and a purposeful DM care model that should target: early disease diagnosis; increased and affordable use of HbA1c monitoring for effective management of glycemia and associated risk factors of diabetic complications; and development of community-oriented structured diabetes-education programs that incorporate motivational interviewing.

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