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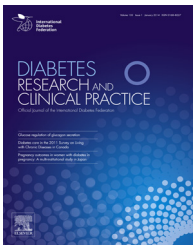

Comparison of fasting plasma glucose and haemoglobin A1c point-of-care tests in screening for diabetes and abnormal glucose regulation in a rural low income setting☆

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ABSTRACT

Aims: Glycated haemoglobin (HbA_{1C}) has been suggested to replace glucose tests in identifying diabetes and pre-diabetes. We assessed agreement between fasting plasma glucose (FPG) and HbA_{1C} rapid tests in classifying abnormal glucose regulation (AGR), and their utility for preventive screening in rural Africa.

Methods: A population-based survey of 795 people aged 35–60 years was conducted in a mainly rural district in Uganda. FPG was measured using On-Call® Plus glucometers, and classified using World Health Organization (WHO) and American Diabetes Association (ADA) criteria. HbA_{1C} was measured using A1cNow® kits and classified using ADA criteria. Body mass index and blood pressure were measured. Percentage agreement between the two tests was computed.

Results: Using HbA_{1C}, 11.3% of participants had diabetes compared with 4.8% for FPG. Prevalence of HbA_{1C}-defined pre-diabetes (26.4%) was 1.2 times and 2.5 times higher than FPG-defined pre-diabetes using ADA (21.8%) and WHO (10.1%) criteria, respectively. With FPG as the reference, agreement between FPG and HbA_{1C} in classifying diabetes status was moderate (Kappa = 22.9; Area Under the Curve (AUC) = 75%), while that for AGR was low (Kappa = 11.0; AUC = 59%). However, agreement was high (over 90%) among negative tests and among participants with risk factors for type 2 diabetes (obesity, overweight or hypertension). HbA_{1C} had more procedural challenges than FPG.

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Conclusions: Although low in the general sample, agreement between HbA_{1C} and FPG is excellent among persons who test negative with either test. A single test can therefore identify the majority at lower risk for type 2 diabetes. Nurses if trained can conduct these tests.

1. Introduction

Identifying individuals with abnormal glucose regulation (AGR) enables intensified preventive measures to be invoked earlier and evidence shows that it is cost-effective [1–3]. Type 2 diabetes and pre-diabetes are detected through an oral glucose tolerance test (OGTT), fasting plasma glucose (FPG) or glycated haemoglobin (HbA_{1C}). Diagnostic cut-offs for these tests have been defined by the World Health Organization (WHO) and the American Diabetes Association (ADA) [4,5]. However, the debate about affordable but valid diagnostics for early detection of high risk persons at primary care levels in low income countries continues.

While the OGTT is the more sensitive test [6], it has a lengthy cumbersome procedure, poor reproducibility, and questionable cost-effectiveness [6–8]. FPG is easier, cheaper and more reproducible, but has lower sensitivity and high pre-analytical variability (4–14%) [9]. In 2009, experts from the ADA, the European Association for the Study of Diabetes, and the International Diabetes Federation recommended that HbA_{1C} should be the primary test for early detection of type 2 diabetes and pre-diabetes in asymptomatic persons [4]. In 2011, WHO too recommended that HbA_{1C} is useful for diabetes screening, 'provided there is stringent quality assurance and standardization' [10]. HbA_{1C} does not require fasting, its analytical variability is less than 2%, and it is relatively stable over 2–3 months [9,11]. However, it is costly [7] and is affected by haemolysis, haemoglobinopathies, triglycerides, and common drugs like Aspirin [9,12]. Evidence of its value in detection of pre-diabetes is also inconclusive [10].

Pre-diabetes is now defined by three criteria: impaired glucose tolerance (determined by the OGTT), impaired fasting glucose (determined by FPG) and HbA_{1C} levels between 5.7 and 6.4% (39–46 mmol/mol). Likewise, each of these tests has cut-off point for diagnosis of diabetes. The challenge is their level of agreement: While many studies have demonstrated that both FPG and HbA_{1C} have a high validity [9,11,13,14], there is limited data on their level of agreement in classification of both diabetes and AGR, feasibility of their use by primary care workers, and their utility in screening for high risk persons at primary care facilities.

Type 2 diabetes is on the rise in low income countries [15]. However, akin to most low income countries, Uganda's policy and strategy for non-communicable disease (NCD) prevention is new and evolving [16]. Uganda's only official guidelines for type 2 diabetes were published in 1998 [17]. These guidelines focus on management of symptomatic persons in secondary care settings with no guidance on preventive screening.

The main objective of this study was to assess the level of agreement between FPG and HbA_{1C} rapid tests in defining diabetes and AGR, factors that enhance their agreement, their utility in preventive screening, and whether primary care workers can perform them. We analyze the implications of using either test in detection of high risk persons at in a low income setting.

2. Materials and methods

2.1. Setting

The Iganga-Mayuge Health and Demographic Surveillance Site (HDSS) where this study was conducted is located in eastern Uganda, about 120 km east of Kampala the capital city. The HDSS has a population of approximately 70,000. It has 65 villages of which 13 are peri-urban and 52 are rural. Surveillance data is collected every 6 months on socio-demographic characteristics, births, deaths, and migrations. Add-on studies are also often conducted within the HDSS, including our study. Data for this study were collected over 8 weeks in March and April 2012.

2.2. Study population

This study was nested into a larger survey that assessed prevalence of diabetes and pre-diabetes among people aged 35–60 years in the HDSS [18]. The study population comprised men and women aged 35–60 years. A multi-stage design was used: Forty-two villages (8 peri-urban and 34 rural) were randomly selected, from which a sample of 1656 participants was taken proportionate to the village populations. From the HDSS database, participants from each village were selected using simple random sampling with the help of Microsoft Excel. HDSS locator information was used to trace participants to their households by Village Scouts who routinely register vital events.

The sample size required for comparing differences in prevalence of AGR as detected by FPG and HbA_{1C} was determined, using the formula for comparative studies by Fleiss et al. [19]. At a significance level of 95%, power of 80%, estimated occurrence of AGR in the general population being 3% [20], and hypothesized difference in prevalence of AGR between the two tests at 3%, the minimum computed sample size was 792 respondents for either comparison group. This was adjusted to 879 respondents to cater for about 10% estimated non-response. For this sub-study therefore, a sub-sample of 879 of the 1656 participants in the larger study was selected by taking a simple random sample from the master database, assisted by Stata 10 (refer to Fig. 1)

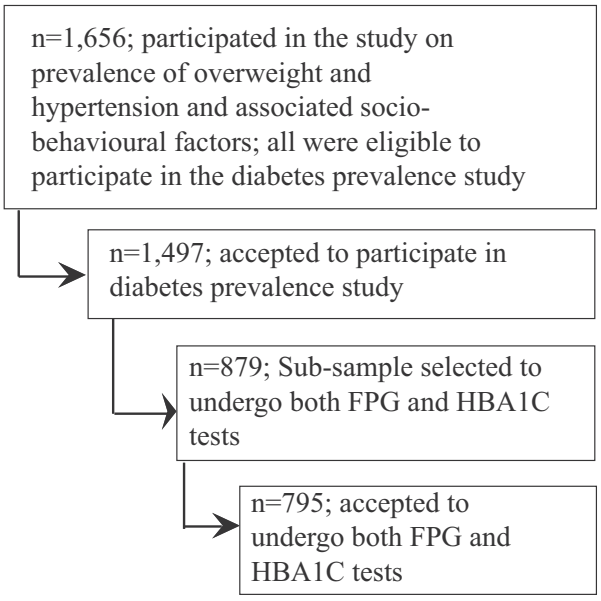


Fig. 1 – Flow-chart showing how the study sample was obtained.

2.3. *Measurements*

Data for this study were collected in three stages: In stage one, participants underwent physical measurements of height, weight, and blood pressure. In the second stage, participants underwent tests to assess their blood sugar status. In the third stage, research assistants were asked about their experiences in applying the two tests to assess the tests' feasibility in this setting. Data were collected by 12 teams, each having two experienced research assistants: a nurse and a social worker. Research assistants underwent a 5 days' training and practice session supervised by a laboratory technician. All measurements were conducted at the participants' homes.

2.3.1. *Stage 1: physical measurements*

Detailed procedures for measurement of the physical characteristics have already been described elsewhere [18]. Height was measured using standard height metres, with the participant standing upright. Weight was measured using calibrated Seca® scales, with the participant lightly clothed. BMI was calculated as weight-in-kilograms divided by the square of height in metres. A participant was classified as overweight if their BMI was 25 kg/m^2 or greater, and obese if their BMI was 30 kg/m^2 or greater.

Two blood pressure (BP) measurements were taken (5–30 min apart), with the participant seated, using a calibrated electronic BP device (Welch-Allyn®). The mean of these two measurements was taken as their BP. Participants were classified as having hypertension if their average systolic BP was 140 mmHg or higher, or if their average diastolic BP was 90 mmHg or higher, or if they were on treatment for hypertension [21].

2.3.2. *Stage 2: assessment of blood sugar levels*

Each participant was contacted on the day prior to their scheduled date for data collection and an appointment was sought for the following day. To obtain an FPG, they were requested not to eat anything on the appointment day until their blood test had been conducted. All appointments were set in the morning hours before 10.30 am and because of this, each data collection team covered only four households per-day. Participants who reported to have eaten anything on the appointment day were rescheduled.

For each consenting participant two blood drops were obtained from a finger prick using an automated lancing device and each was placed on a separate applicator. One sample was analyzed for plasma glucose levels using a glucometer (On-Call Plus®, ACON Laboratories) while the second was analyzed for HbA_{1C} using the A1cNow® (Bayer) Rapid Immuno-Assay. Both tests were in form of rapid kits. Point-of-care (POC) tests are widely recommended for monitoring of blood glucose and some brands have comparable validity to laboratory-based tests [14,22–24]. Because of their simple procedure, the tests were performed by the nurses on the data collection teams.

Classification of AGR was based on the standard cut-offs for FPG and HbA_{1C} as defined by the ADA [4]: For FPG, (1) participants with an FPG <5.6 mmol/l were classified as normal; (2) participants with an FPG >6.9 mmol/l were classified as having diabetes; (3) participants with an FPG between 5.6 and 6.9 mmol/l were classified as having 'pre-diabetes'. All participants with an FPG ≥5.6 mmol/l were classified as having 'AGR'. For HbA_{1C}, (1) participants with an HbA_{1C} <5.7% (or <39 mmol/mol) were classified as having normal glycosylation; (2) participants with an HbA_{1C} ≥6.5% (or ≥48 mmol/mol) were classified as having diabetes; (3) participants with an HbA_{1C} of 5.7–6.4% (39–46 mmol/mol) were classified as having 'pre-diabetes'. For HbA_{1C}, 'AGR' was defined as HbA_{1C} ≥5.7% (or ≥39 mmol/mol). 'AGR' therefore included both diabetes and pre-diabetes.

Because the WHO has different cut-offs for FPG, a separate cross-analysis between FPG and HbA_{1C} was also conducted using the WHO criteria, to assess whether agreement changed significantly when WHO criteria were used compared to ADA criteria for FPG. The WHO cut offs for FPG are as follows [5]: (1) participants with an FPG <6.1 mmol/l were classified as normal; (2) participants with an FPG >6.9 mmol/l were classified as having diabetes; (3) participants with an FPG between 6.1 and 6.9 mmol/l were classified as having 'pre-diabetes'. All participants with an FPG ≥6.1 mmol/l were classified as having 'AGR'.

2.3.3. *Stage 3: assessing feasibility of FPG and HbA_{1C} rapid tests*

The study nurses were interviewed as key informants. Their experiences in using the two tests were explored. Variables included: ease of use, challenges in the test procedure, reversible and irreversible mistakes and device error readings and their causes. This information was triangulated with trainers' observations regarding the duration of practice sessions required for research assistants to master the respective test procedures during their training, as well as observational data on the actual duration of each test as recorded during data collection.

2.4. Statistical analysis strategy

Data were double entered in EpiData, cleaned and exported to STATA10 for analysis. The percentage agreement between the FPG and HBA_{1C} tests in classifying diabetes and AGR was determined at the standard cut-offs and evaluated using the Kappa Statistic. We explored further the predictive value of HbA_{1C} for FPG-defined diabetes status and FPG-defined AGR. The reason for using FPG as the reference was that our data seems to indicate that HbA_{1C} was the less specific one of the two tests. Percentage agreement was also compared for the two tests among sub-groups with risk factors for type 2 diabetes i.e. hypertension, overweight, obesity, and a combination of being overweight and hypertensive. Receiver operating characteristic (ROC) curves were used to evaluate the performance of HBA_{1C} in predicting FPG-defined diabetes status and AGR.

3. Results

3.1. Background characteristics of participants

Table 1 shows the background characteristics of participants. Of the 879 eligible participants contacted, 795 (90.4%) participated in this study. Reasons for non-participation included declining the blood tests (4.2%), and being away from one's home at 3 visits (5.4%). The majority (87%) of participants were from the rural areas. The mean age of participants was 43.7 years (standard deviation (SD) =6.9). The majority (63%) were subsistence farmers. Based on FPG, 4.8% were in the range classified as diabetes while 21.8% and 10.1% were in the range for pre-diabetes (using ADA and WHO criteria, respectively). Based on HbA_{1C}, 11.3% had levels in the range classified as diabetes while 26.4% were in the range for pre-diabetes.

Table 1 – Background characteristics and prevalence of diabetes and AGR.

Characteristic	*n*	%
Sex		
Males	417	52.4
Females	378	47.6
Location of residence		
Rural	691	86.9
Peri-urban	104	13.1
Age-group		
35–39	255	32.1
40–44	204	25.7
45–49	154	19.4
50–54	109	13.7
55–60	73	9.2
Main occupation		
Subsistence farmers	500	62.9
Traders	164	20.6
Formal/salaried	39	4.9
Mechanics	92	11.6
Highest level of education		
None	139	17.5
Lower primary	174	21.9
Higher primary	315	39.6
Secondary	131	16.5
Tertiary	36	4.5
Glycaemia status (FPG)		
Normal	584	73.5
Pre-diabetes	173	21.8
Diabetes	38	4.8
Glycaemia status (HbA_{1C})		
Normal	495	62.3
Pre-diabetes	210	26.4
Diabetes	90	11.3

FPG = fasting plasma glucose (using American Diabetes Association criteria); HbA_{1C} = glycated haemoglobin.

3.2. Agreement between FPG and HbA_{1C} in classifying diabetes status

Table 2 shows the percentage agreement between FPG and HbA_{1C} rapid tests in classifying diabetes status. At the cut-offs recommended by both the WHO and ADA, overall agreement between the two rapid tests in classifying diabetes status was low (Kappa = 22.9). Among persons classified as having diabetes by the FPG test, the HbA_{1C} test provides a similar classification for 53% of them. Likewise, among persons classified as having diabetes by HbA_{1C}, the FPG test only provides a similar classification for 20% of them (Table 2). Based on the ROC curves, the performance of HbA_{1C} in predicting FPG-defined diabetes status was moderate (AUC = 0.75; 95% CI 0.65–0.85) (Fig. 2A). However, despite the sub-optimal agreement in defining diabetes, there is high agreement among the negatives. Among persons classified as not having diabetes by the FPG test, the HbA_{1C} test too classifies 91% of them as not having diabetes. Likewise, among persons classified as not having diabetes based on HbA_{1C}, the FPG test too classifies 97% of them as not having diabetes. ROC curve analysis shows that BMI has lower but moderate performance in predicting diabetes-defining FPG levels (AUC = 0.66; 95% CI 0.57–0.75) (Fig. 2A).

3.3. Agreement between FPG and HbA_{1C} in classifying abnormal glucose regulation

Table 3 shows the percentage agreement between FPG and HbA_{1C} rapid tests in classifying AGR. At the cut-offs recommended by the WHO and ADA, respectively, agreement between FPG and HbA_{1C} rapid tests in classifying AGR was very low (Kappa = 10.6% using the WHO cut-off for FPG; Kappa = 11.0% using the ADA cut-off for FPG). However, agreement among the negatives was good (77.4%). Based on the ROC analysis, the performance of HbA_{1C} in predicting FPG defined AGR was also low (AUC = 0.59; 95% CI 0.54–0.63) (Fig. 2B).

3.4. Agreement among participants with risk factors for type 2 diabetes

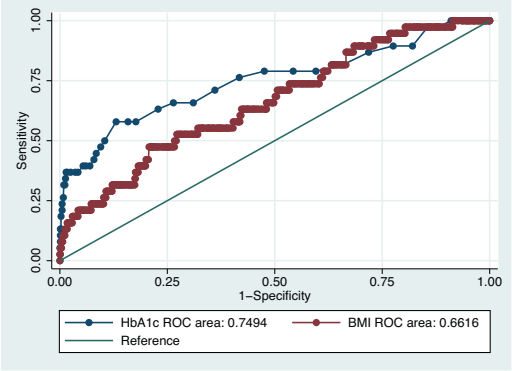
Tables 2 and 3 show variation in percentage agreement between both tests associated with risk factors for type 2 diabetes. Agreement between FPG and HbA_{1C} rapid tests in classifying diabetes status is higher when the tests are conducted among individuals with risk factors for type 2 diabetes. While a Kappa Statistic of 22.9 is obtained when the two tests are applied to the entire sample, a Kappa of 34.9 is obtained for hypertensive persons, 45.4 for overweight persons, 58.8 for persons who are both overweight and

Table 2 – Percentage agreement between FPG and HbA_{1C} in assessing diabetes status.

HbA_{1C} Status	FPG status		PPV of HBA_{1C} for FPG diabetes status	NPV of HBA_{1C} for FPG diabetes status	Percentage Agreement	Kappa
	Diabetes	No diabetes				
Entire sample (n = 795)						
Diabetes	18 (52.6)	72 (9.5)	20.0			
No diabetes	20 (47.4)	685 (90.5)		97.2	88.4	22.9
Among hypertensive persons (n = 159)						
Diabetes	8 (80.0)	21 (14.1)	27.6			
No diabetes	2 (20.0)	128 (85.9)		98.5	85.5	34.9
Among over-weight persons (n = 124)						
Diabetes	10 (83.3)	16 (14.3)	38.5			
No diabetes	2 (16.7)	96 (85.7)		98.0	85.5	45.4
Persons both overweight and hypertensive (n = 42)						
Diabetes	6 (100.0)	6 (16.7)	50.0			
No diabetes	0 (0.0)	30 (83.3)		100.0	85.7	58.8
Among obese persons (n = 42)						
Diabetes	8 (100.0)	5 (14.7)	61.5			
No diabetes	0 (0.0)	29 (85.3)		100.0	88.1	68.8

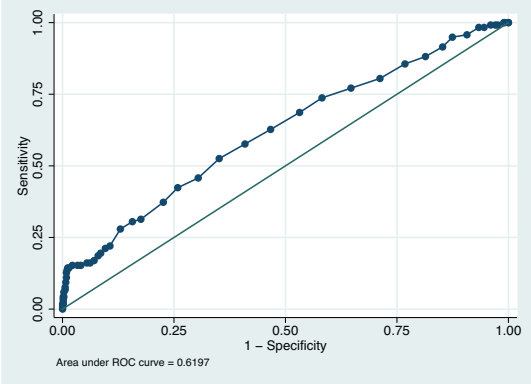
FPG = fasting plasma glucose; HbA_{1C} = glycated haemoglobin; PPV = positive predictive value; NPV = negative predictive value.

A: Relationship between FPG-defined diabetes status and HbA1C values and BMI



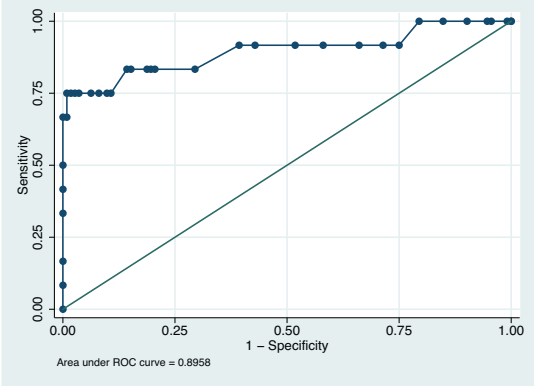
(HBA1C: AUC=0.75; 95% CI 0.65-0.85)
(BMI:AUC=0.66; 95% CI 0.57-0.75)

B: Relationship between FPG-defined AGR and HbA1C values



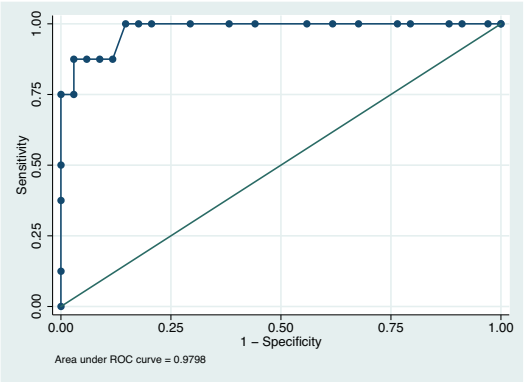
(AUC=0.59; 95% CI 0.54-0.63)

C: Relationship between FPG-defined diabetes status and HbA1C values among overweight persons



(AUC 0.90; 95% CI 0.76-1.00)

D: Relationship between FPG-defined diabetes status and HbA1C values among obese persons



(AUC 0.98; 95% CI 0.94-1.00)

Fig. 2 – Receiver operating characteristic (ROC) curves for the relationship between FPG-defined diabetes status and FPG-defined abnormal glucose regulation (AGR) status and HBA_{1C} values.

Table 3 – Percentage agreement between FPG and HBA_{1C} in assessing abnormal glucose regulation (AGR).

Hba_{1c} status	FPG status		PPV of HBA_{1C} for IFG	NPV of HBA_{1C} for IFG	Percentage agreement	Kappa
	Have AGR	Have no AGR				
Entire sample (n = 795)						
Have AGR	99 (46.9)	201 (34.4)	33.0		60.6	11.0
Have no AGR	112 (53.1)	383 (65.6)		77.4		
Among hypertensive persons (n = 159)						
Have AGR	30 (65.2)	51 (45.1)	37.0		57.9	16.4
Have no AGR	16 (34.8)	62 (54.9)		79.5		
Among over-weight persons (n = 124)						
Have AGR	31 (72.1)	38 (46.9)	44.9		59.7	22.1
Have no AGR	12 (27.9)	43 (53.1)		78.2		
Persons both overweight and hypertensive (n = 42)						
Have AGR	15 (88.2)	16 (64.0)	40.5		57.1	21.4
Have no AGR	2 (11.8)	9 (36.0)		81.8		
Among obese persons (n = 42)						
Have AGR	18 (85.7)	9 (42.9)	66.7		71.4	42.9
Have no AGR	3 (14.3)	12 (57.1)		80.0		

FPG = fasting plasma glucose (based on American Diabetes Association criteria); HbA_{1C} = glycated haemoglobin; PPV = positive predictive value; NPV = negative predictive value.

hypertensive and 68.8 for obese persons (Table 2). ROC analysis shows high performance of HbA_{1C} in predicting FPG-defined diabetes status among overweight persons (AUC 0.90; 95% CI 0.76–1.00) (Fig. 2C) and obese persons (AUC 0.98; 95% CI 0.94–1.00) (Fig. 2D). However, agreement between FPG and HbA_{1C} in classifying AGR does not improve among people with risk factors for type 2 diabetes, except among obese persons (Kappa = 42.9) (Table 3).

3.5. *Feasibility of rapid tests in primary preventive care*

According to the research assistants, the devices used in both FPG and HbA_{1C} measurements were easy to use, with no major procedural challenges. They reported that with training, nurses would be able to conduct either test. The FPG test took a mean of four minutes to perform (including 2 min for preparation of the sample and 2 min for the actual test). On the other hand, the HbA_{1C} test took a mean of nine minutes, including four minutes for preparing the sample and five minutes for running the test.

Challenges were observed. With regard to the FPG test, some participants did not comply with fasting, resulting in re-scheduling of appointments. The FPG test was also associated with some errors from insufficient samples and not sticking to the procedure, but these were reported to be much less frequent compared to the HbA_{1C} test.

The HbA_{1C} procedure was viewed as more complicated than the FPG procedure especially in the steps taken to prepare the sample before running the test. As a result, HbA_{1C} generated more quality control errors arising from insufficient samples and procedural mistakes than the FPG test. It also required precise timing between steps, and a test could be wasted by taking too long or too short between some steps. HbA_{1C} required longer practice before the teams could master the steps, compared to the FPG test. The HbA_{1C} devices failed to operate whenever the room temperature exceeded 28 °C. In hot climatic conditions like those in Iganga district, the HbA_{1C} tests must be conducted before 11.30 am on hot days. Because of its more complicated procedures and likely errors, the HbA_{1C} test was associated with a 10% wastage rate compared to only 2% for the FPG test. Other causes of failure of the HbA_{1C} included accidental contamination with moisture and dust. By design, the HbA_{1C} device was tagged to only 10 tests after which the device was auto-disabled.

4. Discussion

This analysis compares the agreement between FPG and HbA_{1C} rapid tests in identifying diabetes and AGR when used in a screening strategy among 35–60 year old persons. The setting is rural Africa, a context with very low access to laboratories and a paucity of data on performance of screening tests for AGR. We show that whilst overall agreement between the two rapid tests in identifying diabetes is moderate, and that their agreement in identifying AGR is low, their agreement is excellent among 'negatives' (i.e. those who test negative with either test), and is high in those who have risk factors for type 2 diabetes. We also show that these tests are feasible for use by non-physician health care workers.

Our study finds a marked disparity in the prevalence of diabetes and pre-diabetes between FPG and HbA_{1C}. The prevalence of diabetes and pre-diabetes based on HbA_{1C} is more than double the prevalence based on FPG. Similar findings in which HbA_{1C} shows a higher prevalence of diabetes and pre-diabetes have been reported in two recent studies, one in India [25], and another in Europe [26]. In fact, our diabetes prevalence rate of 11.3% using HbA_{1C} is close to that found in India [25]. However, our findings contrast with other studies in American, Arab and Chinese populations that show higher prevalence of AGR with the FPG test compared to HbA_{1C} [27–29]. To use the rapid HbA_{1C} as a primary care screening test in our setting and age-group would result in a high proportion of people classified as having diabetes or pre-diabetes, possibly with many false positives, similar to recent observations by Nazir, Mohan and colleagues among Asian Indians [25]. It would also have cost implications to prevention

programmes. On the other hand, using the FPG test may miss many high risk persons.

A possible explanation for this marked contrast in results from the two tests is that people of African descent have significantly higher average glycosylation of haemoglobin than people of other origins and the differences are glucose independent [30,31]. Several studies have indicated the need to determine region specific cut-offs for HbA_{1C} because of its variation between ethnic groups due to factors that may be genetic [1,32–36]. A second explanation for the disparity is that the FPG test excludes some individuals with impaired glucose tolerance and diabetes but with normal FPG. The disparity between FPG and HbA_{1C} may also be attributed to the age-group in this study (35–60 years). It has been proposed that HbA_{1C} varies with age [33]. There is a possibility too that FPG levels were affected by the occupational habits of the study population, who tend to commence farming work early in the morning. The disparity may also imply a qualitative weakness inherent in rapid tests.

At the standard cut-offs used, the percentage agreement between FPG and HbA_{1C} rapid tests in classifying diabetes status was low, while the performance of HbA_{1C} in predicting FPG defined diabetes status was moderate. Agreement between the two tests in classifying AGR is even much lower. Schöttker and colleagues demonstrate similar findings among European subjects [26]. However, Mohan and colleagues demonstrate higher agreement when the more rigorous quantitative laboratory tests are used, a difference that could be attributed to inherent limitations of rapid tests [37]. The implication of our findings is that either rapid test misses a significant proportion of the people that would otherwise be classified as having either diabetes or AGR by the other test. Multiple tests are therefore necessary to increase the diagnostic accuracy of these tests. Indeed some studies have demonstrated that combined use of FPG with HbA_{1C} or random blood sugar is necessary [1,13,32,38]. There is also a need for follow-on studies to calibrate rapid tests against the OGTT in Africa.

However, our study also finds that while the percentage agreement between FPG and HBA_{1C} is low in the study sample, agreement among the negatives (i.e. those whom either test classifies as not having diabetes or AGR) is high. A classification of normal glycaemia by one test is likely to be classified similarly by the other test, suggesting that for persons who test negative by any of these tests, one test may be sufficient for decision-making; on the other hand, persons testing positive by any of these tests ought to be subjected to a confirmatory test.

Our study finds that agreement between FPG and HbA_{1C} in classifying diabetes status increases when the tests are conducted among people with other risk factors for type 2 diabetes. This change is highest when the test is conducted among obese persons (where agreement is 100% among positives), followed by persons who are both overweight and hypertensive (100% agreement among positives) and then persons who are overweight (83% agreement among positives). The implication of these findings is that among obese persons and persons who are both overweight and hypertensive, rapid tests have diagnostic value for detection of diabetes. These findings also support arguments that the predictive value of HbA_{1C} varies with several factors including prevalence of diabetes [33,39].

Lastly, our study finds that in low resource settings, nurses are able to conduct both rapid tests at point-of-care, given the appropriate training. These findings lend credence to calls for simplification of point-of-care diagnostics for diabetes and AGR [22,40], and calls for task shifting of cardio-vascular risk management to non-physician health care workers [41–43]. However, the HbA_{1C} rapid test was more cumbersome than the FPG test and had higher wastage rates. These limitations of HbA_{1C} have also been observed in other studies [39].

Our study has implications on three of six WHO health system building blocks [44] important for integrating preventive care for type 2 diabetes in low resource settings: diagnostics, financing and human resources. Regarding diagnostics, our findings show that both FPG and HbA_{1C} rapid tests are useful for primary care level screening to detect high risk persons, but because FPG is cheaper and has lower wastage rates, it is the more feasible test in this setting. Since the two tests have high agreement among people who test negative, a single test can reliably screen out the majority without AGR, so that lifestyle counselling is targeted to fewer people who need it most. However, because these two tests have low agreement among those who test positive, mechanisms must be put in place for confirmation of positive results, similar to what is done in HIV testing in Africa. Other studies are necessary to determine the most appropriate confirmatory tests for low income settings. Financial implications may arise from which cut-offs are used. The lower ADA cut-offs will result in larger numbers of persons that need intervention, but may be beneficial in detecting as many high risk persons as possible. Regarding human resources, our findings show that these tests can be performed by nurses if trained.

The major limitation of this study is the use of rapid point-of-care tests rather than laboratory based tests, and therefore could not report on sensitivity and specificity. However, there is now sufficient evidence that some modern point-of-care tests have comparable accuracy to laboratory based tests [22–24]. In addition, the more cumbersome laboratory tests would not be of value to screening in this setting. Our finding that the two tests have high convergence among negatives may be sufficient to defend their utility in identifying non-high risk individuals, so that only those who test positive with either rapid test need the more rigorous and invasive laboratory based tests to confirm their status. Another limitation is that the Oral Glucose Tolerance Test (OGTT) was not performed, hence the lack of data on sensitivity and specificity of the tests, and the exclusion of 'impaired glucose tolerance (IGT)' in our comparisons. However, the OGTT would be a very cumbersome test to apply to this number of respondents, and has limited value in screening [1]. Another limitation was that each participant underwent only one round of tests, with resulting absence of data on repeatability of the test results. However, multiple simultaneous tests are of limited value in screening because of the cost implication. Lastly, HbA_{1C} is also known to be affected by haemolysis, haemoglobinopathies like Sickle Cell disease, triglycerides, and drugs commonly used in Africa like Aspirin and Dapsone [9,12]. However, most of these confounders tend to lower, rather than increase HbA_{1C} values.

We conclude that because the HbA_{1C} and FPG rapid tests have high agreement among people who test negative, a single test can reliably screen out the majority without AGR, so that lifestyle counselling is targeted. However because their agreement among persons who test positive is low, screening programmes should include a mechanism for confirmation of positive test results, especially for individuals do not have other risk factors for type 2 diabetes. While trained nurses can use either test in clinic as well as field surveys to identify persons with suspected diabetes and pre-diabetes, we found FPG to be more practical than HbA_{1C} under field conditions.

Conflict of interest

The authors declare that there was no conflict of interest.

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Author contributions: RWM designed the study, collected and analyzed the data and led the manuscript writing. He is the guarantor for this study. C-GO was the senior co-author on the team. He provided technical guidance in all stages of the study. DG and FEM provided expert support in the design of the statistical analysis strategy and rigorously reviewed the results. SP and GT provided guidance in the conceptualization of the study, and participated in the analysis and development of the discussions, especially the health systems implications. FNN participated in the design as well as the technical review of results. All authors participated in writing the manuscript.

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