RESEARCH ARTICLE

Hyperglycemia in pregnancy diagnosed using glycated hemoglobin (HbA_{1c}) in Uganda: a preliminary cross-sectional report [version 1; peer review: awaiting peer review]

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Abstract

Background: Hyperglycemia in pregnancy (HIP) is a common medical complication during pregnancy and is associated with several short and long-term maternal-fetal consequences. We aimed to determine the prevalence and factors associated with HIP among Ugandan women.

Methods: We consecutively enrolled eligible pregnant women attending antenatal care at Kawempe National Referral Hospital, Kampala, Uganda in September 2020. Mothers known to be living with diabetes mellitus or haemoglobinopathies and those with anemia (hemoglobin <11g/dl) were excluded. Random blood sugar (RBS) and glycated hemoglobin A1c (HbA_{1c}) were measured on peripheral venous blood samples. HIP was defined as an HbA1c ≥5.7% with its subsets of diabetes in pregnancy (DIP) and prediabetes defined as HbA1c of ≥6.5% and 5.7-6.4% respectively. ROC curve analysis was performed to determine the optimum cutoff of RBS to screen for HIP.

Results: A total of 224 mothers with a mean (± SD) age 26±5 years were enrolled, most of whom were in the 2nd or 3rd trimester (94.6%, n=212) with a mean gestation age of 26.6±7.3 weeks. Prevalence of

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HIP was 11.2% (n=25) (95% CI: 7.7-16.0). Among the mothers with HIP, 2.2% (n=5) had DIP and 8.9% (n=20) prediabetes. Patients with HIP were older (28 years vs. 26 years, p=0.027), had previous tuberculosis (TB) contact (24% vs. 6.5%, p=0.003) and had a bigger hip circumference (107.8 (±10.4) vs. 103.3 (±9.7) cm, p = 0.032). However only previous TB contact was predictive of HIP (odds ratio: 4.4, 95% CI: 1.2-14.0; p=0.022). Using HbA_{1c} as a reference variable, we derived an optimum RBS cutoff of 4.75 mmol/L as predictive of HIP with a sensitivity and specificity of 90.7% and 56.4% (area under the curve = 0.75 (95% CI: 0.70-0.80, p<0.001)), respectively.
Conclusions: HIP is common among young Ugandan women, the majority of whom are without identifiable risk factors.

Keywords
Hyperglycemia in pregnancy, prediabetes, Hemoglobin A1c, Uganda

This article is included in the Healthy Lives gateway.

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Introduction

Pregnancy is naturally characterized by insulin resistance and hyperinsulinemia leading to hyperglycemia, the most common endocrinopathy during the gestation period (Farrar, 2016; Saravanan *et al.,* 2020). Previously, any hyperglycemia detected in pregnancy was termed gestational diabetes (GDM) (WHO, 2013). However, recently, the term hyperglycemia in pregnancy (HIP) has been proposed by the World Health Organization (WHO) (Diabetes Canada Clinical Practice Guidelines Expert Committee *et al.,* 2018; WHO, 2018). HIP classifies hyperglycemia based on both onset and severity (Diabetes Canada Clinical Practice Guidelines Expert Committee *et al.,* 2018; WHO, 2018). It includes the more severe manifestations of total diabetes in pregnancy (comprising of known and previously undiagnosed diabetes in pregnancy [DIP]), which may persist in the post-partum period and a more benign form, GDM (WHO, 2013). DIP and GDM are together termed hyperglycemia first detected in pregnancy (WHO, 2013).

HIP is a growing public health concern and adversely affects maternal and child health, and is likely to contribute to the growing global diabetes epidemic (Bianco & Josefson 2019; Guariguata *et al.,* 2014). Depending on the diagnostic criteria used and the population of pregnant women studied, the resulting prevalence of HIP can vary widely. Results from a recent survey on HIP prevalence in 173 countries found country-specific prevalence estimates ranging from <1% in Germany up to 28% for a study in Nepal, using a variety of criteria (Jiwani *et al.,* 2012). Globally, HIP has been estimated to affect nearly 16.9%, or 21.4 million, live births among women of reproductive age, with total diabetes in pregnancy accounting for an estimated 16.0% of these cases (Guariguata *et al.,* 2014). In this report, more than 90% of cases of HIP were estimated to occur in low- and middle-income countries (LMICs), with South-East Asian and African regions having the highest number of live births affected with HIP at over 6.0 (23.2%) and 4.3 (16.0%) million cases, respectively (Guariguata *et al.,* 2014).

Previous studies assessing the prevalence of HIP have mostly concentrated on high risk mothers, such as those with advanced age, high gravidity or in a specific period of gestation age, which may not reflect the true prevalence in the general population of pregnant women (Adefisan *et al.,* 2020; Cosson *et al.,* 2019; Mukuve *et al.,* 2020). Moreover, screening and intervention on HIP during antenatal care (ANC) are not routine in most LMICs, making an accurate estimation of the burden of this treatable condition largely impossible. This could be due to the several caveats associated with current tests, which requires overnight fasts, multiple clinic visits and the oral glucose tolerance test (OGTT) which is labor intensive.

Despite the serious public health implications of HIP, there has been no universal definition and no universal standards for screening and diagnosis, and a wide variety of methods are applied (Guariguata *et al.,* 2014). However, fasting plasma glucose (FPG), 1-hour, 2-hour or 3-hour plasma glucose following a 75g OGTT, interpreted according to the American Diabetes Association (ADA), WHO or the International Association of the Diabetes and Pregnancy Study Group (IADPSG) criteria are the most commonly used methods (Guariguata *et al.,* 2014; Meek *et al.,* 2020). Glycated hemoglobin (HbA_{1c}) can also be used to screen for and diagnose HIP, especially in early pregnancy (Goyal *et al.,* 2020). Trimester specific cutoff values for HbA_{1c} have recently been proposed (Sánchez-González *et al.,* 2018), though not widely validated or adopted by international guidelines (Sánchez-González *et al.,* 2018).

The aim of this study was to determine the prevalence of HIP and its associated risk factors among pregnant women attending ANC in Uganda, irrespective of their gestation age, using HbA_{1c}. Secondarily, we sought to determine an appropriate random blood sugar (RBS) cutoff value for screening for HIP in our setting.

Methods

Study design and setting

We conducted a cross-sectional study in a large specialized obstetrics and gynecology national referral hospital in Kampala, Uganda in September 2020.

This study enrolled pregnant women attending the ANC clinic at the directorate of Obstetrics and Gynecology at Kawempe National Referral Hospital (KNRH), which also serves as the academic teaching hospital for Makerere University College of Health Sciences. KNRH was purposively selected due to its central location attracting a large number of patients from Kampala and its surrounding districts, thus representing the demographics of both urban and peri-urban patient populations. On average, about 50-60 mothers attend the ANC clinic at KNRH from Tuesday to Thursday every week.

Study population

Eligible participants were all pregnant women attending ANC (regardless of gestation age) during the study period who provided informed consent to participate in the study. Pregnant women known to be living with diabetes or haemoglobinopathies were excluded. In addition, patients with anemia (hemoglobin <11g/dl) were excluded at analysis.

Sample size and sampling procedure

With an estimated prevalence of HIP at 15.6% in Uganda (Kiiza *et al.,* 2020), using the formula for the determination of sample size for prevalence studies (Kish-Leslie) (Kish, 1965), with an assumed non-response rate of 10%, precision of 5%, and a Z-score of 1.96 at 95% confidence interval, a sample size of 217 was anticipated. Eligible participants were identified, and consecutively sampled with the assistance of a senior nurse at the ANC clinic and two other trained study nurses.

Data collection

Study clinicians administered a semi-structured study questionnaire through a face-to-face interview to collect information regarding risk factors and symptoms for HIP and maternal characteristics: age, gravidity, education level, occupation, marital status, HIV status, tuberculosis contact, gestation age, history of abortion, smoking and alcohol usage, and the number of ANC

visits in the current pregnancy. Gestation age was estimated using the date of the last normal menstrual period. Polyuria, polydipsia, and polyphagia were considered classic symptoms of diabetes.

Diagnosis of hyperglycemia in pregnancy. All consenting mothers were subjected to a RBS and HbA_{1c} tests. RBS was performed at the point of care on venous blood samples using the On-Call™ Plus Glucometer (ACON Biotech, China) according to manufacturer's instruction. HbA_{1C} was estimated using Cobas® 6000 analyzer series (Roche Diagnostics) at the Central Diagnostic Laboratory Services (CDLS), Medical Research Council/Uganda Virus Research Institute and London School of Hygiene and Tropical Medicine Uganda Research Unit laboratory within 24 hours of sample collection. Prediabetes was defined as HbA_{1c} of 5.7% to 6.4% and overt diabetes (diabetes in pregnancy, DIP) as HbA_{1c} of 6.5% or higher, according to the American Diabetes Association (Goyal *et al.,* 2020) and consistent with guidelines of the IADPSG (Meek *et al.,* 2020; Saravanan *et al.,* 2020), and the WHO classification of hyperglycemia first diagnosed in pregnancy (WHO, 2018). Patients with HIP were referred for the appropriate clinical care according to the national guidelines.

Complete blood count. A complete blood count was performed using the HumaCount 5D Hematology System (Wiesbaden, Germany) using 3 mL of blood samples collected in EDTA tubes within 12 hours from the time of sample collection. Patients with hemoglobin concentration of 11g/dl or lower were regarded as having anemia according to the WHO definition (World Health Organization, 2011) of anemia in pregnancy and were subsequently excluded from the study at analysis. Anemic patients were also referred for appropriate management by the clinical team.

Anthropometrical assessment. Weight was measured with minimal clothing and without shoes using a digital bathroom weighing scale (SECA-Germany), placed on a flat surface and recorded to the nearest 0.1kg. Height was measured using a calibrated stadiometer. Waist and hip circumferences were measured using a tailor's measuring tape to the nearest 0.1 cm. Body mass index and Waist-Hip Ratios were calculated accordingly. Brachial blood pressure was measured from both arms while mothers were sitting down with their feet flat on the ground using an automated machine with an appropriate adult cuff size. The average of the two measurements was considered as the participant's blood pressure. Women were classified as hypertensive if systolic and diastolic blood pressure were ≥140mmHg and ≥90mmHg, respectively, and normal if blood pressure is less than 140/90mmHg.

Statistical analysis

Statistical analyses were performed using STATA version 16 (StataCorp LLC, College Station, TX, USA) and GraphPad Prism version 8.0.4 (GraphPad Software, La Jolla, CA, USA). The data were expressed as absolute numbers and percentages for categorical variables, and as means and standard deviations (mean ± SDs) for continuous variables. Shapiro-Wilk normality test was applied to evaluate all quantitative variables to select the appropriate test. Welch's One-Way ANOVA was used to compare continuous data across groups. Chi-square or Fisher' Exact tests were used to assess associations between HIP across demographic and clinical characteristics of participants. Variables with a p value <0.2 were fitted into a multivariable logistic regression model to adjust for confounders. Receiver operating characteristics (ROC) curve analysis was performed to determine the optimum cutoff of RBS in those patients who met criteria for HIP in relation to HbA_{1c} test. Area under the ROC curve (AUC) was shown with 95% Wilson confidence intervals (CI). Optimal diagnostic cut-off value for RBS were calculated using Youden's J statistic (sensitivity+specificity-1). For this analysis, the hypothesis was that at the optimal RBS cut off, the AUC = 0.7. In all analyses, $P<0.05$ was considered significant at 95% CI.

Ethical considerations

This study was approved by the Makerere University School of Medicine Ethics and Research Committee (reference number #REC REF 2020-113). All mothers provided informed written consent to participate after the study procedure, risks and benefits were explained to them.

Results

In September 2020, a total of 267 pregnant women participated in the study. However, 43 participants were excluded due to either incomplete data or presence of anemia (Figure 1).

Baseline characteristics of study participants

Of the 224 eligible participants, most were married (91.1%, n=204), and attending ANC for the first time in the current

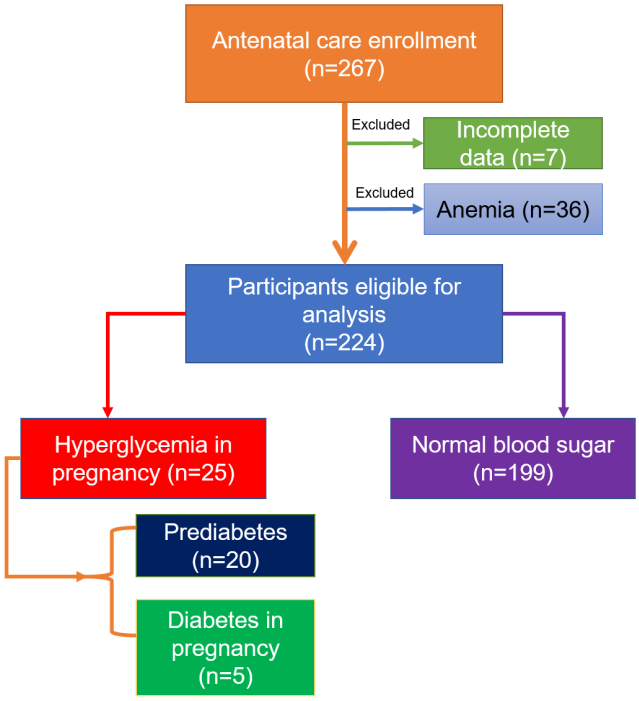

Figure 1. Study flow diagram.

pregnancy (63.4%, n=142). Over three quarters had attended post-primary education (77.7%, n=174) and were business-women (42.2%, n=99). The mean age of the women was 26 years (SD± 5), of which 138 (61.6%) were ≥25 years old. Just over one-third of the participants were primigravida (34.8%, n=78), and the majority of the mothers were in their 2nd or 3rd trimester of pregnancy (94.6%, n=212), with a mean gestation age of 26.6 weeks (SD ± 7.3) (Table 1). In total, 43 (19.2%) women had at least one of the classic symptoms of diabetes.

Table 1. Sociodemographic and maternal characteristics of the study participants.

Participant variable	N (%) or Mean ± SD
Antenatal care visit at enrollment	
First	142 (63.4)
Second	27 (12.1)
Third	19 (8.4)
Fourth and more	36 (16.1)
Age (years)	26 ± 5.0
<25 years	86 (38.4)
≥25 years	138 (61.6)
Marital status	
Married	204 (91.1)
Single	12 (5.4)
Widowed	8 (3.6)
Education level	
Informal	4 (1.8)
Primary	46 (20.5)
Secondary	117 (52.2)
Tertiary	57 (25.5)
Occupational status	
Business	99 (42.2)
Professional	46 (20.5)
Unemployed	79 (35.3)
Smoking status	
Former	2 (0.9)
Never	222 (99.1)
Alcohol usage	
Current	12 (5.4)
Former	38 (17.0)
Never	174 (77.7)
Family history of diabetes	
No	185 (82.6)
Yes	39 (17.4)
District of residence	
Kampala	156 (69.6)
Wakiso	62 (27.7)
Mpigi	1 (0.5)
Mukono	4 (1.8)
Entebbe	1 (0.5)
Residence	
Peri-Urban	63 (28.1)
Urban	161 (71.9)
HIV status	
Positive	6 (2.7)
Negative	218 (97.3)
BCG scar	
Yes	162 (72.3)
No	62 (27.7)
Family history of tuberculosis	
Yes	22 (9.8)
No	202 (90.2)
Tuberculosis contact	
Yes	19 (8.5)
No	205 (91.5)
Family size	
≤4	177 (79.0)
≥5	47 (21.0)
Symptoms of diabetes	
Yes	43 (19.2)
No	181 (80.8)
Gravidity	
Primigravida	78 (34.8)
Multigravida	120 (53.6)
Grand multigravida	19 (8.5)
Great grand multigravida	7 (3.1)
Previous abortion	
Yes	36 (16.1)
No	188 (83.9)

Participant variable	N (%) or Mean ± SD
Gestation age at enrollment (weeks)	26.6 ±7.3
Trimester at enrollment	
1	12 (5.4)
2	101 (45.1)
3	111 (49.6)
Anthropometry	
Weight (kilograms)	68.9 ± 12.4
Height (meters)	1.6 ± 0.06
Body mass index (kg/m2)	27.3 ± 4.8
Waist circumference (centimeters)	95.2 ± 10.4
Hip circumference (centimeters)	103.8 ± 9.8
Waist-hip circumference	0.92 ± 0.08
Blood pressure at enrollment	
Systolic blood pressure (mmHg)*	125 ± 18
Diastolic blood pressure (mmHg)*	78 ± 12.8
Normal	188 (91.5)
Hypertensive	19 (8.5)

*Average of two measurements taken.

Prevalence of HIP

RBS and HbA_{1c} was performed for all the 224 participants. The median (range) RBS was 4.6 (2.8-8.0) mmol/l. The median (range) of HbA_{1c} was 5.2 (3.6-14.9).

The overall prevalence of HIP was 11.2% (n=25) (95% CI: 7.7-16.0); 2.2% (n=5) (95% CI: 1.0-5.1) had DIP, and 8.9% (n=20) (95% CI: 5.9-13.4) prediabetes using the WHO criteria. Patients with HIP were slightly older than those without (28 years vs. 26 years, p=0.027), had previous tuberculosis contact (24% vs. 6.5%, p=0.003), had a bigger hip circumference (107.8 (±10.4) vs. 103.3 (±9.7) cm, p = 0.032) and a higher proportion of urban dwellers had HIP compared to their rural counterparts (88% vs.69.8%), though this was not statistically significant (p=0.062) (Table 2). However, after accounting for important confounders in a multivariable logistic regression models, none of these factors showed a statistically significant association (Table 3).

The mean RBS was slightly higher in those with HIP compared to those with normal HbA_{1c}; however this was not to statistical significance (Figure 2).

Using HbA_{1c} as a reference variable, ROC curve and the AUC for RBS as a predictor of HIP was 0.75 (95% CI: 0.70-0.80,

Table 2. Prevalence of hyperglycemia among pregnant women at Kawempe National Referral Hospital.

Participant variable	HIP (n=25)	No HIP (n=199)	P-value
	N (%)	N (%)	
ANC visit at enrollment	2 (1)	2 (1)	0.857
First	16 (64.0)	126 (63.3)	0.277
Second	5 (20)	22 (11.1)	
Third	0 (0)	19 (9.5)	
Fourth and more	4 (16)	32 (16.1)	
Age, mean (±SD)	28.4 ± 4.8	26.0 ± 5.0	**0.027**
<25 years	7 (28)	79 (39.7)	0.257
≥25 years	18 (72)	120 (60.3)	
Marital status			
Married	25 (100)	179 (89.9)	0.252
Single	0 (0)	12 (6.0)	
Widowed	0 (0)	8 (4.0)	
Education level			
Informal	0 (0)	4 (2.0)	0.661
Primary	7 (28)	39 (19.6)	
Secondary	13 (52)	104 (52.3)	
Tertiary	5 (20)	52 (26.1)	
Occupational status			
Business	13 (52)	86 (43.2)	0.666
Professional	5 (20)	41 (20.6)	
Unemployed	7 (28)	72 (36.2)	
Smoking status			
Former	0 (0)	2 (1.0)	>0.999
Never	25 (100)	197 (99.0)	
Alcohol usage			
Current	2 (8)	10 (5.0)	0.324
Former	6 (24)	32 (16.1)	
Never	17 (68)	157 (78.9)	
Family history of diabetes			
No	20 (80)	165 (82.9)	0.717
Yes	5 (20)	34 (17.1)	
District of residence			
Kampala	17 (68)	139 (69.8)	0.061
Wakiso	6 (24)	56 (28.1)	
Mpigi	1 (4)	3 (1.5)	
Mukono	0 (0)	1 (0.5)	
Entebbe	1 (4)	0 (0.0)	

Participant variable	HIP (n=25)	No HIP (n=199)	P-value
	N (%)	N (%)	
Residence			
Peri-Urban	3 (12)	60 (30.2)	0.062
Urban	22 (88)	139 (69.8)	
HIV status			
Positive	1 (4)	5 (2.5)	0.513
Negative	24 (96)	194 (97.5)	
BCG scar			
Yes	10 (40)	52 (26.1)	0.144
No	15 (60)	147 (73.9)	
Family history of tuberculosis			
Yes	4 (16)	18 (9.0)	0.282
No	21 (84)	181 (91.0)	
Tuberculosis contact			
Yes	6 (24)	13 (6.5)	**0.003**
No	19 (76)	186 (93.5)	
Family size			
≤4	19 (76)	158 (79.4)	0.694
≥5	6 (24)	41 (20.6)	
Symptoms of diabetes			
Yes	4 (16)	39 (19.6)	0.793
No	21 (84)	160 (80.4)	
Gravidity			
Primigravida	4 (16)	74 (37.2)	0.112
Multigravida	16 (64)	104 (52.3)	
Grand multigravida	3 (12)	16 (8.0)	
Great grand multigravida	2 (8)	5 (2.5)	
Previous abortion			
Yes	7 (28)	29 (14.6)	0.085
No	18 (72)	170 (85.4)	
Gestation age at enrollment (weeks; mean ± SD)	25.8 ± 7.7	26.7 ± 7.3	0.558
Trimester at enrollment			
1	1 (4)	11 (5.5)	0.922
2	12 (48)	89 (44.7)	
3	12 (48)	99 (49.7)	
Anthropometry, mean ± SD			
Weight (kilograms)	71.4 ± 15.0	68.6 ± 12.0	0.274
Height (meters)	1.6 ± 0.07	1.6 ± 0.06	0.408
BMI (kg/m2)	28.7 ± 5.9	27.1 ± 4.6	0.113
Waist circumference (centimeters)	97.5 ± 13.4	94.9 ± 10.0	0.227
Hip circumference (centimeters)	107.8 ± 10.4	103.3 ± 9.7	**0.032**
Waist-hip circumference	0.92 ± 0.08	0.92 ± 0.08	0.327
Blood pressure at enrollment, Mean ± (SD)			
Systolic blood pressure (mmHg)*	122 ± 12	125 ± 18	0.394
Diastolic blood pressure (mmHg)*	77 ± 8	78 ± 13	0.759
Normal	23 (92)	165 (82.9)	0.386
Hypertension	2 (8)	34 (17.1)	

HIP, hyperglycemia in pregnancy. *Average of two measurements taken.

Table 3. A multivariable logistic regression model showing factors associated with hyperglycemia among pregnant women at Kawempe National Referral Hospital.

Demographic and clinical characteristics	Adjusted Odds Ratio	95% CI	P-value
Age	1.04	0.92 - 1.16	0.549
District of residence			
Entebbe	1.00		
Kampala	1.55	0.49 - 4.92	0.458
Mukono	9.36	0.6 - 146.93	0.112
Residence			
Rural	1.00		
Urban	3.80	0.92 - 15.63	0.064
BCG scar			
Yes	1.00		
No	1.72	0.64 - 4.58	0.280

Demographic and clinical characteristics	Adjusted Odds Ratio	95% CI	P-value
Tuberculosis contact			
No	1.00		
Yes	4.14	1.23 - 13.98	0.022
Gravidity			
Primigravida	1.00		
Multigravida	1.67	0.43 - 6.43	0.458
Grand multigravida	2.08	0.3 - 14.55	0.462
Great grand multigravida	4.01	0.28 - 56.64	0.304
Previous abortion			
No	1.00		
Yes	1.24	0.37 - 4.21	0.728
Body mass index	0.98	0.84 - 1.15	0.826
Hip circumference	1.06	0.98 - 1.14	0.132

CI, confidence interval.

p<0.001) (Figure 3). We derived optimum cutoffs for RBS of 4.75 mmol/L with a sensitivity and specificity of 90.7% and 56.4%, respectively. At a lower RBS cutoff of 4.0 mmol/L, the sensitivity and specificity was 99.5% and 23.6%, respectively, and at a higher RBS cutoff of 5.5 mmol/L, the sensitivity and specificity was 26.9% and 83.5%, respectively.

Discussion

The use of HbA_{1c} for screening, diagnosis and monitoring of diabetes and prediabetes in pregnancy remains a work in progress with several unanswered questions (Hughes *et al.,* 2016). In the present study, we aimed to determine the prevalence and factors associated with HIP using HbA_{1c} in Uganda. To our knowledge, this is the first study to report on the use of HbA_{1c} to screen for HIP in Uganda. In our study, the prevalence of HIP ranged between 7.5 and 16.0%. This is consistent with the estimated prevalence of HIP of 16% reported in the Africa region (Guariguata *et al.,* 2014). In two previously published studies from Uganda, the prevalence of HIP was 15.6% using FPG criteria (Kiiza *et al.,* 2020) and 31.9% using OGTT criteria (Nakabuye *et al.,* 2017). The observed differences in the prevalence of HIP across these studies could be due to the difference in the diagnostic criteria used. It is well established that due to physiological changes in pregnancy, HbA_{1c} level decreases as gestation age increases (Kumpatla *et al.,* 2013; Rafat & Ahmad, 2012; Schaible *et al.,* 2018). This could explain the low prevalence observed in our study.

HIP is typically diagnosed between 24th and 28th weeks of gestation (WHO, 2018). However, evidence from the metacentric landmark trial, hyperglycemia and adverse pregnancy outcome (HAPO) showed that continued exposure to hyperglycemia

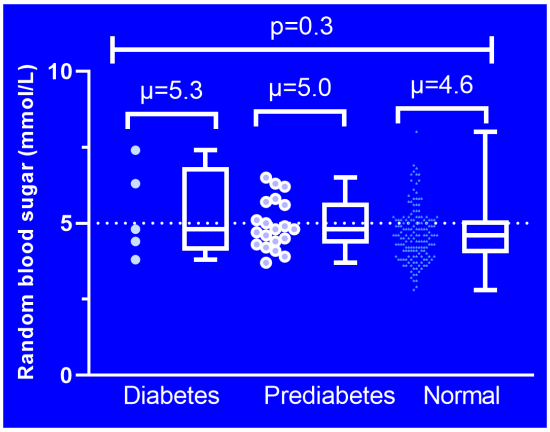

Figure 2. Random blood sugar levels across different glycemic status.

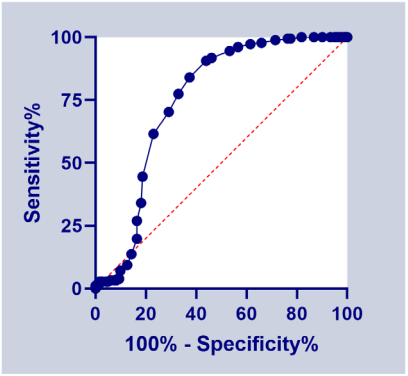

Figure 3. Receiver operating characteristic curve.

non-diagnostic for diabetes was associated with adverse maternal and fetal outcomes (Catalano *et al.,* 2012; HAPO Study Cooperative Research Group *et al.,* 2008). Based on this finding, current guidelines recommend early screening and appropriate management of HIP to improve maternal and fetal outcomes (WHO, 2018). OGTT is generally considered the gold standard for screening for HIP (Coetzee *et al.,* 2020). However, FPG and HbA_{1c} can also be used. HbA_{1c} has been shown to correlate with poor maternal-fetal outcomes (Ho *et al.,* 2017). Studies to establish normal HbA_{1c} reference ranges in pregnancy are scarce. Among healthy non-diabetic pregnant women, a recent study from Mexico has shown that the upper limit of HbA_{1c} increases with gestation age (Sánchez-González *et al.,* 2018). In this population, the cutoff for the diagnosis of HIP was nearly identical to the American Diabetes Association criteria for the diagnosis of diabetes and prediabetes in non-pregnant population and in early pregnancy. However, given the ease of HbA_{1c} compared to OGTT, testing may improve follow-up rates and combining HbA_{1c} analysis with FPG or waist circumference may improve detection rates (Hughes *et al.,* 2016).

Risk factors for HIP include advancing age; obesity; excessive weight gain during pregnancy; a family history of diabetes; HIP during a previous pregnancy; a history of stillbirth or infant with congenital abnormality; and glycosuria during pregnancy significantly overlap with those of type 2 diabetes mellitus (Diabetes Canada Clinical Practice Guidelines Expert Committee *et al.,* 2018; Farrar, 2016; Saravanan *et al.,* 2020). In our study, the majority of the patients were young, and family history of diabetes was only elicited in 20% of the patients. This is consistent with published studies in Uganda and elsewhere that have reported that over one-third to half of mothers do not have known risk factors (Nakabuye *et al.,* 2017; Thacker & Petkewicz, 2009). This has implications for the selection of patients for screening. RBS has been studied as a possible screening tool. It is interesting that none of the patients with DIP in our study had RBS above 11.1 mmol/L. In one study conducted in Nigeria, using OGTT as a reference standard, the best threshold for screening was 5.4 mmol/L for RBS, which had a sensitivity of 45% and a specificity of 90.0% (Adefisan *et al.,* 2020). In our study, with a cutoff of 4.75mmol/L, we found the reverse, a higher sensitivity (90.7%) and a lower specificity (56.4%). However, at a cutoff of 5.5 mmol/L, we found a similar diagnostic performance (sensitivity of 27% and specificity of 84%). Given the high sensitivity of RBS at a relatively lower RBS cutoff and the cost of performing HbA_{1c} especially in LMICs, RBS – a cheap and readily available modality – may be used alongside HbA_{1c} for screening for HIP in our setting.

Our study is not without limitations. Firstly, we had a small sample size derived from a single center and thus our findings may not be generalizable to the general population of pregnant women in Uganda. Secondly, there is no established HbA_{1c} reference ranges among Ugandan women stratified by gestation age. It is therefore likely that we may have missed some cases of HIP since we used HbA_{1c} cutoff for non-/early pregnancy population. However, we excluded anemic patients by performing hemoglobin estimation for all mothers. Lastly, being a pilot study, we were unable to retrieve key risk factors, such as pre-pregnancy weight, and birth weights and perinatal outcomes of previous pregnancies. However, over 60% of the mothers were primigravida. However, the strength of this study lies in its inclusiveness of pregnant mothers of different gestation ages from both urban and peri-urban communities. We report for the first time the feasibility of screening for HIP using HbA_{1c} in a resource limited setting and the utility of RBS as an adjunct to HBA_{1c} to aid in identifying of mothers who are likely to have HIP.

Conclusions

In conclusion, we found a slightly over 10% prevalence of HIP among Uganda women all ages of gestation. The majority of those diagnosed with HIP were young without identifiable risk factors for hyperglycemia. RBS and HbA_{1c} may be used complementarily to diagnose HIP in resource constrained settings. We recommend a larger, multicenter study using different diagnostic modalities to confirm of findings.

Data availability

Underlying data

Figshare: Hyperglycemia in pregnancy diagnosed using glycated hemoglobin (HbA1c) in Uganda: a preliminary cross-sectional report dataset, https://doi.org/10.6084/m9.figshare.13292690.v1 (Bongomin, 2020).

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