

# **ADVOCATING THE USE OF HbA1C FOR DIAGNOSIS OF DIABETES IN AFRICA**

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# INTRODUCTION

Prevalence of type 2 diabetes mellitus is on the increase worldwide and Africa is not an exception.

AS AT 2014 ESTIMATE

- ❖ Worldwide Confirmed people with diabetes is about 387 million
- ❖ Prevalence of diabetes in the world was 9%, among adults aged 18 years or older.

It is projected that by the year 2035, those affected by diabetes will be around 592 million.

# INTRODUCTION CONT.

- Among the total diabetes patients, 77% live in low- and middle-income countries and 40–49-year olds have the largest number of people of any group.
- It is estimated that about 179 million people remain undiagnosed, for various reasons, and they may present with complications of diabetes<sup>1</sup>.
- Many patients with diabetes are without symptoms and will therefore require screening, making use of biomarkers for the detection of the disease.
- Every seven seconds, diabetes causes the death of an individual worldwide, and
- in 2014 alone, 4.9 million deaths were attributed to diabetes with 80% of deaths related to diabetes reported from low- and middle-income countries<sup>2</sup>.

# INTRODUCTION CONT.

- Prompt diagnosis or even the detection of those at risk thereby preventing the disease or delaying its onset will go a long way in preventing complications and the attendant morbidity and mortality.
- Traditionally fasting blood glucose and oral glucose tolerance tests were the methods in use for diagnosis diabetes and newly introduce HbA1c has introduced new dimensions.

# HBA1c BRIEF HISTORY

## HBA1c

- 1955 it was discovered
- 1968 Elevation in Diabetes was noted
- 1977 Correlation with blood glucose
- 1996 NGSP National Glycohemoglobin Standardization Programme was founded
- 1993-1912 Joint NGSP/IFCC Standardization accuracy was improved

# CURRENT SITUATION WITH HBA1c

- HbA1c was accepted by ADA in 2009 and WHO in 2011<sup>4,5,6</sup> for the diagnosis of type 2 diabetes.
- This was based on the use of laboratory methods for the measurement and not for use of point of care testing (POCT) instruments.
- WHO at that time envisaged some problems and this method of diagnosis of Type 2 DM was not recommended for the developing world.
- Such problems include: difficulties with cost, availability and accuracy, alternative method was therefore recommended for the developing world.
- However, with marked Improvement in the instruments in the market there is need to review this position for Africa for reasons that I will put forward .

# PERCULIAR PROBLEMS OF AFRICA

- Despite the fact that HbA1c had been widely introduced for monitoring of diabetes since more than three decades ago and more recently for diagnosis, its use in Africa is still very scanty.
- Most centers in Africa, Nigeria in particular do not assay HbA1c and when they do it is only used for monitoring and not for diagnosis.

# Peculiar problems of Africa cont.

- During revision course of WACP at Ibadan 2 years ago, in an attempt to gather information for the filling of a questionnaire on HbA1c measurement survey by IFCC, I interviewed residents from various part of Nigeria who assembled at Ibadan.
- The responses were that most centers ( Teaching Hospitals) measure HbA1c using PCOT but only for monitoring of glycemic control.

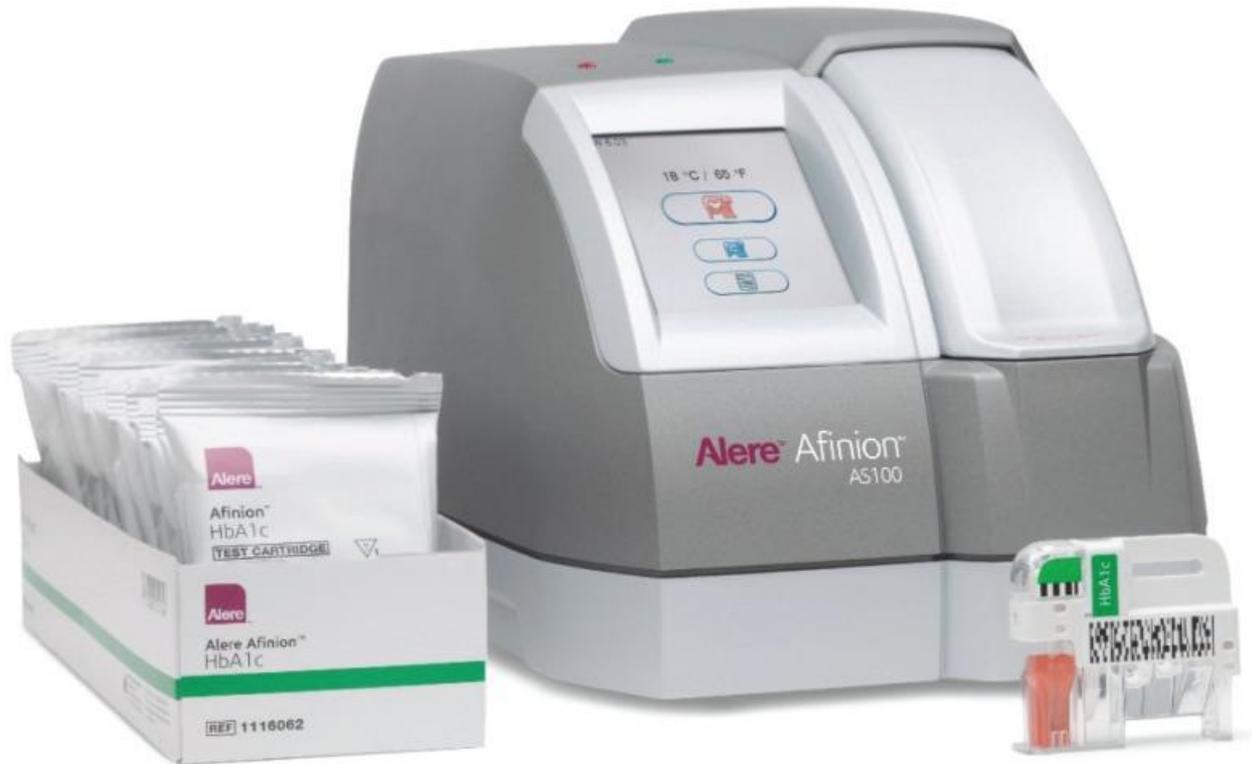
# Perculiar problem of Africa cont.

- Many weeks later as a follow up, I asked examiners who are senior consultants at the WACP examination in Ibadan about the instrument they use in their laboratory for HbA1c measurement. They all said that measurement was by use of POCT instrument.

# POTENTIAL ADVANTAGES OF POCT OF HbA1c Over laboratory Testing

- It provides rapid test results to expedite medical decision-making may not need expert for its measurement.
- It is more convenient for patients.
- It may improve health system efficiency and cost saving.
- It can improve access to testing for underserved populations.
- Prognostic value ( relationship with lipids)

# EXAMPLE OF PCOT INSTRUMENT



Rapid test results for decision-making may not need expert for its measurement.

- The Norwegian study noted that about 75% of general practitioners in Norway are using point-of-care A1C testing in their offices, presumably for both diagnosis and monitoring, thus providing a possible model of uptake.
- The Norwegian study also observed that point-of-care A1C testing quality is closely monitored in their country through a stringent national quality assurance program for laboratory testing in which essentially all general practitioners' offices participate.

# Another evidence of no need for expert for POCT HbA1c

- The aim of this study was to assess the performance of various point-of-care instruments in the hands of **non-laboratory trained personnel**.
- **Two nursing staff tested samples from patients** attending a diabetes research clinic using the following point-of-care devices for HbA1c-Metrica A1C Now, Bayer DCA 2000, Cholestech GDX and Axis-Shield Nycocard HbA1c. In addition they performed regular analysis of quality control samples. The effects on analytical performance of multiple operators as well as laboratory-trained staff, were also assessed. All measurements were compared to a boronate-affinity HPLC method in the central laboratory.
- The analytical performance obtained by laboratory staff was similar to nursing staff for 3 devices and better for the Nycocard device.

## Conclusions

- On the basis of the results obtained by nursing staff, only the DCA of the devices tested, can be recommended for measurement of HbA1c outside of the laboratory.

# improved provider and patient convenience,

- No need for fasting
- Provides value reflecting average 2-3 months blood glucose level therefore reducing frequency of measurements
- Can easily be used to check compliance of patient on treatment

# COST SAVING

- In our laboratory cost of HbA1c is five times to the patient than blood glucose, but when related to the frequency of tests it becomes cheaper
- The cost differences between point-of-care and laboratory testing of A1C for monitoring blood glucose were assessed in a 2014 budget impact analysis by Health Quality Ontario.<sup>8</sup>
- The analysis included A1C point-of-care devices that were available in Canada at the time (the Afinion system was not included).<sup>8</sup>
- Results indicated that if all laboratory testing for A1C monitoring in Ontario was replaced by point-of-care testing, the annual cost savings to the province could be \$4.7 million (\$86.8 million for point-of-care versus \$91.5 million for laboratory testing).<sup>8</sup>

# HbA1c AND LIPID PATTERN

- HbA1c is not only a useful biomarker of long-term glycemic control but also a good predictor of lipid profile; thus, HbA1c measurement could have additional benefits of identifying diabetes patients who are at a greater risk of cardiovascular complications.<sup>10</sup>
- In a series of 1,011 type 2 diabetic patients, HbA1c exhibited direct correlations with cholesterol, triglycerides, and low density lipoprotein cholesterol and inverse correlation with high-density lipoprotein cholesterol.
- They observed a linear relationship between HbA1c and dyslipidemia as the levels of serum cholesterol and triglycerides were significantly higher and that of high-density lipo-protein cholesterol were significantly lower in patients with worse glycemic control as compared to patients with good glycemic control .<sup>10</sup>

# WHY HbA1c .

- In summary,

The use of point-of-care A1C for the diagnosis of diabetes would

- ❖ enable rapid diagnosis,
- ❖ save costs of patients' management,
- ❖ convenience for both patients and care providers,
- ❖ provide prognostic value for prediction of cardiovascular diseases by giving indication of possible dyslipidaemia.

# Challenge of POCT FOR HbA1c

[Clin Chem Lab Med.](#) 2006;44(2):223-7.

- **Measurement of glycated hemoglobin (HbA1c) with an automated POCT instrument in comparison with HPLC and automated immunochemistry method: evaluation of the influence of hemoglobin variants.**
- [Haliassos A<sup>1</sup>](#), [Drakopoulos I](#), [Katritsis D](#), [Chiotinis N](#), [Korovesis S](#), [Makris K](#).

## **Abstract**

- Our study evaluates a fast and easy way to perform point-of-care testing (POCT) measurements of glycated hemoglobin HbA1c in comparison with an immunoassay on an automated biochemistry analyzer and cation exchange chromatography, the two methods routinely used in clinical laboratories for the measurement of HbA1c. A significant finding of our study is that although the POCT instrument insert claims that the method is not affected by the presence of HbS in the heterozygous state or in combination with beta-thalassemia, discrepant results were found in some cases with such hemoglobinopathies. In these cases, the two POCT and laboratory immunoassay methods showed clinically significant positive interferences with samples containing the HbS trait.
- We conclude that samples with the HbS trait should be interpreted with caution when tested using the POCT instrument.

# IMPLEMENTATION ISSUES

- There are several considerations in using A1C systems for the point-of-care diagnosis of type 2 diabetes:
- the suitability of A1C for diagnosing type 2 diabetes (versus its use for monitoring)
- the use of point-of-care tests versus laboratory tests
- the need for methods to ensure sharing test results between information systems and health care providers, and checks to avoid the duplication of testing
- the comparative accuracy and costs of the various devices for point-of-care A1C testing.

What to look for in a POC HbA1c Analyzer, A case for point-of-care testing for HbA1c **By: [Gavin Jones](#)** July 18, 2013

**1. SIMPLICITY**

**2. AUDIT TRAILS**

**3. CERTIFICATION**

**4. METHODOLOGY**

# What to look for in a POC HbA1c Analyzer cont.

Most POC HbA1c analyzers use a drop of blood (4 to 10  $\mu\text{L}$ ) taken from a finger prick (capillary blood) or venous sample that is applied to a reagent cartridge and then inserted into a desktop device for analysis.

Time to reporting of HbA1c results is generally between three and 10 minutes, depending on the analyzer. Keys to the effectiveness of any HbA1c POC analyzer are simplicity, audit trails, certification, and methodology.

# SIMPLICITY

- Ensuring that a POC analyzer is easy to use will minimize possibility of user error. Saving time and costs
- An analyzer that is simple to use also ensures minimal training requirements, again contributing to affordability.
- Features that can support ease of use include employing ready-to-use reagent cartridges that can be inserted straight into the analyzer and the blood sample then added directly, without the need for premixing or pipetting. Minimizing the number of steps in the procedure not only reduces the opportunity for user error but also helps to standardize results by eliminating any variation introduced by different operators, particularly when pipetting and mixing.

# AUDIT TRAILS

For patient safety purposes, audit trails should also be available.

Use of barcode scanning for patient and user identification, as well as for confirmation of the batch of reagents and controls used, ensures that an analyzer can provide such trails.

Quality control results on two levels that are recorded and held within the analyzer's memory are also ideal for auditing purposes.

# CERTIFICATION

- Certification of the analyzer to confirm delivery of accurate, standardized results should also be a key consideration.
- Effort to standardize HbA1c results, the AACC set up the National Glycohemoglobin Standardization Program (NGSP) in 1996. In parallel, the IFCC developed reference methods for glycated hemoglobin. In 2006 and 2007, an international consensus between IFCC and AACC was reached.<sup>12</sup>

# CERTIFICATION

- The calibration and certification of laboratories and manufacturers to the same standards has improved the conformity of results. However, in practice differences can still be observed among technologies and among individual systems.
- These observed differences arise because of heterogeneity of hemoglobins, underlying differences in technologies (e.g., ion exchange, boronate affinity, immunoassay), calibration drifts, or lot-to-lot variability. However, if the manufacturer follows the recommendations of the IFCC and NGSP to ensure instruments and reagents are accurately aligned and traceable to the reference method, this should not prove problematic.\_

# METHODOLOGY

There are POC HbA1c analyzers available whose results are not affected by

- hemoglobin variants (which do not result in reduced erythrocyte life span),
  - labile glycated hemoglobin, or
  - hematocrit levels.
- Such analyzers use Boronate Fluorescence Quenching Technology (BFQT)<sup>25</sup>, which is associated with simple yet powerful multiple optical measurements. This is based on well-documented boronate affinity chromatography systems used in reference laboratories.
  - Since BFQT does not require chromatographic separation, the methodology allows for fast, simple, and accurate POC measurement of HbA1c to deliver results comparable to chromatography-based techniques.

# CONCLUSION

- HbA1c is affected by blood glucose concentration and its measurement reflects 2-3 months glycemic control<sup>11</sup>,
- It must be interpreted with caution in pregnant women, in situations in which there is decreased RBC life span eg haemolysis, splenomegaly, chronic kidney disease, recent blood transfusion, use of erythropoiesis stimulating agents and haemoglobinopathies, just to mention a few.

# CONCLUSION

- Use of HbA1c measurements in diabetes is highly desirable in Africa in view of the various advantages mentioned.
- It is convenient as a single blood draw that does not require fasting, minimum day to day variability and pre-analytical sample stability. Measurement is possible in Nigeria since most centers are currently measuring it, using PCOT methodology. The available evidences point to fact that if instrument is carefully choosing and standardized this measurement can become feasible in Africa.

- **THANK YOU ALL**
- **FOR YOUR ATTENTION**

# REFERENCES

1. WoShariq I. Sherwani,<sup>1</sup> Haseeb A. Khan,<sup>2</sup> Aishah Ekhzaimy,<sup>3</sup> Afshan Masood,<sup>4</sup> and Meena K. Sakharkar. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients Biomark Insights. 2016; 11: 95–104
2. International Diabetes Federation (IDF) 2015. Available from: [www.idf.org](http://www.idf.org).
3. Nathan DM, Cleary PA, Backlund JY Diabetes Control and Complication trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group Intensive Diabetes Treatment and Cardiovascular Diseases in patients with type 1 diabetes . N Engl J.Med. 2005; 353:2643-2653

# REFERENCES

4. World Health Organization. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. Abbreviated result of WHO consultation. World Health Organization web site. <http://www.who.int./diabetes/publication/report-hblac.2011.pdf> Published 2011.
5. World Health Organization, Definition and diagnosis of diabetes mellitus and Intermediate hyperglycaemia: report of WHO/IDF consultation. WHO web site. [http://apps.who.int/iris/bitstream/10665/43588/1/9241594934\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/43588/1/9241594934_eng.pdf). published 2006.S93
6. American Diabetes Association Tests of glycemia in diabetes. Diabetes Care 2004; 27: (Suppl 1):S91-S93
7. Solvik UO, Roraas T, Christensen NG, Sandberg S. Diagnosing diabetes mellitus: performance of hemoglobin A1c point-of-care instruments in general practice offices. Clin Chem [Internet] 2013 Dec;59(12):1790–801. [cited 2017 Feb 9] Available from: <http://clinchem.aaccjnls.org/content/clinchem/59/12/1790.full.pdf>. [PubMed]
8. [Clinica Chimica Acta Volume 365, Issues 1–2](#), March 2006, Pages 257-263 Nurse-based evaluation of point-of-care assays for glycated haemoglobin Author links open overlay pane [Andrew St John](#) <sup>a</sup>[Timothy M.E.Davis](#) <sup>b</sup>[IanGoodall](#) <sup>c</sup>[Mary AnneTownsend](#) <sup>d</sup>[Christopher P.Price](#) <sup>e</sup>

# REFERENCES

- 9. Chadee A, Blackhouse G, Goeree R. Point-of-Care Hemoglobin A1c Testing: A Budget Impact Analysis. *Ont Health Technol Assess Ser* [Internet] 2014;14(9):1–23. [cited 2017 Feb 9] Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4549575/pdf/ohtas-14-1.pdf>. [[PMC free article](#)] [[PubMed](#)]
  - 10. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. *Clin Exp Med*. 2007;7:24–9.
  - 11. Sandler CN, McDonnell ME. The role of hemoglobin A1c in the assessment of diabetes and cardiovascular risk. *Cleveland Clinic J. Med* Vol 83 Suppl 1, 2016
- 12. Geistanger A, Arends S, Berding C, et al; on behalf of the IFCC Working Group on Standardization of Hemoglobin A1c. Statistical Methods for Monitoring the Relationship between the IFCC Reference Measurement Procedure for Hemoglobin A1c and the Designated Comparison Methods in the United States, Japan, and Sweden. *Clin Chem*. 2008;54(8):1379-1385.









