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ORIGINAL RESEARCH ARTICLE

First-trimester glycosylated hemoglobin (HbA1c) and maternal characteristics in the prediction of gestational diabetes: An observational cohort study

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Abstract

Introduction: This study aimed to investigate the extent to which gestational diabetes mellitus (GDM) can be predicted in the first trimester by combining a marker of growing interest, glycosylated hemoglobin A1c (HbA1c), and maternal characteristics.

Material and methods: This observational study was conducted in the outpatient obstetric department of our institution. The values of HbA1c and venous random plasma glucose were prospectively assessed in the first trimester of pregnancy. We determined maternal characteristics that were independent predictors from the regression analysis and calculated areas under the receiver-operating curves by combining the maternal age, body mass index, previous history of GDM, and first-degree family history for diabetes mellitus. Moreover we investigated the predictive capability of HbA1c to exclude GDM. Patients with a first-trimester HbA1c level of 6.5% (48 mmol/mol) or more were excluded. The study was registered at ClinicalTrials.gov ID: NCT02139254.

Results: We included 785 cases with complete dataset. The prevalence of GDM was 14.7% (115/785). Those who developed GDM had significantly higher HbA1c and random plasma glucose values ($p < 0.0001$ and $p = 0.0002$, respectively). In addition, they had a higher body mass index, were more likely to have a history of GDM and/or a first-degree family history of diabetes. When these maternal characteristics were combined with the first-trimester HbA1c and random plasma glucose the combined area under the receiver operating characteristics curve was 0.76 (95% CI 0.70–0.81).

Conclusions: Our results indicate that HbA1c and random plasma glucose values combined with age, body mass index, and personal and family history, allow the identification of women in the first trimester who are at increased risk of developing GDM.

KEYWORDS

gestational diabetes, glycosylated hemoglobin A1c, pregnancy complications, screening method

Abbreviations: AUC, area under the receiver operating characteristics curve; BMI, body mass index; CI, confidence interval; GDM, gestational diabetes mellitus; HAPO, Hyperglycemia and Adverse Pregnancy Outcome; HbA1c, glycosylated hemoglobin A1c; IADPSG, International Association of Diabetes and Pregnancy Study Groups; OGTT, oral glucose tolerance test; OR, odds ratio; ROC, receiver operating characteristic curve.

1 | INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any glucose intolerance that develops or is first diagnosed during pregnancy. Recently, it has been described by the American Diabetes Association as diabetes diagnosed during pregnancy that is not clearly overt diabetes.[1] This definition implies the possible existence of two forms of GDM, one that is based on a pregestational metabolic disorder, and another that is caused by a disturbed metabolic adaptation to the energy requirements of pregnancy under profound physiological insulin resistance. Despite tremendous effort and research a global consensus on GDM screening is still lacking. The original criteria to define GDM were established based on a 3-hour 100-g oral glucose tolerance test (OGTT) by O'Sullivan and Mahan in 1964.[2] However consecutive studies demonstrated that even lower degrees of hyperglycemia were associated with an increased risk of adverse pregnancy outcome.[2-4] Based on the results of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study in 2008, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) developed a new guideline in 2010 recommending a universal one-step screening using the 75-g OGTT between 24 and 28 weeks of gestation.[5]

Key message

The combination of maternal history and characteristics with easily accessible biochemical markers may present a possible screening method. Similar to pre-eclampsia screening, the use of a prediction model for gestational diabetes would allow an early intervention to reduce adverse pregnancy outcome.

The American Diabetes Association amended their guideline in 2014 but stated that there were insufficient data to demonstrate the superiority of one screening to the other.[6]

At present, with the increasing prevalence of dysglycemia among pregnant women, screening for metabolic disorders in the first trimester becomes important. However, existing data are insufficient to determine how and based on which thresholds to screen early for GDM. Moreover, many experts do not recommend GDM screening in the first trimester at all, as there are no valid data regarding the benefits and harms of diagnosing and treating GDM in early gestation.[7]

However, the first trimester might be a clinically relevant opportunity for screening and management of glucose intolerance.[8] In

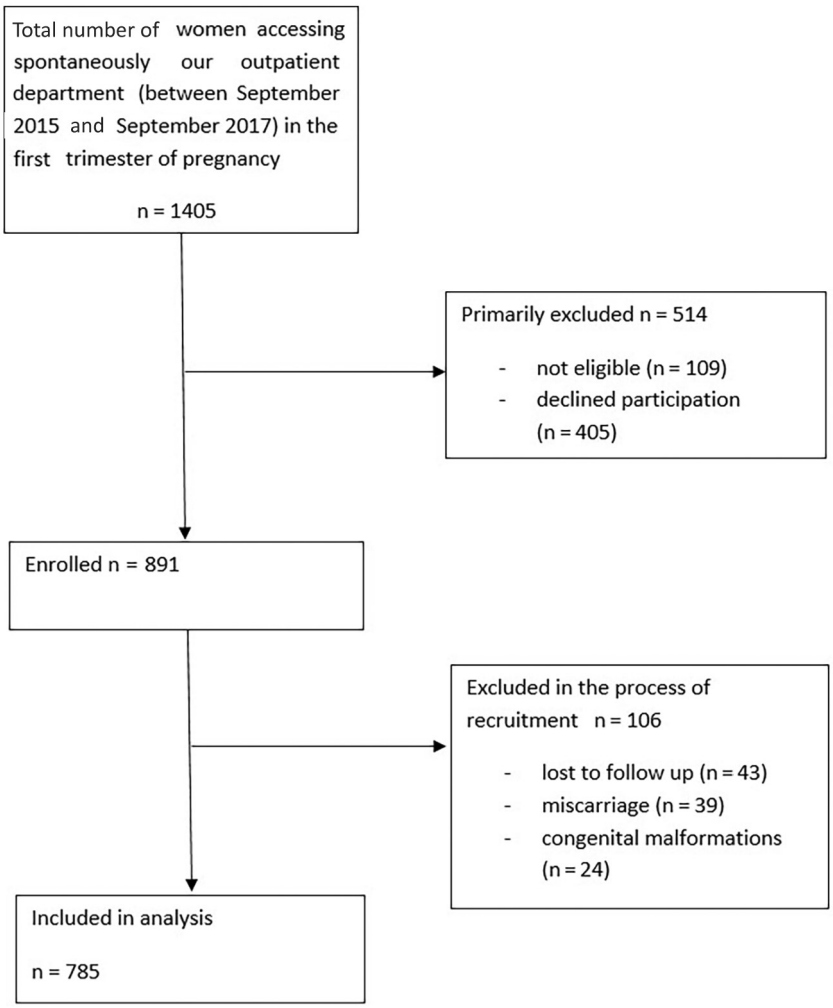

FIGURE 1 Flowchart of patient inclusion.

our recent study we showed, that a first-trimester glycosylated hemoglobin (HbA1c) of 42 mmol/mol (6.0%) or more was predictive of GDM, whereas no GDM was found in pregnancies in women with an HbA1c value less than 26 mmol/mol (4.5%). An HbA1c in the prediabetes range indicates a threefold increased risk of developing GDM.[9]

The aim of this study was to confirm these results in a wider population and establish an early risk stratification tool, which would diminish the need for universal screening from 24 weeks onward.

2 | MATERIAL AND METHODS

In a prospective cohort study, all pregnant women attending the outpatient department at the Division of Obstetrics of the University Hospital of Bern, during a 3-year study period, in the first trimester of pregnancy were invited to participate. The participants consisted of women spontaneously visiting our department or referred to us, who were at high and low risk for GDM. During the study period the number of new consultations in the first trimester reached approximately 500 per year. The primary outcomes of the study were the correlation between first-trimester HbA1c and random plasma glucose and the development of GDM. In all women, the HbA1c and random plasma glucose were assessed during the first trimester of pregnancy (up to 13^{+6} weeks) and a 2-hour, 75-g OGTT was performed according to the national guidelines between 24 and 28 weeks of gestation. The exclusion criteria were a known type 1 or type 2 diabetes or a first-trimester HbA1c of 48 mmol/mol (6.5%) or greater. Women who had a miscarriage before the implementation of the 75-g OGTT screening were also excluded. We determined whether personal and family history would add to the value of HbA1c in predicting GDM. Hence, the following information was obtained: obstetric history, family history of diabetes (first-degree), ethnicity (categorized as Caucasian or non-Caucasian), height, prepregnancy self-reported weight, and age. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Additional parameters were weight gain during pregnancy, GDM treatment with diet or insulin, duration of pregnancy in days, mode of delivery, incidence of pregnancy complications, neonatal birthweight in grams, Apgar score at 1 and 5 minutes, and arterial as well as venous pH from the umbilical cord.

If a woman was diagnosed with GDM, she was treated and monitored according to Swiss national guidelines. All women gave birth at our hospital and had phenotypically normal neonates. During the study period the electronic records, screening procedures, and treatment protocols remained unchanged.

2.1 | Diagnostic criteria for GDM

According to the HAPO Study[5,10] the diagnosis of GDM was made when any of the following criteria were met on the 75-g OGTT between 24 and 28 weeks of gestation: fasting plasma glucose 5.1 mmol/L or more, 10 mmol/L or more at 1 hour, and 8.5 mmol/L or more at 2 hours.

2.2 | Statistical analyses

Data were analyzed using the SPSS software, version 26, and GraphPad PRISM 8.2.1 for Windows. The categorical variables were summarized as numbers and percentages and compared between the

TABLE 1 Maternal and pregnancy characteristics in women with and without gestational diabetes mellitus

Characteristics	GDM ($n = 115$)	Non-GDM ($n = 670$)	p value
Maternal age (years), mean ± SD	32.1 ± 5.2	30.8 ± 6.1	0.02
Body mass index (kg/m^2), mean ± SD	26.4 ± 5.8	23.2 ± 5.9	<0.0001
Gestation at sampling (weeks), mean ± SD	10.1 ± 1.2	10.3 ± 1.4	0.08
Hemoglobin at sampling (g/L), mean ± SD	126 ± 8	124 ± 11	0.08
Gestation at delivery (weeks), mean ± SD	38.5 ± 1.8	39.3 ± 1.9	0.0008
Birthweight (grams), mean ± SD	3289 ± 525	3268 ± 534	0.64
Birthweight percentile (%), mean ± SD	52 ± 3	44 ± 2	0.011
LGA, *n* (%)	11 (9.5%)	21 (3.1%)	0.0036
SGA, *n* (%)	6 (5.2%)	68 (10%)	0.11
Family history of diabetes, *n* (%)	30 (26%)	77 (11.4%)	0.003
Multiparous, *n* (%)	72 (62.6%)	420 (62.7%)	>0.9999
Previous GDM, *n* (%)	15/72 (21%)	7/420 (2%)	<0.0001
Ethnicity			
Caucasian, *n* (%)	73 (70.2%)	474 (72.9%)	0.55
Non-Caucasian, *n* (%)	31 (29.8%)	176 (27%)	
Infertility treatment	7 (6%)	17 (2.5%)	0.06

Abbreviations: GDM, gestational diabetes mellitus; LGA, large for gestational age; SD, standard deviation; SGA, small for gestational age.

control mothers and mothers with GDM using Fisher's exact test. The continuous variables were summarized as means and standard deviation and compared between the control mothers and mothers with GDM using *t* test or Wilcoxon's signed-rank test, as appropriate. For each difference, a *p* value was calculated. Correlations between the potential risk variables of the mothers in the first trimester and a pathological 75-g OGTT between 24 and 28 weeks of gestation were analyzed using Pearson's chi-squared test. Receiver operating characteristic (ROC) curve analyses were conducted to evaluate the prognostic accuracy of first-trimester HbA1c and random plasma glucose in predicting GDM; moreover, the overall model quality was calculated. To assess the role of each variable in predicting GDM, binary logistic regression models (method: inclusion, forward and backward contingent) were fitted adjusting for BMI, age, ethnicity, and personal (previous GDM) and family (first-degree relative) history. The optimal threshold for the random plasma glucose and HbA1c values was calculated using the ROC coordinates and their Youden score and the positive likelihood ratio was also calculated. As resulted from logistic regressions, effect estimates were reported along with 95% confidence intervals (CIs) and *p* values. The comparison of the ROC curves was performed using MedCalc statistical software. A *p* value less than 0.05 was considered to indicate statistical significance.

2.3 | Ethics statement

Ethical approval for the current study was obtained by the local institutional review board Ethics Committee of the Canton of Bern, Switzerland (030_13) on April 25, 2014. The study was registered at ClinicalTrials.gov (NCT02139254).

3 | RESULTS

From September 2015 to September 2017, we were able to include 1000 singleton pregnancies in our study. Of those, 215 (21.5%) had to be excluded because of pre-existing diabetes, miscarriage, fetal malformations, or missing data (Figure 1). The mean gestational age at inclusion was 10.2 ± 1.4 weeks. The prevalence rate of GDM in our cohort was 14.7% (115/785). The clinical maternal characteristics and pregnancy outcomes of our study population were dichotomized between those with and without GDM and are listed in Table 1. The mean first-trimester HbA1c and random plasma glucose values were significantly higher in the GDM group than in the non-GDM group (34 mmol/mol [5.26% ± 0.35%] vs 32 mmol/mol [5.10% ± 0.27%], $p < 0.001$ and 4.63 ± 0.94 mmoL/L vs 4.20 ± 0.76 mmoL/L, $p < 0.001$, respectively). Although the gestational age at delivery was lower, women who later developed GDM had higher BMI, were older, and their infant showed a higher neonatal birthweight centile. The logistic regression analysis revealed that the incidence of GDM was significantly influenced by maternal age, BMI, previous history of GDM, and first-degree family history for diabetes mellitus (Table 2).

Figure 2 presents sequential increase in GDM incidence correlated with higher first-trimester HbA1c values. All the women with a first-trimester HbA1c of 42 mmol/mol (6.0%) or more (4/785) developed GDM. Furthermore, we stratified this wide mixed population based on the prediabetes HbA1c cut-off value of 39 mmol/mol (5.7%). The prediabetes group had a significantly higher GDM

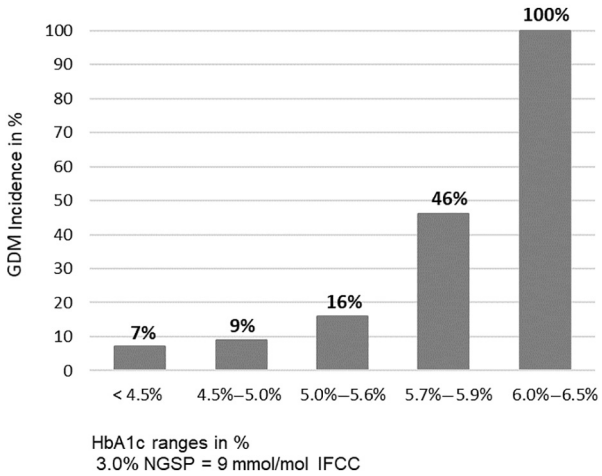

FIGURE 2 First-trimester glycosylated hemoglobin A1c (HbA1c) (%) ranges and gestational diabetes mellitus (GDM) incidence (%) in our population. IFCC, International Federation of Clinical Chemistry and Laboratory Medicine; NGSP, National Glycohemoglobin Standardization Program.

TABLE 2 Univariate and multivariate analysis of factors associated with gestational diabetes mellitus

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value[a]
Maternal age (per year)	1.05	−3.05 to −0.80	0.008	1.04	1.00–1.09	0.02
Body mass index (per kg/m^2)	1.16	−3.45–0.74	<0.0001	1.14	1.01–1.27	<0.0001
Racial origin as risk factor	2.14	1.13–3.98	0.02	1.34	1.14–1.53	0.14
Family history of diabetes						
First-degree relative	2.48	1.49–4.07	0.0005	2.35	1.80–2.91	0.003
Pregnancy with previous GDM	12.2	5.40–30.17	<0.0001	8.92	8.58–9.25	<0.0001

Abbreviations: CI, confidence interval; GDM, gestational diabetes mellitus; OR, odds ratio.

[a]Adjusted for maternal age, body mass index, gestational age at sampling, hemoglobin at sampling, ethnicity, parity, conception status, and previous GDM.

incidence (50% [15/30] vs 13% [100/755]) in the group of HbA1c less than 39 mmol/mol (5.7%) ($p < 0.0001$; 95% CI 2.465–11.94, odds ratio [OR] 5.5).

The ROC analysis showed a significant relation between the HbA1c value and the occurrence of GDM (Figure 3A). The optimal diagnostic HbA1c cut-off value to rule out GDM, derived from the ROC analysis, was 26 mmol/mol (4.5%). Using this cut-off value the test performance yielded a low sensitivity, a specificity of 98%, and positive and negative likelihood ratios of 1.01 and 0.5, respectively. Therefore, if we had used a first-trimester HbA1c cut-off value of 26 mmol/mol (4.5%) or less we would have missed only 2/115 (1.7%) women who developed GDM in the third trimester. Hence, HbA1c alone could not qualify as a screening method for GDM. Similarly, a significant increase in the GDM incidence with rising random plasma glucose value was observed (Figure 3B).

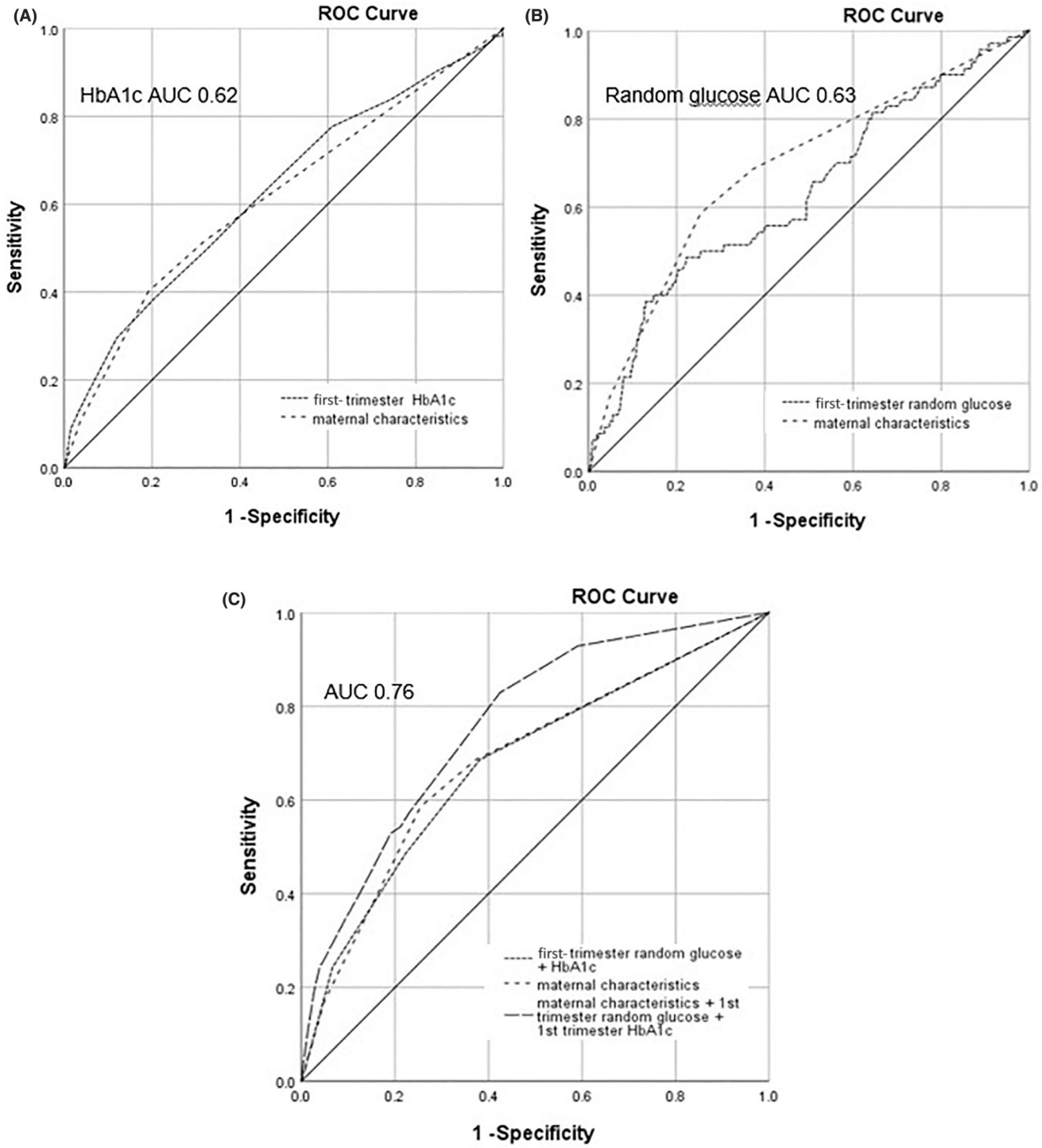

FIGURE 3 Receiver operating curves (ROC) of first-trimester glycosylated hemoglobin A1c (HbA1c) (A) and, random glucose values (B) separately, and the combination of maternal factors and these biochemical markers (C). AUC, area under the ROC.

TABLE 3 Performance of screening for gestational diabetes mellitus by maternal factors, first-trimester HbA1c and random plasma glucose values and their combination

		95% CI			
	AUROC	Lower bound	Upper bound	Standard Error	*p* value
First-trimester HbA1c	0.609	0.534	0.684	0.038	0.003
First-trimester random plasma glucose	0.632	0.557	0.706	0.038	<0.001
Maternal characteristics	0.686	0.615	0.756	0.036	<0.001
First-trimester random plasma glucose + HbA1c	0.679	0.609	0.750	0.036	<0.001
Maternal characteristics + first-trimester HbA1c	0.737	0.679	0.796	0.030	<0.001
Maternal characteristics + first-trimester random plasma glucose	0.717	0.650	0.784	0.034	<0.001
Maternal characteristics + first-trimester random plasma glucose + HbA1c	0.762	0.705	0.819	0.029	<0.001

Abbreviations: AUROC, area under receive operating characteristic curve; CI, confidence interval; GDM, gestational diabetes mellitus; HbA1c, glycosylated hemoglobin A1c; maternal characteristics: age, body mass index, previous GDM, family history for diabetes.

Combining the first-trimester HbA1c and the ransom plasma glucose values the calculated area under the ROC curve (AUC) was 0.67 (95% CI 0.60–0.75). Adding the maternal characteristics such as age, BMI, previous GDM, and family history of diabetes there was a significant improvement in the AUC of the first-trimester HbA1c and random glucose. The combined AUC was 0.76 (95% CI 0.70–0.81) (Figure 3C). Table 3 demonstrates the performance of screening for GDM by maternal factors (age, BMI, previous GDM, family history for diabetes), first-trimester HbA1c and random plasma glucose values and their combination. A comparison of each ROC curve showed a significant difference between the single variable curves and the combined one (see Table S1).

4 | DISCUSSION

This study highlighted some potentially clinically important aspects in the prediction of GDM. We demonstrated that first-trimester HbA1c and random plasma glucose values combined with a panel of simple maternal demographic and clinical characteristics could be used as an early risk stratification tool for GDM. The calculated AUC values are similar to those noted for type 2 diabetes in the general nonpregnant population, in which the reported AUC values were typically located between 0.75 and 0.85.[11] Comparable to our retrospective study[9] the first-trimester HbA1c and random plasma glucose values were significantly higher in pregnant women who later developed GDM according to the IADPSG criteria than in those women who did not. These results are of particular importance in the era of optimizing the diagnosis of pregnancy complications in the first trimester.[12]

This study has several strengths. First, it was conducted prospectively in a single center and in a mixed population with a relatively high GDM prevalence (14.7%). As a result, we could overcome the limitation of our previous study, which was biased towards a high-risk population of women that had at least one risk factor for GDM. Second, all patients underwent the same diagnostic procedures, laboratory workup, and management protocols. The use of random plasma glucose and HbA1c is inexpensive and could be performed during the first antenatal booking visit with no special pretest preparation or fasting state. A noticeable limitation of our study is that we based our calculations on the one-step screening for GDM, which is mainly used in Europe. Furthermore, we had a high number of drop-outs and losses to follow up.

That being said, there is a growing interest in the ability to determine as early as possible whether a pregnant woman will develop GDM. GDM prediction in the first trimester of pregnancy would allow for a more timely intervention to reduce GDM-related short- and long-term adverse pregnancy outcomes. Emerging evidence suggests that lifestyle changes can lessen not only the risk for diabetes in nonpregnant individuals but also the adverse outcomes in pregnant women with GDM.[13] The existing diagnostic guidelines for the first trimester are focused on the exclusion of undiagnosed pregestational diabetes or other forms of dysglycemia. However, most of the women do not appear to have sufficiently elevated glycemia to fulfill the criteria for impaired fasting glucose or impaired glucose tolerance.[14] In the early part of pregnancy (eg first trimester and first half of second trimester) fasting and postprandial glucose concentrations are normally lower compared with those in nonpregnant women.[14] At this time in pregnancy, elevated fasting or postprandial plasma glucose levels may well reflect the existence of a dysglycemia; however, the criteria for designating abnormally high glucose concentrations at this time have not yet been established or proven in studies.

We believe in the heterogeneous nature of GDM, where the group diagnosed early may represent a different range of phenotypes, compared with that diagnosed later in pregnancy. Furthermore, if there are benefits from identifying and treating early GDM, the use of risk factor screening needs to be considered. Risk factor screening is unreliable later in pregnancy.[15] Studies that provided early intervention based on maternal characteristics alone, such as BMI, exhibited no effective improvement in both obstetric and metabolic outcomes.[16] However, Osmundson et al demonstrated that early treatment of women with a first-trimester HbA1c in the prediabetes range reduced the GDM incidence in non-obese women.[17] Hence many study groups suggested diagnosis of GDM in the first trimester. A published prediction model, including five well-established risk factors, exhibited

a moderate predictive performance among nulliparous women, with an AUC of 0.732.[18] On the other hand, a study from the UK combined maternal characteristics with routine and novel parameters such as adiponectin, E-selectin, and tissue plasminogen activator to predict GDM in the first trimester and achieved an AUC of 0.86.[19] A recently published study showed that a machine-learning approach can accurately predict GDM based on retrospective data obtained from patient health records.[20] However, these studies assessed the parameters retrospectively in retrieved samples. Moreover, the criteria used to diagnose GDM in both studies were different from those used in our cohort. The model proposed by Artzi et al also requires that the caring obstetrician gains access to that load of information.[20]

5 | CONCLUSION

Our study shows that a GDM prediction model could be developed based on first-trimester HbA1c and maternal characteristics, potentially allowing early intervention to reduce adverse pregnancy outcomes. Further clinical research on the performance of this proposed novel risk prediction model is warranted to determine if it is effective in reducing the incidence of GDM as well as its potential consequences.

AUTHOR CONTRIBUTIONS

SA, CS, and LR conceived and designed the study. CL gathered the data and conducted the statistical analysis. SA and LR wrote the first draft. BM, GF, and DS contributed essentially with intellectual input into the study design, result analysis, and in the revision of the manuscript. All authors have read and approved the manuscript.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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REFERENCES

1. American Diabetes Association. Standards of medical care in diabetes—2018. *Diabetes Care*. 2018;41:S20-S24.
2. O'Sullivan JB, Mahan CM. Criteria for the oral glucose tolerance test in pregnancy. *Diabetes*. 1964;13:278-285.
3. Sermer M, Naylor CD, Gare DJ, et al. Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. The Toronto tri-Hospital gestational diabetes project. *Am J Obstet Gynecol*. 1995;173:146-156.
4. Yang X, Hsu-Hage B, Zhang H, Zhang C, Zhang Y, Zhang C. Women with impaired glucose tolerance during pregnancy have significantly poor pregnancy outcomes. *Diabetes Care*. 2002;25:1619-1624.
5. Metzger BE, Gabbe SG, Persson B, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care*. 2010;33:676-682.
6. American Diabetes Association. Standards of medical care in diabetes–2014. *Diabetes Care*. 2014;37:S14-S80.
7. McIntyre HD, Sacks DA, Barbour LA, et al. Issues with the diagnosis and classification of hyperglycemia in early pregnancy. *Diabetes Care*. 2016;39:53-54.
8. Hughes RC, Moore MP, Gullam JE, Mohamed K, Rowan J. An early pregnancy HbA1c ≥5.9% (41 mmol/Mol) is optimal for detecting diabetes and identifies women at increased risk of adverse pregnancy outcomes. *Diabetes Care*. 2014;37:2953-2959.
9. Amylidi S, Mosimann B, Stettler C, Fiedler GM, Surbek D, Raio L. First-trimester glycosylated hemoglobin in women at high risk for gestational diabetes. *Acta Obstet Gynecol Scand*. 2016;95:93-97.
10. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2008;358:1991-2002.
11. Sattar N, Wannamethee SG, Forouhi NG. Novel biochemical risk factors for type 2 diabetes: pathogenic insights or prediction possibilities? *Diabetologia*. 2008;51:926-940.
12. Amylidi-Mohr S, Kubias J, Neumann S, et al. Reducing the risk of preterm preeclampsia: comparison of two first trimester screening and treatment strategies in a single Centre in Switzerland. *Geburtshilfe Frauenheilkd*. 2021;81:1354-1361.
13. Yu Y, Xie R, Shen C, Shu L. Effect of exercise during pregnancy to prevent gestational diabetes mellitus: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med*. 2018;31:1632-1637.
14. Immanuel J, Simmons D. Screening and treatment for early-onset gestational diabetes mellitus: a systematic review and meta-analysis. *Curr Diab Rep*. 2017;17:115.
15. Simmons D, Devers MC, Wolmarans L, Johnson E. Difficulties in the use of risk factors to screen for gestational diabetes mellitus. *Diabetes Care*. 2009;32:e8.
16. Vinter CA, Tanvig MH, Christensen MH, et al. Lifestyle intervention in Danish obese pregnant women with early gestational diabetes mellitus according to WHO 2013 criteria does not change pregnancy outcomes: results from the LiP (lifestyle in pregnancy) study. *Diabetes Care*. 2018;41:2079-2085.
17. Osmundson SS, Norton ME, El-Sayed YY, Carter S, Faig JC, Kitzmiller JL. Early screening and treatment of women with prediabetes: a randomized controlled trial. *Am J Perinatol*. 2016;33:172-179.
18. Donovan BM, Breheny PJ, Robinson JG, et al. Development and validation of a clinical model for preconception and early pregnancy risk prediction of gestational diabetes mellitus in nulliparous women. *PLoS ONE*. 2019;14:e0215173.
19. Savvidou M, Nelson SM, Makgoba M, Messow CM, Sattar N, Nicolaides K. First-trimester prediction of gestational diabetes mellitus: examining the potential of combining maternal characteristics and laboratory measures. *Diabetes*. 2010;59:3017-3022.
20. Artzi NS, Shilo S, Hadar E, et al. Prediction of gestational diabetes based on nationwide electronic health records. *Nat Med*. 2020;26:71-76.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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