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Validity of Fasting Plasma Glucose in Reference to HbA1c for the Detection of Diabetes in an Overweight and Obese Population in Sri Lanka

ABSTRACT

Objective: The validity of fasting plasma glucose (FPG) measurements for detecting diabetes was evaluated in reference to HbA1c among a 35-64-year-old overweight and obese population.

Methods: Data were collected from 1200 adults aged 35-64 with a body mass index (BMI) of 25 kg/m^2 or above using a questionnaire-based interview, basic clinical measurements, and biochemical analyses. Sensitivity, specificity, and ROC analyses were performed on 1121 persons for FPG (the index test) and HbA1c (the reference standard). HbA1c ≥6.5% was considered to indicate diabetes.

Results: Approximately 64% were female, 73% were employed, 31% had BMI ≥30 kg/m^2, and 70% lived in urban settings. The mean age (SD) was 47.8 (±7.5) years. The prevalence of diabetes was 25.7% according to HbA1c ≥ 6.5%, and 44% of them were undiagnosed. A significant correlation was found between FPG values and HbA1c (r = 0.863; P < .001). At the FPG cutoff point of 126 mg/dL, the sensitivity was 60% (95% CI: 53.6, 65.5), and the specificity was 99.8% (95% CI: 99.4, 100.1), with high agreement (kappa = 0.69; P < .001). The positive and negative predictive values were 98.7% (96.9, 100.5) and 89.3% (87.4, 91.3), respectively. At FPG 100 mg/dL, the sensitivity increased to 82.0% (77.2, 86.7), and specificity reduced to 88.5% (86.2, 90.7), with a marginal change in kappa (0.66; P < .001). Receiver operating characteristic analysis found an area of 0.91 (P < .001) under the curve at this optimum cutoff point.

Conclusion: A lower threshold of FPG (≥100 mg/dL) may achieve a maximum yield of diabetes during the screening of overweight or obese persons in the age group 35-64 years.

Keywords: Diabetes, fasting plasma glucose, HbA1c, screening, sensitivity and specificity, validity

Introduction

Diabetes mellitus has become a global epidemic affecting an estimated 425 million people across the world, with high prevalence in countries in South Asia, including Sri Lanka.[1] In Sri Lanka, 10.7% (95% CI 8.1-15.2) of adults aged 20-70 years were reported to have type 2 diabetes in 2017.[1] The global burden of disease assessment ranked diabetes as the 14th highest cause of DALYs worldwide and the 16th highest in South Asia.[2,3]

During the 2005-2006 period, 10.3% (95% CI: 9.4%-11.2%) of Sri Lankan adults aged 20 years and above had diabetes according to the oral glucose tolerance test (OGTT).[4] Almost 10 years later, the STEPS survey found that only 7.4% (95% CI: 6.4-8.5%) of adults aged 18-64 years had diabetes (previously diagnosed or FPG > 125 mg/dL).[5] This raises concerns about the diagnostic accuracy of FPG as opposed to OGTT.

In Sri Lanka, at least one-third of people with diabetes remain undiagnosed.[4] The effects of undiagnosed diabetes with longstanding hyperglycemia include long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Early detection through screening can achieve good glycemic control and prevent microvascular and cardiovascular complications through dietary and lifestyle modifications with or without therapeutic measures.[6-8]

The risk of diabetes is higher in overweight or obese persons than in others.[9] Other main risk factors include an unhealthy diet, reduced physical activity, increased sedentary behavior, stress, and genetic predisposition.[10] Addressing the rising trend of non communcable disease (NCD), including diabetes, has been given much attention in the Sri Lankan national health agenda.[11,12] Healthy Lifestyle Centers (HLCs) were introduced in primary healthcare facilities

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in 2011 to reduce the risk of NCDs among those aged 40-65 years of age through early identification of risk factors and appropriate management and referral.[13] Screening for diabetes is provided through HLC using capillary fasting blood glucose (or venous FPG in some centers). It was reported that 10.6% of HLC attendees in 2015 had fasting blood glucose above 126 mg/dL.[13]

An analysis of FPG and OGTT in Sri Lankans revealed that the recommended cutoff point of 7.0 mmol/L (126 mg/dL) has very low sensitivity (47.1%) and very high specificity (99.6%) in predicting diabetes.[14] This study found a lower FPG cutoff point of 5.3 mmol/L (95 mg/dL), with higher sensitivity and adequate specificity for diagnosing pre-diabetes and diabetes in Sri Lankan adults. However, the validity of FPG in predicting HbA1c is not known, especially in overweight and obese adults. In patients with type-2 diabetes, a high correlation ($r = 0.77$) has been found between FPG and HbA1c, but the FPG values failed to predict HbA1c.[15]

Since bridging this information gap would improve the screening services and, thereby, appropriate management, we conducted a study in persons aged 35-64 years who were overweight or obese in the Colombo district. We hypothesized that several persons with diabetes are misclassified as prediabetic or normal when the current reference standard of fasting plasma glucose (FPG ≥126 mg/dL) is used in a sub-population with high-risk people.

The present study determined the validity of FPG measurement in screening a 35-64-year-old, overweight or obese population for the detection of diabetes in reference to HbA1c as per the American Diabetes Association (ADA) reference standard.

Material and Methods

Study Design and Participants

A validation study was conducted using baseline data collected on enrollment in a 2-group, parallel-arm, randomized control trial (RCT) in the Colombo district. The data were planned to be collected prior to performing the index test (FPG) and reference standard (HbA1c).

Persons who were 35-64 years of age and having a body mass index (BMI) of 25 kg/m^2 or above were included as participants. Among those excluded were pregnant women, breastfeeding mothers, any persons who had lost 5% or more of their body weight in the preceding 6 months, and those on medication or following lifestyle modifications known to reduce body weight.

Sample size (n = 1200) was calculated at the inception to conduct a randomized controlled trial, which has been described elsewhere.[16] This number was sufficient to meet the number required to estimate sensitivity and specificity in diagnostic accuracy studies.[17] A predetermined level of sensitivity (55%) and specificity (88%) according to previously published studies was used,[18] with the 95% CIs to be within ±5%. The prevalence of DM in adults was taken as 20%, given due consideration for the epidemiological pattern of diabetes in Sri Lanka.[10,19]

Participants were sampled from Medical Officer of Health (MOH) divisions in 2 stages: In the first stage, 5-6 sub-divisions within each MOH division were sampled. In the second stage, 30-35 participants from each sub-division were shortlisted and assessed for eligibility.

The selected participants were interviewed by trained enumerators following informed consent. Participants in groups of 20-30 were invited to a common place (a clinic center, primary health care facility, community center, premises of a government or community-based organization) in an overnight fasting state of 12 hours for the biochemical investigations.

Ethics Clearance

Ethics standards for involving human subjects in research were followed. The Ethics Review Committee of the Faculty of Medicine University of Colombo Faculty of Medicine granted ethics approval to conduct this study (approval number: EC-16-061, date: May 19, 2016). Results of individual clinical and biochemical assessments were provided to the participants. Written informed consent was obtained from participants prior to interview and blood drawing.

Test Method

An analysis was performed between FPG (the index test) and HbA1c (the reference standard), which was classified as having DM if the HbA1c was 6.5% or higher.

Basic socio-demographic data were gathered through a questionnaire-based interview, and heights and weights were measured using standard anthropometric equipment. A sample of 6 mL of blood was drawn from each participant fasting for 12 hours, using standard precautions by specially trained medical laboratory technicians. Blood specimens were sent for testing within an hour, and testing was performed following standard procedures in 2 accredited laboratories. HbA1c was tested using a high-performance liquid chromatographic assay (Bio-Rad D10, Hercules, California, USA) and FPG using the glucose oxidase method (Randox Imola, UK). The index test and reference standard were performed simultaneously, and there wasn't any time interval between the 2 tests. Results of HbA1c were not available for the performers of the FPG, and results of FPG were not available for assessors of HbA1c.

Statistical Analysis

The following measures of validity were calculated in the analysis as percentages with 95% CIs (95% CI):

Sensitivity: The probability of getting a positive test result (true positives) in subjects with the disease.

Specificity: The new test's ability to correctly detect subjects who do not have the disease (true negatives).

Positive predictive value: The proportion of subjects with a positive disease test.

Negative predictive value: The proportion of subjects without disease with a negative test result in total subjects.

MAIN POINTS

- The present cutoff point of FPG 126 mg/dL does not detect 40% of the diabetic patients identified with HbA1c (≥6.5%) in an overweight/obese and predominantly urban population.
- Lowering the cutoff point of FPG to 100 mg/dL in high-risk populations would yield more individuals with disease but also result in some false positives.
- Despite the majority being highly educated, predominantly employed, and living in urban/suburban areas, a substantial percentage (44%) of the disease remains undiagnosed.

The likelihood ratio of a positive test: the probability of a person who has the disease testing positive divided by the probability of a person who does not have the disease testing positive, i.e., sensitivity/(1-specificity).

The likelihood ratio of a negative test: the probability of a person who has the disease testing negative divided by the probability of a person who does not have the disease testing negative, i.e., (1-sensitivity)/specificity.

Yield: the proportion of correctly classified subjects (true positives + true negatives) among all subjects.

These analyses were carried out using 2 FPG thresholds: 100 mg/dL and 126 mg/dL. Furthermore, ROC analysis was performed (sensitivity vs. 1-specificity), and the area under the curve was calculated to identify the optimum point of FPG to predict diabetes.

Results

Participants

Of the 2518 participants screened for eligibility, 1200 were eligible and participated in the study. As shown in Table 1, 64% of participants were female, 73% were employed, and 70% lived in urban settings. Approximately 31% of participants were obese. The mean (SD) age was 47.8 (±7.5) years, BMI 28.9 (±3.5) kg/m^2, FPG 101.6 (±38.0) mg/dL, and HbA1c percentage 6.34 (±1.63). According to the questionnaire survey, 14% (n = 170) were known to have DM. However, the HbA1c analysis revealed that 25.4% of participants had an HbA1c of 6.5% or higher. The distribution of participants by age group, BMI categories, and HbA1c standard cutoffs are given in Table 1.

Table 1. Baseline Demographic and Clinical Characteristics of Participants (n = 1200)

Characteristic	No.	%
Sex		
Female	765	63.8
Male	435	36.2
Age category (in years)		
35-49	715	59.6
50-64	485	40.4
Education level		
Primary or lower (≤grade 5)	54	4.5
Secondary (grades 6-11)	338	28.2
GCE (ordinary level)	272	22.7
GCE (advanced level)	354	29.5
Degree and above	182	15.2
Employment status		
Employed	873	72.7
Unemployed	327	27.3
Residence		
Urban	840	70.0
Rural	360	30.0
BMI category		
Overweight (25.0-29.9 kg/m^2)	825	68.8
Obese (≥30.0 kg/m^2)	375	31.2
Self-reported diabetes		
Not known or no diabetes	1030	85.8
Known to have diabetes	170	14.2
Diabetes status according to HbA1c		
Normal (≤5.6%)	485	40.4
Increased risk for diabetes (5.7-6.4%)	410	34.2
Diabetes (≥6.5%)	305	25.4

GCE General Certificate of Education; BMI, body mass index.

Figure 1 illustrates the flow of assessments conforming to the Standards for Reporting of Diagnostic Accuracy Studies (STARD), including reasons for non-participation.[20] Fasting plasma glucose and HbA1C were performed simultaneously on all 1200 participants. However, the individuals treated for diabetes were excluded from the analyses.

Test Results

Of 1200 adults, 1121 were selected for the analysis of test results after excluding 79 persons who were already on treatment for diabetes. They were excluded to avoid any differential effects of medication on the 2 parameters, FPG and HbA1c. There was a high and significant correlation between FPG and HbA1c levels ($r = 0.863$; $P < .001$).

Table 2 shows cross-tabulations of FPG results by the HbA1c results. The percentage agreement, as expressed by kappa, was 0.690 and 0.655 and highly significant for the 2 cutoff levels of FPG, 126 mg/dL and 100 mg/dL, respectively.

Table 3 summarizes all measures of validity with their 95% CI. Accordingly, at the FPG cutoff level of 126 mg/dL, the sensitivity was approximately 60%, but the specificity was almost 100%. When the threshold was lowered to 100 mg/dL, the sensitivity increased to 82% while maintaining the level of specificity at 88.5%. At FPG 126 mg/dL, both positive and negative predictive values were high. However, at the lower threshold, the positive predictive value was low (67.6%) in contrast to the high negative predictive value (94.3%).

The positive likelihood ratio was 258 at the threshold of 126 mg/dL, in contrast to 7.1 at the lower threshold. The negative likelihood ratio was 0.4 and 0.2, respectively, for the 2 levels concerned. The yield (both true positives and true negatives) was 90.6% and 87.0% in the 2 instances, i.e., FPG 126 mg/dL and 100 mg/dL, respectively. However, the latter yielded more persons with DM than the former. In contrast, the former excluded more non-diabetic individuals than the latter.

Figure 2 shows the ROC analysis with a very high proportion in the area under the curve: 0.91 (95% CI: 0.89, 0.94); $P < .001$, indicating very high validity of FPG in detecting DM. However, the optimum threshold of FPG is around 100 mg/dL, resulting in a sensitivity above 80% while expecting the least false positives to be less than 12%.

No adverse events have been reported from performing the FPG, HbA1c, or any other assessments in this study.

Discussion

The Main Finding of This Study

This study showed a relatively high prevalence of diabetes (25.4% according to HbA1c ≥ 6.5%) in an adult population with BMI ≥25 kg/m^2, predominantly employed and living in and around urban settings in Sri Lanka. Of those diagnosed with diabetes, 44% were unaware of having the disease. The present sensitivity and specificity analysis indicated that the standard cutoff point for FPG of 126 mg/dL will only detect 50% of the cases of diabetes (sensitivity 59.6%). However, it excludes almost all people without diabetes (specificity 99.8%) in this population. At the FPG level of 100 mg/dL, more than

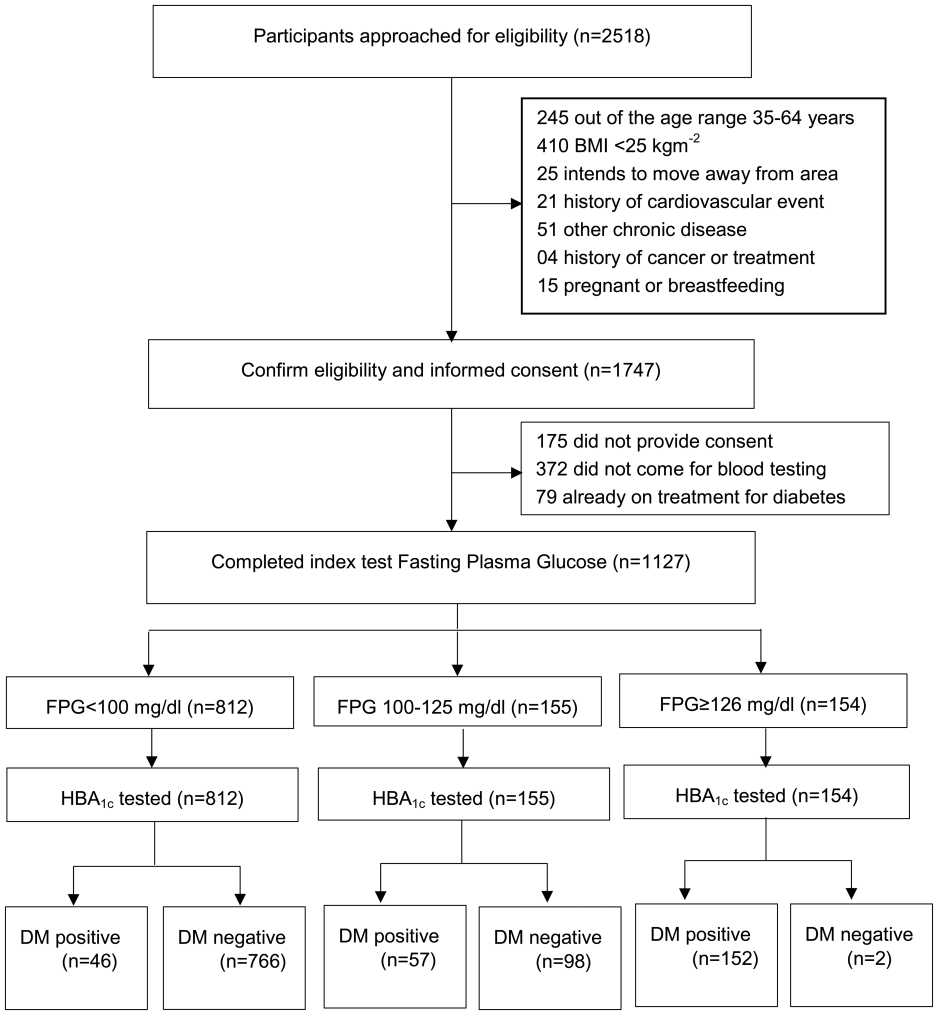

Figure 1. Flow diagram for the evaluation of validity of FPG in reference to HbA1c for the detection of diabetes in overweight/obese individuals aged 35-64 years.

Table 2. Sensitivity and Specificity of Fasting Plasma Glucose for the Detection of Diabetes at the Level of 126 mg/dL and 100 mg/dL (n = 1121)

Diabetes Screening	Diabetes Confirmed, No. % [95% CI]		
	Diabetes	No diabetes	Total
FPG ≥126	152	2	154
	59.6% [53.6, 65.5][a]	0.2% [−0.1, 0.6]	13.7%
FPG <126	103	864	967
	40.4% [34.4, 46.4]	99.8% [99.4, 100.1][b]	86.3%
Total	255	866	1121
	100.0%	100.0%	100.0%
FPG ≥100	209	100	309
	82.0% [77.2, 86.7][c]	11.5% [9.4, 13.7]	27.6%
FPG <100	46	766	812
	18.0% [13.3, 22.8]	88.5% [86.2, 90.7][d]	72.4%
Total	255	866	1121
	100.0%	100.0%	100.0%

At FPG 126 mg/dL, [a]sensitivity = 59.6%; [b]specificity = 99.8%; kappa = 0.690; $P < .001$.At FPG 100 mg/dL, [c]sensitivity = 82.0%; [d]specificity = 88.5%; kappa = 0.655; $P < .001$.Reference standard HbA1c ≥6.5%.

80% of diabetics can be detected (sensitivity 82.0%) while having around 12% false positives (specificity 88.5%).

Fasting plasma glucose test is often carried out at diabetes screening settings and follow-up clinics. This analysis emphasizes that there is a large proportion with high HbA1c (≥6.5%) but without elevated FPG in an overweight/obese population. Therefore, the health staff in these clinical settings should be more concerned about this fact when using FPG only and pay attention to those with marginally low FPG levels, especially 100-125 mg/dL.

What Is Already Known on This Topic?

The diagnostic criteria of diabetes mellitus by the ADA include any one of the values given below:[18] (1) FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours or (2) 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or (3) HbA1c ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP (www.ngsp) certified and standardized to the Diabetes Control and

Table 3. Summary of Measures of Validity of Fasting Plasma Glucose in Detecting Diabetes in Reference to HbA1c (n = 1121)

Measure	FPG ≥ 126 mg/dL		FPG ≥ 100 mg/dL	
	%	95% CI	%	95% CI
Sensitivity	59.6	[53.6, 65.5]	82.0	[77.2, 86.7]]
Specificity	99.8	[99.4, 100.1]	88.5	[86.2, 90.7]
Positive predictive value	98.7	[96.9, 100.5]	67.6	[62.4 72.9]
Negative predictive value	89.3	[87.4, 91.3]	94.3	[92.7, 95.9]
Diagnostic accuracy	90.6	[88.9, 92.2]	87.0	[85.0, 88.9]
	Ratio	95% CI	Ratio	95% CI
Positive likelihood ratio	258	[64.4, 1034]	7.1	[5.9, 8.6]
Negative likelihood ratio	0.4	[035, 0.47]	0.20	[0.16, 0.27]

Reference standard HbA1c ≥6.5%.

Complications Trial (DCCT) assay or (4) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L). Without unequivocal hyperglycemia, criteria (1) to (3) should be confirmed by repeat testing. These tests have been used for screening and confirmatory tests to assess diagnostic accuracy, and the sensitivity and specificity varied markedly depending on the country, target population, laboratory standards, and type of test used as the index test and reference standard.[18,21-25]

A review of evidence on diagnostic accuracy revealed that many studies have used the 2-hour OGTT as the reference standard.[21] The FPG as a screening test has not shown very high sensitivity.[14,18] The Sri Lanka Diabetes and Cardiovascular Study 2005-2006 (SLDCS) found results consistent with our study:[14] a sensitivity of 47.1% and specificity of 99.6% for the diagnosis of diabetes at the FPG cutoff point of 7 mmol/L (126 mg/dL). When the FPG cut-point was lowered to 5.6 mmol/L (100 mg/dL), the sensitivity increased to 80.8% and specificity declined to 92.1%. A study from Korea found a sensitivity of 55% with 100% specificity at the cutoff point of 7 mmol/L (126 mg/dL) based on diagnosis by OGTT among high-risk persons.[18] When the threshold was lowered to 6.1 mmol/L (110 mg/dL), the sensitivity improved to 85.2% and specificity reached 88.5%.

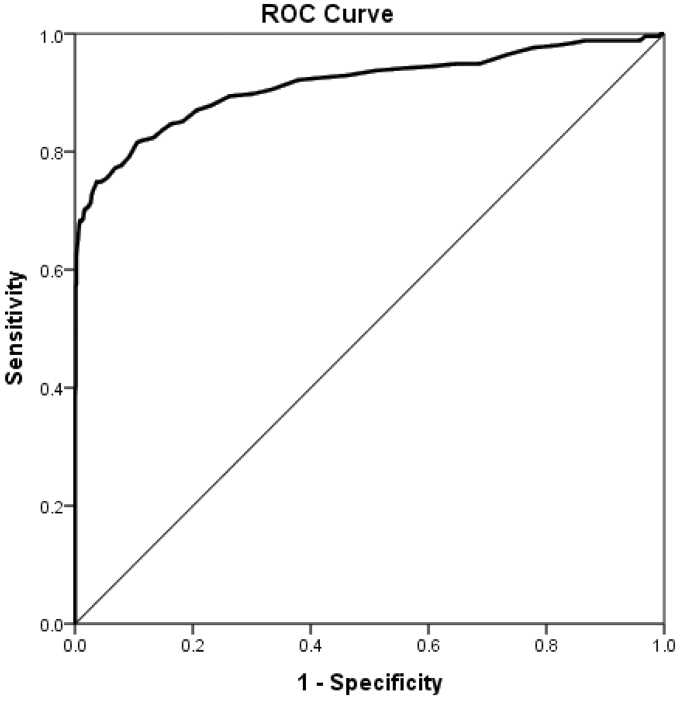

Figure 2. Receiver operating characteristic (ROC) curve of fasting plasma glucose thresholds in reference to HbA1c for the detection of diabetes (n = 1121).

The prevalence of diabetes, according to HbA1c, in our study was consistent with a recent study carried out in Colombo, which reported a prevalence of 27.6%. A high prevalence of diabetes is partially attributed to the increased detection by HbA1c.[26]

Though the HbA1c levels have been used as a diagnostic criterion, their accuracy as a diagnostic criterion for diabetes mellitus has been considered doubtful. HbA1c ≥6.5% had low sensitivity in contrast to FPG (43%) and 2-hour plasma glucose (28%) in a previously undiagnosed diabetic cohort.[27] A review of 6 large studies from 1999 to 2009 compared the validity of HbA1c across different countries.[28] The review pointed out that the proportion of HbA1c ≥6.5% in patients diagnosed with OGTT varied extensively (17.0-78.0%) by the study center, suggesting a strong ethnic variation. The probability of detection through HbA1c was highest in the Indian population. Another study among individuals at increased risk of diabetes found that HbA1c levels were useful in detecting patients with early diabetes in individuals with FPG levels ≥100 mg/dL and, in particular, in patients with FPG levels above 110 mg/dL and below 126 mg/dL.[29] Those few studies indicate that there is a possibility of considering a lower threshold of FPG below the current threshold in detecting diabetes among high-risk individuals.

Obesity, causing the accumulation of adipose tissue in excess, plays a large role in causing prediabetes and diabetes. The extension of adipose tissue in other areas of the body increases certain metabolites, with the increased production of inflammatory cytokines causing systemic inflammation and disturbance of cellular function, resulting in impaired insulin signaling, locally induced loss of β-cell function, the occurrence of hyperglycemia, and diabetes eventually.[30] Thus, detection of hyperglycemia at early stages would provide an opportunity to commence cost-effective preventive interventions in resource-poor settings.

A cost-effectiveness study has shown that lowering FBG thresholds progressively in 5 mg/dL decrements from 120 mg/dL in adults at high risk of diabetes leads to increased quality-adjusted life years (QALYs), cost, and cost per QALY.[31] This study has highlighted that a threshold of 105 mg/dL or higher would be cost-effective. Further lowering of the FPG threshold is possible where the intervention costs are minimal without compromising effectiveness.

HbA1c represents the average plasma glucose level over the past 8-12 weeks.[32] Moreover, it is used as a measure of glycemic control. In conforming to the ADA guidelines, the WHO recommended that HbA1c should be used as a diagnostic test for diabetes provided stringent quality assurance tests are in place; assays are standardized to the international reference values and in the absence of conditions that preclude its accuracy.[33] There are several benefits of defining HbA1c as a diagnostic test: it is equally or better at predicting the retinopathy than FPG;[33] HbA1c is not affected by the day-to-day variability of plasma glucose; and the testing does not require any fasting

state.[34] Evidence suggests that HbA1c is a reliable measure of chronic hyperglycemia, as well as a prognostic marker of long-term diabetes complications, including CVD risk.[35] However, further understanding is required about its suitability as a reference standard since much variation has been described in previous reviews.

What Does This Study Add?

- The present cutoff point of FPG 126 mg/dL does not detect 40% of the diabetic patients identified with HbA1c (≥6.5%) in an overweight/obese and predominantly urban population. Lowering the cutoff point to 100 mg/dL for high-risk populations would identify more people with the disease but result in some false positives to some extent. Our findings were consistent with SLDCS 2005-2006 results, though we used HbA1c as the reference standard in contrast to OGTT by the SLDCS.
- Almost 1 in 4 persons (25.4%) has diabetes according to HbA1c (≥6.5%) in a 35-64-year-old, overweight/obese, and predominantly urban population in Sri Lanka. This indicates a higher prevalence of diabetes than the figures in past surveys for this age group. This could be due to the high-risk nature of our study participants, i.e., high BMI and urbanicity, and the reference test we used.
- Despite the majority being highly educated, predominantly employed, and living in urban/suburban areas, a substantial percentage (44%) of the disease remains undiagnosed. Although diabetes is common and there are screening services free of cost, there seems to be a gap in seeking care for several reasons.

Study Limitations

The main limitation of our analysis is the use of HbA1c as the reference standard, which has a low diagnostic accuracy according to some studies.[27] Many previous studies have used the 2-hour OGTT as the reference standard. The absence of OGTT limited the comparability of our results with other studies. Nevertheless, this will be one of the first studies to report the correlation between the 2 tests concerned. Due to limited resources, the present study has taken only a single FPG assessment from each individual despite the guidelines that suggest 2 measurements for the diagnosis of diabetes.

Exclusion of persons with BMI <25 kg/m^2 prevented the metabolically high-risk group based on the Asian cutoff point (BMI 23.5 kg/m^2). Factors that affect HbA1c levels, such as anemia and hemoglobinopathies, could not be excluded since there was no possibility of screening for these conditions upon enrolment.

Conclusion

Our study revealed that lowering the threshold of FBG from 126 mg/dL to 100 mg/dL would detect more patients with diabetes among 35- to 64-year-old, overweight, or obese adults. At present, the FPG value of 126 mg/dL is taken as the cutoff point to diagnose diabetes irrespective of the risk of having diabetes. Our findings suggest lowering the diagnostic threshold for diabetes from 126 mg/dL to 100 mg/dL in high-risk adults, i.e., those above 35 years with BMI > 18.5 kg/m^2. Thus, we recommend that a 100 mg/dL threshold be used in detecting diabetes among high-risk adults in primary healthcare settings so that low-cost interventions can be initiated early. Further analysis would be required to characterize and compare the participants identified by the 2 tests, FPG and HbA1c. A high rate of undiagnosed diabetes emphasizes the need for active screening of populations at risk through diversifying the services of primary healthcare and strengthening their HLCs.

Other Information: The study was registered in the Sri Lanka Clinical Trials Registry (SLCTR/2016/018). Available at https://slctr.lk/trials. The complete study protocol is available in the open-access journal *Contemporary Clinical Trials Communications*, under the title "*mHealth nutrition and lifestyle intervention (mHENAL) to reduce cardiovascular disease risk in a middle-aged, overweight and obese population in Sri Lanka: study protocol for a randomized controlled trial.*" Available at https://doi.org/10.1016/j.conctc.2019.100453.

Data Availability Statement: The investigators are bound by the ethical condition that no individual data or biological material will be shared with any other party.

Ethics Committee Approval: Ethics clearance was obtained from the Ethics Review Committee of the University of Colombo Faculty of Medicine, Sri Lanka (approval number: EC-16-061; date: May 19, 2016) prior to data collection.

Informed Consent: Written informed consent was obtained from the partcipants who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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References

1. International Diabetes Federation. *The IDF Diabetes Atlas*. 8th ed, 2019 . at:https://reports.instantatlas.com/report/view/704ee0e6475b4af885051bcec15f0e2c/LK. Accessed September 1, 2019.
2. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the global burden of disease study 2010. *Lancet*. 2012;380(9859):2095-2128. [CrossRef]
3. Bhutani J, Bhutani S. Worldwide burden of diabetes. *Indian J Endocrinol Metab*. 2014;18(6). [CrossRef]
4. Katulanda P, Constantine GR, Mahesh JG, et al. Prevalence and projections of diabetes and pre-diabetes in adults in Sri Lanka - Sri Lanka Diabetes, cardiovascular Study (SLDCS). *Diabet Med*. 2008;25(9):1062-1069. [CrossRef]
5. Ministry of Health Nutrition and Indigenous Medicine. *Non-communicable Disease Risk Factor Survey*. Sri Lanka. Colombo; 2015.
6. Stratton IM, Adler AI, Neil HAW, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Br Med J*. 2000;321(7258):405-412. [CrossRef]
7. DCCT Research Group. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial. *Diabetes*. 1995;44(8):968-983.
8. Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med*. 2004 September 21;141(6):421-431. [CrossRef]
9. Wild SH, Byrne CD. Risk factors for diabetes and coronary heart disease. *BMJ*. 2006;333(7576):1009-1011. [CrossRef]

10. Hills AP, Arena R, Khunti K, et al. Epidemiology and determinants of type 2 diabetes in South Asia. *Lancet Diabetes Endocrinol*. 2018;6(12):966-978. [CrossRef]
11. Wijeyaratne C, Arambepola C, Karunapema P, et al. Capacity-building of the allied health workforce to prevent and control diabetes: lessons learnt from the National Initiative to Reinforce and Organize General Diabetes Care in Sri Lanka (NIROGI Lanka) project. *WHO S East Asia J Public Heal*. 2016;5(1):34-39. [CrossRef]
12. Ministry of Health Care and Nutrition Sri Lanka. *The National Policy & Strategic Framework for Prevenetion and Control of Chronic Non-communicable Diseases*. Ministry of Health Care and Nutrition: Colombo; 2009.
13. Mallawaarachchi DSV, Wickremasinghe SC, Somatunga LC, Siriwardena VT, Gunawardena NS. Healthy Lifestyle Centres: a service for screening noncommunicable diseases through primary health-care institutions in Sri Lanka. *WHO S East Asia J Public Heal*. 2016;5(2):89-95. [CrossRef]
14. Katulanda GW, Katulanda P, Dematapitiya C, et al. Plasma glucose in screening for diabetes and pre-diabetes: how much is too much? Analysis of fasting plasma glucose and oral glucose tolerance test in Sri Lankans. *BMC Endocr Disord*. 2019;19(1):11. [CrossRef]
15. Bouma M, Dekker JH, de Sonnaville JJ, et al. How valid is fasting plasma glucose as a parameter of glycemic control in non-insulin-using patients with type 2 diabetes? *Diabetes Care*. 1999;22(6):904-907. [CrossRef]
16. Senarath U, Katulanda P, Fernando DN, et al. MHealth nutrition and lifestyle intervention (mHENAL) to reduce cardiovascular disease risk in a middle-aged, overweight and obese population in Sri Lanka: study protocol for a randomized controlled trial. *Contemp Clin Trials Commun*. 2019;16:100453. [CrossRef]
17. Flahault A, Cadilhac M, Thomas G. Sample size calculation should be performed for design accuracy in diagnostic test studies. *J Clin Epidemiol*. 2005;58(8):859-862. [CrossRef]
18. Kim CH, Kim HK, Bae SJ, Park JY, Lee KU. Discordance between fasting glucose-based and hemoglobin A1c-based diagnosis of diabetes mellitus in Koreans. *Diabetes Res Clin Pract*. 2011;91(1):e8-e10. [CrossRef]
19. De Silva AP, De Silva SHP, Haniffa R, et al. Inequalities in the prevalence of diabetes mellitus and its risk factors in Sri Lanka: A lower middle income country. *Int J Equity Health*. 2018;17(1):45. [CrossRef]
20. Cohen JF, Korevaar DA, Altman DG, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. *BMJ Open*. 2016;6(11):e012799. [CrossRef]
21. Cox ME, Edelman D. Tests for screening and diagnosis of type 2 diabetes. *Clin Diabetes*. 2009;27(4):132-138. [CrossRef]
22. Hu Y, Liu W, Chen Y, et al. Combined use of fasting plasma glucose and glycated hemoglobin A1c in the screening of diabetes and impaired glucose tolerance. *Acta Diabetol*. 2010;47(3):231-236. [CrossRef]
23. Florkowski C. HbA1c as a diagnostic test for diabetes mellitus - Reviewing the evidence. *Clin Biochem Rev*. 2013;34(2):75-83.
24. Silverman RA, Pahk R, Carbone M, et al. The relationship of plasma glucose and HbA1c levels among emergency department patients with no prior history of diabetes mellitus. *Acad Emerg Med*. 2006;13(7):722-726. [CrossRef]
25. Grint D, Alisjhabana B, Ugarte-Gil C, et al. Accuracy of diabetes screening methods used for people with tuberculosis, Indonesia, Peru, Romania, South Africa. *Bull World Health Organ*. 2018;96(11):738-749. [CrossRef]
26. Somasundaram NP, Ranathunga I, Gunawardana K, Ediriweera DS. High prevalence of diabetes mellitus in Sri Lankan urban population – data from Colombo urban study. *Sri Lanka J Diabetes Endocrinol Metab*. 2019;9(2):8. [CrossRef]
27. Karnchanasorn R, Huang J, Ou HY, et al. Comparison of the current diagnostic criterion of HbA1c with fasting and 2-hour plasma glucose concentration. *J Diabetes Res*. 2016;2016:6195494. [CrossRef]
28. Christensen DL, Witte DR, Kaduka L, et al. Moving to an A1C-based diagnosis of diabetes has a different impact on prevalence in different ethnic groups. *Diabetes Care*. 2010;33(3):580-582. [CrossRef]
29. Clark Perry RC, Ravi Shankar RR, Fineberg N, Mcgill J, Baron AD. HbA1c measurement improves the detection of type 2 diabetes in high-risk individuals with nondiagnostic levels of fasting plasma glucose. *Diabetes Care*. 2001;24(3):465-471. [CrossRef]
30. Ruze R, Liu T, Zou X, et al. Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. *Front Endocrinol*. 2023;14:1161521. [CrossRef]
31. Nathan DM, Turgeon H, Regan S. Relationship between glycated haemoglobin levels and mean glucose levels over time. *Diabetologia*. 2007;50(11):2239-2244. [CrossRef]
32. Zhuo X, Zhang P, Kahn HS, Edward W, Gregg EW. Cost-effectiveness of alternative thresholds of the fasting plasma glucose test to identify the target population for type 2 diabetes prevention in adults aged ≥45 years. *Diabetes Care*. 2013;36(12):3992-3998. [CrossRef]
33. Wolrd Health Organization. *Use of glycated. Haemoglobin: (HbA1c) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation*. WHO: Geneva; 2011.
34. Tapp RJ, Tikellis G, Wong TY, et al. Longitudinal association of glucose metabolism with retinopathy: results from the Australian diabetes obesity and lifestyle (AusDiab) study. *Diabetes Care*. 2008;31(7):1349-1354. [CrossRef]
35. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. *Biomark Insights*. 2016;11:95-104. [CrossRef]